

## REACTIONS OF 3,5-DIMETHYL-4-NITROISOXAZOLE WITH CYCLIC ENAMINES AND 1-DIETHYLAMINOPROPYNE

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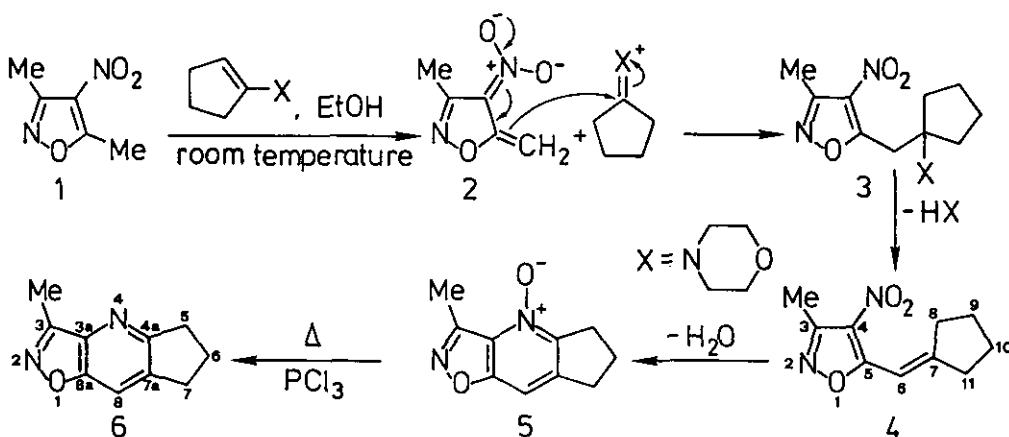
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**Abstract** - 3,5-Dimethyl-4-nitroisoxazole (**1**) was found to undergo tandem condensation-cyclization processes with 4-(1-cyclopenten-1-yl)- and 4-(1-cyclohexen-1-yl)morpholine in ethanol solution to give, through the intermediates (**4**) and (**7**), the *N*-oxides (**5**) and (**9**), respectively. The reactivity of **1** towards 1-diethylamino-propyne in different solvents was also investigated; the structure of the unexpected acyloxime (**13**), coming from the above reagents in acetonitrile, was determined by an X-ray analysis. Plausible mechanistic pathways for these new reactions are suggested.

Despite the interest shown over the past fifty years in the reactivity of the title compound with a variety of reagents,<sup>1</sup> its behaviour towards enamines and ynamines has been completely disregarded. On this basis, we wish now to report some findings on this topic.

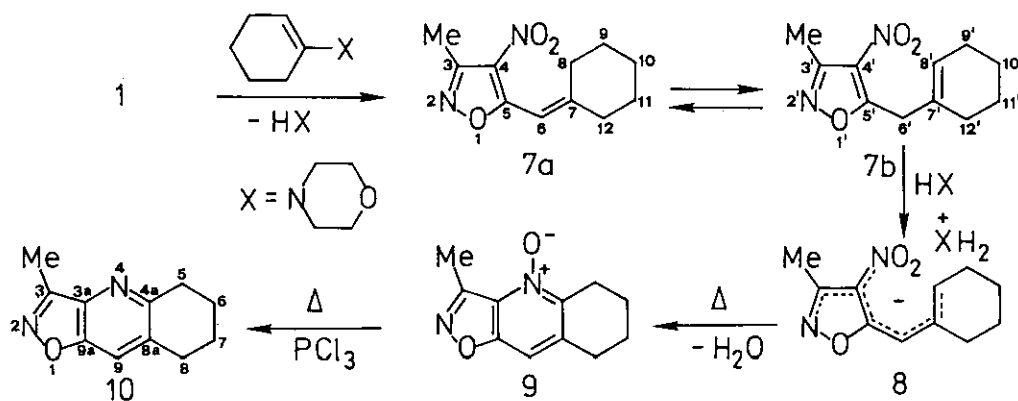


Scheme 1

When the nitro derivative (**1**) was allowed to react with an excess (molar ratio 1:2) of 4-(1-cyclopenten-1-yl)morpholine in anhydrous ethanol at room temperature for 5 days, the tricyclic N-oxide (**5**) was isolated in 80% yield; treatment of the latter with  $\text{PCl}_3$  in refluxing chloroform afforded the cyclopentisoxazolopyridine (**6**) in good yield.

Due to the remarkable acidity of the 5-methyl group of the starting material,<sup>2</sup> the formation of **5** can be accounted for by assuming that the corresponding carbanion (**2**) gives rise to the condensation product (**4**) through the adduct (**3**); the subsequent base-catalyzed cyclization of **4** into **5**, involving the attack of the C-8 carbon on the electrophilic nitrogen of the  $\text{NO}_2$  group, closely resembles other ring closures previously described for suitably ortho-substituted nitrobenzene derivatives<sup>3</sup> (Scheme 1).

