2-Alkyl-1,2,3-Triazole-1-Oxides: Preparation and Use in the Synthesis of 2-Alkyltriazoles

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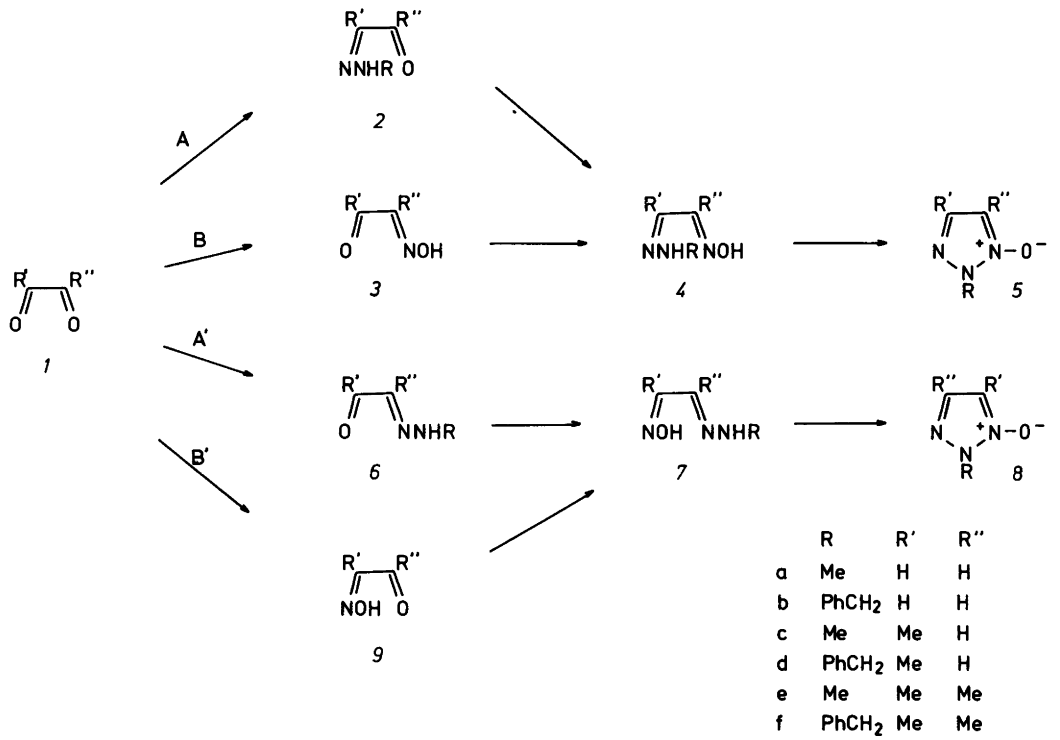
Methylhydrazono oximes were obtained by reaction of glyoxal, methylglyoxal, or diacetyl with methylhydrazine and hydroxylamine or from nitrosoacetone and methylhydrazine. The methylhydrazono oximes cyclize upon oxidation to 2-methyltriazole-*N*-oxides. Benzyl analogues are obtained similarly. This reaction also opens an efficient route to 2-alkyltriazoles since *N*-deoxygenation proceeds smoothly. The 2-alkyltriazole-1-oxides are activated at C-5. Electrophiles and nucleophiles can be introduced prior to deoxygenation. Acetoxytriazoles arise directly by reaction with acetyl chloride. Methylation of the *N*-oxides yields 1-methoxytriazolium salts which react with, *e.g.*, dimethylamine, hydroxide, thioacetate, or cyanide ions in an addition – elimination fashion leading to 5-substituted 2-alkyltriazoles.

The *N*-oxygen of 2-phenyl-1,2,3-triazole-1-oxides activates the adjacent carbon atom towards electrophiles and nucleophiles.[1] Methylation of the oxygen atom yields 1-methoxytriazolium salts in which both the α- and the β-carbon atoms are activated towards nucleophiles, making introduction of substituents into the triazole ring or its α-methyl group easy.[1,2] So far, these transformations have been restricted to 2-phenyl-substituted triazoles. The present work outlines a route to 2-alkyltriazole-1-oxides, and, utilizing the *N*-oxide activation, to 2-alkyltriazoles.

Two obvious, alternative routes may lead from α-dicarbonyl compounds to 2-alkyltriazole-1-oxides (*5*) (Scheme 1). By route A, the α-dicarbonyl compound (*1*) is converted, *via* its monohydrazone (*2*), into the oxime hydrazone (*4*) undergoing oxidative cyclization. By route B the carbonyl groups are functionalized in the opposite order (*1*→*3*→*4*→*5*). Unsymmetric dicarbonyl compounds may give rise to two isomeric hydrazones (*2*) and (*6*) and oximes (*3*) and (*9*) and hence to two, isomeric triazole-1-oxides, (*5*) and (*8*). 2-Phenyltriazole-1-oxide was obtained from glyoxal through route A.[1] This route did not apply to 2-methyltriazole-1-oxide since glyoxal failed to give a monomethylhydrazone. A bismethylhydrazone was the only simple product which could be isolated, even when glyoxal was used in excess. Route B, however, proved passable. Glyoxal monoxime (*3a*) could be prepared *in situ* and transformed to glyoxaloxime methylhydrazone (*4a*). This need not be isolated prior to its oxidative cyclization, thus rendering the synthesis of 2-methyltriazole-1-oxide (*5a*) from glyoxal a one-pot process. The condensations must be run under near neutral conditions. At higher pH-values the monoxime is converted into the dioxime (glyoxime) and in acidic solution, the monoxime undergoes hydrolysis and the glyoxal set free reacts with methylhydrazine to produce glyoxal bis-methylhydrazone. 2-Benzyltriazole-1-oxide (*5b*) was obtained similarly, whereas 2,5-dimethyltriazole-1-oxide (*8c*) was accessible through both route A and B. Methylglyoxal and methylhydrazine produce 1-methylhydrazonopropanone (*6c*) as the thermodynamically stable and isolable product,[3] readily converted into the oxime methylhydrazone (*7c*) and then to *8c*. Route B is less attractive since it leads to 2,5-di-



