# Electrophilic and Nucleophilic Substitution in the Triazole *N*-Oxides and *N*-Methoxytriazolium Salts: Preparation of Substituted 1,2,3-Triazoles

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2-Phenyltriazole 1-oxides are activated at C-5 towards both electrophilic and nucleophilic attack. The *N*-oxides can be selectively halogenated and, in turn, the halogen replaced by strong nucleophiles. On subsequent deoxygenation, the *N*-oxides yield halogeno-, methylthio-, and methoxy-triazoles. Methylation produces *N*-methoxytriazolium salts in which H-5 can be replaced by weak nucleophiles, *e.g.* fluoride ions. Thus fluoro-, chloro-, hydroxy-, alkoxy-, acyloxy-, amino-, substituted amino-, azido-, nitro-, mercapto-, alkylthio-, acylthio-, and cyano-substituents can be introduced in the triazole nucleus. Alternatively deprotonated *N*-methoxytriazolium salts react with electrophiles producing substituted triazole *N*-oxides. The reactions of triazole *N*-oxides with hydrogen chloride to give chlorotriazoles, and with acetyl chloride to give acetoxytriazoles, are explained.

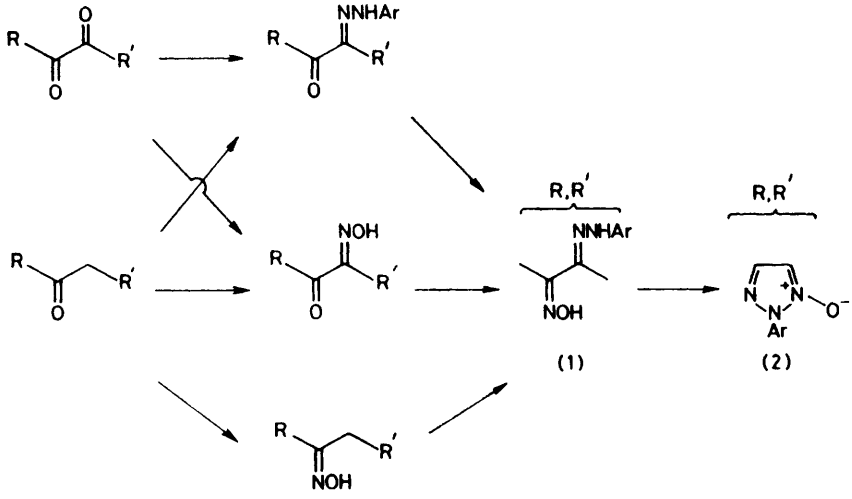


THE present work is directed towards the study of novel, general, and effective ways of introducing substituents into the 1,2,3-triazole nucleus, a ring system of growing interest. It is hoped that the principles described can be put to good use also in other five-membered heteroaromatic ring systems.

Monocarbon-substituted 1,2,3-triazoles, can be obtained by cyclization of suitable precursors or by replacement reactions in pre-formed triazoles.[1–3] The former method suffers from limited accessibility of starting materials, the latter by lack of reactivity and selectivity. In fact, selective monosubstitution at carbon atoms of triazoles has been accomplished in only a few cases. Thus, 1-alkyltriazoles on halogenation produce 4-halogeno-derivatives,[4,5] whereas triazole and 2-alkyltriazoles undergo dihalogenation.[5,6] 1- and 2-Aryltriazoles, when reacting at all, are attacked at the benzene nucleus upon bromination [6–9] or nitration.[10–12] Under forcing conditions, however, 2-aryltriazoles undergo mononitration in the triazole ring.[13,14] Nucleophilic substitution of 1-substituted-5-hydroxytriazoles to the corresponding chloro-compounds,[15,16] replacement of the halogen in these with cyanide,[17] ammonia,[18] or amine,[16] as well as the replacement of the amino-group of aminotriazoles *via* diazotization to give hydroxy-[19] or halogeno-triazoles [18,20] are methods severely limited by the difficult availability of the requisite hydroxy- and amino-triazoles.[1–3] Hence, a need exists for a general and effective method of monosubstituting 1,2,3-triazoles. In the present paper the introduction of substituents into the 2-phenyltriazole system is reported, the required activation of the triazole nucleus being brought about by an *N*-oxide function or alternatively an *N*-methoxy-grouping.

## RESULTS AND DISCUSSION

2-Aryltriazole 1-oxides (2) are readily available through oxidative cyclization [21–25] of *vic*-arylhydrazone oximes

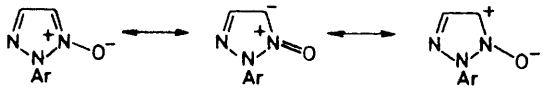



SCHEME 1

(1), accessible in their turn from: (*i*) *vic*-dicarbonyl compounds by selective monoarylhydrazone formation followed by reaction with hydroxylamine; [26,27] (*ii*) carbonyl compounds by coupling with arenediazonium ions at the α-position,[28,29] followed by treatment with hydroxylamine; (*iii*) carbonyl compounds or α-keto-

esters by nitrosation [30,31] and subsequent reaction with arylhydrazine; [26,32] (*iv*) oximation of carbonyl compounds with an activated α-methylene group and subsequent coupling with arenediazonium ions; [33] or (*v*) selective mono-oximation of *vic*-dicarbonyl compounds followed by condensation with arylhydrazine. On the other hand, our attempts to obtain 2-phenyltriazole 1-oxide by oxidation of 2-phenyltriazole with peracetic acid,[34,35] *meta*-chloroperbenzoic acid,[36,37] dichloropermaleic acid,[38] trifluoroperacetic acid,[35] peroxydisulphuric acid,[39] or t-pentyl hydrogen peroxide in the presence of molybdenum pentachloride [40] were of no avail.

2-*Phenyltriazole* 1-*Oxides. Reactions with Electrophiles and Nucleophiles*.—The resonance structures of a triazole *N*-oxide (2a—c) suggest that the carbon atom




(2a) (2b) (2c)

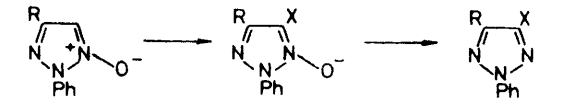
SCHEME 2

adjacent to the *N*-oxide function is activated both towards electrophilic and nucleophilic attack. That (2b) contributes significantly to the hybrid is evident from the carbon-13 chemical shifts. A comparison of these (see Experimental section) with those of 2-phenyltriazole [41] reveals that introduction of the *N*-oxygen atom causes high-field shift changes of C-5 (22.5 p.p.m.) and C-4 (6.7 p.p.m.), reflecting increased negative charge densities,[42] particularly at C-5. Simultaneous enhancement of reactivity towards nucleophiles of the *N*-oxide as compared to 2-phenyltriazole itself is suggested by the 10 Hz (C-5) and 6 Hz (C-4) larger one-bond C–H coupling constants in the former species. Larger coupling constants reflect increased positive charge on the nitrogen atoms in heteroaromatic rings.[42–44]

In previous studies, 2-aryltriazole *N*-oxides with a free 5-position have been reacted only with the acidic electrophile, nitric acid; it was maintained that only the benzenoid *para*-position is attacked.[21c] Our attempts to repeat this selective nitration *via* complicated mixtures of 4′-, 5-, and 4′,5-nitro-substituted derivatives led to 2′,4′,5-trinitrophenyltriazole *N*-oxide, a reaction course similar to that prevailing in the nitration of 2-phenyltriazole,[13,14] indicating a strongly diminished C-5 activation. Most likely, initial protonation of the *N*-oxygen atom, the basicity of which is documented by the ready transformation of triazole *N*-oxides into their hydrochlorides,[21a,c,d,f] is responsible for the deactivation. Thus, the 5-position of triazole *N*-oxides seems activated only towards neutral electrophiles. Accordingly, we found that chlorine and bromine effect selective monosubstitution at C-5 of 2-phenyltriazole 1-oxide and its 4-methyl derivative. That the halogen is introduced adjacent to the *N*-oxide function is evident from the disappearance of the high-field heteroaromatic proton $^1$H n.m.r. signal, and the collapse of the high-field heteroaromatic carbon doublet in the coupled $^{13}$C n.m.r. spectra (Table). Resonance structures indicate activation of the phenyl *ortho* and *para* positions towards electrophiles. However, the shift difference between C-3′ and C-2′ of the parent *N*-oxides (3; R = H or Me) indicates that the *N*-oxygen atom slightly impedes interannular conjugation.[45] Consequently, the phenyl group is deactivated and attack of the phenyl group is not observed.

The simultaneous activation of triazole *N*-oxides towards nucleophiles was demonstrated by displacement of the halogen of the 5-chlorotriazole *N*-oxide (4a; R = H) with methanethiolate, a reagent not affecting the de-oxygenated analogue. The less nucleophilic methoxide ion reacts sluggishly with the chlorotriazole *N*-oxide, while weaker nucleophiles, *e.g.* the thioacetate ion, leave it unaffected.

Only the methoxytriazole *N*-oxide (4n; R = H) exhibits the substituted heteroaromatic carbon n.m.r.




(3) R = H or Me

(4) a; X = Cl; b; X = Br; n; X = OMe; t; X = SMe; R = H or Me

(5) a; X = Cl; b; X = Br; n; X = OMe; t; X = SMe; R = H or Me

SCHEME 3

signal at the lowest field. However, a comparison of 2-phenyltriazole [41] and its 4-methoxy-derivative (5n; R = H) signifies that the methoxy-group causes shift displacements of 22.7 and −18.4 p.p.m. for the substituted and the adjacent carbon atom, respectively. Addition of these contributions to the heteroaromatic carbon n.m.r. shifts of the parent triazole *N*-oxide (3; R = H) provides predicted shifts for the methoxytriazole *N*-oxide (4n; R = H) which actually are inverted in their relative position. The shift difference between C-3′ and C-2′ of the *N*-oxides is 5.8—6.5 p.p.m. indicating that the *N*-oxygen atom impedes interannular conjugation slightly.[45] Like other *N*-oxides,[46] all the triazole *N*-oxides exhibit a characteristic $M^+ - 16$ peak in their mass spectra due to loss of oxygen. The *N*-oxides possessing a free 5-position show an additional $M^+ - OH$ peak. The *N*-oxygen atom can be removed chemically by treatment with phosphorus trichloride. The facile removal of the activating oxygen after the substitution reactions makes selectively monosubstituted 2-phenyltriazoles (5) readily available.

