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Preface

Volume 92 of *Advances in Heterocyclic Chemistry* commences with a survey of 2- and 3-aminofurans authored by C. A. Ramsden (Keele University, UK), and V. Milata (Slovak University of Technology, Bratislava). The review concentrates on the synthesis and properties of furans with primary amino groups; these highly reactive structures are unstable unless substituted with electron-withdrawing groups.

The second chapter by I. D. Sadekov, G. M. Abakarov, and V. I. Minkin of Rostov State University (Russia) is entitled “Five-Membered Heterocycles with Vicinal Te and O Heteroatoms,” a relatively new field of chemistry, which has undergone rapid expansion in the last two decades.

V. P. Litvinov (Zelinsky Institute, Russia) contributes an overview of the chemistry of thienopyrimidines, concentrating on the last 15 years of developments; these compounds have achieved significant importance because of their potential biological activity.

Volume 92 closes with installment IX in the ongoing series entitled “The Literature of Heterocyclic Chemistry”, covers the literature for the years 2002–2004. Authored by L. I. Belen’kii, V. N. Gramenitskaya, and Yu. B. Evdokimenkova (also of the Zelinsky Institute), it continues this series of reviews, which have been published in *Advances in Heterocyclic Chemistry* since 1966, and is the seventh of the series to be composed under the direction of Professor Belen’kii.

The volume closes with a subject index covering these four chapters.

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Gainesville, FL
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2-Aminofurans and 3-Aminofurans

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I. Introduction

This review covers the literature on 2-aminofurans 1 and 3-aminofurans 2 up to the end of 2005. Most of the known derivatives of these amines are associated with electron-withdrawing substituents (typically CO.R or CN) either on the furan ring or on the amine nitrogen. In the case of 2-aminofurans this appears to be essential for the amine to be isolated and characterised. The parent amine 1 (R1 = R2 = R3 = H) is too unstable to be isolated or even trapped in useful yield. The 3-aminofurans seem to be relatively more stable: although the parent system 2 (R1 = R2 = R3 = H) has not been reported, the 2-methyl and 2,5-dimethyl derivatives 2 (R1 = H, Me, R2 = H, R3 = Me) were reported in 1937, but have received no attention since.

![Chemical structures](image-url)
The parent aminofurans 1 and 2 \((R^1 = R^2 = R^3 = H)\) appear to be the least stable of the simple heterocyclic amines and this is consistent with the view that they are the least aromatic. Although unstable, both 2- and 3-aminothiophene 3 and 4 have been isolated and characterised (13MI1155, 14AC403, 73JHC1067). The 2-aminopyrroles 5 have been characterised in solution (95TL9261). We have previously reviewed the chemistry of 4- and 5-aminomidazoles (94AHC1).

The instability of the parent 2-aminofuran ring may be due to facile tautomerism to an imine followed by ring-opening to 4-hydroxybutyronitrile. In spite of the apparent greater stability of the 3-aminofurans, much more is known about the chemistry of the 2-aminofurans and this probably reflects the greater availability of 2-substituted precursors.

This review is principally concerned with the preparation and reactions of the furan primary amines 1 and 2. Where appropriate we have included related secondary and tertiary amines, and also amides and similar N-substituted amines but no attempt has been made to provide comprehensive coverage of non-primary amines or polycyclic derivatives.

II. 2-Aminofurans

A. Physical Properties

1. Molecular Structure

The structures of four 2-aminofuran derivatives have been determined by X-ray crystallography. These are the primary amines 6 (78JOC3821) and an indol-2-one derivative (85CPB544), and the tertiary amines 7 (89AC533) and 8 (97AC1358). The amine nitrogen atoms are sp\(^2\) hybridised and the C–N bonds (1.32–1.33 Å) are intermediate between a single and double bond, indicating a resonance interaction with the stabilising substituents. The structure of an imine derivative (99AC258) and a Cr(CO)\(_3\) complex of a 2-dimethylamino derivative (95JOMC127) have also been reported.

2. Computational Studies (Including 3-Aminofurans)

Properties of aminofurans have been investigated using semi-empirical \(\pi\)-electron methods (70JA2929, 81AQ105), semi-empirical all valence electron AM1
(93JHC113, 01JCS(P1)680), INDO (97JA6575) and PM3 (97JOC4088) methods, and *ab initio* methods (78JA3981, 98JKCS391).

Semi-empirical calculations suggest that the energy difference between aminofurans and their imine tautomers is small, but in each case the amino form was calculated to be the most stable (70JA2929). An *ab initio* study found that furan is destabilised relative to benzene by substituents such as NH$_2$, which are π-electron donors and σ-electron acceptors (78JA3981). These studies identified a stabilising effect in 2-aminofurans that is absent in 3-aminofurans and the authors suggest that this may be either intramolecular hydrogen bonding or a hyperconjugative interaction of an oxygen lonepair with the C–N bond (78JA3981).

For 2-aminofurans the results of semi-empirical calculations have been found to be entirely consistent with the regioselectivity of substitution and cycloaddition reactions (93JHC113, 97JOC4088, 01JCS(P1)680).

3. *Ultraviolet Spectroscopy*

The UV spectral data of representative 2-aminofurans are summarised in Table 1.

4. *NMR Spectroscopy*

The $^1$H-NMR and $^{13}$C-NMR chemical shifts for representative 2-aminofurans are shown in Tables 2 and 3. $^{13}$C-NMR data are very limited and assignments of signals are often not included with the chemical shifts.

Table 1. Ultraviolet spectral data for 2-aminofuran derivatives

<table>
<thead>
<tr>
<th>$R^1$; $R^2$; $R^3$</th>
<th>Solvent</th>
<th>$\lambda_{max}$ ($\varepsilon$) (nm)</th>
<th>References</th>
</tr>
</thead>
<tbody>
<tr>
<td>CHO; H; H</td>
<td>H$_2$O</td>
<td>350 (29,600)</td>
<td>62JMPC513</td>
</tr>
<tr>
<td>CO$_2$Me; H; H</td>
<td>MeOH</td>
<td>316 (–)</td>
<td>85CPB5581</td>
</tr>
<tr>
<td>Me; CO$_2$Et; CO$_2$Et</td>
<td>MeOH</td>
<td>210 (5500), 276 (11,200)</td>
<td>62CB307</td>
</tr>
<tr>
<td>CO$_2$Et; CO$_2$Et; CO$_2$Et</td>
<td>MeOH</td>
<td>264 (9300), 305 (15,850)</td>
<td>62CB307</td>
</tr>
<tr>
<td>H; Me; CN</td>
<td>MeOH</td>
<td>223 (11,000), 257 (17,000)</td>
<td>66CB1002</td>
</tr>
<tr>
<td>Me; Me; CN</td>
<td>MeOH</td>
<td>227 (7600), 266 (8700)</td>
<td>66CB1002</td>
</tr>
<tr>
<td>Ph; CN; Ph</td>
<td>EtOH</td>
<td>362 (19,950)</td>
<td>82S513</td>
</tr>
<tr>
<td>Thiazol-4-yl; H; H</td>
<td>MeOH</td>
<td>296(–)</td>
<td>85CPB5581</td>
</tr>
</tbody>
</table>
B. PREPARATION

1. Cyclisation of Nitriles

a. From γ-Keto-Nitriles (Method A). This is a convenient route (Scheme 1) to substituted 2-aminofurans (Table 4, Method A) and cyclisation can be achieved under either basic or acidic conditions.

Westöö (59ACS692) provided the first examples of this method by reaction of 2-chloroketones 9 (X = Cl, R¹ = Me, R² = COMe, CO₂Et) with the sodium salt of ethyl cyanoacetate. Under these basic conditions cyclisation is considered to occur via the enolate anion 11. Subsequently, further examples of these compounds have been described using the same approach and limitations have been noted (62CB307,

### Table 2. Chemical shifts of ring protons in 2-aminofuran derivatives

<table>
<thead>
<tr>
<th>R¹; R²; R³</th>
<th>Solvent</th>
<th>δH-3</th>
<th>δH-4</th>
<th>δH-5</th>
<th>δNH</th>
<th>References</th>
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</thead>
<tbody>
<tr>
<td>H; Me; CN</td>
<td>CDCl₃</td>
<td>–</td>
<td>–</td>
<td>6.54</td>
<td>5.06</td>
<td>85CPB937</td>
</tr>
<tr>
<td>H; Et; CN</td>
<td>d₆-DMSO</td>
<td>–</td>
<td>–</td>
<td>6.70</td>
<td>7.17</td>
<td>96JHC2007</td>
</tr>
<tr>
<td>H; Ph; CN</td>
<td>d₆-DMSO</td>
<td>–</td>
<td>–</td>
<td>6.99</td>
<td>5.45</td>
<td>01JHC1197</td>
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<tr>
<td>H; PhCH₂; CN</td>
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<td>–</td>
<td>6.76</td>
<td>3.31</td>
<td>01JHC1197</td>
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<tr>
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<td>d₆-DMSO</td>
<td>6.70</td>
<td>–</td>
<td>–</td>
<td>~7.3</td>
<td>98JHC1313</td>
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</table>

### Table 3. Chemical shifts of ring carbons in 2-aminofuran derivatives

<table>
<thead>
<tr>
<th>R¹; R²; R³; R⁴</th>
<th>Solvent</th>
<th>δC-2</th>
<th>δC-3</th>
<th>δC-4</th>
<th>δC-5</th>
<th>References</th>
</tr>
</thead>
<tbody>
<tr>
<td>(CHOH)₂CH₂OH; H; CN; H</td>
<td>d₆-DMSO</td>
<td>164.4</td>
<td>67.6</td>
<td>109.1</td>
<td>146.0</td>
<td>89LA1049</td>
</tr>
<tr>
<td>CN; Ph; COPh; H</td>
<td>CDCl₃</td>
<td>162.1</td>
<td>90.6</td>
<td>97.5</td>
<td>151.1</td>
<td>00H1337</td>
</tr>
<tr>
<td>CO₂Me; H; H; H</td>
<td>CDCl₃</td>
<td>158.5</td>
<td>87.1</td>
<td>122.6</td>
<td>135.1</td>
<td>97JOC4088</td>
</tr>
<tr>
<td>H; H; H; COPh</td>
<td>CDCl₃</td>
<td>164.0</td>
<td>95.7</td>
<td>111.4</td>
<td>145.4</td>
<td>03JOC2609</td>
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</table>
Under these conditions, if the ketone 10 is not sufficiently acidic (e.g. \( R^2 = H \)) cyclisation does not occur (62CB307, 88TL3437). Use of the sodium enolate of cyanoacetone gave esters and ketones 1 (\( R^2 = \text{COMe}, \text{CO}_2\text{Et} \)), but alternative cyclic products were obtained with amides (e.g. \( R^2 = \text{CONH}_2 \)) (78JOC3821). Early work suggested that the chlorides 9 (\( X = \text{Cl} \)) were superior to bromides and avoided alternative products (59ACS692). More recently, bromides have been successfully reacted with malononitrile using diethylamine in DMF (98JHC1313), or triethylamine in THF (78CPB3880), and it is significant to note that under these conditions an electron-withdrawing substituent \( R^2 \) is not necessary for cyclisation. The ketone 10 (\( R^1 = \text{Ph}, R^2 = H, R^3 = \text{CN} \)) has been cyclised in EtOH containing a few drops of triethylamine and the 2-aminofuran 1 (\( R^1 = \text{Ph}, R^2 = H, R^3 = \text{CN} \)) reacted further with in situ reagents without isolation (97EJC105).

In an alternative procedure, the ketones 10 can be cyclised to 2-aminofurans 1 under acidic conditions. For example, phenacylmalononitrile 10 (\( R^1 = \text{Ph}, R^2 = H, R^3 = \text{CN} \)) cyclised in hot AcOH/concentrated HCl (89JPC31) and further examples have been prepared by this method as synthetic intermediates (04BMCL3907). A similar cyclisation of a cyanoester has been achieved using AcOH/concentrated H\(_2\)SO\(_4\), but the 2-aminofuran was accompanied by some 2-hydroxyfuran (90JPC479). Phenacylmalononitrile has also been cyclised to 2-amino-3-cyano-5-phenylfuran (1; \( R^1 = \text{Ph}, R^2 = H, R^3 = \text{CN} \)) by a primary alkylamine and a catalytic amount of concentrated HCl, but it should be noted that similar conditions using aromatic amines led to 1-aryl-2-aminopyrroles (89LA1145).

Treatment of phenacylmalononitrile 10 (\( R^1 = \text{Ph}, R^2 = H, R^3 = \text{CN} \)) with dry HCl in iso-propanol for three days gave only a trace of the 2-aminofuran, which was accompanied by pyrrole derivatives (94TL5989) and this was attributed to the nucleophilic ion attacking the nitrile group. More recently, it has been shown that use of TFA (or trifluoromethane sulphonic acid) gives good yields of 2-aminofurans. On the basis of substituent effects and the rates of cyclisation, the authors conclude that under these conditions (TFA, 20 °C, ~1 h) cyclisation occurs via the keto form 10 (Scheme 1) protonated on the nitrile nitrogen atom (04H127).
Table 4. Preparation of 2-aminofuran derivatives I by nitrile cyclisation

<table>
<thead>
<tr>
<th>R¹</th>
<th>R²</th>
<th>R³</th>
<th>Method</th>
<th>Yield (%)</th>
<th>m.p. (°C)</th>
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<tr>
<td>CH₂CO₂Et</td>
<td>H</td>
<td>CN</td>
<td>A</td>
<td>21</td>
<td>92–93</td>
<td>78CPB3880</td>
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<tr>
<td>CN</td>
<td>Ph</td>
<td>COₚPh</td>
<td>A</td>
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<td>200–202</td>
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<tr>
<td>CO₂Et</td>
<td>CO₂Et</td>
<td>CO₂Et</td>
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<td>–</td>
<td>188–189</td>
<td>70JOC1234</td>
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Two alternative routes to γ-keto-nitriles 10 that have been used to generate unusual 2-aminofuran derivatives are noteworthy. Treatment of the isoquinolinedione–glyoxal products 13 with malononitrile and diethylamine in alcoholic solvent gave the furans 15 via the intermediates 14. The 5-methyl derivative tautomerises to the product 16 (m.p. 224°C), which was isolated in low yield. The 2-phenyl derivative cyclises to the tetracyclic product 17 whose structure was confirmed by X-ray crystallography (85CPB2663) (Scheme 2).

Treatment of the indolone 18 with diazomethane gives the quinolone 19 in high yield. This product equilibrates with the aminofuran 20 in dimethyl sulfoxide (DMSO) solution and the pure 2-aminofuran has been isolated (m.p. 171.5–172.5°C) and characterised (78JOC4383) (Scheme 3).

b. From γ-Hydroxy-Nitriles (Method B). In this approach (Scheme 4), the hydroxynitrile is generated by Knoevenagel reaction of an α-hydroxyketone 21 (acyloin or benzoin) with an acidic nitrile 22 (usually malononitrile) followed by base-catalysed cyclisation to the 2-aminofuran 1 (Table 4, Method B) without isolation of the intermediates. Evidence of initial formation of an iminobutenolide (Scheme 4) has been reported (02JA2190) (see Section II.C.1.a).
Gewald (66CB1002) provided the first fully characterised examples of this approach. Anderson and co-workers (61JCS4705) had previously prepared the furan 1 (R¹ = R² = Ph, R³ = CN) (m.p. 204–206 °C) by condensation of benzoin with malononitrile, but the molecular structure was not recognised (69MC503) until a re-investigation by Ducker and Gunter (74AJC2229). An interesting finding that arose from later studies was that the product from 1-hydroxyacetone and malononitrile, which had been originally described as the 2-aminofuran 1 (R¹ = H, R² = Me, R³ = CN) by Gewald, is in fact a dimer. The Diels–Alder cycloadduct 23 was originally proposed for the dimer structure (73JOC612). However, a later X-ray crystallographic study showed that it had the structure 24 (80LA1952). Other derivatives do not appear to dimerise. Authentic monomer 1 (R¹ = H, R² = Me, R³ = CN) was later prepared by Matsuda and co-workers (85CPB937) by using diethylamine as base rather than potassium hydroxide (Scheme 4). The monomer forms the dimer 24 upon heating at 130–135 °C.

Subsequently, this approach summarised in Scheme 4 has been used for the synthesis of a variety of derivatives of the amines 1 (70BCSJ3290, 78H1503, 80CCC1581, 83CCC3140, 84CCC1788, 96JHC2007, 01MI2424), including the formation of sugar derivatives (89LA1049, 96TA2191) and intermediates for the synthesis of pyrrolo[2,3-d]pyrimidines (see Section II.C.1.c) (96JOC7973, 01JHC1197, 03BMCL59). An alternative procedure employing basic alumina or montmorillonite in ethanol and microwave radiation has been described as giving increased yields of 2-aminofurans and much shorter reaction times (03BCSJ203). Although work on the route shown in Scheme 4 has been mainly restricted to the use of malononitrile, arylsulphonylacetonitriles 22 (R³ = SO₂Ar) have also been successfully condensed to
give 2-arylsulfonyl derivatives 1 (R³ = SO₂Ar) (87JHC757). In another variation of this approach, 1,1,2,2-tetracyanoethane undergoes aldol addition to aromatic aldehydes and subsequent cyclisation and elimination of the hydroxynitrile intermediates gives the amines 1 (R¹ = Ar, R² = R³ = CN) (82KGS1605).

c. From α,β-Unsaturated Ketones and Cyanide (Method C). Soto and co-workers (82S513, 83AQ340) have described a convenient route to the 4-cyanofurans 1 (R² = CN) that involves the addition of cyanide ion to a 3-cyano-enone 25 (R¹, R³ = Ar, R² = CN) (Scheme 5). The enolate anion generated in this way is poured into 1 N HCl leading to cyclisation to the 2-aminofurans 1. In this way, a number of 3,5-diaryl-4-cyano derivatives have been prepared and fully characterised (Table 4, Method C). In terms of substitution pattern this method conveniently complements Methods A and B. In a subsequent study using the aldehydes and methyl ketones 25 (R¹ = H or Me, R² = CN, R³ = Ar or Alk), the 2-aminofurans 1 could not be isolated but were trapped and characterised as the imines 27 (R¹ = H or Me, R² = CN, R³ = Ar or Alk) (85JCS(P1)2581).

In a variation of this approach, the esters 25 (R² = CO₂Et) gave the γ-ketonitriles 26 (R² = CO₂Et) which were isolated. In hot ethanol containing a catalytic amount of piperidine, these nitriles 26 (R² = CO₂Et) cyclise to the 2-aminofurans 1. In this case, the 2-aminofurans 1 (R² = CO₂Et) cannot be isolated but are trapped by p-tolualdehyde to give the imines 27 (R¹ = Me, Ph, R² = CO₂Et, R³ = Ar) (86JHC1583). Attempts to liberate the free amines 1 from the imines 27 were unsuccessful.

A similar cyclisation of p-nitrobenzylideneacetylacetone 28 using KCN followed by dilute HCl to give the 2-aminofuran 29 had previously been reported by Sword (70JCS(C)1916) (Eq. (1)). It is interesting to note that the m-nitro analogue did not cyclise. More recently, some acylated enamines have been shown to react with cyanide to give 2-morpholino-furans (90T8103).
d. Other Methods Employing Nitrile Cyclisation. Treatment of the furylacrylates 30 (R = Et, CH₂Ph) with neat morpholine resulted in an exothermic reaction that gave the 2-aminofurans 31 (R = Et, CH₂Ph) (∼50% yield) after aqueous workup. The formation of these products is rationalised in terms of ring-opening of the furans by the morpholine followed by an alternative recyclication of the intermediate γ-hydroxynitriles and subsequent hydrolysis of the resulting enamines (Scheme 6) (70JOC1234).

Treatment of epichlorohydrin with aqueous sodium cyanide gives the amine 32 in 9% yield (Scheme 7) (64JOC3252). The formation of this product has been
rationalised in terms of formation of 4-hydroxycrotonitrile which (i) cyclises to form 2-aminofuran and (ii) cycloadds to the aminofuran leading to the isolated product (Scheme 7).

2. Reduction of 2-Nitro and 2-Azido Derivatives

a. 2-Nitro Derivatives. In principle, reduction of a 2-nitrofuran 33 is a convenient route to 2-aminofurans 1 but this method has found limited usage. At least one electron-withdrawing group on the ring is necessary to stabilise the amine. Table 5 shows 2-aminofurans 1 that have been prepared and characterised using this procedure. Yields range from poor to moderately good. The amine 1 is often accompanied by a significant yield of the tautomeric $\gamma$-ketonitrile 34, formed by reductive ring-opening, which is a reversal of the synthetic route shown in Scheme 1. For example, electrochemical reduction of the derivatives 33 ($R^1 = CH\equiv N-NHCOAr$, $R^2 = R^3 = H$) gave 5–10% isolated yields of the corresponding nitriles 34 and 35–45% isolated yields of the amines 1 (91TL631). Other examples have been reported and sometimes only the ring-opened isomer is isolated and appears to be favoured by protic solvents (57CI523A). Padwa and Waterson (01ARK29) observed that reduction of the sulphone 33 ($R^1 = SO_2C_6H_4Me$, $R^2 = R^3 = H$) by hydrogen and Lindlar’s catalyst in MeOH gave the imine tautomer 35 (91%) rather than the expected 2-aminofuran 1 ($R^1 = SO_2C_6H_4Me$, $R^2 = R^3 = H$).

A number of different reducing agents have been used to reduce 2-nitrofurans to 2-aminofurans. These include catalytic hydrogenation (34MI13, 57CI523B,
Table 5. Preparation of 2-aminofuran derivatives by nitro reduction

![Diagram of 2-aminofuran](Image)

<table>
<thead>
<tr>
<th>R¹</th>
<th>R²</th>
<th>R³</th>
<th>Method</th>
<th>Yield (%)</th>
<th>m.p. (°C)</th>
<th>References</th>
</tr>
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<tbody>
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<td>H</td>
<td>5%Pd/C/H₂</td>
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<td>150–175</td>
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<tr>
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<td>H</td>
<td>H</td>
<td>5%Pd/C/H₂</td>
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<td>135–136</td>
<td>84ABB234</td>
</tr>
<tr>
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<td>H</td>
<td>Al/Hg</td>
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<td>134</td>
<td>70CZ222</td>
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<tr>
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<td>H</td>
<td>Al/Hg</td>
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<td>96</td>
<td>80CC135</td>
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<td></td>
<td></td>
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<td>H</td>
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<td>169.5</td>
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<td>H</td>
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<td>126–127</td>
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<td>H</td>
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<td>148–151</td>
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<td>H</td>
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<tr>
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<td>H</td>
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<td>H</td>
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<td>H</td>
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<td>–</td>
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<td>H</td>
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<td>Al/Hg</td>
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<td>105–106</td>
<td>75BP291</td>
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59JMPC135, 62JMPC513, 74H391, 83KFZ683, 85CPB5581, 93JHC113, 95JHC1283, aluminium amalgam (1905ACP196, 43CB419, 69CZ139, 70CZ222, 75AQ183, 80CC135, 83KFZ683), sodium amalgam (72KGS1159), Raney nickel (57CI523A), sodium dithionite (00TL6531), stannous chloride (96P386), zinc dust (04BMC-L2041), and electrochemically (58MI121), using a mercury drop or glassy carbon electrode (91TL631, 91JICS562). In addition, xanthine oxidase catalysed reduction of methyl 5-nitro-2-furoate **33** (R¹ = CO₂Me, R³ = R⁴ = H) to the 2-aminofuran **1** (R¹ = CO₂Me, R³ = R⁴ = H), and structurally related metabolites, has been described (82CPB2647, 84ABB234). *In vivo* metabolic reduction in rabbits (62JMPC524), rats (82CPB3435, 84ABB112) and eels (84CPB4193), and by bacteria (56JP(L)1072, 59JMPC135, 59JMPC155) and enzyme extracts (75BM121) has also been reported.

In some preparations, the 2-aminofurans **1** are not isolated but are trapped *in situ* as amides, using acetic anhydride (75AQ183), enamines, using ethyl ethoxymethylene malonate (EtO-CH = C(CO₂Et)₂) (95JHC1283), or vinylfurans, using ethoxymethylene malononitrile (EtO-CH = C(CN)₂) (93JHC113). This...
approach is particularly useful for functionalising 2-aminofurans that are too unstable to be isolated (see also Section II.C.1.d). In this way, the highly unstable parent amine \( R^1 = R^3 = R^4 = H \) has been generated by catalytic reduction (5% Pd/C/H\( \text{H}_2 \)) of 2-nitrofuran and trapped in low yield (15%) as the 5-(2,2-dicyano) vinylfuran \( R^1 = CH = C(CN)_{2}, R^3 = R^4 = H \) (93JHC113).

b. 2-Azido Derivatives. 2-Azido-3-formylbenzo[b]furan 36 is reduced to the 2-amino-3-formyl derivative 37 by hexamethyldisilathiane (HMDST) in MeCN and to the 2-amino-3-thioformyl derivative 38 in MeOH (Eq. (2)) (96S1185). The aldehyde 37 can also be obtained using \( H_2S \) in MeOH as reducing agent (89S530).

![Diagram](image)

(2)

3. Rearrangement of Furan-2-Carboxylate Derivatives

Since the precursor acids, aldehydes and nitriles (e.g. 39 and 44) are stable and readily available, this is a convenient route to 2-aminofuran derivatives. Although it is not a direct route to the primary amines, it is a useful method for making carbamate (42) or amide (43) derivatives, which are usually stable and can be further modified. This method is particularly useful for preparing N-stabilised derivatives when the furan ring does not carry an electron-withdrawing stabilising group (Table 6).

The most convenient routes to carbamates 42 and amides 43 have been developed by Padwa and co-workers and involve Curtius rearrangement of 2-carbonyl azides 40, prepared from the acids 39 (Scheme 8). Thermal rearrangement gives the isocyanate 41, which in the presence of an alcoholic solvent gives the corresponding carbamate 42 (79JHC477, 99JOC4617). \( \text{t-Bu} \) carbamates have also been prepared directly from the acids 39 by heating with diphenyl phosphor azidate \([N_3PO(OPh)_{2}]\) and triethylamine in \( \text{t-Bu} \) alcohol (97JOC4088, 99JOC3595). Alternatively, generation of the isocyanates 41 in benzene/toluene solution followed by treatment with either a Grignard reagent or an alkyl copper lithium reagent gives the amides 43 (00ARK193, 03JOC2609). A number of stable derivatives have been prepared in good yield (Table 6) using the methods shown in Scheme 8.

As part of a study of the oxidative rearrangement of \( N \)-arylamidines, Ramsden and co-workers have shown that reaction of the amidines 45 with phenyliododi-carboxylates \([\text{PhI}(O_2CR_{3})_2]\) results in the formation of the carbodiimides 46 in a reaction analogous to the Hofmann reaction of amides. The carbodiimides 46 are not isolated but react with the liberated carboxylic acid \([R_{3}CO_2H]\) yielding the stable \( N \)-acylureas 47. Upon heating, the ureas 47 eliminate an arylisocyanate providing an alternative route to the amides 43 (Scheme 9) (95JCS(P1)615, 97JCS(P1)2319, 01JCS(P1)680). In this way, a number of amides 43 have been prepared in good yield (Table 6).
4. Substitution of the Furan Ring

Studies in the 1960s showed that reaction of secondary amines with 5-chlorofurfuraldehyde (60MI41, 60MI429, 60MI1534), 2-bromo-5-nitrofuran (64MI705, 65MI2022) and 2,3-dibromofuran (68MI722) gives 2-dialkylaminofurans. One nitro group of 2,5-dinitrofuran is readily displaced by secondary amines (73CB1688, 76JOC2824, 97JOC4088) and \(N\)-alkylsulphonamides (01ARK29) providing a
Table 6. Preparation of 2-aminofuran derivatives 42 and 43 by rearrangement

<table>
<thead>
<tr>
<th>R¹</th>
<th>R²</th>
<th>R³</th>
<th>Method</th>
<th>Yield (%)</th>
<th>m.p. (°C)</th>
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<td>H</td>
<td>H</td>
<td>Et</td>
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<td>27–28</td>
<td>99JOC4617</td>
</tr>
<tr>
<td>H</td>
<td>H</td>
<td>t-Bu</td>
<td>N₃PO(OPh)₂</td>
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<td>98–99</td>
<td>97JOC4088</td>
</tr>
<tr>
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<td>H</td>
<td>t-Bu</td>
<td>N₃PO(OPh)₂</td>
<td>87</td>
<td>76–77</td>
<td>99JOC3595</td>
</tr>
<tr>
<td>P-NO₂·C₆H₄</td>
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<td>t-Bu</td>
<td>N₃PO(OPh)₂</td>
<td>86</td>
<td>147–148</td>
<td>99JOC3595</td>
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</table>

Carbamates (42)

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<th>Method</th>
<th>Yield (%)</th>
<th>m.p. (°C)</th>
<th>References</th>
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</thead>
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<td>H</td>
<td>H</td>
<td>Phl(O₂CR³)₂ R³MgBr</td>
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<td>111–113</td>
<td>97JCS(P1)2319</td>
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<tr>
<td>H</td>
<td>H</td>
<td>R³Cu(CN)Li₂</td>
<td>60</td>
<td>92–94</td>
<td>00ARK193</td>
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<td>H</td>
<td>Phl(O₂CR³)₂ R³Cu(CN)Li₂</td>
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<td>01JCS(P1)680</td>
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<tr>
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<td>R³Cu(CN)Li₂</td>
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<td>87–89</td>
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<tr>
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<td>H</td>
<td>R³Cu(CN)Li₂</td>
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<td>85–86</td>
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<tr>
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<td>H</td>
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<td>CH₂CH(CH₂CH₂)₂</td>
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<td>67–70</td>
</tr>
<tr>
<td>H</td>
<td>H</td>
<td>(CH₂)₂CH(CH₂CH₂)₂</td>
<td>R³Cu(CN)Li₂</td>
<td>42</td>
<td>65–66</td>
</tr>
<tr>
<td>H</td>
<td>H</td>
<td>Ph</td>
<td>R³MgBr</td>
<td>63</td>
<td>121–122</td>
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<tr>
<td>H</td>
<td>H</td>
<td>R³Cu(CN)Li₂</td>
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<td>H</td>
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<td>R³MgBr</td>
<td>60</td>
<td>100–101</td>
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<td>Me</td>
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<td>170–172</td>
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<td>240–245</td>
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<tr>
<td>P-Me·C₆H₄</td>
<td>H</td>
<td>Phl(O₂CR³)₂</td>
<td>49</td>
<td>162–164</td>
<td>01JCS(P1)680</td>
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<tr>
<td>P-MeO·C₆H₄</td>
<td>H</td>
<td>Phl(O₂CR³)₂</td>
<td>45</td>
<td>153–155</td>
<td>01JCS(P1)680</td>
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<tr>
<td>P-Br·C₆H₄</td>
<td>H</td>
<td>Phl(O₂CR³)₂</td>
<td>43</td>
<td>219–221</td>
<td>01JCS(P1)680</td>
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<tr>
<td>[4,5]Benzo</td>
<td>Me</td>
<td>Phl(O₂CR³)₂</td>
<td>89</td>
<td>129–30</td>
<td>01JCS(P1)680</td>
</tr>
</tbody>
</table>

Amides (43)

<table>
<thead>
<tr>
<th>R¹</th>
<th>R²</th>
<th>Method</th>
<th>Yield (%)</th>
<th>m.p. (°C)</th>
<th>References</th>
</tr>
</thead>
<tbody>
<tr>
<td>H</td>
<td>H</td>
<td>Me Phl(O₂CR³)₂ R³MgBr</td>
<td>88</td>
<td>92–94</td>
<td>99JOC3595</td>
</tr>
<tr>
<td>H</td>
<td>H</td>
<td>Me Phl(O₂CR³)₂ R³MgCl</td>
<td>55</td>
<td>62–64</td>
<td>01JCS(P1)680</td>
</tr>
<tr>
<td>H</td>
<td>H</td>
<td>Me Phl(O₂CR³)₂ R³MgI</td>
<td>45</td>
<td>170–172</td>
<td>01JCS(P1)680</td>
</tr>
<tr>
<td>H</td>
<td>H</td>
<td>Me Phl(O₂CR³)₂ R³MgBr</td>
<td>48</td>
<td>170–172</td>
<td>01JCS(P1)680</td>
</tr>
<tr>
<td>H</td>
<td>H</td>
<td>Me Phl(O₂CR³)₂ R³MgCl</td>
<td>40</td>
<td>240–245</td>
<td>01JCS(P1)680</td>
</tr>
<tr>
<td>H</td>
<td>H</td>
<td>Me Phl(O₂CR³)₂ R³MgI</td>
<td>49</td>
<td>162–164</td>
<td>01JCS(P1)680</td>
</tr>
<tr>
<td>H</td>
<td>H</td>
<td>Me Phl(O₂CR³)₂ R³MgBr</td>
<td>45</td>
<td>153–155</td>
<td>01JCS(P1)680</td>
</tr>
<tr>
<td>H</td>
<td>H</td>
<td>Me Phl(O₂CR³)₂ R³MgCl</td>
<td>43</td>
<td>219–221</td>
<td>01JCS(P1)680</td>
</tr>
<tr>
<td>H</td>
<td>H</td>
<td>Me Phl(O₂CR³)₂ R³MgI</td>
<td>89</td>
<td>129–30</td>
<td>01JCS(P1)680</td>
</tr>
</tbody>
</table>

A convenient route to the 2-amino-5-nitrofuran derivatives 49 (Eq. (3)). In a similar way, 2-amino-5-vinyl derivatives 51 can be prepared from the pyridinium derivatives 50 (X = pyridinium) using a range of amines (e.g. pyrrolidine, n-butylamine or aniline) (Eq. (4)) (83MI1). Treatment of the S-methyl derivative 50 (R = CO₂Et, X = SM) with ammonium formate in dry ethanol (40–50 °C) affords the primary amine 51 (R = CO₂Et, R¹ = R² = H) (Eq. (4)) (94CCC444).
Padwa and co-workers have demonstrated a convenient route to 2-amido derivatives 53, which provides an alternative to Curtius rearrangement (Section II.B.3). In this approach, C–N cross-coupling between a 2-bromofuran 52 and an amide is achieved using copper (I) iodide in the presence of \(\text{N,N}^-\text{dimethylethylenediamine}\) and a base (\(\text{K}_2\text{PO}_4\) or \(\text{K}_2\text{CO}_3\)) (Eq. (5)) (02TL7365, 03JOC2609). Yields of the amides 53 are usually good.

\[
\begin{align*}
\text{R}^1\text{O} & \quad \text{Br} \quad \text{O} \quad \text{R}^1 \\
\text{N} & \quad \text{R}^2 \\
\text{R}^3 & \quad \text{H} \\
\text{R}^2 & \quad \text{O} \quad \text{R}^3 \\
\text{CuI} & \quad \text{Cul} \quad \text{R}^1 \text{O} \quad \text{N} \quad \text{R}^2 \quad \text{O} \quad \text{R}^3
\end{align*}
\]

5. Oxazole Cycloaddition

Padwa and co-workers have shown that the amides 55 can be conveniently prepared in high yield by [4+2]-cycloaddition of an acetylenic dienophile to the corresponding 2-amino oxazole derivative 54 (Eq. (6)). The reaction was extended to intramolecular reactions (e.g. 56 → 57, Eq. (7)), giving convenient 2-aminofuran precursors for further intramolecular Diels–Alder furan (IMDAF) reactions (see Section II.C.1.e) (99JOC3595, 99TL1645).

6. Elimination from Dihydrofuran Derivatives

A number of cyclisation methods described in Section II.B.1 involve transient formation of a dihydrofuran intermediate. For nitrile cyclisations this section
describes methods in which a 2-amino-dihydrofuran derivative is isolated and characterised and converted into the aromatic product as a separate step.

Reaction of an arylidenemalononitrile with potassium cyanide and an aromatic aldehyde in DMF gives the 2,3-dihydrofurans 58. The reaction appears to proceed via equilibration of intermediate carbanions (Scheme 10). Thermal elimination of HCN in hot ethylene glycol gives the aromatic 2-amino-4,5-diaryl-3-cyanofurans 59 in good yield (83AQ340, 84JCS(P1)2009).

The dihydrofurans 60 can be prepared by reaction of malononitrile with either 2-chloroethanols or epoxides (Scheme 11; R1 or R2 = H, Me, Ph). Conversion into the benzamides 61 and oxidation with N-bromosuccinimide gives the 2-amidofurans 62 (20–40%) (85CPB937).

The imides 63 are cyclised by dimethyl(methylthio)sulphonium tetrafluoroborate (DMTSF) to give the dihydrofurans 64 that readily lose acetic acid to give high yields of the 2-amidofurans 65 (Scheme 12) (00TL9387).

\[ \text{Ar}^2\text{CN} \xrightarrow{\text{Ar}^1\text{CHO}} \text{CN-} \xrightarrow{\Delta} \text{HCN} \]

Scheme 10

\[ \text{Ar}^2\text{CN} \xrightarrow{\text{Ar}^1\text{CHO}} \text{CN-} \xrightarrow{\Delta} \text{HCN} \]

Scheme 11

Reagents: i, CH2(CN)2/EtONa; ii, PhCOCl/pyridine; iii, NBS/(PhCO2)2/CCl4
An interesting approach to 5-vinyl derivatives has been described by Slovakian workers. A variety of substrates treated with malononitrile and sodium azide lead to derivatives of the general type \( \text{67} \). A typical transformation is shown in Scheme 13. The final stages in each process appear to involve displacement of a 2-nitro substituent by azide and subsequent reduction, under the reaction conditions, to the amines \( \text{67} \) (79CCC3301, 80CCC752, 84CCC984, 90CCC718, 94CCC2481).

Cyclodehydration of \( \gamma \)-keto-amides \( \text{68} \) using either triflic anhydride (\( \text{Tf}_2\text{O} \)) or trifluoroacetic anhydride (\( \text{TFAA} \)) gives the derivatives \( \text{69} \) in good yield (Eq. (8)) (03JOC2609). 2-Dialkylaminofurans have been prepared in good yield by cyclodehydration of 3-arylpropionamides (\( \text{ArCOCH}_2\text{CH}_2\text{CONR}_2 \)) using acetic anhydride and perchloric acid followed by treatment with base (\( \text{Et}_3\text{N} \)) (73JCS(P1)2523).

![Scheme 12](image1)

![Scheme 13](image2)

7. Miscellaneous Methods

An interesting approach to 5-vinyl derivatives has been described by Slovakian workers. A variety of substrates treated with malononitrile and sodium azide lead to derivatives of the general type \( \text{67} \). A typical transformation is shown in Scheme 13. The final stages in each process appear to involve displacement of a 2-nitro substituent by azide and subsequent reduction, under the reaction conditions, to the amines \( \text{67} \) (79CCC3301, 80CCC752, 84CCC984, 90CCC718, 94CCC2481).

Cyclodehydration of \( \gamma \)-keto-amides \( \text{68} \) using either triflic anhydride (\( \text{Tf}_2\text{O} \)) or trifluoroacetic anhydride (\( \text{TFAA} \)) gives the derivatives \( \text{69} \) in good yield (Eq. (8)) (03JOC2609). 2-Dialkylaminofurans have been prepared in good yield by cyclodehydration of 3-arylpropionamides (\( \text{ArCOCH}_2\text{CH}_2\text{CONR}_2 \)) using acetic anhydride and perchloric acid followed by treatment with base (\( \text{Et}_3\text{N} \)) (73JCS(P1)2523).
A notable recent innovation is the coupling of dimethyl acetylenedicarboxylate (DMAD), cyclohexyl isocyanide and an aromatic aldehyde in benzene under reflux giving the 2-aminofurans 70 in good yield (60–70%) (Eq. (9)) (00CC1019, 03ACR899). The method can be carried out at room temperature in higher yield in an ionic liquid (1-butyl-3-methylimidazolium tetrafluoroborate) from which the product is easily isolated by extraction with ether (04S2376).

\[
\begin{align*}
\text{MeO}_2\text{C} & \equiv \text{CO}_2\text{Me} \\
+ & \\
\text{RCHO} & \text{CN-cycloHex} \\
\rightarrow & \\
\text{MeO}_2\text{C} & \equiv \text{CO}_2\text{Me} \\
\text{R} & \text{O} \text{N-cycloHex}
\end{align*}
\]

(9)

It has been reported that [1+4]-cycloaddition between alkyl isocyanides and 3-benzylidene-2,4-pentadione followed by tautomerisation of the resulting iminolactone gives the N-alkyl-2-aminofurans 71 (R = cyclohexyl, 'Bu, PhCH₂) (Scheme 14) (97MC697). However, subsequent studies have shown that the isolated products are the pyrrol-2-ones 72, which are probably formed by oxidation of the intermediate 2-aminofurans 71 (04TL1413) (see also Section II.C.1.a).

\[
\begin{align*}
\text{MeCO} & \equiv \text{Ph} \\
\text{Me} & \text{MeCO} \\
\xrightarrow{\text{R-NC}} & \\
\text{MeCO} & \equiv \text{Ph} \\
\text{Me} & \text{Me} & \text{MeCO} & \equiv \text{Ph} \\
\rightarrow & \\
\text{O}_2 & \\
\text{MeCO} & \equiv \text{Ph} \\
\text{Me} & \text{Me} & \text{MeCO} & \equiv \text{Ph}
\end{align*}
\]

Scheme 14

Trimethylsilyl cyanide reacts with diphenylcyclopropenone in the presence of Fe₂(CO)₉ or PPh₃ as catalyst to give the aminofuran derivative 73 (40–60%) (Eq. (10)). Other phosphines and transition metal phosphine complexes are effective catalysts. A similar reaction was achieved using cycloheptenocyclopropenone. Desilylprotonation of compound 73 was achieved in hot MeOH containing a trace of p-TsOH, but the primary amine was trapped \textit{in situ} as a cycloadduct without isolation (87JOC4408).

\[
\begin{align*}
\text{Ph} & \text{Ph} \\
+ & \\
\text{Me}_3\text{SiCN} & \text{Fe}_2\text{(CO)}_9 \\
\text{or} & \text{PPh}_3 \\
\rightarrow & \\
\text{Ph} & \text{Ph} \\
\text{Ph} & \text{Ph} & \text{N(SiMe})_3\text{)}_2
\end{align*}
\]

(10)

Treatment of the nitrogen ylides 74 (R¹ = Me, Ph; R², R³ = alkyl) with sulphur in hot benzene gives the amines 75 (~30% yield) (Eq. (11)). A mechanism for this Dimroth-type rearrangement has been proposed. The structure of the product 75 (R¹ = Ph, R² = R³ = Me) has been confirmed by X-ray crystallography (95JOMC127).
Methods of liberating simple 2-aminofurans from phthalimides (71CB681, 75AP713) and imines (84JA5753) by displacement using hydrazine and oxime, respectively, have been described but the products are not well-characterised.

