Reactions of Nitrile Oxides and Nitrile Imines with Derivatives of 4,5-Dihydrooxazole and 4,5-Dihydrothiazole and with Related Compounds

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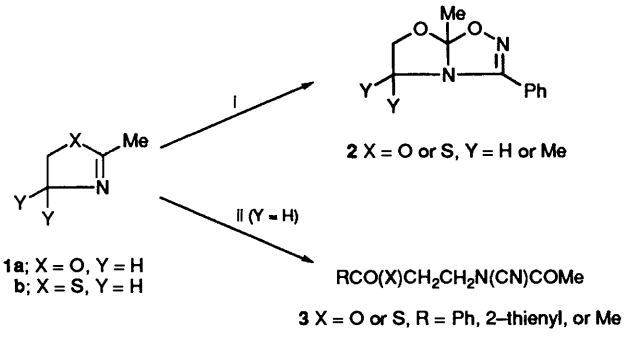
2-Phenyl-4,5-dihydrooxazole **4** gives a cycloadduct **6** when treated with benzonitrile *N*-oxide; with a 1-oxoalkane- or α-oxoarene-nitrile *N*-oxide (RCOCNO), an open-chain product, $RCO_2CH_2CH_2N(CN)COPh$, is obtained. The six-membered-ring analogue of compound **4** undergoes similar reactions. Depending on the nature of the ring substituents, a substituted 4,5-dihydrooxazole reacts with a *C,N*-diarylnitrile imine, to give either a cycloadduct, *e.g.* **17**, or a 1,2,4-triazol-4-ium salt, *e.g.* **19**. The product from the reaction of 4,5-dihydro-2-methylthiazole **1b** with a nitrile imine depends upon the nature of the C- and N-substituents in the latter. In all cases it is postulated that a 4-substituted triazolium salt **24** is formed. This may lose thiirane to give a substituted 1,2,4-triazole **25**, or it may react with a second molecule of the precursor of the nitrile imine, to give a 4-substituted 1,2,4-triazolium salt, *e.g.* **27**, in which the precursor moiety is incorporated into the C-4 side chain.

We have previously[1] shown that 2-methyl-4,5-dihydrooxazole **1a**, 2-methyl-4,5-dihydrothiazole **1b**, and their 4,4-dimethyl derivatives, all of which may be regarded as cyclic imidate esters, give the expected cycloadducts **2** on reaction with benzonitrile *N*-oxide. However, when compounds **1a** and **1b** are treated with 1-oxoalkane- or α-oxoarene-nitrile *N*-oxides (RCOCNO), a ring-opening reaction takes place to give products **3** (Scheme 1). We now continue these studies and extend them by the use of nitrile imines.



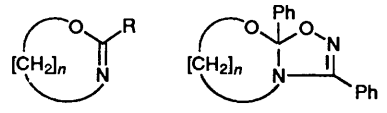
Scheme 1 *Reagents:* i, $PhC{\equiv}\overset{+}{N}{-}\bar{O}$; ii, $RCO{-}C{\equiv}\overset{+}{N}{-}\bar{O}$

Results and Discussion

In order to investigate further the scope of the cycloaddition/ring-opening reaction[1] we first replaced the 2-methyl group in compound **1a** by a 2-phenyl group, and so studied the reactions of 2-phenyl-4,5-dihydrooxazole **4**. This gave the cycloadduct **6** (62%) when treated with benzonitrile *N*-oxide and underwent the expected ring-opening reaction with the α-oxonitrile oxides, RCOCNO (R = Ph, Me or 2-thienyl), to give the open-chain compounds, **8** (58%), **9** (65%) and **10** (90%), respectively. Structures were confirmed spectroscopically by the methods described in our earlier[1] work.

We increased the size of the dipolarophile-containing ring and showed that the six-membered 2-phenyl-5,6-dihydro-4*H*-oxazine **5** behaved in a similar way to the five-membered analogue **4**. It gave the cycloadduct **7** with benzonitrile *N*-oxide and open-chain compounds **11**–**13** with the appropriate α-oxonitrile oxide.