Tlc monitoring of the reaction course clearly showed the presence of a key intermediate that slowly evolved into the final product; thus, when the reaction was carried out with 1 equiv. of the same reagent for 12 h, we succeeded in isolating compound (**4**) by flash chromatography.

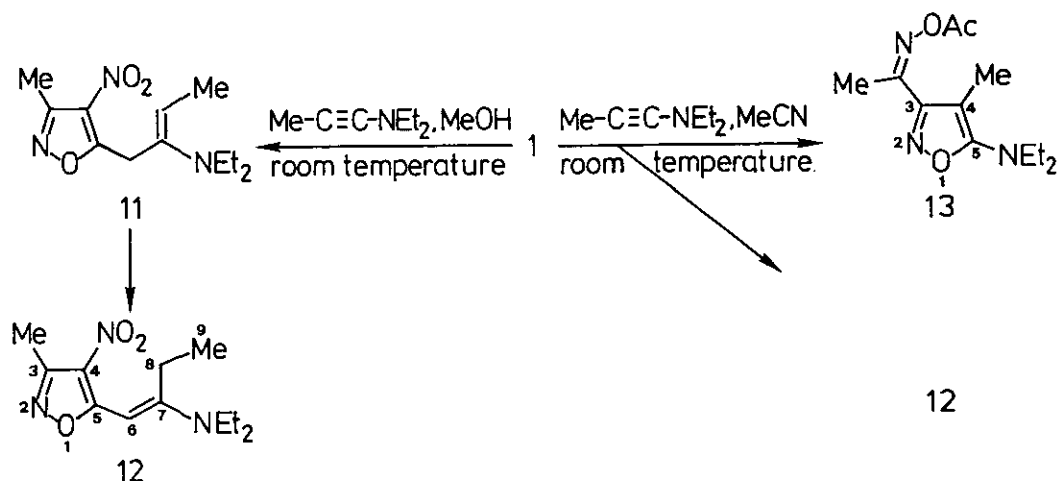


Replacement of the above enamine with the corresponding cyclohexene derivative afforded, under the original conditions, only a small amount of the N-oxide (**9**); the reaction mixture now contained predominantly the salt (**8**), that separated as a pure product by treatment with ether. Likewise for **4**, the precursor (**7**) was obtained with 1 equiv. of the same reagent and shorter reaction times; on the contrary, when the reaction was carried out under forcing conditions, we isolated in 39% yield the desired compound (**9**) which was easily converted into the tetrahydroisoxazoloquinoline (**10**) (Scheme 2). Comparable results were obtained by treatment of **1** with the same reagents in dry acetonitrile.

The dramatic difference observed for the terminal ring closure of the nitro derivatives (**4**) and (**7**) can be explained on the basis of the Brown's generalization for the reactivity trend of five- and six-membered rings containing an exocyclic double bond.<sup>4</sup>

On the same ground, whereas the former compound exists exclusively as **4** in chloroform solution,

the latter gives rise to a tautomeric equilibrium between **7a** and **7b** (ca. 2:1) in the same solvent. The structures of the isoxazoles (**4**), (**7**), and (**8**), as well as those of the novel ring systems (**5**), (**6**), (**9**), and (**10**) were determined by analytical and spectral evidence (Experimental). In particular, the ir bands of **4** and **7** ( $1570$  and  $1360\text{ cm}^{-1}$ ) were replaced by a strong  $\text{N}^+-\text{O}^-$  absorption at  $1342$  and  $1322\text{ cm}^{-1}$  in the spectra of compounds (**5**) and (**9**), respectively. Moreover, whereas the  $^1\text{H}$  nmr spectrum of **4** showed a quintet at  $\delta$  7.11 for the vinyl proton, the coupled  $^{13}\text{C}$  nmr pattern was characterized by a doublet and a singlet at  $\delta$  105.85 and 169.87, attributable to the C-6 and C-7 carbons of the exocyclic double bond; similar resonances also appeared in the corresponding spectra of **7** for the same moiety of the form (**7a**), but the concomitant presence of **7b** was easily ascertained on the basis of a signal at  $\delta$  3.81 (6'-CH<sub>2</sub>) in the former, and a singlet and a doublet at  $\delta$  130.70 and 126.66 in the latter, for the endocyclic C(7')-C(8') double bond. Finally, both the  $^1\text{H}$  and  $^{13}\text{C}$  nmr resonances of the CH group exhibited diagnostic downfield shifts on going from compounds (**5**) and (**9**) to the corresponding deoxygenation products (**6**) and (**10**) ( $\delta$  7.205, 7.17 and  $\delta$  105.15, 108.24 vs.  $\delta$  7.57, 7.77 and  $\delta$  113.69, 120.95, respectively).