Reaction between 1-alkynyl sulphones and alkynylamines has been reported to give 2-amino-5-sulphinylfurans (88CB2163, 87CB71, 84AC321). The primary products of these reactions appear to be cyclobutadienes and the furans may be formed by a subsequent isomerisation (91JOC4095). An addition of ynamines to cyclopropanes has been reported to give tertiary amino derivatives (82TL3159)

C. Reactions

1. Reactions of the Furan Ring

a. Oxidation. UV irradiation of methanol solutions of the 4,5-diphenyl-, 4,5-dimethyl- and 4,5-tetramethylene derivatives 76 gives the corresponding 5-hydroxypyrrrolin-2-ones 77 in yields ranging from 20% to 67% (Scheme 15) (81AP127). Subsequent workers demonstrated a similar transformation when acetonitrile solutions of diaryl derivatives 76 were exposed to air and Spanish daylight over three days (84JCS(P1)2009). Under these conditions, the diphenyl derivative 76 (R¹ = R² = Ph) gave only a trace of the product 77 (R¹ = R² = Ph) and the p-chlorophenyl derivative 76 (R¹ = Ph, R² = p-CIC₆H₄) underwent no oxidation at all. However, derivatives with an electron-donating substituent (R¹ or R² = p-MeC₆H₄ or p-MeOC₆H₄) gave the products 77 in 65–80% yield.

![Scheme 15](image_url)
A similar transformation of 2-furylcarbamates (e.g. 42) to N-carboxy-5-hydroxyxypyrrolin-2-ones has been reported (78H1603, 80H1073). This type of oxidative rearrangement probably also accounts for the failure to isolate the 2-aminofurans 71 formed from 3-benzylidene-2,4-pentanediones and alkyl isocyanides (Scheme 14) (97MC697, 04TL1413).

An elegant application of the oxidation of 2-aminofurans has been described by Nicolaou and co-workers (02JA2190, 02JA2202) in model studies directed towards the total synthesis of CP molecules. In this study, the isolable iminobutenolide 80 is formed by cyclisation of the alkoxide 79 (Method B, Section II.B.1.b). Without a stabilising substituent on the ring the equilibrium favours the imine 80 rather than the amine 81 (Scheme 16). However, it is postulated that there is sufficient 2-aminofuran in equilibrium for this to be rapidly oxidised to the hydroperoxide 83. At this stage, the final product is determined by the reaction conditions. In strongly acidic conditions, tautomerism to the amine 85 and hydrolysis rationalises the formation of the isolated anhydride 88. Under weakly acidic conditions, formation of

![Scheme 16](image-url)
the molozonide 82 and rearrangement to hydroperoxide 84 rationalises the formation of the 5-hydroxypyrrolin-2-one 87, together with a small amount of the maleimide 86. The formation of compound 87 under these conditions is entirely consistent with the other oxidation reactions of 2-aminofurans described above.

**b. Reaction with Oxygen Nucleophiles. Water:** Little has been reported on the hydrolysis of aminofurans. Treatment of the derivative 76 (R¹ = R² = Ph) with concentrated HCl/EtOH followed by aqueous workup gave compound 78 (R¹ = R² = Ph) (35%) (Scheme 15) (66CB1002). Reaction of the ester 89 with warm aqueous alkali resulted in saponification and ring-opening to give the acid 90 characterised as its barium salt (Eq. (12)) (63JBC1625). Under similar conditions the ester 91 gives 3-cyano-2,5-hexanedione 92 (35%) (Eq. (13)) (78JOC3821).

**Alcohols:** Reaction of the ketone 93 with malononitrile gave the tetracyclic product 95 which is presumed to be formed via intramolecular cyclisation of the intermediate 2-amino-5-phenylfuran 94 (Scheme 17). The structure of product 95 was confirmed by X-ray crystallography. The corresponding 2-amino-5-methylfuran does not appear to cyclise (85CPB2663).

c. Reaction with Nitrogen Nucleophiles: Formation of Pyrroles and Pyrrolo[2,3-d]pyrimidines. **Ammonia:** Treatment of 3-acetyl derivatives 96 (R = CN, CO₂Et or COMe) with hot concentrated ammonia gives 3-cyano-2-methylpyrroles 97 (ca. 60%) (Eq. (14)). The reaction is presumed to occur via nucleophilic attack of the ring leading to an intermediate acyclic cyanoketone (78JOC3821). The proposed ring-opening step is analogous to the reaction with alkali shown in Eq. (13).
Reaction of the derivative 98 with a hot methanolic solution of ammonium acetate, containing a small amount of MeONa, gives the 2-aminopyrrole 99 (Eq. (15)). The same product was obtained when the ammonium salt was replaced by urea or thiourea (97EJC105).

**Amidines and Guanidines:** A convenient route to 4-aminopyrrolo[2,3-d]pyrimidines 101, including the DHFR inhibitor TNP-351 101 (R₁ = H, R₂ = (CH₂)₃ C₆H₄CONH·CH(CO₂H)CH₂CH₂CO₂H, R₃ = NH₂) (96JOC7973) and related structures of biological interest (01JHC1197, 03BMCL59), has been achieved by reacting 2-amino-3-cyanofurans 100 with amidines or guanidines (Scheme 18) (95JOC6684, 96BKCS676). The reaction probably involves nucleophilic attack at the 2-position followed by ring-opening and a recyclisation in which the amino nitrogen becomes the pyrrole nitrogen (Scheme 18) (95JOC6684, 96BKCS676).

d. **Reaction with Electrophiles.** 2-Aminofurans behave like enamines or dienamines towards electrophiles with reaction occurring on the furan ring. NMR studies have shown that in TFA or sulphuric acid, 2-amino-3-cyanofurans protonate on the ring at positions 5 (e.g. 102) rather than on the exocyclic nitrogen (68TL4605). In DMSO/TFA protonation of the exocyclic nitrogen atom occurs (95JHC985).
The parent 2-aminofuran 103 is extremely unstable but when generated in situ, by catalytic reduction of 2-nitrofuran, and immediately reacted with the electrophiles ethoxymethylene malononitrile (EMMN) and ethyl ethoxymethylene cyanoacetate (EMCA) the 5-substitution products 104 were formed in low yield (Eq. (16)) (93JHC113). If the 5-position is blocked as in the case of the 5-methyl derivative 105, or 2-aminobenzo[b]furan, then substitution occurs at position 3, e.g. 106 (Eq. (17)) (93JHC113).

\[
\text{103} \xrightarrow{\text{EtO} \equiv \text{CN}} \text{104; } X = \text{CO}_2\text{Et}, \text{CN}
\]

(16)

It is significant to note that when the furan ring is deactivated, as in the case of ethyl 5-amino-2-furoate 107, then reagents such as EMME and EMCA react on the exocyclic nitrogen atom (66JHC202). However, in ethanolic HCl the furoate 107 gave a 50% yield of the diastereomeric dilactones 108 (68JOC1105). These stereoisomers are presumed to form from the aminofuran 107 by acid-catalysed electrophilic addition of the \(\alpha,\beta\)-unsaturated ester function to the dieneamine function of a second molecule giving the intermediate 109, which undergoes hydrolysis leading to the diastereomeric lactones 108. The same product was obtained (48%) upon diazotisation of aminofuran 107, probably via a similar mechanism (81H231). Reaction of isatins with compound 107 also results in substitution of the furan ring at position 3 (02SL1140).

The product originally thought to be the amine 110 (66CB1002) was subsequently shown to be a dimer but was incorrectly assigned the cycloadduct structure 113.
Later workers showed that the properties of the dimer were consistent with structure 111 (Scheme 19), which was confirmed by X-ray crystallography (80LA1952). Subsequently, it was shown that the monomer 110 (m.p. 108–109 °C) can be isolated and that it undergoes thermal dimerisation upon heating (130–135 °C) to give dimer 111 (m.p. 156–158 °C) (85CPB937). We suggest that a plausible mechanism for the formation of the dimer 111 involves partial tautomerism of the amine 110 to the imine tautomer 112, which reacts as an electrophile with the dieneamine 110 to form the electrophilic substitution product 111. Imine tautomers are sometimes encountered during the preparation of 2-aminofurans (see Sections II.B.2.a and II.C.1.a).

The thermal dimerisation 110 → 111 appears to be reversible in solution and reaction of compound 111 with phenyl thioisocyanate in hot THF gives the thioamide 114 (80LA1952).

e. Cycloaddition Reactions. A 2-amino substituent activates the furan ring and, as expected, 2-aminofurans are particularly reactive towards electron-deficient dienophiles. The initially formed cycloadducts readily ring-open to give synthetically useful products.

The earliest example of a Diels–Alder reaction of a 2-aminofuran was described by Johnson and Heeschen (64JOC3252), who found that the 3,4-dihydroaniline derivative 32 (Scheme 7) is formed in the reaction of epichlorohydrin with potassium cyanide. These workers rationalised the formation of product 32 in terms of transient formation of 2-aminofuran 103 which undergoes cycloaddition with its nitrile precursor (HOCH₂CH═CHCN) (see Scheme 7, Section II.B.1.d).
Gewald (66CB1002) described the first examples of Diels–Alder reactions of fully characterised 2-aminofurans. In particular he showed that the 2-amino-3-cyanofurans 100 react with maleic anhydride in hot acetone to give, after spontaneous dehydration of the cycloadducts 115, the phthalic anhydrides 116 (Scheme 20). It should be noted that one of the 2-aminofurans used in this study (100; \( R_1 = H, R_2 = Me \)) was in fact the dimer 111, which under the conditions of the reaction is presumed to be in equilibrium with the monomer (Section II.C.1.d). Further examples of maleic anhydride cycloadditions have subsequently been reported (82S513, 87JOC4408, 90T8103), together with cycloadditions of \( N \)-arylmaleimides (89JPC31).

Because the carbamate derivative 117 is particularly electron-rich and mild conditions can be used for Diels–Alder reaction, the cycloadducts 118 can be isolated (Eq. (18)), and only upon heating in toluene solution (110 \( ^\circ \)C) does dehydration occur (97JOC4088).

In 1980, Nixon and co-workers (80S56, 82JOC2483) recognised that cycloadditions of the 2-amino-3-cyanofurans 100 with acrylates or vinyl ketones provided a convenient route to anthanilic acid derivatives (84JMC772, 90H651). 6-Methoxy-2H-pyran-3-one has also been used as dienophile (87AP(W)813). Later, the synthetic potential of 2-aminofuran cycloadditions was systematically studied by Padwa and co-workers who investigated a wider range of dienophile and aminofuran derivatives. Reaction of the methyl ester 119 with a range of mono- and disubstituted alkene dienophiles gave the ring-opened adducts 120 in high yield (96TL2903, 97JOC4088). Using unsymmetrical dienophiles, the additions were regioselective with the electron-withdrawing group adding to the amino carbon. This selectivity is entirely in accord with FMO theory. Treatment of the adducts 120 with \( BF_3 \cdot OEt_2 \) at 80 \( ^\circ \)C results in dehydration giving high yields of the anilines 123. Alternatively, a trace of \( p \)-TsOH in aqueous THF gives the cyclohexenones 122, which on further treatment with \( BF_3 \cdot OEt_2 \), give high yields of the phenols 121. The approach summarised in Scheme 21 therefore provides good access to selectively substituted anilines and phenols. An unusual mode of addition of the amine 100 (\( R_1 = R_2 = Me \)) with dimethyl acetylenedicarboxylate has been reported (88S632).
The carbamate 124 and the amide 125 are more reactive towards dienophiles than the ester 119 and this is attributed to their higher HOMO energies (97JOC4088). Calculated HOMO energies are as follows: 119 (−8.8 eV), 124 (−8.6 eV), 125 (−8.5 eV), furan (−9.3 eV) (97JOC4088, 01JCS(P1)680). Derivatives 124 and 125 react readily with acetylenic esters giving the phenol derivatives 126 (Scheme 22) (97JOC4088, 01JCS(P1)680).

An interesting result was observed when the 2-morpholinofuran 127 was reacted with methyl vinyl ketone in hot toluene (Scheme 23). This reaction resulted in a mixture of the three phenols 129, 130 and 131. These products are formed by ring-opening of the initial cycloadduct 128 followed by either loss or 1,2 migration of the nitro substituent (97JOC4088).

In a series of elegant studies during the last decade, Padwa and co-workers have demonstrated the value of IMDAF of 2-aminofurans for the synthesis of various alkaloid skeletons and their analogues (98JOC5304, 98JOC3986, 99JOC4617, 99JOC3595, 00OL3233, 00TL9387, 03JOC2609). In particular, these transformations are achieved using 2-aminofurans with an appropriate alkenyl group tethered to the nitrogen atom. This approach is best illustrated by three selected examples.
A versatile approach to pyrrolophenanthradine alkaloids, which occur in various *Amaryllidaceae* species, is exemplified by the synthesis of oxoassoanine \( \text{136} \) (Scheme 24) (98JOC3986). Acylation of the 2-aminofuran \( \text{119} \) gave the amide \( \text{132} \) which was N-alkylated using 4-bromo-but-1-ene. The resulting alkene derivative \( \text{133} \) underwent intramolecular cycloaddition and loss of water from the cycloadduct upon heating at 100 °C with LiClO\(_4\) etherate in a sealed tube to give the 2,3-dihydroindole \( \text{134} \) in 79% yield. Radical cyclisation followed by decarboxylation then gave the alkaloid oxoassoanine \( \text{136} \).

Using IMDAF cycloaddition of the carbamate \( \text{138} \), the azabicyclo[3.2.2]nonanone \( \text{141} \) has been prepared in 81% overall yield (Scheme 25) (99JOC4617). N-alkylation of the carbamate \( \text{137} \) readily gives the alkene \( \text{138} \), which upon heating in benzene at 190 °C in a sealed tube gives the tetrahydro-2\(H\)-indole \( \text{139} \) in 89% yield. The formation of a single diastereoisomer (\( \text{139} \)) is consistent with the exo-mode of the IMDAF cycloaddition being energetically favoured. Calculations suggest that formation of the exo-adduct is favoured by ca. 10 kcal mol\(^{-1}\). Treatment of the imine \( \text{139} \) with methyl iodide followed by aqueous workup gave the azabicyclo[3.2.2]nonanone \( \text{141} \) in 90% yield. This product is presumed to be formed by an intramolecular Michael addition of an intermediate cyclohexenone \( \text{140} \).

Styryl derivatives of 2-aminofurans, as well as alkenyl compounds, also undergo intramolecular cycloaddition and the alkene function can be introduced by Stille coupling of a suitably functionalised aryl iodide. This approach is illustrated by the tetrahydroquinoline synthesis summarised in Scheme 26 (99JOC3595). The iodo derivative \( \text{143} \) is readily prepared from the carbamate ester \( \text{142} \) (67% yield) and Stille coupling with vinyltributyltin gives the styrene \( \text{144} \) (72% yield). Intramolecular cycloaddition and dehydration is then achieved simply by heating compound \( \text{144} \) in toluene under reflux (24 h) to give the tetrahydroquinoline \( \text{145} \) in 79% yield.

Intramolecular cycloadditions of allene derivatives have also been reported (Eq. (19)) (97LAR435).

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**Scheme 23**

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**Scheme 24**

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**Scheme 25**

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**Scheme 26**

---
2. Reactions of Ring Substituents

a. Reactions of 2-Amino Substituents. Although 2-aminofurans often react as die-namines with electrophiles (Section II.C.1.d), it is well established that they react like conventional aromatic amines with carbonyl reagents giving N-functionalised products. For example, treatment with acid chlorides or acid anhydrides under
standard conditions gives amides in moderate to good yield. Many examples of the formation of 2-amidofurans by acylation of primary 2-aminofurans have been reported (62JMPC513, 70JCS(C)1916, 79JHC477, 80CCC1581, 85CPB937, 85CPB5581, 95IJHC191, 96P386, 01BMC1123, 02HCA4485). A typical procedure is shown in Eq. (20) (85CPB937). It is interesting to note that acetylation of the dinitro derivative 146 gave a mixture of the N-acetyl (147) and N,N-diacetyl (148) products (Eq. (21)) (79JHC477). Isocyanates give ureas (77CS199, 02BMCL1379). Bromoacetyl bromide (BrCO·CH₂Br) gives amides and not ring-acylated products (95JHC985) as previously claimed (68TL4605).

Scheme 25

\[
\begin{align*}
\text{Me\,N\,Me} & \quad \xrightarrow{i, \text{NaOH, K}_2\text{CO}_3, \text{Bu}_4\text{N}^+\text{HSO}_4^-/ \text{CH}_2=\text{C(Me)}\text{CH}_2\text{CH}_2\text{Br} / \text{C}_6\text{H}_6 \text{ at } 80 \, ^\circ\text{C}} \text{Me\,N\,Me} \\
\text{Me\,Me} & \quad \xrightarrow{\text{ii, benzene, sealed tube, } 190 \, ^\circ\text{C}; \text{iii, MeI; iv, H}_2\text{O.}} \text{Me\,Me}
\end{align*}
\]

Reagents: i, NaOH, K₂CO₃, Bu₄N⁺HSO₄⁻/CH₂=C(Me)CH₂CH₂Br / C₆H₆ at 80 °C; ii, benzene, sealed tube, 190 °C; iii, Mel; iv, H₂O.
Primary 2-aminofurans react with aldehydes to give a Schiff base (69CZ187, 80CCC1581, 83CCC3140, 84CCC1788, 85JCS(P1)2581, 86JHC1583) and this condensation reaction has been used to form stable derivatives of 2-aminofurans that
are too unstable to be isolated (e.g. Scheme 27) (86JHC1583). Reaction with dimesdone gives the enaminoketone tautomer (01MI2428).

Reaction of the derivative 149 ($R_1 = R_2 = 2,5$-dimethyl-3-thienyl) with DMF acetal gives the amidine 150 (85%) (Scheme 28) (01MI2424). Condensation of the derivatives 149 ($R_1, R_2$ = alkyl or aryl) with 2,5-dimethoxytetrahydrofuran, in the presence of 4-chloropyridinium chloride, gives the pyrrole derivatives 151 (25–86%) (Scheme 28) (96JHC2007, 98JHC1313).

It should be noted that alkene electrophiles do not always react on a ring carbon atom (Section II.C.1.d). The ester 152 reacts with diethyl ethoxymethylenemalonate at 120°C to give the N-substitution product 153 (78%) (Eq. (22)). At a higher temperature (150°C), the amide 154 (14%) was also formed by competing 1,2-addition of the amine to the diester (95JHC1283).

The nitrogen atom of amides and carbamates 155 can be alkylated using standard procedures (Eq. (23)) and this type of transformation has been studied extensively in the context of using the products 156 in IMDAF (see Section II.C.1.e, Schemes 24–26).
The $N$-acyl ureas 157, prepared by amidine rearrangement (Section II.B.3), undergo thermal elimination of phenyl isocyanate with formation of the amides 158 (Eq. (24)) (01JCS(P1)680). This approach provides access to amides of unstable 2-aminofurans that cannot be prepared by acylation of the primary amine.

b. Reactions of Other Substituents. Most of the reactions involving another substituent also involve the amino group resulting in the formation of a new bicyclic system, and this type of reaction is covered in Section II.C.2.c.
The thioamide 159 has been prepared (22%) by treatment of the corresponding nitrile with H₂S in DMF at 50–60 °C (83CCC3140). The thioaldehyde 160 is formed in 63% yield by treatment of the corresponding aldehyde with HMDST ((Me₃Si)₂S) (96S1185). 5-Amino-2-furaldehyde forms compound 161 upon treatment with 3-amino-2-oxazolidinone (62JMPC513, 68JOC2552).

c. Formation of Furo[2,3-b]pyridines and Furo[2,3-d]pyrimidines. Reaction of 2-aminofurans with bifunctional reagents provides access to bicyclic heterocycles. It should be noted that some reagents, such as amidines, result in ring-opening of the furan ring and recyclisation to give bicyclic pyrroles, and these transformations are discussed in Section II.C.1.e. The reactions discussed below are those in which the furan ring remains intact leading to furan-based bicycles.

Furo[2,3-b]pyridines: 2-Amino-5-furoates 162 with diethyl ethoxy methylene-malonate undergo thermal cyclisation (ca. 240 °C) to give furo[2,3-b]pyridine diesters 163 in good yield (Scheme 29) (66JHC202, 95JHC1283). In a similar manner, trifluoroacetoacetate (CF₃COCH₂CO₂Et) gives the derivative 164 (R = Et) and sodium nitromalonaldehyde (Na⁺⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻~-~-~C·NO₂(CHO)₂) gives the nitro derivative 165 (R = Et) (66JHC202). Other reagents give similar products (03S1531).

Reagents: i, EtOCH=C(CO₂Et)₂, heat; ii, CF₃CO.CH₂CO₂Et, 130 °C; iii, Na⁺⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻⁻~-~-~C·NO₂(CHO)₂; iv, HCl.

Scheme 29

3-Cyano amines provide access to 4-aminofuro[2,3-b]pyridines. Heating (7 h) of the 4,5-diaryl amines 166 with ethyl acetoacetate gives the bicyclic derivatives 167 (55–60% yield) (Eq. (25)) (95IJHC191). Similarly, 2-amino-3-cyano-5-phenylfuran 168 with either cyanoacetamide or ethyl cyanoacetate in hot ethanol containing catalytic Et₃N gives the 4-amino-3-cyano derivative 169 (Eq. (26)) (97EJC105). Use of cyanothioacetamide or malononitrile gives the corresponding thio and imino products. Cyclisation to 4-aminofuro[2,3-b]pyridines is also achieved using cyclohexanone and AlCl₃ in hot 1,2-dichloroethane (02BMC2077, 02APMC347). Cyclisation using diethyl acetonedicarboxylate has also been reported (95MC333).
Access to 2-aminofuro[2,3-\(b\)]pyridines (e.g. \(\text{171}\)) is provided by thermal cyclisation of the dinitrile \(\text{170}\) (Eq. (27)), although the yield of the precursor \(\text{170}\) (Section II.C.1.d) is low (93JHC113).

The thioaldehyde \(\text{160}\) reacts with electron-deficient alkynes to give the corresponding furo[2,3-\(a\)]pyridines in moderate yield via an intermediate dihydropyridine (Eq. (28)) (97TL2171).

**Furo[2,3-\(d\)]pyrimidines**: Reaction of 2-amino-3-cyanofurans \(\text{172}\) with hot formamide provides a high yielding route to 4-aminofuro[2,3-\(d\)]pyrimidines \(\text{173}\) (\(R^3 = H\)) (Scheme 30) (66CB1002, 80CCC1581, 84CCC1788, 04BMCL3907). 2-Substituted products \(\text{173}\) (\(R^3 \neq H\)) can be prepared by condensation of a nitrile (\(R^3\)CN) in the presence of dry HCl: the 4-amino product \(\text{173}\) is usually accompanied by the corresponding 4-chloro derivative (80JHC1497, 83TL4611, 90JHC119). Similar transformations using nitriles and dry HBr have been achieved (99H2723).

Use of formic acid, instead of formamide, gives pyrimidin-4-ones \(\text{175}\) (\(R^3 = H\)) (01M12424). Alternatively, microwave irradiation with montmorillonite and an acid chloride (\(R^3\)COCl) gives the derivatives \(\text{175}\) (\(R^3 = \text{aryl or alkyl}\)) (03BCSJ203). Reaction of the amines \(\text{172}\) with carbon disulphide in pyridine leads to the dithiones \(\text{174}\), and related derivatives have been obtained using a variety of condensation reagents (69JCS(C)1937, 91JICS660, 95IJHC191, 96JHC659, 96JPC206, 00M826, 02SC3749). Reaction of the 4,5-dimethyl derivative \(\text{172}\) (\(R^1 = R^2 = \text{Me}\)) with \(\text{EtO}_2\text{CCH}_2\text{-NCX}\) (\(X = \text{O or S}\)), and related reagents, leads to tricyclic derivatives (01CPB391, 01H1747, 01JHC743).
Reaction of 2-amino-3-ethoxycarbonyl-5-phenylfuran with trichloroacetonitrile in ethanol gives the pyrimidinone \( 175 \) (\( R_1 = \text{Ph}, R_2 = \text{H}, R_3 = \text{OEt} \)) \( (90\text{JPC}479) \).

\[ \text{Scheme 30} \]

Reagents: i, HCONH\(_2\); ii, \( R_3 \text{CN}, \text{HCl} \); iii, HCO\(_2\)H; iv, \( R_3 \text{COCl} \), montmorillonite, \( \mu \nu \); v, CS\(_2\), pyridine, heat.

\( \text{Reagents: i, HCONH}_2; \text{ii, R}_3\text{CN, HCl; iii, HCO}_2\text{H; iv, R}_3\text{COCl, montmorillonite, } \mu \nu; \text{v, CS}_2, \text{pyridine, heat.} \)

\( \text{Reagents: i, HCONH}_2; \text{ii, R}_3\text{CN, HCl; iii, HCO}_2\text{H; iv, R}_3\text{COCl, montmorillonite, } \mu \nu; \text{v, CS}_2, \text{pyridine, heat.} \)

\subsection{d. Formation of Furo[3,2-b]thiazines and Furo[2,3-d]thiazoles. Furo[3,2-b]thiazines:} The 3-cyanomethylsulphonyl substituent (\(-\text{SO}_2\text{CH}_2\text{CN}\)) provides access to furo[3,2-b]thiazine derivatives \( (97\text{JHC}857) \). An illustrative example is shown in Eq. (29).

\[ (29) \]

\( \text{Furo[2,3-d]thiazoles:} \) Oxidation of furylthioureas \( 176 \) using bromine in acetic acid gives good yields of the furo[2,3-\(d\)]thiazoles \( 177 \) (Eq. (30)) \( (77\text{CS}199) \).
III. 3-Aminofurans

A. Physical Properties

1. Molecular Structure

The structure of the 3-aminofuran 178 has been determined by X-ray crystallography (05OL1343). The exocyclic C–N bond is longer (1.4 Å) than that observed for 2-aminofurans (1.32–1.33 Å) (Section II.A.1) indicating less resonance interaction with the furan ring. In the benzofuran derivative 179, the C–N bond is shorter (1.36 Å) (88AC1449) consistent with a greater resonance interaction. In the N-tosyl derivative 180, the C–N bond increases to 1.41 Å due to competing resonance with the sulphone (88AC300).

2. Computational Studies

The results of quantum mechanical calculations on 3-aminofurans are included in Section II.A.2.

3. Ultraviolet Spectroscopy

The UV spectral data of representative 3-aminofurans are summarised in Table 7.

Table 7. Ultraviolet spectral data for 3-aminofuran derivatives

<table>
<thead>
<tr>
<th>R¹; R²; R³</th>
<th>Solvent</th>
<th>λ_max (ε) (nm)</th>
<th>References</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ph; Ph; COPh</td>
<td>EtOH</td>
<td>253 (15,100), 281 (14,800), 368 (17,800)</td>
<td>84LA1702</td>
</tr>
<tr>
<td>H; Ph; COPh</td>
<td>EtOH</td>
<td>243 (15,800), 349 (12,900)</td>
<td>84LA1702</td>
</tr>
<tr>
<td>Ph; Ph; COMe</td>
<td>EtOH</td>
<td>267 (11,750), 327 (12,600)</td>
<td>84LA1702</td>
</tr>
<tr>
<td>Ph; CN; COPh</td>
<td>EtOH</td>
<td>283 (24,550), 318 (9300), 369 (15,850)</td>
<td>84LA1702</td>
</tr>
<tr>
<td>Ph; CN; COMe</td>
<td>EtOH</td>
<td>253 (15,100), 281 (14,800), 368 (17,800)</td>
<td>84LA1702</td>
</tr>
</tbody>
</table>
4. **NMR Spectroscopy**

The $^1$H-NMR and $^{13}$C-NMR chemical shifts for representative 3-aminofurans are shown in Tables 8 and 9. Conformational studies of the aldehydes and thioaldehydes $^2 (R^1 = R^2 = H, R^3 = CHO, CHS)$ have been reported (97JOC2263).

### Table 8. Chemical shifts of protons in 3-aminofuran derivatives

<table>
<thead>
<tr>
<th>$R^1; R^2; R^3$</th>
<th>Solvent</th>
<th>$\delta H-2$</th>
<th>$\delta H-4$</th>
<th>$\delta H-5$</th>
<th>$\delta NH$</th>
<th>References</th>
</tr>
</thead>
<tbody>
<tr>
<td>$t$-Bu; H; CO$_2$Et</td>
<td>CDCl$_3$</td>
<td>5.75</td>
<td>–</td>
<td>–</td>
<td>4.51</td>
<td>00OL2061</td>
</tr>
<tr>
<td>Ph; H; CO$_2$Et</td>
<td>CDCl$_3$</td>
<td>6.37</td>
<td>–</td>
<td>–</td>
<td>4.65</td>
<td>00OL2061</td>
</tr>
<tr>
<td>H; Ph; CO$_2$Et</td>
<td>CDCl$_3$</td>
<td>7.37</td>
<td>6.11</td>
<td>7.29</td>
<td>~5.4</td>
<td>75ACS(B)224</td>
</tr>
<tr>
<td>H; H; CH = S</td>
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<td>6.17</td>
<td>7.23</td>
<td>~4.2</td>
<td>75ACS(B)224</td>
</tr>
<tr>
<td>Me; H; CH = O</td>
<td>CDCl$_3$</td>
<td>5.2</td>
<td>5.79</td>
<td>–</td>
<td>–</td>
<td>98H1431</td>
</tr>
<tr>
<td>H; 3-PyCH$_2$; CO$_2$Me</td>
<td>$d_6$-DMSO</td>
<td>–</td>
<td>–</td>
<td>7.38</td>
<td>5.52</td>
<td>99JHC423</td>
</tr>
</tbody>
</table>

### Table 9. Chemical shifts of ring carbons in 3-aminofuran derivatives

<table>
<thead>
<tr>
<th>$R^1; R^2; R^3; R^4$</th>
<th>Solvent</th>
<th>$\delta C-2$</th>
<th>$\delta C-3$</th>
<th>$\delta C-4$</th>
<th>$\delta C-5$</th>
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<tr>
<td>$t$-Bu; H; H; CO$_2$Et</td>
<td>CDCl$_3$</td>
<td>144.8</td>
<td>124.5</td>
<td>98.5</td>
<td>160.4</td>
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<td>Ph; H; H; CO$_2$Et</td>
<td>CDCl$_3$</td>
<td>145.1</td>
<td>124.9</td>
<td>99.9</td>
<td>156.1</td>
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<tr>
<td>H; H; H; CH = S</td>
<td>CDCl$_3$</td>
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<td>149.8</td>
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<td>151.0</td>
<td>96S1185</td>
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<td>Me; H; H; CH = O</td>
<td>CDCl$_3$</td>
<td>147.3</td>
<td>137.9</td>
<td>101.4</td>
<td>160.3</td>
<td>98H1431</td>
</tr>
<tr>
<td>H; H; CO$_2$t-Bu; H</td>
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<td>125.17</td>
<td>105.15</td>
<td>141.67</td>
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<tr>
<td>H; H; CO$_2$t-Bu; N(CO$_2$Et)NHCO$_2$Et</td>
<td>CDCl$_3$</td>
<td>132.35</td>
<td>120.65</td>
<td>107.27</td>
<td>139.17</td>
<td>82T2783</td>
</tr>
</tbody>
</table>

4. **NMR Spectroscopy**

The $^1$H-NMR and $^{13}$C-NMR chemical shifts for representative 3-aminofurans are shown in Tables 8 and 9. Conformational studies of the aldehydes and thioaldehydes 2 ($R^1 = R^2 = H, R^3 = CHO, CHS$) have been reported (97JOC2263).

### B. Preparation

1. **Cyclisation of Cyanovinyl Ethers (Method A)**

This approach has previously been reviewed (99AHC79). Several groups have prepared stable crystalline 3-aminofuran derivatives 2 by treatment of cyanovinyl ethers.
ethers 181 with strong base (Scheme 31). A good variety of substituents have been introduced at positions 4 and 5 of the furan ring using this method (Table 10). However, this approach requires an acidic proton \( z \) to the ether and all derivatives prepared by this method have an electron-withdrawing substituent at the 2-position. These 2-substituents probably also stabilise the amines since the other ring substituents are cross-conjugated. The best way of preparing the ethers 181 appears to be the treatment of the enolates 182 with the appropriate halo derivative, e.g. diethyl chloromalonate (84LA1702, 86TL815, 99JHC423, 02S753). A good alternative route is to treat the ketones 183 with ethyl glycolate under Mitsunobu conditions (00OL2061). Some ethers have also been prepared from 2-halovinyl nitriles 184 and alcohol derivatives (84LA1702, 00OL2061, 00JMC4288) and from a 1-bromovinyl nitrile 185 (76HCA945).

2. Reduction of 3-Nitro and 3-Azido Derivatives (Method B)

Little has been reported on the reduction of 3-nitrofurans to the amines. An early report (34MI13) described the reduction of the derivative 186 to ethyl 2-acetamido-3-amino-5-furoate 187 in 10% yield using PtO\(_2\)/H\(_2\) in ethanol (Eq. (31)). Reduction of a 2-alkenyl derivative using H\(_2\) and Raney nickel has been described more recently but the product was not characterised (98H1431).

More attention has been directed to the reduction of 3-azidofurans 188 which give simple 3-aminofurans 2 in good yield (Table 10). The azides are prepared from the
3-bromofurans and are conveniently reduced by H$_2$S/EtOH, containing a trace of base, e.g. piperidine (75ACS(B)224), or by NH$_4$SH/MeOH (98H1431). The reduction has been proposed to occur via the triaza intermediate $^{189}$ (Scheme 32). HMDST can also be used to reduce 3-azido-2-formylfurans $^{188}$ ($R^3=CHO$). Use of MeOH as solvent gives the 3-amino-2-formylfurans $^{2}$ ($R^3=CHO$) and use of MeCN gives the thioformyl products $^{2}$ ($R^3=CHS$) (Table 10) (95JOC2254, 97JOC2263).

Table 10. Preparation of 3-aminofuran derivatives

$^{2}$

<table>
<thead>
<tr>
<th>$R^1$</th>
<th>$R^2$</th>
<th>$R^3$</th>
<th>Method</th>
<th>Yield (%)</th>
<th>m.p. [b.p.] (°C)</th>
<th>References</th>
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<tbody>
<tr>
<td>Ph</td>
<td>Ph</td>
<td>PhCO</td>
<td>A</td>
<td>55</td>
<td>121–123</td>
<td>84LA1702</td>
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<tr>
<td>$-(CH_2)_4-$</td>
<td>$p$-BrC$_6$H$_4$CO</td>
<td>A</td>
<td>96</td>
<td>152–153</td>
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<td></td>
</tr>
<tr>
<td>H</td>
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<td>124–126</td>
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<td>H</td>
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<tr>
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<tr>
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<td>C</td>
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<td>[55–56 (4 mm Hg)]</td>
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<tr>
<td>Me</td>
<td>Ph</td>
<td>Ph</td>
<td>C</td>
<td>–</td>
<td>[120–121 (0.07 mm Hg)]</td>
<td>73TL3353</td>
</tr>
</tbody>
</table>
3. Rearrangement of Furan-3-Carboxylate Derivatives (Method C)

A detailed study of the Curtius rearrangement of the furoyl azides 190 (R\textsuperscript{1} = H, Me, R\textsuperscript{2} = H, R\textsuperscript{3} = Me) gave the furyl isocyanates 191 which are transformed into the amides 192 by Grignard reagents and the carbamates 194 by alcohols (Scheme 33) (34JA146, 34JA666). Heating these isocyanates with water gave symmetrical difuryl-ureas (34JA146). Rearrangement in glacial formic acid gives the formamide derivatives 193 and these were found to be the best precursors of the free primary amines 2. Rapid alkaline hydrolysis of the corresponding formamides 193 gave the amines 2 (R\textsuperscript{1} = H, Me, R\textsuperscript{2} = H, R\textsuperscript{3} = Me) (Table 10) in good yield (37JA2525).

More recently, two carbamate derivatives of the parent amine 196 (R\textsuperscript{1} = R\textsuperscript{2} = R\textsuperscript{3} = H, R\textsuperscript{4} = Me, t-Bu) have been prepared in moderate yield (ca. 50%) by treatment of
3-furanoic acid 195 with diphenylphosphoryl azide and triethylamine in the presence of the appropriate alcohol (Eq. (32)) (82T2783).

\[
\begin{align*}
\text{CO}_2\text{H} & \quad \xrightarrow{(\text{PhO})_2\text{PO.N}_3 / \text{Et}_3\text{N}} \quad \text{NHCO}_2\text{R} \\
195 & \quad \xrightarrow{\text{R-OH}} \quad 196
\end{align*}
\]

(32)

4. Substitution of the Furan Ring

\[
\begin{align*}
\text{Br} & \quad \xrightarrow{\text{R}^1\text{NHCO}_2\text{R} / \text{CuI}} \quad \text{R}^1\text{NCO}_2\text{R} \\
197 & \quad \xrightarrow{110 \degree \text{C}} \quad 197
\end{align*}
\]

(33)

A promising new route to 3-aminofuran derivatives has been described by Padwa and co-workers. Copper-catalysed amidation of 3-bromofuran using CuI and four different amides gave excellent yields of furan-3-ylamides 197 (Eq. (33)), including the benzamide 197 (R^1 = H, R^2 = Ph) (98%) (03JOC2609).

5. Miscellaneous Methods

An innovative new route to the secondary amines 198 (R^2 = alkyl) has recently been described (05OL1343, 05JOC8919). This novel approach involves a multicomponent reaction of thiazole carbenes, DMAD and aryl, \(\alpha,\beta\)-unsaturated or aliphatic aldehydes. The thiazole carbenes are generated \textit{in situ} by treatment of a thiazolium salt with sodium hydride (Scheme 34). The yields of 3-aminofurans 198 are moderate.
to good (ca. 30–80%). This approach is not suitable for the primary amines 198 ($R_2 = H$) but 26 representative secondary amines 198 ($R_2 = Me, Et, n-Bu, Bn$) have been prepared by this method. The reaction probably involves the formation of a spirocyclic intermediate that undergoes hydrolysis on workup to give the isolated products 198 (Scheme 34) (05JOC8919).

The preparation of two $N,N$-diethylaminofurans 200 ($R = Me, Et$) by ring-opening of the cyclobutenone 199 using a Grignard reagent has been described (Eq. (34)) (73TL3353).

Treatment of $N$-acetyl-$p$-glucosamine with dilute alkali is reported to give 3-acetamidofuran 192 ($R^1 = R^2 = R^3 = H, R^4 = Me$) (56CB1473). An imine derivative of 3-aminofuran has been obtained by reaction of 3-furyllithium with the oxime $O$-tosylate of tetraphenylcyclopentadienone (84JA5753).

C. REACTIONS

1. Reactions of the Furan Ring

a. Oxidation. Upon exposure to air the amines 2 ($R^1 = H, Me, R^2 = H, R^3 = Me$) rapidly darken and are converted into a soft resinous ill-defined product (37JA2525).

b. Reaction with Nucleophiles. The amines 2 ($R^1 = H, Me, R^2 = H, R^3 = Me$) are reported to be unstable in hot aqueous acids or alkalis. Treatment of the 2-methyl derivative with hot dilute sulphuric acid resulted in quantitative elimination of ammonia. With aqueous KOH, or Ba(OH)$_2$, the 2,5-dimethyl derivative gives ammonia, acetic acid and acetoin (37JA2525).

c. Reaction with Electrophiles. NMR studies have shown that in the presence of D$_2$O H/D exchange occurs at the 2-position of the carbamate 201. Reaction of the carbamate 201 with methyl 3-nitroacrylate gives the 2-substituted product 202 (10%), as well as a cycloadduct in very low yield (3%) (see Section III.C.1.d). Diethyl azodicarboxylate gives only the substitution product 203 (14%) (82T2783).
d. Cycloaddition Reactions. Reaction of the furan 201 with DMAD in hot toluene gave the adduct 205 (24%). This is presumed to have been formed via the initial [4 + 2]-cycloadduct 204, which hydrates on workup (Scheme 35). Reaction with methyl 3-nitroacrylate in ether gave a low yield (3%) of the cycloadduct 206 (82T2783).

A series of diastereoselective Diels–Alder reactions of 3-proline derivatives have been reported (94JOC3246, 95JOC16, 96TL2133). In a typical example, the derivative 207 reacts with methyl acrylate to give predominantly the isomer 208 (Eq. (35)).

\[
\begin{align*}
207 & \xrightarrow{\text{methyl acrylate}} 208
\end{align*}
\]

(35)

2. Reactions of Ring Substituents

a. Reactions of 3-Amino Substituents. Treatment of the amines with benzoyl chloride/pyridine gives the benzamides (37JA2525). Use of Boc₂O/DMAP gives the carbamates (98H1431). The ureas 209 (R = CO₂Me, CONHMe) have been prepared by reacting the corresponding primary amine with either an aryl isocyanate or phosgene followed by aniline (01BMCL9). Ethyl 2-acetamido-3-amino-5-furoate 187 has been diazotised and coupled with β-naphthol to give a red azo compound, m.p. 223.5–224.5 °C (11%) (34MI113).

The guanidines 210 can be prepared from the corresponding primary amines by treatment with the S-methyl isothiourea 211 and HgCl₂/Et₃N in DMF. The products
210 can be isolated but have been cyclised to the furo[3,2-\textit{d}]pyrimidines (see Section III.C.2.c) without characterisation (99JHC423).