Next we studied the cycloaddition reactions of dihydrooxazoles and dihydrothiazoles with nitrile imines. 2,4,4-Trimethyl-

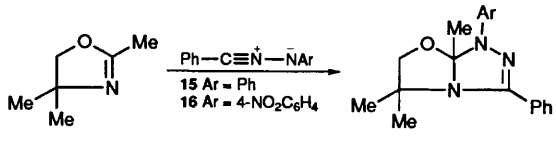


4 R = Ph, *n* = 2
5 R = Ph, *n* = 3
1a R = Me, *n* = 2

6 *n* = 2
7 *n* = 3

8 R = Ph, *n* = 2
9 R = Me, *n* = 2
10 R = 2-thienyl, *n* = 2
11 R = Ph, *n* = 3
12 R = Me, *n* = 3
13 R = 2-thienyl, *n* = 3

4,5-dihydrooxazole **14** reacted with the *C,N*-diarylnitrile imines **15** and **16**, to afford the expected cycloadducts **17** and **18** (Scheme 2). Surprisingly, however, when the attempted



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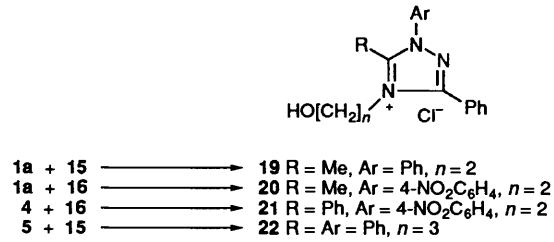
17 Ar = Ph
18 Ar = 4-$NO_2C_6H_4$

Scheme 2

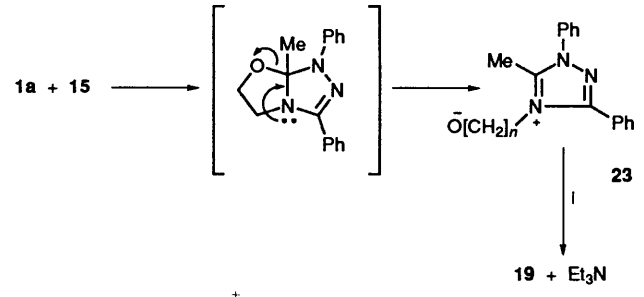
cycloaddition reaction was repeated on the dihydrooxazoles **4** and **1a** or on the dihydrooxazine **5** the 4-substituted 1,2,4-triazolium salts **19**–**22** were obtained in high yields (~70%) (Scheme 3). It is interesting that the presence (in substrate **14**) or



Scheme 3

absence (from substrate **1a**) of a 4,4-dimethyl group should alter the chemistry so markedly. The ionic nature of the products **19**–**22** was evident from the high m.p.s of compounds **19**, **20** and **22** (**21** was obtained as a homogeneous gum) and

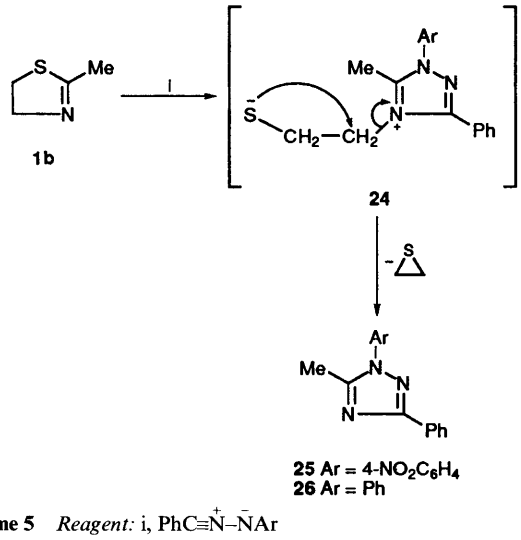
from the immediate precipitation of silver chloride when they were treated with silver nitrate. The ^{13}C NMR spectrum of each of the products showed two aromatic signals additional to those due to the benzenoid carbon atoms, consistent with the formation of a 1,2,4-triazole system; in the ^{1}H NMR spectrum the methylene protons of the side chain showed simple splitting, in contrast to the complex couplings observed for the ring protons in the starting materials. In order to explain the formation of the 1,2,4-triazolium salts **19–22**, we suggest that the initially formed cycloadduct undergoes fission of the bridgehead carbon–oxygen bond with concomitant aromatisation of the nitrogen-containing ring (illustrated for the conversion **1a** ⟶ **19** in Scheme 4). The resulting base **23** then



Scheme 4 *Reagent:* $Et_3\overset{+}{N}H\ Cl^-$

liberates Et_3N from triethylamine hydrochloride [formed during the *in situ* preparation of the nitrile imine from the *N*-phenylbenzohydrazonoyl chloride (PhCCl=NNHPh) and Et_3N], to give the triazolium salt **19** (and triazolium salts **20–22** *via* analogous intermediates).

