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Received March 8, 1990

The Schmidt reaction of 6,7-dihydro-3-phenyl-1,2-benzisoxazol-4(5*H*)-one (**1**) is described. In addition to the expected isomeric lactams, 3-phenyl-5,6,7,8-tetrahydro-4*H*-isoxazolo[4,5-*c*]azepin-4-one (**3**) and 7,8-dihydro-3-phenyl-4*H*-isoxazolo[4,5-*b*]azepin-5(6*H*)-one (**4**), 4-amino-3-phenyl 1,2-benzisoxazole (**5**) was isolated, along with 4,5-dihydro-3*H*-isoxazolo[5,4,3-*kl*]acridine (**6**). Possible mechanisms for the formation of these products are discussed and some chemistry of the little-known ring system represented by **6** is also described.

J. Heterocyclic Chem., **27**, 1617 (1990).

As part of our continuing interest in the biological activity of novel fused heterocyclic ring systems containing the isoxazole group [1], we were interested in synthesizing the 5,6,7,8-tetrahydro-4*H*-isoxazolo[4,5-*c*]azepin-4-one system (exemplified by **3**, Scheme 1). Our efforts in this direction have resulted not only in the synthesis of this heterocycle, but also in the synthesis of a heretofore unknown 4,5-dihydro-3*H*-isoxazolo[5,4,3-*kl*]acridine. This paper describes the preparation of this little-known heterocycle as well as some of its chemical and spectral properties.

Lactams of the type represented by **3** (containing an *n* membered ring) are known to be available from the corresponding cyclic (*n*-1 membered) ketones by reaction with hydrazoic acid under acidic conditions (the Schmidt reaction [2]). Since an appropriate starting material, 6,7-dihydro-3-phenyl-1,2-benzisoxazol-4(5*H*)-one (**1**), was readily available [3], the Schmidt reaction was carried out on **1**, using sodium azide in concentrated sulfuric acid. It was recognized that the anticipated iminodiazonium ion intermediate, **2** (Scheme 1), could rearrange along either of two pathways--alkyl migration (path a) would lead to the desired heterocycle, while aryl migration (path b) would lead to the isomeric isoxazolo[4,5-*b*]azepine. The migratory aptitudes of the sigma bonds adjacent to the ketone in the Schmidt reaction are known to be very sensitive to inductive effects caused by neighboring groups [4]. Thus, while it was known that aryl migration is usually favored in cyclic alkyl aryl ketones [2a], it was felt that the electron deficient nature of the isoxazole group would favor alkyl migration and formation of the desired isoxazolo[4,5-*c*]azepine. We were also encouraged by a previous report with the 6,7-dihydroindazol-4(5*H*)-one system [5], in which alkyl migration was shown to be favored, leading to analogous lactams.

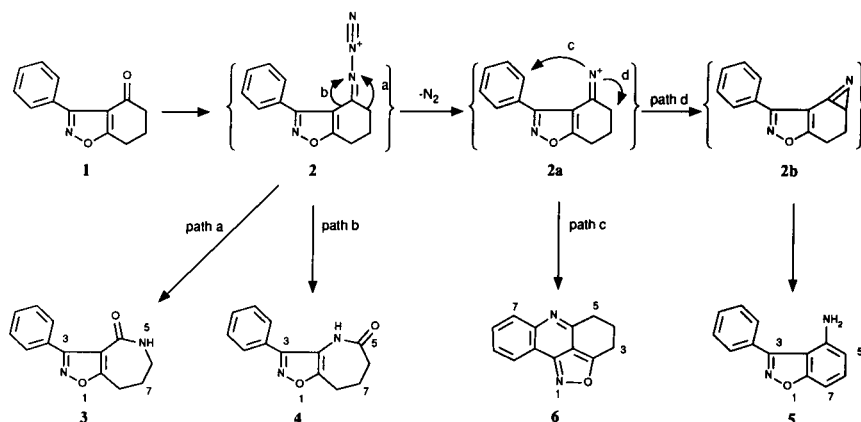
When **1** was subjected to Schmidt conditions, both lactams were formed (Scheme 1), but, as predicted, lactam **3**, the product of alkyl migration, predominated over lactam **4**, the product of aryl migration (31% yield and 3.8% yield, respectively). As indicated in Scheme 1, two other