1-*Methoxy-2-Phenyltriazolium Salts. Nucleophilic Addition–Elimination*.—The limitations that only neutral electrophiles and strong nucleophiles can be introduced at C-5 of triazole *N*-oxides led us to try *O*-alkylation of these as a mode of further activation. *N*-Methoxytriazolium salts (6) are obtained in virtually quantitative yield by alkylation of the *N*-oxides with

trimethyloxonium tetrafluoroborate. The *N*-methoxytriazolium ion possesses a strongly electrophilic C-5 since *O*-alkylation cancels the negative charge on the oxygen atom. This is confirmed by the $^{13}C$ n.m.r. shift, C-5 is similar to that of C-5 of 1-methyl-2-phenyltriazolium bromide, which readily loses H-5 on treatment with base.[47]

Introduction of substituents into the activated position

$^1H$ N.m.r. shifts (p.p.m. relative to tetramethylsilane) and $^{13}C$ n.m.r. shifts [a] of 2-phenyl-1,2,3-triazole 1-oxides dissolved in deuteriochloroform (0.7M) (p.p.m. relative to the $CDCl_3$ centre peak at δ 76.90) and of 1-methoxy-2-phenyl-1,2,3-triazolium tetrafluoroborates dissolved in acetonitrile (0.7M) (p.p.m. relative to the $CD_3CN$ centre peak at δ −0.22). One- and two-bond C–H coupling constants are given in parentheses

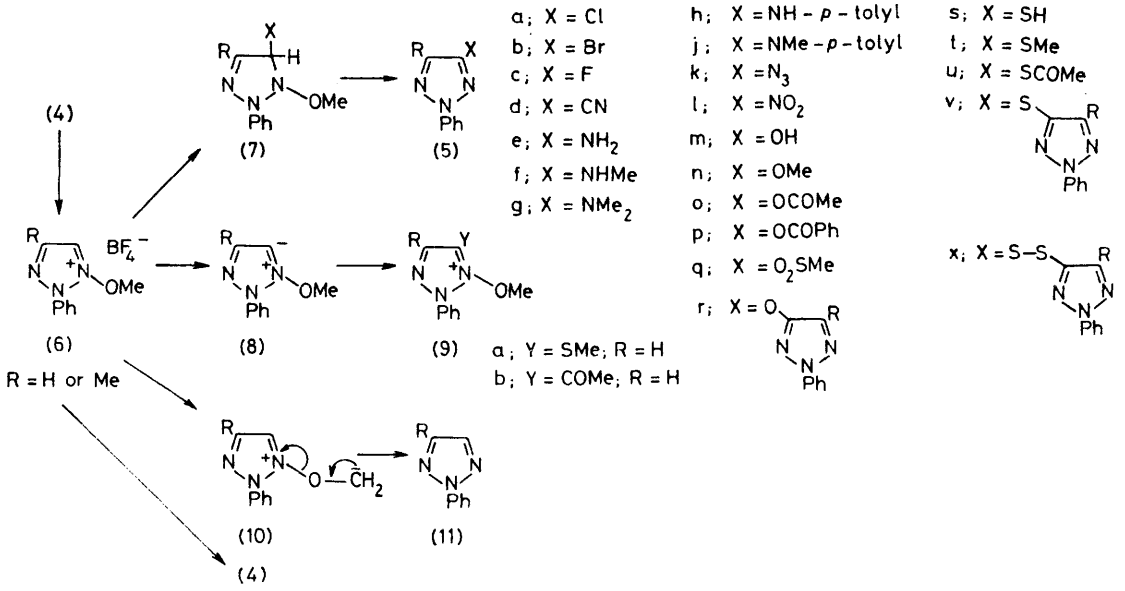
| | | H-4 | H-5 | $CH_3$ | C-4 | C-5 | C-1′ | C-2′ | C-3′ | C-4′ | $CH_3$ |
|---|---|---|---|---|---|---|---|---|---|---|---|
| 2-Phenyl-1,2,3-triazole 1-oxide | (3; R = H) | 7.67 [b] | 7.46 | | 132.7 [c] | 116.9 | 134.6 | 123.0 | 128.8 | 129.0 | |
| | | $J_{H-4,H-5}$ 0.9 Hz | | | (200; 9) | (204; 13) | | | | | |
| 4-Methyl- | (3; R = Me) | | 7.27 | 2.28 | 142.2 | 124.2 | 134.7 | 122.8 | 128.8 | 128.8 | 12.0 |
| 5-Methyl- | (4; R = H, [d] X=Me) | 7.56 | | 2.28 | 132.6 (195) | 125.2 | 135.0 | 122.6 | 128.7 | 128.7 | 8.1 |
| 5-Chloro- | (4a; R = H) | 7.71 | | | 131.1 | 119.1 | 134.9 | 122.6 | 129.0 | 129.4 | |
| 5-Bromo- | (4b; R = H) | 7.70 | | | 133.8 | 105.5 | 135.1 | 122.7 | 129.0 | 129.4 | |
| 5-Methoxy- | (4n; R = H) | 7.47 | | 4.04 | 120.1 | 143.4 | 134.8 | 122.5 | 128.9 | 128.9 | 59.4 |
| 5-Methylthio- | (4t; R = H) | 7.67 | | 2.47 | 134.7 | 123.9 | 135.0 | 122.5 | 128.9 | 128.9 | 14.6 |
| 5-Chloro-4-methyl- | (4a; R = Me) | | | 2.37 | 139.9 | 118.3 | 134.9 | 122.3 | 128.8 | 128.8 | 11.1 |
| 5-Bromo-4-methyl- | (4b; R = Me) | | | 2.33 | 142.0 | 105.9 | | 122.3 | 128.8 | 128.8 | 11.8 |
| 1-Hydroxy-2-phenyl-1,2,3-triazolium hydrogensulphate [e] | | 8.31 | 8.52 | | 136.3 (215; 8) | 128.1 (214; 14) | 132.4 | 125.9 | 131.2 | 134.4 | |
| 1-Methoxy-2-phenyl-1,2,3-triazolium tetrafluoroborate | (6; R = H) | 8.44 [b] | 8.99 | 4.36 | 135.9 [c] (214; 8) | 126.9 (215; 13) | 132.4 | 125.7 | 130.3 | 133.2 | 72.4 |
| 4-Methyl- | (6; R = Me) | | 8.78 | 4.32 2.55 | 146.2 (8) | 125.1 (214) | 132.5 | 125.7 | 130.3 | 133.0 | 72.1 |
| 5-Methyl- | (9; R = H, Y = Me) [f] | 8.28 | | 4.39 2.66 | 138.7 (208) | 134.8 | 132.6 | 125.1 | 129.9 | 132.6 | 70.6 7.4 |

[a] Signals were assigned through the coupled spectra as described in ref. 45. [b] The assignments of the H-4 and H-5 signals are based on the position of H-4 in the 5-methyl derivative and H-5 of the 4-methyl derivative. [c] The assignment of the C-4 and C-5 signals is based on the position of C-4 in the 5-methyl derivative and C-5 of the 4-methyl derivative. [d] Obtained by cyclization of methylglyoxal-2-oxime-1-phenylhydrazone. [e] Dissolved in concentrated sulphuric acid with the lock ($D_2O$) and chemical-shift standard (dioxan, δ 67.40 p.p.m.) in concentric tube. [f] Obtained by alkylation of 5-methyl-2-phenyltriazole 1-oxide.

being shifted 10 p.p.m. towards lower field by the *O*-alkylation.* Even more convincing is the simultaneous 10-Hz increase of the one-bond C–H coupling constant, a sensitive probe for estimating the charge on the nitrogen atoms of heteroaromatic rings.[42-44] In fact, the magnitude of the one-bond coupling constant of C-5 of the 1-methoxy-2-phenyltriazolium salt (6; R = H) is similar to that of C-5 of 1-methyl-2-phenyltriazolium bromide, which readily loses H-5 on treatment with base.[47]

* *O*-Alkylation also causes a decrease of the shift difference between C-3′ and C-2′ indicating increased impediment of the interannular conjugation.[45]

Introduction of substituents into the activated position of the *N*-methoxytriazolium ion seems possible by nucleophilic addition followed by elimination of methanol [(6) → (7) → (5)] or, alternatively, by abstraction of H-5 followed by electrophilic addition [(6) → (8) → (9)]. Competitive, but undesirable, transformations are (Scheme 4): (*i*) nucleophilic attack at the *O*-methyl group leading to dealkylation with regeneration of the *N*-oxide; (*ii*) deprotonation of the *O*-methyl group with subsequent loss of formaldehyde and the formation of 2-substituted-triazole; and (*iii*) ring-fission rather than




SCHEME 4

elimination when nucleophiles possessing an acidic hydrogen are used.

