Syntheses and Reactivities of 3-Methylisoxazolo[4,5-*b*]pyridines

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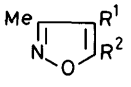
A synthetic pathway to 3-methylisoxazolo[4,5-*b*]pyridine and some of its derivatives is described. The determination of methoxydechlorination rates for the 5,7-dichloro- (12) and 5-chloro-derivative (14) showed a noteworthy activation in respect of 2,4-dichloropyridine (22) and 2-chloropyridine (23).

RECENTLY we have undertaken a study of the synthesis and chemical behaviour of 1,2-benzisoxazole analogues with a nitrogen atom in the benzene ring. The syntheses of 3-methylisoxazolo[4,5-*c*]-[1a] and 3-methylisoxazolo-[5,4-*b*]-pyridine [1b] have been reported. The photochemical behaviour of some derivatives of the former compound,[2] and the kinetics of the reaction of chloro-3-methylisoxazolo[4,5-*c*]- and chloro-3-methylisoxazolo-[5,4-*b*]-pyridines with methoxide ion were investigated.[3] Our results show a remarkable variation of the reactivity, dependent on the position of fusion of the isoxazole and pyridine rings. Surprisingly, the methoxydehalogenation of 6-chloro-3-methylisoxazolo[5,4-*b*]pyridine (21) showed a smaller activation energy, by *ca.* 3 kcal mol^{-1}, than did 6-chloro-3-methylisoxazolo[4,5-*c*]pyridine (20).

In order to gain more insight into the influence of the different fusions of pyridine and isoxazole rings on the reactivity of the chlorine atoms, we prepared 3-methylisoxazolo[4,5-*b*]pyridine (16) and some of its derivatives. Only one derivative of this system has been previously reported in the literature.[4]

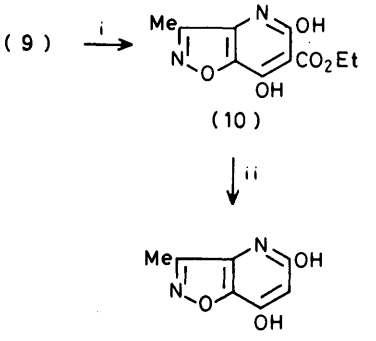
RESULTS AND DISCUSSION

Substitution of the chlorine atom in the 5-chloroisoxazole (1) proceeded efficiently to give the nitrile (2) which, on subsequent treatment with ammonia, afforded the diamide (3). Alkaline hydrolysis of compound (3) gave 4-carbamoyl-3-methylisoxazole-5-carboxylic acid, (4), whose structure was established by comparison with 5-carbamoyl-3-methylisoxazole-4-carboxylic acid (5), prepared unambiguously from the nitrile (2) and aqueous alkali. Compound (5) gave the imide (6) on dehydration with thionyl chloride.



(1) R^1 = CO_2Et, R^2 = Cl
(2) R^1 = CO_2Et, R^2 = CN
(3) R^1 = R^2 = $CONH_2$
(4) R^1 = $CONH_2$, R^2 = CO_2H
(5) R^1 = CO_2H, R^2 = $CONH_2$
(6) R^1 R^2 = CONHCO
(7) R^1 = NH_2, R^2 = CO_2H
(8) R^1 = NH_2, R^2 = CO_2Me
(9) R^1 = $NHCOCH_2CO_2Et$, R^2 = CO_2Me

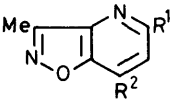
Hofmann degradation of the amido-acid (4) afforded 4-amino-3-methylisoxazole-5-carboxylic acid (7), which was esterified to the amino-ester (8) with methanolic hydrogen chloride. Condensation of compound (8) with ethyl (chloroformyl)acetate gave the amide (9) which cyclized with sodium ethoxide to afford the ester (10).



Reagents: i, NaOEt; ii, OH^-

5,7-Dihydroxy-3-methylisoxazolo[4,5-*b*]pyridine (11), obtained from the ester (10) by alkaline hydrolysis and decarboxylation, can exist in numerous tautomeric forms: in the solid state an hydroxyoxo-form (ν_{OH} 3 300—2 300, ν_{CO} 1 660 cm^{-1}) is present, and in $(CD_3)_2SO$ solution an equilibrium mixture of tautomers can be postulated on the basis of D_2O exchange of the proton from the 6-OH group.