products were isolated from the Schmidt reaction of **1**, namely 4-amino-3-phenyl-1,2-benzisoxazole (**5**) and 4,5-dihydro-3*H*-isoxazolo[5,4,3-*kl*]acridine (**6**). Compound **5** probably arises from a Semmler-Wolff aromatization [5,6], in which the intermediate nitrenium ion **2a** gives rise to an azirine **2b** through insertion into a coplanar α -C-H bond (Scheme 1). Protonation of the azirine nitrogen with subsequent ring opening to the imine and proton transfer yields the fully aromatic **5**.

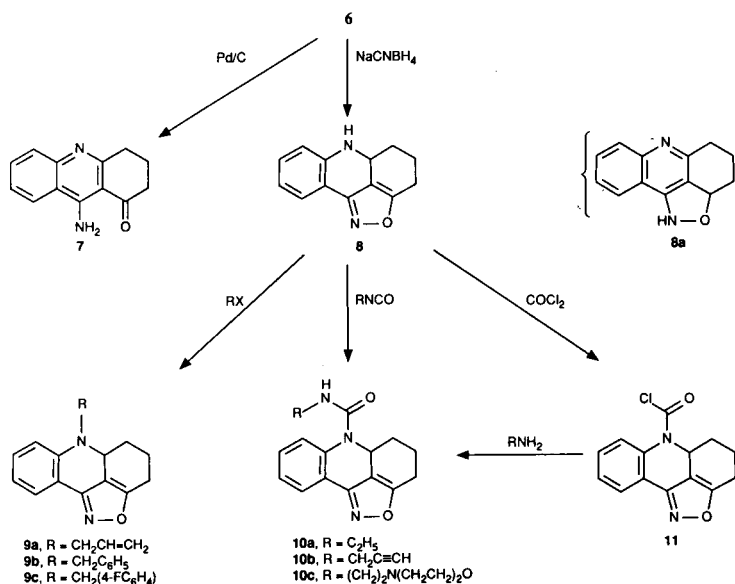
Compound **6** arises from the intramolecular attack of **2a** on the ortho position of the favorably oriented phenyl group. Examples of the formation of a new 6-membered nitrogen-containing ring through such an intramolecular attack by a nitrenium ion on a suitably disposed C-H bond are known in the literature [5,7], but to our knowledge this is the first case where the reaction proceeds in high enough yield to allow the preparation of useful amounts of the new heterocycle. We know of only one other example in the literature of the isoxazolo[5,4,3-*kl*]acridine ring system [8]. This compound, 1,2a,3,4,5,5a,10b,10c-octahydro-1-methyl-6*H*-isoxazolo[5,4,3-*kl*]acridine-6-carboxaldehyde, was synthesized *via* an intramolecular nitrene cycloaddition, and its further chemical transformations were not explored. We have investigated some of the chemistry of **6**, results which are reported later in this paper.

The structural assignments of compounds **3-6** were supported by infrared and mass spectral data, as well as by proton and carbon-13 nmr data (see experimental section). The isomeric lactams **3** and **4** were easily distinguished on the basis of their proton and carbon-13 spectra. The proton nmr of **3** (see experimental) showed that the amide NH proton was split into a triplet by the adjacent methylene group, while the NH of **4** was a broad singlet. In addition, the carbon-13 spectra of **3** and **4** showed the expected differences in the chemical shifts of the methylene groups at position-6 (42.2 and 36.2 ppm, respectively). The structure of **5** was assigned immediately upon inspection of the mass and nmr spectra: the molecular ion was correct and there were neither aliphatic protons nor sp³ carbons in the nmr

Scheme 1



Scheme 2



spectra. Finally, while the mass spectrum suggested the structure of **6**, it was confirmed by the carbon-13 spectrum, which, while showing that the isoxazole portion of the molecule was intact, indicated an additional quaternary carbon (147.5 ppm), due to the formation of the new bond to the phenyl group.