	R	R'	R''
a	Me	H	H
b	$PhCH_2$	H	H
c	Me	Me	H
d	$PhCH_2$	Me	H
e	Me	Me	Me
f	$PhCH_2$	Me	Me

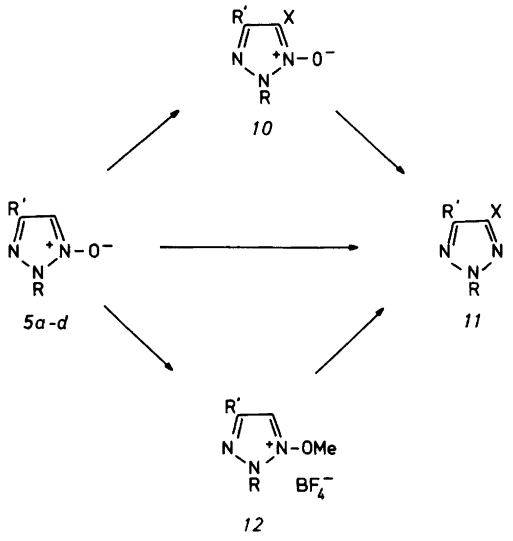
methyltriazole-1-oxide (*8c*) contaminated with the 4-methyl isomer (*5c*). Minimum contamination was observed when methylhydrazine was added immediately after hydroxylamine. This suggests that the formylketoxime (*9c*) is the kinetically formed monoxime as is the analogous formylmethylhydrazone.[3] The contaminating 4-methyl isomer could be removed by treatment with bromine, converting the 4-methyl isomer into its 5-bromoderivative (*10c; X=Br*) which can be easily separated from the non-affected 5-methyl compound.

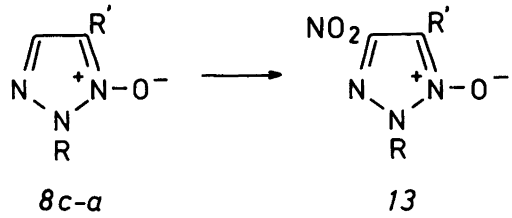
2-Benzyl-5-methyltriazole-1-oxide (*8d; R* = $C_6H_5CH_2$) could not be directly produced free of the 4-methyl isomer (*5d*) even by route A since in the benzyl case the equilibrium between the isomeric methylglyoxal hydrazones (*2d* and *6d*) is not completely in favour of the former but contains a 2.1:1 mixture of the two. The latter leads to the 4-methyl isomer which could again be removed *via* bromination.

Isomer-free 2,4-dimethyltriazole-1-oxide (*5c*) was prepared by reaction of nitrosoacetone (*3c*) (from acetoacetic ester) with methylhydrazine followed by oxidation. The absence of isomeric triazole-*N*-oxides confirms that the ketoaldoxime (*3c*) is the thermodynamically more stable monoxime. 2-Benzyl-4-methyltriazole-1-oxide (*5d*) was obtained in the same manner.

2,4,5-Trimethyltriazole-1-oxide (*5e*) was accessible from diacetyl. The one-pot process, route B, is convenient but only gives a 7% yield. A major byproduct is the dioxime (dimethylglyoxime). The more cumbersome route A affords 27% total yield. Again, the 2-benzyl analogue (*5f*) was obtained similarly.

2-Methyltriazole gives no well defined products upon chlorination.[4] Bromination requires iron as a catalyst and leads to a dibromo derivative.[4] In contrast, 2-alkyltriazole-1-oxides (*5a–d*) were chlorinated or brominated at room temperature to the 5-substituted derivatives (10). Halogen did not attack the 4-position of the triazole-oxides even after several h at 60°C. However, both C-4 and C-5 were attacked upon mild nitration. Thus, 2-methyltriazole-1-oxide gave a 3.3:1 mixture of the 5- and the 4-nitro derivative (*10a; X=*NO_2) and (*13a*). The 5-substituted 2-





methyltriazole-1-oxides (*8c*) and (*10a; X=Br*) likewise underwent nitration at C-4 producing *13c* and *13, R=Me, R' = Br*. The similar reactivity at C-4 and C-5 of 2-alkyltriazole-1-oxides towards nitration may be looked upon as a compromise between activation at C-4 by the N-2 lone pair and a moderated activation at C-5 due to protonation of the *N*-oxygen. In 2-phenyltriazole-1-oxides, not attacked at C-4,[1] the N-2 lone pair is engaged in conjugation with the benzene ring. This leads to activation of the *o*- and *p*-positions hence explaining the observed nitration at these positions.

