Reaction of Azoles with Ethyl Bromopyruvate Oxime: Alkylation by Substitution and by Elimination–Addition

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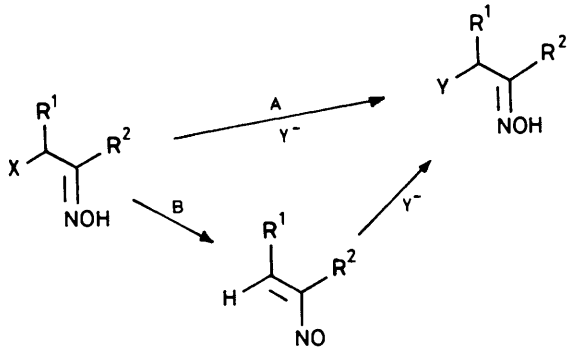
Ethyl bromopyruvate oxime (**1a**) reacts with imidazole, 1-methylimidazole, pyrazole, 3-methylpyrazole, 3,5-dimethylpyrazole, and 1,2,4-triazole to give products of *N*-alkylation of the azoles. The rates of reaction of (**1a**) with imidazole, 1-methylimidazole, and 3,5-dimethylpyrazole are much faster than with the other azoles. The *O*-alkylated oxime (**1b**) reacts much more slowly than (**1a**) with imidazole and with 3,5-dimethylpyrazole. Imidazole is shown to be a strong enough base to eliminate HBr from the bromo oxime (**1a**), and the reaction of pyrazole with (**1a**) is greatly accelerated when an external base (sodium carbonate) is added. As a result, it is concluded that the more basic azoles, with pK_a values above 4, react with (**1a**) by an elimination–addition mechanism whereas the others react by direct displacement of bromide. Related reactions of imidazole and of 1,2,4-triazole with ethyl chloro(hydroxyimino)acetate have also been carried out and the *N*-substituted azoles (**12**), (**13**), and (**14**) have been isolated.

Oximes of α-halogenocarbonyl compounds react easily with many nucleophiles to give products in which the halide is displaced by the nucleophile. Such reactions can, in principle, take place either by direct nucleophilic displacement or by elimination of hydrogen halide followed by addition of the nucleophile (Scheme 1). The elimination–addition mechanism

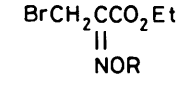


Scheme 1.

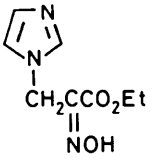
(path B) can be brought about by the use of an external base, or, if the nucleophile is sufficiently basic, by the nucleophile itself. Evidence for an elimination–addition mechanism in some such reactions is provided by the isolation or detection of intermediate nitrosoalkenes.[1]

As part of an investigation of the use of α-halogen oximes as aklylating agents we have studied the reactions of heteroaromatic diazoles and triazoles with ethyl 3-bromo-2-hydroxyiminopropanoate (ethyl bromopyruvate oxime) (**1a**). This is a useful alkylating agent because the products are readily transformed into esters of α-amino acids[2] and of hydroxyamino acids.[3]

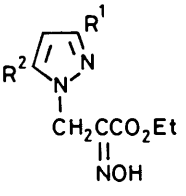
Reactions of the oxime with imidazole, 1-methylimidazole, pyrazole, 3-methylpyrazole, 3,5-dimethylpyrazole, and 1,2,4-triazole have been investigated and a variety of mono- and di-alkylated azoles have been isolated. The rates of the reactions differed widely with different azoles and the heterocycles studied were chosen partly to elucidate the mechanisms of the reactions. There is evidence, detailed below, that either of the mechanisms shown in Scheme 1 can operate and that the mechanism is related to the basicity of the azole.



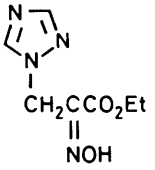
(1) a; R = H
b; R = C(OMe)Me$_2$



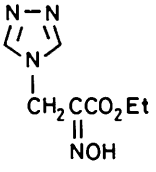
(2)



(3) a; R^1 = R^2 = H
b; R^1 = R^2 = Me
c; R^1 = Me, R^2 = H
d; R^1 = H, R^2 = Me



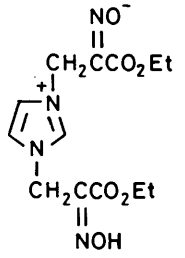
(4)