Because of our aforementioned interest in the biological activity of heterocycles containing the isoxazole group, we were interested in derivatives of the little known ring system represented by **6**. Transfer hydrogenation of **6** with Pd/C in the presence of 1-octene gave 9-amino-3,4-dihydroacridin-1(2*H*)-one (**7**, Scheme 2), the product of reduction of the 1,2 N-O bond. This product was identical to that synthesized by us by another route, and its chemistry is discussed elsewhere [9]. Reduction of **6** with sodium cyanoborohyde in acetic acid gave 4,5,5a,6-tetra-

hydro-3*H*-isoxazolo[5,4,3-*k*]acridine (**8**), the product of reduction of the 5a,6 C=N bond. We were aware that the mass and proton nmr spectra also fit the tautomeric structure **8a**, but here again the issue was decided conclusively by the carbon-13 spectrum: the single methine carbon (46.96 ppm), which bears a hetero atom, is clearly bonded to nitrogen, as in **8**, and not to oxygen, as in **8a** [10].

Compound **8** was resistant to alkylation by primary alkyl halides and mesylates and to acylation by acid chlorides. It could, however, be alkylated with the more reactive allyl or benzyl halides to give compounds **9a-c** and it reacted with an isocyanate to give a urea (**10a**, Scheme 2). Ureas were more conveniently obtained by the reaction of **8** with the highly reactive phosgene to give a crystalline carbamoyl chloride (**11**), which then reacted smoothly with amines to give ureas **10b-c**. Further investigations of the chemistry of **8** are in progress.

EXPERIMENTAL

Melting points were determined on a Thomas-Hoover capillary melting point apparatus and are uncorrected. The mass spectra were obtained from a Finnigan Model 4000 spectrophotometer with an INCOS data system at 70 eV by direct insertion. Nuclear magnetic resonance spectra were taken on a Varian Gemini-200 instrument. The ^1H and ^{13}C assignments were made on the basis of single frequency homonuclear decoupling experiments, APT, HETCOR and fully proton coupled experiments. Thin-layer chromatography was performed on pre-coated glass plates (E. Merck 5.0 x 10.0 cm, silica gel 60, F-254). E. Merck 230-400 mesh silica gel was used for flash chromatography. Elemental analyses were performed by Micro-Tech Laboratories, Skokie, IL.

Schmidt Reaction of **1**.

Compound **1** (2.374 g, 11.1 mmoles) was dissolved in 15 ml of concentrated sulfuric acid. When dissolution was complete, 25 ml of dichloromethane was added, followed by 0.80 g (12.3 mmoles) of sodium azide. The reaction mixture was stirred at room temperature for 3 hours and then poured over cracked ice. After increasing the volume of the organic phase with additional dichloromethane (25 ml), concentrated hydrochloric acid was added until all the solids had dissolved (3 ml). The aqueous phase was separated and then the organic phase was extracted three times with dilute (5%) hydrochloric acid. The combined aqueous phase was adjusted to pH 4-5 with 50% sodium hydroxide solution and then to pH 7-8 with saturated sodium bicarbonate solution. Extraction with dichloromethane, followed by drying (magnesium sulfate) and evaporation gave a solid residue that was purified by flash chromatography (50% ethyl acetate/dichloromethane). Evaporation of the product-containing fractions gave 0.705 g (30%) of **6**, mp 148-149°. Recrystallization from ethyl acetate/hexane gave material of mp 149-150°; ^1H nmr (deuteriochloroform): δ 2.47 (quintet, $J = 6$ Hz, 2H, 4- CH_2), 3.08 (t, $J = 6$ Hz, 2H, 5- CH_2), 3.27 (t, $J = 6$ Hz, 2H, 3- CH_2), 7.57 (ddd, $J_o = 8$ Hz, $J_m = 1$ Hz, 1H, H-9), 7.78 (ddd, $J_o = 8$ Hz, $J_m = 1$ Hz, 1H, H-8), 8.00 (dd, $J_o = 8$ Hz, $J_m = 1$ Hz, 1H, H-7), 8.30 (dd, $J_o = 8$ Hz, $J_m = 1$ Hz, 1H, H-10); ^{13}C nmr (deuteriochloroform): δ 174.24 (C-2a), 160.48 (C-5a), 153.69 (C-10b), 147.55 (C-6a), 131.53 (C-8), 129.66 (C-7), 126.89 (C-9), 124.68 (C-10), 116.23 (C-10a), 112.70 (C-10c), 29.67 (C-5), 24.42 (C-3), 23.92 (C-4); ms: m/e 210 (M^+).