When the corresponding *N*-methoxypyridinium salts are treated with nitrogen, oxygen, sulphur, or halogen nucleophiles, dealkylation, deprotonation with elimination of formaldehyde, and addition followed by ring-fission are the major processes.[48a-53] Clean addition–elimination is observed only when carbon nucleophiles are employed.[49] However, when the *N*-methoxytriazolium ion is treated with these nucleophiles the reactions can be conducted to give, mainly, or solely, addition–elimination products. Thus, a variety of substituents can easily be introduced into the triazole nucleus. By way of example, while sodium azide dealkylates the *N*-methoxypyridinium ion it reacts readily at room temperature with 1-methoxy-2-phenyltriazolium tetrafluoroborate (**6**; R = H) in acetonitrile solution to give 4-azido-2-phenyltriazole (**5k**; R = H) in 73% yield. Similarly, ammonia in acetonitrile reacts with the methoxytriazolium salt (**6**; R = H) to give the aminotriazole (**5e**; R = H) in 79% yield. In addition, 7% of triazole *N*-oxide (**4**; R = H) is formed by dealkylation. The 4-methyl-substituted *N*-methoxytriazolium salt (**6**; R = Me) reacts similarly producing 73% of the aminotriazole (**5e**; R = Me). This confirms that C-5 of *N*-methoxytriazolium ions is the position most susceptible to nucleophilic attack. Methylamine reacts with the *N*-methoxytriazolium salt (**6**; R = H) producing methylaminotriazole (**5f**; R = H) together with a small amount of *N*-oxide. A second by-product here is dimethylaminotriazole (**5g**; R = H), obtained even in the presence of a hundred-fold excess of methylamine, indicating that dimethylamine, formed by alkylation of methylamine, is not a progenitor for the dimethylaminotriazole; more likely the initially formed methylaminotriazole undergoes *N*-methylation by the *N*-methoxytriazolium ion.

Aromatic amines also react smoothly with the *N*-methoxytriazolium ion. Thus, *p*-toluidine in two-fold excess yields *p*-toluidinotriazole (**5h**; R = H) as the major product. By-products are triazole *N*-oxide, *N*-methyl-*p*-toluidinotriazole (**5j**; R = H), and *N*-methyl-*p*-toluidine. In this case, the *N*-methyl-*p*-toluidinotriazole probably arises *via* alkylation of *p*-toluidine followed by addition–elimination.

Triethylamine dealkylates the *N*-methoxytriazolium ion quantitatively.

Nitrite ions react with the *N*-methoxytriazolium ion as an ambident nucleophile, yielding nitro- (**5l**) and nitrite-substituted triazoles. The latter species reacts further to give a complicated mixture.[7]

Potassium nitrate in acetonitrile dealkylates the *N*-methoxytriazolium ion quantitatively.

With two equivalents of aqueous sodium hydroxide the *N*-methoxytriazolium salt (**6**; R = H) produces a mixture of addition–elimination and dealkylation products. Hydroxytriazole (**5m**; R = H) is the initial addition–elimination product which then competes with the hydroxy-ions producing bistriazolyl ether (**5r**; R = H) by an additional addition–elimination reaction. Triazole *N*-oxide arises by *O*-dealkylation. Again, initially formed hydroxytriazole competes with the hydroxy-ions, being alkylated by (**6**; R = H) to give methoxytriazole (**5n**; R = H). The reaction conditions can be optimized to give either the single or the double addition–elimination product. Thus, low concentration of *N*-methoxytriazolium salt in an excess of strong base (aqueous sodium hydroxide) favours formation of hydroxytriazole (obtained in 83% yield), while a high concentration of *N*-methoxytriazolium salt and use of a weak base (sodium hydrogencarbonate) expedites formation of bistriazolyl ether (obtained in 74% yield). Again, the 1-methoxy-4-methyltriazolium salt (**6**; R = Me) reacts similarly with aqueous base.

Oxygen nucleophiles devoid of hydrogen also react predominantly with addition–elimination. Thus sodium methoxide in methanol, potassium benzoate in acetonitrile, and sodium methanesulphinate in acetonitrile produce methoxy-, benzoyloxy-, and methylsulphinyltriazole (**5n**, **5p**, **5q**; R = H), respectively.

When the *N*-methoxytriazolium salt (**6**; R = H) is treated with sulphide ions in methanol a double addition–elimination sequence, leading to bistriazolyl sulphide (**5v**; R = H), is the major process. The intermediate mercaptotriazole (**5s**; R = H) could not be detected even under conditions of high dilution of *N*-methoxytriazolium ion. Small amounts of methoxytriazole (**5n**; R = H) and 2-phenyltriazole are formed as by-products; the latter by deprotonation of the methoxy-group followed by elimination of formaldehyde, the former most likely *via* addition to the starting material (**6**; R = H) of methoxide ions present in the methanolic sulphide solution.

Methylthiolate ions in methanol convert the *N*-methoxytriazolium ion (**6**; R = H) into methylthiotriazole (**5t**; R = H) with 2-phenyltriazole as the sole by-product, while thioacetate ions in acetonitrile react in a clean addition–elimination fashion to give acetylthiotriazole (**5u**; R = H), which upon hydrolysis gives mercaptotriazole (**5s**; R = H) in high yield. 5-Mercapto-4-methyl-2-phenyltriazole (**5s**; R = Me) was obtained analogously from (**6**; R = Me) *via* the acetylthiotriazole (**5u**; R = Me).

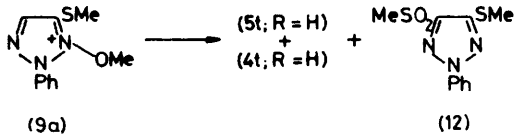
Clean addition–elimination also takes place when the *N*-methoxytriazolium anion is treated with cyanide ions to afford the cyanotriazole (**5d**; R = H).

Most remarkably, even the extremely weak nucleophilic fluoride ion reacts with the *N*-methoxytriazolium ion (**6**; R = H or Me) in acetonitrile solution at room temperature furnishing fluorotriazole (**5c**; R = H or Me) as the major product. Methoxytriazole (**5n**; R = H or Me) appears as a by-product, observed also when azide and cyanide ions are used as nucleophiles. Its formation by competitive addition of water, contained in the starting materials, to give hydroxytriazole, followed by *O*-alkylation by unchanged *N*-methoxytriazolium salt, is an unlikely event since the addition of 10 equiv. of water does not influence the fluorotriazole :

methoxytriazole ratio. Again, formation of methoxytriazole by addition of methanol, liberated during the production of fluorotriazole, to unchanged *N*-methoxytriazolium salt is unlikely since neither the presence of equimolar amounts of ethanol nor the use of ethanol as a solvent influences the fluorotriazole : methoxytriazole ratio significantly.* This indicates that the methoxtriazole is formed by intermolecular transfer of a methoxy-group, presumably from the initial adduct (7c), to unchanged starting material. Subsequent elimination of methanol then affords the methoxytriazole.

When the *N*-methoxytriazolium salt is treated with chloride ions the product composition depends on the nature of the cation. Thus, lithium, potassium, or tetrabutylammonium chlorides cleanly dealkylate the triazolium salt (6; R = H), while calcium or magnesium chloride also enter the addition–elimination reaction course to give the chlorotriazole (5a; R = H) in 13% yield.

1-*Methoxy-2-phenyltriazolium Salts. Deprotonation-Electrophilic Addition.*—Abstraction of an aromatic hydrogen followed by addition of an electrophile to the carbanion thus generated has so far not been reported for *N*-methoxypyridinium salts. Clean deprotonation of *N*-methoxytriazolium salts requires a base which must not act as a nucleophile causing addition or dealkylation. Therefore, the *N*-methoxytriazolium salt (6; R = H) was treated with the sterically hindered base, ethyldi-isopropylamine, in the presence of methylthiomethanesulphonate as the electrophile. This afforded the 5-methylthiotriazole 1-oxide (4t; R = H) as the main product. Isolated by-products were the methylthio- (5t; R = H), the methylsulphinyl- (5q; R = H), and most interestingly the 4-methylsulphinyl-5-methylthiotriazole (12), where both triazole hydrogen atoms




SCHEME 5

have been replaced, one with an electrophile, the other with a nucleophile. The methylthio-substituted products can all be derived from 1-methoxy-5-methylthio-2-phenyltriazolium ion, the expected result of electrophilic addition of methylthiomethanesulphonate to the carbanion (8; R = H) with simultaneous loss of methanesulphinate. Thus, dealkylation of (9a) induced by the liberated methanesulphinate will produce the methylthiotriazole *N*-oxide (4t; R = H) while deprotonation of the methoxy-group of (9a) with subsequent elimination of formaldehyde will give rise to the methylthiotriazole (5t; R = H). In fact, pure 1-methoxy-5-methylthio-2-phenyltriazolium tetrafluoroborate (9a), prepared by alkylation of 5-methylthio-2-phenyltriazole-*N*-oxide (4t; R = H), on treatment with methanesulphinate ions gave methylthiotriazole *N*-oxide (4t; R = H) and methylthiotriazole (5t; R = H). In the presence of ethyldi-isopropylamine, however, the 4-methylsulphinyl-5-methylthiotriazole (12) became the sole additional product.[7] It did not arise when the 1-methoxy-5-methylthiotriazolium salt (9a) was treated with the methylsulphinyltriazole (5q; R = H), even in the presence of ethyldi-isopropylamine. The mechanism of the formation of the 4-methylsulphinyl-5-methylthiotriazole (12) will be discussed in a forthcoming paper. The formation of the methylsulphinyltriazole by the reaction of 1-methoxy-2-phenyltriazolium tetrafluoroborate (6; R = H) with methylthiomethanesulphonate is most likely due to addition of methanesulphinate, liberated by the electrophilic addition, to unchanged starting material followed by elimination of methanol.

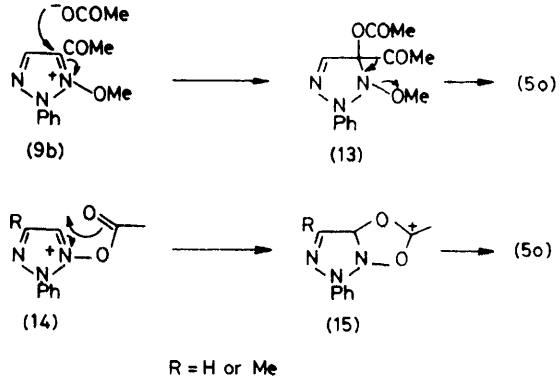
When the *N*-methoxytriazolium salt (6; R = H) is treated with ethyl di-isopropylamine and acetic anhydride deprotonation–addition is apparently involved. The main product is acetoxytriazole (5o; R = H) (67% yield) but its progenitor does not seem to be the *N*-oxide (3; R = H), formed by dealkylation of the *N*-methoxytriazolium ion, since pure *N*-oxide does not react with acetic anhydride, even in the presence of ethyldi-isopropylamine. The fact that *N*-methoxytriazolium salt only affords acetoxytriazole in the presence of ethyldi-isopropylamine suggests that a deprotonation–acetylation sequence has occurred producing the acetyl-*N*-methoxytriazolium ion (9b). The acetyl group supposedly activates the iminium centre of (9b) to attack by the acetate ion liberated during the acetylation. The adduct (13) formed finally eliminates methyl acetate to give the acetoxytriazole.