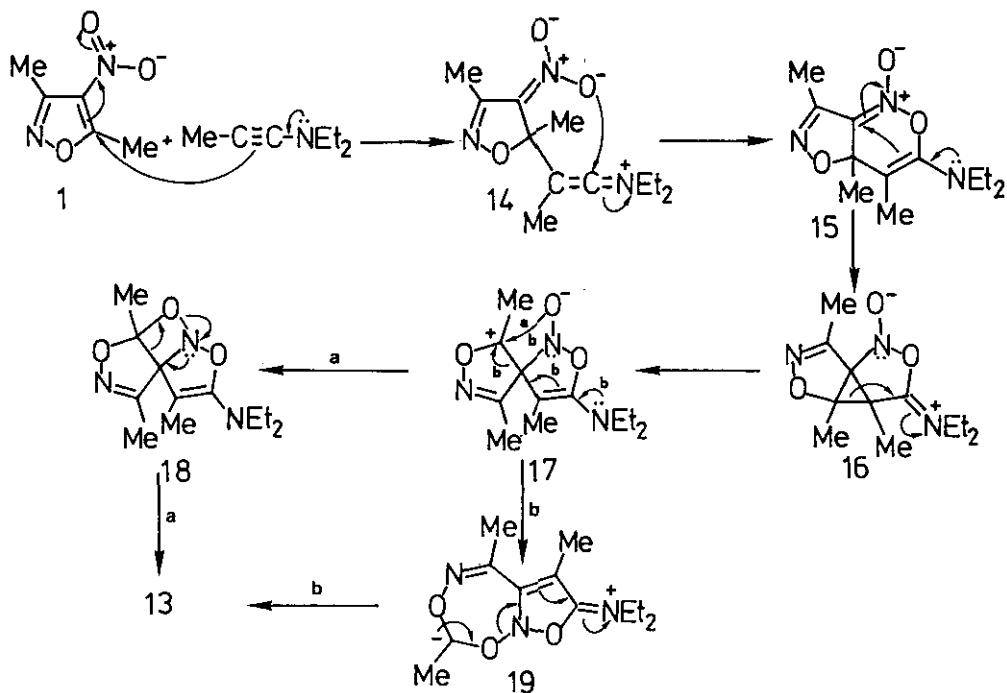


Scheme 3

Treatment of **1** with 1 equiv. of 1-diethylaminopropyne in methanol<sup>5</sup> at room temperature gave almost quantitatively compound (**12**), whose stereochemistry followed from a NOESY experiment; although **12**, coming from a prototropic isomerization of the enamine intermediate (**11**), formally resembled the nitro derivatives (**4**) and (**7**), no cyclization was observed for this product even under more drastic conditions (molar ratio 1:2, prolonged reflux), probably due to the reduced electrophilic properties of the NO<sub>2</sub> nitrogen at  $\delta$  position of a dienamine system (Scheme 3).

On the other hand, when methanol was replaced with acetonitrile, surprisingly we isolated from the complex reaction mixture only a small amount of **12** together with the more abundant isoxazole derivative (**13**), whose structure was determined by a single crystal X-ray analysis.

This not straightforward alternative reaction of **1** was tentatively explained as shown in the Scheme 4.



Scheme 4

According to the well known behaviour of 4-nitrosoisoxazoles with nucleophiles,<sup>6</sup> it probably starts with a Michael addition leading to the nitronate (14) that, in turn, evolves into the derivative (15), through a formal [4 + 2] cycloaddition; ring contraction of the oxazine moiety of 15 gives rise to the spiran (17) via the unstable cyclopropane derivative (16). The final product can then arise from 17 through the tricyclic compound (18) (route a), or by conversion of the same intermediate into the seven-membered bicyclic system (19), followed by N-O ring opening of the latter (route b).

This mechanistic rationale appears to be confirmed by the firmly established Z configuration of the acyloxime (13) (see Figure).

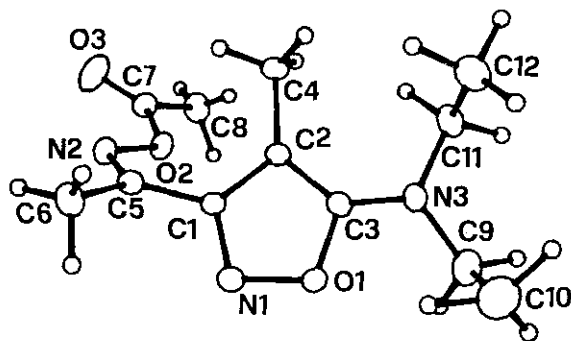


Figure: A computer-generated drawing of 13 derived from the X-ray coordinates with hydrogens omitted for clarity.