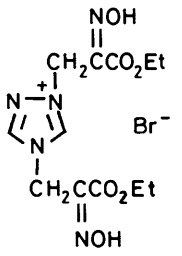
(5)

Reactions were carried out by dissolving the oxime and an excess (2—5 mol equiv.) of the appropriate azole in

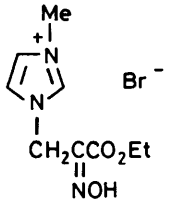
dichloromethane or acetonitrile at room temperature. Azoles with free NH groups all gave mono-*N*-alkylation products [structures (**2**)—(**5**)]. The symmetrical diazoles gave the expected oximes (**2**), (**3a**), and (**3b**), which were isolated in moderate yield. 3-Methylpyrazole gave a 2:1 mixture of isomers (**3c**) and (**3d**) in good yield. 1,2,4-Triazole gave both possible oximes (**4**) and (**5**), which were separated and isolated. It proved difficult to remove residual 1,2,4-triazole from the reaction mixture and this reduced the yield of the purified oximes. Two 2:1 adducts were also isolated from this series of reactions: the zwitterion (**6**) (from imidazole) and the quaternary salt (**7**) (from 1,2,4-triazole). 1-Methylimidazole also gave a quaternary salt, compound (**8**).



(**6**)



(**7**)

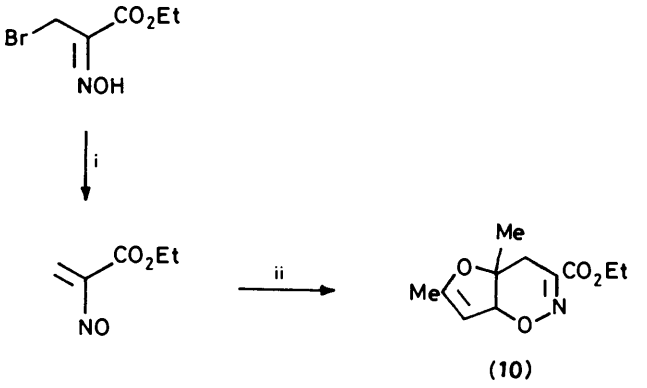


(**8**)

The course of these reactions was monitored by t.l.c. and there were striking differences in the times required for the reactions to go to completion. A semiquantitative investigation was carried out in which each azole was treated with ethyl bromopyruvate oxime under identical conditions (1 mmol of oxime with 2 mmol of azole in 25 ml acetonitrile at 20 °C). The times taken for the bromo oxime to be completely consumed (as indicated by t.l.c.) are shown in the Table. 1-Methylimidazole, as the only azole without a free NH group, was not included in this comparison but its reaction with (**1a**) was rapid. Reactions were also carried out under the same conditions in which the protected oxime (**1b**) [prepared from (**1a**) and 2-methoxypropene] was used as the alkylating agent for imidazole [giving the adduct (**9**)] and for 3,5-dimethylpyrazole. Times taken for complete consumption of the protected oxime are included in the Table.

As the Table indicates, imidazole and 3,5-dimethylpyrazole both reacted rapidly with the bromo oxime (**1a**) but much more slowly with the oxime (**1b**). Reactions of the other azoles with (**1a**) were comparably slow. Since only the bromo oxime (**1a**) is capable of reacting by an elimination–addition mechanism it is possible that the rapid reactions observed between this oxime and imidazole, 1-methylimidazole, or 3,5-dimethylpyrazole involve such a mechanism and that all the other reactions are nucleophilic displacements. There is some correlation between the times of reaction of the azoles with (**1a**) and their basicity (Table). The p*K* values of the azoles in aqueous solution are not directly applicable to these reactions, which were carried out in dichloromethane, but the order of basicities of the azoles does correlate with the times taken for the reactions. The most striking difference is between the reaction times for 3,5-dimethylpyrazole and for 3-methylpyrazole, since these compounds differ in basicity by less than one p*K* unit.