When 2-methyl-4,5-dihydrothiazole **1b** reacted with *N*-(4-nitrophenyl)(benzonitrile imine) **16**, the product (55%) was clearly not the thiol analogue of the salt **20**. Instead, the side chain of the salt had been lost, to give 5-methyl-1-(4-nitrophenyl)-3-phenyl-1*H*-1,2,4-triazole **25**.[2] Our structural assignment was kindly confirmed by Professor R. N. Butler, University College of Galway, who showed that the IR spectrum of our sample was identical with that of an authentic sample of compound **25**. The isolation of thiirane from the reaction mixture confirmed our suggested mechanism (Scheme 5) for the loss of the $-CH_2CH_2S^-$ side chain. Ethene (6%) and

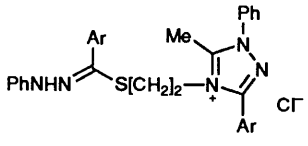


Scheme 5 *Reagent:* i, $PhC\overset{+}{\equiv}\overset{-}{N}-NAr$

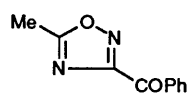
elemental sulfur, which were also formed in the reaction, may have arisen either by thermal decomposition of thiirane or by direct fragmentation of the $-CH_2CH_2S^-$ side chain.

In order to account for the different behaviour of the oxygen and sulfur heterocycles **1a** and **1b** towards nitrile imines the structures of the two zwitterionic intermediates **23** and **24** need to be considered. We suggest that the alkoxide side chain in intermediate **23** is sufficiently basic to displace triethylamine from its salt, and thus give the hydroxy salt, *e.g.* **19** (Scheme 4), whereas the less basic thiolate anion is unable to do this.[3] Further, the nucleophilic thiolate anion in intermediate **24** is better able to participate in an intramolecular nucleophilic substitution reaction than its more weakly nucleophilic oxygen counterpart in species **23**.

The reaction of 2-methyl-4,5-dihydrothiazole **1b** with *N*-phenyl(benzonitrile imine) **15** contrasted markedly with that just described for the nitro-substituted nitrile imine **16**. The expected 5-methyl-1,3-diphenyl-1*H*-1,2,4-triazole **26** (Scheme 5) was isolated in only 2% yield. Instead, the major product (56%) was the 1,2,4-triazolium salt **28**. In this case we assume that an intermediate of type **24** (Ar = Ph) is formed, and that its sulfur atom undergoes intermolecular nucleophilic substitution with PhCCl=NNHPh (the precursor of compound **15**) [contrast the case of compound **25**, which is formed from intermediate **24** (Ar = 4-$NO_2C_6H_4$) by intramolecular nucleophilic substitution]. When the dihydrothiazole **1b** reacted with 4-chlorobenzonitrile *N*-phenyl imine, there was no evidence of the intermediate **24** degrading to a 4-unsubstituted triazole; instead the 4-substituted triazolium salt **28** was isolated (60%).



27 Ar = Ph
28 Ar = 4-ClC_6H_4



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We conclude with a serendipitous observation. We have already reported[1] that 2-methyl-4,5-dihydrooxazole **1a** reacts with benzonitrile *N*-oxide, to give the ring-opened *N*-cyano compound **3** (R = Ph, X = O). Each time we carried out the experiment we isolated trace amounts (<0.5%) of another compound, which we did not identify at first; indeed we did not even mention its formation in our earlier[1] communication. We now recognise that it is 3-benzoyl-5-methyl-1,2,4-oxadiazole **29**, formed from the appropriate zwitterionic intermediate (*i.e.*, an oxygen analogue of intermediate **24**) by the (unfavoured) loss of oxirane (*cf.* Scheme 5).

Work is now in progress to investigate in more detail the electronic and structural factors which determine the subsequent fate of the cycloadduct formed when the C=N group of 4,5-dihydrooxazoles and 4,5-dihydrothiazoles reacts with 1,3-dipoles.

Experimental

General details are given in ref. 1. Appropriate NMR signals for aromatic rings were observed, but have been excluded in order to simplify the text. *J* Values are recorded in Hz. IR Spectra were determined for samples as KCl discs.