Chlorination of the diol (11) with phenylphosphonic



(12) R^1 = R^2 = Cl
(13) R^1 = Cl, R^2 = $NHNH_2$
(14) R^1 = Cl, R^2 = H
(15) R^1 = $NHNH_2$, R^2 = H
(16) R^1 = R^2 = H
(17) R^1 = Cl, R^2 = OMe
(18) R^1 = OMe, R^2 = H

dichloride easily gave 5,7-dichloro-3-methylisoxazolo[4,5-*b*]pyridine (12), which underwent regiospecific nucleophilic substitution at the 7-position. Thus, the dichloride (12) reacted with hydrazine hydrate or sodium methoxide to afford the hydrazine (13) or the ether (17), respectively. The structure of the product as (13) is supported by its oxidative decomposition in alkaline medium to the 5-chloro-derivative, (14), whose coupling constant ($J_{6,7}$ 9.0 Hz) is in agreement with typical $J_{3,4}$ values for pyridines.[5] The structure of compound (17) followed from the formation

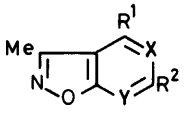
of compound (13) by substitution of the methoxy-group with hydrazine. The chlorine atom of compound (14) can be substituted, but this needs more severe conditions than those required in the case of the dichloro-derivative (12). Concentrated sodium methoxide attack on compound (14) gave the ether (18), and anhydrous hydrazine led to the 5-hydrazino-derivative (15) which, by oxidation, as previously reported for compounds (13), gave 3-methylisoxazolo[4,5-*b*]pyridine (16). The chemical shifts and coupling constants of compound (16) are similar to those of the monochloroderivative (14).

Rate constants (k_2/l mol^{-1} sec^{-1} ±2%) for the methoxydechlorination of some chloroisoxazolopyridines and chloropyridines

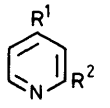
Compound	$10^4 k_2$	T/°C
(12)	12.6	20
(19)	266.1 [a]	20
(22)	0.0317 [a]	20
(14)	0.88	80
(20)	1.99 [b]	80
(21)	291.0 [b]	80
(23)	0.0152 [b]	80

[a] The value refers to attack at the 4-position and was calculated from data reported either in ref. 3 or by M. Forchiassin, G. Illuminati and G. Sleiter, *J. Heterocycl. Chem.*, **1969**, **6**, 899. [b] The value was calculated from data reported either in ref. 3 or by M. Forchiassin *et al.*, *loc. cit.*

Methoxydechlorination of compounds (12) and (14) is second-order overall. From the value of the rate constant for the dichloro-derivative (12) (Table) it is evident that there is a noteworthy activation compared with 4-methoxydechlorination of 2,4-dichloropyridine (22) [$k_{(12)}/k_{(22)}$ = 397.5]. However, a higher reactivity, due to the different type of fusion of the isoxazole and pyridine rings, results in the case of the isoxazolo[5,4-*b*]pyridine (19) [$k_{(19)}/k_{(12)}$ = 21.1]. Similar effects on the reactivity are found when comparing the reaction rate of the 5-chloroisoxazolo[4,5-*b*]-pyridine (14) with that of 2-chloropyridine (23) [$k_{(14)}/k_{(23)}$ = 57.9] and with that of the 6-chloroisoxazolo[4,5-*c*]- or 6-chloroisoxazolo[5,4-*b*]pyridine (20) or (21) [$k_{(20)}/k_{(14)}$ = 2.3, $k_{(21)}/k_{(14)}$ = 330].