Anal. Calcd. for $\text{C}_{13}\text{H}_{10}\text{N}_2\text{O}$: C, 74.27; H, 4.79; N, 13.33. Found: C, 74.50; H, 4.87; N, 13.39.

The original dichloromethane extract of the acidic aqueous phase was evaporated and purified by flash chromatography (20% ethyl acetate/hexane, then 50% ethyl acetate/hexane, then 20% ethyl acetate/dichloromethane). In the 50% ethyl acetate/hexane was eluted, sequentially, **5** and unreacted **1**. Evaporation of the fractions containing **5** gave 0.041 g (1.8%), mp 122-123°. Recrystallization from cyclohexane gave mp 125-126°; ^1H nmr (deuteriochloroform): δ 4.2 (s, 2H, exchanges with deuterium oxide, NH_2), 6.45 (d, $J_o = 10$ Hz, 1H, H-5), 6.90 (d, $J_o = 10$ Hz, 1H, H-7), 7.30 (dd, $J_o = 10$ Hz, 1H, H-6), 7.52 (m, 3H, H-3',4',5'), 7.73 (m, 2H, H-2',6'); ^{13}C nmr (deuteriochloroform): δ 165.46 (C-7a), 157.63 (C-3a), 142.27 (C-4), 131.72 (C-6), 130.16 (C-4'), 129.68 (C-1'), 129.18 (C-2',3',5',6'), 108.69 (C-3a), 107.73 (C-5), 99.32 (C-7); ms: m/e 210 (M^+).

Anal. Calcd. for $\text{C}_{13}\text{H}_{10}\text{N}_2\text{O}$: C, 74.27; H, 4.79; N, 13.33. Found: C, 73.85; H, 4.94; N, 13.35.

The unreacted **1** amounted to 0.211 g (8.9%) after evaporation of the appropriate fractions. Its identity was confirmed by tlc, ^1H nmr, and ms.

The next product, eluted with 20% ethyl acetate/dichloromethane, was established to be **4**, 0.095 g (3.8%), mp 147-148° after recrystallization from ethyl acetate/pentane; ^1H nmr (DMSO- d_6): δ 2.03 (m, 2H, 7- CH_2), 2.51 (m, 2H, 6- CH_2), 3.03 (m, 2H, 8- CH_2), 7.55 (m, 3H, H-3',4',5'), 7.68 (m, 2H, H-2',6'), 9.02 (s, 1H, exchanges with deuterium oxide NH); ^{13}C nmr (DMSO- d_6): δ 173.47 (C-5), 158.49 (C-3), 155.84 (C-8a), 130.27 (C-4'), 129.38 (C-2',6'), 128.00 (C-3',5'), 127.11 (C-1'), 115.07 (C-3a), 36.18 (C-6), 26.52 (C-8), 18.11 (C-7); ms m/e 228 (M^+).

Anal. Calcd. for $\text{C}_{13}\text{H}_{12}\text{N}_2\text{O}_2$: C, 68.40; H, 5.30; N, 12.28. Found: C, 68.11; H, 5.16; N, 12.16.