## EXPERIMENTAL

Melting points were taken on a Büchi 510 apparatus and are uncorrected. Except where otherwise stated, infrared spectra were measured for dispersions in KBr with a Perkin-Elmer 283 spectrophotometer, while  $^1\text{H}$  and  $^{13}\text{C}$  nmr spectra were recorded in  $\text{CDCl}_3$  solutions on a Varian Gemini-200 instrument operating at 200 MHz and 50 MHz, respectively; the relative assignment of the  $^{13}\text{C}$  resonances was achieved on the basis of the coupled spectra and long-range heteronuclear correlation experiments. Elemental analyses were obtained by a Perkin-Elmer 240C Analyzer. Silica gel plates (Merck F254) and silica gel 60 (Merck; 230-400 mesh) were used for analytical and flash chromatographies, respectively. Petroleum ether refers to the fraction bp 40-70°C.

### Reactions of the Nitroisoxazole (1) with 4-(1-Cyclopenten-1-yl)morpholine. Preparation of Compounds (4) and (5).

**A** - Compound **(1)** (0.142 g, 1 mmol) was allowed to react with the title enamine (0.153 g, 0.16 ml, 1 mmol) in anhydrous ethanol (1 ml) at room temperature for 12 h; removal of the solvent left a semi-solid orange residue, which was subjected to flash chromatography with petroleum ether-ethyl acetate (12:1 v/v) as eluent. The first fraction ( $R_f=0.57$ ) afforded 5-cyclopentylidenemethyl-3-methyl-4-nitroisoxazole (**4**) as a pale yellow solid [0.030 g, 33% yield based on the starting material recovered from the second band ( $R_f=0.38$ ; 0.080 g)], mp 62-62.5°C (from pentane); ir  $\nu_{\text{max}}$ : 3075 (CH), 1570, and 1360  $\text{cm}^{-1}$  ( $\text{NO}_2$ );  $^1\text{H}$  nmr  $\delta$ : 1.70-1.90 (m, 4H, 9- $\text{CH}_2$  and 10- $\text{CH}_2$ ), 2.55 (s, 3H, 3- $\text{CH}_3$ ), 2.60-2.70 (m, 2H, 8- $\text{CH}_2$ /11- $\text{CH}_2$ ), 2.80-2.90 (m, 2H, 11- $\text{CH}_2$ /8- $\text{CH}_2$ ), 7.11 (quintet,  $J=2.2$  Hz, 1H, H-6);  $^{13}\text{C}$  nmr  $\delta$ : 11.88 (q, 3- $\text{CH}_3$ ), 25.79 (t, 9- $\text{CH}_2$ /10- $\text{CH}_2$ ), 26.71 (t, 10- $\text{CH}_2$ /9- $\text{CH}_2$ ), 34.12 (t, 8- $\text{CH}_2$ /11- $\text{CH}_2$ ), 37.50 (t, 11- $\text{CH}_2$ /8- $\text{CH}_2$ ), 105.85 (d, C-6), 126.60 (br s, C-4), 155.49 (s, C-3), 168.05 (s, C-5), 169.87 (s, C-7). Anal. Calcd for  $\text{C}_{10}\text{H}_{12}\text{N}_2\text{O}_3$ : C, 57.69; H, 5.81; N, 13.45. Found: C, 57.46; H, 5.79; N, 13.23.

**B** - Treatment of **1** (0.142 g, 1 mmol) with an excess of the above reagent (0.306 g, 0.32 ml, 2 mmol) under the same conditions for 5 days gave 3-methylcyclopent[*b*]isoxazolo[5,4-*e*]pyridine-4-oxide (**5**), that was separated by filtration as an ivory-coloured solid (0.082 g, 43%); a second crop of the same product was recovered from the residue left by evaporation to dryness of the filtrate, by flash chromatography with ethyl acetate-acetone (5:1 v/v) as eluent ( $R_f=0.33$ , 0.070 g, 80% overall yield): silk needles mp 183-184°C (from ethyl acetate); ir  $\nu_{\text{max}}$ : 3080, 3060 (CH), and 1342  $\text{cm}^{-1}$  ( $\text{N}^+-\text{O}$ );  $^1\text{H}$  nmr  $\delta$ : 2.14-2.29 (m, 2H, 6- $\text{CH}_2$ ), 2.75 (s, 3H, 3- $\text{CH}_3$ ), 3.02-3.14 (m, 4H, 5- $\text{CH}_2$  and 7- $\text{CH}_2$ ), 7.21 (m, 1H, H-8);  $^{13}\text{C}$  nmr  $\delta$ : 11.02 (q, 3- $\text{CH}_3$ ), 22.79 (t, 6- $\text{CH}_2$ ), 27.90 (t, 5- $\text{CH}_2$ ), 31.53 (t, 7- $\text{CH}_2$ ), 105.15 (d, C-8), 129.85 (s, C-3a), 143.98 (s, C-7a), 150.24 (s, C-4a), 152.52 (s, C-3), 160.73 (s, C-8a). Anal. Calcd for  $\text{C}_{10}\text{H}_{10}\text{N}_2\text{O}_2$ : C, 63.15; H, 5.30; N, 14.73. Found: C, 63.04; H, 5.29; N, 14.45.