Both nitro-substituted 2-methyltriazole-1-oxides (*10a; X=NO_2*) and (*13a*) gave the 4,5-dinitro triazole-1-oxide (*13; R=Me, R'=NO_2*) upon further nitration. Nitration of 2-methyltriazole also proceeded stepwise through 2-methyl-4-nitrotriazole to 2-methyl-4,5-dinitrotriazole (*11; R=Me, R'=X=NO_2*). The dinitrotriazoles, the first to be described, are thermally stable above their melting points.

2-Substituted 4-halogenotriazoles are inert towards nucleophiles.[5] The 5-halogen of the corresponding N-oxides is activated and replaceable on treatment with methanethiolate ions.

The triazole *N*-oxides described were readily deoxygenated by phosphorus trichloride to give the parent, hitherto inaccessible or difficultly available 2-alkyltriazoles (*11*). An exception are the nitrosubstituted *N*-oxides which are insoluble in phosphorus trichloride. This limitation is not a serious one since 2-alkyltriazoles can be nitrated directly.

The 2-alkyltriazole-1-oxides are quantitatively methylated at the *N*-oxygen by trimethyloxonium tetrafluoroborate. The 1-methoxytriazolium tetrafluoroborates (*12*) formed may react in several ways[1,2] but only the reaction between 1-methoxy-2-benzyltriazolium tetrafluoroborate (*12b*) and selected nucleophiles was studied. Thus cyanide ions, dimethylamine, hydroxide ions, and thioacetate ions underwent addition-elimination reactions with the 1-methoxytriazolium salt to give substituted 2-benzyltriazoles (*11b* and *d*) as the main products. 2-Benzyltriazole-1-oxide was invariantly formed as a byproduct, arising from *O*-dealkylation of the starting material. The two-step sequence: alkylation of the triazole-1-oxide and nucleophilic addition followed by elimination of methanol could be performed as a one-pot process. By this method, carbon, nitrogen, oxygen, and sulfur substituents can easily be introduced into the triazole ring.

2-Phenyltriazole-1-oxides and acetyl chloride produced 4-acetoxy- and 4-chlorotriazoles. 2-Alkyltriazole-1-oxides yielded only 4-acetoxytriazoles (*11; X=OAc*). These were hydrolyzed to 4-hydroxytriazoles (*11; X=OH*).

In conclusion, 2-alkyl substituted triazole-1-oxides are readily available and well suited as precursors of 2-alkyltriazoles (*11*) without or with a variety of substituents in the triazole ring.

Experimental

Solvents were removed under reduced pressure. Flash chromatography was performed as described in Ref. 6. All new compounds were colourless, unless otherwise stated. The purity and identity of all compounds were confirmed using TLC, melting points, and IR, ^{1}H NMR, and mass spectra. ^{1}H NMR spectra were recorded on a

Bruker HX-90 instrument. ^{13}C NMR spectra were obtained on a Bruker WH-90 instrument and assigned as described previously.[7] Mass spectra were obtained on a V.G. Micromass 7070F instrument.

Preparation of monoalkylhydrazones of α-dicarbonyl compounds. A solution of alkylhydrazine (0.10 mol) and acetic acid (12 ml) in water (80 ml) was added with stirring during 15 min to a 1.0 % aqueous solution of the α-dicarbonyl compound (730 ml). The mixture was kept at 20 °C for 48 h and extracted with dichloromethane (4×120 ml). The organic solution was washed with water (4×30 ml), dried ($MgSO_4$), and evaporated leaving the crude monohydrazone. It was characterized through its ^1H NMR spectrum and used without further purification.

1-Benzylhydrazonopropane (*6d*), containing 32 % of the isomer (*2d*). (93 % yield) from benzylhydrazine[8] and methylglyoxal. ^1H NMR ($CDCl_3$) (6d): δ 7.4–7.15 (5H, m, Ph), 6.88 (1H, s, HC=N), 4.36 (2H, d, *J* 4.0 Hz, collapses on exchange with D_2O, CH_2), 2.27 (3H, s, MeC=O). (2d): δ 9.27 (1H, s, HC=O), 7.4–7.15 (5H, m, Ph), 4.64 (2H, d, *J* 4.7 Hz, collapses on exchange with D_2O, CH_2), 1.75 (3H, s, MeC=N).

2-Methylhydrazonobutan-3-one (*6e*), a yellow semicrystalline mass (63 % yield) from methylhydrazine and diacetyl. ^1H NMR ($CDCl_3$): δ 5.65 broad (1H, s, NH), 3.23 (3H, d, *J* 4 Hz, collapses on irradiation at 5.65, NMe), 2.33 (3H, s, MeC=O), 1.79 (3H, s, MeC=O), 1.79 (3H, s, MeC=N).

2-Benzylhydrazonobutan-3-one (*6f*), with 97 % yield from benzylhydrazine and diacetyl. ^1H NMR ($CDCl_3$): δ 7.29 (5H, s, Ph), 6.03 broad (1H, s, exchangeable, NH), 4.59 (2H, d, *J* 5 Hz, CH_2), 2.33 (3H, s, MeC=O), 1.78 (3H, s, MeC=N).