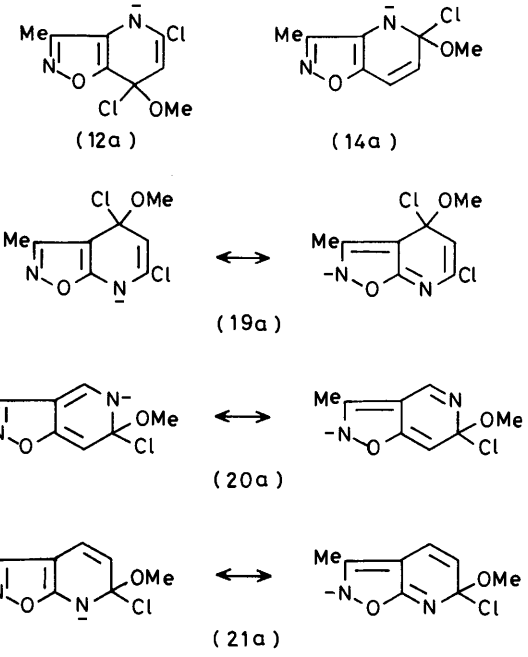


(19) X = CH, Y = N, $R^1 = R^2$ = Cl
(20) X = N, Y = CH, R^1 = H, R^2 = Cl
(21) X = CH, Y = N, R^1 = H, R^2 = Cl



(22) $R^1 = R^2$ = Cl
(23) R^1 = H, R^2 = Cl

Negative-charge delocalization in intermediate σ-complexes can account for the rate differences in the methoxydechlorination of the aforementioned compounds. Thus, in the intermediates (19a)—(21a), the negative charge can be distributed both at the pyridine and at the isoxazole nitrogen atoms, whereas in the case of intermediates (12a) and (14a) the negative charge is located only at the pyridine atom. The higher reactivity [3] of compound (19) compared with compounds (20) and (21) follows from the increased stabilization of the negative charge over seven atoms instead of five; however, compound (21) is more activated than its isomer (20) since, in the *ortho*-quinonoid resonating structure of the σ-complex (21a), aromaticity of the isoxazole nucleus is preserved.



EXPERIMENTAL

I.r. spectra were recorded on a Perkin-Elmer 457 spectrometer for KBr discs. ^{1}H N.m.r. spectra were recorded with a Perkin-Elmer R600 instrument; chemical shifts (J in Hz) are reported in p.p.m. downfield from internal tetramethylsilane. U.v. spectra were measured for solutions in methanol with a Cary 14 spectrometer. Silica gel plates (Merck F_{254}) were used for analytical t.l.c. Extracts were dried over sodium sulphate and were evaporated under reduced pressure. Light petroleum refers to that fraction boiling in the range 40—70 °C.

Ethyl 5-Cyano-3-methylisoxazole-4-carboxylate (2).—Ethyl 5-chloro-3-methylisoxazole-4-carboxylate (1) [6] (51.9 g) was added dropwise to a stirred suspension of sodium cyanide (17.5 g) in *NN*-dimethylformamide (130 ml). The mixture was heated at 100 °C for 1 h and was then kept overnight at room temperature. Dilution with water (1 300 ml) and extraction with diethyl ether afforded, after work-up, a residue which, on distillation at 46—48 °C and 0.1 mmHg, gave (on cooling to 0 °C) the *nitrile* (2) as crystals (42.5 g, 86%), m.p. 26 °C (Found: C, 53.2; H, 4.4; N, 15.5. $C_8H_8N_2O_3$ requires C, 53.3; H, 4.5; N, 15.55%); $\nu_{max.}$ 2 245 (CN) and 1 735 cm^{-1} (CO); $\lambda_{max.}$ 234 nm (log ε 3.90); δ($CDCl_3$) 1.45 (3 H, t, J 7.2, CH_2CH_3), 2.56 (3 H, s, Me), and 4.45 (2 H, q, J 7.2, CH_2CH_3).