### Reactions of 1 with 4-(1-Cyclohexen-1-yl)morpholine. Synthesis of Compounds (7), (8), and (9).

**A** - A mixture of **1** (0.142 g, 1 mmol) and the title enamine (0.167 g, 0.17 ml, 1 mmol) in anhydrous ethanol (1 ml) was stirred at room temperature for 12 h and evaporated to dryness; the residue was

resolved into two components by flash chromatography with petroleum ether-ethyl acetate (16:1 v/v) as eluent. The first fractions ( $R_f=0.46$ ) gave 5-cyclohexylidenemethyl-3-methyl-4-nitroisoxazole (**7**) [0.030 g, 60% yield based on **1** recovered from the following band ( $R_f=0.31$ , 0.11 g)] as a pale yellow oil; an analytical sample was obtained as a colourless liquid by dissolution in pentane, treatment with charcoal, filtration, evaporation to dryness, and prolonged evacuation under reduced pressure ( $10^{-2}$  mmHg);  $\nu_{\max}$  (neat): 3040 (CH), 1570, and  $1360\text{ cm}^{-1}$  ( $\text{NO}_2$ );  $^1\text{H nmr } \delta$ : 1.50-1.80 [m, 6H, (9- $\text{CH}_2$ , 10- $\text{CH}_2$ , and 11- $\text{CH}_2$ ) and 4H, (10'- $\text{CH}_2$  and 11'- $\text{CH}_2$ )], 1.93-2.06 (m, 4H, 9'- $\text{CH}_2$  and 12'- $\text{CH}_2$ ), 2.38-2.45 (m, 2H, 8- $\text{CH}_2$ /12- $\text{CH}_2$ ), 2.56 [s, 3H, (3- $\text{CH}_3$ ) and 3H, (3'- $\text{CH}_3$ )], 2.74-2.81 (m, 2H, 12- $\text{CH}_2$ /8- $\text{CH}_2$ ), 3.81 (br s, 2H, 6'- $\text{CH}_2$ ), 5.58 (m, 1H, H-8'), 6.78 (quintet,  $J=1.1\text{ Hz}$ , 1H, H-6);  $^{13}\text{C nmr } \delta$ : 11.73 (q, 3'- $\text{CH}_3$ ), 11.83 (q, 3- $\text{CH}_3$ ), 21.75 (t, 10'- $\text{CH}_2$ /11'- $\text{CH}_2$ ), 22.58 (t, 11'- $\text{CH}_2$ /10'- $\text{CH}_2$ ), 25.25 (t, 9'- $\text{CH}_2$ /12'- $\text{CH}_2$ ), 25.92 (t, 9- $\text{CH}_2$ /10- $\text{CH}_2$ /11- $\text{CH}_2$ ), 28.04 (t, 10- $\text{CH}_2$ /11- $\text{CH}_2$ /9- $\text{CH}_2$ ), 28.58 (t, 12'- $\text{CH}_2$ /9'- $\text{CH}_2$ ), 28.82 (t, 11- $\text{CH}_2$ /9- $\text{CH}_2$ /10- $\text{CH}_2$ ), 32.13 (t, 8- $\text{CH}_2$ /12- $\text{CH}_2$ ), 35.49 (t, 6'- $\text{CH}_2$ ), 38.97 (t, 12- $\text{CH}_2$ /8- $\text{CH}_2$ ), 106.85 (d, C-6), 126.66 (d, C-8'), 128.20 (br s, C-4), 129.50 (br s, C-4'), 130.70 (s, C-7'), 155.52 (s, C-3), 155.65 (s, C-3'), 163.94 (s, C-7), 168.14 (s, C-5), 173.36 (s, C-5'). Anal. Calcd for  $\text{C}_{11}\text{H}_{14}\text{N}_2\text{O}_3$ : C, 59.45; H, 6.35; N, 12.60. Found: C, 59.68; H, 6.56; N, 12.27.