2,5-Dimethyl-3-aminofuran gives a crystalline adduct (29\%) (C\textsubscript{13}H\textsubscript{15}O\textsubscript{2}N) upon treatment with benzaldehyde in aqueous ethanol. The structure of this additional product has not been established (37JA2525).

\textit{b. Reactions of Other Substituents (Formation of Furo[3,2-\textit{b}]Pyridines and Furo[3,2-\textit{d}]Pyrimidines).} The ester 212 (R = CO\textsubscript{2}Me) has been converted into the amide 212 (R = CONHMe) in 100\% yield using MeNH\textsubscript{2}/HCl/AlMe\textsubscript{3} (01BMCL9).

\[
\text{NH}_2
\]

Reaction of the 2-formyl derivative 213 with either acetone or pyruvic acid in EtOH/H\textsubscript{2}O/NaOH gives the corresponding furo[3,2-\textit{b}]pyridines 214 in 40–70\% yield (Eq\textsubscript{(36)})(75ACS(B)233). 2-Thioformyl-3-aminofurans react with diethyl acetylenedicarboxylate to give the corresponding furo[3,2-\textit{b}]pyridine diesters (97TL2171).

The 2-cyano derivative 215 (R\textsubscript{1} = H, R\textsubscript{2} = protected ribofuranosyl) has been cyclised using formamidine acetate to give the 4-amino-furo[3,2-\textit{d}]pyrimidine 216 (R\textsubscript{1} = H, R\textsubscript{2} = ribofuranosyl) (86TL815). The derivative 215 (R\textsubscript{1} = Ph, R\textsubscript{2} = H) has been cyclised using the chloro imidate of N,N-dimethylacetamide to give a 4-chlorofuro[3, 2-\textit{d}]pyrimidine (00JMC4288). The guanidines 210 have been cyclised to the furo[3, 2-\textit{d}]pyrimidin-4-ones 217 for evaluation as purine nucleoside phosphorylase inhibitors (99JHC423).
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2-AMINOFURANS AND 3-AMINOFURANS

Refs.


Five-Membered Heterocycles with Vicinal Te and O Heteroatoms

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I. Introduction

Of all the Te, O-containing heterocycles, the most currently studied are those containing these heteroatoms in positions 1, 4 of the six-membered rings of derivatives of 1,4-phenoxatellurine and 1-oxa-4-telluracyclohexane (85SR(4)63, 93AHC(58)48, 94MI1). The parent phenoxtellurine prepared 80 years ago (26JCS223) is the first representative of tellurium-containing heterocycles with two heteroatoms in a ring.

While no Te, O-heterocyclic compounds with heteroatoms in the positions 1, 3 have yet been reported, the syntheses and reactions of their analogues with vicinal tellurium and oxygen centers in five-membered rings received considerable attention during the last two decades. The study of the five-membered heterocycles with vicinal Te and O heteroatoms began with the preparation of 1,2-oxatellurol-1-ium chlorides performed by M.R. Detty et al. (83JA875). 1-Bromo-1-butyl-3H-benzoxatellurole-2,1, which was the first representative of benzoxatelluroles-2,1, was obtained in 1990 (90ZOB471), and three years later the first derivatives of 5H-oxatellurole-1,2 system
were synthesized (93ZOK1068). The later studies of the five-membered heterocycles with vicinal Te and O heteroatoms have been mainly focused on investigation into their reactions extending the synthetic potential of organotellurium chemistry. Thus, the reaction of 1-bromo-1-butylbenzoxatelluroles-2,1 with bromine giving rise to \( \sigma \)-alkylltellurobenzaldehydes and benzophenones represents a new method for the synthesis of \( \sigma \)-functionalized aromatic carbonyl compounds (90ZOB471, 94KGS266, 96T3365). Another example is a new approach to the enantiomerically pure telluronium salts based on the reaction of 1-chloro(bromo)hexahydro-3\( H \)-benzoxatelluroles-2,1 with organolithium or Grignard compounds (97TA3357, 98JOC5423, 99T2545).

Some data on the preparation and reactions of oxatelluroles and their benzoanalogues can be found in reviews (86SR(6)15, 93AHC(58)48, 01A125, 95RCR(64)491) and those concerned with oxatellurol-1-ium halides in review papers (93AHC(58)48, 96SR(18)295, 02UK1051). This review is intended to collect all the data available on the synthesis and reactions of various classes of five-membered heterocycles with vicinal Te and O heteroatoms and to provide a comprehensive treatment of the subject with literature coverage to 2005.

II. 1,2-Oxatellurol-1-ium Halides

A. SYNTHESIS

Under the action of \( \text{AlCl}_3 \) in a dichloromethane solution or upon refluxing, a deuterochloroform solution, \( \beta \)-aryltelluropropenoyl chlorides 1 rearrange to \( \beta \)-chlorotellurenylvinylaryl ketones 2 in 31–96% yields (83JA875, 83JA883, 86JOC1692, 87O1597, 88O2188) (Scheme 1). Owing to the strong intramolecular coordination \( \sigma \)-Te bond (01CR1247), the \( \sigma \)-\( \sigma \) distances in 2 are significantly shorter than the sum of the van der Waals radii of the respective atoms and are almost indistinguishable in length from the covalent two-center, two-electron O–Te

![Scheme 1](image-url)

\( R^1 = \text{Me, Et}; \)
\( R=\text{H, Ar}=\text{Ph}; \quad R=\text{Me}: \quad \text{Ar}=\text{Ph, 4-FC}_6\text{H}_4, 4-\text{MeOC}_6\text{H}_4, 4-\text{Me}_2\text{NC}_6\text{H}_4; \quad R=\text{Ph}: \quad \text{Ar}=\text{Ph, 2-MeC}_6\text{H}_5, 3-\text{MeC}_6\text{H}_5, 4-\text{MeC}_6\text{H}_5, 3-\text{MeOC}_6\text{H}_4, 4-\text{MeOC}_6\text{H}_4, 3-\text{FC}_6\text{H}_4, 4-\text{MeCOC}_6\text{H}_4, 1-\text{C}_{10}\text{H}_7; \)
\( \text{Ar}=\text{Ph}: \quad R=4-\text{MeOC}_6\text{H}_4, 2,5-(\text{MeO})_2\text{C}_6\text{H}_3, 4-\text{BuC}_6\text{H}_4 \)
bond (2.11 Å). The covalency factor \(^{88}\text{CR}^{899}\) of the intramolecular coordination Te⋯O bonds in 2 exceeds 90%, whereas the lengths of the C(3)C(4) and CO bonds indicate the double-bond character (Section VI). These findings are corroborated by the results of quantum chemical calculations \(^{95}\text{JC}^{1287}\) employing the theory of atoms in molecules and point to the existence of a chemical bond between the tellurium and oxygen centers. The molecular structure of the \(\beta\)-chlorotellurenylvinylcarbonyl compounds must, thus, be attributed to the heterocyclic system of 1,2-oxatellurol-1-ium chlorides 3, the five-membered ring of which contains a \(\pi\)-electron sextet and, therefore, acquires substantial aromatic character.

The mechanism of the catalyzed rearrangement of \(\beta\)-aryltelluropropenoyl chlorides 1, Scheme 2, involves the intermediacy of an acylium cation, which undergoes the cyclization reaction through the ipso addition to the carbon linked to the tellurium followed by breaking a C–Te bond in the spirocyclic \(\sigma\)-complex 4 and making a Te–O bond resulting in the formation of 3. As typical for electrophilic substitution reactions, the rates of the rearrangement are strongly influenced by the substituent \(R^1\) in the aryl ring attached to the tellurium. The larger electron donation of the substituent \(R^1\), the faster is the rearrangement and the higher are yields of 1,2-oxatellurolium chlorides 3. Thus, the rearrangement of \(\beta\)-phenyltellurocinnamyl chloride 1 (\(R = \text{Ph}\), \(Ar = 4\text{-MeOC}_6\text{H}_4\)) occurs smoothly at room temperature and gives the corresponding 1,2-oxatellurolium chloride in almost quantitative yield, whereas for the compound 1 (\(R = Ar = \text{Ph}\)) without an activating methoxy group in the aryl ring, the half-time of the rearrangement at the same conditions is as long as 30 h and in the case of the compound 1 (\(R = \text{Ph}\), \(Ar = 4\text{-MeCOC}_6\text{H}_4\)) with a strong electron-withdrawing group in the ring, the heterocycle 3 was obtained in only 1% yield even after refluxing a deuterochloroform solution of the reactants for 72 h \(^{83}\text{JA}^{875}\).

For the propenoyl chlorides 1 with \(p\)-substituted aryl groups attached to the tellurium, the reaction pathway involving ipso-acylation of the aryl group attached to the tellurium as depicted by Scheme 2 is the only course of the rearrangement. Introduction into the aryl groups of strong electron-releasing \(m\)-substituents results in activation of \(o\)-positions in the ring and in the appearance of an additional reaction channel leading to the formation of telluroflavones 5. As seen from the data listed in Table 1, the ratio of products, 3 and 5, changes drastically depending on the structure of the initial propenoyl chlorides 1 (Scheme 3).

The above method for the synthesis of heterocycles 3 has some shortcomings, such as its multistep character, applicability to only Te-aryl derivatives and unsuitability for the preparation of the compounds 3 containing a substituent in the position 4 of
the ring. Some of these shortcomings may be obviated by an extension of the method employing as the starting material \( \beta \)-methyldihalogenotellurovinylcarbonyl compounds \( 6 \) instead of \( 1 \). The reductive elimination of a molecule of methyl halide from \( 6 \) occurs smoothly under reflux of its acetic acid solution in the presence of catalytic amounts of the corresponding hydrogen halide. Although up to now the use of compounds \( 6 \) in this reaction was exemplified only by the preparation of 3,4-tetramethylene-1,2-oxatellurol-1-ium halides \( 7-9 \) (96ZOK1434, 97JOM(536–537)233), there is little doubt that the method featured in Scheme 4 may be applied to the

### Table 1. Yields of 1,2-oxatellurol-1-ium chlorides 3 and telluroflavones 5 as obtained by the cyclization reaction (Scheme 3) of \( \beta \)-aryltelluropropenoyl chlorides 1

<table>
<thead>
<tr>
<th>Compound 1</th>
<th>Yield of 3 (%)</th>
<th>Yield of 5 (%)</th>
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<td>Ph</td>
<td>Me</td>
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</tr>
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<td>MeO</td>
</tr>
<tr>
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<td>H</td>
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<td>3,4-(MeO)(_2)C(_6)H(_3)</td>
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<td>MeO</td>
</tr>
<tr>
<td>2,5-(MeO)(_2)C(_6)H(_3)</td>
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<td>H</td>
</tr>
<tr>
<td>2,5-(MeO)(_2)C(_6)H(_3)</td>
<td>MeO</td>
<td>MeO</td>
</tr>
</tbody>
</table>

![Scheme 3](image)

![Scheme 4](image)
synthesis of a wider range of 1,2-oxatellurolium halides with various substituents in the carbon triad.

-o-Aryltellurobenzoyl chlorides 10 are susceptible to the rearrangement similar to that of \( \beta \)-aryltelluropropenoyl chlorides to give \( o \)-chlorotellurenyl benzophenones 11 in high yields (75CS(A)116, 78T655, 85JOM(287)81). By analogy with 3, the structure of compounds 11 should more properly be regarded as benzoatellurol-1-iium-2,1 chlorides 12 (Scheme 5). It is worth noting that this rearrangement giving rise to the benzoderivatives of 1,2-oxatellurolium-1-iium chlorides 3 was described even earlier than the rearrangement shown in Scheme 1 that leads to the parent compounds.

A series of derivatives of benzoatellurol-1-iium-2,1 chlorides, 2-(\( \beta \)-halogenopropionyl)phenyltellurenyl halides 14, was obtained by a thermal rearrangement of 1,1-dihalogenotellurochromanones 13 (90ZOB2764) occurring under long-term refluxing of its chloroform, nitrobenzene or bromobenzene solutions. The mechanism of this rearrangement, specific to organotellurium compounds, includes a predissociation of 13 with the formation of a solvated ion pair and the subsequent nucleophilic addition of a halide ion at the \( \alpha \)-carbon center of the six-membered ring (Scheme 6).

In the case of dichlorotellurochromanone 13 (\( X = \text{Cl} \)), the final product of this reaction is 2-(acryloyl)phenyltellurenyl chloride 15 formed in 80% yield by the elimination of a molecule hydrogen chloride from the intermediate 2-(\( \beta \)-propionyl)phenyltellurenyl chloride 14 (\( X = \text{Cl} \)).

A general method for the synthesis of organyltellurenyl halides stabilized by an intramolecular coordination O\( \rightarrow \)Te bond is based on the cleavage of a C\( _{sp}^{3} \)–Te bond by hydrogen halides in an acetic acid solution. Scheme 7 featuring the scope of the method involves the reactions of \( o \)-alkyltellurobenzaldehydes (72BSF3559), \( o \)-alkyltelluroacetophenones (72BSF3559, 81JOM(208)35,
As for all the other above-considered rearrangements (Schemes 1–6), the stabilization of the \( \sigma \)-halogenotellurenylvinylcarbonyl products is due to the formation of a strong intramolecular coordination \( \sigma \)-Te bond serving as the driving force for the protodealkylation reactions shown in Scheme 7. The energies of these bonds (or, equivalently, the energies of the hypervalent three-centered, four-electron \( \sigma \)-Te–Hal bonds in the 10-Te-3 telluranes (see 80JA7753 for the nomenclature) were evaluated by \textit{ab initio} MP2/6-31G** and MP2/LanL2DZ calculations and found to fall in the range of 16–30 kcal/mol (01CR1247).

**B. REACTIONS**

\( \beta \)-Chloro- and \( \beta \)-bromotellurenylvinylaryl ketones, 2 and 16, readily enter into the oxidation–addition reaction with the corresponding dihalogen to give \( \beta \)-trihalogenotellurovinylaryl ketones 17 (X = Cl) and 18 (X = Br) in 39–92% yields (86JOC1692) (Scheme 8). In contrast with 2 and 16, \( \beta \)-iodotellurenylvinylaryl ketones do not react with iodine. \( \sigma \)-Chloro-(72BSF3559) and \( \sigma \)-bromotellurenylbenzaldehyde (96T3365) as well as \( \sigma \)-chloro- (78T655) and \( \sigma \)-bromotellurenyl benzophenone (81JOM(205)167) react with dihalogens in similar way to form \( \sigma \)-trihalogenotellurobenzaldehydes and benzophenones, respectively, in high yields.

Contrary to expectations, the reactions of tellurenyl chlorides 2 with bromine as well as tellurenyl bromides 16 with chlorine do not afford non-symmetric \( \beta \)-trihalogenotellurovinylcarbonyl compounds, but various mixtures of tellurium trichlorides 17 and tellurium tribromides 18 (86JOC1692). For example, tellurenyl chloride 2a reacts with bromine to give a 1:2 mixture of tellurium trichloride 17a and tellurium tribromide 18a. Under the same conditions treatment of tellurenyl bromide 16a with chlorine gives a mixture of the same trihalides, but in a 2:1 ratio (Scheme 9).

\[
\begin{align*}
2 (X=\text{Cl}) \quad & \quad 16 (X=\text{Br}) \\
& + X_2 \\
& \to \\
& X_3 \quad \text{Te} \quad \text{O} \\
& \quad \text{R} \quad \text{Ar} \\
2 (X=\text{Cl}) \quad & \quad 16 (X=\text{Br}) \\
17 (X=\text{Cl}) \quad & \quad 18 (X=\text{Br})
\end{align*}
\]

\( X=\text{Cl}: \text{R}=\text{H}, \text{Ar}=\text{Ph}; \text{R}=\text{Me}: \text{Ar}=\text{Ph}, 4-\text{FC}_6\text{H}_4, 4-\text{Me}_2\text{NC}_6\text{H}_4; \text{R}=\text{Ph}: \text{Ar}=\text{Ph}, 3-\text{FC}_6\text{H}_4, 4-\text{FC}_6\text{H}_4, 4-\text{MeOC}_6\text{H}_4, 2-\text{MeC}_6\text{H}_4; \text{Ar}=\text{Ph}: \text{R}=4-\text{MeOC}_6\text{H}_4, 4-\text{Bu}^1\text{C}_6\text{H}_4.

\( X=\text{Br}: \text{R}=\text{Me}, \text{Ar}=\text{Ph}; \text{R}=\text{Ar}=\text{Ph}

\text{Scheme 8}

\[
\begin{align*}
\text{Cl-Te(O)} \quad & \quad \text{Br}_2 \\
\to \\
\text{Cl}_2 \text{Te(O)} \quad & \quad \text{Br}_3 \text{Te(O)} \\
\text{Me} \quad & \quad \text{Me} \\
2a \quad & \quad 17a \quad & \quad 18a \quad & \quad 16a
\end{align*}
\]

\text{Scheme 9}
At the same time, oxidation of tellurenyl iodide 19 with bromine occurs with fission of the Te–I bond, probably, through formation of the mixed tellurium trihalide 20 (86JOC1692) (Scheme 10).

The cyclic structure of tellurenyl halides 2 stabilized by an intramolecular coordination $O\rightarrow$Te bond provides for their peculiar reactivity unusual for tellurenyl halides without such a bond. Whereas reduction of the latter gives diaryl ditellurides (99ZOK981), 2 under the same conditions are transformed into bis(2-arylvinylltellurides 21 (in more than 80% yield), ditellurides 22 being formed as a minor product (86JOC1692) (Scheme 11).

The partial ionic character of chlorine in $\beta$-chlorotellurenylvinylaryl ketones 2 reveals itself in the readiness of the exchange reactions (Scheme 12) providing convenient access to $\beta$-bromo-, iodo- and trifluoroacetotellurenylvinyl ketones obtained in almost quantitative yields. $\beta$-Fluorotellurenylvinyl ketone 24 was obtained on treatment of 2 with silver tetrafluoroborate in acetonitrile solution (83JA875).

Less studied are similar exchange reactions of halogens of benzoannulated 1,2-oxatellurol-1-ium halides ($o$-chlorotellurenylbenzaldehyde and $o$-chlorotellurenylbenzophenone) (72BSF3559) (Scheme 13).

Reactions of aromatic aldehydes and ketones containing a tellurenyl halide group in an $o$-position with organometallic compounds provide an approach to less accessible $o$-alkyltellurocarbonyl compounds (72BSF3559, 78T655, 81JOM(208)11) (Scheme 14).

$o$-Halogenotellurenylphenylcarbonyl compounds and their vinyl analogues are useful precursors to a number of tellurium-containing heterocycles. Thus, treatment of $o$-bromotellurenylacetonophenone with various basic reagents, such as potassium hydroxide in ethanol (76BSF294), potassium acetate (81JOM(208)35) or ammonia (78JHC865) affords telluroindoxyl 25 (Scheme 15).

By coupling $o$-bromotellurenylacetonophenone with benzaldehydes telluroaurones (arylidene-2-dihydro-2,3-oxo-3-benzo[b]tellurophenones) 26 were obtained in 80% and

![Scheme 10](image1)

![Scheme 11](image2)
higher yields \(73\text{CR}(C)(276)1035\). As shown in Scheme 16, the reaction proceeds through the intermediate formation of chalcones \(27\).

The condensation of \(\sigma\)-bromotellurenylacetophenone with dimethylformamide and dimethylacetamide was used for the synthesis of tellurochromones \(28\) \(79\text{PS}73, 81\text{JOM}(208)11\). The initially formed \(\beta\)-(\(\sigma\)-bromotellurenylaroyl)enamines \(29\) were reduced by hypophosphoric acid to \(28\) in about 45\% yields (Scheme 17). In a similar way, telluropyrans \(30–32\) with fused thiophene rings were prepared \(79\text{PS}73, 81\text{JOM}(208)11\).
It is worth noting that under the action of triethylamine enamine 29a undergo dehydrobromination to give 2\(H\)-dimethylaminomethylene-2-oxo-3-benzo\([b]tellurophene\) 33 (81JOM(208)11) (Scheme 18).

2-Bromotellurenylbenzaldehyde (or its oxime) serves as the precursors to another tellurium-containing heterocyclic system, namely benzoisotellurazole 34 (78JHC865). The reaction of the aldehyde with ammonia proceeds through the formation of imine 35 followed by its dehydrobromination. The cyclization reaction of oxime 36 is catalyzed by polyphosphorous acid (Scheme 19).
A similar cyclization of $\beta$-bromotellurenylvinyl aldehyde $8$ ($R_1$, $R_2 = (\text{CH}_2)_4$, $X = \text{Br}$) occurring under treatment of its benzene solution with ammonia affords isotellurazole $37\text{a}$ in 71% yields (97DAN(357)504) (Scheme 20).

A more convenient approach to isotellurazoles is based on the use of $\beta$-methyldibromotellurovinylaldehydes $6$ as the starting material. The reaction occurs smoothly upon bubbling ammonia through benzene solutions of $6$ and gives rise to isotellurazoles $37$ obtained in more than 70% yields (97DAN(357)504) (Scheme 21). Since $\beta$-halogenotellurenylvinyl aldehydes $7$–$9$ are prepared from the compounds $6$, this method allows one to avoid this preliminary step.

$\beta$-Halogenotellurenylvinyl aldehydes (1,2-oxatellurol-1-ium halides) $8$ and $9$ readily react with aromatic amines to give $N$-aryl-$\beta$-halogenotellurenylvinyl imines ($N$-aryl-1,2-azatellurol-1-ium halides) $38$ in high yields (96ZOK1434) (Scheme 22).
A more general method for the synthesis of N-arylimines 38 involves the use of tellurium dihalides 6 instead of compounds 8 and 9 (96ZOK1434, 97JOM(536–537)233, 97DAN(357)504, 00ZOK631, 05JOM(690)103). The elimination of methyl halide and the subsequent cyclization occur smoothly under refluxion of methanolic solutions of equimolar mixtures of the reactants (Scheme 22). The formulation of 38 as heterocycles with a three-center, four-electron hypervalent bond stems from the results of X-ray structural studies of the representative examples of the compounds 38b and 38c (04IAN66, 05JOM(690)103). The lengths of the Te–N bonds in these compounds (2.170 and 2.147 Å, respectively) are only 0.04–0.06 Å longer than the covalent Te–N bond in benzoisotellurazole 34 (78JHC745).

The reaction of β-chlorotellurenylvinylaryl ketones 2 with acyl chlorides in dichloromethane or acetonitrile promoted by nitrogen bases (triethylamine, pyridine, 2,6-dimethylpyridine) gives rise to 1,6-dioxa-6a-tellurapentalenes 39 in 11–85% yields (87O1597) (Scheme 24).

By the use of imidoyl chloride 40 instead of acyl chlorides in this reaction, 1-oxa-6-aza-6a-tellurapentalene 41 was obtained in low (11%) yield (87O1597) (Scheme 25).

III. 5H-Oxatelluroles-1,2 and 3H-benzoxatelluroles-2,1

Of all the possible oxa- and benzoxatelluroles, the currently known are only those containing tetracoordinate tellurium centers, 2-aryl-2-halogeno-5H-oxatelluroles-1,2
A. SYNTHESIS

For the synthesis of the heterocycles 42 and 43, two important groups of precursors, 3-aryltelluropropene-2-oles-3 44 and 2-butylltellurobenzylic alcohols 45, have been used. The route to 44 lies through the nucleophilic addition of aryltellurolate anions to a triple bond of propargyl alcohol (93ZOK1068, 94KGS266) or reduction of Z-β-aryltellurovinylaldehydes and ketones 46 (77ZOB1999, 94DAN(339)366, 96ZOK1061, 97JOM(536–537)233) with sodium borohydride (Scheme 26).

42 (93ZOK1068, 94KGS266) and 1-butyl-1-halogeno-3H-benzoatelluroles-2,1 43 (90ZOB471, 94KGS266, 96T3365).
The oxidation of alcohols 44 with tert-butyl hypochlorite proceeding through the intermediacy of σ-telluranes 47 leads to the formation of diastereomeric mixtures (in case R³ ≠ H) 1,2-oxatelluroles 42 in 44–82% yields (93ZOK1068, 94KGS266) (Scheme 27).

2-Butyltellurobenzylic alcohols 45 are prepared by the reduction of 2-butyltellurobenzaldehyde 48 with sodium borohydride, by coupling 48 with Grignard reagents (94KGS266, 96T3365) or, as is the case of compound 45a, by treatment of 2-bromo(iodo)benzyl alcohol with butyl lithium followed by a reaction with powdered tellurium and hydrolysis (90ZOB471, 94KGS266) (Scheme 28).

Treatment of 2-butyltellurobenzylic alcohols 45 with tert-butylhypochloride gives 1-butyl-1-chlorobenzoxatelluroles-2,1 43 (X = Cl) (94KGS266). These compounds and their 1-bromo analogues 43 (X = Br) can also be obtained by dehydrohalogenation of Te-dihalogeno derivatives 49 of alcohols 45, which, like other alkylaryl tellurides (95SR(17)1), readily add a molecule of dihalogen to a Te(II) center (90ZOB471, 94KGS266, 96T3365). The conditions of the dehydrohalogenation of 49 are determined by the identity of the halogens attached to tellurium. Whereas 2-butyldifluorotellurobenzylic alcohol 49d spontaneously converts into 1-butyl-1-fluorobenzoxatellurole-2,1 when being prepared by a treatment of its dibromo analogue 49b with AgF in acetone (94KGS266), similar transformations of other benzylic alcohols 49 (X = Cl, Br, I) occur only under the action of an equimolar amount of a strong base or by passing a chloroform solution of the alcohol through a column of aluminum oxide (X = Cl) (Scheme 29). The yields of 1-butyl-1-halogenobenzoxatelluroles-2,1 43 (X = Hal) vary in the range 54–86% (90ZOB471, 94KGS266) (Scheme 29).
Compounds 43 are obtained as mixtures of two diastereomers, the ratio of which depends on the origin of the halogen and increases on passing from lighter to heavier halogens. Thus, in the case of benzoxatelluroles 43h–j (R = 4-MeC₆H₄) the ratio of the diastereomers was 1:2, 1:2.5 and 1:3.5 for X = Cl, Br and I, correspondingly (94KGS266).

Recently, the synthesis of 2-bromo-2-methyl-3,4-tetramethylene-5-aroylmethyl oxatelluroles-1,2 50 based on coupling phenacyl bromides with 2-methyltellurocyclohexen-1-al-1 (97JOM(536–537)233) has been reported (04MI1). In contrast with the usual course of reactions of dialkyl or alkylaryl tellurides, see e.g. (02JOC3096), this reaction affords in 45–60% yields diastereomeric mixtures of compounds 50 (Scheme 30). The ratio of the diastereomers strongly depends on the substituent in the aryl ring and extends from 31:69 (50b) and 35:65 (50a) to 13:87 (50c). The double set of the diastereomers 50 is characterized by two sets of ¹³C, ¹²⁵Te and ¹H nuclear magnetic resonance (NMR) resonances. In the case of oxatellurole-1,2 50a, signals of the carbonyl carbons appear at 197.2 and 197.7 ppm and...
the $^{125}\text{Te}$ NMR spectrum contains two signals at 1177.8 and 1179.5 ppm. Four quartet signals of the methylene protons are present in the $^1\text{H}$ NMR spectrum. The peculiar behavior of 2-methyltellurocyclohexen-1-al-1 in this reaction was explained by the presence of a strong intramolecular coordination O→Te bond, the X-ray determined (04IAN66) length of which (2.692 Å) is 0.9 Å shorter than the van der Waals contact (60MI1).

The methodology used for the synthesis of benzoxatelluroles-2,1 43a-c, e-m (Scheme 29) has been successfully applied to the preparation of their oxo derivatives. The oxidation of 2-phenyltellurobenzoic acid by butylhypochlorite or dehydrohalogenation of 2-aryldichlorotellurobenzoic acids under the action of triethylamine affords 1-aryl-1-chlorobenzoxatellurol-2,1-ones-3 51 in 75–92% yields (94KGS266) (Scheme 31).

B. REACTIONS

Oxatelluroles-1,2 42 and benzoxatelluroles-2,1 43 readily exchange the halogen atoms attached to the tellurium center for other anionic groups. Under treatment of 2-aryl-2-chloroxatelluroles-1,2 42a,c with potassium iodide in an acetone solution, the corresponding 2-iodoxatelluroles were obtained in 82–84% yields and bromoxabenzotellurole 43b reacts with silver acetate to give 1-acetoxy-1-butylbenzoxatellurol-2,1-ones-3 51 in 62% yield. At the same time, the reaction of 43b with an ethanolic solution of sodium hydroxide leads not to the expected 1-butyl-1-hydroxybenzoxatellurol-2,1 52, but to the product of its dehydration bis-(1-butylbenzoxatellurol-2,1-yl-1) oxide 53 in 32% yield (94KGS266) (Scheme 32).
The reaction between equimolar amounts of bromobenzoxatelluroles 43b,f,i and bromine in boiling chloroform or tetrachloromethane results in the cleavage of the Te–O bond and depending on the origin of substituent R in position 3 of the ring affords in 73–98% yields of either 2-butyldibromotellurobenzaldehyde 54a (R = H) (90ZOB471, 94KGS266, 96T3365) or 2-butyldibromotellurobenzophenones 54b,c (R = Ph, 4-MeC₆H₄) (94KGS266, 96T3365). The suggested mechanism involves the hexacoordinated tellurium intermediate 55 and its rearrangement to the hypobromite 55a followed by the elimination of a molecule of hydrogen bromide (Scheme 33). The reduction of 54 to 2-butyltellurophenylcarbonyl compounds 56 occurs with almost quantitative yields.

With the use of two moles of bromine in this reaction and performing it in acetic acid 2-tribromobenzaldehyde 57 was obtained in 60% yield (94KGS266, 96T3365) (Scheme 34). That the reaction proceeded through the intermediate formation of tellurenyl bromide 58 was confirmed by the preparation of 57 by bromination of 58 in acetic acid.

Considering the fact that the precursors for bromobenzoxatelluroles unsubstituted in the position 3 are 2-butyltellurobenzaldehydes 48 and 2-butyltellurobenzyl alcohols 45, respectively, the reactions shown in Schemes 33 and 34 may be regarded as a new methodology for the conversion of o-alkyltellurobenzaldehydes into o-alkyltellurobenzophenones and o-alkyltellurobenzylic alcohols into o-alkyltellurobenzaldehydes, which is specific to organotellurium chemistry. It must be noted that the attempts at direct oxidation of alcohols 45 to the aldehydes failed (71BSB669). In the case of 1-bromo-1-butyl-3-methylbenzoxatellurole 43l, the initially formed ketone 59 enters into further bromination reactions at the methyl group to give the bromo- and dibromomethyl derivatives 59a and 59b (Scheme 35), which can be separated using a partial crystallization technique (94KGS266, 96T3365).
IV. 1,1′-Spirobis-[3H-benzoxatelluroles-2,1]

A. SYNTHESIS

The first representative of 1,1′-spirobis-[3H-benzoxatelluroles-2,1], 60, was synthesized in almost quantitative yield by dehydrochlorination of bis-(hydroxymethylphenyl)tellurium dichloride 61 (81KGS122, 94KGS266) (Scheme 36).

The configuration of the tetracoordinated tellurium atom in 60 corresponds to a trigonal bipyramid with a lone electron pair as the phantom ligand. The compounds containing such centers are prone to fast and reversible polytopal intramolecular rearrangements leading to permutations of the axial and equatorial ligands. In the case of the spirotellurane 60, a rearrangement of this type occurs at room temperature in deuterochloroform or nitrobenzene with frequencies higher than $10^4$/s resulting in the averaging of the diastereotopic protons of methylene groups appearing in the $^1$H NMR spectrum as four-proton singlet signals at 5.28 and 5.34 ppm, respectively. The polytopal rearrangement of the spirotellurane 60 is much more rapid than the similar rearrangement of its sulfurane analogue (77JOC4006). This trend is in accord with the quantum chemical analyses of the mechanisms of polytopal rearrangements of chalcogenuranes (75ZOK1993, 77ZOB2011). An approach to derivatives of the parent spirotellurane 60 (spirotelluranes 62) is based on the reaction of tellurolates 63 with tellurium tetra-chloride, which occurs in moderate yields (20–61%) in tetrahydrofuran or ether (84JA7529) (Scheme 37).
B. REACTIONS

Reactions of spirotelluranes 60, 62 have been little studied. Under the action of ozone spirotellurane 62a readily oxidizes into the dimer of the tellurane oxide 64 in 64% yield (84JA7529). Interestingly, another spirotellurane 62b is inert in this reaction. The oxidation of 62a,c to trans 12-Te-6 pertelluranes, 1,1-difluoro-1,1-dihydro-3,3,3′,3′-tetramethyl-1,1′-spiro[3H-benzoxatellurole-2,1] 65a (30% yield) and 6,6′-bis-(1,1-dimethylpropyl)-1,1-difluoro-3,3,3′,3′-tetra(trifluoromethyl)-1,1′-spiro[3H-benzoxatellurole-2,1] 65b (75% yield) occurs under the action of bromine trifluoride in a solution of CF₂ClCFCl₂ (Scheme 38).

\[ R = H, R' = Me, CF₃; R = Bu, R' = CF₃; R = H, R' = Me (a), CF₃ (b) \]

Scheme 37

\[ R = H, R' = Me, CF₃; R = Bu, R' = CF₃; R = H, R' = Me (a), CF₃ (b) \]

Scheme 38
C. 1,1'-SPIROBIS-[3H-BENZOATELLUROL-2,1]-3,3'-DIONE

The only currently known representative of this group of spirotelluranes is 66 prepared in low (15%) yield (95HC481) from bis-(2-carboxyphenyl) telluride 67. A likely way to 67 includes, most probably, dehydration of the intermediate tellurium oxide 68. The spiran 66 can be hydrolyzed by aqueous sodium hydroxide to salt of the acid 68, which cyclizes again on acidification (Scheme 39).

V. OXATELLUROLANES-1,2 AND HEXAHYDRO-3H-BENZOATELLUROLES-2,1

A. SYNTHESIS

A series of oxatellurolanes-1,2 69 with various halogen atoms attached to the tetracoordinated tellurium center was prepared in 53–86% yields by the reaction of dehalogenation of α-halogenocarbonyl compounds (α-chloro-, bromo- and iodo-acetophenones, diethylbromo- and diethyl dibromomalonates) by 3-organyltelluropropanoles-1 70 (97H(45)575) (Scheme 40).

The suggested mechanism for the formation of heterocycles 69 involves addition of dicoordinated tellurium center to a halogen of the α-halogenocarbonyl compound followed by deprotonation of the adduct and intramolecular cyclization to 69 (Scheme 41).

The yields of the tellurolanes 69 are in the range 53–86%, whereas those of carbonyl compounds 71 are almost quantitative (90–98%).

Hexahydro-3H-benzoateelluroles-2,1 72 and 73 containing tetracoordinated tellurium centers have been obtained using the methodology applied to the syntheses of 5H-oxatellurolanes-1,2 and 3H-benzoateelluroles-2,1. The oxidation of (S)-10-organyltelluro-2-exoborneols 74 with tert-butyl hypochlorite affords 72 in 86–97% yields.

\[
\text{Scheme 39}
\]

\[
\text{Scheme 40}
\]

\[R = \text{Me}; \ X = \text{Cl, Br, I}; \ X = \text{Br}; \ R = \text{Et, Ph}\]
The bromo derivatives 73 are obtained in about 50% yields by treatment of alcohols 74 with N-bromosuccinimide (NBSI) (96TA2797, 99T2545) (Scheme 42).

Owing to the chirality of the 2-exohydroxyborneol ligand in the telluride 74, the reactions shown in Scheme 42 may lead to the formation of mixtures of diastereomers of telluranes 72 and 75 and 73, 75. However, these transformations are fully stereospecific and give rise to a single diastereomer. As stems from an X-ray study of a fluorine derivative 78 (R = Ph) (Section V.B) is obtained by the halogen exchange reaction with 72 (R = Ph) (Scheme 44), the preferred diastereomers of these compounds have the (R) stereochemical configuration at the tetracoordinated tellurium centers possessing the geometry of a distorted trigonal bipyramid (the angle of F–Te–F in 78 is 166.8°).

The derivatives of the heterocycles 69, 72 and 73 are represented by only 2-aryl-2-halogenoxatellurrolan-1,2-ones 76 (X = Cl, Br), which were prepared in 90–94% yields by the oxidation of β-aryltelluropropionic acids (88ZOB717) with tert-butylnhypochlorite or via dehydrobromination of β-aryldibromotelluropropionic acids (93KGS1700) (Scheme 43).

### B. REACTIONS

The chloro-containing hexahydro-3H-benzoatelluroles-2,1 72 are susceptible to facile anionic exchange reactions occurring under treatment of their acetonitrile solutions with NaBr (96TA2797, 98JOC5423, 99T2545), NaI or AgF (96TA2797, 99T2545). The yields of the products (Scheme 44) are almost quantitative.
The interaction of 2-chloro(bromo)hexahydro-3\textit{H}-benzoxatelluroles-2,1 with organolithium compounds or Grignard reagents afford enantiomerically pure telluronium salts of type 79 and 80 in 67–97% yields (96TA2797, 98JOC5423, 99T2545). Thus, by treating 72 (R = Et) with methyllithium only the diastereomer of the telluronium salt 79 is obtained in 79% yield. Compound 73 (R = Me) reacts with ethylmagnesium bromide to give ethyl(2-exo-hydroxy-10-bornyl)methyltelluronium chloride 80 (Scheme 45).

The enantiomerically pure telluronium salts 81 can also be obtained in moderate to high (41–73%) yields by the reaction between tellurides 74 and benzyl bromide or bromoethylacetate (00TA3323) (Scheme 46). The reaction is highly diastereoselective. Thus, the ratio of diastereomers of the salts 81 formed under treatment of telluride 74 (R = Me) with benzyl bromide is 6:1. According to the data of an X-ray study, the main product of this reaction possesses the (\textit{R}) configuration at the pyramidal tricoordinated tellurium.
VI. Molecular and Crystal Structures

The heterocyclic compounds with vicinal tellurium and oxygen atoms whose molecular and crystal structures have been determined by X-ray analysis are listed in Table 2. It contains data on important structural parameters featuring the stereochemical configuration at the tellurium centers.

The T-shaped configuration of the tricoordinated tellurium atoms in compounds 2, 14, and 58 with the almost linear Hal–Te–O fragments clarifies the hypervalent (10-Te-3) type of bonding realized at these centers. An important feature of the intramolecular coordination O→Te–X bonds is the extremely strong dependence of their lengths and strengths on the electronegativity of X (96SR(18)295, 99RKZ10, 98CJC766, 01CR1247). By varying the electronegativity in a series of compounds
with similar molecular frameworks, it becomes possible to cover a wide range of intramolecular distances, ranging from those close to normal van der Waals contacts to those indistinguishable from covalent Te–O bonds, as is the case of compounds 2, 14 and 58 containing strongly electronegative atoms attached to tellurium. The principal factor that accounts for this tendency is the donation of an electron pair from the nonbonding orbital of the oxygen to the lowest \( s^* \) orbital of the Te–X bond. This \( n_O \rightarrow \sigma^*_{Te-X} \) orbital interaction (negative hyperconjugation) in the compounds of 7–9 and 11 type leads to the expansion of the valence shell of the tellurium atoms and results in the formation of the hypervalent Hal–Te–O triad, where the Te–Hal bonds are 0.3–0.4 Å lengthened compared with the ordinary two-center,

<table>
<thead>
<tr>
<th>Compound</th>
<th>Te–C</th>
<th>Te–O</th>
<th>Te–Hal</th>
<th>O–Te–Hal(O)</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ph[TeCl(C6H4OMe-4)]O+</td>
<td>2.08</td>
<td>2.190</td>
<td>2.476</td>
<td>170.1°</td>
<td>83JA875</td>
</tr>
<tr>
<td>Ph[Te]=O</td>
<td>2.081</td>
<td>2.310</td>
<td>2.618</td>
<td>168.6°</td>
<td>74AX(B)139</td>
</tr>
<tr>
<td>CH2CH2[TeBr(CH2CH2Br)]O+</td>
<td>2.111</td>
<td>2.368</td>
<td>2.784</td>
<td>169.5°</td>
<td>90ZOB2764</td>
</tr>
<tr>
<td>CH2CH2[TeBr(CH2CH2I)]O+</td>
<td>2.122, 2.136</td>
<td>2.005</td>
<td>2.796</td>
<td>172.1°</td>
<td>94KGS417</td>
</tr>
<tr>
<td>CH2CH2[TeBu]O+</td>
<td>2.103, 2.106</td>
<td>2.077, 2.082</td>
<td>—</td>
<td>160.5°</td>
<td>84JA7529</td>
</tr>
<tr>
<td>CH2CH2[TeO(CF3)2]O+</td>
<td>2.100</td>
<td>2.106, 2.137</td>
<td>—</td>
<td>161.3°</td>
<td>95HC481</td>
</tr>
</tbody>
</table>
two-electron bonds of this type. It is worth noting that in contrast with diorganyl-
tellurium dihalides TeR₂ (91UK1229), no shortened intermolecular Te⋯Hal con-
tacts were observed in the crystal structures of compounds 2, 14 and 58. The
aromatic delocalization in the 6π-electron heterocycles of these compounds
(00MC171) reveals itself in the notable shortening the formally double C = C and
C = O bonds and the lengthening of the C–C bond.