The final product to be eluted from the column was **3**, 0.788 g (31%), mp 161-162° after recrystallization from ethyl acetate; ^1H nmr (DMSO- d_6): δ 2.00 (m, 2H, 7- CH_2), 3.16 (m, 2H, 8- CH_2), 3.26 (m, 2H, 6- CH_2), 7.46 (m, 3H, H-3',4',5'), 7.60 (m, 2H, H-2',6'), 8.05 (t, $J = 5$ Hz, 1H, exchanges with deuterium oxide, NH); ^{13}C nmr (DMSO- d_6): δ 173.43 (C-4), 163.07 (C-3), 162.79 (C-8a), 129.41 (C-4'), 129.10 (C-2',6'), 128.97 (C-1'), 127.90 (C-3',5'), 110.37 (C-3a), 39.80 (C-6), 25.68 (C-8), 24.96 (C-7); ms m/e 228 (M^+).

Anal. Calcd. for $\text{C}_{13}\text{H}_{12}\text{N}_2\text{O}_2$: C, 68.40; H, 5.30; N, 12.28. Found: C, 68.34; H, 5.31; N, 12.33.

9-Amino-3,4-dihydroacridin-1(2H)-one (**7**).

In 100 ml of 1-octene were combined 2.00 g (9.42 mmoles) of **6** and 1.0 g of 5% Pd/C. The reaction mixture was refluxed for 16 hours and then filtered through celite and concentrated under reduced pressure. Recrystallization of the residue from dichloromethane gave 1.18 g (59%) of **7**, mp 237-239° (lit [9] mp 237-239°); ^1H nmr (DMSO- d_6): δ 2.03 (quintet, $J = 6$ Hz, 2H, 3- CH_2), 2.64 (t, $J = 6$ Hz, 2H, 2- CH_2), 2.98 (t, $J = 6$ Hz, 2H, 4- CH_2), 7.43 (m, 1H, H-7), 7.71 (m, 2H, H-5 and H-6), 8.37 (d, $J_o = 8$ Hz, 1H, H-8), 8.42 (s, 1H, exchanges with deuterium oxide, NH), 10.00 (s, 1H, exchanges with deuterium oxide, hydrogen bonded NH); ^{13}C nmr: δ 200.74 (C-1), 163.43 (C-4a), 154.76 (C-9), 147.94 (C-10a), 131.76 (C-6), 128.37 (C-5), 124.16 (C-7), 123.28 (C-8), 117.99 (C-8a), 105.43 (C-9a), 39.25 (C-2), 33.86 (C-4), 21.11 (C-3) [11].

4,5,5a,6-Tetrahydro-3H-isoxazolo[5,4,3-*k*]acridine (**8**).

In 100 ml of glacial acetic acid was dissolved 4.75 g (22.6 mmoles) of **6**. To this solution was added sodium cyanoborohydride (2.84 g, 44.6 mmoles) with vigorous stirring. After stirring for 30 minutes the reaction was neutralized with excess solid sodium carbonate and extracted two times with dichloromethane. Drying and evaporation of the organic phase gave a solid that was purified by flash chromatography (50% tetrahydrofuran/hexane). Evaporation of the product-containing fractions and recrystallization from dichloromethane/hexane gave 2.78 g (58%) of **8**, mp 152-154°; ^1H nmr (deuteriochloroform): δ 1.44 (m, 1H, H-5), 1.80 (m, 1H, H-4), 2.16 (m, 2H, H-4 and H-5), 2.72 (m, 2H, H-3), 4.24 (s, 1H, exchanges with deuterium oxide, NH), 4.42 (m, 1H, H-5a), 6.66 (d, $J_o = 10$ Hz, 1H, H-7), 6.79 (ddd, $J_o = 10$ Hz, $J_m = 1$ Hz, 1H, H-9), 7.16 (ddd, $J_o = 10$ Hz, $J_m = 1$ Hz, 1H, H-8), 7.73 (dd, $J_o = 10$ Hz, $J_m = 1$ Hz, 1H, H-10); ^{13}C nmr (deuteriochloroform): δ 165.40 (C-2a), 154.96 (C-10b), 146.67 (C-6a), 131.37 (C-8), 125.02 (C-10), 118.94 (C-9), 115.73 (C-7), 113.25 (C-10a or C-10c), 112.64 (C-10c or C-10a), 46.95 (C-5a), 30.66 (C-5), 22.26 (C-3), 20.72 (C-4); ms: m/e 212 (M^+).