Preparation of 2-hydroximino alkylhydrazonoalkanes (*7*). Aqueous sodium hydroxide (2M, 200 ml) was added with stirring during 1 h to a solution of alkylhydrazonoalkanone (0.10 M) and hydroxylammonium chloride (6.0 g) in water (260 ml). After 24 h pH was adjusted to 6 with hydrochloric acid and the volume was reduced to ~80 ml. Extraction with dichloromethane (4×130 ml), drying ($MgSO_4$), and removal of the dichloromethane furnished the crude 2-hydroximino alkylhydrazonoalkane (*7*) as a yellow-orange semicrystalline mass which was used without further purification.

In this way *2-hydroximino-1-methylhydrazonopropane* (*7c*) (100 %) from 1-methylhydrazonopropanone (*6c*);[3] *2-hydroximino-1-benzylhydrazonopropane* (*7d*) (87 %); and *2-hydroximino-3-methylhydrazonobutane* (*7e*) (88 %) were obtained.

2-Hydroximino-3-benzylhydrazonobutane (*7f*). Aqueous sodium hydroxide (2M, 200 ml) was added with stirring during 1 h to a solution of 2-benzylhydrazonobutan-3-one (*6f*) (20 g) and hydroxylammonium chloride (6.0 g) in methanol above to give 20 g (94 %) of *7f* a cream-coloured, semicrystalline mass.

Preparation of 1-hydroximino alkylhydrazono alkanes (*4*). The alkylhydrazine (0.12 mol) dissolved in ether (16 ml) was added to a solution of

Table 1. Preparation, yields, purification and analytical data of 2-alkyltriazole-1-oxides

Product *5* R	R′	R″	Procedure	Yield of crude product[a]/%	Recrystallization media	M.p. of pure compound/°C	Analysis
Me	H	H	a	22	EtOAc-hexane	81–83	$C_3H_5N_3O$
Bn	H	H	b	27	EtOAc	95–97	$C_9H_9N_3O$
Me	H	Me	c	21	EtOAc-hexane	*ca.* 0	$C_4H_7N_3O$
			d	17			
Bn	H	Me	e	11	EtOAc-hexane	*b*	$C_{10}H_{11}N_3O$
Me	Me	H	f	20	Ether-hexane	*ca.* 20[c]	$C_4H_7N_3O$
Bn	Me	H	g	10	EtOAc-hexane	46–53[c]	$C_{10}H_{11}N_3O$
Me	Me	Me	a	7	Ether-hexane	*d*	$C_5H_9N_3O$
			d	27			
Bn	Me	Me	d	11	EtOAc-hexane	*d*	$C_{11}H_{13}N_3O$

[a]Total yields from alkylhydrazine are given. [b]Yellow. [c]Light brown. [d]Slightly yellow.

nitrosoacetone[1] (*3c*) (0.10 mol) in ether (32 ml) during 10 min. After stirring for 0.5 h the ether was removed to give the crude 1-hydroximino alkylhydrazono alkane (*4*) as an orange semicrystalline mass, used without further purification.

In this way *1-hydroximino-2-methylhydrazonopropane* (*4c*) (quantitative yield) and *1-hydroximino-2-benzylhydrazonopropanone* (*4d*) (quantitative yield) were obtained.

Preparation of 2-alkyltriazole-1-oxides. Conditions are those specified below under (*a*)–(*g*). Yields, m.p.s and recrystallization media are given in Table 1, ^{1}H NMR data in Table 2.

(*a*) Hydroxylammonium chloride (0.1 mol) and sodium carbonate (0.105 mol), thoroughly mixed, were added as fast as possible to an aqueous solution of the α-dicarbonyl compound (8 % if glyoxal, 10 % if methylglyoxal, and 18 % if diacetyl) (0.1 mol) with efficient stirring. Immediately after all had dissolved, the hydrazine (0.1 mol), dissolved in methanol (40 ml), was added. After stirring for 0.5 h the suspension was added during 10 min to a refluxing mixture of copper (II) sulphate (100 g), pyridine (100 ml), and water (400 ml). After heating to reflux for 0.5 h and cooling to 20 °C 2M sulphuric acid was added to pH *ca.* 3.

After filtration, the residue and filtrate were successively washed with ether (100+2×30 ml) and then extracted with dichloromethane (4×100 ml). The extract was washed with 2M aqueous sodium hydroxide (2×25 ml), dried ($MgSO_4$), and evaporated to dryness to give the crude product.

(*b*) As in (*a*) but after filtration only the filtrate was washed and extracted. After the washing with sodium hydroxide and removal of dichloromethane the product was dissolved in ethyl acetate. Filtration through silica gel (8 g) and activated carbon (2 g) followed by removal of the ethyl acetate gave the crude product.

(*c*) The crude product obtained as in *a,* chloroform (60 ml), sodium carbonate (2.0 g), water (10 ml), and bromine (1.9 ml) were stirred for 3 h. The chloroform was removed and sodium thiosulphate (1.0 g) was added. Extraction with dichloromethane (3×20 ml), drying ($MgSO_4$), and flash chromatography (ethyl acetate-hexane, [1:1]) gave 0.45 g (2 %) of 2,4-dimethyl-5-bromotriazole-1-oxide (R_F 0.32), identical with the material described below. Subsequent elution with ethyl acetate-methanol 1:1 afforded the crude product.