Experiments were performed to test the hypothesis that there are two different mechanisms for these reactions. One was based on the earlier demonstration that the nitrosoalkene ethyl 2-nitrosopropenoate can be intercepted efficiently as a heterodiene in cycloaddition reactions.[4] A solution of imidazole was added dropwise to a solution of the bromo oxime (**1a**) and 2,5-dimethylfuran, and the furo-oxazine (**10**) was isolated in 50% yield. This experiment demonstrates that imidazole is a strong enough base to generate the nitrosoalkene from the bromo oxime (**1a**) by elimination of HBr (Scheme 2). In contrast, an

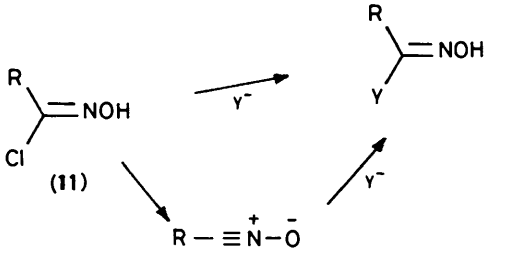


(**10**)

Scheme 2. *Reagents:* i, imidazole; ii, 2,5-dimethylfuran

analogous reaction carried out with pyrazole instead of imidazole gave only the oxime (**3a**) (52%) and none of the furo-oxazine (**10**). In another experiment, sodium carbonate was added to a solution containing the bromo oxime (**1a**) and pyrazole under the standard conditions shown in the Table. In the presence of sodium carbonate the reaction was complete in ten minutes and the oxime (**3a**) was isolated in 85% yield. The drastic reduction in the reaction time is evidence for a change in the mechanism.

A similar mechanistic dichotomy exists in the reaction of chloro oximes (**11**) with nucleophiles: products could be formed either by way of intermediate nitrile oxides or by direct displacement of halide (Scheme 3). We carried out a brief



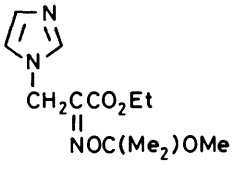
Scheme 3.

investigation of the reaction of ethyl chloro(hydroxyimino)acetate (**11**; R = CO_2Et) with imidazole and with 1,2,4-triazole. Imidazole reacted rapidly with the chloro oxime to give the adduct (**12**) in good yield. This compound has recently been prepared independently from the same reagents in the presence of triethylamine.[5] In contrast, 1,2,4-triazole did not react with the chloro oxime unless an external base (triethylamine) was present. The triazoles (**13**) and (**14**) were then formed. In a related investigation Dalla Croce and his co-workers showed that 1-methylimidazole reacted with the hydrazonyl chloride (**15**) only in the presence of triethylamine. Evidently,

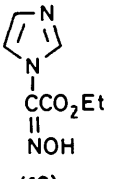
Table. Comparison of reaction times of azoles with the bromo oximes (**1a**) and (**1b**)[a]

Azole	pK_a[b]	Reaction time (h) (**1a**)	(**1b**)
Imidazole	7.10	0.2	24
3,5-Dimethylpyrazole	4.12	0.5	48
3-Methylpyrazole	3.32	24	
Pyrazole	2.52	72	
1,2,4-Triazole	2.27	72	

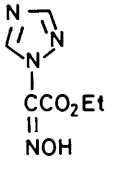
[a] Reactions were carried out with the azole (2.0 mmol) and the bromo oxime (1.0 mmol) in acetonitrile (25 ml) at 20 °C. [b] Values are for aqueous solutions at 20 °C: D. D. Perrin, 'Dissociation Constants of Organic Bases in Aqueous Solution: Supplement 1972,' Butterworths, London, 1972.



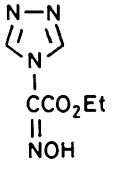
(**9**)



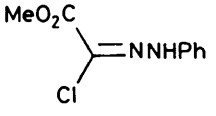
(**12**)



(**13**)



(**14**)



(**15**)

substitution reactions of compounds (**11**) and (**15**) with azoles take place much more readily by the elimination–addition mechanism than by direct displacement.

Experimental

Melting points are uncorrected. I.r. spectra were recorded for KBr discs on a Perkin-Elmer R34 spectrophotometer. Except where indicated otherwise, n.m.r. spectra were recorded for solutions in $CDCl_3$ on a Perkin-Elmer R34 spectrometer operating at 220 MHz. Mass spectra were recorded by electron impact at 70 eV, using a direct insertion probe. Medium pressure chromatography was carried out on S.O. t.l.c. silica gel (Whatman).[7] Flash chromatography was carried out with Kieselgel 60 (Merck) as the stationary phase.[8] Light petroleum refers to the fraction b.p. 40—60 °C and it was distilled before use. Other solvents were used as supplied.