3-Methylisoxazole-4,5-dicarboxamide (3).—A mixture of the nitrile (2) (42 g) and 32% aqueous ammonium hydroxide was stirred at room temperature for 24 h. The solid

product was filtered off and crystallized from water to yield the *diamide* (3) (23.6 g). A second crop (total 75%) was recovered by concentration of the mother-liquors. An analytical sample, obtained by crystallization from water (charcoal), had m.p. 235—236 °C (Found: C, 42.8; H, 4.2; N, 25.0. $C_6H_7N_3O_3$ requires C, 42.6; H, 4.2; N, 24.8%); $\nu_{max.}$ 3 360, 3 290, and 3 180 (2 × NH_2), 1 710 (CO), and 1 695 cm^{-1} (CO); $\lambda_{max.}$ 230 nm (log ε 3.98); δ[$(CD_3)_2SO$] 2.47 (3 H, s, Me) and 7.75br, 8.49br, 8.80br, and 9.14br (4 H, 4 × D_2O-exchangeable s, 2 × NH_2).

4-Carbamoyl-3-methylisoxazole-5-carboxylic Acid (4).—The diamide (3) (5.6 g) and 10% aqueous potassium hydroxide (30 ml) were stirred at 50 °C for 35 min. Acidification with concentrated hydrochloric acid (pH 1) afforded, by refrigeration at 0 °C overnight, the *acid* (4) (4.3 g). A second crop was obtained from the mother-liquors (total 95%). An analytical sample, obtained by crystallization from water, had m.p. 183—184 °C (decomp.) (Found: C, 42.15; H, 3.5; N, 16.3. $C_6H_6N_2O_4$ requires C, 42.4; H, 3.55; N, 16.5%); $\nu_{max.}$ 3 340 and 3 190 (NH_2), 3 050—2 200br (OH), 1 720 (CO_2H), and 1 675 cm^{-1} ($CONH_2$); $\lambda_{max.}$ 223 (log ε 3.92) and 228 nm (3.92); δ[$(CD_3)_2SO$] 2.38 (3 H, s, Me), 7.64br (1 H, D_2O-exchangeable s, OH), and 8.92br (2 H, D_2O-exchangeable s, NH_2).

5-Carbamoyl-3-methylisoxazole-4-carboxylic Acid (5).—A suspension of the nitrile (2) (2 g) in 1M aqueous sodium hydroxide (10 ml) was stirred at room temperature for 12 h. Acidification with concentrated hydrochloric acid (pH 1) gave the *acid* (5) (1.75 g, 86%), m.p. 263—264 °C (sublimation at 200 °C and 0.03 mmHg) (Found: C, 42.6; H, 3.6; N, 16.7. $C_6H_6N_2O_4$ requires C, 42.4; H, 3.55; N, 16.5%); $\nu_{max.}$ 3 290 and 3 130 (NH_2), 2 800—2 000 (OH), 1 710 (CO_2H), and 1 660 cm^{-1} ($CONH_2$); $\lambda_{max.}$ 226 nm (log ε 4.04); δ[$(CD_3)_2SO$] 2.45 (3 H, s, Me), 8.69br and 9.08br (2 H, 2 × D_2O-exchangeable s, NH_2), and 9.50br (1 H, D_2O-exchangeable s, OH).

3-Methylisoxazole-4,5-dicarboximide (6).—A mixture of the acid (5) (1 g) and thionyl chloride (10 ml) was refluxed until the solid had dissolved (2 h). Evaporation of the solution gave a residue which was treated with diethyl ether. The extract was evaporated to dryness and the residue was sublimed at 75 °C and 0.02 mmHg to give the *imide* (6) (0.58 g, 65%), m.p. 150—152 °C (Found: C, 47.5; H, 2.8; N, 18.2. $C_6H_4N_2O_3$ requires C, 47.4; H, 2.65; N, 18.4%); $\nu_{max.}$ 3 270 (NH) and 1 790 and 1 740 cm^{-1} (CO); $\lambda_{max.}$ 224 nm (log ε 4.03); δ[$(CD_3)_2SO$] 2.41 (3 H, s, Me), and 11.25br (1 H, D_2O-exchangeable s, NH).