**B** - When **1** (0.142 g, 1 mmol) was treated with 2 equiv. of the above reagent (0.334 g, 0.34 ml) under the same conditions for 5 days, a small amount of compound (**9**) (0.015 g) was separated by filtration; evaporation to dryness of the filtrate gave a red-brown semisolid residue (0.285 g) containing (tlc,  $^1\text{H}$  and  $^{13}\text{C}$  nmr) morpholinium 5-[(1-cyclohexen-1-yl)methylene]-3-methyl-4,5-dihydroisoxazole-4-nitronate (**8**) as the largely predominant product (ca. 90%). An analytical sample, obtained as a pale yellow solid by repeated treatments with ether, gradually wrinkled above  $85^\circ\text{C}$  and melted at  $102\text{-}103^\circ\text{C}$ ;  $\nu_{\max}$ :  $3300\text{-}2300$  and  $2200\text{-}1700\text{ cm}^{-1}$  ( $\text{NH}_2^+$ );  $^1\text{H nmr } \delta$ : 1.05-1.53 (m, 3H, methylene protons), 1.67-1.86 (m, 2H,  $\text{CH}_2$ ), 1.91-2.20 (m, 2H,  $\text{CH}_2$ ), 1.98 (s, 3H, 3- $\text{CH}_3$ ), 2.52-2.68 (m, 1H, methylene proton), 2.80-2.87 (m, 4H, 2  $\text{H}_2\text{N}^+\text{CH}_2$ ), 3.61-3.67 (m, 4H, 2  $\text{OCH}_2$ ), 4.56-4.68 (m, 1H, H-8), 5.25 (t,  $J=2.0\text{ Hz}$ , 1H, H-6), 7.30 (br s, 2 H, exchangeable  $\text{NH}_2^+$ );  $^{13}\text{C nmr } \delta$ : 9.68 (q, 3- $\text{CH}_3$ ), 22.57 (t, 10- $\text{CH}_2$ /11- $\text{CH}_2$ ), 25.91 (t, 11- $\text{CH}_2$ /10- $\text{CH}_2$ ), 27.01 (t, 9- $\text{CH}_2$ /12- $\text{CH}_2$ ), 32.39 (t, 12- $\text{CH}_2$ /9- $\text{CH}_2$ ), 45.37 (t, 2  $\text{H}_2\text{N}^+\text{CH}_2$ ), 66.88 (t, 2  $\text{OCH}_2$ ), 84.34 (d, C-8), 111.39 (s, C-4), 112.52 (d, C-6), 149.11 (s, C-7), 153.06 (s, C-3), 154.22 (s, C-5). Anal. Calcd for  $\text{C}_{15}\text{H}_{23}\text{N}_3\text{O}_4$ : C, 58.24; H, 7.49; N, 13.58. Found: C, 58.45; H, 7.25; N, 13.42.

**C** - Heating of **1** (0.142 g, 1 mmol) with the enamine (0.334 g, 0.34 ml, 2 mmol) in the same solvent (1 ml) under reflux for 24 h yielded 3-methyl-5,6,7,8-tetrahydroisoxazolo[4,5-*b*]quinoline-4-oxide (**9**), that was isolated by filtration (0.040 g); chromatographic workup [toluene-methanol (5:1 v/v) as eluent] of the residue recovered from the filtrate, afforded a further amount of the same compound ( $R_f=0.51$ , 0.040 g, 39% overall yield): white crystals mp  $206\text{-}207^\circ\text{C}$  (from ethyl acetate);  $\nu_{\max}$ : 3070, 3040 (CH), and  $1322\text{ cm}^{-1}$  ( $\text{N}^+\text{-O}^-$ );  $^1\text{H nmr } \delta$ : 1.70-1.98 (m, 4H, 6- $\text{CH}_2$  and 7- $\text{CH}_2$ ), 2.80 (s, 3H, 3- $\text{CH}_3$ ), 2.85-2.98 (m, 4H, 5- $\text{CH}_2$  and 8- $\text{CH}_2$ ), 7.17 (br s, 1H, H-9);  $^{13}\text{C nmr } \delta$ : 11.42 (q, 3- $\text{CH}_3$ ), 21.51 (t, 6- $\text{CH}_2$  and 7- $\text{CH}_2$ ), 24.12 (t, 5- $\text{CH}_2$ /8- $\text{CH}_2$ ), 29.80 (t, 8- $\text{CH}_2$ /5- $\text{CH}_2$ ), 108.24 (d, C-9), 129.10 (s, C-

3a), 137.45 (s, C-8a), 145.31 (s, C-4a), 152.46 (s, C-3), 157.96 (s, C-9a). Anal. Calcd for  $C_{11}H_{12}N_2O_2$ : C, 64.69; H, 5.92; N, 13.72. Found: C, 64.78; H, 5.90; N, 13.71.