Ethyl 3-Bromo-2-[(1-methoxy-1-methylethoxy)imino]propanoate (**1b**).—Ethyl 3-bromo-2-hydroxyiminopropanoate (ethyl bromopyruvate oxime (**1a**)[4] (0.21 g, 1.0 mmol) and 2-methoxypropene (0.07 g, 1.0 mmol) were dissolved in dichloromethane (5 ml). The solution was kept at room temperature for 6 h, after which period the reaction was judged to be complete (by t.l.c.). The solvent was distilled off to leave the oxime ether (**1b**) (0.28 g, 100%), $\nu_{max.}$ 1 725 (CO) and 1 600 cm^{-1} (C=N); δ 1.32 (3 H, t), 1.51 (6 H), 3.28 (3 H), 4.20 (2 H), and 4.32 (2 H, q). The compound was not characterised further.

Ethyl 2-Hydroxyimino-3-imidazol-1-ylpropanoate (**2**) and *1,3-Bis[(2-ethoxycarbonyl-2-hydroxyimino)ethyl]imidazolium Hydroxide Inner Salt* (**6**).—A solution of ethyl 3-bromo-2-hydroxyiminopropanoate (10.5 g, 50 mmol) was added dropwise during 1 h to a stirred solution of imidazole (6.8 g, 100 mmol) in dichloromethane (250 ml). A precipitate appeared during the addition. The reaction mixture was stirred for a further 0.5 h and the solvent was then removed. The residue, an oil, was dissolved in the minimum volume of aqueous HCl (2M) and the solution was washed with dichloromethane (50 ml) and ether (50 ml). Aqueous sodium carbonate (2M) was then added to the aqueous solution slowly until a precipitate appeared. This was filtered off, washed with water, ethanol, and ether, and crystallised to give the *imidazole* (**2**) (5.4 g, 55%), m.p. 155—165 °C (decomp.) (from acetonitrile) (Found: C, 48.6; H, 5.85; N, 21.15. $C_8H_{11}N_3O_3$ requires C, 48.7; H, 5.6; N, 21.3%); $\nu_{max.}$ 2 560 (br, OH), 1 710 (CO) and 1 620 cm^{-1} (C=N); δ[$(CD_3)_2SO$] 1.20 (3 H, t), 4.22 (2 H, q), 5.02 (2 H), 6.92 (1 H, 4-H of imidazole), 7.12 (1 H, 5-H of imidazole), 7.72 (1 H, 2-H of imidazole), and 10.32 (1 H, br, OH); *m/z* 197 (M^+) and 81 (base).

The filtrate obtained after removal of this precipitate was allowed to stand. After 15 min a further precipitate appeared. This was filtered off, washed with cold ethanol and ether, and dried to give the *zwitterion* (**6**) (5.2 g, 32%), m.p. 165 °C (decomp.) (Found: C, 47.6; H, 5.8; N, 16.8. $C_{13}H_{13}N_4O_6$ requires C, 47.85; H, 5.6; N, 17.2%); $\nu_{max.}$ 1 705, 1 680, and 1 550 cm^{-1}; δ (CF_3CO_2H) 1.10 (6 H, t), 4.18 (4 H, q), 5.15 (4 H), 7.14 (2 H), and 8.70 (1 H); *m/z* 326 (M^+), 197 (base), and 81.

3-(2-Ethoxycarbonyl-2-hydroxyimino)ethyl-1-methylimidazolium Bromide (**8**).—Ethyl 3-bromo-2-hydroxyiminopropanoate (0.21 g, 1.0 mmol) in dichloromethane (5 ml) was added dropwise during 0.5 h to a stirred solution of 1-methylimidazole (0.166 g, 2.0 mmol) in dichloromethane (10 ml). After the addition was complete the brown solution was reduced in volume and the residue was triturated with acetonitrile to remove 1-methylimidazole. Crystallisation of the residual solid gave the *imidazolium bromide* (**8**) (0.20 g, 68%), m.p. 175—180 °C (decomp.) (from ethanol) (Found: C, 36.7; H, 4.9; N, 13.8. $C_9H_{14}BrN_3O_3$ requires C, 37.0; H, 4.8; N, 14.4%); $\nu_{max.}$ 2 725 (OH), 1 705 (CO), and 1 570 cm^{-1} (C=N); δ[$(CD_3)_2SO$] 1.28 (3 H, t), 4.00 (3 H), 4.20 (2 H, q), 5.28 (2 H), 7.79 (1 H), 7.90 (1 H), 9.40 (1 H), and 13.50 (1 H, br, OH).