(*d*) The 2-hydroximinoalkylhydrazonoalkane (*7*) (0.10 mol) was dissolved in pyridine (45 ml) and water (100 ml) and added during 5 min to a stirred, boiling solution of copper (II) sulphate (39 g) in water (430 ml). The mixture was stirred and heated to reflux for 1 h and worked up as in (*a*).

(*e*) The crude product obtained as in (*d*) was treated with bromine as in (*c*). Flash chromatography (ethyl acetate-hexane [1:1]) gave 3 % of 2-benzyl-4-methyl-5-bromotriazole (*10 d; X=Br*), identical with the material described below. The column was then eluted with ethyl acetate to give 11 % of *2-benzyl-5-methyl-1,2,3-triazole-1-oxide* (*8d*).

(*f*) The 1-hydroximino alkylhydrazono alkane (*4*) (0.10 mol) was dissolved in water (32 ml), cyclized, and worked up as in (*a*).

(*g*) Like (*f*). The crude product then obtained by work-up as in (*a*) was flash-chromatographed (ethyl acetate-hexane [1:1]) to give 10 % of *2-benzyl-4-methyl-1,2,3-triazole-1-oxide* (*5d*), R_F=0.20.

Chlorination of 2-alkyltriazole-1-oxides. (*a*) 15 % Aqueous sodium hypochlorite (17.5 ml) was added during 10 min with stirring and cooling in an ice bath to a mixture of the triazole-1-oxide (10 mmol), 4M hydrochloric acid (13.8 ml), and chloroform (25 ml) for 10 min. After stirring at 20 °C for 8 h sodium thiosulfate (3 g) was added. The organic solution was isolated. The aqueous solution was extracted with dichloromethane (2×30 ml). The organic extracts were dried ($MgSO_4$), the solvent was removed, the residue was extracted with hot methanol (3×10 ml), the solution filtered through activated carbon, and the methanol removed.

In this way, 2-methyltriazole-1-oxide (*5a*) afforded 78 % of *2-methyl-5-chloro-1,2,3-triazole-1-oxide* (*10a; X=Cl*), m.p. 67–70 °C. Recrystallization (ethyl acetate) gave m.p. 75–77 °C Anal. $C_3H_4N_3OCl$: C,H,N. ^{1}H NMR ($CDCl_3$): δ 7.53 (1H, s, H-4), 4.00 (3H, s, Me).

By the same procedure 2-benzyltriazole-1-oxide (*5b*) gave a residue which was dissolved in dichloromethane (10 ml). Filtration through silica gel (5 g), elution with further 4×10 ml of dichloromethane gave 72 % of *2-benzyl-5-chloro-1,2,3-triazole-1-oxide* (*10b; X=Cl*) as an oil. Reprecipi-

Table 2. ^{1}H NMR data (δ values in ppm in $CDCl_3$, relative to tetramethylsilane) of 2-alkyl substituted 1,2,3-triazole-1-oxides.

Compound (*5*)			H-4	H-5	Ph	CH_2	NMe	CMe	*J*/Hz
R	R′	R″							
Me	H	H	7.29	7.48			3.98		0.9
Bn	H	H	7.31	7.51	7.33		5.52		1.0
Me	H	Me	7.38				3.96	2.22	
Bn	H	Me	7.39		7.45–7.25	5.51		2.23	
Me	Me	H		7.14			3.91	2.24	
Bn	Me	H		7.12	7.45–7.2	5.45		2.23	
Me	Me	Me					3.92	2.22	
								2.18	
Bn	Me	Me			7.4–7.2	5.44		2.20	
								2.16	

tation (ethyl acetate-hexane) gave an analytical specimen. Anal. $C_9H_8N_3OCl$: C,H,N. ^{1}H NMR ($CDCl_3$): δ 7.53 (1H, s, H-4), 7.4–7.2 (5H, m. Ph), 5.51 (2H, s, CH_2).

Bromination of 2-alkyltriazole-1-oxides. Bromine (10 ml) was added during 5 min with stirring and cooling to 0 °C to a mixture of the 2-alkyltriazole-1-oxide (0.05 mol), chloroform (60 ml), sodium carbonate (10.6 g), and water (80 ml). Stirring was continued for 3 h. Bromine and chloroform were removed, sodium thiosulfate (4 g) added, and the aqueous solution extracted with dichloromethane (3×400 ml). Drying ($MgSO_4$), removal of the dichloromethane, extraction with boiling methanol (3×400 ml), filtration through activated carbon, and removal of the methanol gave the crude product.

In this way, 2-methyltriazole-1-oxide (*5a*) produced 86 % of *2-methyl-5-bromo-1,2,3-triazole-1-oxide* (*10a; X=Br*), m.p. 92–93 °C. Recrystallization (ligroin) did not raise the m.p. Anal. $C_3H_4N_3OBr$: C,H,N. ^{1}H NMR ($CDCl_3$): δ 7.59 (1H, s, H-4), 4.05 (3H, s, Me).