#### Deoxygenation of the N-oxides (5) and (9) into 6 and 10.

**A** - A solution of  $PCl_3$  (0.412 g, 0.262 ml, 3 mmol) in chloroform (5 ml) was added dropwise to **5** (0.19 g, 1 mmol) in the same solvent (5 ml); the mixture was stirred at room temperature for 3 h and then refluxed for 1 h. The resulting solution was cooled, treated with ice water (15 ml), and made basic (pH 10) with 20% aqueous NaOH. After removal of the organic phase, the aqueous solution was extracted with  $CHCl_3$  (3x10 ml); evaporation to dryness of the combined extracts left a solid residue which was sublimed at  $50^\circ C$  ( $10^{-2}$  mmHg) to give 3-methylcyclopent[*b*]isoxazolo[5,4-*e*]pyridine (**6**) as a white solid (0.16 g, 92%), mp  $101.5-102^\circ C$  (from ether);  $ir \nu_{max}$ :  $3045\text{ cm}^{-1}$  (CH);  $^1H\text{ nmr } \delta$ : 2.18 (quintet,  $J=7.5$  Hz, 2H, 6- $CH_2$ ), 2.56 (s, 3H, 3- $CH_3$ ), 2.99 (dt,  $J=7.5$  and 1.2 Hz, 2H, 7- $CH_2$ ), 3.05 (t,  $J=7.5$  Hz, 2H, 5- $CH_2$ ), 7.57 (t,  $J=1.2$  Hz, 1H, H-8);  $^{13}C\text{ nmr } \delta$ : 9.11 (q, 3- $CH_3$ ), 24.16 (t, 6- $CH_2$ ), 30.60 (t, 7- $CH_2$ ), 33.00 (t, 5- $CH_2$ ), 113.69 (d, C-8), 138.52 (s, C-3a), 139.82 (s, C-7a), 155.08 (s, C-3), 155.98 (s, C-8a), 164.37 (s, C-4a). Anal. Calcd for  $C_{10}H_{10}N_2O$ : C, 68.95; H, 5.79; N, 16.08. Found: C, 69.21; H, 5.90; N, 15.87.

**B** - Operating as above, compound (**9**) (0.204 g, 1 mmol) afforded 3-methyl-5,6,7,8-tetrahydroisoxazolo[4,5-*b*]quinoline (**10**) as a white solid (0.162 g, 86 %), mp  $88-88.5^\circ C$  after sublimation at  $50^\circ C$  ( $10^{-2}$  mmHg);  $ir \nu_{max}$ :  $3040\text{ cm}^{-1}$  (CH);  $^1H\text{ nmr } \delta$ : 2.68-2.88 (m, 4H, 6- $CH_2$  and 7- $CH_2$ ), 2.62 (s, 3H, 3- $CH_3$ ), 2.85-2.96 (m, 2H, 5- $CH_2$ /8- $CH_2$ ), 3.10-3.19 (m, 2H, 8- $CH_2$ /5- $CH_2$ ), 7.77 (br s, 1H, H-9);  $^{13}C\text{ nmr } \delta$ : 9.83 (q, 3- $CH_3$ ), 21.38 (t, 6- $CH_2$ /7- $CH_2$ ), 21.49 (t, 7- $CH_2$ /6- $CH_2$ ), 29.15 (t, 8- $CH_2$ ), 30.08 (t, 5- $CH_2$ ), 120.95 (d, C-9), 134.00 (s, C-3a), 135.63 (s, C-8a), 153.36 (s, C-3), 154.60 (s, C-4a), 155.51 (s, C-9a). Anal. Calcd for  $C_{11}H_{12}N_2O$ : C, 70.19; H, 6.43; N, 14.88. Found: C, 70.09; H, 6.54; N, 14.64.

#### Reactions of Compound (1) with 1-Diethylaminopropyne. Synthesis of the Isoxazole Derivatives (12) and (13).

**A** - A solution of **1** (0.142 g, 1 mmol) and ynamine<sup>7</sup> (0.111 g, 0.137 ml, 1 mmol) in methanol (5 ml) was stirred at room temperature for 24 h; removal of the solvent left a residue which was resolved into two components by flash chromatography with petroleum ether-ethyl acetate (3:1 v/v) as eluent. After the unreacted starting material was isolated from the first band ( $R_f=0.64$ , 0.060 g), the second one afforded 5-[(*E*)-2-diethylamino-1-buten-1-yl]-3-methyl-4-nitroisoxazole (**12**) as a yellow solid ( $R_f=0.30$ ; 0.14 g, 96% yield based on the recovered **1**), mp  $64-65^\circ C$  (from pentane);  $ir \nu_{max}$ :  $1571\text{ cm}^{-1}$  ( $NO_2$ );  $^1H\text{ nmr } \delta$ : 1.21 (t,  $J=7.5$  Hz, 3H, 9- $CH_3$ ), 1.26 (t,  $J=7.2$  Hz, 6H, 2  $NCH_2CH_3$ ), 2.46 (s, 3H, 3- $CH_3$ ), 2.82 (br q,  $J=7.5$  Hz, 2H, 8- $CH_2$ ), 3.43 (q,  $J=7.2$  Hz, 4H, 2  $NCH_2CH_3$ ), 6.23 (br s, 1H, H-6);  $^{13}C\text{ nmr } \delta$ : 12.40 (q, 9- $CH_3$ ), 12.70 (br q, two slowly interchangeable  $NCH_2CH_3$ ), 12.95 (q, 9- $CH_3$ ), 23.84 (t, 8- $CH_2$ ), 45.15 (br t, two slowly interchangeable  $NCH_2CH_3$ ), 81.75 (d, C-6), 121.86 (br s, C-4), 155.47 (s, C-3), 166.13 (s, C-7), 168.65 (s, C-5). Anal. Calcd for  $C_{12}H_{19}N_3O_3$ : C, 56.90; H, 7.56; N, 16.59. Found: C, 57.21; H, 7.75; N, 16.30.