Ethyl 2-Hydroxyimino-3-pyrazol-1-ylpropanoate (**3a**).—(*a*) Ethyl 3-bromo-2-hydroxyiminopropanoate (1.05 g, 5.0 mmol) in dichloromethane (25 ml) was added dropwise to a solution of pyrazole (0.68 g, 10 mmol) in dichloromethane (25 ml). The reaction mixture was stirred for 72 h. The solvent was then distilled off. Medium pressure chromatography of the residue eluting with dichloromethane gave the *pyrazole* (**3a**) (0.56 g, 57%), m.p. 68—69 °C (from tetrachloromethane) (Found: C, 48.8; H, 5.7: N, 21.4. $C_8H_{11}N_3O_3$ requires C, 48.7; H, 5.6; N, 21.3%); $\nu_{max.}$ 3 400 (OH), 1 710 (CO), and 1 600 cm^{-1} (C=N); δ 1.20 (3 H, t), 4.21 (2 H, q). 5.29 (2 H), 6.20 (1 H, t), 7.61 (2 H, m, 3-H and 5-H), and 12.70 (1 H, br, OH); *m/z* 197 (M^+) and 81 (base).

(*b*) A solution of pyrazole (0.27 g, 4.0 mmol), ethyl bromopyruvate oxime (0.42 g, 2.0 mmol), and 2,5-dimethylfuran (0.5 g) in dichloromethane (25 ml) was allowed to stand at room temperature for 96 h. The solvent was distilled off. The residue was subjected to medium pressure chromatography as in (*a*), which gave the pyrazole (**3a**) (0.21 g, 52%). None of the furo-oxazine (**10**) was detected in the reaction mixture.

(*c*) To a solution of pyrazole (0.13 g, 2.0 mmol) in acetonitrile (20 ml) was added anhydrous sodium carbonate (2.1 g). The mixture was stirred vigorously and a solution of ethyl 3-bromo-2-hydroxyiminopropanoate (0.21 g, 1.0 mmol) in acetonitrile (5 ml) was added. The bromo oxime was consumed after 10 min

(by t.l.c.). The reaction mixture was filtered through Celite and the filtrate was evaporated to dryness. Medium pressure chromatography of the residue gave (with dichloromethane) the pyrazole (**3a**) (0.17 g, 85%).

Ethyl 2-Hydroxyimino-3-(3-methypyrazol-1-yl)propanoate (**3c**) *and Ethyl 2-Hydroxyimino-3-(5-methylpyrazol-1-yl)propanoate* (**3d**).—To a stirred solution of 3-methylpyrazole (0.166 g, 2.0 mmol) in acetonitrile (20 ml) was added ethyl 3-bromo-2-hydroxyiminopropanoate (0.21 g, 1.0 mmol) in acetonitrile (5 ml). The solution was kept at room temperature for 24 h, then the solvent was distilled off. Medium pressure chromatography gave [with ether–light petroleum (5:1)] the *pyrazoles* (**3c**) and (**3d**) (0.16 g, 76%) as a mixture, m.p. 93—96 °C (from tetrachloromethane) (Found: C, 51.3; H, 6.1; N, 20.0. $C_9H_{13}N_3O_3$ requires C, 51.2; H, 6.2; N, 19.9%); $\nu_{max.}$ 3 400 (OH), 1 710 (CO), and 1 600 cm^{-1} (C=N). ^1H N.m.r. spectroscopy indicated that the two isomers were present in the ratio 61 : 39; δ for the major isomer [assigned structure (**3c**)] 1.25 (3 H, t), 2.25 (3 H), 4.29 (2 H, q), 5.25 (2 H), 6.05 (1 H, br, 4-H of pyrazole), 7.50 (1 H, br, 5-H of pyrazole), and 13.50 (1 H, br, OH); δ for the minor isomer [assigned structure (**3d**)] 1.20 (3 H, t), 2.40 (3 H), 4.25 (2 H, q), 5.21 (2 H), 6.04 (1 H, 4-H of pyrozole), 7.49 (1 H, 3-H of pyrazole), and 13.50 (1 H, br, OH); *m/z* (mixture of isomers) 211 (M^+) and 95 (base).