The stereochemical configuration of the tetracoordinated tellurium centers in
benzoxatellurole 43b and spirotelluranes 62b and 66 do not differ from that in
diorganyl tellurium dihalides R₂TeHal₂ (02SR(23)125) or organyltellurium trihalides
RTeHal₃ (00UK940) and may be described as a slightly distorted trigonal bipy-
ramid. In these molecules, the electronegative oxygen or bromine atoms are found in
the apical positions whereas carbon atoms and an electron lone pair (phantom
ligand) take the equatorial ones. The triad O–Te–Br in benzoxatellurole 43b is more
aligned (the corresponding angle is 172.1°) than the O–S–Cl in its close structural
analogue 1,1-dichloro-3,3-bis-(trifluoromethyl)-5-methyl-3,4-benzothiazol-2,1 (the
O–S–Cl angle is 167.6°) (79JA3595). Somewhat larger are the deviations from lin-
earity of the O–Te–O fragments in the spirotelluranes 62b and 66 (see Table 2). The
decrease in the values of the O–chalcogen–O angle observed for spirossoxygenuran-
anes of type 66 (177.7° for spirosulfurane, 172.4° for spiroselenurane and 161.3° for
spirotellurane (95HC481)) is primarily caused by steric factors due to the inclusion of
a long O–chalcogen bond into the five-membered rings. The Te–Br bond in ben-
zoxtellurole 43b (2.796 Å) is 0.1–0.3 Å longer than those in the acyclic σ-telluranes
ArTeBr₃ and Ar₂TeBr₂ (91UK1229). In the crystal, molecules of 43b form planar
dimers by virtue of the secondary intermolecular Te⋯Br bonds, the lengths of which
(3.592 Å) are 0.7 Å shorter than the sum of the van der Waals radii of tellurium and
bromine. Taking into account of these secondary bonds, the coordination polyhe-
dron of tellurium in 43b may be considered as a distorted octahedron.

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74AX(B)139 P. M. Bauwir, G. Llabres, O. Dideberg, and L. Dupont, Acta Cryst-


I. Introduction


Thienopyrimidines occupy a special position among these compounds. Along with some other pyrimidine systems containing an annulated five-membered heteroaromatic ring, thienopyrimidines are structural analogs of biogenic purines and can be considered as potential nucleic acid antimetabolites. Earlier, various aspects of the chemistry and biology of isomeric thienopyrimidines have been reviewed (1954MI1, 1966AHC235, 1970MI1, 1976KGS1299, 1984MI1, 1984P4, 1985MI1, 1985MI2, 1985RCR450, 1986SR97, 1987MI1, 1989MI1, 1990P545, 1992SR1, 1995MI1, 1996AHC193, 2004IZV487).

The present review analyzes results of studies on the synthesis, chemical transformations, and biological activities of thienopyrimidines published primarily over the last 10–15 years.
II. Synthesis of Thienopyrimidines

Synthetic approaches to the construction of thienopyrimidines are sufficiently well developed. Three possible types of annulation of thiophene to the pyrimidine ring and, correspondingly, three isomeric thienopyrimidines are known: thieno[2,3-d]pyrimidine (1), thieno[3,2-d]pyrimidine (2), and thieno[3,4-c]-pyrimidine (3). The structures and the conventional numbering of these heterocyclic systems are shown below.

The known approaches to the synthesis of thienopyrimidines can be divided into two main groups: construction of the pyrimidine ring by intramolecular cyclization of thiophene derivatives and thiophene ring closure in pyrimidine derivatives.

A. SYNTHESIS OF THIENOPYRIMIDINES BY PYRIMIDINE RING CLOSURE

Appropriately substituted aminothiophenes, accessible by various methods (1976KGS1299, 1984MI1, 1984P4, 1986SR97), serve as the main starting compounds for the preparation of thienopyrimidines with this approach. Syntheses involving pyrimidine ring closure starting from both 2- and 3-aminothiophenes proceed under similar conditions and in virtually the same reaction sequences, due to which all three types of thienopyrimidines become accessible. Hence, it is reasonable to classify the reactions leading to these compounds according to the type of substitution in the pyrimidine rings formed.

One of the most popular approaches to the synthesis of thienopyrimidinediones 4 is based on the pyrimidine ring closure in thienylureas 5.

Hereinafter, A is the thiophene ring bearing substituents at positions 2 and 3 or 3 and 4; thienopyrimidine structure 4 is thiophene analogously annulated to the pyrimidine ring; the ester group is most widely used as the COX group.

The starting thienylureas are synthesized according to known procedures based on the reactions of aminothiophenes with isocyanates (1969CB3698, 1987USP4670560, 1988JMC1786, 1989GEP3712782, 1995EUP640606), KOCN–HC1 (1972BEP769843), C1SO2NCO (1985S190) and some other reagents. The substituent R in
thienylureas can be replaced with other hydrocarbon groups using reactions with amines (1988JMC1786).


Thienopyrimidine diones containing the hydrogenated thiophene ring were synthesized starting from the corresponding tetrahydrothienylureas (1967BCJ2636, 1989GEP3712782, 1989JAP63126884, 1989USP4835157). Thienopyrimidine diones 4 unsubstituted at the nitrogen atom (R = H) were prepared starting from aminothiophenes 6, whose successive treatment with chloroformates (or phosgene) and primary amines (1989INP8902432, 1989JAP63126884, 1990JAP0253788, 1990JHC1761, 1993P95) afforded the target products 4.

\[
\begin{array}{c}
\text{A} \quad \overset{\text{ClCO}_2R^1}{\xrightarrow{\text{RNH}_2}} \quad \text{A} \quad \overset{\text{COX}}{\xrightarrow{\text{NHCONHR}}} \quad \text{A} \quad \overset{\text{NH}_2}{\xrightarrow{\text{COX}}} \quad \text{A}
\end{array}
\]

Although intermediate thienylureas were not isolated, their transient formation is quite probable (1990PS181, 1991SL57).

Substituted thienopyrimidine dione 7 was prepared in 91% yield by heating \(N,N'-\)diethyl-\(N\)-methoxycarbonyl-\(N'\)-(3-methylamino-5-phenyl-2-thenoyl)thiourea (8) in methanol (2000JOC3690).

\[
\begin{array}{c}
\text{S} \quad \text{N} \quad \text{Me} \quad \text{O} \quad \text{Et} \quad \text{O} \quad \text{Ph} \quad \text{N} \quad \text{Me} \quad \text{O} \quad \text{S} \quad \text{N} \quad \text{Et} \quad \text{O} \quad \text{Ph} \quad \text{OMe}
\end{array}
\]

Salts of thieno[2,3-\(d\)]pyrimidine-2,4-dione with alkali metals were synthesized and their IR spectra were studied (2000MM11).

it has been demonstrated that for \( R = \text{Acyl} \), the latter reactions resulted in hydrolysis to give unsubstituted thioxopyrimidinone 10 (\( R = \text{H} \)).

\[
\begin{align*}
\text{Reagents: } i. & \text{ RNCS or 1) CSCl}_2, \ 2) \text{RNH}_2; \text{ KOH-EtOH or HCl-EtOH.}
\end{align*}
\]

As in the case of the corresponding ureas, thioureas 9 need not be isolated in the pure form. For example, treatment of esters 6 with isothiocyanates in the presence of bases directly afforded thioxopyrimidinones 10 (1966AHC235, 1981JHC1227, 1989JIC48) the reactions of compounds bearing a \(-\text{CONH}_2\) group proceeded in the absence of bases as well (1984JCSP(1)2005). The reactions with \( N \)-arylthioureas are accompanied by elimination of aniline to form unsubstituted thioxopyrimidinone 10 (\( R = \text{H} \)) (1991SL57), which was also prepared by treating aminothiophene 6 with potassium thiocyanate in acetic acid or with formamide and elemental sulfur (1990DOK32).

Thiourea 9 can be prepared by the reactions of the corresponding isothiocyanates with an excess of primary amines (1982EUP43054, 1995JHC69) or hydrazine (1993H1315, 1994P64) as well as by the reactions of esters 6 with \( N \)-arylthiocarbamates (1987H1303).

Fused 2-amino-3-ethoxycarbonylthiophenes 11 were successfully used in analogous reactions for the synthesis of tricyclic thioxothienopyrimidinones. For example, the reactions of compounds 11 with isothiocyanates gave rise to thioureido derivatives 12, which underwent intramolecular cyclization under the action of ethanolic KOH to form 2-thioxodihydropyrano(thiopyran)-thienopyrimidine-4-ones 13 in yields higher than 95% (1998KGS1388, 2001KFZ6, 2001KFZ8, 2001KFZ9, 2001KGS1116) (see also Ref. 2001CHC1025).

Condensation of diethyl 2-amino-4,5,6,7-tetrahydrothieno[2,3-\( c \)]pyridine-3,6-dicarboxylate (14) with SCN\( \text{CO}_2\text{Et} \) followed by treatment of intermediate 15 with
NaOEt afforded ethyl 4-oxo-2-thioxo-1,2,3,4,5,6,7,8-octahydropyrido[4’,3’:4,5]thieno[2,3-\textit{d}]pyrimidine-7-carboxylate (16) (1999JHC1119).

2-Thioxopyrido[3’,2’:4,5]thieno[3,2-\textit{d}]pyrimidin-4(3\textit{H})-ones 17 isomeric to compound 16 were prepared by cyclocondensation of 2-ethoxycarbonyl-4-phenyl-6-substituted thieno[2,3-\textit{b}]pyridines 18 with isothiocyanates in the presence (or in the absence) of a phase-transfer catalyst (1997JHC937).

A one-pot procedure was developed (2001JHC419) for the synthesis of (2-alkylthio-4-oxothieno[3,2-\textit{d}]pyrimidine-3-yl)acetonitriles (19) based on the treatment of methyl 3-aminothiophene-2-carboxylate (20) successively with CSCI, NH\textsubscript{2}CH\textsubscript{2}CN, and alkyl halides.

The reactions of aminocarbonyl derivatives of thiophene (21) with potassium thiocyanate afforded (4-oxo-3,4-dihydrothieno[2,3-\textit{d}]pyrimidin-2-ylthio)acetic acid derivatives (22) in yields up to 51%. Analogously, the isomeric aminocarbonyl derivative 23 gave ethyl (7-cyano-6-methylthio-4-oxo-3,4-dihydrothieno[3,2-\textit{d}]pyrimidin-2-ylthio)acetate (24) in 85% yield (2000H2363).
Thioxothienopyrimidinones 25 were prepared (1993SL71) by recyclization of thiazines in an acidic medium.


Selenium analogs of compounds 10, viz., selenoxothienopyrimidinones 26, were prepared by intramolecular cyclization of selenoureas 27 in the presence of ethanolic KOH (1977KGS753).

A procedure was developed (1988JPR585, 1991JPR229, 1993JCR(S)302, 1993M11) for the synthesis of thienopyrimidinedithiones 28 involving thermal recyclization of thiazines 29, which, in turn, are prepared by the reactions of substituted 2-amino-3-cyanothiophenes 30 with carbon disulfide in the presence of bases.
The reaction of carbon disulfide with amino derivatives of thienopyridine 31 was used for the synthesis of pyridothienopyrimidinedithione 32 (1998M523).

3-Cyano-2-thioureidothiophenes 33, which are prepared by the reactions of aminoocyanothiophenes 30 with isothiocyanates or by reactions successively with CSCl₂ and amines, undergo intramolecular cyclization in the presence of bases at room temperature to give 3-thioxothieno[2,3-d]pyrimidine-1-imines 34 (1985CB4473, 1989MI1, 1990CP229). The latter reaction requires thorough control over the temperature to prevent the possible rearrangement (such as the Dimroth rearrangement) into aminothienopyrimidinethiones. Attempts to isolate the corresponding cyclization products of cyanourea failed due, apparently, to the rapid rearrangement into aminothienopyrimidinones (1985CB4473).

Aminothiophenes 35 react with 5,5'-dimethyl N-cyanoiminocarbodithioate to give isothioureas 36, which cyclize in the presence of amine (if X = OR) or by heating with a base (if X = NR₂) to yield compounds 37 (1988GEP249023, 1993P347).
The dicyanomethylene substituent as well as its ester analog can cause a substantial shift of the tautomeric equilibrium in the pyrimidine moiety. Dicyanomethylene derivatives and their ester analogs \(38\) were prepared (1988GEP249020, 1988GEP249021, 1988GEP249022) by reactions of compounds \(35\) successively with (di)cyanoketene dithioacetal followed by cyclization of intermediate \(39\) in the presence of bases.

Thienopyrimidinone \(40\) was prepared (1991HCA579) by the reaction of 3-amino-2-ethoxycarbonylthiophene with ethyl dicyanoacetate (see also Ref. 2002RCB854).

Aminothienopyrimidinones \(41\) were synthesized by cyclization of vic-cyanothiénylureas \(42\) generated in situ by the reaction of 2-amino-3-cyanothiophenes \(30\) with isothiocyanates (1985CB4473) or urea (1990MI1). Compound \(41\) with \(R^3 = H\) exists predominantly as the tautomeric 4-NH form. The reactions with isothiocyanates are accompanied by dimerization as a side process (1991JPR229).
l-Aminothieno[2,3-\(d\)]pyrimidine-3(4\(H\))-thiones (43) were prepared by cyclization of vic-cyano(thioureo)thiophenes 33 followed by the Dimroth rearrangement of intermediates 34 under the action of bases (1989AP227, 1989MI2, 1990IJC1070, 1991GEP287503, 1992PS93) or by heating 2-amino-3-cyanothiophenes 30 with thiourea (1990MI1).

Thioureas 44 undergo cyclization to give annulated thienopyrimidines 45 (1987JHC1125).

Angularly annulated thienopyrimidinethiones 46 were synthesized (1987JHC1125) from 2-amino-3-thienyl-1,2,4-triazoles 47 with isothiocyanates or carbon disulfide.
2-Aminothienopyrimidine-4-imines 48 were prepared (1993JHC435) by the reaction of aminothiophenes 30 with cyanamides in an acidic medium.

Treatment of 2-acylamino-3-cyanothiophenes 49 with amines afforded thienopyrimidineimines 50, some of which are rather unstable and rearrange into aminothienopyrimidines 51 under the reaction conditions (1981CS245, 1988CS195, 1993S1129).

More stable compounds 52 in which the imino group is involved in the fused triazole ring were prepared (1988JHC615, 1990MI1) according to the following
A general procedure for the synthesis of aminothienopyrimidinones (thiones, selenones) 53 is based on the reaction of α-thienylchloroformamidines 54 with salts KXCN (X = O, S, or Se) (1980LA699).

In recent years, many more studies were devoted to the synthesis of thienopyrimidinones and their derivatives. There are two types of such structures depending on the position of the C = O group, viz., the A structure containing the amide group and the B structure, a cyclic urea.

As in earlier studies, three main procedures were used for the synthesis of thienopyrimidinones. One procedure involves intramolecular cyclization of vic-ethoxycarbonylthienylamidines 55, which are formed in the reaction of 2-amino-3-ethoxycarbonylthiophenes of type 6 with amides, to give thienopyrimidinones 56, cyclization being so rapid that it is impossible to isolate amidines 55 (1981JHC1277, 1984JCS(P1)100, 1985IZV1858, 1986KFZ39, 1988LA633, 1990GEP272089, 1990MI1, 1991KFZ38, 1992IJC492, 1993P192). Secondary amides, including cyclic amides, react analogously (1991KFZ38).


$\text{vic}$-Amino(carbamoyl)thiophenes 58 react with aromatic and heteroaromatic aldehydes to give hydrogenated thienopyrimidinones (1985JHC825, 1992JHC1963, 1992MI1, 1996PS271) that are oxidized to the corresponding thienopyrimidinones on heating in an acidic medium (1992MI1).

Thienopyrimidinones 59 were prepared (1986KFZ1312, 1988JMC(E)453, 1988TL3537, 1992GEP295381, 1992P577, 1993P26) by the reactions of thiophenes
containing the ethoxycarbonyl and amide groups with amines. It was postulated that these reactions proceed via intermediate diamides 57.


An unusual closure of the pyrimidine ring was observed with 2-chloroacetylamino-3-ethoxycarbonylthiophenes 66 and salts KXCN (X = S or Se) giving substituted thienopyrimidinones 67 (1993GEP4119767).

\[
\begin{align*}
\text{66} & \quad \text{KXCN} & \quad \text{67}
\end{align*}
\]

\(X = S, \text{Se.}\)

Successive treatment of 2-amino-3-cyanothiophenes 30 with carbon disulfide in the presence of sodium methoxide and then with methyl iodide gave \(\text{vic-bis(methylthio)methylideneamino(cyano)thiophenes 68, which were transformed into alklythiothienopyrimidineimines 69 under the action of amines (1993JCR(S)302). It was emphasized that it is necessary to thoroughly control the reaction conditions to prevent the possible Dimroth rearrangement.}\)

\[
\begin{align*}
\text{30} & \quad \text{1) } \text{CS}_2, \text{NaOMe} & \quad \text{2) } \text{MeI} & \quad \text{68} & \quad \text{69}
\end{align*}
\]

2-Benzoylamino-4,5-dihydrothiophene-3-carbonitrile (70) with ethyl acetoacetate in the presence of tin(Iv) chloride and triethylamine afforded ethyl 2-(5,6-dihydro-2-phenylthieno[2,3-d]pyrimidin-4-yl)-3-oxobutanoate (71) (2001JHC269).

\[
\begin{align*}
\text{70} & \quad \text{MeCOCH}_2\text{CO}_2\text{Et} & \quad \text{SnCl}_4, \text{Et}_3\text{N} & \quad \text{H}_2\text{N} & \quad \text{CO}_2\text{Et} & \quad \text{NHCOPh} & \quad \text{71}
\end{align*}
\]

An efficient procedure was developed for pyridothienopyrimidines containing various substituents at position 2 of the pyrimidine fragment. For example, iminophosphoranes 72 react with isocyanates, CO_2, and CS_2 under mild conditions to give functionalized 2,3-dihydropyrido-[3',2':4,5]thieno[3,2-d]pyrimidines 73–75 (1994T6705).
A new efficient approach to the previously unknown trihalomethyl-substituted thienopyrimidinones 76 is based on the reaction of methyl N-(1-chloro-2,2,2-trihaloethylidene)carbamates 77 with thienylamines 78 (2003MI1). Intermediate trihaloacetamidines 79 undergo intramolecular cyclization into thienopyrimidinones 76 on heating.


Two main procedures for the construction of thienopyrimidinethiones 80 containing a cyclic thioamide fragment are known. One of them is based on the cyclization of vic-acylamino(thiocarbamoyl)thiophenes 81.

Thioamides required for this reaction are prepared from the corresponding nitriles 30, which undergo cyclization to thienopyrimidinethiones 80 upon successive treatment with carbon disulfide in the presence of bases and then with orthoesters.
The reverse order of the reaction steps can also be used: an imidate or amide is initially formed from nitrile 30 and then these intermediates are transformed into compounds 80 upon treatment with NaSH (1986JHC1757, 1988JPR585).

Another procedure for the synthesis of thiones 80 involves recyclization of thienothiazinethiones 82, which are prepared by the reactions of amides 83 or thienooxazinones 63 with P2S5 and Na3S, under the action of amines (1983CZ344, 1987GEP234677). These reactions proceed via intermediate bis-thioamides 84. In the case of R4 = Bu′, the intermediates were isolated (1986P95). An excess of amine should not be used in recyclization because of the possible replacement of the thione group with the imino group (1988P756, 1989GEP258233).

Thienopyrimidinethiones 85 isomeric to thiones 80 were synthesized by cyclization of thioureas 86 prepared from the corresponding amino(aroyl)thiophenes (1990JHC269).

In recent years, the development of synthetic methods for thienopyrimidines containing two substituents in the pyrimidine moiety has also attracted attention. For example, a general procedure was devised for diaminothienopyrimidines 87 involving pyrimidine ring closure in vic-cyano(guanidino)thiophenes 88.
Compounds 87 are prepared in situ from 2-amino-3-cyanothiophenes with chloroformamidine (1993JMC3103, 1995JMC2763) or guanidine. The latter route proceeds via guanidines 88 or 89 as intermediates (1986JHC1757, 1989M12, 1990HCA797, 1990IJC1070).

Diaminothienopyrimidines 87 were also prepared from thiophenes 30 with cyanamides under acidic conditions (1990JHC119) or by cyclization of guanidines 88 derived from the corresponding carbodiimides 90 (1991JHC1857).

Diaminothienopyrimidines were also prepared (1981CS245) by treatment of thiophenes 30 successively with carbon disulfide and ammonia.

An original procedure was developed for the synthesis of thienopyrimidines 87 involving the simultaneous closure of the thiophene and pyrimidine rings (1993MC149, 1994KGS122, 1995MI11, 1996T1011). For example, treatment of enethiolates 91 with N-cyanochloroacetamidine triggers a chain of successive reactions: alkylation at the sulfur atom to form 92, the Thorpe–Ziegler cyclization to give thiophenes 93, and pyrimidine ring closure. Intermediates need not be isolated and
the target thienopyrimidine 87 can be synthesized by a one-pot procedure. The last step, viz., pyrimidine ring closure, can be performed both in basic and acidic media.

Alkoxo- and alkylthio-substituted aminothienopyrimidines 94 were prepared by cyclization of the corresponding isourreas and isothioureas 95. Isourreas are generated in situ from thiophenes 30 with cyanates in the presence of acids (1984INDP151496). Isothioureas are produced by alkylation of thioureas 33 (1991GEP287503).

Another procedure is based on the use of iminothienothiazinethiones 29 as the starting substrates. For example, their reactions with one equivalent of methyl iodide afforded compounds 96, which underwent recyclization into thienopyrimidines 97 under the action of amines. Two equivalents of methyl iodide gave di(methylthio)thienopyrimidines 98 (1993JCR(S)302).
The two possible isomers of aminothienopyrimidines contain either the amidine (99) or guanidine (100) fragment.

Two general procedures for the direct synthesis of aminothienopyrimidines 99 are documented. One method involves cyclization of vic-amidino(cyano)thiophenes 101.


Imidates react with thiophenes 30 analogously. In the reactions of N-substituted imidates, the initially formed thienopyrimidineimines 50 undergo cyclization to give aminothienopyrimidines 51 (1986CB1070). Amidines 101 can also be prepared from

A very mild procedure for the generation of amidines 101, allowing their isolation, is based on aminolysis of imidates 102, which are prepared by treatment of thiophenes 30 with orthoesters. The reaction with ammonia directly affords aminothienopyrimidine 99 (1986JHC1757), whereas in the case of primary amines, recyclization of intermediate thienopyrimidineimine 50 takes place. Thienopyrimidineimines 50, like amidines 101, can be isolated. Both these compounds give aminothienopyrimidines 99 on heating in the presence of a catalytic amount of bases (1988M12, 1992CP34).

Amidines 101 can also be generated by treatment of amides 103 with arylamine hydrochlorides in the presence of dehydrating agents, such as P2O5. In this case, attempts to isolate the corresponding amidines failed, but this procedure made it possible to prepare thienopyrimidines 99 (1981CS245, 1988CS195).

Another synthesis of aminothienopyrimidines 99, which is used much more rarely, is based on pyrimidine ring closure in vic-acylaminothiophenecarbamidines 104 generated in situ from compounds 103 and amines (1983CPB401, 1993P26).
Aminothienopyrimidines 99 can also be prepared by substitution of an amine for the halogen atom in halothienopyrimidines synthesized from thienopyrimidinones of type A. An analogous synthesis based on thienopyrimidinones of type B provides the only approach to derivatives of isomeric aminothienopyrimidine 100 (1987JAP6200426).

Most compounds of this group are accessible only by an indirect route involving thienopyrimidinones, preparation of chlorothienopyrimidines from these compounds, and the replacement of the chlorine atom with OR, SR, or other groups. However, procedures for the direct construction of the target pyrimidine ring were described for the preparation of specific compounds.


1-Chlorothieno[2,3-d]pyrimidines (108) are formed (sometimes as by-products) from thiophenes 30 with nitriles and dry hydrogen chloride (1990HCA797, 1990JHC119). Apparently, the attack of HCl on the nitrile group in amidine 109 is followed by pyrimidine ring closure in the imidoyl chloride 110 produced. Chlorothienopyrimidines 108 can selectively be prepared from thiophenes 30 with the Vilsmeier reagent. In this case, the competitive reactions of the nitrile and amino groups are not observed (1989GEP258015).
The synthesis of 2,4-dithioxotetrahydropyrrolo[4',3':4,5]thienopyrimidine \(111\) was described (2003M13). Interaction of the 2-amino-3-cyanotetrahydrothieno[2,3-\(c\)]pyridine \(112\) with carbon disulfide in pyridine results in the formation of 4-imino-2-thioxotetrahydropyrimidothieno[3,2-\(c\)]-1,3-thiazene \(113\), which undergoes Dimroth rearrangement by boiling in water containing calcium dihydroxide and finally converts into \(111\).

The reactivity of 2-amino-4,5,6,7-tetrahydrobenzo[\(b\)]thiophene-3-carboxamide \(114\) toward a variety of chemical reagents gave thienopyrimidines, e.g., \(115\) (\(X = \text{N}\)) and thienopyridines, e.g., \(115\) (\(X = \text{CCN}\)) (2003HAC459).

The previously unknown polyannulated heterocyclic system, viz., tetrahydrocycloheptathieno-1,2,4-triazolopyrimidine \(116\), was constructed starting from 2-amino-3-cyanotetrahydropyrimidine \(117\) in four steps (2002PS123).
In recent years, procedures were devised for the synthesis of thienopyrimidines using recyclization of derivatives of thieno[2,3-d]oxazinones (2002JCR(S)5, 2002MI2, 2002JCR(S)0149), thieno[3,2-d]oxazines (1998P775), and pyrano[3,4-d]pyrimidines (1999P858).

B. SYNTHESIS OF THIENOPYRIMIDINES BY THIOPHENE RING CLOSURE

As earlier, procedures for the synthesis of thienopyrimidines by thiophene ring closure starting from the available pyrimidine are used much more rarely than the pyrimidine ring closure, because the appropriately substituted pyrimidines are less readily accessible. In this section, data are systematized according to the types of reactions giving rise to the thiophene ring.

Generally, the synthesis of thienopyrimidines using the Claisen, Thorpe–Ziegler, and Friedläender condensations can be represented by the following scheme:

\[
\text{A} \begin{array}{c}
\overset{Y}{\text{S}}
\end{array}\begin{array}{c}
\text{z}
\end{array}
\overset{Y}{\text{A}}
\begin{array}{c} 
X
\end{array}
\begin{array}{c} 
\text{B}
\end{array}
\begin{array}{c} 
\text{Y=CO}_2\text{Et, X=OH (}=\text{O}) ; Y=\text{CN, X=NH}_2 ; Y=\text{COR, X=R;}
\end{array}
\begin{array}{c} 
Z\text{ is an electron-withdrawing group, B is the pyrimidine ring.}
\end{array}
\]

In the case of \(Y=\text{CO}_2\text{Et,}\) the reaction affords 5-hydroxythienopyrimidines, which exist predominantly as the oxo form (118). Pyrimidines 119 starting compounds can be prepared by two methods. One of them involves substitution of the mercaptoacetic acid residue for the chlorine atom in 4-chloro-5-ethoxycarbonylpyrimidines 120. Pyrimidines 119 are then cyclized in the presence of bases to thieno[2,3-d]pyrimidin-5-ones 118 (1988JHC959, 1993INP13664).
The sulfonyl group at position 4 of a pyrimidine can be replaced like a chlorine atom. The starting sulfonylpyrimidines were prepared (1988JHC959) by oxidation of the corresponding arylthio compounds.

Another procedure for the synthesis of pyrimidines involves alkylation of 5-ethoxycarbonylpyrimidine-4(3H)-thiones with chloroacetic acid derivatives. In this case, thienopyrimidines were prepared without isolation of intermediate pyrimidines (1988GEP258012, 1988SL201, 1990SL75).


In some cases, pyrimidines formed as intermediates in the 5-alkylation of pyrimidinethiones were isolated (1987KGS1377, 1990P216). In the presence of catalytic amount of bases, compounds undergo cyclization to give the target products. In addition to compounds containing the above-mentioned groups Z, 6-aryl-substituted derivatives can also be prepared, but cyclization of intermediates is carried out in metallic sodium or sodium hydride (1993INP13664).
Both these procedures allow one to isolate intermediate pyrimidines 127 (1988JIC695, 1988P537, 1989P492). The Michael reaction of thione 129 with acrylonitrile affords pyrimidine 130, which, however, does not undergo cyclization. After oxidation of pyrimidine 130 to sulfone 131, the acidity of the methylene fragment becomes sufficiently high to allow cyclization of the latter to give thienopyrimidine 132 (1990CCC1049, 1993P26).

\[
\begin{align*}
\text{N} & \text{N} \\
\text{Me} & \text{S} \\
\text{Ar} & \text{COMe} \\
\text{CN} & \\
\rightarrow & \text{CN} \\
\text{N} & \text{N} \\
\text{Me} & \text{S} \\
\text{Ar} & \text{COMe} \\
\rightarrow & \text{CN} \\
\text{N} & \text{N} \\
\text{Me} & \text{S} \\
\text{Ar} & \text{SO}_2 \\
\rightarrow & \text{Cl} \\
\end{align*}
\]

5-Ethoxycarbonyl-4-methyl-2-phenylpyrimidine-6(1H)-thione 133 reacted with a series of α-halocarbonyl compounds to give S-alkyl derivatives 134. Upon treatment of 134 with sodium dioxide, cyclization to thienopyrimidines 135 occurred (2002MI2, 2002PS2745).

\[
\begin{align*}
\text{N} & \text{N} \\
\text{Me} & \text{S} \\
\text{CO}_2\text{Et} & \\
\rightarrow & \text{S} \\
\text{Me} & \text{COR} \\
\rightarrow & \text{OH} \\
\end{align*}
\]

R = EtO, Ph, 4-ClC₆H₄, 4-BrC₆H₄, 4-ClC₆H₄NH, 4-MeOClC₆H₄NH.

Treatment of aminoisothiazolopyrimidine 136 with chloroacetone gave an unexpected transformation. A thienopyrimidine formed, apparently, through the intermediate opening of the isothiazole ring and the formation of the corresponding nitrile (1988JCR(S)46).

\[
\begin{align*}
\text{N} & \text{N} \\
\text{Me} & \text{NH}_2 \\
\text{Ph} & \text{Ni} \\
\rightarrow & \text{Cl} \\
\text{Ph} & \text{Me} \\
\rightarrow & \text{COMe} \\
\end{align*}
\]
Alternative approaches to the synthesis of thienopyrimidines by thiophene ring closure are also documented. For example, the thio-Claisen rearrangement of propargyl sulfide 137 (X = S) affords thienopyrimidinodiones 138, the rearrangement of sulfoxide 137 (X = SO) gives the corresponding formyl derivative 138 (R² = CHO) (1989JHC1851).

Another approach to the construction of a thiophene ring based on functionalized pyrimidines involves thiolation of the methyl group in vic-methylpyrimidinocarbonitriles 139 with elemental sulfur followed by cyclization of the intermediate thiols 140 to give thienopyrimidines 141. The reactions were carried out with pyrimidinethiones (1990LA1215) and pyrimidinediones (1990MI5, 1991MI3).

Ethyl 4,5-diamino-2-(dimethylamino)thieno[2,3-d]pyrimidine-6-carboxylate (142) was prepared in 93% yield from 4-amino-6-chloro-2-(di-methylamino)pyrimidine-5-carbonitrile (143) with ethyl 2-mercaptoacetate in refluxing EtOH–THF (5:1) (2000S255).

Bromination of 5-allyl-6-methyl-2-methylthio(phenyl)pyrimidine-4-thiols (144) in chloroform afforded 6-bromomethyl-4-methyl-2-methylthio(phenyl)-5,6-dihydrothieno[2,3-d]pyrimidines 145. The latter were transformed into 4,6-dimethyl-2-methylthio(phenyl)thieno[2,3-d]pyrimidines 146 by refluxing with ethanolic sodium ethoxide (1999KZA60).
The thermal [3,3]-sigmatropic rearrangement of 1,3-dimethyl-5-(isopropylthio)uracils gave 1,3,6-trialkylthieno[2,3-d]pyrimidines in yields up to 82% (2000SC4183).

Ethyl ester 147 was synthesized by the reaction of 4,6-dichloro-2-(methylthio)pyrimidine-5-carbonitrile (148) with o-fluoroaniline followed by treatment of the intermediate fluoroanilino derivative with ethyl mercaptoacetate and NaOH (1999MI12).

First representatives of the previously unknown tricyclic annulated system, viz., ethyl 7-methylthio-4,5-dihydro-3H-thieno[2,3,4-de]pyrimido[4,5-d]pyrimidine-2-carboxylates 149, were prepared by a three-step synthesis from 4,6-dichloro-2-methylthiopyrimidine-5-carbonitrile (2000MI13).

Some other approaches to thienopyrimidines from derivatives of pyrimidine were described (2002M13, 2003EJC11, 2003HCM89, 2003M14, 2003PS737).
III. Chemical Properties of Thienopyrimidines

A. NUCLEOPHILIC SUBSTITUTION

In the chemistry of thienopyrimidinones and thienopyrimidinediones, the replacement of an oxygen atom with a chlorine atom is used rather often. Earlier, it was found (1968CR(C)128, 1973CR(C)93) that this reaction with thienopyrimidinediones proceeds on heating with either POCl₃ (an excess of POCl₃, pyridine, or N,N-dimethylaniline is used as the solvent) or SOCl₂. The reaction is accompanied by the formation of the corresponding dichlorothienopyrimidines.


Thienopyrimidinones react analogously to afford chlorothienopyrimidines (1983CPB401, 1986EUP150469).

Compounds containing the thioxo group undergo the same transformations. Under the action of POCl₃, thienopyrimidinethiones are converted into chlorothienopyrimidines (1986JHC1757).

Thienopyrimidinones and thienopyrimidinethiones undergo intramolecular condensation involving the primary amino group and the oxo- or thioxo group to form compounds with a five- or six-membered ring (1989GEP258233, 1992P333, 1993P26, 1993P588).
Nucleophilic substitution occurs particularly easily in chlorothienopyrimidines. The chlorine atom can be replaced with virtually any nucleophilic residue. In the last 10–15 years, the replacement of the chlorine (or bromine) atom in the pyrimidine fragment of thienopyrimidines with an amino group has been studied most extensively.

The nucleophilic substitution reactions of dichlorothienopyrimidines 155 with amines and hydrazines proceed stepwise. Initially, the chlorine atom involved in a fragment of cyclic imidoyl chloride is replaced to give aminochlorothienopyrimidines 156, which can be isolated in good yields. Compounds 156 are further transformed into diaminothienopyrimidines 157 in the presence of an excess of the amine or by treatment with another amine under more drastic conditions (1968CR(C)128, 1973CR(C)93, 1986GEP226893, 1986P23, 1992INP17021, 1992INP18887, 1994IZ-V181).

The chlorine atom in aminochlorothienopyrimidines 158, readily derived from thienopyrimidinones 159 and POCl₃, is also replaced by the amino group to give 157 (1968USP3318883, 1991EUP404356).

\[
\begin{align*}
\text{Cl} & \quad \text{NR}_2 \\
\text{A} \quad \text{NAr} & \quad \text{O} \\
& \quad \text{NR}_2 \\
\end{align*}
\]


\[
\begin{align*}
\text{Cl} & \quad \text{NR}_2 \\
\text{A} \quad \text{NAr} & \quad \text{NR}_2 \\
& \quad \text{R}_1 \\
\end{align*}
\]

Chlorothienopyrimidines 163 isomeric to compounds 108 react with amines under more drastic conditions to give aminothienopyrimidines 164 (1983CPB401, 1994JAP0616557).

\[
\begin{align*}
\text{Cl} & \quad \text{NR}_2 \\
\text{A} \quad \text{NAr} & \quad \text{NR}_2 \\
& \quad \text{R}_1 \\
\end{align*}
\]


Reactions with thiourea produce the corresponding thiones 167 (1968CR(C)128). The replacement of a chlorine atom with a thiocyanate group is also documented (1997AF1005).

The halogen atoms in these compounds can exchange with another halogen (1968CR(C)128). For example, 1-chlorothieno[2,3-\(d\)]pyrimidine (168) and NaI yield the iodothienopyrimidine 169.

CH-acids also substitute the chlorine atom in chlorothienopyrimidines 170 to give methylidenethienopyrimidines 171 (1986CPB516, 1993P585).
Replacement of the methylthio group in monothiomethylthieno-pyrimidines \textbf{172} with the amino group to form \textbf{173} was studied (1987KGS1131, 1994JPR160).

The alkylthio groups in thienopyrimidines are saponified with alkalis (1989GEP258017, 1989KGS413).

Yet another example of nucleophilic substitution in the pyrimidine fragment of thienopyrimidines is the replacement of the 1,2,4-triazolyl substituent with a nucleophile (1992EUP452002).

\[ \text{HNu} = R_1^2\text{NH}, R_1^1\text{SH}. \]

\section*{B. ELECTROPHILIC SUBSTITUTION}

Both in earlier (1966AHC235, 1984MI11, 1985MI1, 1990JHC717, 1990USP4939137) and more recent (1992JHC1963, 1992SR1, 1993JHC1065, 1993JMC3103, 1996AHC193) studies on chlorination, bromination, Vilsmeier formylation, and nitration demonstrated that electrophilic substitution in thieno[2,3-\textbf{d}]pyrimidine \textbf{1} and thieno[3,4-\textbf{d}]pyrimidine \textbf{3} involves position 6 and equivalent position 7, respectively (in the presence of an excess of an electrophilic reagent, the latter reaction leads to disubstitution at positions 5 and 7), which is typical of
thiophene itself and suggests a weak influence of annulation with the pyrimidine ring. A different situation is observed for electrophilic substitution in thieno[3,2-d]pyrimidine 2, where the influence of annulation on the pyrimidine ring is stronger than the effect of orientation of the sulfur atom in the thiophene ring and, consequently, attack occurs at position 7.


N-alkylation of thienopyrimidinediones and thienopyrimidinones is often used with thienopyrimidines. Thienopyrimidinediones 4 (R = H) are alkylated with alkyl halides in the presence of bases to give N-alkylthienopyrimidinediones 176 (1983P135, 1986P661, 1990EUP329168, 1992SC3221). The reactions were carried out with NaH or K$_2$CO$_3$ as the base or under conditions of phase-transfer catalysis.

A method was developed for selective glycosylation of thienopyrimidines at position 4. Initially, dione 4 is transformed into disilyl derivative 179, which is alkylated with sugar derivatives in the presence of Lewis acids (most often, trimethylsilyl triflate). Glycosylation was carried out on 1-OH (1993NN937, 1994NN883, 1994NN1135) and 1-OAc derivatives (1994JPR129) and methyl glycosides (1995LA1371, 1995M593).

The Michael reaction of thienopyrimidinediones 4 bearing a substituent at position 2 with ethyl acrylate and acrylonitrile affords thienopyrimidinediones 180 (1990JHC1761, 1990USP4939137).

An intramolecular alkylation of thienopyrimidinones 183 giving tricyclic compounds 184 is also documented (1989CPB2122, 1989P153).

If the nitrogen atom at position 2 bears a substituent, alkylation proceeds at the nitrogen atom in position 4 of the thienopyrimidine system, as exemplified (1988DOK1135, 1989KGS413) by the formation of thiazolothienopyrimidinium salts 185 from S-allyl derivatives 186.

Thienopyrimidinethiones react with alkyl halides and alkyl sulfonates at the sulfur atom to give alkylthiothienopyrimidines. In thienopyrimidinedithiones 187, the distinction between the two sulfur atoms is insufficient for the reaction to proceed selectively. Therefore, the reactions are conducted to afford di(alkylthio)thienopyrimidines 188 (1993MI1).

\[
\begin{array}{c}
\text{A} \quad \text{O} \\
\text{N} \\
\text{NCH}_2\text{NR}_2 \\
\text{CH}_2\text{O}, \text{R}_2\text{NH} \\
\text{A} \\
\end{array}
\]


\[
\begin{array}{c}
\text{A} \quad \text{N} \\
\text{NR} \quad \text{SAlk} \\
\end{array}
\]

Examples of O-alkylation of thienopyrimidinones are scarce. However, such an alkylation can be carried out intramolecularly. For example, treatment of 2-(2-chloroethyl)thienopyrimidine-1,3-dione (191), prepared from the corresponding hydroxy compound and PC1₃, with a base led to the closure of the oxazolidine ring giving tricyclic 192 (1989CPB1197, 1989CPB2096, 1989CPB2717).

\[
\begin{array}{c}
\text{A} \quad \text{O} \\
\text{NCH}_2\text{CH}_2\text{OH} \\
\text{PCl}_3 \\
\text{AlkHal} \\
\text{Et}_3\text{N}, \text{EtOH} \\
\text{A} \quad \text{O} \\
\text{NCH}_2\text{CH}_2\text{OH} \\
\text{PCl}_3 \\
\text{AlkHal} \\
\text{Et}_3\text{N}, \text{EtOH} \\
\text{A} \quad \text{N} \\
\text{NR} \quad \text{SAlk} \\
\text{A} \quad \text{N} \\
\text{SAlk} \\
\end{array}
\]

Analogous reactions of 4-(2-chloroethyl)thienopyrimidine-1,3-diones were also described (1989H985). In both cases, alkylation proceeds at the oxygen atom.
involved in the cyclic urea fragment because of the higher basicity of this oxygen atom compared to the oxygen atom at position 1.

2-(Carboxymethylthio)thieno[2,3-d]pyrimidin-4-ones (193) react with acetic anhydride in the presence of pyridine to form mesoionic heterocycles 194 (1990CRTK249).

A new approach to 4,5-dihydro-9H-pyrido[1,2-a]thieno[3,2-e]pyrimidine-4,9-diones 198 is based on 1,3-dipolar cycloaddition of the above-mentioned mesoionic compounds with dimethyl acetylenedicarboxylate (2001JCR(S)304).
Intramolecular cyclization of allylthio derivatives of thienopyrimidines 199 under the action of concentrated sulfuric acid and halogens (Br or I) was studied. (1990LA1215, 2000S714, 2000S741, 2000UKZ47, 2000ZOR1091, 2002PS889). Treatment with sulfuric acid afforded linearly annulated thiazolothienopyrimidines 200, whereas the reactions with halogens as cyclizing agents gave rise to angular isomers 201.