Similarly, 2,4-dimethyltriazole-1-oxide (*5c*) gave 76 % of *2,4-dimethyl-5-bromo-1,2,3-triazole-1-oxide* (*10c; X=Br*), m.p. 67–69 °C. Recrystallization (ligroin) gave m.p. 70–71 °C. Anal. $C_4H_6N_3OBr$: C,H,N. ^{1}H NMR ($CDCl_3$): δ 3.96 (3H, s, NMe) 2.25 (3H, s, CMe).

Similarly, 2-benzyltriazole-1-oxide (*5b*) gave a crude product which was filtrated through silica gel as by the chlorination of (*5b*). This gave 83 % of *2-benzyl-5-bromo-1,2,3-triazole-1-oxide* (*10b, X=Br*) m.p. 38–39 °C (ethyl acetate-hexane). Anal. $C_9H_8N_3OBr$: C,H,N. ^{1}H NMR ($CDCl_3$): δ 7.54 (1H, s, H-4), 7.45–7.15 (5H, m, Ph) 5.52 (2H, s, CH_2).

Similarly, 2-benzyl-4-methyltriazole-1-oxide (*5d*) produced 67 % of the yellow *2-benzyl-4-methyl-5-bromo-1,2,3-triazole-1-oxide* (*10d; X = Br*), m.p. 59–61 °C (ethyl acetate-hexane), Anal. $C_{10}H_{10}N_3OBr$: C,H,N. ^{1}H NMR ($CDCl_3$): δ 7.4–7.25 (5H, m. Ph), 5.49 (2H, s, CH_2), 2.23 (3H, s, Me).

Nitration of 2-alkyltriazole-1-oxides. The 2-alkyltriazole-1-oxide (1 mmol), conc. sulphuric acid (1.02 ml), and fuming nitric acid (d=1.55 g/ml, 0.51 ml) were stirred for 3 h. Water (5 ml) was added. Extraction with dichloromethane (5+2×3 ml), drying (K_2CO_3) and removal of the dichloromethane, gave the crude product.

In this way 2-methyltriazole-1-oxide (*5a*) gave a mixture which by preparative t.l.c. (toluene-ether, 3:1) gave 109 mg (75 %) of *2-methyl-5-nitro-1,2,3-triazole-1-oxide* (*10a; X=NO$_2$*) (R_F 0.31) m.p. 121 °C, after recrystallization (chloroform): m.p. 124 °C. Anal. $C_3H_4N_4O_3$: C,H,N. ^{1}H NMR ($CDCl_3$): δ 8.15 (1H, s, H-4), 4.03 (3H, s, Me). MS *m/z* (rel. int.): 144 (38 %, M^+), 128 (7, M-O), 112 (9, M-O_2), 98 (100, M-NO_2); and 33 mg (23 %) of *2-methyl-4-nitro-1,2,3-triazole-1-oxide* (*13a*) (R_F 0.22) m.p. 180–181 °C. After recrystallization (chloroform): m.p. 182 °C. Anal. $C_3H_4N_4O_3$: C,H,N. ^{1}H NMR ($CDCl_3$): δ 7.85 (1H, s, H-5), 4.08 (3H, s, Me); MS *m/z* (rel. int.): 144 (62 %, M^+), 128 (5, M-O), 114 (43, M-O_2), 98 (27, M-NO_2), 68 (92), 53 (100).

If the nitration of 2-methyltriazole-1-oxide was

performed by heating it to 100 °C for 0.5 h *2-methyl-4,5-dinitro-1,2,3,-triazole-1-oxide (13; R=Me, R'=NO$_2$)*, m.p. 127–128 °C was formed in 77 % yield. Recrystallization (chloroform) gave m.p. 130–131 °C. anal. $C_3H_3N_5O_5$: C,H,N. ^{1}H NMR ($CDCl_3$): δ 4.13 (3H, s, Me); MS *m/z* (rel. int.): 189 (26 %, M^+), 173 (2, M-O), 143 (16, M-NO_2), 97 (100).

Similarly nitration of 2,5-dimethyltriazole-1-oxide (*8c*) (20 °C, 3 h) produced 92 % of *2,5 dimethyl-4-nitro-1,2,3-triazole-1-oxide* (*13c*), m.p. 114–116 °C. Recrystallization (chloroform-hexane) gave m.p. 120–122 °C. Anal. $C_4H_6N_4O_3$: C,H,N. ^{1}H NMR ($CDCl_3$): δ 4.08 (3H, s, NMe), 2.57 (3H, s, CMe); MS *m/z* (rel. int.): 158, (57 %, M^+), 128 (3, M-NO), 112 (3, M-NO_2), 82 (45), 67 (100).

Nitration of 2-methyl-5-bromotriazole-1-oxide (*10a; X=Br*) (100 °C, 0.5 h) gave 80 % of *2-methyl-4-nitro-5-bromo-1,2,3-triazole-1-oxide* (*13; R=Me, R'=Br*), m.p. 175–182 °C. Recrystallization (chloroform) gave m.p. 182 °C. Anal. $C_3H_3N_4C_3Br$: C,H,N. ^{1}H NMR ($CDCl_3$) 4.15 (3H, s, Me); MS *m/z* (rel. int.): 222+224 (60 %, M^+) 206+208 (1, M-O), 176+178 (7, M-NO_2), 146+148 (82), 131+133 (70).