Ethyl 3-(3,5-Dimethylpyrazol-1-yl-2-hydroxyiminopropanoate (**3b**).—A solution containing ethyl 3-bromo-2-hydroxyiminopropanoate (0.21 g, 1.0 mmol) and 3,5-dimethylpyrazole (0.495 g, 5.2 mmol) in dichloromethane (30 ml) was kept at room temperature for 1 h. The solvent was then distilled off. Medium pressure chromatography of the residue gave (with dichloromethane) the *pyrazole* (**3b**) (0.15 g, 65%), m.p. 164—165 °C (from dichloromethane–hexane) (Found: C, 53.35; H, 6.6; N, 18.9. $C_{10}H_{15}N_3O_3$ requires C, 53.3; H, 6.7; N, 18.7%); $\nu_{max.}$ 3 400 (OH), 1 705 (CO), and 1 600 cm^{-1} (C=N); δ 1 25 (3 H, t), 2.22 (3 H, 3-Me), 2.39 (3 H, 5-Me), 4.24 (2 H, q), 5.15 (2 H), 5.81 (1 H, 4-H), and 9.50 (1 H, br, OH); *m/z* 225 (M^+) and 109 (base).

Ethyl 2-Hydroxyimino-3-(1,2,4-triazol-1-yl)propanoate (**4**) *and Ethyl 2-Hydroxyimino-3-(1,2.4-triazol-4-yl)propanoate* (**5**).—A solution of 1,2,4-triazole (0.69 g, 10.0 mmol) and ethyl 3-bromo-2-hydroxyiminopropanoate (0.42 g, 2.0 mmol) in acetonitrile (50 ml) was maintained at room temperature for 18 h. The solvent was distilled off and the residue was subjected to medium pressure chromatography which gave [with dichloromethane–ethanol (9:1)] the 1,2,4-*triazol-4-yl derivative* (**5**) (0.071 g, 18%), m.p. 165—166 °C (from ethanol) (Found: C, 42.8; H, 5.0; N, 28.25. $C_7H_{10}N_4O_3$ requires C, 42.4; H, 5.1; N, 28.3%); $\nu_{max.}$ 3 115, 2 550, 1 710 (CO), and 1 640 cm^{-1} (C=N); δ[$(CD_3)_2SO$] 1.25 (3 H, t), 4.21 (2 H, q), 5.06 (2 H), 8.40 (2 H, 3-H, and 5-H), and 13.40 (1 H, br, OH); *m/z* 198 (M^+) and 82 (base). A second, more polar component was then eluted and was identified as the 1,2,4-*triazol-1-yl derivative* (**4**) (0.071 g, 18%), m.p. 154—157 °C (from ethanol–hexane) (Found: C, 42.75; H, 5.0; N, 28.6%); $\nu_{max.}$ 3 045, 2 670, 1 710 (CO), and 1 615 cm^{-1} (C=N); δ[$(CD_3)_2SO$] 1.20 (3 H, t), 4.22 (2 H, q), 5.31 (2 H), 8.05 (1 H, 3-H), 8.65 (1 H, 5-H), and 12.05 (1 H, br, OH): *m/z* 198 (M^+) and 109 (base).

1,4-bis-[(2-*Ethoxycarbonyl-2-hydroxyimino)ethyl*]-1,2,4- *triazolium Bromide* (**7**).—A solution of 1,2,4-triazole (0.69 g, 10.0 mmol) and ethyl 3-bromo-2-hydroxyiminopropanoate (1.05 g, 5.0 mmol) in tetrahydrofuran (50 ml) was allowed to stand at room temperature for 2 weeks. During this period a solid precipitated. This was filtered off and dried to give the *triazolium bromide* (**7**) (0.85 g, 82%), m.p. 180—182 °C (decomp.) (Found: C, 35.7; H, 4.4; N, 16.9. $C_{12}H_{18}BrN_5O_6$ requires C, 35.3; H, 4.4; N, 17.15%); $\nu_{max.}$ 3 400 (OH), 3 150, 1 730 (CO), 1 700 (CO), and 1 615 cm^{-1} (C=N); δ[$(CD_3)_2SO$] 1.24 (3 H, t), 1.27 (3 H, t), 4.25 (2 H, q), 4.29 (2 H, q), 5.38 (2 H), 5.49 (2 H), 9.39 (1 H, 3-H), 10.35 (1 H, 5-H), 13.40 (1 H, OH), and 13.50 (1 H, OH); *m/z* 328 ($C_{12}H_{18}N_5O_6^+$) and 70 (base).