The reactions described for hydrazinothienopyrimidines can also be assigned to electrophilic substitution reactions. For example, treatment of 1-hydrazinothienopyrimidines 204 with formic acid (1968CR(C)128, 1973CR(C)93, 1985JHC831), acetic acid (1973CR(C)93), or orthoesters (1991P409) led to the closure of the s-triazole ring to form 205 (1985JHC831).
Compounds 205 were also prepared using unstable aminothienopyrimidineimines 206 with orthoesters (1993P20) or with acetylacetone, which undergoes acid catalyzed loss of acetone under the reaction conditions (1992IJC223).


\[
\begin{align*}
207-209 & \\
X = \text{CO}_2\text{Et} (207), \text{CH}_2\text{CO}_2\text{Et} (212), \text{NH}_2 (209) \\
Z = \text{O} (210), \text{S} (211).
\end{align*}
\]

Nitrosation of 4-hyrazinothieno[2,3-\(d\)]pyrimidine (204) led to tetrazole ring closure giving tetrazolothienopyrimidine 212 (1968CR(C)128, 1973CR(C)93, 1991MI4, 1992IJC223). The same compound can be prepared by cyclization of 4-azidothienopyrimidine 213 (1991P409).

\[
\begin{align*}
204 & \xrightarrow{\text{HNO}_2} 212 \\
213
\end{align*}
\]

2-Hyrazinothieno[2,3-\(d\)]pyrimidines 214 undergo cyclization to the corresponding triazolothienopyrimidines 215 under the action of aliphatic acids (2000ML835, 2000ZOR448, 2001ZN(B)826).

\[
\begin{align*}
214 & \xrightarrow{\text{HNO}_2} 215
\end{align*}
\]

In the synthesis of tetracyclic systems 216–218, hyrazino derivatives of pyrano- and tetrahydropyridothienopyrimidines were used as the starting compounds (2001KGS681, 2002HAC280, 2003KFZ15).

Aroylation of thieno[2,3-d]pyrimidines (1997H2159) and complex formation of 2,6-dimethylthieno[2,3-d]pyrimidine-2,4-dione with CuII, MnII, and VIV ions (2000M14) were investigated. 2-(Arylideneamino)thieno[2,3-d]pyrimidin-4-ones were studied by mass spectrometry (2000M15).

IV. Biological Activity and Some Aspects of the Practical Use of Thienopyrimidines

From the standpoint of biological activity, fused heteroaromatic systems are often of much greater interest than the constituent monocyclic compounds. The appearance of qualitatively new properties of an annulated molecule, enlargement of the possibility of varying pharmacophore groups in different positions of the molecule, and the ability of the latter to interact with a wider spectrum of receptors adopting various conformations are apparently of crucial importance. In addition, the structure of the molecule can be varied due to annulation at different positions of individual heterocyclic fragments.

Biological activities of thienopyrimidines have been partially reviewed (1985RCR450, 1996AHCI93). The structure–activity relationships for certain types of derivatives have been discussed (2000JMC(E)677, 2000M16, 2002AF448, 2002CBC1023). Thienopyrimidine derivatives are characterized by a very broad spectrum of biological activities, which includes several dozens of activities. To analyze this problem in more detail, it is worthwhile to survey both recent studies, including patents, and, in part, some earlier investigations. Since the detailed analysis of biological activities of this class of compounds is beyond the scope of the present review, only various activities and the corresponding references are mentioned below.

Novel classes of thienopyrimidines have been identified as potent inhibitors of VEGFR-2 kinase (2003PCT2003022852, 2004BMC(L)21), ErbB kinase (2004PCT2004112714, 2005PCT2005007083), and p38 kinase (2003PCT2003074530). The application of thienopyrimidines as selective inhibitors of nitrogen oxide synthases was discussed (2003MI5).


Of other aspects, practical use of 4-[4-(arylazo)phenoxy]-5,6,7,8-tetrahydrobenzo[b]thieno[2,3-d]pyrimidines as disperse dyes (2002MI7) and 2,4-dimethylthio-6-phenylthieno[3,2-d]pyrimidine as a material for nonlinear optics (1993JAP305630) is documented.

V. Conclusions

Analysis of the data on the chemistry of isomeric thienopyrimidines published over the last 10–15 years shows that this class of heteroaromatic compounds, which are structural analogs of natural compounds of the purine class, attracts increasing interest of chemists and biochemists. In the first half of the 21st century, new approaches to the synthesis of derivatives of these fused heterocyclic systems will be, undoubtedly, extensively developed. These derivatives are not only of theoretical interest but also possess a broad spectrum of practical use, primarily, due to various biological activities. Of the approaches to their synthesis, multicomponent cascade heterocyclization, which allows one to construct various functionalized thienopyrimidines and their fused analogs in one technologically and ecologically safe step, holds the most promise.
Acknowledgment

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I. Introduction

This survey is a sequel to eight reviews already published in *Advances in Heterocyclic Chemistry* (66AHC(7)225, 79AHC(25)303, 88AHC(44)269, 92AHC(55)31, 98AHC(71)291, 99AHC(73)295, 01AHC(79)199, 04AHC(87)1). It includes monographs and reviews published during the period 2002–2004 as well as some published earlier but omitted in Part VIII.

Like Parts III–VIII, this survey is based mainly on short bibliographic papers published by the authors in *Khimiya Geterotsiklicheskikh Soedinenii* since 2003 (03KGS776, 04KGS1416, 05KGS927, 05KGS1265, 05KGS1408, 05KGS1705). Sources not only in English but also in Russian, Japanese, Chinese, Czech, and other languages are surveyed and classified. This feature of the survey should cause no problem, because some of the sources are available in English translations and practically all others have informative English abstracts as well as quite understandable and useful schemes and lists of references. As before, carbohydrates are not covered. Such compounds are mentioned only in general cases (e.g., anomeric effect) as well as when carbohydrates serve as starting compounds for the synthesis of other heterocycles or they are present as fragments of a complex system including another heterocyclic moiety such as a nucleoside.

II. General Sources and Topics

A. General Books and Reviews

1. Textbooks and Handbooks

   Drugs, general handbooks: 02MI30, 03MI84.
   Fundamentals of combinatorial organic chemistry: 03MI63.
   Means of protection, medical treatment, and growth regulation of animals and plants: 04MI3.
   Selected topics of organic chemistry based on the Nenitescu reaction: 03MI1

2. Annual Reports

   a. Comprehensive Reports. 03PHC1, 04PHC1, 05PHC1.

   b. Specialized Reports Devoted to a Basic Series of Heterocycles. Three-membered heterocycles: 03PHC75, 04PHC54.
      Four-membered heterocycles: 03PHC100, 04PHC82, 05PHC64.
Pyrrole and its benzo derivatives: 03PHC140, 04PHC128, 05PHC109.
Furan and its benzo derivatives: 03PHC167, 04PHC156, 05PHC142.
Thiophenes, selenophenes, and tellurophenes: 03PHC116, 04PHC98, 05PHC84.
Five-membered heterocycles with more than one N atom: 03PHC206, 04PHC198, 05PHC172.
Five-membered heterocycles with N and S (Se) atoms: 03PHC230, 04PHC228, 05PHC197.
Five-membered heterocycles with O and S (Se, Te) atoms: 03PHC249, 04PHC272, 05PHC227.
Five-membered heterocycles with O and N atoms: 03PHC261, 04PHC283, 05PHC238.
Pyridine and its benzo derivatives: 03PHC284, 04PHC309, 05PHC261.
Diazines and their benzo derivatives: 03PHC306, 04PHC347, 05PHC304.
Triazines, tetrazines, and fused polyaza-systems: 03PHC339, 04PHC385, 05PHC337.
Six-membered heterocycles with O and/or S atoms: 03PHC360, 04PHC405, 05PHC362.
Seven-membered heterocycles: 03PHC385, 04PHC431, 05PHC386.
Heterocycles with eight-membered and large rings: 03PHC431, 04PHC451, 05PHC418.
Heterocyclic chemistry: 03AR(B)161.

c. Reports Devoted to Individual Problems. Anion and ion-pair receptors based on pyrroles and polyammonium macrocycles: 03CCR(240)191.
Bioinspired reactions of heterocycles: 03AR(B)447.
Highlights of the total synthesis of natural heterocycles: 03AR(B)208.
Lanthanides and actinides complexes with heterocyclic ligands: 03CCR(241)249.
Marine natural heterocycles: 03AR(B)183.
Natural heterocyclic polymers chemistry: 03AR(B)263.
Oxidation and reduction of heterocycles: 03AR(B)21.
Photochemistry of heterocycles: 03AR(B)396.
Supramolecular chemistry of heterocycles: 03AR(B)244.
Synthesis of P-, S-, Se-, Te-, and Si-heterocycles: 03AR(B)63.
Transition metal complexes with heterocycles as ligands in hydroformylation including hydroformylation of heterocycles: 02CCR(228)61, 03CCR(241)295.
Transition metals in organic synthesis: 03CCR(247)79, 04CCR(248)1085.
Transition metals in stochiometric reactions of heterocycles: 03AR(B)138.
Transition metals in formation and transformation reactions of heterocycles: 03CCR(241)147.
Use of transition metals as catalysts in the synthesis of heterocycles: 03AR(B)104.

3. Nomenclature

Nomenclature for the C_{60}-I_{h} and C_{70}-D_{5h(6)} fullerenes (IUPAC Recommendations, 2002): 02PAC629.

4. History of Heterocyclic Chemistry, Biographies

Emil Fischer, his personality, his achievements, and his scientific progeny: 02EJO4095.
100 Years of the Wolff rearrangement, particularly, heterocycles in the Wolff rearrangement: 02EJO2193.

5. Bibliography of Monographs and Reviews

The literature of heterocyclic chemistry, 1999–2001: 04AHC(87)1.

a. Specialized Surveys. 03KGS776, 04KGS1416, 05KGS927, 05KGS1265, 05KGS1408, 05KGS1705.

B. GENERAL TOPICS BY REACTION TYPE

We have classified the many reviews dealing with these materials under following headings:

1. General Sources and Topics.
2. Structure and Stereochemistry (it is self-subdivided into Theoretical Aspects, Stereochemical Aspects, Betaines and Other Unusual Structures, Miscellaneous Substituted Heterocycles).
3. Reactivity (General Topics, Reactions with Electrophiles and Oxidants, Reactions with Nucleophiles and Reducing Agents, Reactions toward Free Radicals, Carbenes, etc., Reactions with Cyclic Transition State, Reactivity of Substituents, Heterocycles as Intermediates in Organic Synthesis).
4. Syntheses (General Topics and Nonconventional Synthetic Methodologies, Synthetic Strategies and Individual Methods, Versatile Synthons and Specific Reagents, Ring Synthesis from Nonheterocyclic Compounds, Syntheses by Transformation of Heterocycles).
5. Properties and Applications (Dyes and Intermediates, Substances with Luminescent and Related Properties, Organic Conductors, Coordination Compounds, Polymers, Miscellaneous).

1. General Sources and Topics

Aromaticity as a cornerstone of heterocyclic chemistry: 04CRV2777.
Asymmetric catalysis (general aspects): 03MI55.
Dependence of physical, chemical, biological, and technological properties on chemical structure: 03MI58.

Development of asymmetric reactions using a glucose-scaffold: 02YGK232.

1,3-Dipolar cycloadditions, the problem of concertedness: 03MI57.

From conventional homogeneous to green homogeneous and heterogeneous catalysis with Lewis acids (ring opening and electrocyclic formation of heterocycles, reactions in ionic liquids, N,N'-dialkylimidazolium and N-alkylpyridinium salts): 03CRV4307.

Isomerization of free radicals, in particular, cyclization of aminyl radicals, cyclization and decyclization of oxygen-containing radicals, and decomposition of peroxyalkyl radicals to give epoxides: 04UK1181.

Organocopper compounds in syntheses and transformations of heterocycles: 02MI13.

Organopalladium compounds in syntheses and transformations of heterocycles: 02MI14.

Solid-phase heterocyclic chemistry: 02CRV61.

The logic of multistep synthesis of complex molecules: 03MI154.

2. Structure and Stereochemistry

a. Theoretical Aspects. Hydrophobic interactions and chemical reactivity in reactions and syntheses of heterocycles: 03OBC2809.

Methods of modulating hydrogen-bonded interactions in a synthetic “host” (O-, N-macroheterocycles)–“guest” (small heterocycles) systems: 02CSR275.

New perspective of electron transfer chemistry (porphyrin and porphyrin–fullerene systems): 03OBC609.

Non-standard stereochemistry and hypercoordination in non-classical heterocycles: 02UK989.

Purines, pyrimidines, triazines as components of quadruple hydrogen-bonded systems: 03CC5.

b. Stereochemical Aspects. Chiral auxiliary applications: 02MI11.

Configurational stability and transfer of stereochemical information in the reactions of enantioenriched lithium derivatives of heterocycles: 02AG(E)716.

Stereoselective formation of quaternary carbon centers and related functions (reactions with participation and formation of heterocycles, heterocycles as ligands in molecules of catalysts, and heterocycles as catalysts): 03T10105.

Metal-assisted stereocontrol of 1,3-dipolar cycloaddition reactions: 02SL1371.


Cyclopropahetarenes: 03CRV1327.

P-, As-, Si-, Ge-, Sn-heterocycles as new organoelement betaines with fragments \(+E_{15}^c \cdot C \cdot E_{14}^d \cdot X^{(+)}\) and \(+E_{15}^c \cdot C \cdot E_{14}^d (-)\) \((E_{15}^c = P, \text{As}; E_{14}^d = \text{Si}, \text{Ge}, \text{Sn}; X = \text{C, S, O, NR})\): 02IZV665.

Syntheses, properties, and biological activities of cyclobutahetarenes: 03CRV1539.
3. Reactivity

a. General Topics. Activation of carbonyl and related compounds in aqueous media: 00MI13.

Asymmetric Michael-type addition reactions with participation and/or formation of heterocycles: 00MI11.

Asymmetric organocatalysis of aldol and related reactions using imidazolidinones or proline as catalysts: 04ACR558.

Asymmetric two-center catalytic Reissert-type reactions: 02CC1989.

Baylis–Hillman reaction in syntheses and transformations of heterocycles: 03CRV811.

Carbon–carbon bond-forming reactions mediated by silicon Lewis acids in syntheses and transformations of heterocycles: 03CRV733.

Development of novel oxidation reactions in water using $I,O$-heterocycles with hypervalent iodine as oxidants: 04YGK116.

Design of reversible one-electron redox systems using five-membered S-, Se-, and Te-heterocycles: 04YGK140.

Flash vacuum pyrolysis of Meldrum acid, pyrrol-3(2$H$)-ones, thiophen-3(2$H$)-ones, azepin-3(2$H$)-ones, and pyrrolizin-3-ones: 04ACA19.

Is there stereoelectronic control in the formation and cleavage of tetrahedral intermediates (in reactions with participation of heterocycles): 02ACR28.

Methodology and stereochemistry of aldol reactions with participation of heterocycles: 00MI7.

Methodology and stereochemistry of allylation of carbonyl derivatives of heterocycles: 00MI19.

Molecular designs of tautomeric interconversions of heterocycles: 02IZV197.

Molybdenum in reactions of heterocycles: 04OPP205.

New aspects of the Ireland and related Claisen rearrangements (syntheses and transformations of lactones and lactams, morphine synthesis): 02T2905.

Organocatalysis (acceleration of reactions in the presence of substoichiometric quantities of organic compounds, particularly, heterocycles): 04AG(E)5138.

Photoinduced electron-transfer reactions in heterocyclic chemistry: 03H(60)1921.

Rare-earth metal triflates as catalysts in reactions with formation and participation of heterocycles: 02CRV2227.

Reactions of heterocycles in ionic liquids: 03MI61.
Reactions with participation of heterocycles in the presence of Pd-catalysts: 02PAC1327.
Ring-chain tautomerism of naphthalene-based heterocyclic systems: 03UK498.
Stereoselective cyclopropanation of heterocycles: 03CRV977.
Stereoselective oxidative and reductive coupling using chiral 2-oxazolidinones and 2-imidazolidinones as auxiliaries: 04YGK306.
Stereoselective radical reactions of carbonyl derivatives of heterocycles: 00MI12.
Suzuki–Miyaura cross-coupling reaction in organic synthesis (review contains many examples of reactions with participation of heterocycles): 02T9633.
Tautomerism in diazoles, pyridines, and nucleic bases: 02UK1120.
Thermo- and photochemical reactions of carbonyl compounds in the solid state: 00M114.
Versatile transformations of heterocycles in aqueous media: 03YGK454.

Formylation of naphthalene-based heterocyclic systems: 03UK498.
α-Haloketones in reactions of N-alkylation of heterocyclic compounds: 03ZOR1759.
Heterocycles as nucleophiles in nucleophilic substitution reactions by electron transfer: 03CRV899.
Heterocyclic compounds as nucleophiles in asymmetric Michael additions to nitroalkenes: 02EJO1877.
Metallocomplex asymmetric oxidation of sulfides including oxidation of cyclic sulfides and derivatives of heterocycles with sulfide groups as substituents: 03ZOR1607.
New catalytic approaches in the stereoselective Friedel–Crafts alkylation reaction: 04AG(E)550.
Oxidation of heterocyclic compounds with permanganate anion: 04KGS643.
Palladium-catalyzed reactions of aryl halides with soft, non-organometallic nucleophiles, in particular heterocycles as one type of N-containing nucleophiles: 02T2041.
Polyvalent iodine compounds in the oxidation of heterocycles: 02CRV2523.

c. Reactions with Nucleophiles and Reducing Agents. Activation of X–Y bonds (Y is sulfur and related elements), in particular, in heterocyclic compounds: 01MI139.
Asymmetric hydrosilylation (including reactions with heterocycles): 01MI39.
1-Azaallylic anions in heterocyclic chemistry: 04CRV2353.
O–H bond activation and addition to unsaturated systems (in particular reactions of heterocycles): 01MI42.
Catalytic hydroamination of unsaturated carbon–carbon bonds, particularly, in heterocycles: 01MI40.
Enantioselective addition of dialkylzinc to aldehydes of pyridines, pyrimidines, and quinolines leading to chiral hetarylalkanoles which act as asymmetric autocatalysts: 04BCJ1063.

Hydroboration, diboration, silylboration, and stannylboration reactions with participation of heterocycles: 01MI38.

Hydrocirconation, particularly, of heterocycles: 01MI44.

Hydrophosphination and related reactions (including reactions of heterocycles): 01MI41

Molecular complexes of heteroaromatic N-oxides and their reactions with nucleophiles: 03H(60)419.

Nucleophilic substitution of hydrogen in heterocyclic chemistry: 04CRV2631.

Nucleophilic substitution of a nitro group, fluorine, and chlorine atoms in heteroaromatics: 03UK764.

Reactions of chiral enolate equivalents with derivatives of heterocycles: 02OPP1.

Reactions of highly functionalized heterocyclic organomagnesium reagents prepared through halogen-metal exchange: 03AG(E)4302.

Reductive amination of carbonyl compounds (including those belonging to heterocyclic series) with borohydride- and borane-reducing agents: 02OR(59)1.

Ring opening of heterocycles by arene-catalyzed lithiation: 03PAC1453.

d. Reactions toward Free Radicals, Carbenes, etc. Catalytic carbonylation of heteroaromatic halides: 04MI40.

Radical-mediated oxidative annulation of heteroaromatic compounds: 03S803.

Stereoactive radical reactions of carbonyl derivatives of heterocycles: 00MI12.

e. Reactions with Cyclic Transition State. Diels–Alder reactions with participation and formation of heterocycles in an unconventional solvent, 5.0 M lithium perchlorate/diethyl ether: 02T6777.

Heterocycles as dienes and dienophiles in catalytic asymmetric Diels–Alder reactions: 02MI5.

Heterocycles as ligands in enantioselective cyclopropanion reactions with zinc carbenoids: 02MI17.

Masked o-benzoquinones (one CO group is acetal- or acylal-protected) as active dienes in Diels–Alder reactions with dienophiles (among them thiophene and pyrrole derivatives): 02ACR856.

Mesoionic ring systems in 1,3-dipolar cycloaddition reactions: 02HC(59)681.

Participation of heterocycles in Pd-catalyzed cycloadditions involving trimethylenemethane and its analogs: 02M16.

Recoverable catalysts for asymmetric hetero Diels–Alder reactions: 02CRV3385.


Advances in the nitro to carbonyl conversion (Nef reaction), particularly, in heterocyclic series: 04T1017.
**g. Heterocycles as Intermediates in Organic Synthesis.** Application of heterocycles as non-metallic organocatalysts in organic chemistry: 04MI142.

Chiral diketopiperazines in enantioselective Strecker reactions: 03CRV2795.

Chiral heterocyclic N-oxides as catalysts or ligands in enantioselective reactions: 03YGK1081.

Cyclic α-oxy sulfones as versatile intermediates: 02JCS(P1)275.

1,3-Dialkylimidazolium, 1,1-dialkylpyrrolidinium, and 1-alkylpyridinium salts as ionic liquids in catalysis: 04CCR(248)2459.

Dynamic kinetic resolution; atroposelective lactone ring opening and its use in the synthesis of natural products and chiral auxiliaries: 03T8291.

Enantioselective catalysis using heterogeneous bis(oxazoline) ligands: 02CRV3467.

Enantioselective chemo- and bio-catalysis in ionic liquids (1,3-dialkylimidazolium salts): 04CC1033.

Enantioselective conjugate addition reactions of strongly coordinating nucleophiles with the use of chiral 4,6-dibenzo furylendiy1-2,2'-bis(4-phenyloxazoline)-based aqua complexes as catalysts: 03YGK1073.

Heterocycles as ligands in molecules of chiral catalysts supported on inorganic materials: 02CRV3495.

Heterocycles in engineered asymmetric catalysis: 00MI16.

Heterocyclic chiral enolate equivalents as ligands in catalysts: 02OPP1.

Heterocyclic intermediates in asymmetric syntheses of peptides from α-amino acids: 02SL1388.

Heterocyclic protecting groups in organic syntheses by heterogeneous catalysis: 04CRV199.

Imidazolium and pyridinium salts as peptide-coupling reagents: 04T2447.

Industrial methods for the production of optically active intermediates: 04AG(E)788.

Ionic liquid (molten salt)-phase organometallic catalysis: 02CRV3667.

Mechanism of asymmetric induction in catalytic hydrogenation, hydrosilylation, and cross-combination by metal complexes (N,O-heterocycles as ligands): 02UK39.

Metalated heterocycles and their applications in synthetic organic chemistry: 04CRV2667.

New syntheses of alkynes through oxazolinone formation: 02CC1555.

Polymer-supported hypervalent iodine heterocyclic reagents: 02SL1966.

Preparation and exploitation of chiral building blocks having a dioxaboricyclo[3.2.1]octane framework: 02YGK317.

Reactions with participation of tritium-labeled heterocycles: 02S1781.

Syntheses and applications of heterocyclic boronic acids: 03S469.

Synthetic applications of Lewis acid-induced hexahydro-1,3,5-triazines as N-methyleneamine equivalents: 02H(57)1525.

Synthetic uses of functionalized heteroaromatic organolithium reagents prepared by non-deprotonating methods: 03T9255.

Thiazole-mediated synthetic methodology: 04CRV2557.
4. Syntheses

Aromatic nucleophilic denitrocyclization reactions leading to annulated five-, six-, seven-, and eight-membered heterocycles: 02AHC(83)189.
Asymmetric 1,3-dipolar cycloaddition reactions: 02HC(59)817, 02MI10.
Azides in 1,3-dipolar cycloaddition reactions: 02HC(59)623.
Azomethine ylides in 1,3-dipolar cycloaddition reactions: 02HC(59)169.
Bismuth(III) compounds in syntheses and transformations of heterocycles: 02T8373.
Capto-dative aminoalkenes in syntheses of heterocycles: 02UK225.
Carbonyl ylides in 1,3-dipolar cycloaddition reactions: 02HC(59)253.
Catalytic enantioselective aza Diels–Alder reactions: 02MI9.
The chemistry of pericyclic reactions and their application to syntheses of heterocycles: 03YZ717.
The combinatorial synthesis of bicyclic heterocycles: 03CRV893.
Cyclic 1,3-diones and their derivatives as versatile reactive intermediates in the syntheses of fused heterocycles: 04JHC807.
Diacetylene and its derivatives in heterocyclization reactions: 02AHC(82)157.
Diazooalkanes in 1,3-dipolar cycloaddition reactions: 02HC(59)539.
Effects of external reagents in 1,3-dipolar cycloaddition reactions: 02HC(59)755.
Enyne metathesis catalyzed by ruthenium carbene complexes (cyclization of enynes to heterocycles; combination of metathesis with cycloaddition leading to the formation of heterocycles): 03S1.
Fluorous syntheses of heterocyclic systems: 04CRV2531.
Formation of heterocycles under high pressure: 02MI28.
Formation of heterocycles upon catalytic carbonylation of acetylenic compounds: 03MI30.
Formation of heterocycles in Pd-catalyzed cycloadditions involving trimethylenemethane and its analogs: 02M16.
Formation of five- and six-membered heterocyclic rings by radical cyclization: 04H(63)1903, 04T6239.
Free radical methods for the synthesis of lactones, lactams, and thiolactones: 00M15.
Halo- and selenolactonization as two major strategies for cyclofunctionalization: 04T5273.
Heteroaromatic molecular tweezers involving multiple hydrogen-bonding sites: 04M18.
Heterocycles derived from heteroatom-substituted carbenes: 04CRV2507.
Heterocycles from sterically hindered phenols and their derivatives: 02KGS1323.
Heterocyclization of propargyl compounds: 03MI35.
KF/Al₂O₃-mediated syntheses, particularly, in heterocyclic series: 02T9301.
Methods, mechanistic fundamentals, pathways and applications of catalytic enantioselective Diels–Alder reactions: 02AG(E)1651.
Molybdenum in syntheses of heterocycles: 04OPP205.
Nitrile oxides in 1,3-dipolar cycloaddition reactions: 02HC(59)361.
Nitrile ylides and nitrile imines in 1,3-dipolar cycloaddition reactions: 02HC(59)473.
α-Nitrocarbonyl compounds and α,β-unsaturated nitro compounds in syntheses of heterocycles: 03MI46.
Nitrogen derivatives of aromatic aldehydes and enamines in syntheses of heterocycles: 03MI49.
Nitronates in 1,3-dipolar cycloaddition reactions: 02HC(59)83.
Nitrones in 1,3-dipolar cycloaddition reactions: 02HC(59)1.
One-pot syntheses of annulated derivatives of furan, pyrrole, pyridine, pyrane, and thiophene based on reactions of quinones with enamines: 04YGK811.
Oxidative spiroacetalizations and spirolactonizations of arenes: 04S2767.
PdI$_2$-catalyzed synthesis of heterocycles: 04SL2468.
Preparation, reactivity and biological activity of enaminoketones and enaminothiones and their utilization to prepare N-heterocyclic compounds: 04JHC461.
Radical cyclization of olefins with formation of lactones, lactams and other heterocycles: 02MI62.
Recent advances in the synthesis of heterocycles via ring-closing metathesis: 03PHC1.
Selective rhodium(II)-catalyzed reactions of diazo compounds leading to heterocycles: 03S1137.
Spontaneous resolution under supramolecular control by crystallization of some heterocycles and their binary mixtures: 02CSR342.
Stereoselective organic reactions in water, among them syntheses of heterocycles: 02CRV2751.
Sulfonium salts in syntheses of heterocycles: 03ZOR323.
Sulfur ylides in syntheses of heterocyclic compounds: 03MI38.
Syntheses of alkynylheteroaromatics using Ti-catalyzed intermolecular hydroamination of alkynes: 04SL1653.
Syntheses of heterocycles via group VI Fischer carbene complexes: 04CRV2259.
Syntheses of heterocycles via palladium-olefin and -alkyne chemistry: 04CRV2285.
Syntheses of heterocyclic compounds under microwave irradiation: 04H(63)903.
Syntheses and reactions of N-ethyl-heterocycles: 04H(63)1455.
Syntheses of heterocyclic compounds by the reactions of exocyclic α,β-unsaturated ketones: 04JHC229.
Syntheses of five- and six-membered N- and N,O-heterocycles using oximes: 04YGK38.
Syntheses of heterocycles by carbonylation of acetylenic compounds: 04T5499.
Syntheses of heterocycles by catalytic intramolecular cyclization of acetylenic compounds: 03MI31.
Syntheses of heterocycles from chloro- and bromoketones: 03MI41.
Syntheses of heterocycles in catalytic asymmetric processes: 01JCS(P1)1729.
Syntheses of heterocycles in ionic liquids: 03MI61.
Syntheses of heterocycles on polymeric supports: 02MI33.
Syntheses of heterocycles on a solid phase: 02MI29.
Syntheses of heterocyclic compounds with hypervalent organoiodine reagents: 04AHC(86)225.
Tandem reactions involving organolithium reagents (reactions with formation and participation of heterocycles): 03OPP445.
Theoretical calculations of metal-catalyzed hetero Diels–Alder and 1,3-dipolar cycloaddition reactions: 02MI112.
Thiocarbonyl ylides in 1,3-dipolar cycloaddition reactions: 02HC(59)315.
Transition metal-catalyzed reactions in heterocyclic syntheses: 04CRV2127.
The virtue of multifunctional triazene linkers in the efficient solid-phase synthesis of heterocyclic libraries: 04ACR805.

Asymmetric synthesis of heterocycles containing an \( \alpha \)-amino propargyl fragment: 02OPP459.
Atom transfer radical cyclization reactions mediated by copper complexes to form furan and pyrrole rings, lactones and \( \beta \)-lactams: 02CSR1.
Controlled microwave heating in syntheses and transformations of heterocycles: 04AG(E)6250.
Diels–Alder reactions with \( N \)-methylanilines as azadienes: 02H(57)1525.
Diels–Alder and of hetero Diels–Alder reactions in asymmetric syntheses using catalysts containing heterocycles as ligands: 03MI103.
Double catalytic activation with chiral Lewis acid and amine catalysts in the syntheses of heterocycles, in particular, enol lactones: 04EJO4741.
Enantioselective palladium-catalyzed transformations in syntheses and reactions of heterocycles: 04CRV3453.
Formation of five- and six-membered heterocyclic rings by radical cyclization: 02H(57)2413.
Heterocyclization reactions using chiral catalysts supported on inorganic materials: 02CRV3495.
Nickel-catalyzed reductive cyclizations and couplings in the syntheses of heterocycles including coupling of alkynes with epoxides and syntheses of indole and indolizidine alkaloids: 04AG(E)3890.
Nucleophilic trifluoromethylation and introduction of fluorinated moieties in the syntheses of bioactive fluorinated heterocycles: 03S185.
Palladium-catalyzed reactions of aryl halides with soft, non-organometallic nucleophiles in the syntheses of heterocycles: 02T2041.
Palladium-mediated syntheses of aldehydes and ketones from thiol esters (many examples of syntheses of \( N \)-heterocycles and natural compounds containing heterocyclic fragments): 04ACA87.
Parallel kinetic resolution of racemic mixtures as a new strategy for the preparation of enantiopure heterocycles: 02CSR365.
The Pummerer reaction in the synthesis of heterocyclic compounds: 04CRV2401.
Recent advances in microwave-assisted synthesis including the syntheses of heterocycles: 04ACA66.
Silyl-protected stable 1,3-dipole equivalents in cycloaddition reactions leading to N-, S-, or O-heterocycles: 04BCJ835.

Suzuki coupling reaction in syntheses and transformations of heterocycles: 04MI141.

Syntheses of γ-lactams, epoxides, furans, etc. by transition metal-catalyzed-mediated reactions of allenes with a nucleophilic functionality connected to the α-carbon atom: 03ACR701.

Transition metal-catalyzed annulations (cycloisomerizations of alkynylimines to pyrroles, alkynylketones to furans, and syntheses of multisubstituted heterocycles, particularly, alkaloids): 03SL2265.

c. Versatile Synthons and Specific Reagents. Allenamides in organic synthesis (including synthesis and transformations of heterocycles): 03ACR773.

Allylsilanes in organic synthesis: 04EJO3173.

Alkyl phosphines as reagents and catalysts in the formation and transformation of heterocycles: 03S317.

β-Aminocarboxylic acids containing a cyclopropane ring in syntheses of heterocycles: 03CRV1603.

Application of Sm₂I in organic synthesis (review contains examples of syntheses and transformations of heterocycles): 03MI87.

The chemistry of diaminomaleonitrile and its utility in heterocyclic synthesis: 03T2749.

Chiral enolate equivalents (reactions with formation and participation of heterocycles): 03OPP1.

Cycloaddition to ynlolates as functional carbanions with formation of β-lactones, N- and O-heterocycles: 03S2275.

Diacetylene and its derivatives in heterocyclization reactions: 02AHC(82)157.

γ-Halogen-substituted carbanions as useful intermediates in organic synthesis (particularly, cyclization to tetrahydrofurans and pyrrolidines: 04IZV1771.

Heterocyclization of acetylenes with nitriles, isocyanates, and carbodiimides: 03MI62.

Internal perfluoroolefins in syntheses of fluorinated heterocycles: 02ZOR967.

Ketenes in polymer-assisted synthesis, mainly of heterocycles: 03AG(E)2340.

Methods for preparation of γ- and δ-oxo acids as useful synthons for heterocycles: 02H(57)1353.

Synthesis of aziridines, benzimidazoles, flavones, quinolines thiazoles, etc. using clay and clay-supported reagents: 02T1235.

Use of 3-halo-1-azaallylic anions in heterocyclic chemistry: 03PAC1433.

d. Ring Synthesis from Nonheterocyclic Compounds. Acetylene derivatives of quinones as key intermediates in the synthesis of fused heterocyclic quinoid structures: 04UK171.

Application of cascade processes toward heterocyclic synthesis: 03PAC47.

Pd-Assisted multicomponent syntheses of heterocycles: 03EJO4101.

Asymmetric syntheses of N- and O-heterocyclic compounds using ketenes: 03T3545.
Carbon–carbon bond formation with electrogenerated nickel and palladium complexes in cyclization reactions leading to the formation of heterocycles: 03EJO1605.

Cyclizations involving attack of carbo- and heteronucleophiles on carbon–carbon π-bonds activated by organopalladium complexes in the syntheses of heterocycles: 03S2115.

CycloadDITION reactions to fullerene C₆₀ leading to fullerenedotriazolines, -pyrrolidines, -oxiranes, isoxazolines: 02IZV343.

[2 + 2] Cycloaddition, Diels–Alder reactions, epoxidation of aromatic aldehydes, isomerization of aryl-substituted epoxides, and aziridination catalyzed by the iron Lewis acid [(η⁵-C₅H₅)Fe(CO)2(THF)]: 03ACA3.

Cyclobutane derivatives in syntheses of heterocycles: 03CRV1485.

1,3-Dipolar cycloaddition reactions in syntheses of heterocycles: 02HC(59)1, 02HC(59)83, 02HC(59)169, 02HC(59)253, 02HC(59)315, 02HC(59)361, 02HC(59)473, 02HC(59)539, 02HC(59)623, 02HC(59)755, 02HC(59)817.

Donor–acceptor-substituted cyclopropane derivatives and their application in organic synthesis (with many examples of synthesis of various heterocyclic compounds including drugs: 03CRV1151.

Formation of functionalized heterocycles in Et₂O·BF₃-catalyzed radical cyclization of oxime ethers: 03YZ285.

Formation of heterocycles in heterocyclization, cycloaddition, and 1,3-dipolar cycloaddition reactions of alkenynamines: 03ZOR169.

Guanidines in syntheses of heterocycles: 02MI60.

Heterocycles from alkylidencyclopropanes: 03CRV1213.

Isonitrile-based multicomponent syntheses of heterocycles: 03EJO1133.

Monothiooxamides and oxaminic acids thiohydrazides in syntheses of N- and S-heterocycles: 04IZV491.

Multiple stereoselectivity and its application in asymmetric epoxidation, 1,3-dipolar cycloaddition, [2 + 2] cycloaddition and Diels–Alder reactions: 03T5953.

New asymmetric reactions utilizing tartaric acid esters as chiral auxiliaries (formation of N- and N,O-heterocycles by nucleophilic addition of iminoderivatives or 1,3-dipolar cycloaddition of nitrile oxides and nitrones): 03SL1075.

Oxidation, epoxidation, and sulfoxidation reactions catalyzed by haloperoxidases, among them reactions with participation of heterocycles: 03T4701.

Photochemical reactions of nitrogen-containing thio carbonyl compounds ([2 + 2] cycloaddition to alkenes with formation of thietanes, transformations of thiourea to lactams and cyclic amines, cyclizations of thioamides): 03H(59)399.

Reactions of arynes with heterodienes: 03T701.

Reactions of enaminones with formation of heterocycles: 03T8463.

Reactions of naphthaldehyde leading to the formation of heterocyclic derivatives: 03UK498.

Schiff’s bases in syntheses of heterocycles: 02MI61.

Solution-phase multicomponent methodology for the synthesis of heterocyclic compounds. (non-catalytic syntheses, catalysis with acids and metals, multicomponent reactions including cycloaddition are reviewed): 03S1471.
Spin-selectivity in photocyclization and photoaddition reactions with formation or transformation of heterocycles: 03SL451.

Stereoselective syntheses of heterocyclic compounds by cyclopropylcarbinol ring opening with mercury(II) salts: 03ACR766.

Stereoselective synthesis of non-aromatic $O\,-\,$, $N\,-\,$, and $O\,-\,N\,$-heterocycles using dia-stereotopic groups: 04S2075.

Strategies for heterocyclic construction $via$ novel multicomponent reactions based on isocyanides and nucleophilic carbenes: 03ACR899.

Syntheses and transformations of heterocycles mediated by fluoride ion-activated organosilicon compounds: 02H(57)361.

Syntheses of cyclic chiral ynamides and their transformations to mono- and fused binuclear heterocycles: 03SL1379.

Syntheses of fluorinated azaheterocycles by nickel-mediated C–F activation of heteroaromatics: 02CC2749.

Syntheses of heterocycles from fluorinated vinylsulfides: 03UK394.

Syntheses of heterocycles by cyclization reactions of dianions: 04CRV4125.

Syntheses of heterocycles by the Friedländer condensation reaction: 04MI10.

Syntheses of heterocycles by reactions of 3-oxobutyl isothiocyanate with amines: 03EJO415.

Syntheses of heterocycles through carbonates and carbamates obtained by CO$_2$ fixation with alcohols and amines: 03MI104.

Syntheses of perfluoroalkyl heterocycles from carbonyl compounds: 04AHC(87)273.

Template-controlled regioselective biscycloaddition to [60]fullerene with formation of fused heterocyclic derivatives: 03BCJ865.

Thioamides as useful synthons in the synthesis of heterocycles: 03CRV197.

Transition metal-based Lewis acid, base, and ambiphilic catalysis in syntheses of $O\,-\,$ and $N\,$-heterocycles: 03YGK425.

Transition metal-catalyzed addition of heteroatom–hydrogen bonds to alkynes in syntheses of cyclic amines and pyrroles by hydroamination reactions, in syntheses of $O\,$-heterocycles by hydroalkoxylation of alkynes, and in syntheses of S- and Se-heterocycles: 04CRV3079.

Use of enantiomerically enriched sulfoxides in stereoselective heterocyclizations: 02OPP273.

Use of products of the Claisen rearrangement for the synthesis of heterocyclic compounds: 04CRV2939.

e. Syntheses by Transformation of Heterocycles. Modern methods for the syntheses of substituted naphthalenes, among them naphthalenes fused with heterocycles and naphthalenes bearing heterocyclic substituents: 03T7.

Polyfluoro-2,3-epoxyalkanes in the syntheses of perfluoroalkyl heterocycles: 04AHC(87)273.


Syntheses of optically active silicon-containing amino acids, particularly, of silaproline-, imidazolidine-, and oxazolidine-based amino acids: 03MI86.
5. **Properties and Applications (Except Drugs and Pesticides)**

   **a. Dyes and Intermediates.** Indigoid and flavonoid compounds as the natural constituents of historical textile dyes: 04CSR329.
   Stabilization of anthocyanine color via formation of supramolecular complexes with metals: 04YGK490.

   **b. Substances with Luminescent and Related Properties.** Compounds with heterocyclic fragments as mono-, bi-, and polydentate ligands in manganese clusters with relevance to photosystem II: 04CRV3981.
   Construction of light-harvesting materials including porphyrin fragments: 04YGK480.
   Crowned spirobenzopyrans as ion-responsive photochromic materials: 03YGK322.
   Design and synthesis of dioxetanes as highly efficient chemiluminescent substrates: 03YGK595.
   Femtosecond studies of solvation and intramolecular configurational dynamics of fluorophores containing heterocyclic fragments in liquid solution: 04CRV1929.
   \(N\)-heterocycles as ligands in organo lanthanide metal complexes for electroluminescent materials: 02CRV2357.
   Heterocycles as monomers for plastic optical fiber lasers and amplifiers containing lanthanide complexes: 02CRV2347.
   \(N\)- and \(N, O\)-heterocycles as second-order nonlinear optical chromophores with both large first-order molecular hyperpolarizability and good transparency: 03MI108.
   Macroheterocycles with fragments of crown ethers, thiacrowns, pyrazoles as highly efficient fluorescent sensors and switches: 02CSR116.
   Organic solar cell based on fullerene modified by heterocycles, porphyrin systems, and polymers with heterocyclic fragments: 04MI53.
   Photochromic \(trans\)–\(cis\)-isomerization and molecular switching properties of azo-conjugated metal complexes with heterocycles as ligands: 04BCJ407.
   Photo-, thermo-, solvato-, and electrochromic spiroheterocyclic compounds: 04CRV2751.
   Recent applications of oxazoline-containing ligands in asymmetric catalysis: 04CRV4151.