Similar nitration of 2-methyltriazole[5] (*11a; X=H*) gave 98 % of *2-methyl-4-nitro-1,2,3-triazole* (*11a; X=NO$_2$*), m.p. 97–99 °C. recrystallization (ligroin) gave m.p. 99–101 °C. Anal. $C_3H_4N_4O_2$: C,H,N. ^{1}H NMR ($CDCl_3$): δ 8.11 (1H, s, H-5), 4.27 (3H, s, Me).

Nitration of 2-methyltriazole at 100 °C for 10 h afforded 97 % of *2-methyl-4,5-dinitro-1,2,3-triazole* (*11; R=Me, R'=X=NO$_2$*) m.p. 78–80 °C. Recrystallization (ethyl acetate-hexane) gave m.p. 81–82 °C. Anal. $C_3H_3N_5O_4$: C,H,N. ^{1}H NMR ($CDCl_3$): δ 4.35 (3H, s, Me); MS, *m/z* (rel. int.): 173 (100 %, M^+), 157 (34, M-O), 81 (26).

Reaction of 2-alkyltriazole-1-oxides with nucleophiles. 2-Benzyl-5-chlorotriazole-1-oxide (*10b; X=Cl*) (0.26 g), lithium methanethiolate[9] (0.21 g), and dry methanol (2.6 ml) were heated with stirring in a screw cap reaction vessel to 100 °C for 1 h. Removal of the methanol, addition of water (5 ml), extraction with dichloromethane (3×5 ml), drying ($MgSO_4$), and removal of the dichloromethane afforded 0.26 g (94 %) of *2-benzyl-5-methylthio-1,2,3-triazole-1-oxide* (*10b; X=SMe*) as an oil which was reprecipitated from ethyl acetate-hexane. Anal. $C_9H_9N_3OS$: C,H,N. ^{1}H NMR ($CDCl_3$): δ 7.51 (1H, s, H-4), 7.45–7.25 (5H, m, Ph), 5.53 (2H, s, CH_2), 2.43 (3H, s, Me).

Preparation of 1-methoxy-2-alkyltriazolium tetrafluoroborates. 2-Benzyl-triazole-1-oxide (*5b*) (10 mmol) and trimethyloxonioum tetrafluoroborate (10.8 mmol) were dissolved in sulfur dioxide (*ca.* 7.5 ml). After reflux (condenser with dry ice and drying tube [with calcium sulfate]) for 1 h the sulfur dioxide was allowed to evaporate. Recrystallization (methanol-ether) gave yellow *1-methoxy-2-benzyl-1,2,3-triazolium tetrafluoroborate* (*12b*) (96 %) m.p. 45–47 °C. Anal. $C_{10}H_{12}N_3OBF_4$: C,H,N. ^{1}H NMR ($CDCl_3$): δ 8.66 (1H, d, *J* 1.1 Hz, H-5), 8.06 (1H, d, *J* 1.1 Hz, H-4), 7.5–7.15 (5H, m, Ph), 6.00 (2H, s, CH_2), 4.35 (3H, s, Me).

Reaction of 1-methoxy-2-alkyltriazolium salts with nucleophiles. 1-Methoxy-2-benzyltriazolium tetrafluoroborate (*12b*) (0.45 g), potassium cyanide (0.21 g), and dry acetonitrile[1] (4.5 ml) were stirred for 72 h. The solvent was removed and the residue extracted with dichloromethane (3×10 ml). Drying ($MgSO_4$), removal of the dichloromethane, and flash chromatography (ethyl acetate-hexane [1:6]) gave 0.17 g (58 %) of *2-benzyl-4-cyano-1,2,3-triazole* (*11b; X=CN*) R_F 0.28 as an oil which was reprecipitated from ethyl acetate-hexane. Found: C, 64.25; H, 4.35; N, 29.75. Calc. for $C_{10}H_8N$: C, 65.2; H, 4.4; N, 30.4 %. ^{1}H NMR ($CDCl_3$): δ 7.90 (1H, s, H-5) 7.32 (5H, s, Ph), 5.58 (2H, s, CH_2). The column was then eluted with ethyl acetate, first to give several unidentified compounds in minor amounts, then 0.067 g (24 %) of *2-benzyltriazole-1-oxide* (*5b*).

Dimethylamine (5 ml) was condensed at −80 °C in a flask with 1-methoxy-2-benzyltriazolium tetrafluoroborate (*12b*) (1.31 g). Dry acetonitrile (13 ml) was added and the mixture stirred at 20 °C for 72 h. Work-up as above using ethyl acetate-hexane (1:4) as the eluant gave 0.67 g (71 %) of *2-benzyl-4-dimethylamino-1,2,3-triazole* (*11b, X=NMe$_2$*) R_F 0.31 as an oil (m.p. *ca.* 0 °C) which was reprecipitated from ethyl acetate-hexane. Anal. $C_{11}H_{14}N_4$: C,H,N. ^{1}H NMR ($CDCl_3$): δ 6.92 (1H, s, H-5), 7.24 (5H, s, Ph), 5.36 (2H, s, CH_2), 2.82 (6H, s, NMe_2).