3,7a-*Diphenyl*-5,6-*dihydro*-7a*H*-*oxazolo*[3,2-d]-1,2,4-*oxadiazole* **6**.—Prepared (62%) from α-chlorobenzaldoxime, triethylamine and 2-phenyl-4,5-dihydrooxazole **4** by the method described in ref. 1, this was obtained as a *powder*, m.p. 98–99 °C (attempted recrystallisation caused decomposition) (Found: C, 72.45; H, 5.1; N, 10.25. $C_{16}H_{14}N_2O_2$ requires C, 72.15; H, 5.3; N, 10.5%); ν_{max}/cm^{-1} 1565 (C=N); δ_H 3.41 (1 H, ddd, $J_{c,d}$ 13.0, $J_{b,c}$ 9.5, and $J_{a,c}$ 6.0, H^c), 3.74 (1 H, ddd, $J_{a,b}$ 12.0, $J_{b,d}$ 5.5, H^b), 3.75 (1 H, ddd, $J_{a,d}$ 7.0, H^d) and 4.08 (1 H, ddd, H^a) (the signals H^a, H^b, H^c and H^d relate to the protons 5-H^aH^b-

6-H^{c}H^d, *i.e.* the protons attached to C-5 and C-6 of the reduced oxazole ring); δ_C 49.6 (C-5) and 64.5 (C-6); *m/z* 266 (M^+), 222 ($M^+ - OCH_2CH_2$), 147 ($M^+ - PhCNO$) and 77 (Ph^+, 100%).

3,8a-*Diphenyl*-6,7-*dihydro*-5H,8aH-1,2,4-*oxadiazolo*[5,4-b]-[1,3]*oxazine* **7**.—Prepared likewise from 2-phenyl-5,6-dihydro-4*H*-oxazine **5**,[4] this formed *needles* (42%), m.p. 121–122 °C (from diethyl ether–light petroleum) (Found: C, 72.65; H, 5.85; N, 9.75. $C_{17}H_{16}N_2O_2$ requires C, 72.85; H, 5.75; N, 10.0%); ν_{max}/cm^{-1} 1590 (C=N); δ_H 1.42 and 1.80 (each 1 H, m, 6-H_2), 3.34 and 3.65 (each 1 H, m, 5-H_2) and 3.82 and 4.24 (each 1 H, m, 7-H_2); δ_C 24.9 (C-6), 40.3 (C-5) and 61.4 (C-7); *m/z* 280 (M^+), 250 ($M^+ - OCH_2$), 119 ($PhCNO^+$) and 77 (Ph^+, 100%).

2-(N-*Cyanobenzamido*)*ethyl Benzoate* **8**.—This was prepared (58%) by heating compound **4** with *N*-hydroxy-α-oxo-α-phenylacetohydroxinoyl chloride [PhCOCCl(=NOH)] in dry toluene (*cf.* ref. 1). After purification by column chromatography [$CHCl_3$–light petroleum (1:1)], the product formed *crystals*, m.p. 89–90 °C (from EtOH) (Found: C, 69.1; H, 4.95; N, 9.35. $C_{17}H_{14}N_2O_3$ requires C, 69.35; H, 4.8; N, 9.5%); ν_{max}/cm^{-1} 2215 (C≡N), 1720 (ester C=O) and 1690 (amide C=O); δ_H 4.19 (2 H, t, *J* 6.5, NCH_2) and 4.66 (2 H, t, OCH_2); δ_C 43.7 (NCH_2), 67.1 (OCH_2), 111.0 (C≡N), 166.3 and 168.2 (C=O); *m/z* 105 ($PhCO^+$, 100%) and 77 (Ph^+); no M^+.

2-(N-*Cyanobenzamido*)*ethyl Acetate* **9**.—Prepared similarly (65%) from pyruvohydroximoyl chloride [MeCOCCl(=NOH)] and compound **4**, the title compound was purified by column chromatography [$CHCl_3$–light petroleum (1:1)], then by distillation (Kugelrohr). It formed an *oil*, b.p. 165 °C at 0.2 mmHg (Found: C, 62.1; H, 5.2; N, 12.1. $C_{12}H_{12}N_2O_3$ requires C, 62.05; H, 5.2; N, 12.05%); ν_{max}/cm^{-1} 2215 (C≡N), 1740 (ester C=O) and 1705 (amide C=O); δ_H 2.15 (3 H, s, MeCO), 4.19 (2 H, t, *J* 6.5, NCH_2) and 4.66 (2 H, t, OCH_2); δ_C 43.7 (NCH_2), 67.1 (OCH_2), 111.0 (C≡N), 166.3 and 168.2 (C=O); *m/z* 105 ($PhCO^+$, 100%) and 77 (Ph^+); no M^+.