2-*Phenyltriazole* 1-*Oxides. Reactions with Hydrogen Chloride and Acetyl Chloride.*—The observed properties of the triazole *N*-oxides and the *N*-methoxytriazolium salts make it possible to rationalize the previously reported reactions of other triazole *N*-oxides with hydrogen chloride to give chlorotriazoles [21c,24,27] and the reaction with acetic anhydride to give acetoxytriazole.[27] The first reaction is performed at elevated temperature with hydrogen chloride in dioxan [24] or diethyl ether [21c] or with concentrated hydrochloric acid.[21c] The chlorine thus introduced into 4-methyl-2-phenyltriazole 1-oxide (3; R = Me) was assumed to adopt the phenyl-*para*-position.[21c] Reproducing the experiments we found that 4-methyl-2-phenyltriazole 1-oxide (3; R = Me) produces the 5-chlorotriazole (5a; R = Me). Similarly, 2-phenyltriazole 1-oxide affords 4-chloro-2-phenyltriazole (5a; R = H). Mechanisms involving oxidation of hydrogen chloride to chlorine, then halogenation of either the 2-phenyltriazole formed [21c] or unchanged *N*-oxide to give its 5-chloro-derivative, reduced by hydrogen chloride to the final chlorotriazole, could be excluded. Thus, halogenation of triazole was not observed, neither when a 1 : 1 mixture of 2-phenyltriazole and the 4-

* Ethoxytriazole is, in fact, produced, but only in the same amount as the methoxytriazole suggesting that addition of alcohol is slower than the process responsible for the methoxytriazole formation.

methyltriazole *N*-oxide (3; R = Me) was treated with hydrochloric acid to give the 4-chloro-5-methyltriazole (5a; R = Me) as the sole halogenotriazole, nor when a 1 : 1 mixture of 4-methyl-2-phenyltriazole and the triazole *N*-oxide (3; R = H) was treated in the same manner to produce 4-chloro-2-phenyltriazole, exclusively. The sequence involving reduction of the intermediate chlorotriazole *N*-oxide is unlikely since it is not converted, when heated in the pure state with hydrochloric acid, into the corresponding chlorotriazole. More likely, the transformation of triazole *N*-oxides into chlorotriazoles is initiated by protonation of the *N*-oxide, known to form hydrochlorides,[21a,c,d,f] and in sulphuric acid solution exhibiting $^{13}C$ n.m.r. shifts and C–H coupling constants (Table) similar to those of the *N*-methoxytriazolium ion. Subsequent addition of chloride ions to C-5 of the *N*-hydroxytriazolium ion, with final elimination of water, is analogous to the facile addition–elimination reactions of *N*-methoxytriazolium ions described above. A similar mechanism was observed in hydrogen-bromide-induced deoxygenative bromination of 1,2,4-triazine 2-oxides.[54]

Reaction of a triazole *N*-oxide with acetic anhydride to yield acetoxytriazole has previously been observed.[27] Neither 2-phenyltriazole 1-oxide, nor its 4-methyl derivative, reacted with acetic anhydride at room temperature. However, acetyl chloride converted the former compound into a mixture of chlorotriazole (5a; R = H) (11%) and acetoxytriazole (5o; R = H) (86%). The process obviously involves the position adjacent to the *N*-oxide function, since the 4-methyltriazole *N*-oxide reacts similarly. Again, an addition–elimination sequence seems to be operative, the iminium centre required arising by acylation to give an *N*-acetoxytriazolium ion (14). This may be attacked at




SCHEME 6

the iminium carbon atom by chloride ions liberated in the first step; subsequent elimination of acetic acid yields the chlorotriazole. Alternatively, the carbonyl oxygen atom may attack the iminium carbon atom to give the cyclic azadioxolenium ion (15) which may open either by nucleophilic addition of chloride ions at the triazole carbon atom to give (upon elimination of acetic acid) the chlorotriazole (5a) or, by deprotonation, to give the acetoxytriazole (5o). This mechanism is slightly different from that proposed, but apparently never proved, for the quantitative conversion of pyridine *N*-oxide into 2-acetoxypyridine when heated to 140 °C with acetic anhydride.[48b,55] It was assumed that the pyridine *N*-oxide after *O*-acetylation is attacked at C-2 by acetate ions, whereupon acetic acid is eliminated to give the final product.

## EXPERIMENTAL

Solvents were removed *in vacuo*. The purity and identity of all compounds were secured through t.l.c., m.p., i.r., $^1H$ n.m.r., and mass spectra. $^1H$ and $^{19}F$ n.m.r. spectra were recorded on a Bruker HX-90 instrument. $^{13}C$ N.m.r. spectra were obtained on a Bruker WH-90 instrument. Mass spectra were obtained on a V.G. Micromass 7070 F instrument.

*Preparation of Triazole* N-*Oxides*.—(*a*) Phenylhydrazine (26 ml) dissolved in 50% acetic acid (80 ml) was added with stirring to a 1.6% aqueous solution of glyoxal (1 500 ml) during 30 min. Stirring was continued for 2 h and the mixture was then filtered; the precipitate was washed with water, dried, and recrystallized (ethanol, 60 ml) to give 33.5 g (85%) of glyoxal phenylhydrazone, m.p. 107—109 °C [lit.,[56] 108 °C (decomp.)]. This material and hydroxylamine hydrochloride (25.4 g) were dissolved in ethanol (400 ml). A 17% solution of sodium hydroxide (96 ml) was added with stirring during 30 min and the mixture was filtered; the filtrate was concentrated at 40 °C to *ca.* 80 ml, kept at 5 °C for 4 d, and filtered to give 36.6 g (99%) of 2-phenylhydrazonoglyoxal 1-oxime as yellow crystals, m.p. 95—99 °C. This material was dissolved in boiling 15% aqueous pyridine (925 ml). A solution of copper(II) sulphate (88 g) in water (357 ml) was added with stirring, and heated to reflux during 30 min. Stirring and heating were continued for 4 h. The mixture was cooled to 20 °C, acidified to pH *ca.* 2 with 25% sulphuric acid, and extracted with dichloromethane (4 × 200 ml). The extract was washed twice with 2N sodium hydroxide (300 ml), dried ($MgSO_4$), and evaporated to dryness. Hexane (50 ml) was added and decanted off after 1 d at −25 °C. The residue was dissolved in methanol (400 ml) and filtered through activated carbon. Removal of the methanol afforded 23.0 g (80%) of light brown 2-*phenyl*-1,2,3-*triazole* 1-*oxide* (3; R = H), m.p. 56—59 °C. Recrystallization (ethanol) gave colourless crystals, m.p. 60—61 °C (Found: C, 59.6; H, 4.45; N, 26.15. $C_8H_7N_3O$ requires C, 59.6; H, 4.4; N, 26.1%); *m/e* 161 (100%, $M^+$), 145 (14, *M* − O), 144 (2, *M* − OH), 91 (55, $C_6H_5N$), and 77 (63, $C_6H_5$); n.m.r., see Table.

(*b*) A 5% sodium hydroxide solution (274 ml) and a 26% sodium nitrite solution (88 ml) were added to ethyl acetoacetate (42 ml). The mixture was stirred for 2 d, cooled to −10 °C, and 6N sulphuric acid (120 ml) added at such a rate that the temperature did not exceed 0 °C. The mixture was kept at 0—5 °C for 30 min, filtered, the precipitate and the filtrate extracted with ether (3 × 65 and 7 × 65 ml, respectively), the combined extracts dried ($MgSO_4$), and the ether removed to give 25.5 g (99%) of colourless, crystalline nitrosoacetone,[57] which was dissolved in ether (200 ml). Phenylhydrazine (30 ml) was added with cooling to 0 °C during 5 min. The mixture was kept at 20 °C for 3 h, dried ($MgSO_4$), filtered through activated carbon, and the volume reduced at 20 °C to 50 ml; it was

then cooled to −25 °C, filtered, and the precipitate dried to give 35.1 g (68%) of methylglyoxal 1-oxime 2-phenylhydrazone, m.p. 122—124 °C (lit.,[26] 134 °C). This material was oxidized as described in (*a*) to give 16.8 g (90%) of 4-methyl-2-phenyl-1,2,3-triazole 1-oxide (3; R = Me), m.p. 63—65 °C (lit.,[21c] 67—68 °C); *m/e* 175 (38%, $M^+$), 159 (45, $M^+ - O$), 158 (32, $M^+ - OH$), 91 (100, $C_6H_5N$), and 77 (43, $C_6H_5$); n.m.r. data in Table.

*Electrophilic and Nucleophilic Substitution Reactions of Triazole N-Oxides.*—(*a*) 2-Phenyl-1,2,3-triazole 1-oxide (3; R = H) (1.00 g) dissolved in chloroform (11 ml), sodium carbonate (0.43 g), and a solution of chlorine in tetrachloromethane (saturated at 0 °C; 5.3 ml) were stirred for 3 d. The solvents were then removed and water (30 ml) was added. Extraction with dichloromethane (4 × 30 ml), drying ($MgSO_4$), and removal of the dichloromethane gave 1.22 g of crude (4a; R = H) which was dissolved in ethyl acetate. Filtration through activated carbon, removal of the ethyl acetate, and recrystallization afforded 0.92 g (75%) of *5-chloro-2-phenyl-1,2,3-triazole 1-oxide* (4a; R = H) as colourless crystals, m.p. 70 °C (Found: C, 49.3; H, 3.15; N, 21.45; Cl, 17.95. $C_8H_6ClN_3O$ requires C, 49.1; H, 3.1; N, 21.5; Cl, 18.15%); *m/e* 195 (77%, $M^+$), 179 (6, $M^+ - O$), 91 (13, $C_6H_5N$), and 77 (100, $C_6H_5$); n.m.r. data in Table.