Ethyl 3-Imidazol-1-yl-[2-(1-methoxy-1-methylethoxy)-imino]propanoate (**9**).—To a solution of the oxime ether (**1b**) (0.28 g, 1.0 mmol) in dichloromethane (25 ml) was added imidazole (0.136 g, 2.0 mmol) and the reaction mixture was stirred for 24 h. The solvent was then distilled off and the residue was purified by medium pressure chromatography. This gave [with dichloromethane–ethyl acetate (19:1)] the imidazole (**9**) (0.23 g, 86%) as a yellow oil; δ 1.32 (3 H, t), 1.53 (6 H), 3.18 (3 H), 4.33 (2 H, q), 5.02 (2 H), 7.03 (2 H, 4-H, and 5-H), and 7.62 (1 H, 2-H). The compound was not characterised further.

Generation of Ethyl 2-Nitrosopropenoate by Imidazole. Reaction with 2,5-Dimethylfuran.—To a stirred solution of ethyl 3-bromo-2-hydroxyiminopropanoate (0.21 g, 1.0 mmol) and 2,5-dimethylfuran (0.48 g, 5.0 mmol) in dichloromethane (10 ml) was added, during 1 h, a solution of imidazole (0.069 g, 1.0 mmol) in dichloromethane (15 ml). A solid was precipitated during this period. When the addition was complete the solid was filtered off and the filtrate was evaporated to small volume. Medium pressure chromatography of the residue gave [with dichloromethane–ethyl acetate (19:1)] ethyl 4a,7a-dihydro-4a,6-dimethyl-4*H*-furo[2,3-*e*]-1,2-oxazine-3-carboxylate (**10**) (0.112 g, 50%), m.p. 85—87 °C (from ether–hexane) which was identical to an authentic specimen.[9]

Ethyl Hydroxyimino(imidazol-1-yl)acetate (**12**).—To a vigorously stirred solution of imidazole (0.68 g, 10 mmol) in dichloromethane (20 ml) was added, dropwise during 30 min, a solution of ethyl chloro(hydroxyimino)acetate[10] (0.75 g, 5 mmol) in dichloromethane (10 ml). After a further 15 min, during which time a precipitate appeared, the solvent was evaporated off. Column chromatography (silica) gave (with dichloromethane) the imidazole (**12**) (0.69 g, 75%), m.p. 141—142 °C (decomp.) (from acetonitrile) [lit.,[5] m.p. 156—157 °C (decomp.)] (Found: C, 45.8; H, 5.0; N, 23.15. Calc. for $C_7H_9N_3O_3$: C, 45.9; H, 4.9; N, 22.95%). I.r. and n.m.r. spectra were as reported.[5]

Ethyl Hydroxyimino(1,2,4-triazol-1-yl)acetate (**13**) and *Ethyl Hydroxyimino(1,2,4-triazol-4-yl)acetate* (**14**).—To a vigorously stirred solution of 1,2,4-triazole (0.69 g, 10 mmol) and triethylamine (1.01 g, 10 mmol) in dichloromethane (50 ml), was added, dropwise during 1 h, a solution of ethyl chloro(hydroxyimino)acetate (1.51 g, 10 mmol). The reaction mixture was then stirred for a further 15 min and the solvent was distilled off. Flash chromatography gave [with dichloromethane–ethanol (9:1)] the 1,2,4-*triazol-4-yl derivative* (**14**) (0.40 g, 22%), m.p. 154—155 °C (from ethanol) (Found: C, 38.9; H, 4.3; N, 30.4. $C_6H_8N_4O_3$ requires C, 39.1; H, 4.35; N, 30.4%); $\nu_{max.}$ 2 650 (OH) and 1 715 cm^{-1} (CO); δ[$(CD_3)_2SO$] 1.28 (3 H, t), 4.25 (2 H, q), 8.65 (2 H, 3-H, and 5-H), and 13.50 (1 H, br, OH); *m/z* 184 (M^+), 156, and 69 (base); *m** (184 → 156) 132.2. Further elution gave the 1,2,4-*triazol-1-yl derivative* (**13**) (0.36 g, 20%), m.p. 142—145 °C (from ethanol) (Found: C, 39.5; H, 4.6%); $\nu_{max.}$ 2 655 (OH) and 1 720 cm^{-1} (CO); δ[$(CD_3)_2SO$] 1.31 (3 H, t), 4.32 (2 H, q), 8.24 (1 H, 3-H), 8.95 (1 H, 5-H), and 12.05 (1 H, br, OH); *m/z* 184 (M^+), 156, 101, and 86 (base).

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