2-(N-*Cyanobenzamido*)*ethyl Thiophene*-2-*carboxylate* **10**.—Prepared as before from compound **4** and α-oxo-α-(2-thienyl)acetohydroximoyl chloride [ThCOCCl(=NOH), Th = 2-thienyl], the title compound was chromatographed on silica [$CHCl_3$–light petroleum (1:1)], then was distilled to give an *oil* (90%), b.p. 155 °C (Kugelrohr) at 0.5 mmHg (Found: C, 60.05; H, 4.0; N, 9.4. $C_{15}H_{12}N_2O_3S$ requires C, 60.0; H, 4.05; N, 9.35%); ν_{max}/cm^{-1} 2215 (C≡N) and 1705br (ester and amide C=O); δ_H 4.17 (2 H, t, *J* 5.0, NCH_2) and 4.63 (2 H, t, OCH_2); δ_C 47.2 (NCH_2), 61.1 (OCH_2), 111.0 (C≡N), 161.8 and 168.2 (C=O); *m/z* 300 (M^+), 105 ($PhCO^+$, 100%) and 77 (Ph^+).

Compounds **11**–**13**.—These were prepared as just described from 2-phenyl-5,6-dihydro-4*H*-oxazine **5** and the appropriate nitrile oxide precursor.

3-(N-*Cyanobenzamido*)*propyl benzoate* **11** (58%), purified by chromatography on silica ($CHCl_3$), had b.p. 240 °C at 1 mmHg (Kugelrohr) (Found: C, 69.85; H, 5.25; N, 8.95. $C_{18}H_{16}N_2O_3$ requires C, 70.1; H, 5.25; N, 9.1%); ν_{max}/cm^{-1} 2215 (C≡N) and 1720br (ester and amide C=O); δ_H 2.31 (2 H, m, $CH_2CH_2CH_2$), 3.95 (2 H, t, *J* 7.0, NCH_2) and 4.45 (2 H, t, OCH_2); δ_C 27.6 ($CH_2CH_2CH_2$), 41.6 (NCH_2), 61.6 (OCH_2), 111.0 (C≡N), 166.4 and 168.4 (C=O); *m/z* 308 (M^+), 105 ($PhCO^+$, 100%) and 77 (Ph^+).

3-(N-*Cyanobenzamido*)*propyl acetate* **12** (53%), after elution from silica [$CHCl_3$–light petroleum (10:1)], had b.p. 175 °C at 0.05 mmHg (Kugelrohr) (Found: C, 63.6; H, 5.7; N, 11.4. $C_{13}H_{14}N_2O_3$ requires C, 63.4; H, 5.75; N, 11.4%); ν_{max}/cm^{-1} 2215 (C≡N) and 1725br (ester and amide C=O); δ_H 2.16 (2 H, m, $CH_2CH_2CH_2$), 1.85 (3 H, s, MeCO), 3.90 (2 H, t, *J* 6.5, NCH_2) and 4.23 (2 H, t, OCH_2); δ_C 20.9 (*Me*CO), 26.8 ($CH_2CH_2CH_2$), 45.2 (NCH_2), 60.1 (OCH_2), 110.9 (C≡N), 168.4 and 170.9 (C=O); *m/z* 105 ($PhCO^+$, 100%) and 77 (Ph^+); no M^+.

3-(N-*Cyanobenzamido*)*propyl thiophene*-2-*carboxylate* **13** (66%) was obtained from its precursor by the use of triethylamine (*cf.* ref. 1), then was purified on silica [$CHCl_3$–light petroleum (10:1)]. The resulting *oil* had b.p. 180 °C at 0.05 mmHg (Kugelrohr) (Found: C, 60.95; H, 4.45; N, 8.9. $C_{16}H_{14}N_2O_3S$ requires C, 61.1; H, 4.5; N, 8.9%); ν_{max}/cm^{-1} 2215 (C≡N) and 1720br (ester and amide C=O); δ_H 2.27 (2 H, m, $CH_2CH_2CH_2$), 3.90 (2 H, t, *J* 6.5, NCH_2) and 4.45 (2 H, t, OCH_2); δ_C 26.8 ($CH_2CH_2CH_2$), 45.3 (NCH_2), 61.3 (OCH_2), 111.0 (C≡N), 162.1 and 168.4 (C=O); *m/z* 314 (M^+), 105 ($PhCO^+$, 100%) and 77 (Ph^+).