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   Heterocycles as unimolecular electrical rectifiers: 03CRV3803.
   Dithiadiazafulvalenes as promising precursors of molecular materials: 04CRV5185.
   Magnetic TTF-based charge-transfer complexes: 04CRV5449.
   New trends in the synthesis of tetraselenafulvalene and tetrathiafulvalene derivatives as \(\pi\)-electron donors for molecular conductors and superconductors: 04CRV5057.
   NMR studies of \(\kappa\)-(BEDT-TTF)\(_2\)X as two-dimensional molecular conductors: 04CRV5635.
   Recent synthetic advances of tetrathiafulvalene-based organic conductors: 04BCJ43.
   Single-component molecular metals with extended-TTF dithiolate ligands: 04CRV5243.
   Tetraselenafulvalene and tetrathiafulvalene derivatives as organic conductors with unusual band fillings: 04CRV4947.
   Tetraselenafulvalene and tetrathiafulvalene derivatives in conducting organic radical cation salts with organic and organometallic anions: 04CRV5203.
   Tetraselenafulvalene derivatives as new organic conductors: 04YGK150.
   Tetrathiafulvalene derivatives in conducting and magnetic Langmuir–Blodgett films: 04CRV5479.
   Tetrathiafulvalenes, oligoacenes, and their buckminsterfullerene derivatives as the brick and mortar of organic electronics: 04CRV4891.

d. Coordination Compounds. Application of chiral binuclear complex catalysts with heterocycles as ligands to asymmetric synthesis: 03M190.
   Asymmetric additions of alkynylzinc reagents (pyridines and alkaloids as N-containing ligands) to aldehydes and ketones: 03T9873.
   Asymmetric metallocomplex catalysis and synthesis of coordination compounds with participation of chiral \(P,N\)-bidentate phosphites and amidophosphites bearing peripheral azine or oxazoline fragments: 04MI46.
   Asymmetric syntheses of natural products; cyclization reactions using molybdenum and tungsten imido alkylidene complexes as efficient olefin-metathesis catalysts: 03AG(E)4592.
   Asymmetric catalysis of hetero Diels–Alder reactions using chiral lanthanide complexes: 02CRV2211.
   Asymmetric catalysis using chiral ferrocene ligands containing an oxazoline substituent: 03ACR659.
   \(1,1'\)-Binaphthyl-2,2'-dial and 2,2'-diamino-1,1'-binaphthyl functionalized with heterocycles as versatile chiral ligands in coordination and metallosupramolecular chemistry: 03CCR(242)33.
   Binding affinities of host–guest (macrocycles as host molecules), protein–ligand (biologically active heterocycles as ligands), and protein transition-state complexes: 03AG(E)4872.
Bipyridine- and porphyrin-based metal complexes as receptors for anions: 03CCR(240)77.

Bridge complexes with heterocyclic ligands, derivatives of triazoles, oxa- and thiadiazoles, pyridazine, phthalazine, etc.: 04CRV349.

Chelates and metal complexes with heterocyclic ligands as modifiers for epoxy resins: 02CCR(224)67.

Catalytic enantioselective C–H activation by means of metal-carbenoid-induced C–H insertion (heterocycles as ligands): 03CRV2861.

Chromatographic and related electrophoretic methods in the separation of transition metal complexes or their ligands (many examples of complexes with heterocyclic ligands: 03CCR(247)159.

Classification of polygons and polyhedra of metallocycles and complexes with heterocyclic ligands according to their mode of self-assembly: 02CCR(225)91.

Combinatorial libraries of chiral heterocyclic ligands for enantioselective catalysis: 03CRV3071.

Complexes of porphyrins with metals as perspective ionophores for anion-selective electrodes with improved selectivity: 02M163.

Conformational and linkage isomerizations for dihapto-coordinated arenes and aromatic heterocycles: controlling the stereochemistry of ligand transformations: 04CCR(248)853.

Coordination copper compounds with N- and N, S-heterocycles: 03MI106.

Copper carbene complexes with N-heterocyclic ligands as advanced catalysts: 03AG(E)1088.

Copper-catalyzed allylic oxidation with complexes of peresters (oxazole derivatives as ligands): 02T845.

Criptands as ligands of lanthanide coordination complexes: 02CRV1977.

Cyclic chiral aminophosphine and phosphinite ligands in enantioselective catalysis: 03CCR(242)145.

Derivatives of oxazolines, pyridines and phosphabicyclic compounds as chiral thioether ligands for asymmetric catalysis: 03CCR(242)159.

Design of chiral catalysts for asymmetric epoxidation of olefins: 04MI50.

Development of the first spiro bis(isoxazoline) ligands and their applications to catalytic enantioselective reactions: 04YGK59.

Electrochemical and photochemical control of host–guest complexation at surfaces (macroheterocycles as host molecules): 03AG(E)4860.

Electronic interactions in metallated polythiophenes: 03CCR(246)89.

Electron-rich P,N-heterocycles as ligands in metallocomplex catalysts: 03S2437.

Electron transfer by copper complexes with imidazole and polypyridines: 04CRV651.

Enantioselective addition of allylic organometallic reagents to aldehydes and ketones using heterocycles as ligands: 03CRV2763.

Enantioselective copper-catalyzed conjugate addition with heterocycles as ligands: 02EJO3221.

Femtosecond absorption spectroscopy of transition metal charge-transfer complexes with polypyridines: 03ACR876.
Ferrocenes functionalized by azamacrocycles, porphyrins, calixpyrroles, and imidazoles as anion complexation agents: 03CCR(240)167.

Functionalized gold nanoparticles chemisorbed by oligothiophenes as π-ligands and their networked structures: 04YGK447.

Heterocyclic ligands in catalysts of stereoselective cyclopropanation: 03CRV977.

Heterocycles as ligands in homogeneous transitional metal catalysts: 02IZV854.

Heterocyclic ligands in catalysts of enantioselective radical processes: 03CRV3263.

Heterocycles as ligands in sequestering agents for plutonium and other actinides: 03CRV4207.

P- and N-heterocycles as ligands in asymmetric reactions catalyzed by metal complexes: 04UK1269.

P-heterocycles and phosphorus derivatives of heterocycles as new chiral ligands for enantioselective hydrogenation: 03CRV3029.

Heterocycles as ligands in molybdenum catalysts for asymmetric allylic alkylations: 04ACR159.

N-heterocycles as ligands in high-turnover palladium catalysts for cross-coupling and Heck chemistry: 04MI47.

Heterocycles as ligands in rhodium catalysts for olefin-oxygenation: 04AG(E)4142.

P-heterocycles, bisisoquinolines, bipyridines, and bis(2-imidazole)biphenyls as achiral and meso ligands to convey asymmetry in enantioselective catalysis: 03CRV3297.

O-, N-, and P-heterocycles as ligands in chiral lanthanide complexes: 02CRV1807.

Heterocyclic ligands derived from carbohydrates for asymmetric catalysis: 04CRV3189.

Heterogeneous enantioselective catalysts with heterocycles, mainly oxazoline derivatives, as ligands in aziridination reactions: 04CSR108.

High-symmetry cage complexes containing pyrazole and pyridine rings: 02ACR972.

Lanthanide complexes of porphyrins and phthalocyanins as liquid crystals and surfactants: 02CRV2303.

Macrocyclic amides as anion receptors based on directed hydrogen-bonding interactions: 03CCR(240)101.

Metal complexes from aryl and hetarylazocompounds: 04MI48.

Metal complexes with N-heterocyclic ligands as solid-state hosts with modular functionality: 03CCR(246)169.

Metal complexes of hexaazatriphenylene (hat) and its derivatives: 03CCR(246)73.

Oxo transfer reactions of perchlorate and other substrates catalyzed by rhenium oxazoline and thiazoline complexes: 03CC2102.

Peptide/metal–ligand hybrids (pyridines and bipyridines as ligands) for the metal-assisted stabilization of peptide microstructures: 03S1307.

Phosphacycles and phosphino-substituted heterocycles as chiral ligands in asymmetric catalysis: 03MI107.

Polycatenation, polythreading and polyknotting in coordination network chemistry (complexes with N-heterocyclic ligands): 03CCR(246)247.
Poly-nuclear Ru complexes with pyrazine and 4,4'-bipyridine “bridges”: 03CCR(238–239)127.

Predetermination of chirality at octahedral centres with tetradentate (particularly, pyridine) ligands as a prospect for enantioselective catalysis: 03CCR(242)125.

Pyrrole derivatives and P-heterocycles as ligands in non-cyclopentadienyl organo-lanthanide complexes: 02CRV1851.

Rational design of coordination compounds of metals with azomethine ligands: 02UK1064.

Reactivity of dioxygen–copper systems with N-heterocycles as ligands: 04CRV1047.

Ru catalysts with phophetane chiral ligands in asymmetric hydrogenation: 03ACR908.

Scandium complexes with phospha- and borabenzenes, azamacrocycles, pyrazoles, porphyrins: 03CC1797.

Spin-state control in cobalt(II) complexes of pyridazine- or triazole-containing ligands: 03CCR(245)17.

Stereoselective epoxidation of alkenes, desymmetrization of meso-N-sulfonylaziridines, Baeyer–Villiger oxidation of cyclobutanones, Diels–Alder reactions of 1,2-dihydropyridines, and polymerization of lactides using metal complexes of chiral binaphthyl Schiff-base ligands: 03CCR(242)97.

Structural diversity of building blocks in complexes of M(NO₃)₂ with bipyridyl ligands: 03CCR(246)145.

Structure and spectroscopy of copper–dioxygen complexes with N-heterocycles as ligands: 04CRV1013.

Structure and function of metallosupramolecular squares with N-heterocycles as ligands: 04CSR133.

Structures of enantiopure ruthenium trisdiimine complexes with polypiridines, phenanthroline and other N-heterocycles: 03CCR(242)47.

Syntheses and characterization of new N,S-macroheterocyclic ligands: 03CCR(245)65.

Syntheses of metal complexes with porphyrins and bipyridines as mimetics of natural photo systems: 03CCR(245)139.

Syntheses and applications for asymmetric reactions of chiral transition metal Lewis acids bearing bis(oxazolinyl)phenyl as an anionic pincer ligand: 03YGG343.


Synthetic routes to homoleptic and heteroleptic tris(diimine)ruthenium(II) complexes incorporating bidentate imine ligands and used, particularly, as photosensitizers in transformations of solar energy to chemical or electric energy: 04CCR(248)1329.

e. Polymers. Alkylsulfonylarylene and thioarylene polymers containing heterocyclic fragments derived from sulfonium electrophiles: 03BCJ15.

Aromatic condensing polymers with fragments of benzimidazole or quinoxaline as base in electrolytic proton-conducting membranes: 02UK862.
Carbohydrate reagents in the syntheses of conjugated polymers containing heterocyclic fragments: 02S1147.

Cationic complexes of Pd$^{II}$, Ni$^{II}$, and Ru$^{II}$ in syntheses of alternating copolymers of CO with heterocyclic vinylic monomers: 02IZV1475.

Construction and functions of supramolecular polymers including heterocyclic molecules, polyrotaxanes, and catenanes: 04YGK464.

Coumarins in polymers: from light harvesting to photo-cross-linkable tissue scaffolds: 04CRV3059.

Di- and tetraphenylsilyl-containing heterochain and heterocyclic polymers such as poly-1,3,4-oxadiazoles, poly-4-phenyl-1,2,4-triazoles, polynaphthylenebenzimidazoles, etc.: 04MI54.

Features of photoluminescence of polyvinylcarbazole doped by polymethine and xanthene dyes: 02MI65.

Functional porous coordination polymers with heterocycles as ligands: 04AG(E)2334.

Polydiaminophenazine, polyquinoxaline, polydiaminopyridine, polyphenothiazine as novel multifunctional polymers from aromatic diamines by oxidative polymerizations: 02CRV2925.

Polyimides in creating modern structural composition materials: 03MI109.

Polymers with phenylquinoxaline fragments: 04IZV1739.

Sensors and sensor arrays based on conjugated polymers containing fragments of crown ethers and thiophene rings in a main chain: 02PAC1753.

Syntheses, chemical properties, and applications of $\pi$-conjugated polymers bearing electronic and optical functionalities (mainly heterocyclic fragments) by organometallic polycondensations: 03SL425.

Syntheses, properties, and applications of porphyrin polymers: 04MI55.


Artificial ionic channels based on crown ethers, O-, and S-calixarenes: 03UK1190.

Aziridines and oxazolines as valuable intermediates in the synthesis of unusual amino acids: 03ACA39.

Control of the magnetic and optical properties in molecular compounds containing heterocyclic, in particular, porphyrinic fragments by electrochemical, photochemical, and chemical methods: 03BCJ443.

Crown ethers, pyridinium salts, pyridines, cyclic amines, and alkaloids as polymer-supported organic catalysts: 03CRV3401.

Fluorogenic and chromogenic chemosensors and reagents for anions based on aromatic heterocycles (phenanthridine, calixpyrroles polypyridines, etc.): 03CRV4419.

Heterocycles as analytical reagents in spectrophotometric methods for the determination of noble metals: 02ZAK1158.

Heterocyclic amines, natural heterocycles as tin-free anti fouling reagents: 03CRV3431.

Heterocyclic compounds as ionic liquids: 03MI60.
sym-Triazine derivatives and sulfurized terpenes as components of additives to lubricating oils: 02MI64.

Preparation and properties of cyclic nitroxide radical compounds directed toward spin systems with multiple properties: 03YGK670.

C. SPECIALIZED HETEROCYCLES

Cyclization of 2-halobenzoyl chlorides with binucleophiles as a convenient method for the construction of bi- and polycyclic N-, O-, and S heterocycles: 04IZV1091.


1. Nitrogen Heterocycles (Except Alkaloids)

a. General Sources and Topics. Basicity and nucleophilicity of aryl-containing N-anions formed by some N-heterocycles including cyclic carboxamides and triazolidinediones: 02ZOR1767.


N-heterocyclic germynes and related compounds: 04CCR(248)411.

Supramolecular compounds of cucurbituril and chalcogenide cluster aquocomplexes of molybdenum and tungsten: 03IZV987.

c. Reactivity. Benzannulated N-heterocycles as substrates in aromatic nucleophilic substitution in phase-transfer systems: 02M158.

Catalytic redox processes involving hydrocarbymetal (N-heterocyclic carbene) complexes and associated imidazolium salts: 04CCR(248)671.

Deprotonating functionalization of N-heteroaromatic compounds with phospha- zene base: 04YZ509.

Fluorous technologies for reactions with participation of N-heterocycles: 03T4475.

Generation and reactions of organic radical cations in zeolites, particularly, reactions of N-heterocycles: 02CRV3947.

Homogeneous catalytic applications of chelate and pincer N-heterocyclic carbenes: 04CCR(248)2239.

N-heterocycles as amination agents in reactions of olefins and alkynes: 02SL1579.

N-heterocyclic carbenes as reagents: 04AG(E)5130.

N-heterocyclic carbenes in organometallic catalysis: 02AG(E)1290.

Hydrogen-bonding-induced phenomena in bifunctional heteroazaaromatics: 03ACR832.

Intermolecular electron transfer reactions of N-heterocycles: 02ACR247.

Methods for oxidation of N-heterocycles: 02MI32.

New reactions in the field of N-heterocycles found by the Dr. M. Ikeda group: 04YZ165.
Nucleophilic chiral cyclic amines as catalysts in asymmetric synthesis: 03CRV2985.
Phenyliodonium derivatives of N-heterocycles and CH-acid compounds, their syntheses and application in chemistry of heterocycles: 03KGS1769.
Reactions of nitrogen-containing heterocyclic compounds using iodosyl reagents: 02M159.
Sequential metathesis in azanorbornene derivatives: 03EJO611.
Stability and reactivity of N-heterocyclic carbene complexes: 04CCR(248)2247.
Substitution and addition reactions of nitrogen-containing analogs of 5-nitro-1,3-dioxanes: 02M120.

**d. Synthesis.** Acylaminosubstituted vinylphosphonium salts in the syntheses of derivatives of N-heterocycles: 02ZOB1764.
Acylpyruvic acids in the syntheses of N-heterocycles: 03MI16.
Acylpyruvic acids in the syntheses of O- and N-containing heterocycles: 03MI39.
Arylcyclopropanes in the syntheses of N-containing heterocycles: 03KGS1123.
Asymmetric electrophilic α-amination of carbonyl groups in syntheses of α-amino acids and N-heterocycles: 04EJO1377.
Azadienes in the syntheses of four-, five- and six-membered heterocycles: 02T379.
Barbituric acids in the syntheses of N-heterocycles: 03MI19.
N-tert-butanesulfanyl imines as versatile intermediates for the asymmetric synthesis of cyclic amines: 02ACR984.
Carbamates and their derivatives in the syntheses of N-heterocycles: 03MI29.
Catalysts for hetero Diels–Alder reactions of imines: 03MI89.
Chiral heterocycles by iminium ion cyclization: 04CRV2311.
Chloramines-T as a nitrogen source in new aziridination of alkenes and in pyrrolidine syntheses from 1,6-dienes and 4-alkenyl iodides: 03YGK706.
Cyclizations of N-acyliminium ions: 04CRV1431.
Cyclocondensation of aromatic and heteroaromatic 1,2-diamines with α,β-unsaturated carbonyl compounds: 03MI10.
Cyclocondensations of 1,3-dicarbonyl compounds in syntheses of O-, N-, and S-heterocycles: 03MI43.
Fischer carbene complexes in stereoselective syntheses of N-heterocycles through [3+2] cycloaddition: 02PAC1317.
Formation of five-membered S,N-heterocycles by 5-endo-trig radical cyclizations: 02S695.
Free radical methods for the synthesis of lactams: 00M15.
Functionalization of anthra- and naphthaquinone derivatives annulated by five- to seven-membered N,O-heterocycles: 03MI32.
Guanidines in the syntheses of N-heterocycles: 03MI24.
Homoallylamine-based syntheses of N-heterocycles including azetidines, pyrrolidines, azepines, quinolines: 02JHC595.
Hyaluronate halides as building blocks for the synthesis of arylazo heterocycles: 03JHC725.
Oxime ethers from (R)- or (S)-O-(1-phenylhydroxylamine) in asymmetric syntheses of N-containing compounds, in particular, of piperidine alkaloids, lactams, five- to eight-membered N-heterocycles: 04CC1341.
Radical translocation/cyclization reactions in syntheses of bridged azabicyclic compounds: 03H(59)429.

Reactions of intramolecular hydroamination of alkenes, alkynes, and allenes with the formation of N-heterocycles in the presence of lanthanocene catalysts: 02CRV2161.

Stereo- and regiocontrol in the formation of lactams by rhodium-carbenoid C–H insertion of α-diazoacetamides: 04EJO3773.

Stereoselective syntheses of substituted cyclic amines by acid-catalyzed cyclization of vinylsilanes bearing an amino group: 03SL143.

Syntheses and reactions of heterocyclic compounds including a fragment of 1-aminocyclopropane-1,2-dicarboxylic acid: 03UK379.

Synthesis and biological activity of aza-heterocyclic phosphonates: 04CRV6177.

Syntheses of aza-heterocycles from oxime derivatives: 03PAC19.

Syntheses and applications of benzosultams: 02H(56)693.

Syntheses of biologically active furyl-substituted and nitrogen-containing 1,3-diheteracycloalkanes: 02MI21.

Syntheses of nitrogen-containing heterocycles by ring-closing metathesis: 04CRV2199.

Syntheses of N- and N,O-heterocycles by reactions of olefins with nitrogen oxides and other nitrosating and nitrating reagents: 03UK363.

Syntheses of N-heterocycles by cyclization of bis(nucleophiles) with oxalidiimidoyl dichlorides: 02EJO221.

Syntheses of N-heterocycles by the linked Pummerer–Mannich ion cyclization: 02SL851.

Syntheses of N-heterocycles via palladium-catalyzed reactions of alkynes with organic halides or triflates: 02H(58)667.

Syntheses of heterocycles from alkyl 3-(dimethylamino)propenoates and related enamiones: 04CRV2433.

Syntheses of N,N-linked bisaza-heterocycles: 02S1311.

Traceless solid-phase syntheses of hydantoins, benzimidazoles, indoles, and diketopiperazines: 02CRV2607.

Unsaturated N-heterocycles from carbohydrate feedstocks: 02ACR728.

2. Oxygen Heterocycles

a. Chemistry of Individual Classes of O-Heterocycles. Cyclic acetals and related compounds as inhibitors of corrosion of metals: 02MI23.

Formation and transformations of endoperoxides and diepoxides using reversible binding of oxygen to aromatic compounds: 03ACR668.

Removing dioxolane and oxathiolane-protecting groups using the CeCl₃·nH₂O/NaI system as an efficient water-tolerant Lewis acid: 03SL2101.

Syntheses and transformations of 6,8-dioxabicyclo[3.2.1]octane skeletal system: 03SL1759.

Syntheses, stereochemistry, rate of formation, properties, and applications of 2-furyl-1,3-dioxacyclanes: 02MI14.

Syntheses, structure, and application of sugar spiroorthioethers: 02YGK206.
b. Reactivity. Asymmetric alcoholysis of cyclic anhydrides: 03CRV2965.
Benzannulated O-heterocycles as substrates in aromatic nucleophilic substitution in phase-transfer systems: 02MI158.
Catalytic liquid-phase transformations of 1,3-dioxacycloalkanes: 02MI122.
5-Nitro-1,3-dioxanes in substitution and addition reactions: 02MI120.
Reactions of cyclic acetals with carbenes 02MI118.
Reduction of cyclic acetals and orthoethers with organoaluminum reagents: 02MI117.
Sequential metathesis in oxanorbornene derivatives: 03EJO611.
Thermolysis of organic peroxides including dioxiranes, dioxetanes, and cyclic trioxides: 03UK1055.
Transformations of 1,3-dioxacycloalkanes by the action of organic and inorganic oxidants: 02MI119.
Transition metal-catalyzed enantioselective ring-opening reactions of oxabicyclic alkenes: 03ACR48.

Application of microwave radiation in the syntheses of cyclic acetals and their heteroanalogs: 02MI115.
Arylcyclopropanes in the syntheses of O-containing heterocycles: 03KGS1123.
Asymmetric Baeyer–Villiger oxidation of prochiral ketones to optically active lactones: 04IZV1784.
Cycloaddition reactions of vinyl oxocarbenium ions with the formation of O-heterocycles: 03T2371.
Cyclocondensations of 1,3-dicarbonyl compounds in the syntheses of O-heterocycles: 03MI143.
Cyclohexadienone ketals and quinols as building blocks in the syntheses and reactions of O-heterocycles, mainly epoxidation, and syntheses of biologically active compounds: 04CRV1383.
Flavin-dependent monooxygenase-mediated Baeyer–Villiger oxidations leading to chiral lactones: 02EJO3711.
Formation of lactones, lactoles, muconic acids, and their derivatives by oxidative degradation of benzene rings: 03T1105.
Formation of polychlorinated dibenzo-p-dioxins and dibenzofurans during municipal solid waste incineration and other combustion processes: 03ACR652.
Free radical methods for the synthesis of lactones: 00M15.
Functionalization of anthra- and naphthaquinone derivatives annulated by five- to seven-membered N,O-heterocycles: 03MI132.
Peroxo Mo and W complexes catalyzed oxidation of alcohols and olefins with hydrogen peroxide to form oxiranes and lactones: 03MI105.
Progress in selective iodolactonization: 03MI88.
Progress in the synthesis of 1,3-dioxanes: 02MI116.
Stereoselective syntheses of substituted cyclic ethers by acid-catalyzed cyclization of vinylsilanes bearing an hydroxy group: 03SL143.

Syntheses and reactions of cyclopropenone acetals (mainly cyclic acetals): 03CRV1295.

Syntheses and uses of exo-glycals: 04CRV263.

Syntheses of biologically active furyl-substituted and nitrogen-containing 1,3-diheteracycloalkanes: 02M121.

Syntheses of O-heterocycles, particularly, γ-lactones by radical cyclizations in aqueous media: 02SL674.

Syntheses of oxygen-containing heterocycles by ring-closing metathesis: 04CRV2199.

Syntheses, physical and chemical properties, and technology of production of epichlorhydrin: 03MI85.

Unsaturated O-heterocycles from carbohydrate feedstocks: 02ACR728.

Use of the Baeyer–Villiger reaction for the oxidation of cycloalkanones to lactones: 04CRV4105.

3. Sulfur Heterocycles


Syntheses and reactions of cyclic polysulfides: 02CRV3905.

Syntheses and reactivity of cyclic sulfamidites and sulfamidates: 03T2581.


Intermolecular electron transfer reactions of S-heterocycles: 02ACR247.

Removing dithiolane- and oxathiolane-protecting groups using CeCl₃·nH₂O/NaI as an efficient water-tolerant Lewis acid: 03SL2101.

Synthesis and utilization of chiral sulfoxides (enantioselective sulfoxidation of S-heterocycles and derivatives of other heterocycles): 03CRV3651.

c. Synthesis. Asymmetric synthesis of C₂-symmetric bis(sulfoxides), among them cyclic bis(sulfoxides): 02EJO3507.

Catalytic syntheses of some S-heterocycles: 02KGS579.

Cyclocondensations of 1,3-dicarbonyl compounds in the syntheses of S-heterocycles: 03MI43.

Formation of five-membered S,N-heterocycles by 5-endo-trig radical cyclizations: 02S695.

Formation of S-heterocycles mediated by sulfonate- and sulfonamide-stabilized carbanions: 03EJO3713.

Free radical methods for the synthesis of thiolactones: 00MI15.

2-Substituted 1-haloethane-2-thiones and -2,2-dithiols as precursors of heterocyclic systems: 03MI65.

Sulfur-containing heterocycles from 1,2-diaza-1,3-butadienes: 03MI64.

Synthesis and applications of benzosultams: 02H(56)693.
Syntheses of \( S \)-heterocycles on the basis of isothocyanate derivatives of perfluoroolefines: 02KGS147.

Syntheses of \( S \)-heterocycles (thiazepines, thiazinones and other) using metalated sulfonamides: 02SL1181.

Syntheses of \( S \)-heterocycles using tetrathiomolybdate: 02SL1762.

Syntheses of sulfur heterocycles via ring-closing olefin metathesis: 04CRV2239.

D. NATURAL AND SYNTHETIC BIOLOGICALLY ACTIVE HETEROCYCLES

We have classified the many reviews dealing with these materials under following headings:

1. General Sources and Topics (it is self-subdivided into Biological Functions, Syntheses).
2. Alkaloids (General, Syntheses, Individual Groups).
3. Antibiotics (General, Antitumor, \( \beta \)-Lactam, Macrocyclic, Miscellaneous).
4. Vitamins.
5. Drugs (General, Activity Types, Individuals and Groups).
6. Pesticides.
7. Miscellaneous (Enzymes, Amino Acids and Peptides, Plant Metabolites, Marine, Cyclodextrins, Other).

1. General Sources and Topics

Analytical chemical studies on high-performance recognition and detection of biomolecules in life: 03YZ901.

Betainic alkaloids and nucleobases: 03AHC(85)67.

Comparative QSAR at the interface between chemistry and biology (chem-bioinformatics): 02CRV783.

Ecological problems of heterocycles: 02MI31.

History of the research on deoxylfluoroglucose, a milestone in the development of positron emission tomography: 02CL704.

cis–trans Isomerization of biomolecules: 03CRV2475.

MATRIX, a new algorithm for the prediction of biological activity of organic molecules based on multidimensional analysis of physicochemical descriptors of modern drugs: 02ZOR1618.

Naturally occurring halogenated pyrroles and indoles: 03PHC56.

Nitrosubstituted heteroaromatic compounds as environmental pollutants with carcinogenic potential for humans: 02CL784.

\( O \)- and \( S \)-heterocycles as donors of oxygen oxide and inhibitors of NO-synthases. 03MI66.

QSAR prediction of environmental toxicity of oxygen- and sulfur-containing heterocycles. 03MI67.

Recognition and sensing of chiral biological substrates via lanthanide coordination chemistry using complexes with porphyrins: 02CCR(226)227.
a. **Biological Functions of Natural and Synthetic Bioactive Heterocycles.** Biological radical sulfur-insertion reactions: 03CRV2149.

Biologically active terpenoids, phenols, and antibiotics from mushrooms in Yunnan, China: 02H(57)157.

Biosynthesis, synthetic analogs, and biological activity of phenazine natural products: 04CRV1663.

*Bis* (μ-oxo)dimetal “diamond” cores in copper and iron complexes with heterocycles as ligands relevant to biocatalysis: 02AG(E)1114.

Chemical activities and biological applications of diazetidines, furoxans, triazolominines, guanidines and other heterocycles as nitric oxide donors: 02CRV1091.

Chemistry and biology of biosynthetic Diels–Alder reactions: 03AG(E)3078.

Chemosensors based on quinoline or *bis*(2-pyridylmethyl)amine and biosensors based on peptides, proteins, and nucleic acids for fluorescent detection of zinc in biological systems: 04CCR(248)205.

Heterocycles as fluorescence probes for the analysis of mono- and oligosaccharides: 03M194.

Heterophanes, β-lactams, polymers including pyrrole rings, etc. as components of hybrid systems through natural product leads: 02CSR324.

Lanthanide complexes with heterocyclic ligands in molecular recognition and chirality sensing of biological substrates: 02CRV2389.

Macroheterocycle–aromatic ring interactions in chemical and biological recognition: 03AG(E)1210.

Molecular mechanics and molecular dynamics simulations of porphyrins, metalloporphyrins, heme proteins, and cobalt corrinoids: 02CCR(225)123.

Natural products in the synthesis of chiral organophosphorus ligands with heterocyclic fragments: 03UK902.

Prospects of genetic code engineering using unconventional amino acids: 04AG(E)6426.

Resonance Raman spectra and biological significance of high-valent iron(IV,V) porphyrins: 02CCR(226)153.

Solid-phase methods of tritium probe introduction: 03UK471.

Sources, biological activities, and syntheses of naturally occurring cyclohexane epoxides: 04CRV2857.

Structure and interaction of cyclodextrins and their complexes: 02CL693.

Synthetic models for the active site of cytochrome P450: 02CCR(226)219.

b. **General Approaches to Syntheses of Biologically Active Heterocycles.** Acid-catalyzed rearrangement of epoxy alcohol derivatives protected by electron-withdrawing groups in asymmetric syntheses of natural products with chiral quaternary carbon and spiro centers: 03YGK133.

Advances in the synthesis of *trans*-fused polycyclic ethers by hydroxy-epoxide cyclization and ether-ring-expansion reactions: 04BCJ2129.

Applications of the allylation reaction to the synthesis of natural products: 00M110.
Applications of asymmetric transition metal-catalyzed allylic alkylations in total synthesis: 03CRV2921.

Application of a hetero Diels–Alder reaction of imines in the syntheses of natural products: 03MI96.

The asymmetric intramolecular Heck reaction in total syntheses of terpenoids and alkaloids: 03CRV2945.

Birch reduction and its application in the total syntheses of natural products: 03PAC1443.

Combinatorial biosynthesis, a new genetic tool for preparing polyketide natural products: 04YGK1095.

Control of regiochemistry of radical cyclizations in the synthesis of physiologically active N-heterocycles: 04YGK325.

Diels–Alder reactions in total synthesis: 02AG(E)1668.

Enantioselective total syntheses based on asymmetric catalysis including total synthesis of strychnine, asymmetric epoxidation of \( \alpha,\beta \)-unsaturated acid derivatives, and ring opening of oxiranes: 04CPB1031.

Methods for the synthesis of (\( E \))-alkene units in \( O \)-macroheterocyclic natural products: 03AG(E)2826.

Progress in the synthesis of NADH and some bioactive porphyrin derivatives: 02MI40.

Perspectives on the total synthesis of antibiotics and other natural biologically active compounds: 03T6683.

Progress in the total syntheses of styrylactone natural products: 03MI95.

Recent achievements in biomimetic organic syntheses: 04AG(E)160.

Recent progress in the syntheses of natural cyclic tetrapyroles: 04MI31.

The role of 1,3-dithianes in natural product syntheses: 03T6147.

Samarium(II)-iodide-mediated cyclizations in natural product syntheses: 04CRV3371.

Stereoselective aldol reactions in the syntheses of polyketide natural products: 00MI8.

Syntheses and properties of allenic natural products and pharmaceuticals: 04AG(E)1196.

Syntheses of natural \( O \)-heterocycles using ring-contraction reactions: 02T9-137.

Syntheses of azaspiro[4.4]nonanes as key structures of several bioactive natural products: 04S2249.

Syntheses of natural compounds and \( S \)-heterocycles by the thio-Claisen rearrangement: 03T7251.

Syntheses of natural compounds and their precursors including fused \( \beta \)-lactams, indole alkaloids, metabolites of marine origin, enzyme inhibitors, and biologically active depsipeptides: 04ACR687.

Syntheses of optically active pheromones, hormones, and other bioregulators: 04YGK2.

Synthetic efforts toward the phomoidrides, biologically active \( O \)-heterocycles: 03CRV2691.
Synthetic methodology and total syntheses of nitrogen-containing natural products, such as the antibiotic 593A, β-lactams, indole alkaloid vincadifformine, po-rothramycin B, vindolin, vinblastin: 03YGK620.

Tandem reactions, cascade sequences, and biomimetic strategies in total synthesis: 03CC551.

The total syntheses of phorboxazoles: 03AG(E)2711.

2. Alkaloids

a. General. Alkaloids and their role in nature: 02MI12.
   Asymmetric organic catalysis with modified Cinchona alkaloids: 04ACR621.
   Biotransformation of alkaloids: 01M134, 02H(56)711, 02MI24.
   Heterogeneous enantioselective hydrogenation over Cinchona alkaloid modified platinum: 04ACR909.
   Morphine, the Proteus of organic molecules: 02CC1159.

b. Synthesis. Advances in the total synthesis of piperidine and pyrrolidine natural alkaloids with ring-closing metathesis as a key step: 03EJO3693.
   Asymmetric syntheses of isoquinoline alkaloids: 04CRV3341.
   Asymmetric syntheses of polyfunctionalized pyrrolidines and related alkaloids: 04SL2670.
   Biogenetically patterned syntheses of monoterpenoid indole alkaloids from secologanin and its derivatives: 03MI97.
   Current topics in biomimetic alkaloid syntheses: 02YGK350.
   Heterocyclic derivatives of ephedrine alkaloids: 03MI50.
   Iminophosphorane-based methodologies (aza-Wittig reaction) in the syntheses of β-carboline, pyrimidine, oxazole, and imidazole alkaloids: 04SL1.
   Mannich and related reactions in total syntheses of alkaloids: 04CL1096.
   Progress in syntheses of pumiliotoxin alkaloids: 04MI32.
   Pyridine and piperidine strategies of syntheses of the Sedum and related alkaloids: 02T5957.
   SmI$_2$-induced cyclizations with participation of indole and pyrrole derivatives in stereoselective syntheses of alkaloids: 04SL422.
   Spiro[pyrrolidine-3,3'-oxindoles] construction in the syntheses of oxindole alkaloids: 03EJO2209.
   Syntheses of (−)-physostigmine: 02H(57)1327.
   Syntheses of pyrrolidine alkaloids via [3 + 2] cycloadditions: 02PAC1339.
   Syntheses of pyrrolo[1,2-b]pyrazole alkaloid vitasomnin and its structural analogs: 03MI21.
   The tethered Biginelli condensation in the syntheses of guanidine alkaloids: 04CC253.
   Use of radical cyclizations to form the indole system in total syntheses of alkaloids: 03YZ1007.
Vinylogous Mannich reaction with participation of N- and O-heterocycles in alkaloid syntheses: 02ACR895.

c. Individual Groups of Alkaloids. Acridone alkaloids: 00MI4.
Alkaloids of the Menispermaceae: 00MI12.
Amphibian skin as a remarkable source of biologically active arthropod alkaloids: 03JMC445.
Chemical and biological aspects of melanin: 03MI83.
Chemistry and biology of roseophilin and the prodigiosin alkaloids: 03AG(E)3582.
Chemistry and pharmacology of analgesic indole alkaloids from the Rubiaceous plant, Mitragyna speciosa: 04CPB916.
Clinical studies of camptothecin and derivatives: 03MI79.
Daphniphyllum alkaloids, unique ring systems with an azaadamantane fragment, and biogenetic path to: 03MI80, 03YGK35.
C20-diterpenoid alkaloids: 02MI26.
Ellipticine, uleine, apparicine, and related alkaloids: 01MI37.
History, chemistry, and biology of alkaloids from Lobelia inflata: 04T10127.
HPLC–MS and CE–MS with atmospheric pressure ionization in analyses of morphine and related compounds: 04CL336.
Ibogaine and Iboga alkaloids, occurrence, biochemistry, physiological, pharmacological, and medicinal aspects: 01MI18, 01MI19, 01MI20, 01MI21, 01MI22, 01MI23, 01MI24, 01MI25, 01MI27, 01MI26, 02MI27, 01MI28, 01MI29, 01MI30, 01MI31, 01MI32, 01MI33.
Indole alkaloids from Strychnos species and their anti-plasmodial and cytotoxic activities: 03KPS425.
Isolation and synthesis of biologically active carbazole alkaloids: 02CRV4303.
Isoniazid alkaloids: 01MI36.
The manzamine alkaloids: 03MI81.
Nitrogen-containing metabolites from marine cyanobacteria: 01MI35.
Putrescine, spermidine, spermine, and related polyamine alkaloids: 02MI25.
Quinoline alkaloids of Turkish Papaver species: 02PAC557.
Recent advances in Cinchona alkaloid chemistry: 04EJO4293.
Recent synthetic studies on the ergot alkaloids and related compounds: 00MI13.
Sesquiterpene pyridine alkaloids: 03MI82.
Studies on the total synthesis of batrachotoxins (steroid alkaloids found in the skin of frogs of the Phyllobates species and the feathers of birds of the Pitohui and Iflíta families from New Guinea): 04YGK1205.
Syntheses of the pyrrole–imidazole alkaloids: 03S1753.
Synthetic approaches to carnegine, a simple tetrahydroisoquinoline alkaloid: 04T10575.
Tremorgenic and nontremorgenic 2,3-fused indole diterpenoids: 03MI80.
Total syntheses of biologically important alkaloids and design of leading compounds for new pharmaceuticals: 03Y225.
Total synthesis of gelsemine: 03AG(E)36.
Two new types of polyhydroxylated alkaloids containing dihydroxypyrrolidine moieties as glycosidase inhibitors from higher plants: 02H(57)1539.

3. Antibiotics


   Syntheses of chemically modified glycopeptide antibiotics related to vancomycin and fight against vancomycin resistance: 03YGK752.
   Synthesis of cryptophycin: 02T4343.
   Total synthesis of the potent anti-tumor alkaloid ecteinascidin: 03YGK949.
   Total synthesis of streptonigrin and related antitumor antibiotics with quinoline and pyridine fragments: 04T3539.
   Total synthesis of vancomycin: 02YGK240.


d. Macrocyclic Antibiotics. Ability of valinomicin to form complexes with neutral molecules: 02SL201.
   Chemistry and biology of rhizoxins, novel anti-tumor macrolides from Rhizopus chinensis: 04T5653.
   Progress in the synthesis of clarithromycin (antibiotic from erythromycin group): 02MI42.

e. Miscellaneous Antibiotics. Analytical methods for the determination of polyether antibiotics: 03CL146.
   Chemistry and biology of the leptomycin family: 02S981.
   Chemistry of structurally confused kinamicins (antibiotics with benzo[b]carbazoloquinone skeleton): 04YGK49.
   Syntheses of indolizidine and diazatricyclic mazangamine alkaloids using cyclic N,O-acetals: 03YGK868.
   Synthetic studies on structurally novel bioactive nine-membered cyclic enediyne with an annulated oxirane fragment: 04YGK226.
   Total synthesis and absolute stereochemistry of the DNA-cleaving nine-membered enediyne antibiotic N1999-A2: 04YGK184.

4. Vitamins

L-Ascorbic acid biosynthesis: 01MI14.
Biosynthesis of biotin and lipoic acid: 01MI18.
Biosynthesis of calcitriol (dihydroxy vitamin D): 01MI17.
Biosynthesis of coenzyme A in bacteria: 01MI11.
Biosynthesis of folate: 01MI17.
Biosynthesis of menaquinone (vitamin K₃) and ubiquinone (coenzyme Q): 01MI12.
Biosynthesis of methanogenic cofactors: 01MI16.
Biosynthesis of molybdopterin guanine dinucleotide: 01MI17.
Biosynthesis of nicotinamide adenine dinucleotides in bacteria: 01MI19.
Biosynthesis of pyrroloquinoline quinone: 01MI17.
Biosynthesis of retinal: 01MI17.
Biosynthesis of riboflavin: 01MI17.
Biosynthesis of thiamin pyrophosphate in *Escherichia coli*: 01MI17.
Biosynthesis of tocopherol (vitamin E): 01MI17.
Biosynthesis of vitamin B₆ and structurally related derivatives: 01MI10.

Historical development and recent synthetic innovations in the total synthesis of cobyric acid, a vitamin B₁₂ precursor: 03EJO30.
Multiple biosynthetic pathways for vitamin B₁₂: 01MI15.

A novel and practical synthesis of (+)-biotin via the Fukuyama-coupling reaction: 03YZ43.

5. Drugs

a. General. Analysis of drugs by photometric methods: 02MI43.
Application and limitations of X-ray crystallographic data in structure-based ligand and drug design for screening: 03AG(E)2718.
Applications of biocatalysts in the preparation of pharmaceuticals: 03MI98.
Biologically active fragment-based drug discovery: 04JMC3463.
Boron-containing nucleosides, carboranyl-substituted nucleotides, porphyrins, and boron analogs of acridine in neutron-capture therapy: 04IZV1795.
Exogenous NO donors (chemical aspect): 02IZV1269.
Glycosaminio acids as building blocks for combinatorial synthesis connected with drug discovery, particularly search for glyco- and peptidomimetics: 02AG(E)231.
Green chemistry in process research and developments in the pharmaceutical industry: 03YGK464.
Histamine H³-receptors and pharmacolgical regulation of their functions by heterocyclic agonists and antagonists: 02KFZ(7)3.
Integrase inhibitors as a possible future of HIV/SPID therapy: 02KFZ(11)3.
The interactions of metal ions with quinolone anti-bacterial agents: 02CCR(232)27.
Mass spectrometry and chromatography mass spectrometry in the analysis of drugs: 02ZAK566.
Medicinal chemistry in the new millennium. A glance into the future: 02PAC703.
Medicinal chemistry of carboranes: 02CCR(232)173.
Modalities of DNA base–mercury-binding mechanisms: 04CRV5911.
Natural and synthetic substances related to human health (anti-tumor substances, antibiotics, antihistamins, dioxines): 02PAC1959.
Natural product hybrids as new leads for drugs: 03AG(E)3996.
Nitrogen oxide donors as potential drugs: 04MI12.
Photoprocesses of photosensitizing drugs within cyclodextrin cavities: 02CSR287.