(*b*) 4-Methyl-2-phenyl-1,2,3-triazole 1-oxide (3; R = Me) (2.19 g) similarly produced 1.99 g (76%) of *5-chloro-4-methyl-2-phenyl-1,2,3-triazole 1-oxide* (4a; R = Me) as colourless crystals, m.p. 93—94 °C (Found: C, 51.75; H, 3.95; N, 20.0; Cl, 16.8. $C_9H_8ClN_3O$ requires C, 51.55; H, 3.85; N, 20.05; Cl, 16.9%); n.m.r. data in Table.

(*c*) Compound (3; R = H) (6.00 g), chloroform (50 ml), sodium carbonate (5.2 g), and water (67 ml) were cooled to 0 °C and bromine (7.4 ml) was added with efficient stirring during 1 min. Stirring was continued at 20 °C. After 3 h, when t.l.c. (toluene–ether [4 : 1]) indicated complete conversion, excess of bromine was removed by evaporation. Subsequent extraction with dichloromethane (30 + 3 × 10 ml), drying ($MgSO_4$), and removal of the dichloromethane gave crude (4b; R = H) which was purified as in (*a*) to give 9.00 g (100%) of *5-bromo-2-phenyl-1,2,3-triazole 1-oxide* (4b; R = H) as colourless crystals, m.p. 86—87 °C (Found: C, 40.15; H, 2.6; N, 17.5; Br, 33.1. $C_8H_6BrN_3O$ requires C, 40.0; H, 2.5; N, 17.5; Br, 33.3%); *m/e* 239 (33%, $M^+$), 223 (3, $M^+ - O$), 91 (12, $C_6H_5N$), and 77 (100, $C_6H_5$); n.m.r. data in the Table.

(*d*) Similarly (3; R = Me) (2.58 g) gave 3.46 g (93%) of *5-bromo-4-methyl-2-phenyl-1,2,3-triazole 1-oxide* (4b; R = Me) as colourless crystals, m.p. 61 °C (Found: C, 42.65; H, 3.3; N, 16.45; Br, 30.8. $C_9H_8BrN_3O$ requires C, 42.55; H, 3.15; N, 16.55; Br, 31.45%); n.m.r. data in the Table.

(*e*) Compound (3; R = H) (48 mg) dissolved in concentrated sulphuric acid (0.42 ml) and concentrated nitric acid (0.13 ml) were kept at room temperature. According to t.l.c. a mixture of products arose. Quenching by dilution with water, filtration, and preparative t.l.c. (ether–ethyl acetate–hexane [2 : 1 : 1]) gave 2-*p*-nitrophenyltriazole 1-oxide, m.p. 150—155 °C, 5-nitro-2-phenyltriazole 1-oxide, m.p. 114—120 °C, and 5-nitro-2-*p*-nitrophenyltriazole 1-oxide, m.p. 140—145 °C as initial products, identified through their $^1H$ n.m.r. spectra. These products were detectable after 1 min of reaction time. The final product, 2-(2,4-dinitrophenyl)-5-nitrotriazole 1-oxide emerges after *ca.* 2 h. The starting material was consumed after 13 d. Performing the reaction at −20 °C or omission of the sulphuric acid did not improve the specificity. A preparative experiment using four times the amount of nitric acid and heating to 100 °C for 2 h gave on dilution 50% of *5-nitro-2-(2,4-dinitrophenyl)-1,2,3-triazole 1-oxide*, m.p. 163—167 °C. Recrystallization (dichloromethane–ether) gave a product of m.p. 173 °C (Found: C, 32.1; H, 1.5; N, 26.6. $C_8H_4N_6O_7$ requires C, 32.45; H, 1.35; N, 28.4%); δ($CDCl_3$) 9.06 (1 H, d, *J* 2.7 Hz, H-3′), 8.72 (1 H, dd, *J* 2.7 and 9.2 Hz, H-5′), 8.48 (1 H, s, H-4), and 7.95 (1 H, d, *J* 9.2 Hz, H-6′).

(*f*) 5-Chloro-2-phenyl-1,2,3-triazole 1-oxide (4a; R = H) (0.48 g) was heated to reflux with 1.3M methanolic sodium methoxide (2.0 ml) for 9 h. The methanol was removed and the residue worked up as in (*g*) below to give an ether extract which on evaporation to dryness gave a residue which was flash-chromatographed[58] (ethyl acetate). The first fraction contained 0.16 g (33%) of unchanged (4a; R = H). The next fraction contained 68 mg (14%) of *5-methoxy-2-phenyl-1,2,3-triazole 1-oxide* (4n; R = H), yellow crystals, m.p. 73—74 °C. Recrystallization (ethyl acetate–hexane) gave a product of m.p. 81 °C (Found: C, 56.65; H, 4.75; N, 21.85. $C_9H_9N_3O_2$ requires C, 56.55; H, 4.75; N, 22.0%); *m/e* 192 (45%, $M^+$), 176 (11, $M^+ - O$), 91 (15, $C_6H_5N$), and 77 (100, $C_6H_5$); n.m.r. data in the Table.

(*g*) (4a; R = H) (0.67 g) and a 55% suspension of sodium hydride in mineral oil (Fluka) (0.18 g) were placed in a flask equipped with a solid $CO_2$–acetone-cooled reflux condenser with a drying tube. Methanethiol (5 ml) distilled from $CaSO_4$ was condensed in the flask. After stirring under reflux for 2 h the methanethiol was allowed to evaporate, methanol (4 ml) was added, and the mixture heated to reflux for 1 h. Subsequent evaporation to dryness, extraction with dichloromethane (4 × 10 ml), and removal of the dichloromethane gave a residue which was washed with hexane (3 × 4 ml) (decanting performed after cooling to −25 °C). The residue was extracted with ether (50 + 3 × 10 ml). The extract was filtered, and its volume reduced to 10 ml. On cooling to −25 °C, 0.70 g (98%) of *5-methylthio-2-phenyl-1,2,3-triazole 1-oxide* (4t; R = H), m.p. 71—73 °C, separated. Recrystallization (ether) gave off-white crystals, m.p. 76—79 °C (Found: C, 52.1; H, 4.4; N, 20.3; S, 15.55. $C_9H_9N_3OS$ requires C, 52.15; H, 4.4; N, 20.3; S, 15.45%); *m/e* 207 (33%, $M^+$), 191 (5, $M^+ - O$), 190 (20, $M - OH$), 119 (17), 117 (18), 91 (7, $C_6H_5N$), and 77 (100, $C_6H_5$); n.m.r. data in the Table.

(*h*) (3; R = H) (0.13 g) and concentrated hydrochloric acid (1.5 ml) were heated in a sealed tube to 150 °C for 3 h. The mixture was neutralized (sodium hydrogencarbonate) and extracted with dichloromethane (2 × 5 ml). Drying ($MgSO_4$) and removal of the dichloromethane afforded 0.10 g (71%) of *4-chloro-2-phenyl-1,2,3-triazole* (5a; R = H), m.p. 33—36 °C. Recrystallization (hexane) gave colourless crystals, m.p. 39—40 °C (Found: C, 53.7; H, 3.45; N, 23.45; Cl, 19.65. $C_8H_6ClN_3$ requires C, 53.5; H, 3.35; N, 23.4; Cl, 19.75%); *m/e* 179 (100%, $M^+$); δ($CDCl_3$) 7.66 (1 H, s, H-5), and 8.2—7.9 and 7.6—7.25 (2 H, m, and 3 H, m, Ph).

(*j*) Similarly, (3; R = H) (53 mg), 4-methyl-2-phenyl-1,2,3-triazole (11; R = Me) (53 mg)[59] and concentrated hydrochloric acid (0.6 ml) gave a crude product which was flash-chromatographed (toluene).[58] The first fraction contained 34 mg (58%) of 4-chloro-2-phenyltriazole (5a; R = H) identical with the material above. The second fraction contained 49 mg (92%) of unchanged 4-methyl-2-phenyltriazole.

(*k*) Similarly (3; R = Me) (0.26 g), 2-phenyl-1,2,3-triazole (11; R = H) [12] (0.22 g), and concentrated hydrochloric acid (2.6 ml) yielded 0.26 g (90%) of *5-chloro-4-methyl-2-phenyl-1,2,3-triazole* (5a; R = Me), m.p. 41—45 °C; recrystallization (hexane) gave a product of m.p. 45 °C (lit.,[21c] 45—46 °C); δ($CDCl_3$) 8.0—7.85 and 7.55—7.15 (2 H, m, and 3 H, m, Ph) and 2.33 (3 H, s, Me).

(*l*) (3; R = H) (0.16 g) and acetyl chloride (1.6 ml) were kept at 20 °C for 1 d. The acetyl chloride was removed, the residue extracted with ether (4 × 10 ml), the ether removed, and the residue flash-chromatographed; [58] dichloromethane–hexane (1 : 3) gave 20 mg (11%) of 4-chloro-2-phenyltriazole (5a; R = H), m.p. 37 °C; then elution eith ethyl acetate–hexane (1 : 4) gave 0.17 g (86%) of *4-acetoxy-2-phenyl-1,2,3-triazole* (5o; R = H), m.p. 33—34 °C. Recrystallization (hexane) gave a product of m.p. 34 °C (Found: C, 59.25; H, 4.45; N, 20.9. $C_{10}H_9N_3O_2$ requires C, 59.1; H, 4.45; N, 20.7%); *m/e* 203 (10%, $M^+$), 161 (100, $M^+ - C_2H_2O$), δ($CDCl_3$) 7.79 (1 H, s, H-5), 8.05—7.85 and 7.55—7.15 (2 H, m, and 3 H, m, Ph), and 2.34 (3 H, s, Me).