5,5,7a-*Trimethyl*-1,3-*diphenyl*-5,6-*dihydro*-7aH-*oxazolo*[2,3-c][1,2,4]*triazole* **17**.—A mixture of 2,4,4-trimethyl-4,5-dihydrooxazole **14** (0.56 g, 5.0 mmol), *N*-phenylbenzohydrazonoyl chloride (PhCCl=NNHPh) (1.15 g, 5.0 mmol), triethylamine (0.51 g, 5.0 mmol) and dry benzene (100 cm^3) was stirred for 7 days, then the precipitated triethylamine hydrochloride was filtered off. Removal of the solvent under reduced pressure and trituration of the resulting oil with hexane gave the title compound as *needles* (0.55 g, 36%), m.p. 81–82 °C (from EtOH) (Found: C, 74.0; H, 6.9; N, 13.7. $C_{19}H_{21}N_3O$ requires C, 74.2; H, 6.9; N, 13.7%); ν_{max}/cm^{-1} 1595 (C=N); δ_H 1.05, 1.40 and 1.70 (each 3 H, s, Me), 3.65 (1 H, d, J_{gem} 4.0, *gem*-CH) and 3.85 (1 H, d, *gem*-CH); δ_C 23.52, 23.57 and 28.1 (each Me), 64.9 (C-5) and 77.2 (OCH_2); *m/z* 307 (M^+), 306 ($M^+ - H$) and 194 ($PhCNNPh^+$).

5,5,7a-*Trimethyl*-1-(4-*nitrophenyl*)-3-*phenyl*-5,6-*dihydro*-7aH-*oxazolo*[2,3-c][1,2,4]*triazole* **18**.—Prepared (36%) from *N*-(4-nitrophenyl)benzohydrazonoyl chloride by the method just described, the *title product* had m.p. 159–160 °C (from EtOH) (Found: C, 64.7; H, 5.7; N, 15.8. $C_{19}H_{20}N_4O_3$ requires C, 64.75; H, 5.7; N, 15.9%); ν_{max}/cm^{-1} 1585 (C=N); δ_H 1.00, 1.45 and 1.80 (each 3 H, s, Me), 3.55 (1 H, d, J_{gem} 4.0, *gem*-CH) and 3.90 (1 H, d, *gem*-CH); δ_C 23.4, 24.0 and 27.9 (each Me), 65.3 (C-5) and 77.8 (OCH_2); *m/z* 352 (M^+), 337 ($M^+ - Me$) and 239 ($4\text{-}NO_2C_6H_4NNCPh^+$).

4-(2-*Hydroxyethyl*)-5-*methyl*-1,3-*diphenyl*-1,2,4-*triazol*-4-*ium Chloride* **19**.—Reaction of 2-methyl-4,5-dihydrooxazole **1a** with PhCCl=NNHPh, using the conditions described for the preparation of compound **17**, gave solid material, which was purified by chromatography [$CHCl_3$–MeOH (9:1)], then by successive recrystallisations from ethanol (×2), ethanol–light petroleum, and water. The resulting *needles* (69%) had m.p. 179–180 °C (Found: C, 64.45; H, 5.9; Cl, 11.2. $C_{17}H_{18}ClN_3O$ requires C, 64.65; H, 5.75; Cl, 11.2%); ν_{max}/cm^{-1} 3130 (OH) and 1600 (C=N); δ_H[$(CD_3)_2SO$] 3.05 (3 H, s, Me) 3.95 (2 H, br t, NCH_2), 4.35 (2 H, br t, OCH_2) and 6.10 [1 H, br t, OH (coupled to CH_2)]; δ_C[$(CD_3)_2SO$] 12.1 (Me), 49.4 (NCH_2) and 58.1 (OCH_2); *m/z* 280 ($M^+ - Cl$), 279 ($M^+ - HCl$), 261 (279 – H_2O), 194 ($PhCNNPh^+$), 91 (PhN^+) and 77 (Ph^+).

The following compounds were obtained similarly.

4-(2-*Hydroxyethyl*)-5-*methyl*-1-(4-*nitrophenyl*)-3-*phenyl*-1,2,4-*triazol*-4-*ium chloride* **20** (90%) was purified by recrystallisation from EtOH (×3), column chromatography [$CHCl_3$–MeOH (9:1)], and further successive recrystallisations from EtOH and water. The resulting *needles* had m.p. 217–218 °C (Found: C, 55.4; H, 4.75; N, 15.45; Cl, 9.55. $C_{17}H_{17}ClN_4O_3$ requires C, 55.6; H, 4.75; N, 15.55; Cl, 9.7%); ν_{max}/cm^{-1} 3200br (OH) and 1600 (C=N); δ_H[$(CD_3)_2SO$] 3.05 (3 H, s, Me), 3.85 (2 H, br t, NCH_2), 4.45 (2 H, br t, OCH_2) and 6.05 [1 H, br t, OH (coupled to CH_2)]; δ_C[$(CD_3)_2SO$] 11.9 (Me), 49.1 (NCH_2)

and 58.0 (OCH_2); *m/z* 324 (M^+ – HCl), 239 (4-$NO_2C_6H_4NNCPh^+$) and 77 (Ph^+).