Methyl 4-Amino-3-methylisoxazole-5-carboxylate (8).—To the acid (4) (2.4 g) a solution of potassium hypochlorite [prepared from chlorine (1.4 g) and potassium hydroxide (4.0 g)] in water (20 ml) was added dropwise at room temperature. The mixture was treated with 20% aqueous potassium hydroxide (12 ml), then heated at 60 °C (2 h), cooled in ice, and acidified (pH 1) with 1M hydrochloric acid. The *amino-acid* (7) (0.9 g) crystallized out overnight in a refrigerator. A second crop of compound (7) (total 60%) was obtained from the mother-liquors. An analytical sample, obtained by crystallization from water (charcoal), had m.p. 159—160 °C (decomp.) (Found: C, 42.0; H, 4.2; N, 19.9. $C_5H_6N_2O_3$ requires C, 42.3; H, 4.3; N, 19.7%); $\nu_{max.}$ 3 460 and 3 340 (NH_2), 3 200—2 120 (OH), and 1 670 cm^{-1} (CO); $\lambda_{max.}$ 293 nm (log ε 3.86).

A solution of the amino-acid (7) (3.25 g) in methanol which had been saturated with gaseous hydrogen chloride under refrigeration (ice–salt bath) (75 ml) was kept at room temperature for 3 d. The mixture was evaporated to afford a solid residue which was washed with diethyl ether and dissolved in water to give, after neutralization with saturated aqueous sodium carbonate, the *ester* (8) (2.7 g, 75%). An analytical sample, obtained by recrystallization from diethyl ether, had m.p. 110—111 °C (Found: C, 46.0; H, 5.05; N, 17.8. $C_6H_8N_2O_3$ requires C, 46.2; H, 5.2; N, 17.9%); $\nu_{max.}$ 3 440 and 3 350 (NH_2) and 1 690 cm^{-1} (CO); $\lambda_{max.}$ 222 (log ε 3.67) and 298 nm (3.94); δ($CDCl_3$) 2.27 (3 H, s, Me), 3.94 (3 H, s, OMe), and 4.27br (2 H, D_2O-exchangeable s, NH_2).

Ethyl N-(5-Methoxycarbonyl-3-methylisoxazol-4-yl)malonamate (9).—To a solution of compound (8) (6.7 g) in methylene dichloride (35 ml) were added ethyl (chloroformyl)-acetate (9.7 g) and triethylamine (8 ml). The mixture was refluxed for 2 h and then evaporated; the residue was then extracted with hot benzene to yield the *ester* (9) (10.6 g, 91%). A sample was crystallized from light petroleum, m.p. 123—125 °C (Found: C, 48.7; H, 5.3; N, 10.5. $C_{11}H_{14}N_2O_6$ requires C, 48.9; H, 5.2; N, 10.35%); $\nu_{max.}$ 3 270 (NH), 1 735 (CO_2Et), 1 725 (CO_2Me), and 1 660 cm^{-1} (CONH); δ($CDCl_3$) 1.34 (3 H, t, *J* 8.0, CH_2CH_3), 2.40 (3 H, s, Me), 3.52 (2 H, s, $COCH_2$), 3.99 (3 H, s, OMe), 4.30 (2 H, q, *J* 8.0, CH_2CH_3), and 9.53br (1 H, D_2O-exchangeable s, NH).

Ethyl 5,7-Dihydroxy-3-methylisoxazolo[4,5-b]*pyridine-6-carboxylate* (10).—A solution of sodium ethoxide, prepared from sodium (1.1 g) in anhydrous ethanol (70 ml), and the ester (9) (10.6 g) was refluxed for 90 min. The precipitate which formed was filtered off and dissolved in the minimum amount of water. The solution was acidified with concentrated hydrochloric acid to afford *compound* (10) (8.4 g, 90%), m.p. 229—231 °C (Found: C, 50.5; H, 4.1; N, 11.7. $C_{10}H_{10}N_2O_5$ requires C, 50.4; H, 4.2; N, 11.8%); $\nu_{max.}$ 3 200—2 300 (NH and/or OH) and 1 650 cm^{-1} (CO); $\lambda_{max.}$ 233 (log ε 4.21), 270 (3.82), and 330 nm (3.68); δ[$(CD_3)_2SO$] 1.28 (3 H, t, *J* 7.2, CH_2CH_3), 2.40 (3 H, s, Me), 4.25 (2 H, q, *J* 7.2, CH_2CH_3), and 4.90—7.00br (D_2O-exchangeable s, NH and/or OH).