(*m*) Similarly, (3; R = Me) (0.37 g) and acetyl chloride (3.5 ml) furnished 0.17 g (42%) of 4-chloro-5-methyl-2-phenyltriazole (5a; R = Me) and 0.26 g (57%) of *4-acetoxy-5-methyl-2-phenyl-1,2,3-triazole* (5o; R = Me), m.p. 51 °C. Recrystallization (hexane) gave a product of m.p. 53—54 °C (Found: C, 61.15; H, 5.3; N, 19.4. $C_{11}H_{11}N_3O_2$ requires: C, 60.8; H, 5.1; N, 19.35%); δ($CDCl_3$) 8.0—7.8 and 7.55—7.25 (2 H, m, and 3 H, m, Ph), 2.38 (3 H, s, Me), and 2.26 (3 H, s, Me).

*Deoxygenation of Triazole N-Oxides.*—(*a*) 5-Chloro-2-phenyl-1,2,3-triazole 1-oxide (4a; R = H) (0.94 g) and phosphorus trichloride (0.91 ml) were stirred and heated to reflux for 1 h. Subsequent stirring with water (10 ml) for 1 h, extraction with dichloromethane (3 × 7 ml), drying ($K_2CO_3$), removal of the dichloromethane, dissolution in ether, filtering through activated carbon, and evaporation to dryness left 0.82 g (95%) of 4-chloro-2-phenyl-1,2,3-triazole (5a; R = H), m.p. 38—39 °C, identical with the material described above.

(*b*) Similarly, 5-chloro-4-methyl-2-phenyl-1,2,3-triazole 1-oxide (4a; R = Me) produced 90% of 5-chloro-4-methyl-2-phenyltriazole (5a; R = Me), identical with the material above.

(*c*) Similarly, 4-bromo-2-phenyl-1,2,3-triazole 1-oxide (4b; R = H) (1.31 g) and phosphorus trichloride (1.0 ml) yielded 1.18 g (97%) of *4-bromo-2-phenyl-1,2,3-triazole* (5b; R = H) as colourless crystals (hexane), m.p. 48—50 °C (Found: C, 43.0; H, 2.7; N, 18.9; Br, 36.05. $C_8H_6BrN_3$ requires C, 42.9; H, 2.7; N, 18.75; Br, 35.65%); *m/e* 223 (100%, $M^+$); δ($CDCl_3$) 7.74 (1 H, s, H-5), and 8.1—7.9 and 7.6—7.3 (2 H, m, and 3 H, m, Ph).

(*d*) Similarly, 5-bromo-4-methyl-2-phenyl-1,2,3-triazole 1-oxide (4b; R = Me) produced 100% of *5-bromo-4-methyl-2-phenyl-1,2,3-triazole* (5b; R = Me), m.p. 55 °C (hexane) (Found: C, 45.45; H, 3.35; N, 17.5; Br, 32.95. $C_9H_8BrN_3$ requires C, 45.4; H, 3.4; N, 17.65; Br, 33.55%); δ($CDCl_3$) 8.05—7.85 and 7.55—7.2 (2 H, m, and 3 H, m, Ph), and 2.36 (3 H, s, Me).

(*e*) Similarly, 4-methylthio-2-phenyl-1,2,3-triazole 1-oxide (4t; R = H) (0.36 g) and phosphorus trichloride (0.34 ml) produced an oil which was dissolved in hexane and filtered through activated carbon. Removal of the hexane gave 0.33 g (100%) of *4-methylthio-2-phenyl-1,2,3-triazole* (5t; R = H) as a colourless oil (Found: C, 56.35; H, 4.7; N, 22.05; S, 16.95. $C_9H_9N_3S$ requires C, 56.55; H, 4.75; N, 22.0; S, 16.8%); *m/e* 191 (100%, $M^+$); δ($CDCl_3$) 7.62 (1 H, s, H-5), 8.05—7.9 and 7.55—7.25 (2 H, m, and 3 H, m, Ph), and 2.58 (3 H, s, Me).

*Preparation of 1-Methoxytriazolium Salts.*—(*a*) 2-Phenyl-1,2,3-triazole 1-oxide (3; R = N) (1.30 g) dried over $P_2O_5$, trimethyloxonium tetrafluoroborate [60] (1.43 g), and dichloromethane (14 ml), dried over $K_2CO_3$ and then over molecular sieves (3 Å), were stirred for 3 d. Then ether, distilled from $LiAlH_4$ (35 ml) was added. The mixture was pressure-filtered (in order to avoid moisture) to give 1.99 g (94%) of *1-methoxy-2-phenyl-1,2,3-triazolium tetrafluoroborate* (6; R = H), colourless crystals, m.p. 131—134 °C (Found: C, 41.1; H, 3.95; N, 15.9. $C_9H_{10}BF_4N_3O$ requires C, 41.25; H, 3.45; N, 16.0%); n.m.r. data in the Table.

(*b*) Analogously, 4-methyl-2-phenyl-1,2,3-triazole 1-oxide (3; R = Me) gave 98% of colourless *1-methoxy-4-methyl-2-phenyl-1,2,3-triazolium tetrafluoroborate* (6; R = Me), m.p. 82—83 °C (Found: C, 43.3; H, 4.55; N, 15.15; $C_{10}H_{12}BF_4N_3O$ requires C, 43.35; H, 4.35; N, 15.15%); n.m.r. data in the Table.

*Reactions of 1-Methoxy-2-phenyl-1,2,3-triazolium Tetrafluoroborates with Nucleophiles.—General.* All solid nucleophiles used were finely ground and carefully dried over $P_2O_5$ at 1.3 Pa. Acetonitrile was purified [61] and dried over molecular sieves (3Å). Methanol was distilled from magnesium.[62] Moisture was carefully excluded during the reactions.

(*a*) 1-Methoxy-2-phenyl-1,2,3-triazolium tetrafluoroborate (6; R = H) (0.62 g), potassium hydrogenfluoride (3.5 g), and acetonitrile (20 ml) were stirred for 3 d. The solvent was removed and the residue extracted with dichloromethane (4 × 10 ml). The dichloromethane was removed and the residue flash-chromatographed [58] using dichloromethane–hexane (1 : 4) as the eluant. The first fraction contained 0.24 g (61%) of *4-fluoro-2-phenyl-1,2,3-triazole* (5c; R = H), a colourless oil which crystallizes at low temperature, m.p. 5 °C (Found: C, 59.0; H, 3.75; N, 25.65. $C_8H_6FN_3$ requires C, 58.9; H, 3.7; N, 25.75%); *m/e* 163 (100%, $M^+$); $\delta_H$($CDCl_3$) 7.42 (1 H, d, *J* 7.3 Hz), 8.0—7.85 and 7.55—7.25 (2 H, m, and 3 H, m, Ph); $\delta_F$ ($CDCl_3$; reference $CFCl_3$) 144.3 (d, *J* 7.3 Hz); $\delta_C$ ($CDCl_3$) 162.6 (d, $J_{CF}$ 248 Hz, C-4), 119.7 (d, $J_{CCF}$ 29 Hz, C-5), 139.5 (C-1′), 118.1 (C-2′), 129.1 (C-3′), and 127.5 (C-4′). The next fraction contained 36 mg (9%) of 4-methoxy-2-phenyltriazole (5n; R = H), identical with the material described below. The column was then eluted with ethyl acetate to give 27 mg (7%) of 2-phenyltriazole 1-oxide (3; R = H), identical with the material described above.

(*b*) Similarly, 1-methoxy-4-methyl-2-phenyl-1,2,3-triazolium tetrafluoroborate (6; R = Me) produced colourless *5-fluoro-4-methyl-2-phenyl-1,2,3-triazole* (5c; R = Me) (64%), m.p. *ca.* 7 °C (Found: C, 61.25; H, 4.6; N, 24.05. $C_9H_8FN_3$ requires C, 61.0; H, 4.55; N, 23.7%); *m/e* 177 (100%, $M^+$); δ($CDCl_3$) 7.95—7.8 and 7.55—7.2 (2 H, m, and 3 H, m, Ph) and 2.32 (3 H, s, Me); $\delta_F$ ($CDCl_3$, reference $CFCl_3$) 147.8 (s); $\delta_C$ ($CDCl_3$) 129.1 (C-4, d, $J_{CCF}$ 20 Hz), 160.8 (C-5, d, $J_{CF}$ 250 Hz), 139.6 (C-1′), 117.6 (C-2′), 129.1 (C-3′), 126.8 (C-4′), and 8.1 (Me). The second product was the colourless *5-methoxy-4-methyl-2-phenyl-1,2,3-triazole* (5n; R = Me) (9%) as an oil; *m/e* 189.089 9 (100%) ($C_{10}H_{11}N_3O$ requires 189.090 2); δ($CDCl_3$) 7.95—7.75 and 7.5—7.15 (2 H, m, and 3 H, m, Ph), 3.99 (3 H, s, OMe), and 2.25 (3 H, s, CMe).

(*c*) (**6**; R = H) (**0.11 g**), non-aqueous magnesium chloride * (0.13 g), and acetonitrile (1.3 ml) were stirred for 3 d and the mixture worked up as in (*a*). The first fraction contained 10 mg (13%) of 4-chloro-2-phenyltriazole (5a; R = H), identical with the material described above. Subsequent elution with ethyl acetate gave 42 mg (62%) of triazole *N*-oxide (3; R = H).

(*d*) (6; R = H) (0.15 g), potassium cyanide (75 mg), and acetonitrile (1.5 ml) were stirred for 3 d. Removal of the solvent, extraction with dichloromethane (4 × 10 ml), and removal of the dichloromethane afforded 96 mg (97%) of *4-cyano-2-phenyl-1,2,3-triazole* (5d; R = H), m.p. 81—83 °C. The material was dissolved in ether, the solution filtered through activated carbon, the ether removed, and the residue recrystallized (hexane) producing colourless crystals, m.p. 89 °C (Found: C, 63.7; H, 3.5; N, 33.0. $C_9H_6N_4$ requires C, 63.5; H, 3.55; N, 32.95%); δ($CDCl_3$) 8.12 (1 H, s, H-5), 8.15—8.0 and 7.6—7.4 (2 H, m, and 3 H, m, Ph); *m/e* 170 (100%, $M^+$).