4-(2-*Hydroxyethyl*)-1-(4-*nitrophenyl*)-3,5-*diphenyl*-1,2,4-*triazol*-4-*ium chloride* **21** was obtained as a homogeneous *gum* (70%) following column chromatography [$CHCl_3$–EtOAc (19:1); then by gradual addition of MeOH to remove polar material] (Found: C, 62.6; H, 4.6; N, 13.3; Cl, 8.55. $C_{22}H_{19}ClN_4O_3$ requires C, 62.5; H, 4.55; N, 13.25; Cl, 8.4%); ν_{max}/cm^{-1} 3380br (OH) and 1605 (C=N); δ_H[$(CD_3)_2SO$] 1.75 (1 H, br s, OH), 3.60 (2 H, br t, NCH_2) and 4.35 (2 H, br t, OCH_2); δ_C[$(CD_3)_2SO$] 50.6 (NCH_2) and 58.6 (OCH_2); *m/z* 387 (M^+ – Cl), 386 (M^+ – HCl), 239 (4-$NO_2C_6H_4NNCPh^+$) and 77 (Ph^+).

4-(3-*Hydroxypropyl*)-1,3,5-*triphenyl*-1,2,4-*triazol*-4-*ium chloride* **22** formed a *glass* (70%), softening point 213–214 °C, after chromatography [$CHCl_3$–EtOAc (13:1); followed by the gradual addition of MeOH to remove polar material] (Found: C, 70.7; H, 5.7; N, 10.85; Cl, 9.1. $C_{23}H_{22}ClN_3O$ requires C, 70.5; H, 5.65; N, 10.7; Cl, 9.05%); ν_{max}/cm^{-1} 3200br (OH) and 1590 (C=N); δ_H[$(CD_3)_2SO$] 1.65 (2 H, m, $CH_2CH_2CH_2$), 1.95 (1 H, br s, OH), 3.35 (2 H, br t, NCH_2) and 4.45 (2 H, br t, OCH_2); δ_C[$(CD_3)_2SO$] 30.2 ($CH_2CH_2CH_2$), 46.6 (NCH_2) and 58.5 (OCH_2); *m/z* 355 (M^+ – HCl), 194 (PhCNNPh$^+$) and 77 (Ph^+).

5-*Methyl*-1-(4-*nitrophenyl*)-3-*phenyl*-1H-1,2,4-*triazole* **25**.—2-Methyl-4,5-dihydrothiazole **1b** (1.01 g, 10.0 mmol) reacted in solution in benzene with *N*-(4-nitrophenyl)benzohydrazonolyl chloride (2.76 g, 10.0 mmol) and triethylamine (2.02 g, 20.0 mmol) (*cf.* the preparation of the cycloadduct **17**) to give a solid, which was recrystallised first from EtOH (×2), then from aq. AcOH, to form compound **25** as needles (1.46 g, 55%), m.p. 139–149 °C (decomp.) (lit.,[2] 139–140 °C) (Found: C, 64.1; H, 4.1; N, 19.7. Calc. for $C_{15}H_{12}N_4O_2$: C, 64.3; H, 4.3; N, 20.0%); δ_H 2.65 (3 H, s, Me); δ_C 14.1 (Me); *m/z* 280 (M^+) and 239 (4-$NO_2C_6H_4NNCPh^+$); the IR spectrum was identical with that of authentic material.

The reaction was repeated in dichloromethane. The distillate obtained when the solvent was removed at the end of the reaction contained thiirane; δ_H 2.25 (s, CH_2); *m/z* 60 (M^+); its spectra were identical with those of an authentic sample. Ethene (6%) (determined iodometrically) was trapped as 1,2-dibromoethane. Shaking of the crude solid from the reaction with cold carbon disulfide extracted a small amount of elemental sulfur (identified by the mass spectrum).

5-*Methyl*-1,3-*diphenyl*-4-[2-(N-*phenylbenzohydrazonoylsulfanyl*)*ethyl*]-1H-1,2,4-*triazol*-4-*ium Chloride* **27** *and* 5-*Methyl*-1,3-*diphenyl*-1H-1,2,4-*triazole* **26**.—The solid material from the reaction of 2-methyl-4,5-dihydrothiazole **1b** with *N*-phenylbenzohydrozonoyl chloride in the presence of triethylamine (*cf.* the method just described for compound **25**) was chromatographed on silica [$CHCl_3$–MeOH (20:1)]. Eluted first, the triazole **26** formed needles (2%), m.p. 93–94 °C (shrinks at 80–85 °C) (lit.,[5] 92–93 °C) (Found: C, 76.3; H, 5.8; N, 17.75. Calc. for $C_{15}H_{13}N_3$: C, 76.55, H, 5.55; N, 17.85%); δ_H 2.60 (3 H, s, Me); δ_C 13.4 (Me); *m/z* 235 (M^+) and 194 (PhCNNPh$^+$).