5,7-Dihydroxy-3-methylisoxazolo[4,5-b]*pyridine* (11).—A solution of compound (10) (8.4 g) in 4M aqueous sodium hydroxide (84 ml) was heated at 100 °C for 2 h. After being cooled, the solution was acidified with concentrated hydrochloric acid to give *compound* (11) (5.4 g, 92%), m.p. 250 °C (decomp.) (Found: C, 50.8; H, 3.5; N, 16.8. $C_7H_6N_2O_3$ requires C, 50.6; H, 3.6; N, 16.9%); $\nu_{max.}$ 3 300—2 300 (NH and OH) and 1 660 cm^{-1} (CO); $\lambda_{max.}$ 222 (log ε 4.04), 2.52 (3.66), and 306 nm (3.86); δ[$(CD_3)_2SO$] 2.40 (3 H, s, Me), 5.82 (1 H, D_2O-exchangeable s, 6-H), and 8.00—10.30br (D_2O-exchangeable s, 2 OH and/or NH).

5,7-Dichloro-3-methylisoxazolo[4,5-b]*pyridine* (12).—A mixture of compound (11) (5.4 g) and phenylphosphonic dichloride (9.3 ml) was heated at 160 °C for 90 min, and was then cooled and poured into ice–water (180 ml). After decomposition of the excess of phenylphosphonic dichloride, the solid product was filtered off, washed with water, and treated with 0.5M sodium hydroxide (100 ml). The insoluble *dichloro-derivative* (12) was washed with water, dried, and sublimed at 100 °C and 0.02 mmHg (3.5 g, 52%), m.p. 135 °C (Found: C, 41.5; H, 2.1; Cl, 34.9; N, 13.8. $C_7H_4Cl_2N_2O$ requires C, 41.4; H, 2.0; Cl, 35.0; N, 13.8%); $\nu_{max.}$ 3 080 cm^{-1} (CH); $\lambda_{max.}$ 207 (log ε 4.29), 242 (3.81), 294 (3.80), and 307sh nm (3.59); δ($CDCl_3$) 2.66 (3 H, s, Me) and 7.53 (1 H, s, 6-H).

5-Chloro-7-hydrazino-3-methylisoxazolo[4,5-b]*pyridine* (13).—To a stirred solution of compound (12) (1 g) in dioxan (8 ml), was added hydrazine hydrate (1 ml). The resultant mixture was heated at 100 °C for 1 h. The solvent was removed under reduced pressure and the residue was washed with water to give the *hydrazine* (13) (0.9 g, 92%). A sample crystallized from ethanol had m.p. 186—188 °C (Found: C, 42.2; H, 3.6; Cl, 17.7; N, 28.4. $C_7H_7ClN_4O$ requires C, 42.3; H, 3.55; Cl, 17.85; N, 28.2%); $\nu_{max.}$ 3 340 and 3 300—3 120br (NH_2 and NH) and 3 080 cm^{-1} (CH); δ[$(CD_3)_2SO$] 2.51 (3 H, s, Me), 4.66 (2 H, D_2O-exchangeable s, NH_2), 6.94 (1 H, s, 6-H), and 8.91 (1 H, D_2O-exchangeable s, NH).

5-Hydrazino-3-methylisoxazolo[4,5-b]*pyridine* (15).—The chloro-derivative (14) (*vide infra*) (0.38 g) and anhydrous hydrazine (1.5 ml) were heated at 90—95 °C for 2 h. The resulting solution was kept over concentrated sulphuric acid overnight and the residue was crystallized from light petroleum to give the *hydrazine* (15) (0.260 g, 70%), m.p. 111—112 °C (Found: C, 51.0; H, 4.95; N, 34.0. $C_7H_8N_4O$ requires C, 51.2; H, 4.9; N, 34.1%); δ($CDCl_3$) 2.57 (3 H, s, Me), 3.99br (2 H, D_2O-exchangeable s, NH_2), 5.98br (1 H, D_2O-exchangeable s, NH), 6.87 (1 H, d, *J* 9.0, 6-H), and 7.48 (1 H, d, *J* 9.0, 7-H).