QSAR studies on non-benzodiazepine compounds binding to benzodiazepine receptor: 04CRV3751.

Ruthenium complexes with porphyrines as metallopharmaceuticals: 02CCR (232)69

Selective optimization of side activities as a way for drug discovery: 04JMC1303.

Sports drug testing: 04CSR1.

Some characteristics of marketed and investigational prodrugs: 04JMC2393.

Syntheses of chiral drug substances: 02SL837.

Synthetic metalloporphyrins as biomimetic catalysts (cytochrome P450 models) in the oxidative activation of drugs: 04MI33.

Theory and applications of NMR-based screening in pharmaceutical research, in particular among heterocyclic compounds: 04CRV3641.

b. **Definite Types of Activity.**

Agenerase (a tetrahydrofuran derivative) as a new anti-HIV preparation: 02M147.

Angiotensin II, AT1 receptor antagonists, and clinical implications of active metabolites: 03JMC2261.

Antibiotic glycosyltransferases: 03JMC3425.

Antiestrogens and selective estrogen receptor modulators as multifunctional medicines: 03JMC883, 03JMC1081.

Aziridine, furocumarine, and thiazine derivatives as preparations for blood product disinfection: 02CSR128.

Chemistry and anti-tumor activity of epothilones: 04OBC2137.

Construction of the chiral quaternary carbon in the discovery directed toward 1-(4-isopropyl-4-phenyl-4-cyanobutyl)-4-[2-(n-fluorophenoxy)ethyl]piperazine, the novel neuroprotective agent E 2050: 03YGK67.

Derivatives of isoquinoline and porphyrin as new antimalarial drugs: 01PAC1173.

Design and development of substituted pyrimidine-2,4-diones as potassium channels blockers: 04YFK27.

Directed search for anti-convulsants, particularly, among azepines, furans, and pyrazoles: 04KGFZ(9)3.

Epibatidin and the problem of non-opioid analgesics: 03M123.

Haemozoin formation as a target for the rational design of new antimalarials: 04M134.

Heterocycles as agonists and antagonists of opioid receptors: 03JMC1775.

Higher-end serotonin receptors (5-HT5, 5-HT6, and 5-HT7): 03JMC2795.

Inhibitors of de novo nucleotide biosynthesis as drugs: 02ACR961.

Mechanism of action, efficiency, and safety of drugs (among them indole derivative arbidol) for therapy and prophylactic of grippe: 04KGFZ(11)8.

Mechanistic studies on artemisinin derivatives and design of new antimalarials: 02ACR167, 02ACR225.

Multi-nuclear platinum complexes with N-heterocyclic ligands as anti-cancer drugs: 03CCR(241)133.

Natural and synthetic O- and N-heterocycles as new anti-malarial drugs: 03AG(E)5274.
Natural *O*-heterocycles as *z*-glucosidase inhibitors and antioxidants: 02PAC511.

New antidiabetic vanadyl–pyridone complexes: 03CCR(245)31.

Porphyrins, thia- and selenaporphyrins, and phthalocyanines as current clinical and preclinical photosensitizers for use in photodynamic therapy: 04JMC3897.

Recent developments in the maytansinoid anti-tumor macroheterocycles with *N*,*O*-heterocyclic and oxirane fragments: 04CPB1.

5-HT4 Receptor ligands (benzimidazolones, cyclic benzamides, indole, imidazopyridine, and indazole derivatives as agonists and antagonists of 5-HT4 receptors): 03JMC319.

Synthesis of camptothecins and related alkaloids as new anti-cancer drugs: 03T8649.

Synthesis of sumanitrole, aziridine derivative used in the therapy of Parkinson’s disease: 02PAC1359.

Synthetic analogs of cocaine: 03JMC1775.

Synthetic and natural compounds as well as plants in the treatment of male sexual disfunctions: 04CL1119.

c. *Individual Substances and Groups of Compounds.* Anti-microbial activity and pharmacokinetic properties of moxifloxacin: 02MI45.

Complexes of 14-membered macrocyclic tetramines (cyclams) and their use in medicine: 04CSR246.

3D-QSAR studies on 5,6-diarylimidazo[2,1-*b*]thiazole: Selective COX-2 inhibitors: 03MI69.

Design and synthesis of nitrosoamines (derivatives of *N*-heterocycles) as nitric oxide donors: 03YGK45.

Determination of purine bases with anti-herpetic activity using HPLC: 04KFZ(7)44.

The discovery of ezetimibe, cholesterol-formation inhibitor, substituted azetidinone: 04JMC1.

Fluoroquinolones as anti-bacterial compounds and their use in the therapy of tuberculosis: 02MI46.

(4-Hydroxyypyridine-2,6-dicarboxylato)oxovanadate(V), a new insulin-like compound: 03CCR(237)13.

Inhibitors of farnesyltransferase and their possible use in cancer chemotherapy: 04JMC1869.

Macro cyclic peptides, inhibitors of serine proteases, as potential therapeutic agents: 04JMC769.

A medicinal chemistry perspective on artemisinin and related endoperoxides: 04JMC2945.

Nicotinamide and its pharmacological properties for clinical therapy: 04MI35.

Nucleoside analogs as anti-cancer agents: 03MI99.

Oxazolidinone structure–activity relationships leading to linezolid: 03AG(E)2010.

Pharmacokinetics of some benzimidazole derivatives: 02MI50.

Research and development of the free radical scavenger 3-methyl-1-phenyl-2-pyrazolin-5-one (edaravone) as a neuroprotectant: 04YZ99.
Side effect of fluoroquinolines; safety and endurability of levofloxacin as drug: 02M149.
Sparfloxacin (prolongated difluoroquinolone) as anti-bacterial preparation of wide spectrum of action: 02M144.
Synthesis and biological activities of pyrancarboxylic acid derivatives toward LPS-antagonists as antisepticemia drugs: 02YGK604.
Thiazolidinethiones as hypoglycemic preparations: 02M148.

6. Pesticides

Coumarins, flavonoids, terpenoids, etc. as leads for new herbicides and agrochemicals: 02T1631.
Ethyl 2-chloro-5-(4-chloro-5-difluoromethoxy-1-methylpyrazol-3-yl)-4-fluorophenoxyacetate as a new cereal herbicide, Pyraflufen-ethyl: 03YGK2.

7. Miscellaneous

Catechol oxidase activity of dicopper complexes with 2-(2-pyridyl)ethylamine derivatives and other N-donor ligands: 03CCR(245)191.
Chemical and catalytic mechanisms of carboxyl transfer in biotin-dependent enzymes: 02ACR113.
Comparative geometric and electronic structure of low-spin ferro- and ferrihemes as models of the bis-histidine-ligated electron-transferring cytochromes: 04CRV589.
Zn-complexes of pyrazoles and pyridinones as synthetic analogs relevant to the structure and function of zinc enzymes: 04CRV699.
Fe- and Co-complexes of pyridines and triazacyclononane as synthetic analogs of cysteinate-ligated non-heme iron and non-corrinoid cobalt enzymes: 04CRV825.
Computational studies on the mechanism of orotidine monophosphate decarboxylase: 03MI78.
Construction and synthesis of ribonucleases based on 1,4-diazabicyclo[2.2.2]octane and imidazole: 02IZV1014.
Diels–Alderase, a novel C–C bond-formation enzyme involving natural products biosynthesis: 04YGK778.
Dioxygen activation at mononuclear nonheme iron active sites (enzymes, models, and intermediates with pyridines as ligands): 04CRV939.
Electron-nuclear double resonance spectroscopy of metallocoenzymes with N- and S-heterocycles as ligands: 03ACR522.
Enzymatic transition state equilibrium and heterocyclic transition state models: 03ACR588.
Epoxides, aziridines, β-lactams as irreversible inhibitors of serine, cysteine, and threonine proteases: 02CRV4639.
Flavones, purines, pyrimidines, oxoindoles as inhibitors of cyclin-dependent kinases: 03AG(E)2122.
Functional analogs of cytochrome c oxidase, myoglobin, and hemoglobin: 04CRV561.
Heterocycles as histone deacetylase inhibitors: 03JMC5097.
\(N\)-heterocycles as protein kinase inhibitors: 03ACR462.
Heterocyclic compounds as inhibitors of enzymes and biological processes: 03AG(E)2462.
Heterocycles as cyclooxygenase inhibitors (a comparative QSAR study): 03CRV703.
Heterocycles as inhibitors of viral proteases: 02CRV4609.
Introduction of P450, peroxidase, and catalase activities into myoglobin by site-directed mutagenesis: 03BCJ1309.
Mechanism of HIV-1 protease action and search for inhibitors (with heterocyclic fragment): 03OBC5.
Mechanism of olefin epoxidation catalyzed by cytochrome P450 enzymes: 04CRV3947.
A mechanistic perspective on the chemistry of DNA repair glycosylases: 03CRV2729.
Nitropyrazoles, benzotetrazines, benzodifuroxans, diazetidines as NO donors: 02MI51.
Pyridine derivatives as A3 adenosine antagonists: 03CC2949.
Radical carbon skeleton rearrangements catalyzed by coenzyme B\(_{12}\)-dependent mutases: 03CRV2083.
Radical catalysis in coenzyme B\(_{12}\)-dependent isomerization (eliminating) reactions: 03CRV2095.
The role of soluble guanylate cyclase in mechanisms of physiological effects of NO: 02MI51.
Roscovitine and other purines as kinase inhibitors. From starfish oocytes to clinical trials: 03ACR417.
Site-specific synthetic ribonucleases based on oligonucleotide conjugates with metal-independent organic catalysts of hydrolysis of phosphodiester bonds: 02IZV1025.
Structural, spectroscopic, and reactivity models for the manganese catalases with heterocycles as ligands: 04CRV903.
Structure and function of DNA photolyase and cryptochrome blue-light photoreceptors: 03CRV2203.
Structure, mechanism, biological activity, inhibition, and synthetic utility of sulfotransferases: 04AG(E)3526.
Synthetic artificial peptidases and nucleases using macromolecular catalytic systems: 03ACR562.
Synthetic models for heme-copper oxidases: 04CRV1077.
Tetrahydrobiopterin radical enzymology: 03CRV2365.
Thiamin phosphate and coferment A as cofactors of pyruvate ferredoxin oxidoreductase: 03CRV2333.
Tyrosinase autoactivation in transformations of ortho-quinone amines to benzothiazines and indole derivatives as well as in spiro-cyclization with formation of betaines: 03ACR300.
Vanadium-containing enzymes, mainly V-complexes of pyridines: 04CRV849.

Application, structure, and related photophysical behavior of green fluorescent protein with an imidazole ring in the chromophore: 02CRV759.

Asymmetric synthesis of β-amino acids with participation of oxazolidine, furan, and pyrrole derivatives: 02MI53.

Autocatalytic radical reactions in physiological prosthetic heme modification: 03CRV2305.

Biologically active N-heterocycles as regulators of protein–DNA interactions: 03AG(E)4138.

Chemical modification via thioamide intermediates and conformation–activity relationships of an antitumor bicyclic hexapeptide: 04YGK993.

Chirality organization induced by self-assembling properties of amino acid units: 02YGK1195.

Conformationally rigid cyclic α-amino acids in the design of peptidomimetics, peptide models, and bioactive compounds: 04UK849.

Conversion of hemoprotein function by chemical modification: 02YGK573.

Cyclic amino acid derivatives with aziridine and azetidine rings, as well as proline derivatives: 02T8629.

Design and synthesis of novel bioactive peptides and peptidomimetics: 03JMC5553.

Design, synthesis, conformational analysis, and application of azabicycloalkane amino acids as constrained dipeptide mimics: 04SL1499.

Direct and indirect enzymatic methods for the preparation of enantiopure cyclic β-amino acids and derivatives from β-lactams: 04MI36.

Enantioselective synthesis of α-amino acids by phase-transfer catalysis with achiral Schiff base esters using Cinchona alkaloids as phase-transfer catalysts: 04ACS506.

Expanding the genetic code using unnatural amino acids with heterocyclic fragments: 02CC1.

Formation of C-type cytochrome: 04ACR999.

Glycosaminic acids as building blocks for combinatorial synthesis of new drugs: 02AG(E)231.

Glyoxylates as versatile building blocks for the synthesis of α-amino acid (including cyclic α-amino acids) and α-alkoxy acid derivatives via cationic intermediates: 03EJO2519.

Heterosubstituted carbocyclic α-amino acids from heterocyclic compounds: 02OPP143.

Hydroxyproline-containing plant proteins: 03KPS176.

Insulin/insulin receptor interaction: 02CL698.

Macrocyclic peptides as β-strand mimetics: 04CRV6085.

New functionalization of myoglobin by chemical modification of heme-propionates: 02ACR35.

Production of cyclic oligopeptides as secondary metabolites by freshwater cyanobacteria: 04CPB889.

Ring-closing metathesis in the synthesis of cyclic amino acids: 03ZOR1287.
Stereocontrolled construction of conformationally constrained and rigid bis(α-amino acid) derivatives including those based on pyrazine and other heterocycles: 03PAC279.

The structure–function relationship of hemoglobin in solution at atomic resolution: 04CRV1219.

Study on the synthesis of (Arg-Gly-Asp)-containing cyclopeptide and its analogs: 02MI52.

Synthesis of N-methyl-δ-amino acids using oxazolidinones: 04CRV5823.

Total synthesis of natural products containing α-substituted α-amino acid structures from aldohexoses using Overman rearrangement as the key reaction: 04YGK693.

c. Plant Metabolites. Anodic oxidation of phenols towards the synthesis of bioactive natural products containing a furan ring: 02SL533.

Biologically active higher furan terpenoids and their derivatives: 03MI71.

Biosynthesis of cyclic bromo-ethers derived from red algae: 02YGK1181.

Chemical synthesis of brassinosteroids, phytohormones with a seven-membered O-heterocycle in some of them: 02KPS99.

Chemistry and biology of terpene trilactones from Ginkgo Biloba: 04AG(E)1640.

Development of palladium-catalyzed cycloalkenylation and its application to the synthesis of natural bioactive O-heterocycles and terpenoids: 02SL1211.

Distribution, classification, structural analysis, and biological activity of phenylpropanoids (lignanes) of medicinal plants: 03KPS87.

Distribution in nature, spectral, and biological properties of neoflavones: 03KPS47.

Enantioselective synthesis of dihydrobenzofuran neolignans: 03S2595.

Flavanoids of beer as natural antioxidants: 02CL90.

Heterocyclic phytohormones, phytochromes, and sensory principles of higher plants: 03AG(E)392.

Identification and characterization of isoflavones in plant material by tandem HPLC–DAD–MS: 03CL530.

Induction of the phase-II enzyme, quinone reductase, by withanolides and norwithanolides from solanaceous species: 04MI37.

Polyestrogens from plants (secondary metabolites, among them compounds containing isoflavone and dihydro[3.2-c]coumarin fragments) in nutrition: 02CL282.

Progress in the synthesis of fumagillin, a sesquiterpene containing two oxirane fragments: 03PAC235.

Recent progress in the chemistry of polyacylated anthocyanins as flower color pigments: 02H(56)633.

Structure, distribution, and properties of flavones and similar compounds in plants of Scutellaria L. species: 02KPS299.

Structures and functions of naturally occurring nano molecules, tannins: 04YGK500.

Study of plant flavones with antimicrobial activity at the University of Botswana: 02PAC1197.
Syntheses of gibberellins, antheridiogens, and incrustoporins: 03CL1061.
Synthesis and biological activity of Celastraceae sesquiterpenoids (furan and agarofuran derivatives with anti-viral and anti-tumor activity): 02CSR43.
Synthesis of furofuran lignans: 04S811.
Synthesis of mintlactone and isomintlactone, terpene lactones from mint oil: 02S2155.
Synthesis of sesquiterpenoids substituted in a lactone ring: 03M127.
Terpenoid coumarins of the genus Ferula: 03H(60)689.

d. Heterocycles Produced by Marine Organisms. Bromo- and iodo-containing alkaloids (pyrrole and indole derivatives) from marine microorganisms and sponges: 02MI54.
Chemical studies of shellfish toxins from northern adriatic mussels (O- and S-heterocycles): 04EJO2533.
Detection of pharmacologically active pyridoacridine and other alkaloids from indopacific marine invertebrates and sponge-derived fungi: 03PAC343.
Heterocycles among biologically active compounda of marine animals and plants: 03IZV1.
Heterocyclic natural products of gorgonian corals of genus Briareum exclusive of briarane-type diterpenoids: 02H(57)1705.
Lamellarins, marine pyrrole alkaloids: 04PHC1.
Search for drug leads from Japanese marine invertebrates: 04YGK1073.
Stereoactive total syntheses of Zincophorin, the ionofore antibiotic (substituted tetrahydropyrane), and Scytophycin C, an antitumor marine macrolide: 04YGK1080.
Studies in bioactive marine alkaloids: 03YGK1099.
Studies of palytoxin (O-macroheterocycle): 02T6239.
Survey of briarane-type diterpenoids of marine origin: 02H(57)535.
Synthetic approaches and anti-tumor activity of microtubule-stabilizing marine metabolite laulimalide and its derivatives: 03CRV3753.
Synthetic studies on the macrolides from marine sponges halichondrins: 03PAC1.
Total synthesis and its role in structure elucidation of lepadiformine, alkaloid of marine invertebrates: 03ACR59.
Total synthesis of bioactive tricyclic marine alkaloids with N-heterocyclic fragments, lepadiformine, and related compounds: 03BCJ2059.
Total synthesis of gambierol, a marine polycyclic ether: 03YGK742.
Total synthesis of marine cyclic guanidine compounds and development of novel guanidine-type asymmetric organocatalysts: 03YZ387.
Total synthesis of polycyclic ether ciguatoxin CTX3C: 03YGK562, 04ACR961, 04SL577.
Toxins (condensed and spiro-O-heterocycles) from adriatic blue mussels: 03PAC325.

e. Cyclodextrins. Capped cyclodextrins containing heteroatoms in “bridges” and “capes”: 03CRV4147.
Metallocyclodextrins and related species: 03H(60)2147.
f. Other Topics. Biosynthesis of defensive compounds from beetles and ants (aka-
loids and other natural products): 03EJO2733.
   The chemistry of chemokine receptor ligands (heterocycles as receptor antago-
nists): 03CRV3733.
   N-heterocycles for DNA recognition: 03MI101.
   Molecular recognition and assembly of cucurbituril: 03MI100.
   Semisynthesis and degradation of the tubulin inhibitors epothilone (macrocyclic
   ketolactone) and tubulysin (thiazole derivative): 03PAC167.
   Synthesis and biosynthesis of paraherquamides, brevianamides, and asperpar-
alines, bicyclo[2.2.2]diazaoctane derivatives: 03ACR127.

III. Three-Membered Rings

   A. General Topics

   Heteroanalogs of cyclopropenylium cations and cyclopropenones: 03CRV1371.
   Similarities and differences between aziridines and epoxides: 02CSR247.

   B. One Heteroatom

   1. One Nitrogen Atom

   Bismuth(III) triflate in the synthesis of aziridines: 04EJO2517.
   Chemistry of enantiomerically pure aziridine-2-carboxylates: 03ACA57.
   Enantioselective catalytic aziridination: 03CRV2905.
   Nucleophilic ring opening of aziridines: 04T2701.
   Preparation, properties, and synthetic applications of 2H-azirines: 02OPP221.
   Synthesis of aziridines: 04SL2051.

   2. One Oxygen Atom

   Epoxides of alicyclic compounds: 03MI2.

   Discrete metal-based catalysts for the copolymerization of CO₂ and epoxides: 04AG(E)6618.
   Enantioselective ring opening of epoxides to alcohols: 02EJO393.
   Fluorinated alcohols as a new medium for activation of oxirane ring opening by
   aromatic amines, thiols, or carboxylic acids: 04SL18.
   Reactions of epoxides as a chiral enolate equivalent: 02OPP1.
   Reactions of epoxides with amines, azides, hydrazines, etc., formation of N-
heterocycles by epoxide ring opening: 04ZOR11.
   Recent developments in the chemistry of lithiated epoxides: 02S1625.
Ring opening of oxiranes: 04SL2051.
Transformation of oxiranes to another heterocyclic system: 04ZOR1279.

Catalysts for asymmetric epoxidation of olefins: 02YGK342.
Catalytic asymmetric epoxidation of \(\alpha,\beta\)-unsaturated carbonyl compounds: 02YGK94.
Enantioselective oxidation methodologies of olefins to oxiranes and other heterocycles: 02T4981.
Epoxide oxidations as a valuable tool in organic synthesis: 03S2753.
Fluorinated alcohols as a new medium for selective epoxidation with dioxirane or \(\text{H}_2\text{O}_2\): 04SL18.
Ketone-catalyzed asymmetric and diastereoselective epoxidation of olefins by dioxiranes generated *in situ* from chiral ketones and oxone (2KHSO\(_5\)·KH\(\text{SO}_4\)·K\(\text{2SO}_4\)): 04ACR497.
Metal-catalyzed epoxidations of alkenes with hydrogen peroxide: 03CRV2457.
Olefin epoxidation with inorganic peroxides: 04ACR645.
Organocatalytic asymmetric epoxidation of olefins by chiral ketones: 04ACR488.
Origins of enantio- and diastereocontrol in sulfur ylide-mediated epoxidation reactions: 03CC2644.
Recoverable catalysts for asymmetric epoxidation reactions: 02CRV3385.
Scope, selectivity, and applications in the synthesis of catalytic, asymmetric sulfur ylide-mediated epoxidation of carbonyl compounds: 04ACR611.
Synthesis, structure, spectral, and photochromic properties of spirooxiranes: 02UK1015.

3. *One Sulfur Atom*

Synthesis of thiranes by direct sulfur transfer: 04CRV251.

C. *Two Heteroatoms*

Chiral sulfonyloxaziridines as oxidants in \(\alpha\)-hydroxylation of \(\beta\)-dicarboxyl compounds: 04MI39.
Design and synthesis of dioxetanes as highly efficient chemiluminescent substrates: 03YGK595.
Dimethyldioxirane as oxidant in \(\alpha\)-hydroxylation of \(\beta\)-dicarboxyl compounds: 04MI39.
Fluorinated alcohols as a new medium for selective epoxidation with dioxirane: 04SL18.
Ketone-catalyzed asymmetric and diastereoselective epoxidation of olefins by use of dioxiranes generated *in situ* from chiral ketones and oxone (2KHSO\(_5\)·KH\(\text{SO}_4\)·K\(\text{2SO}_4\)): 04ACR497.
Thermolysis of organic peroxides including dioxiranes: 03UK1055.
IV. Four-Membered Rings

A. General Topics

Chemistry of azetidin-3-ones, oxetan-3-ones, and thietan-3-ones: 02CRV29. 
Formation of four-membered heterocycles through electrophilic heteroatom cyclization: 02EJO3099. 
Four-membered fused heterocyclo-quinolines containing one nitrogen atom: 03AHC(84)71.

B. One Heteroatom

1. One Nitrogen Atom

Advances in the catalytic, asymmetric synthesis of β-lactams: 04ACR592. 
α-Imino esters as versatile substrates for the catalytic, asymmetric synthesis of β-lactams: 03ACR10. 
Recent progress in the synthesis and chemistry of azetidinones: 03T7631. 
Selective bond cleavage of the β-lactam nucleus in stereocontrolled synthesis: 02SL381. 
Synthesis of β-lactams and amino acids by enyne methathesis (enyne bond reorganization): 04CRV1317.

2. One Oxygen Atom

Nucleophilic substitution and electron transfer in the ring-opening reactions of β-lactones: 02JHC1249. 
Regio- and stereochemistry of Paterno–Büchi photocyclo additions of carbonyl compounds and cyclic vinyl ethers leading to formation of oxetanes: 04ACR919.

3. One Sulfur Atom

Four-membered heterocycles containing high coordinate S as heteroatom: 03CCR(244)137.

C. Two Heteroatoms

1,2-Oxathietanes and 1,2-oxathietes containing high-coordinate S heteroatom: 03CCR(244)137. 
Thermolysis of organic peroxides including dioxetanes: 03UK1055.

D. Three Heteroatoms

1,2,4-Oxadithietanes and 1,2,4-oxadithietes containing high-coordinate S heteroatoms: 03CCR(244)137.
V. Five-Membered Rings

A. General Topics

Five-membered fused heterocyclo-quinolines containing one nitrogen atom: 03AHC(84)71.
Metallocomplex catalysis in electrosynthesis of five-membered heterocycles: 02UK126.
Organometallic complexes of polyheteroatom azoles other than pyrazole: 02AHC(83)117.
Organometallic compounds of chalcogenoazoles and their benzannulated derivatives: 03AHC(84)191.
Syntheses and transformations of cyclopentadiene-annulated five-membered heterocycles: 03KGS643.
Syntheses of five-membered heterocycles through palladium-catalyzed reactions: 04MI11.
Vicarious nucleophilic substitution of hydrogen in nitro-substituted azoles and benzoazoles: 02KGS435.
N-ylides in 1,3-dipolar cycloaddition reactions: 03M122.

B. One Heteroatom

We have classified many reviews dealing with these materials under following headings:

1. General
3. One Oxygen Atom (Furans, Hydrofurans, Annulated Furans, Five-Membered Lactones).
4. One Sulfur Atom (Thiophenes, Annulated Thiophenes).

1. General

Five-membered heterocycles with two vicinal oxo groups: 04M17.

2. One Nitrogen Atom

Naturally occurring halogenated pyrroles and indoles: 03PHC56.

a. Monocyclic Pyrroles. Amino acids and peptides (including derivatives of proline and dioxopiperazine derivatives) as asymmetric organocatalysts: 02T2481.
Nucleophilic transition metal-based cyclization of allenes to form pyrrole rings: 02CSR12.
One-pot pyrrole–aldehyde condensations as versatile self-assembly processes: 04AG(E)1918.
Pyrimidine cyclization based on 3-amino derivatives of pyrrole: 03MI47.
Pyrrolic and polypyrrolic anion-binding agents: 03CCR(240)17.
Reactivity of pyrrole-2-ones: 04KGS1443.
Synthesis and application of pyrrocarbodithioates in the design of complicated heterocyclic systems: 03MI72.
Syntheses of pyrrol-2-ones: 03MI12.
Syntheses of C-vinylpyrroles: 02UK641.
Syntheses, reactions, and biological activity of pyrrole oximes: 04KGS3.
Two-step synthesis of pyrroles from ketones and acetylenes via the Trofimov reaction: 03MI20.
Vicarious nucleophilic substitution of hydrogen in nitro-substituted pyrroles: 02KGS435.
C-vinylpyrroles as pyrrole building blocks: 04CRV2481.

b. Hydropyrroles. Addition of azomethine ylides to [60]fullerene leading to fullerenopyrrolidines: 03SL768.
Amino acids and peptides (including proline derivatives) as asymmetric organocatalysts: 02T2481.
Cyclizations of organolithiums onto pyrrole or aromatic rings leading to a fused heterocycle; activation of the cyclizations by oxazolinyl substituents; use of “dearomatization” cyclization in the synthesis of cainoids, pyrrolidine-2,3-dicarboxylic acid derivatives capable of interaction with receptors of neurotransmitters: 04S1721.
[3 + 2] CycloadDITION of nonstabilized 2-azaallyllithiums (2-azaallyl anions) and azomethine ylides with alkenes to form pyrrolidines and its application to alkaloid total synthesis: 03SL903.
Enamine-based organocatalysis with proline and diamines as the development of direct catalytic asymmetric aldol, Mannich, Michael, and Diels–Alder reactions: 04ACR580.
Formation of pyrrolidines and related compounds via reverse Cope cyclization: 04T243.
N-halosuccinimides in organic synthesis and chemistry of natural compounds: 02ZOR327.
Proline-catalyzed asymmetric reactions: 02T5573, 04MI52.
The SAMP-/RAMP-hydrazone methodology in asymmetric synthesis [SAMP and RAMP = (S)- and (R)-1-amino-2-methoxypyrrolidines]: 02T2253.
Sulfinimines (N-sulfinyl imines) in asymmetric synthesis of pyrrolidines: 04T8003.
Synthesis and chemical transformations of 3,4-2H-dihydropyrroles (Δ1-pyrrolines): 03KGS483.

c. Porphyrins and Related Systems. Aromatic core-modified expanded porphyrinoids with meso-aryl substituents: 02AG(E)2045.
Bioinspired molecular design of light-harvesting multiporphyrin arrays: 04AG(E)150.

Calixphyrins, hybrid macromolecules at the structural crossroads between porphyrins and calixpyrroles: 02PAC1041.

Calixpyrroles and related compounds: 02H(57)169.

Catalytic systems based on immobilized porphyrins and metalloporphyrins: 03UK1081.

Chemical transformations of chlorophyll and its use for producing ecologically pure dyes of new type: 04UK197.

Coordination chemistry of tin porphyrin complexes: 04CCR(248)299.

Confused and inverted porphyrins: 02CC1795.

Core-modified expanded porphyrins as a new generation of organic materials: 03ACR676.

Developments in the metal chemistry of N-confused porphyrin: 03CCR(247)1.

DFT/TDDFT interpretation of the ground and excited states of porphyrin complexes: 02CCR(230)5.

Directly linked porphyrin arrays with tunable excitonic interactions: 04ACR735.

Electronic structure and reactivity of high-valent oxo iron porphyrins: 02CCR(226)51.

Energy-transfer pathways in pyridylporphyrin metal adducts and side-to-face arrays: 02CCR(229)51.

Fullerene-porphyrin architectures as photosynthetic antenna and reaction center models: 02CSR22.

Kinetics and mechanisms of dissociation of manganese complexes with porphyrins in mixed protolytic solvents: 04MI14.

Metalloporphyrin-mediated biomimetic oxidations as a useful tool for the investigation of cytochrome P450-catalyzed oxidative metabolism: 04MI16.

Modifications in aryl groups of meso-phenylsubstituted porphyrins: 04MI12.

Modification of peripheral substituents of a and b chlorophylls and their derivatives: 04KGS483.

Optically active ruthenium porphyrins: chiral recognition and asymmetric catalysis: 02CCR(228)43.

Organoelement chemistry of main-group porphyrin complexes: 02MI13.

Organometallic chemistry of transition metal porphyrin complexes: 00MI11.

Organometallic complexes of the bidentate porphyrin: 04YGK1227.

Origin, control, and application of supramolecular chirogenesis in bisporphyrin-based systems: 04ACR449.

Oxidations catalyzed by metallocorroles: 04MI15.

Photophysical properties of porphyrinoid sensitizers non-covalently bound to host molecules as models for photodynamic therapy: 04CCR(248)321.

Porphyrin–fullerene-linked systems as artificial photosynthetic mimics: 04OBC1425.

Porphyrins as light harvesters in the dye-sensitized TiO₂ solar cell: 04CCR(248)1363.

Porphyrin supramolecules for artificial photosynthesis and molecular photonic/electronic materials: 03BCJ689.
Probing electronic communication in covalently linked multiporphyrin arrays: 02ACR57.

Recent advances in the synthesis of corroles and core-modified corroles: 02EJ01735.

Solid-state structures of metalloporphyrin NO\textsubscript{x} compounds: 02CRV1067.

Synthesis and structure of ruthenium and osmium porphyrin carbene complexes and their role in the metal-mediated cyclopropanation of alkenes: 02CCR(231)151.

Synthesis of conjugation-expanded porphyrins based on the retro Diels–Alder reaction: 02YGBK581.

Synthetic expanded porphyrin chemistry: 03AG(E)5134.

Synthesis and application perspectives of immobilized porphyrins: 04MI13.

Superstructured porphyrins as effectors in dynamic supramolecular assemblies with receptors, rotaxanes, and catenanes: 04EJO1655.

Supramolecular metallocomplex systems on the basis of crown-substituted tetrapyrroles: 04UK6.


Versatility of the titanium(IV)-porphyrin reagent for determining hydrogen peroxide: 03BCJ1873.


Heterocyclization of indoxyl and oxindole derivatives: 03MI8.

Hydrodenitrogenization of indole derivatives: 99MI11.

1-Hydroxyindoles, 1-hydroxytryptophans, and 1-hydroxytryptamines: 02AHC(82)101.

Indole-based multicomponent reactions towards functionalized biologically active heterocycles: 04MI17.

Indolylalkylamines and related structures from \textgamma- and \textdelta-halocarbonyl compounds and arylhydrazines: 03MI7.

Novel chemistry of indole in the synthesis of heterocycles: 03PAC1417.

Rearrangement reactions of indoles and related compounds: 04YZ481.

SmI\textsubscript{2}-induced cyclizations with participation of indole and pyrrole derivatives in stereoselective synthesis of alkaloids: 04SL422.

Spiro[pyrrolidine-3,3’-oxindoles] construction in the synthesis of oxindole alkaloids: 03EJO2209.

Synthesis of \textit{N}-alkynyl-substituted indolines by Ti-catalyzed intermolecular hydroyamination of alkynes: 04SL1653.

Syntheses, reactions, and catalytic activity of indole and izatin oximes: 03KGS5.

Syntheses and properties of benzo[\textit{b}]furoindoles and their derivatives: 04KGS1123.

Syntheses and reactions of sulfur-containing indole derivatives: 03MI56.

Syntheses of derivatives of indole, carbazole, and other \textit{N}-heterocycles using Pd-catalyzed C–N coupling of amines with aryl halides: 04MI44.

Synthetic approaches to indoles on a solid phase: 03T5395.
Vicarious nucleophilic substitution of hydrogen in nitro-substituted benzannulated pyrroles: 02KGS435.


Design, synthesis, structure, and spectral and electrochemical properties of phthalocyanines: 02BCJ1.

4,7-Dihydro-, 4,5,6,7-tetrahydro-, and octahydro iso(and methanoiso)indoles: 04KGS1763.

DFT/TDDFT interpretation of the ground and excited states of porphyrazine complexes: 02CCR(230)5.

Dimers, trimers, and oligomers of phthalocyanines and related compounds: 02CCR(227)129.

Electrochemical and spectroscopic characterization of self-assembled molecular films of tetraaminometal (Co, Cu, Fe) phthalocyanines on gold and silver: 02PAC1609.

Electrochemically activated reactions of phthalocyanines: 02UK255.

Methods for the synthesis and properties of pyrido- and pyrimidinoisoindoles: 04UK833.

Phthalocyanines as versatile components of molecular conductors: 04CRV5503.

Syntheses, structural features, and acid–base interactions in non-central symmetric thia-diazole and triazole phthalocyanine analogs: 04MI124.

Syntheses, reactivity, and physical properties of subphthalocyanines (macrocyclic compounds containing three diiminoisoindole fragments connected with a boron atom by N–B bonds): 02CRV835.

Synthetic, spectroscopic, and theoretical study of novel supramolecular structures composed of lanthanide phthalocyanine double-decker complexes: 02CCR(226)93.

f. Polycyclic Systems Including Two Heterocycles. Asymmetric Heck reaction in the syntheses of indolizidines, spirocyclic systems, natural compounds and in transformations of heterocycles: 04MI43.

Pyrimidine cyclization based on 3-amino derivatives of pyrrole: 03MI147.

Pyrrolotetraethylfulvalenes and their applications in molecular and supramolecular chemistry: 03EJO3245.

Sulfinimines (N-sulfinyl imines) in asymmetric synthesis of quinolizidines and indolizidines: 04T8003.

Synthesis and reactivity of hydrogenated pyrrolopyridines: 02S155.

Synthesis of derivatives of heteroaromatic systems with a bridge nitrogen atom possessing a pyrrole fragment: 03MI118.

Synthesis of N-alkynyl-substituted indolyzidines, and pyrrolizidines by Ti-catalyzed intermolecular hydroamination of alkynes: 04SL1653.

Transition metal complexes in the syntheses of naturally occurring furocarbazoles: 04H(63)2393.

Triazolo- and tetrazoloisoindoles: 02KGS1171.
3. One Oxygen Atom


Furans as versatile synthons for target- and diversity-oriented synthesis: 05PHC1.

Nucleophilic transition metal-based cyclization of allenes to form furan rings: 02CSR12.

Palladium catalysis in the construction of the furan rings from alkynes and organic halides or triflates: 02H(56)613.

Selectivity in cyclizations of oxygen-centered radicals with the formation of furans: 02S1469.


Syntheses and properties of 4,5-disubstituted 2,3-dihydrofuran-2,3-diones: 03MI44.

Syntheses, structure, and biological properties of N-substituted 2(3)-imino-2,3-dihydrofuran-3(2)-ones: 04KGS183.

Syntheses and chemistry of tetronic acids: 04OPP35.

c. Annulated Furans. Palladium catalysis in the construction of benzo[b]furan rings from alkynes and organic halides or triflates: 02H(56)613.

Syntheses and photochromic properties of naphtofurans: 05PHC33.

Syntheses and properties of benzo[b]furoindoles and their derivatives: 04KGS1123.

Syntheses, properties, and biological activity of benzofuro[2,3-c]pyridines: 03MI48.

Transition metal complexes in the syntheses of naturally occurring furocarbazoles: 04H(63)2393.

d. Five-Membered Lactones. o-Quinone methides as intermediates in the syntheses of γ-lactones: 02T5367.

Syntheses of γ-lactones using the Ueno–Stork reaction of radical cyclization of haloacetals: 04S1903.

4. One Sulfur Atom


Methods for the synthesis of oligothiophenes: 03H(60)663.

Molecular structure of thiophene-1,1-dioxides, thiophene-S-oxides and their derivatives: 02KGS725.

Preparative chemistry of stable thiophenium ions: 03MI28.

Pyrimidine cyclizations based on 3-amino derivatives of thiophene: 03MI47.

Syntheses and properties of nano-scale oligothiophenes as materials for molecular electronics: 02YGBK52.

Syntheses of thiophenes, comprehensive monograph: 04MI6.
Pyrimidine cyclization based on 3-amino derivatives of thiophene: 03MI47.
Studies on π-face selective additions with 3,4-di-tert-butylthiophene 1-oxide and 1-imide: 03YGGK1106.
Syntheses and properties of heterohelicenes including thiophene rings as “molecular springs”: 02YGK593.
Syntheses and reactions of 1-aryl-1-benzothiophenium salts: 02YGK218.
Syntheses, properties, and biological activity of benzothieno[2,3-c]pyridines: 03MI48.
Syntheses, properties, and biological activity of thienopyrimidines: 04IZV463.

C. TWO HETEROATOMS

We have classified the many reviews dealing with these materials under following headings:

1. General.
2. Two Nitrogen Atoms (it is self-subdivided into Pyrazoles, Imidazoles, and Annulated Imidazoles).
3. One Nitrogen and One Oxygen Atom (1,2-Heterocycles, 1,3-Heterocycles).
4. One Nitrogen and One Sulfur Atom.
5. Two Oxygen Atoms.
6. Two Sulfur Atoms.

1. General

Achievements in the application of hydrazine and related compounds for the synthesis of five-membered azole heterocycles: 04MI119.
Current methods for the synthesis of 2-substituted azoles: 04T8991.
Photochemical isomerizations of some azoles: 03PHC37.
Ring-chain tautomerism of five-membered N-unsubstituted 1,3-X,N-heterocycles (X = O, S, NR): 03EJO3025.
Syntheses and reactions of benzoiodoxoles, benzoiodazoles: 02CRV2523.

2. Two Nitrogen Atoms

Fused systems based on amino- and oxopyrazoles: 03MI33.
Non-classical spin transitions in Cu-complexes with pyrazole derivatives: 02M156.
3-Phenyl-l-menthopyrazole [(4R,7S)-7-isopropyl-4-methyl-3-phenyl-4,5,6,7-tetrahydroindazole] as a new type of chiral auxiliary: 03H(60)959.
Preparation and transformations of pyrazolinecarboxylic acid derivatives: 03MI3.
Reactions of the ring atoms of pyrazol-3-ones: 04AHC(87)141.
Structural revision in pyrazole chemistry: 04H(63)145.
Syntheses and properties of acetylenic derivatives of pyrazoles: 02AHC(82)1.
Syntheses of 2-pyrazolines by the reactions of \( \alpha,\beta \)-unsaturated aldehydes, ketones, and esters with diazoalkanes, nitrile imines, and hydrazines: 02JHC1.
Synthetic utilities of \( N \)-acylpyrazoles: 03H(60)437.

b. Imidazoles. Copper(II) complexes with multidentate Schiff-base ligands containing imidazole groups: 02CCR(226)199.
Crystal engineering on controlled crystal arrays using hydrogen bonding biimidazolate metal complexes: 04YGK629.
Cyclization with the formation of imidazolidinediones: 02T2701.
Development of a general process for the synthesis of highly substituted imidazoles: 02PAC1349.
Glycolurils: 04H(63)419.
Recent developments in hydantoin chemistry: 04OPP391.
Syntheses and applications of 1,3-dihydro-2\( H \)-imidazol-2-one in biotin synthesis: 04KFZ(5)28.
Spectroscopic implications for magnetic interactions in metal complexes with nitroxide radicals (pyridylsubstituted 4,4,5,5-tetramethyl-4,5-dihydro-1\( H \)-imidazole-1-oxyl 3-oxides): 03BCJ673.


3. One Nitrogen and One Oxygen Atom

a. 1,2-Heterocycles. Molecular rearrangements of isoxazoles as a route to fluorinated heterocyclic compounds: 04H(63)2627.

b. 1,3-Heterocycles. Advances in the total syntheses of oxazole-containing natural products: 04T11995.
Cyclization with the formation of oxazolidinones: 02T2701.
Dimethyl carbonate in the syntheses of oxazolines: 02ACR706.
Homogeneous rhodium(I)-catalyzed reductive amination of 1,3-oxazolidines: 04OPP99.
New achievements in the chemistry of functional oxazole derivatives: 03MI68.
Novel oxazoline-mediated syntheses of heterocycles: 03MI73.
Progress of chiral bis(oxazoline)–metal complexes utilized in asymmetric cyclopropanation: 04MI51.
Progress in the syntheses of chiral bis(oxazoline) ligands: 04MI20.
Pyridine-2,6-bis(oxazolines) as helpful ligands for asymmetric catalysts: 03CRV3119.
Syntheses and properties of oxazolidine-4,5-diones: 03MI45.
The use of \( N \)-boc-1,3-oxazolidines as chiral auxiliaries in asymmetric syntheses: 04EJO677.
4. **One Nitrogen and One Sulfur Atom**

Chemistry of isothiazoles: 03T7445.
1,3-Dihydro-2,1-benzisothiazole 2,2-dioxides (benzosultams) in organic synthesis: 02H(57)1717.
Syntheses and properties of azoles with benzothiazolyl substituents: 03KGS1443.
Syntheses of 2-chloro-5-chloromethylthiazole and its use in the preparation of chlorothiazole neonicotinoids: 04ZOR1759.
Syntheses, properties, and applications of isothiazoles (1,2-thiazoles): 02UK764.
Thiazole-mediated synthetic methodology: 04CRV2557.
Thiazole S-oxides: 02AHC(83)71.