1-Methoxy-2-benzyltriazolium tetrafluoroborate (*12b*) (0.92 g) and 10 % aqueous sodium hydroxide (34.5 ml) were mixed at 0° and stirred at 20° for 72 h. Washing with dichloromethane (3×10 ml), acidification with hydrochloric acid to pH *ca.* 2, extraction with dichloromethane (3×31

ml), drying ($MgSO_4$), and removal of the dichloromethane gave 0.29 g (50 %) of *2-benzyl-4-hydroxytriazole* (*11b; X=OH*), identical with the material described below.

1-Methoxy-2-benzyltriazolium tetrafluoroborate (*12b*) (1.61 g), potassium thioacetate (0.74 g), and dry acetonitrile (16 ml) were stirred for 72 h. The solvent was removed leaving the crude *2-benzyl-4-acetylthiotriazole* (*11b; X=SAc*) which was hydrolyzed by stirring and heating to reflux for 3 h with 10 % aqueous sodium hydroxide (5.5 ml) and methanol (5.5 ml). Washing with dichloromethane (3×10 ml), acidification with hydrochloric acid to pH *ca.* 2, extraction with dichloromethane (3×10 ml), drying ($MgSO_4$), and removal of the dichloromethane, dissolution in ethyl acetate, filtration through silica gel (1 g) and activated carbon (1 g), and removal of the ethyl acetate furnished 0.76 g (69 %) of *2-benzyl-4-mercapto-1,2,3-triazole* (*11b; X=SH*) as an oil which was reprecipitated from ethyl acetate-hexane. Anal. $C_9H_9N_3S$: C,H,N. ^{1}H NMR ($CDCl_3$): δ 7.46 (1H, s, H-5), 7.26 (5H, s, Ph), 5.47 (2H, s, CH_2).

Reaction of 2-alkyltriazole-1-oxides with acetyl chloride. The triazole-1-oxide (25 mmol) and acetyl chloride (50 ml) were kept at 20 °C for 1 d. The acetyl chloride was removed and the residue stirred and heated to reflux with 1 M 50 % methanolic sodium hydroxide (53 ml). Washing with dichloromethane (3×10 ml), acidification with hydrochloric acid to pH *ca.*3, extraction with dichloromethane, drying ($MgSO_4$), and removal of the dichloromethane gave the crude 2-substituted 4-hydroxytriazole.

Thus, 2-methyltriazole-1-oxide (*5a*) (in this case the acidic aqueous solution was evaporated to dryness prior to the extraction with dichloromethane) produced 42 % of 2-methyl-4-hydroxytriazole (*11a; X=OH*), m.p. 99–100 °C, identical with an authentic specimen.[10]

2-Benzyltriazole-1-oxide (*5b*) gave 52 % of *2-benzyl-4-hydroxy-1,2,3-triazole* (*11b; X=OH*) m.p. 70–76 °C. Recrystallization (ethyl acetate) gave m.p. 85–87 °C. Anal. $C_9H_9N_3O$: C,H,N. ^{1}H NMR ($CDCl_3$: δ 7.03 (1H, s, H-5), 7.28 (5H, s, Ph), 5.32 (2H, s, CH_2).

Deoxygenation of 2-alkyltriazole-1-oxides. The triazole-N-oxide (0.1 mol) and phosphorous trichloride (0.22 mol) were stirred and heated to reflux for 1 h. subsequent stirring with water (200 ml) for 1 h, extraction with dichloromethane (3×400 ml), drying (K_2CO_3), removal of the dichloromethane, dissolution in ether, filtration through activated carbon, and removal of the ether left the crude triazole.

2-Methyl-4-chlorotriazole-1-oxide (*10a; X=Cl*) in this way furnished 83 % of *2-methyl-4-chlorotriazole* (*11a; X=Cl*) as an oil b.p. 61 °C/40 mm Hg. (Reported[11] b.p. 62–65 °C/39 mm Hg). ^{1}H NMR ($CDCl_3$): δ 7.44 (1H, s, H-5), 4.14 (3H, s, Me).

2-Benzyltriazole-1-oxide (*5b*) gave 82 % of *2-benzyl-1,2,3-triazole* (*11b; X=H*), m.p. 37–41 °C. Recrystallization (hexane) gave m.p. 43–44 °C. Anal. $C_9H_9N_3$: C,H,N. ^{1}H NMR ($CDCl_3$): δ 7.59 (2H, s, H-4 and H-5), 7.29 (5H, s, Ph), 5.58 (2H, s, CH_2).

2-Benzyl-5-chlorotriazole-1-oxide (*10b; X=Cl*) produced 99 % of *2-benzyl-4-chloro-1,2,3-triazole* (*11b; X=Cl*) as a yellow oil which was dissolved in ether and filtrated through activated carbon. Anal. $C_9H_8N_3Cl$: C,H,N. ^{1}H NMR ($CDCl_3$): δ 7.46 (1H, s, H-5), 7.30 (5H, s, Ph), 5.48 (2H, s, CH_2).

2-Benzyl-5-methylthiotriazole-1-oxide (*10b; X=SMe*) produced 97 % of *2-benzyl-4-methylthio-1,2,3-triazole* (*11b; X=SMe*) as a yellow oil which was dissolved in ether and filtrated through activated carbon. Anal. $C_{10}H_{11}N_3S$: C,H,N. ^{1}H NMR ($CDCl_3$): δ 7.44 (1H, s, H-5) 7.27 (5H, s, Ph) 5.49 (2H, s, CH_2), 2.46 (3H, s, Me).

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