Oxidative Decomposition of the Hydrazines (13) *and* (15).—Benzene (40—80 ml) was added to a mixture of the hydrazines (13) and (15) (10 mmol) in 2M aqueous sodium hydroxide (40 ml). Air was bubbled gently into the stirred mixture. After the disappearance (t.l.c.) of the starting material, evaporation of the organic layer afforded a solid which was separated into two components by sublimation. *5-Chloro-3-methylisoxazolo*[4,5-b]*pyridine* (14), yield 82%, m.p. 97—98 °C (sublimation at 70 °C and 0.06 mmHg) (Found: C, 50.1; H, 3.0; Cl, 20.8; N, 16.7. $C_7H_5ClN_2O$ requires C, 49.9; H, 3.0; Cl, 21.0; N, 16.6%); $\nu_{max.}$ 3 070 cm^{-1} (CH); $\lambda_{max.}$ 204 (log ε 4.04), 236 (3.54), 287sh (3.81), 292 (3.85), 297sh (3.80), and 303sh nm (3.63); δ($CDCl_3$) 2.66 (3 H, s, Me), 7.47 (1 H, d, *J* 9.0, 6-H), and 7.86 (1 H, d, *J* 9.0, 7-H).

3-Methylisoxazolo[4,5-b]*pyridine* (16), yield 50%, m.p. 43—45 °C (sublimation at room temperature and 0.06 mmHg) (Found: C, 62.4; H, 4.65; N, 20.6. $C_7H_6N_2O$ requires C, 62.7; H, 4.5; N, 20.9%); $\nu_{max.}$ 3 070 cm^{-1} (CH); $\lambda_{max.}$ 203 (log ε 3.81), 234 (3.67), 278sh (3.77), 282 (3.81), 287sh (3.75), and 292 nm (3.62); δ($CDCl_3$) 2.70 (3 H, s, Me), 7.46 (1 H, dd, $J_{6,7}$ 8.4, $J_{5,6}$ 4.3, 6-H), 7.89 (1 H, dd $J_{5,7}$ 1.4, $J_{6,7}$ 8.4, 7-H), and 8.69 (1 H, dd, $J_{5,6}$ 4.3, $J_{5,7}$ 1.4, 5-H).

Kinetic Measurements.—Solvent and methoxide reagent were prepared as previously described.[3] All experiments were performed using the sealed-tube technique. The concentrations were 0.024 7M for the dichloro-derivative (12) and 0.045M for sodium methoxide; 0.022 2M for the chloro-derivative (14) and 0.142M for sodium methoxide. The progress of the reaction was followed by titration of liberated chloride ion by the Volhard method, and the rate constants were corrected for the thermal expansion of methanol. Samples of the reaction mixture were left for a sufficient time to ensure completion of the reaction. The solution was then evaporated and the residue was washed with water, then dried and purified by sublimation. Thus prepared were *5-chloro-7-methoxy-3-methylisoxazolo*[4,5-b]*pyridine* (17), m.p. 119—121 °C (Found: C, 48.6; H, 3.65; Cl, 17.7; N, 13.9. $C_8H_7ClN_2O_2$ requires C, 48.4; H, 3.55; Cl, 17.85; N, 14.1%); $\nu_{max.}$ 3 080 cm^{-1} (CH); δ($CDCl_3$) 2.62 (3 H, s, Me), 4.14 (3 H, s, OMe), and 6.90 (1 H, s, 6-H), and *5-Methoxy-3-methylisoxazolo*[4,5-b]*pyridine* (18), m.p. 80—82 °C (Found: C, 58.25; H, 4.8; N, 17.0. $C_8H_8N_2O_2$ requires C, 58.5; H, 4.9; N, 17.05%); $\nu_{max.}$ 3 080 cm^{-1} (CH); δ($CDCl_3$) 2.59 (3 H, s, Me), 4.01 (3 H, s, OMe), 6.89 (1 H, d, *J* 9.0, 6-H), and 7.74 (1 H, d, *J* 9.0, 7-H).

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