Anal. Calcd. for $C_{13}H_{12}N_2O$: C, 73.57; H, 5.70; N, 13.20. Found: C, 73.84; H, 5.82; N, 13.22.

6-(2-Propenyl)-4,5,5a,6-tetrahydro-3H-isoxazolo[5,4,3-*k*]acridine (9a).

In 20 ml of *N,N*-dimethylformamide was combined 4.00 g (18.8 mmoles) of **6**, 4.56 g (37.7 mmoles) of allyl bromide and 8.0 g (57.9 mmoles) of finely milled potassium carbonate. The reaction mixture was then warmed at 90° with vigorous stirring. Every hour an additional 2.8 g (23.1 mmoles) of allyl bromide was added. After 3 hours the reaction mixture was partitioned between water and ethyl acetate and the organic phase was separated, dried, and evaporated. The residue obtained in this manner was purified by flash chromatography (20% ethyl acetate/hexane). Evaporation of the product-containing fractions and recrystallization from ethyl acetate/hexane gave 2.88 g (61%) of **9a**, mp 115-117°; ¹H nmr (deuteriochloroform): δ 1.45 (m, 1H, H-5), 1.83 (m, 1H, H-4), 2.36 (m, 2H, H-4 and H-5), 2.75 (m, 2H, H-3), 3.98 (ddd, $J_{gem} = 14$ Hz, $J_{vic} = 6$ Hz, $J_{vic} = 2$ Hz, 2H, $CH_2CH=CH_2$), 4.36 (m, 1H, H-5a), 5.22 (m, 1H, $CH_2CH=CH_2$), 5.30 (m, 1H, $CH_2CH=CH_2$), 5.88 (m, 1H, $CH_2CH=CH_2$), 6.80 (d, $J_o = 9$ Hz, 1H, H-7), 6.83 (dd, $J_o = 9$ Hz, 1H, H-9), 7.27 (dd, $J_o = 9$ Hz, 1H, H-8), 7.80 (d, $J_o = 9$ Hz, 1H, H-10); ms *m/e* 252 (M^+).

Anal. Calcd. for $C_{16}H_{16}N_2O$: C, 76.16; H, 6.39; N, 11.10. Found: C, 75.90; H, 6.39; N, 11.15.

6-Benzyl-4,5,5a,6-tetrahydro-3H-isoxazolo[5,4,3-*k*]acridine (9b).

In the same manner as for **9a** above, **9b** was obtained in 70% yield after flash chromatography and recrystallization from ethyl acetate/hexane, mp 162-164°; ¹H nmr (deuteriochloroform): δ 1.58 (m, 1H, H-5), 1.81 (m, 1H, H-4), 2.25 (m, 2H, H-4 and H-5), 2.75 (m, 2H, H-3), 4.42 (m, 1H, H-5a), 4.59 (dd, $J_{gem} = 16$ Hz, 2H, $CH_2C_6H_5$), 6.63 (d, $J_o = 9$ Hz, 1H, H-7), 6.80 (dd, $J_o = 9$ Hz, 1H, H-9), 7.18 (dd, $J_o = 9$ Hz, 1H, H-8), 7.31 (m, 5H, $CH_2C_6H_5$), 7.82 (d, $J_o = 9$ Hz, 1H, H-10); ms: *m/e* 302 (M^+).

Anal. Calcd. for $C_{20}H_{18}N_2O$: C, 79.44; H, 6.00; N, 9.26. Found: C, 79.60; H, 6.23; N, 9.17.