(*e*) Dry ammonia (1 ml) was condensed in a flask with (6; R = H) (0.2 g) cooled to −80 °C. Acetonitrile (2 ml) was added, and the mixture stirred at 20 °C for 3 d and worked up as in (*a*) using ethyl acetate–hexane (1 : 3) as the eluant. The first fraction contained 2 mg of an unidentified 2-phenyltriazole. The second fraction contained 0.1 g (79%) of 4-amino-2-phenyl-1,2,3-triazole (5e; R = H), m.p. 72—73 °C. Recrystallization (hexane) gave a product of m.p. 74—75 °C (lit.,[63] 70 °C) (Found: C, 60.5; H, 5.25; N, 35.3. Calc. for $C_8H_8N_4$: C, 60.0; H, 5.05; N, 35.0%); δ($CDCl_3$) 7.2 (1 H, s, H-5), 8.15—8.0 and 7.6—7.3 (2 H, m, and 3 H, m, Ph), and 3.86 (2 H, br s, exchangeable, $NH_2$). The column was then eluted with ethyl acetate producing 6 mg (7%) of triazole *N*-oxide (3; R = H).

(*f*) Similarly, (6; R = Me) (0.3 g) and ammonia in acetonitrile produced 11 mg of unidentified triazoles, then 10 mg (5%) of *4-methyl-5-methylamino-2-phenyl-1,2,3-triazole* (5f; R = Me) as a colourless oil; *m/e* 188.106 2 (100%) ($C_{10}H_{12}N_4$ requires 188.106 2); δ($CDCl_3$) 7.95—7.8 and 7.5—7.05 (2 H, m, and 3 H, m, Ph), 3.33 (1 H, br s, exchangeable, NH), 3.02 (3 H, br, s, NMe), and 2.23 (3 H, s, CMe). The next fraction contained 0.13 g (73%) of 5-amino-4-methyl-2-phenyl-1,2,3-triazole (5e; R = Me), m.p. 83—85 °C. Recrystallization (hexane) gave m.p. 85—87 °C (lit.,[19] 84 °C); δ($CDCl_3$) 7.9—7.75 and 7.5—7.05 (2 H, m, and 3 H, m, Ph), 3.78 (2 H, br s, exchangeable, $NH_2$), and 2.22 (3 H, s, Me). Subsequent elution with ethyl acetate gave 36 mg (19%) of the triazole *N*-oxide (3; R = Me).

(*g*) Methylamine (1 ml), distilled from $CaSO_4$, was concondensed at −80 °C in a flask with (6; R = H) (0.37 g). Acetonitrile (3.7 ml) was added, the mixture stirred at 20 °C for 3 d, and worked up as in (*e*). The first fraction contained 19 mg (10%) of 4-dimethylamino-2-phenyltriazole (5g; R = H), identical with the material below. The next fraction contained 0.10 g (59%) of *4-methylamino-2-phenyl-1,2,3-triazole* (5f; R = H) as a colourless oil, crystallizing on cooling, m.p. 37 °C, unchanged after recrystallization (hexane) (Found: C, 62.15; H, 5.75; N, 32.45. $C_9H_{10}N_4$ requires C, 62.05; H, 5.8; N, 32.15%); *m/e* 174 ($M^+$, 100%); δ($CDCl_3$) 7.12 (1 H, s, H-5), 8.0—7.8 and 7.5—7.05 (2 H, m, and 3 H, m, Ph), 3.88 (1 H, br s, NH), and 2.89 (3 H, d, *J* 3.4 Hz, collapses on irradiation at 3.88, NMe). The column was then eluted with ethyl acetate giving 31 mg (19%) of the triazole *N*-oxide (3; R = H).

(*h*) Similarly, dimethylamine (1 ml), distilled from $CaSO_4$, and (6; R = H) produced 90% of *4-dimethylamino-2-phenyl-1,2,3-triazole* (5g; R = H) as a colourless oil (Found: C, 63.9; H, 6.55; N, 29.65. $C_{10}H_{12}N_4$ requires C, 63.8; H, 6.45; N, 29.75%); *m/e* 188 ($M^+$, 100%); δ($CDCl_3$) 7.16 (1 H, s, H-5), 8.0—7.8 and 7.5—7.05 (2 H, m, and 3 H, m, Ph), 2.94 (6 H, s, NMe), and 10% of the triazole *N*-oxide (3; R = H).

(*j*) Compound (6; R = H) (0.12 g), triethylamine (0.12 ml) dried over calcium sulphate, and acetonitrile (1.2 ml), after standing for 3 d and removal of the solvent, extraction with chloroform (4 × 5 ml), removal of the solvent, extraction with ethyl acetate (4 × 5 ml), removal of the solvent, extraction with ether (4 × 10 ml), and removal of the ether gave 62 mg (88%) of 2-phenyltriazole 1-oxide (3; R = H).

(*k*) Compound (6; R = H) (0.15 g) and *p*-toluidine (0.18 g) were stirred in acetonitrile (1.5 ml) for 3 d and the mixture worked up as in (*e*) using ethyl acetate–hexane (1 : 4) as the eluant. The first fraction contained 12 mg (8%) of *4-methyl-2-phenyl-*p*-toluidino-1,2,3-triazole* (5j; R = H) [Found: *m/e* 264.137 6 (100%). $C_{16}H_{16}N_4$ requires 264.137 5]; δ($CDCl_3$) 7.30 (1 H, s, H-5), 8.05—7.85 and 7.55—7.15 (2 H, m, and 3 H, m, Ph), 7.15 (4 H, s, $C_6H_4$), 3.45 (3 H, s, NMe), and 2.33 (3 H, s, ArMe). The next fraction contained 80 mg of a mixture of *2-phenyl-4-*p*-toluidino-1,2,3-triazole* (5 H; R = H) and *N*-methyl-*p*-toluidine. Recrystallization (hexane) gave 78 mg (56%) of pure (5h; R = H) (Found: C, 71.6; H, 5.45; N, 22.5. $C_{15}H_{14}N_4$ requires C, 72.0; H, 5.65; N, 22.4%); *m/e* 250 (100%, $M^+$). The next fraction contained 33 mg of unchanged *p*-toluidine. The column was then eluted with ethyl acetate to give 26 mg (24%) of triazole *N*-oxide (3; R = H).

(*l*) (6; R = H) (0.14 g), sodium azide (Merck p.a.) (68 mg), and acetonitrile (1.4 ml) were stirred for 3 d and the mixture was worked up as in (*a*) using dichloromethane–hexane (1 : 3) as the eluant. The first fraction contained 71 mg (73%) of *4-azido-2-phenyl-1,2,3-triazole* (5k; R = H) as colourless crystals, m.p. 28 °C. Recrystallization by dissolution in hexane at room temperature followed by cooling to −30 °C did not raise the m.p. The compound deteriorates in the course of some days at 20 °C and is best kept in the refrigerator (Found: C, 51.6; H, 3.15; N, 45.5. $C_8H_6N_6$ requires C, 51.6; H, 3.25; N, 45.15%); *m/e* 186 (22%, $M^+$); δ($CDCl_3$) 7.37 (1 H, s, H-5), 8.05—7.9 and 7.55—7.25 (2 H, m, and 3 H, m, Ph). The next fraction contained 13 mg (14%) of 4-methoxy-2-phenyltriazole (5n; R = H), identical with the material described below. Elution of the column with ethyl acetate gave 1.0 mg (1%) of triazole *N*-oxide (3; R = H).

(*m*) Compound (6; R = H) (0.17 g) and 10% aqueous sodium hydroxide (6.7 ml) were mixed at 0 °C. Stirring was continued at 0 °C for 30 min and at 20 °C for 1 d. Extraction with dichloromethane [3 × 3 ml), acidification (hydrochloric acid), extraction with dichloromethane (3 × 3 ml), and removal of the dichloromethane gave 85 mg (83%) of 4-hydroxy-2-phenyl-1,2,3-triazole (5m; R = H), m.p. 126—127 °C (lit.,[63] 124 °C).

(*n*) (6; R = H) (0.16 g), sodium hydrogencarbonate (0.16 g), and saturated aqueous sodium hydrogencarbonate (0.8 ml) were mixed at 0 °C. Stirring was continued at

* Prepared by the neutralization of t-butylmagnesium chloride in ether with dry hydrogen chloride, followed by evaporation to dryness.

0 °C for 30 min and at 20 °C for 1 d. Extraction with dichloromethane (3 × 5 l), washing of the extract with 1N aqueous sodium hydroxide (5 ml), filtration through silica gel (0.06—0.10 mm) (1 g), extracting the silica gel with further 5 × 3 ml of dichloromethane, removal of the dichloromethane, extraction with ether (3 × 5 ml), removal of the ether, and recrystallization (hexane) produced 70 mg (74%) of *bis-(2-phenyl-1,2,3-triazol-4-yl) ether* (5r; R = H) as colourless crystals, m.p. 75—76 °C. Recrystallization (hexane) gave m.p. 77—78 °C (Found: C, 63.05; H, 4.0; N, 27.65. $C_{16}H_{12}N_6O_2$ requires C, 63.15; H, 3.95; N, 27.6%); *m/e* 304 (100%, $M^+$); δ($CDCl_3$) 7.76 (2 H, s, 2 × H-5), 8.1—7.9 and 7.6—7.25 (4 H, m, and 6 H, m, 2 Ph).

(*o*) Compound (6; R = H) (0.13 g) and 10% aqueous sodium hydroxide (0.43 ml) were stirred for 1 d and the mixture worked up as in (*m*) to give 25 mg (31%) of 4-hydroxy-2-phenyltriazole (5 ; R = H). The first dichloromethane extract was evaporated to dryness and flash-chromatographed [58] (ethyl acetate–hexane [1 : 10]) to give 12 mg (14%) of 4-methoxy-2-phenyltriazole (5n; R = H) and 14 mg (19%) of bis-(2-phenyltriazol-4-yl) ether (5r; R = H), identical with the material above. Subsequent elution with ethyl acetate–hexane (1 : 1) gave 1 mg (2%) of the triazole *N*-oxide (3; R = H).