5. **Two Oxygen Atoms**

1,3-Dioxolane-based polymeric electrolytes: 02UK878.

6. **Two Sulfur Atoms**

*Bis*(ethylenethio)tetrathiafulvalene (BET-TTF) and related dissymmetrical electron donors: 04CRV5289.
Interplay of metal/ligand electronic delocalization and solid-state magnetic behavior of paramagnetic Cp/dithiolene complexes as molecular hinges: 04ACR179.
Pyrrolotetrathiafulvalenes and their applications in molecular and supramolecular chemistry: 03EJO3245.
Redox-switched binding with participation of heterocycles, in particular tetra-thiafulvalenes: 02CSR147.
Synthetic trail from electrophilic alkynes to highly functionalized tetra-thiafulvalenes: 04CRV5151.

**D. Three Heteroatoms**

1. **Three Nitrogen Atoms**

*a. Monocyclic systems.* 5-Amino-3-nitro-1,2,4-triazole and its derivatives: 02ZOR1289.
Coordination chemistry of 4-substituted 3,5-di(2-pyridyl)-4*H*-1,2,4-triazoles and related ligands: 03CCR(241)119.
Diels–Alder and ene reactions of singlet oxygen, nitroso compounds, and triazolinediones: 02CC1243.
Synthesis of stable heteroaromatic carbenes in the 1,2,4-triazole series and their precursors: 03MI17.
1,2,3-Triazole formation under mild conditions *via* 1,3-dipolar cycloaddition of acetylenes with azides: 03H(60)1225.

*b. Annulated Triazoles.* Chemistry of the triazolopyridines: 02AHC(83)1.
Triazoloisoindoles: 02KGS1171.
2. **Two Nitrogen Atoms and One Oxygen Atom**

Progress in the chemistry of furazano[3,4-b]pyrazines and their analogs: 03UK93.

3. **Two Nitrogen Atoms and One Sulfur Atom**

Chemistry of 1,2,3-thiadiazoles (general monograph): 04CH(62)1.
Chemistry and biological activity of 1,3,4-thiadiazolo[3,2-a]pyrimidine derivatives: 04MI11.
Rearrangements and transformations of 1,2,3-thiadiazoles in organic synthesis: 03KGS803.
Thiadiazole S-oxides: 02AHC(83)71.

4. **Three Oxygen Atoms**

Thermolysis of organic peroxides including cyclic trioxides: 03UK1055.

**E. FOUR HETEROATOMS**

1,3- and 1,4-Substituted tetrazolium salts: 02UK819.
2-Substituted and 2,5-disubstituted tetrazoles: 03ZOR489.
1-Substituted 5-alkyl(aryl)sulfanyltetrazoles and their derivatives: 04ZOR479.
Syntheses and properties of vinyltetrazoles: 03UK159.
Syntheses of 2-allyltetrazoles from nitriles by a new catalytic reaction via π-allylpalladium azide complexes: 04YGK682.
Tetrazoloisoindoles: 02KGS1171.

VI. **Six-Membered Rings**

**A. GENERAL**

Conformational analysis of saturated heterocyclic six-membered rings: 04AHC(86)41.
Development and regioselective control of new ring transformations of pyridine and pyrimidine derivatives by action of nucleophiles: 03YGK882.
Diazapyrenes: 03KGS1612.
1,3-Dicarbonyl derivatives in multicomponent reactions leading to pyridines, pyrimidines, and other heterocycles: 04EJO4957.
Nucleophilic attack on unsubstituted carbon atom of azines and nitroarenes as an effective methodology of construction of heterocyclic systems: 02UK803.
Nucleophilic properties of azines: 03MI159.
Oxidative amino-dehydrogenation of azines: 04AHC(86)1.
Syntheses and applications of perhydroazines: 03MI14.
Syntheses of azine-type heterocycles and their condensation into functional molecules: 04YGK335.
Syntheses of six-membered heterocycles through palladium-catalyzed reactions: 04MI11.

Syntheses of six-membered heterocycles (pyrimidines, pyridines, quinolines, pyrans and others) using reactions of functionally substituted alkoxyethylenes with nucleophiles: 03ZOR807.

B. ONE HETEROATOM

We have classified the many reviews dealing with these materials under following headings:

1. **One Nitrogen Atom** (it is self-subdivided into Pyridines, Pyridinium Compounds, Ylides, Pyridine N-Oxides, Applications of Pyridines, Bipyridines and Related Systems, Hydropyridines, Biologically Active Pyridines and Hydropyridines, Pyridines Annulated with Carbocycles, Pyridines Annulated with Heterocycles).

2. **One Oxygen Atom** (Pyrans and Hydropyrans, Annulated Pyrans and Pyrylium Salts).

1. **One Nitrogen Atom**

Radical Additions to Pyridines, Quinolines, and Isoquinolines: 04PHC27.

* a. **Pyridines**. Activated alkoxyethylenes in the syntheses of bioactive pyridine derivatives: 03MI34.

   Addition of organometallic reagents to imino derivatives of pyridine bearing stereogenic N-substituents: 02S651.

   Crystal structures of the coordination products of reactions of di-2-pyridylketone oxime in the presence of vanadium(III): 03CCR(237)197.

   1,4-Dilithio-1,3-diene and 1-lithio-1,3-diene derivatives in reactions with nitriles leading to pyridine derivatives: 04EJO2773.

   Energy-transfer pathways in pyridylporphyrin metal adducts and side-to-face arrays: 02CCR(229)51.

   Highly enantioselective asymmetric syntheses of pyridyl by addition of organometallic reagents to aldehydes, “autocatalysis” by the formed chiral adduct: 04YGK673.

   Hydrodenitrogenation of pyridine derivatives: 99MI11.

   Metallocomplex catalysis in the synthesis of pyridine bases: 03MI62.

   Construction of pyridine rings by metal-mediated [2 + 2 + 2] cycloaddition of alkynes to nitriles and isocyanates: 03CRV3787.

   *De novo* synthesis of substituted pyridines: 04T6043.

   Synthetic methods and some properties of hydrazinopyridines: 03KGS323.

   Multicomponent cascade heterocyclization as a route to directed syntheses of polyfunctionalized pyridines: 03UK75.

   Organometallic complexes of pyridines: 04AHC(86)293.

   Pyrylium salts in the synthesis of pyridines: 03MI62.
Pyrimidine–pyridine ring interconversions: 03AHC(84)31.
Reactions of vinylpyridines with 1,3-dienes: 03MI62.
Syntheses and reactions of nitropyridines: 03PAC1403.
Syntheses, reactions, and biological activity of pyridine oximes: 03KGS963.
Transition metal complexes with 2,2′-bipyridines, pyridine–phosphines, and pyridine N-oxides as ligands: 04IZV1733.


Coordination compounds with 1,10-phenanthroline, 2,2′-bipyridine and other polypyridine ligands as synthetic building blocks: 02SL1043.
Pyridylthioethers as polydentate ligands in palladium and platinum coordination: 04CCR(248)945.
Recent advances with luminescent polymetallic dendrimers containing the 2,3-bis(2′-pyridyl)pyrazine bridging ligand: 02CCR(229)67.
Ruthenium d-orbital delocalization in bis(bipyridine) ruthenium derivatives of redox active quinonoid ligands: 02CCR(230)97.
Ultrafast electron injection from metal polypyridyl complexes to metal-oxide nanocrystalline thin films: 04CCR(248)1231.

d. Bipyridines and Related Systems. Luminescence that lasts from Pt(trpy)Cl+ derivatives (trpy = 2,2′,6′,2″-terpyridine): 02CCR(229)113.
Photophysical, electrochemical, and electrochromic properties of copper-bis(4,4′-dimethyl-6,6′-diphenyl-2,2′-bipyridine) complexes: 02CCR(230)253.
Pyridine-2,6-bis(oxazolines) as helpful ligands for asymmetric catalysts: 03CRV3119.
Recent developments in the supramolecular chemistry of terpyridine–metal complexes: 04CSR373.
Ruthenium(II) and iridium(III) bis-terpyridine complexes: 04CSR147.
Supramolecular coordination compounds with chiral pyridine and polypyridine ligands derived from terpenes: 03CCR(242)87.
Syntheses of chiral 2,2′-bipyridines and 2,2′:6′:2″-terpyridines and their applications in asymmetric homogeneous catalysis: 02CRV3129.
Syntheses of bipyridine complexes as rigid molecules in the investigation of electron and energy transfer: 02CCR(230)28.
Syntheses of 2,2′-bipyridines as versatile building blocks for complex architectures and functional nanomaterials: 04EJO235.
Syntheses of functionalized 2,2′:6′,2″-terpyridines: 03EJO947.
Syntheses of 4′-substituted-2,2′:6,2′-terpyridines: 03S155.
Viologens, diquaternary salts of 4,4′- and 2,2′-bipyridines, embedded in zeolites: 04CCR(248)477.
e. **Hydropyridines.** $n$-BuLi/Lithium aminoalkoxide aggregates as new and promising lithiating agents for pyridine derivatives: 02EJO3375.

Preparation of tetramethylpiperidine-1-o xoammonium salts and their use as oxidants in organic chemistry: 04OPP1.

Reactions of 1,5-diketones with ammonia and its substituted derivatives: 03KGS1283.

Recent advances in the synthesis of piperidones and piperidines: 03T2953.

Stereoselected syntheses of monocyclic and annulated $N$-hydroxyalkylpyperidines: 03MI6.

Sulfinimines ($N$-sulfinyl imines) in asymmetric syntheses of piperidines and 1,2,3,4-tetrahydroisoquinolines: 04T8003.

Syntheses of 2,6-dialkyl-1,2,5,6-tetrahydropyridines and their applications in total synthesis: 04MI23.

Syntheses of piperidines: 04T1701.

f. **Biologically Active Pyridines and Hydropyridines.** Syntheses of chloropyridines ($\beta$-picoline derivatives) and 2-nitroiminoimidazolidine and their use for the preparation of chloropyridine neonicotinoids: 04ZOR1759.

g. **Pyridines Annulated with Carbocycles.** Activated alkoxyethylenes in the syntheses of bioactive quinoline derivatives: 03MI34.

Organometallic complexes of benzannulated pyridines: 04AHC(86)293.

Pfitzinger reaction: 04KGS323.

Phenanthroline ligands as chiral derivatives for asymmetric catalysis: 03EJO1145.

Reactivity of the acridine ring: 04S313.

$\text{SmI}_2$-induced reductive cyclizations of $\alpha$- and $\beta$-aminoketones to form isoquinoline and quinoline derivatives: 04SL422.

1-Substituted 3,3-dialkyl-3,4-dihydroisoquinolines as nucleophilic and electrophilic reagents: 03MI26.

Syntheses of chiral 1,10-phenanthrolines and their applications in asymmetric homogeneous catalysis: 02CRV3129.

Syntheses and biological properties of isoquinolines spiro-fused at the 4-position with carbo- and heterocycles: 02KGS1475.

Syntheses of 3,3-dialkyl-3,4-dihydroisoquinolines: 03MI25.

Syntheses of quinolines and phenanthrolines using metallocomplex catalysis: 03MI62.

h. **Pyridines Annulated with Heterocycles.** Chemistry and biological activity of naphthyridines: 03MI11, 04UK692.

Chemistry of aza coumarins: 03MI36.

Chemistry of bicyclic pyridines containing a ring-junction nitrogen: 02T6143.

Four- and five-membered fused heterocyclo-quinolines containing one nitrogen atom: 03AHC(84)71.
Methods for the synthesis and properties of pyridoisoindoles: 04UK833.
Palladium in quinoline synthesis: 03AHC(84)1.
Pyrido-oxazines, pyrido-thiazines, pyrido-diazines, and their benzologs: 03AHC-(84)219, 03AHC(85)173.
Syntheses and reactivity of hydrogenated pyrrolopyridines: 02S155.
Syntheses of naphthridines using metallocomplex catalysis: 03MI62.

2. One Oxygen Atom

a. Pyrans and Hydropyrans. Application of 8-oxabicyclo[3.2.1]oct-6-en-3-ones to the asymmetric synthesis of polyoxygenated building blocks: 04AG(E)1934.
    Catalytic enantioselective syntheses of 2H-3,4-dihydropyrans involving cycloaddition reactions of carbonyl compounds: 02MI8.
    Dehydroacetic acid and its derivatives in the syntheses of heterocyclic compounds: 04H(63)1193.
    Hetero-Diels–Alder reactions of ketones: 04EJO2093.
    Pyrylium salts in the syntheses of pyridines: 03MI62.
    Selectivity in cyclizations of oxygen-centered radicals with the formation of pyrans: 02S1469.
    Syntheses, properties, and biological activities of 4-hydroxy-2H-pyran-2-ones and of their derivatives: 02ZOB1701.

b. Annulated Pyrans and Pyrylium Salts. Chemistry of aza coumarins: 03MI36.
    Flavones, isoflavones, 2- and 3-hetarylchromones in reactions with hydroxylamine: 02KGS1019.
    Heterocycles directly linked to the 3-position of 1-benzopyran-4-ones: 04H(63)2875.
    New redox reaction of 2-trifluoromethylchromones with alkylmercaptoacetates: 03MI70.
    New synthetic methods for flavones: 04MI22.
    o-Quinone methides as intermediates in the syntheses of chromans, benzopyrans, and δ-lactones: 02T5367.
    Syntheses and reactions of halogen-containing chromones: 03UK550.
    Syntheses and transformations of fluorine-containing chromones: 03MI74.
    Syntheses of 3-aryl and 3-hetarylchromones: 03MI51.
    Syntheses and biological activity of substituted 2-amino-4H-pyrans: 03MI53.
    Syntheses and reactivity of styrylchromones: 04MI21.
    Syntheses of flavones and 2-hetarylchromones: 03MI37.
    Syntheses of hetarylcoumarins: 03MI52.
    Syntheses of isoflavones: 04JHC449.
C. TWO HETEROATOMS

We have classified the many reviews dealing with these materials under following headings:

1. General

1. Two Nitrogen Atoms (it is self-subdivided into 1,2-Heterocycles, 1,3-Heterocycles: Monocyclic Pyrimidines and Hydropyrimidines Except Pyrimidine Nucleoside Bases and Nucleosides, Annulated Pyrimidines Except Purines, Pteridines, and Flavins, Pyrimidine Nucleoside Bases and Purines, Nucleotides and Nucleosides, Nucleic Acids, Pyrazines, and Hydropyrazines).

2. One Nitrogen and One Oxygen Atom.

3. One Nitrogen and One Sulfur Atom.

4. Two Oxygen Atoms.

Ring-chain tautomerism of six-membered N-unsubstituted 1,3-X,N-heterocycles (X = O, S, NR): 03EJO3025.

2. Two Nitrogen Atoms

Pyrido-diazines and their benzologs: 03AHC(84)219, 03AHC(85)173.

a. 1,2-Heterocycles. Chemistry of aza coumarins: 03MI36.

New pathways towards pyridazino-fused ring systems: 04SL1123.

b. 1,3-Heterocycles: Monocyclic Pyrimidines and Hydropyrimidines (Except Pyrimidine Nucleoside Bases and Nucleosides). Asymmetric autocatalytic PRICE reactions (Product Recruitment for the Increase in the Chiral Environment) on examples of pyrimidine derivatives: 02CSR211.

Condensation of hydroxypyrimidines with barbituric acids: 02ZOK487.

Condensation of hydroxypyrimidines with carbonyl compounds: 04ZOR167.

Highly enantioselective asymmetric syntheses of pyrimidylcarbinols by the addition of organometallic reagents to aldehydes, “autocatalysis” by the formed chiral adduct: 04YGK673.

Methods for the syntheses and chemical properties of natural uracils: 03KFZ(7)3.

Pyrimidine–pyridine ring interconversions: 03AHC(84)31.

Syntheses of cyclobutanobis[d]pyrimidindiones as model compounds for the investigation of photoreactivation of DNA: 02MI35.


Barbituric acids in the syntheses of pyrimidine derivatives annulated with O- and S-heterocycles: 03MI40.

Chemistry of aza coumarins: 03MI36.
Chemistry and biological activity of 1,3,4-thiadiazol[3,2-a]pyrimidine derivatives: 04M11.

Methods for the syntheses and properties of pyrimidoisoindoles: 04UK833.

Progress in the chemistry of furazano[3,4-b]pyrazines and their analogs: 03UK93.

Pyrimidine cyclization based on 3-amino derivatives of thiophene and pyrrole: 03M147.

Syntheses, properties, and biological activities of thienopyrimidines: 04IZV463.


Purinediones, purinones, and purineimines fused with five-membered heterocycles: 04AHC(87)85.

Syntheses of purines bearing carbon substituents in positions 2, 6, or 8 by metal- or organometal-mediated C–C bond-forming reactions: 03EJO245.

Theoretical and experimental dipole moments of purines: 02CCC1109.

Xanthine cyclohomologs: 03M113.

e. Nucleotides and Nucleosides. Anionic migration of silyl and stannyl groups as new aspects in the lithiation chemistry of nucleosides: 02YGK145.

Application of imidazole C-nucleoside derivatives to histamine H3- and H4-ligands: 03YGK682.

Carbon–carbon bond formation at the unsaturated sugar part of nucleosides: 03YGK1065.

Chemical syntheses of 13C- and 15N-labeled nucleosides: 02S301.

Development of novel artificial nucleosides for the expansion of triplex-recognition codes: 04YGK1026.

The disclosure of the stepwise supramolecular organization of guanosine derivatives: 04SL596.

5-Guanosine monophosphate and hydrogen-bonded guanosine-based macrocycles (G-quartets) in molecular biology and supramolecular chemistry: 04AG(E)668.

Metal ion complexes of antivirally active acyclic nucleoside phosphonates as nucleotide analogs: 04CSR191.

C(4')-modified nucleotides as chemical tools for the investigation and modulation of DNA polymerase function: 04SL217.

Nucleotides functionalized by carboranyl clusters as a new entity for DNA–oligonucleotide modification: 03EJO4489.

Oligonucleotide syntheses based on chemoselective phosphorylation: 03YGK961.

Palladium-assisted routes to nucleosides: 03CRV1875.

Probing DNA polymerase function with synthetic nucleotides: 04S1.

Site-specific synthetc ribonucleases based on conjugates of oligonucleotides with metal-independent organic catalysts of phosphodiester bond hydrolysis: 02IZV1025.

Studies on H-nucleoside phosphonates: 02ACR952.

Syntheses and applications of nucleosides and oligonucleotides with reactive groups at the C(2) atom: 04UK747.

Syntheses of oxetanocin A (a nucleoside with anti-viral activity) and related unusual nucleosides with bis(hydroxymethyl)-branched sugars: 02S1.
Syntheses of the hypermodified nucleosides of phenylalanine transfer ribonucleic acids: 03YZ267.

Syntheses of nucleoside analogs and new tat protein inhibitors: 02PAC1189.

Syntheses of oligonucleotides with reactive electrophilic groups: 02UK1173.

Syntheses of oligonucleotides modified with polyamines and their properties as antisense antigene molecules: 03YGK890.

Syntheses and properties of oligonucleotides containing 5-substituted pyrimidine nucleoside: 04YGK1238.

Synthetic methodologies for C-nucleosides: 04S1533.

Syntheses and functional properties of bridged structures including an N-heteroaromatic fragment, in particular NADH analogs: 03YGK352.

**f. Nucleic Acids.** Chemistry and biology of DNA repair: 03AG(E)2946.

Design, synthesis, and biological evaluation of DNA minor-groove binders, ligands structurally related to CC-1065, distamycin, and anthramycin: 03PAC187.

Development of bridged nucleic acid analogs for antigene technology: 04CPB1399.

DNA hydrolyses promoted by di- and multi-nuclear metal complexes: 04CCR(248)147.

A fluorescent intercalator displacement assay for establishing DNA-binding selectivity and affinity: 04ACR61.

Free-radical DNA oxidation and its biomarker, oxidized guanosine (8-oxodG): 02M155.

Heteroaromatic oligoamides with dDNA affinity: 03EJO3473.

Identifying hydrogen bond alignments in multistranded DNA architectures by NMR: 02ACR1.

Mechanisms of in situ activation for DNA-targeting antitumor agents: 02CRV2477.

Modern methods for the synthesis of oligonucleotidopeptides: 02UK273.

Novel nucleic acid analogs with a bridged sugar moiety (BNAs): 02CC1653.

Purine base derivatives as indicators of damage to DNA: 02CL276.

Recognition in the minor groove of double-stranded DNA by microgonotropens: 02ACR86.

Replacing the nucleobases in DNA with designer molecules: 02ACR936.

Structural control of DNA and nano-assembly of artificial metallo-DNA complexes: 04YGK508.

Structural preorganization of peptide nucleic acids with the formation of chiral cationic analogs with a five- or six-membered ring structure: 02EJO2021.

Structure, properties, application, strategy, and practice of chemical synthesis of peptide-nucleic acids: 02UK81.

Supramolecular chain polymerization with the formation of DNA-templated assembly of helical cyanine dye aggregates: 04ACR845.

The synthesis and electrochemical properties of nucleic acids containing a ferrocene moiety: 03UK602.

Thermodynamics of DNA interactions from single molecule-stretching experiments: 02ACR159.
Understanding nucleic acids using synthetic chemistry: 04ACR784.
Visualization of oncogenous m-RNA using \(^{99m}\)Tc chelate-forming component – PNA peptide conjugates: 02IZV997.
Zinc–nucleic acid interaction: 04CRV769.

\textit{g. 1,4-Heterocycles: Pyrazines and Hydropyrazines}. Amino acids and peptides (including diketopiperazine derivatives) as asymmetric organocatalysts: 02T2481.
Electrophilic fluorination with 1-chloromethyl-4-fluoro-1,4-diazaonabicyclo[2.2.2]octane \textit{bis}(tetrafluoroborate): 04ACR31.
Mono-functionalization of symmetrical derivatives of pipеразine and other cyclic polyamines: 02T3111
Pyrazines, Supplement I to general monograph: 02HC(58)1.
Recent advances in luminescent polymetallic dendrimers containing the 2,3-\textit{bis}(2'-pyridyl)pyrazine bridging ligand: 02CCR(229)67.
Recent advances in the synthesis of diketopiperazines: 02T3297.
Syntheses and transformations of pipеразинone rings: 02OPP369.

3. \textit{One Nitrogen and One Oxygen Atom}

1,4-Benzoxazines and their 2,3-dihydro derivatives: 04SL2449.
4H-3,1-benzoxazines, their salts and dihydroderivatives: 03KGS163.
Biological relevance and syntheses of C-substituted morpholine derivatives: 04S641.
1,2-Oxazines and their N-oxides in synthesis: 02H(57)915.
Pyrido-oxazines and their benzologs: 03AHC(84)219, 03AHC(85)173.
Syntheses of 1,2-oxazines and their N-oxides: 02H(57)1149.

4. \textit{One Nitrogen and One Sulfur Atom}

Pyrido-thiazines and their benzologs: 03AHC(84)219, 03AHC(85)173.
Syntheses and properties of 1,4-benzothiazine derivatives: 03MI42.
Syntheses, structural analysis, and reactivity of 1,3-oxathiane derivatives: 03H-(60)1447.

5. \textit{Two Oxygen Atoms}

1,4-Benzodioxins and their 2,3-dihydro derivatives: 04SL2449.

D. \textbf{THREE HETEROATOMS}

Cyanuric acid and cyanurates: 02MI34.
Syntheses and properties of 1,3,5-triazine nitroderivatives: 03UK311.
Syntheses and transformations of 1,3,5,7-tetraazabicyclo[3.3.1]nonanes: 02ZOB1383.
1,2,4-Triazine N-oxides: 02AHC(82)261.
E. Four Heteroatoms

Coordination chemistry of 1,2,4,5-tetrazines: 02CCR(230)126.
Progress in 1,2,3,4-tetrazine chemistry: 04CRV2601.

VII. Rings with More Than Six Members

A. Seven-Membered Rings

1. One Heteroatom

3-Benzazepines: 03MI5.
Polymerization and copolymerization of hexano-6-lactam: 02CL296.
Syntheses and applications of dibenzo[b,f]oxepines: 04OPP297.
Xanthine cyclohomologs: 03MI13.

2. Two and More Heteroatoms

Simple four-step synthesis of unsaturated seven-membered carbo- and heterocycles from catechols and quinones via an entropy/strain-reduction strategy: 04SL933.
Syntheses of benzodiazepines by palladium-catalyzed reactions in solid phase: 03T885.
Pentathiepins: 04CRV2617.

B. Medium Rings

Anionic triazacyclononananes as new supporting ligands in main group and transition metal organometallic chemistry: 03CC1025.
One-stage synthesis of medium-sized unsaturated lactones, thiolactones, and lactams of E-configuration using the Bellu–Claisen rearrangement: 04AG(E)3516.
Syntheses of 1,4,7,10-tetraazacyclododecane and its derivatives: 03MI91.

C. Large Rings

1. General Problems

Macroheterocycles and molecular encapsulation: 02AG(E)1488.
Macroheterocycles and their complexes as supramolecular systems: 02AG(E)899.
Redox-switched binding with participation of heterocycles, in particular, macroheterocycles: 02CSR147.

Shape-persistent, nano-sized macroheterocycles: 02EJO3075.
Syntheses of macrocyclic compounds, particularly heterophanes and crowns, by utilizing metal complexation, their structure, and function: 02YGK184.

A planning strategy for diversity-oriented syntheses of macroheterocycles: 04AG(E)46.
One-step syntheses of macrocyclic compounds: 01JHC1239.
Syntheses and functions of \(N\)- and \(N,O\)-macroheterocycles utilizing self-assembling: 04YGK194.

c. Applications. Cryptands and crown-compounds as components of lanthanide-containing molecular and supramolecular polynmetallic functional assemblies: 02CRV1897.
Pyridine analogs of [2.2]paracyclophane in asymmetric catalysis: 03OBC1256.

2. Crown Ethers and Related Compounds

Complexation of calixcrowns with Cs\(^+\) and its application in treating radioactive waste water: 02MI38.
Crown ethers and cryptands as electrolytes with encapsulated lithium ion: 02UK878.
Crowned Schiff base: 02MI39.
Crown ethers and aza-crowns as allosteric supramolecular receptors and catalysts: 04CRV3161.
Crown ethers as sensors for ions and molecular scaffolds for materials and biological models: 04CRV2723.
Hydrogen bonding of 18-crown-6 ether to ruthenium–ammine complexes at second sphere: 04CCR(248)185.
Liquid-crystal crown ethers: 02ZOB1625.
Molecular complexes of crown ethers in crystals and solutions: 02MI36.
Molecular design and recognition of crown ethers: 02MI37.
Molecular design and applications of photochromic crown compounds: 03BCJ225.
New trends in the chemistry of condensed azacrown ethers and azathiacrown ethers: 03JHC1.
Problems of the chemistry of \(N\)- and \(S\)-containing crown ethers: 03MI92.
Syntheses of oxathiacrown compounds based on reactions of sulfuryl chloride with unsaturated compounds and their extraction properties: 02KGS291.

3. Calixarenes and Related Compounds

Calixarenes, cavitands, carcerands, and cyclophanes as nanoscale molecular containers: 02BCJ393.
Calixpyrins, hybrid macromolecules at the structural crossroads between porphyrins and calixpyrroles: 02PAC1041.

Calixpyrroles and related compounds: 02H(57)169.

Chemistry of thiacalixarenes: 04EJO1675.

Coordination chemistry of the larger thia-, phosphacalixarenes, calixarenes with heterocyclic substituents and heterobridges: 03CCR(244)45.

Heterocalixarenes: 04KGS805.

Homooxacalixarenes: 04MI25, 04ZOR1599, 04ZOR639.

Hydrogen bonds around hydrophobic cavities of cyclocalixarenes with heteroatoms and heterocyclic fragments in bridges: 03ACR246.


The spirodienone route for the functionalization of calixarenes: 03SL1.

Thiacalixarenes as a new class of synthetic receptors: 03ZOR13.

Thiacalixarenes as a new molecular scaffold for host molecules: 02YGK550.

4. Catenanes, Rotaxanes and Related Compounds

Catenanes and rotaxanes as components of supramolecular systems self-assembled by donor–acceptor interaction between neutral organic subunits: 04MI27.

Rotaxanes containing quaternary azaaromatic moieties: 04H(63)2131.

From kinetic to thermodynamic assembly of catenanes (error checking, supramolecular protection, and oligocatenanes): 02SL1743.

Mechanically interlocked molecules incorporating cucurbituril and their supramolecular assemblies: 02CSR96.


Rotaxanes and catenanes built around octahedral transition metals: 04EJO1627.

Rotaxanes and catenanes as prototypes of molecular machines and motors: 03PAC1383.

5. Miscellaneous Macroheterocycles

Catalytic asymmetric aldol reactions in aqueous media using praseodymium triflate–chiral tetraoxa[4.4]-2,6-pyridinophane as catalyst: 03YGK445.

Cavitands and related container molecules: 02H(57)2179.

Chemistry and biology of salicylhalamide A (macrocyclic lactone of salicylic acid) and related compounds: 03CRV4283.

Chemistry of condensed macrocyclic formazans: 04JHC135.

Coordination chemistry of (E,E)-1,6,11-tris(arenesulfonyl)-1,6,11-triazacyclpentadeca-3,8,11-trienes and the catalytic properties of their palladium metal complexes: 04MI149.

Heteroannulenes: 02ACR944.

Recent advances in macrocyclic polyamines and their metal complexes: 04MI28.

Supramolecular chemistry of cucurbiturils, macroheterocycles including \( n \) glycoluril fragments, linked by \( 2n \cdot \text{CH}_2 \) (\( n = 5–10 \), mainly cucurbr[6]urils): 02UK840.

Syntheses and coordination chemistry of topologically constrained azamacrocycles: 03CCR(241)27.

Syntheses, characterizations, and reactivities of some macrobicyclic and macrotricyclic hetero-clathrochelate complexes: 02CCR(233–234)255.

Syntheses of amines using nitrobenzenesulfonamides (N-amides), in particular, total syntheses of natural macrocyclic polyamines: 04CC353.

Syntheses, reactivities, and physical properties of subphthalocyanines (macrocyclic nonplanar aromatic compounds containing three diiminoisoindole fragments connected with a boron atom by N–B bonds): 02CRV835.

Tetrathiafulvalene cyclophanes and cage molecules: 04CRV5115.

Ultrashort nonbonded contacts with molecular iron in hetero- and heteraphanes: 04EJO3763.

Use of bile acids as building blocks for the synthesis of macrocyclic “holophanes”, components of supramolecular systems: 04EJO3385.

Use of cavitands for molecular recognition and as supramolecular sensors: 04EJO451.

VIII. Heterocycles Containing Unusual Heteroatoms

A. GENERAL

Organometallic oxides of main group and transition elements (inorganic heterocycles): 03CRV2579.

Structure and stability of \( N_4 \) and \( N_5 \) systems: 03CCR(244)93.

Syntheses, structures, and thermolyses of three- and four-membered heterocyclic compounds containing highly coordinate main group elements (1,2-oxaphosphethanes, as intermediates in the Wittig reaction, 1,2-oxasiletanydes as intermediates in the Peterson reaction, 1,2-oxagermanides, 1,2-oxastannetanides, iodooxethanes, oxazaphosphetidines as intermediates of the aza Wittig reaction, diazaphosphetidines, thiasiliranides, selenaphosphiranes): 03BCJ471.

Synthesis, arrangement, and reactivity of arene–lanthanide compounds, among them complexes with phosphazobenzene, borabenzenes, phenazine ligands: 02CRV2089.

Unusual geometries in main group chemistry, particularly in Se-, Ge-, B-, and P-heterocycles: 04CSR210.

B. PHOSPHORUS HETEROCYCLES

Panorama and perspectives of phospha-organic chemistry: 03AG(E)1578.
Phosphorus heterocycles as ligands in highly efficient catalysts: 02AG(E)563.
1. **Chemistry of Individual Classes of P-Heterocycles**

   Carbene-like reactions, applications, and mechanistic insights of phosphinidene complexes (particularly, formation of $P$-heterocycles): 02EJO1127.

   Chemistry of $\lambda^3$-$2H$-azaphosphirene metal complexes: 02CCR(227)175.

   Electronic structures and syntheses of phospholes and their oligomers: 03CCR(244)1.

   Enantioselective catalysis using cyclic phosphamidodiesters of BINOL as ligands, containing two or three $P$–$N$ or $P$–$O$ bonds: 02CSR259.

   Organometallic complexes of phosphorus analogs of azoles: 03AHC(85)1.

   Syntheses and properties of phosphetanes: 02CRV201.

   Syntheses and properties of phosphorus–sulfur compounds on the basis of 1,3,2,4-dithiadiphosphetane 2,4-disulfides: 02ZOB1442.

   Syntheses, some properties, and structural features of 1,2-thiaphosphocyclanes (1,2-thiaphosphiranes, thiaphosphetanes, thiaphospholanes, and thiaphosphinanes: 03UK884.

   Transition metal complexes bearing a phosphenium ligand (cyclic phosphenium ions in the synthesis of $N,P$-heterocycles): 04MI15.

2. **Structure and Stereochemistry**

   Coordination complexes of bis(amido)cyclodiphosph(III/V and V/V)azane imides and chalcogenides: 02CCR(233–234)237.

3. **Reactivity**

   Applications of Lawesson’s reagent (2,4-bis(p-methoxyphenyl)-1,3-dithiadiphosphetane 2,4-disulfide) in organic and organometallic syntheses: 03S1929.

   Asymmetric hydroformylation catalyzed by highly cross-linked polystyrene-supported RS–BINAPHOS–Rh(I) complexes (phosphin–phosphite catalysts including dinaphtho-1,3,2-dioxaphosphepine ligands): 03YGK694.

   Asymmetric syntheses of compounds containing stereogenic phosphorus centers (reactions with participation of phosphines): 04ACR169.

   Asymmetric syntheses with chiral cyclic phosphorus auxiliaries (1,3,2-oxazaphosphorinanes, 1,3,2-oxazaphospholynes): 02S2633.

   Isolable 1,2-oxaphosphetanes as starting materials for the synthesis of olefins: 04M130.

   Recent applications of proazaphosphatranes in organic synthesis: 04ACA3.

   Transient 2$H$-phospholes as synthetic intermediates in organophosphorus chemistry: 04ACR954.

   Transition metal complexes and related catalytic, medicinal, and photoluminescent applications of 1,3,5-triaza-7-phospaadamantane: 04CCR(248)955.

4. **Synthesis**

   Catalytic methods of $P$–$C$ bond formation in the syntheses of phospholanes and phosphorus-containing derivatives of other heterocycles: 02ZOR1447.
Novel synthetic methodologies of $1H$-phospholes mediated by organometallic compounds: 04MI29.

Reactions of $\alpha$-diketones and $o$-quinones with phosphorus compounds in the syntheses of $P$-heterocycles (cyclophosphates, phosphorans, spirocyclic compounds): 02CRV629.

Syntheses of chiral $P,N$-ligands with pyridine–nitrogen and phosphorus donor atoms and their applications in asymmetric catalysis: 03T9471.

Synthesis of phosphorus heterocycles via ring-closing olefin metathesis: 04CRV2239.

C. BORON HETEROCYCLES

Synthesis, structure, reactivity, and potential applications of Group 13/15 organometallic compounds (four- and six-membered B-, Al-, Ga-, In-heterocycles): 03MI177.

1. Chemistry of Individual Classes of B-Heterocycles

C-aryl monocarbaborane chemistry: 02CCC869.
Cage C–H···X interactions in solid-state structures of icosahedral carboranes: 04CCR(248)457.
Chemistry of $o$-carboranyl derivatives: 01MI2.
Chemistry of closo-dodecaborate anion $[B_{12}H_{12}]^{2-}$: 02CCC679.
Organometallic complexes of boron analogs of azoles: 03AHC(85)1.

2. Reactivity

Phosphorus insertion into borane clusters: 02CCC843.

3. Applications

Chiral 1,3,2-oxazaborolidines in asymmetric synthesis: 04UK632.
Derivatives of closo-dodecaborate anion and their use in medicine: 02IZV1256.
Polyhedral boron compounds as potential linkers for the attachment of radiohalogens to targeted proteins and peptides: 02CCC913.
Use of small metallocarboranes: 02CCC728.

D. SILICON, GERMANIUM, TIN, AND LEAD HETEROCYCLES

1. Chemistry of Individual Classes of Heterocycles

$\text{Bis}$\((\text{cyclopentadienyl})\) metal complexes doubly bridged by silicon atoms: 03MI93.
Chemistry of octasilacubane: 04YGK107.
Cyclic ladder polysilanes with “staircase” structure: 03MI75.
Electronic structure and syntheses of siloles and related metalloles: 03CCR(244)1.
Group 14–16 double-bond compounds in the syntheses of Si-, Ge-, Sn-, and Pb-heterocycles: 01M14.
Heterocycles with endo- and exo Si–Si multiple bonds: 04YGK94.
Hydrazide-based hypercoordinate silicon compounds (Si-helates): 04M14.
Organometallic complexes of silicon analogs of azoles: 03AH(C85)1.
Relationship between photophysical properties and conformation of cyclic oligosi-
lanes with two or more silicon atoms: 02YGK762.
Sila-, germa-, and stannacycloprenenes: 03CRV1429.

2. Reactivity

[2 + 2] Cycloreversion of silacyclobutanes: 03CCR(244)149.
New, silicon-based, cross-coupling reactions with the participation of silatranes,
cyclic polysiloxanes, and Si-derivatives of heterocycles: 02ACR835.

3. Synthesis

Syntheses of Si- and Ge-hetarenes by taking advantage of kinetic stabilization: 04BCJ429.
Syntheses, structures, and reactions of anions and dianions of sila-, germa-, stanna-, and plumba-cyclopentadienes and related benzannulated systems: 04YGK790.

E. Selenium and Tellurium Heterocycles

1. General Sources and Topics

Intermolecular electron-transfer reactions of Se-heterocycles: 02ACR247.

2. Chemistry of Individual Classes of Heterocycles

Benzisoselenazol-3(2H)-ones as oxygen-transfer agents: 04M118.
Chemistry of selenoethers and telluroethers (Se- and Te-analogs of crown ethers,
tellurophenes, selenophenes and other Se- and Te-heterocycles as well as complexes
on their basis): 02CCR(225)159.
Cycloaddition reactions of selenoaldehydes and their generation via retro Die-
ls–Alder reaction of substituted 2-selenabicyclo[2.2.1]heptene derivatives, cycload-
ducts of selenoaldehydes with anthracene as a stable source of selenoaldehydes: 03YGK661.
Derivatives of tellurocarboxylic acids: 02ZOB1685.
Four-membered heterocycles containing high coordinate Se and Te as heteroat-
oms: 03CCR(244)137.
Molecular structure of selenophenes and tellurophenes: 02KGS867.
Organic metals and superconductors based on bis(ethylenedithio)tetraselenaf-
fulvalene (BETS): 04CRV5265.
Syntheses and reactions of Te-heterocycles containing a Te element of 14 group
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Synthesis strategies and chemistry of nonsymmetrically substituted tetrachalcogenafulvalenes: 04CRV5133.
Syntheses of selenochromans by reactions of allylic alcohols with TMSSe-Ph–AlBr₃ and cinnamyl aryl selenides with AlBr₃: 03YZ423.
Syntheses, structures, and reactions of β-telluroacroleins and β-tellurovinyl ketones leading to Te-heterocycles: 02UK1051.
Transformations of 1,2,3-selenadiazoles: 02KGS1629.

F. OTHER UNUSUAL HETERO CYCLES

1. Metallacycles

Catalytic multistep reactions via palladacycles: 03SL298.
Chemistry of stable metallaaromatic compounds of heavier group 14 elements, including silabenzene, 1- and 2-silanaphthalene, 9-silaanthacene, germabenzene, and 2-germanaphthalene: 04ACR86.
Chemistry of 1,2-dehydroosmabenzene derivatives: 04ACR479.
Chiral molecular tweezers: 04ACR862.
Features of structure and coordination in transition metal complexes of metalacyclopentadienes: 04UK563.
From AlX/GaX monohalide molecules to metalloid aluminum and gallium clusters (inorganic Al- and Ga-heterocycles): 01MI6.
Grid-type metal ion architectures in functional metallosupramolecular arrays: 04AG(E)3644.
Nonalternating inorganic heterocycles containing hydrazine as a building block: 02CCR(235)53.
Self-assembly of In-heterocycles: 02MI57.
Structure–reactivity relationships in the cyclo-oligomerization of 1,3-butadiene catalyzed by zerovalent nickel complexes (Ni-heterocycles as intermediates): 03MI76.
Syntheses of heterocycles by transition metal-catalyzed cycloaddition with the formation of metallacycles as intermediates: 02YGK26.
Syntheses, structures, reactivities, and potential applications of group 13/15 organometallic compounds (four- and six-membered B-, Al-, Ga-, In-heterocycles): 03MI77.
Titanocene derivatives with Ti–C σ-bonds: 02UK341.

2. Metal Chelates and Related Complexes

Chemistry of β-diketiminatometal complexes: 02CRV3031.
Metalloccyclophanes with N-heterocyclic fragments as transition metal-based supramolecular systems, their synthesis, photophysics, photochemistry, and potential applications as luminescent anion chemosensors: 02CCR(230)170.
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