6-(4-Fluorobenzyl)-4,5,5a,6-tetrahydro-3H-isoxazolo[5,4,3-*k*]acridine (9c).

In the same manner as for **9a** above, **9c** was obtained in 49% yield after flash chromatography and recrystallization from dichloromethane/hexane, mp 214° dec; ¹H nmr (deuteriochloroform): δ 1.56 (m, 1H, H-5), 1.80 (m, 1H, H-4), 2.21 (m, 2H, H-4 and H-5), 2.80 (m, 2H, H-3), 4.41 (m, 1H, H-5a), 4.54 (dd, $J_{gem} = 16$ Hz, 2H, $CH_2(4-FC_6H_4)$), 6.60 (d, $J_o = 9$ Hz, 1H, H-7), 6.80 (dd, $J_o = 9$ Hz, 1H, H-9), 7.00 (dd, $J_o = 9$ Hz, 1H, H-8), 7.25 (m, 4H, $CH_2(4-FC_6H_4)$), 7.82 (d, $J_o = 9$ Hz, 1H, H-10); ms: *m/e* 320 (M^+).

Anal. Calcd. for $C_{20}H_{17}FN_2O$: C, 74.98; H, 5.35; N, 8.74. Found: C, 75.06; H, 5.52; N, 8.78.

N-Ethyl-4,5,5a,6-tetrahydro-3H-isoxazolo[5,4,3-*k*]acridine-6-carboxamide (10a).

In 200 ml of carbon tetrachloride were combined 5.00 g (23.5 mmoles) of **6** and 8.1 g (114 mmoles) of ethyl isocyanate. The reaction mixture was then refluxed for 48 hours, adding an additional 8.1 g of ethyl isocyanate after 24 hours. At the end of this time the reaction was chilled with an ice/water bath, causing a precipitate to form. The precipitated product was filtered off and dried to give 3.91 g (59%) of **10a** mp 189-190°; ¹H nmr (DMSO-*d*₆): δ 1.11 (t, $J = 6$ Hz, $NHCH_2CH_3$), 1.21 (m, 1H, H-5), 1.80 (m,

1H, H-4), 2.16 (m, 1H, H-4), 2.55 (m, 1H, H-5), 2.72 (m, 2H, H-3), 3.20 (m, 2H, $NHCH_2CH_3$), 4.52 (m, 1H, H-5a), 7.00 (m, 2H, H-7 and H-9), 7.37 (dd, $J_o = 9$ Hz, 1H, H-8), 7.68 (dd, $J_o = 9$ Hz, $J_m = 1$ Hz, 1H, H-10), 8.01 (t, $J = 4$ Hz, 1H, exchanges with deuterium oxide, *NH*); ms: *m/e* 283 (M^+).

Anal. Calcd. for $C_{16}H_{17}N_3O_2$: C, 67.83; H, 6.05; N, 14.83. Found: C, 67.82; H, 6.05; N, 14.84.

4,5,5a,6-Tetrahydro-3H-isoxazolo[5,4,3-*k*]acridine-6-carbonyl Chloride (11).

In 50 ml of dichloromethane was dissolved **8** (4.08 g, 19.2 mmoles). Phosgene in benzene (26 ml of 12.5%, 2.86 g of phosgene, 28.9 mmoles) was then added all in one portion. This solution was then chilled with an ice/water bath as a solution of triethylamine (2.92 g, 28.8 mmoles) in 20 ml of dichloromethane was added dropwise. After the addition was complete (30 minutes), the reaction was washed with dilute hydrochloric acid and then dried and evaporated. The residue obtained in this manner was recrystallized from dichloromethane/hexane to give 3.66 g (69%) of **11**, mp 189° dec; ¹H nmr (deuteriochloroform): δ 1.82 (m, 2H, H-4 and H-5), 2.17 (m, 1H, H-4), 2.69 (m, 2H, H-3), 3.11 (m, 1H, H-5), 4.63 (m, 1H, H-5a), 7.42 (m, 3H, H-7,8,9), 7.96 (dd, $J_o = 9$ Hz, $J_m = 1$ Hz, H-10); ms: *m/e* 274, 276 (M^+).