Eluted next, the salt **27** (56%) was recrystallised from EtOH (×2), then from water, to give *needles*, m.p. 126–127 °C (Found: C, 63.15; H, 5.65; N, 12.1; Cl, 6.15; S, 5.7. $C_{30}H_{28}ClN_5S$·2.5 H_2O requires C, 63.1; H, 5.8; N, 12.25; Cl, 6.2; S, 5.6%); ν_{max}/cm^{-1} 3200br [OH (from water of crystallisation)], 1605 (C=N) and 1555 (NH); δ_H 2.45 [br s, H_2O (from water of crystallisation)], 3.0 (3 H, s, Me), 3.30 (2 H, t, *J* 6.5, SCH_2), 4.75 (2 H, t, NCH_2) and 8.85 (1 H, s, NH); δ_C 11.5 (Me), 29.1 (CH_2S) and 46.1 (NCH_2); *m/z* 254 (CH_2=CHSCPh=NNHPh), 235 (2-methyl-1,3-diphenyl-1,2,4-triazole fragment), 194 (PhCNNPh$^+$) and 91 ($C_6H_5N^+$, 100%); no M^+.

3-(4-*Chlorophenyl*)-5-*methyl*-1-*phenyl*-4-[2-(N-*phenylbenzohydrazonoylsulfanyl*)*ethyl*]-1H-1,2,4-*triazol*-4-*ium Chloride* **28**.—Prepared (60%) from compound **1b** and 4-chlorobenzonitrile *N*-phenylimine by the method just described, this was purified by chromatography [$CHCl_3$–MeOH (20:1)] and successive crystallisations from ethanol and water. Compound **28** formed *needles*, m.p. 122–123 °C (Found: C, 60.25; H, 5.15; N, 11.7· Cl, 17.95; S, 5.4. $C_{30}H_{26}Cl_3N_5S$ requires C, 60.55; H, 4.5; N, 11.7; Cl, 17.95; S, 5.4%) (reproducible C and H analyses could not be obtained owing to the presence of small amounts of tenaciously held water of crystallisation); ν_{max}/cm^{-1} 3400br [OH (from water of crystallisation)], 1600 (C=N), 1555 and 1310 (NH); δ_H 2.45 [br s, H_2O (from water of crystallisation)], 3.10 (3 H, s, Me), 3.35 (2 H, t, *J* 6.5, SCH_2), 4.75 (2 H, t, NCH_2) and 9.0 (1 H, s, NH); δ_C 12.8 (Me), 29.9 (CH_2S) and 47.8 (NCH_2); *m/z* 288/290 [CH_2=CHSC(4-ClC_6H_4)=NNHPh], 269/271 (substituted 1,2,4-triazole fragment), 228/230 (4-$ClC_6H_4CNNPh^+$) and 91 ($C_6H_5N^+$, 100%); no M^+.

Reinvestigation of the Reaction of 2-*Methyl*-4,5-*dihydrooxazole* **1a** *with Benzonitrile* N-*Oxide* (*with Mr. S. Hollas*).—The reaction was repeated as described in ref. 1, then the product was examined by TLC [$CHCl_3$–light petroleum (1:10)]. Material from the faint, faster running spot had spectra identical with those of authentic 3-benzoyl-5-methyl-1,2,4-oxidiazole **29**[6] (Found: M^+, 188.0585. Calc. for $C_{10}H_8N_2O_2$: M, 188.0586); ν_{max}/cm^{-1} 1650 (C=O); δ_H 2.69 (3 H, s, Me); *m/z* 111 (M^+ – Ph) and 105 ($PhCO^+$).

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References

1 D. J. Miller, R. M. Scrowston, P. D. Kennewell and R. Westwood, *Tetrahedron*, 1992, **48**, 7703.
2 R. N. Butler and K. J. Fitzgerald, *J. Chem. Soc., Perkin Trans. 1*, 1988, 1587.
3 see J. March, *Advanced Organic Chemistry*, Wiley, New York, 4th edn., 1992, p. 251.
4 S. Gabriel and P. Elfeldt, *Ber. Dtsch. Chem. Ges.*, 1891, **24**, 3213.
5 M. A. Pérez, C. A. Dorado and J. L. Soto, *Synthesis*, 1983, 483.
6 H. Brachwitz, *J. Prakt. Chem.*, 1971, **313**, 667.

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