(*p*) (6; R = H) (0.24 g) and 1N sodium methoxide in methanol (1.02 ml) were stirred for 1 h. The methanol was removed, the residue extracted into ether (4 × 8 ml), the solution filtered through activated carbon, and the ether removed leaving 0.15 g (94%) of *4-methoxy-2-phenyl-1,2,3-triazole* (5n; R = H) as a colourless oil, m.p. *ca.* 0 °C (Found: C, 61.85; H, 5.6; N, 23.85. $C_9H_9N_3O$ requires C, 61.7; H, 5.18; N, 24.0%); *m/e* 175 (100%, $M^+$); δ($CDCl_3$) 7.25 (1 H, s, H-5), 8.0—7.85 and 7.55—7.15 (2 H, m, and 3 H, m, Ph), and 4.0 (3 H, s, Me).

(*q*) Compound (6; R = H) (0.14 g), potassium benzoate (96 mg), and acetonitrile (5.6 ml) were stirred for 1 d and the mixture worked up as in (*p*) to give 0.11 g (72%) of 4-benzoyloxy-2-phenyl-1,2,3-triazole (5p; R = H), m.p. 82—87 °C. One recrystallization (hexane) gave a product of m.p. 86—90 °C (lit.,[64] 94 °C).

(*r*) Compound (6; R = H) (74 mg), sodium methanesulphinate [65] (57 mg), and acetonitrile (0.7 ml) were stirred for 3 d. The acetonitrile was then removed, the residue extracted with dichloromethane, the solvent removed, the residue dissolved in ethyl acetate, the solution filtered through activated carbon, the ethyl acetate removed, and the residue recrystallized (ethyl acetate–hexane) to produce 83 mg (78%) *4-methylsulphinyl-2-phenyl-1,2,3-triazole* (5q; R = H) as colourless crystals, m.p. 115 °C (Found: C, 48.55; H, 4.05; N, 18.9; S, 14.35. $C_9H_9N_3O_2S$ requires C, 48.4; H, 4.05; N, 18.8; S, 14.35%); *m/e* 223 (100%, $M^+$); δ($CDCl_3$) 8.2 (1 H, s, H-5), 8.15—8.0 and 7.6—7.4 (2 H, m, and 3 H, m, Ph), and 3.29 (3 H, s, Me). Alternative work-up using flash-chromatography [58] (dichloromethane) yields 96% of (5q; R = H), m.p. 115 °C, and, after elution with ethyl acetate, 4% of the triazole *N*-oxide (3; R = H).

(*s*) Compound (6; R = H) (0.13 g), potassium disulphide (Riedel de Häen) (82 mg), and methanol (1.3 ml) were stirred for 1 d. Acetic acid (63 ml) and methanol (7 ml) was then added. Filtration, removal of the methanol, extraction with dichloromethane (3 × 10 ml), removal of the solvent, and preparative t.l.c. (dichloromethane) gave sulphur, an unidentified compound (4 mg), *m/e* 255, containing three sulphur atoms, a mixture of bis(phenyltriazolyl) sulphide (5v; R = H), and 4-methoxy-2-phenyltriazole (5n; R = H) and 2-phenyltriazole (11; R = H) (1 mg, 1%). Compounds (5v) and (5n) were separated by preparative t.l.c. (ethyl acetate–hexane [1 : 10]) to give 7 mg (8%) of (5n; R = H) ($R_F$ 0.48) and 40 mg (51%) of *bis-(2-phenyl-1,2,3-triazol-4-yl) sulphide* (5v; R = H) ($R_F$ 0.40) as colourless crystals, m.p. 84—85 °C (hexane) (Found: C, 59.85; H, 3.8; N, 26.1; S, 10.15. $C_{16}H_{12}N_6S$ requires C, 60.0; H, 3.8; N, 26.25; S, 10.0%); *m/e* 320 (100%, $M^+$); δ($CDCl_3$) 7.81 (2 H, s, 2 H-5), 8.1—7.95 and 7.55—7.25 (4 H, m, and 6 H, m, 2 Ph).

(*t*) Compound (6; R = H) (0.15 g) and a 55% suspension of sodium hydride in mineral oil (85 mg) were treated with methanethiol as above. Methanol (1.5 ml) was added, the mixture stirred for 3 d, and worked up as in (*a*) using dichloromethane–hexane (1 : 2) as the eluant. This afforded 86 mg (78%) of 4-methylthio-2-phenyl-1,2,3-triazole (5t; R = H), identical with the material above. The second fraction contained 5 mg (5%) of 2-phenyltriazole (11; R = H).

(*u*) Compound (6; R = H) (0.38 g), potassium thioacetate (0.18 g), and acetonitrile (3.8 ml) were set aside for 1 d and the mixture worked up as in (*p*); recrystallization of the crude product (hexane) yielded 0.26 g (82%) of *4-acetylthio-2-phenyl-1,2,3-triazole* (5u; R = H) as colourless crystals, m.p. 54—55 °C (Found: C, 54.95; H, 4.05; N, 19.0; S, 14.55. $C_{10}H_9N_3OS$ requires C, 54.8; H, 4.15; N, 19.15; S, 14.6%); δ($CDCl_3$) 7.93 (1 H, s, H-5), 8.1—7.9 and 7.55—7.2 (2 H, m, and 3 H, m, Ph), and 2.44 (3 H, s, Me).

(*v*) Similarly (6; R = Me) gave 90% of the colourless *5-acetylthio-4-methyl-2-phenyl-1,2,3-triazole* (5u; R = Me), m.p. 37—39 °C (Found: C, 56.9; H, 4.85; N, 18.15; S, 13.75. $C_{11}N_{11}N_3OS$ requires C, 56.65; H, 4.85; N, 18.0; S, 13.75%); δ($CDCl_3$) 8.1—7.85 and 7.55—7.2 (2 H, m, and 3 H, m, Ph), 2.44 (3 H, s, COMe), and 2.32 (3 H, s, CMe).

*Deprotonation of 1-Methoxy-2-phenyl-1,2,3-triazolium Tetrafluoroborate followed by Electrophilic Addition.*—Compound (6; R = H) (0.42 g), methylthiomethanesulphonate [66] (1.5 ml) and ethyldi-isopropylamine (0.27 ml) were set aside for 3 d. The methylthiomethanesulphonate was removed at 100 °C and 0.1 kPa. Preparative t.l.c. (dichloromethane) gave 8 mg (3%) of 4-methylthio-2-phenyltriazole (5t; R = H) ($R_F$ 0.87). The next fraction contained 0.12 g (29%) of colourless *4-methylsulphinyl-5-methylthio-2-phenyl-1,2,3-triazole* (12) ($R_F$ 0.44), m.p. 128 °C. Recrystallization (ethyl acetate–hexane) did not raise the m.p. (Found: C, 43.95; H, 3.9; N, 15.6. $C_{10}H_{11}N_3O_2S_2$ requires C, 44.6; H, 4.12; N, 15.6%); *m/e* 269 (100%, $M^+$); δ($CDCl_3$) 8.15—7.95 and 7.6—7.35 (2 H, m, and 3 H, m, Ph), and 3.27 (3 H, s, $O_2SMe$). The third fraction contained 56 mg (16%) of 4-methylsulphinyl-2-phenyl-1,2,3-triazole (5q; R = H) ($R_F$ 0.34), the next fraction contained 0.12 g (36%) of 5-methylthio-2-phenyltriazole 1-oxide (4t; R = H), and the last fraction 33 mg (13%) of the triazole *N*-oxide (3; R = H). The latter compounds were identical with the substances described above.

Compound (6; R = H) (0.32 g), acetic anhydride (2.3 ml), and ethyldi-isopropylamine (0.22 ml) were set aside for 3 d. Evaporation to dryness and flash-chromatography [58] (dichloromethane–ether [1 : 4]) gave 19 mg (9%) of 4-methoxy-2-phenyltriazole (5n; R = H). Subsequent elution with dichloromethane gave 0.16 g (67%) of 4-

acetoxy-2-phenyltriazole (5o; R = H). Finally, elution with ethyl acetate gave 27 mg (9%) of the triazole *N*-oxide (3; R = H). All compounds were identical with the substances described above.

*Miscellaneous Experiments.*—4-Acetylthio-2-phenyl-1,2,3-triazole (5u; R = H) (0.56 g), sodium hydroxide (0.31 g), methanol (3 ml), and water (3 ml) were refluxed for 3 h. The solvents were removed, and the residue was dissolved in water (6 ml), filtered, extracted with dichloromethane (3 × 6 ml), acidified to pH 3 with hydrochloric acid, and extracted with dichloromethane (3 × 10 ml). The extract was dried ($MgSO_4$) and evaporated to dryness giving 0.39 g (87%) of *4-mercapto-2-phenyl-1,2,3-triazole* (5s; R = H) as a yellow oil, crystallizing on cooling, m.p. *ca.* 10 °C (Found: C, 54.3; H, 4.05; N, 23.45; S, 18.2. $C_8H_7N_3S$ requires C, 54.2; H, 4.0; N, 23.7; S, 18.1%); $\nu_{max.}$ (KBr) 2 550 $cm^{-1}$ (SH); δ($CDCl_3$) 7.65 (1 H, s, H-5), 8.1—7.9 and 7.6—7.3 (2 H, m, and 3 H, m, Ph), and 3.55 (1 H, s, exchangeable with $D_2O$, SH). On standing at 20 °C for some weeks the compound is converted into bis-(2-phenyl-1,2,3-triazol-4-yl) sulphide (5x; R = H), m.p. 103 °C; *m/e* 352 (100%, $M^+$).

Similarly, 4-acetoxy-2-phenyl-1,2,3-triazole (5o; R = H) produced 98% of 4-hydroxy-2-phenyl-1,2,3-triazole (5m; R = H), m.p. 124—125 °C (lit.,[64] 124 °C).

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