**B** - The reaction was carried out in dry acetonitrile (5 ml) under the same conditions for 48 h; the raw

product was resolved into three components by chromatographic workup with toluene-ethyl acetate (5:1 v/v) as eluent. Whereas the fastest running fractions gave the unreacted nitro derivative (0.070 g), the second band afforded compound (**12**) ( $R_f=0.58$ , 0.015 g, 12% yield based on the recovered **1**) identical (ir,  $^1\text{H}$  and  $^{13}\text{C}$  nmr) with the material obtained as above; finally, the following band gave 3-[(Z)-1-acethoxyimino-1-ethyl]-5-diethylamino-4-methylisoxazole (**13**) ( $R_f=0.42$ , 0.030 g, 23% yield based on the recovered **1**) that was crystallized from pentane as colourless needles, mp 67-68°C; ir  $\nu_{\text{max}}$  1780  $\text{cm}^{-1}$  (CO);  $^1\text{H}$  nmr  $\delta$ : 1.19 (t,  $J=7.1$  Hz, 6H, 2  $\text{NCH}_2\text{CH}_3$ ), 1.83 (s, 3H, 4- $\text{CH}_3$ ), 2.08 (s, 3H,  $\text{CH}_3\text{CO}$ ), 2.33 (s, 3H,  $\text{CH}_3\text{C}=\text{N}$ ), 3.38 (q,  $J=7.1$  Hz, 4H, 2  $\text{NCH}_2\text{CH}_3$ );  $^{13}\text{C}$  nmr  $\delta$ : 8.27 (q, 4- $\text{CH}_3$ ), 13.78 (q, 2  $\text{NCH}_2\text{CH}_3$ ), 19.25 (q,  $\text{CH}_3\text{CO}$ ), 21.01 (q,  $\text{CH}_3\text{C}=\text{N}$ ), 43.61 (t, 2  $\text{NCH}_2\text{CH}_3$ ), 85.63 (s, C-4), 156.13 (s,  $\text{CH}_3\text{C}=\text{N}$ ), 160.07 (s, C-3), 167.15 (s, C-5), 168.20 (s, CO). Anal. Calcd for  $\text{C}_{12}\text{H}_{19}\text{N}_3\text{O}_3$ : C, 56.90; H, 7.56; N, 16.59. Found: C, 57.01; H, 7.76; N, 16.40.

#### X-ray Crystal Structure Determination for **13**.

A single crystal of the product  $\text{C}_{12}\text{H}_{19}\text{N}_3\text{O}_3$ , grown from pentane, was mounted on an Enraf-Nonius CAD4 diffractometer. No loss of intensity of three standard reflections was observed. Computer programs were those of SHELX76.<sup>8</sup> An absorption correction was applied once the structure was solved.<sup>9</sup> Crystal data: monoclinic; space group  $P2_1/n$ ;  $M = 253.3$ ;  $a = 6.749(6)$  Å,  $b = 21.574(5)$  Å,  $c = 9.799(3)$  Å,  $\beta = 105.77(5)^\circ$ ; cell vol = 1373(1) Å<sup>3</sup>;  $Z = 4$ ;  $d = 1.22$  g  $\text{cm}^{-3}$ ; abs coeff  $\mu = 6.99$   $\text{cm}^{-1}$ ; Cu-K $\alpha$  radiation ( $\lambda = 1.5418$  Å), graphite monochromator. Intensity data were collected in the range  $5 \leq 2\theta \leq 120^\circ$  by using the  $\theta/2\theta$  scan. A total of 2230 reflections were collected of which 1795 having  $I \geq 3\sigma(I)$  were used in the structure solution and refinement. The structure was solved by using direct methods and successive Fourier syntheses; then it was refined with the full-matrix least-squares technique. Anisotropic temperature factors were assigned to all the atoms except the hydrogen ones which were refined isotropically. The final difference map showed no significant features. A weighting scheme of  $w = 1/\sigma^2(F)$  was used. Final agreement factors were  $R = 0.063$  and  $R_w = 0.063$  (239 parameters).

Crystallographic data were deposited at the Cambridge Crystallographic Data Centre, University Chemical Laboratory, Lensfield Road, Cambridge CB2 1EW, England, and are available from there.

#### ACKNOWLEDGMENT

We wish to thank Mrs. Brunella Innocenti and Dr. Cristina Faggi for the analytical data.

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Received, 17th June, 1991