Anal. Calcd. for $C_{14}H_{11}ClN_2O_2$: C, 61.20; H, 4.03; N, 10.20. Found: C, 60.83; H, 4.13; N, 9.98.

N-(2-Propynyl)-4,5,5a,6-tetrahydro-3H-isoxazolo[5,4,3-*k*]acridine-6-carboxamide (10b).

In 100 ml of carbon tetrachloride were combined **11** (12.2 mmoles) and propargyl amine (1.47 g, 26.7 mmoles). This mixture was refluxed for 2 hours and then cooled and shaken with dilute hydrochloric acid. A precipitate, which was soluble in neither phase, was filtered off and recrystallized from methanol/water to give 2.00 g (60%) of **10b**, mp 220° dec; ¹H nmr (DMSO-*d*₆): δ 1.20 (m, 1H, H-5), 1.80 (m, 1H, H-4), 2.18 (m, 1H, H-4), 2.58 (m, 1H, H-5), 2.78 (m, 2H, H-3), 3.20 (t, $J = 1$ Hz, 1H, $C \equiv CH$), 3.92 (complex dd, $J_{gem} = 14$ Hz, 2H, $CH_2C \equiv CH$), 4.58 (m, 1H, H-5a), 7.05 (dd, $J_o = 9$ Hz, 1H, H-9), 7.16 (d, $J_o = 9$ Hz, 1H, H-7), 7.37 (ddd, $J_o = 9$ Hz, $J_m = 1$ Hz, 1H, H-8), 7.71 (dd, $J_o = 9$ Hz, $J_m = 1$ Hz, 1H, H-10), 8.20 (t, $J = 4$ Hz, 1H, exchanges with deuterium oxide, *NH*); ms: *m/e* 293 (M^+).

Anal. Calcd. for $C_{17}H_{15}N_3O_2$: C, 69.61; H, 5.15; N, 14.33. Found: C, 69.56; H, 5.29; N, 14.49.

N-[2-(4-Morpholino)ethyl]-4,5,5a,6-tetrahydro-3H-isoxazolo[5,4,3-*k*]acridine-6-carboxamide (10c).

In the same manner as for **10b** above, **10c** was obtained in 67% yield after recrystallization from ether/hexane, mp 176-178°; ¹H nmr (DMSO-*d*₆): δ 1.20 (m, 1H, H-5), 1.80 (m, 1H, H-4), 2.16 (m, 1H, H-4), 2.5 (m, 8H, $NCH_2CH_2N(CH_2CH_2)_2O$), 2.75 (m, 1H, H-5), 3.10 (m, 1H, H-3), 3.48 (m, 1H, H-3), 3.62 (m, 4H, $N(CH_2CH_2)_2O$), 4.58 (m, 1H, H-5a), 7.00 (dd, $J_o = 9$ Hz, 1H, H-9), 7.36 (ddd, $J_o = 9$ Hz, $J_m = 1$ Hz, 1H, H-8), 7.57 (d, $J_o = 9$ Hz, 1H, H-7), 7.68 (dd, $J_o = 9$ Hz, $J_m = 1$ Hz, 1H, H-10), 7.90 (t, $J = 4$ Hz, 1H, exchanges with deuterium oxide, *NH*); cims: *m/e* 369 (MH^+).

Anal. Calcd. for $C_{20}H_{24}N_4O_3$: C, 65.20; H, 6.57; N, 15.21. Found: C, 65.13; H, 6.59; N, 15.29.

Acknowledgement.

The author wishes to thank Frank A. Pierrat for technical

assistance; Marc Agnew, Anastasia Linville, Dana Hallberg, and Tina Bower for spectra data; and Margaret Hill for literature assistance.

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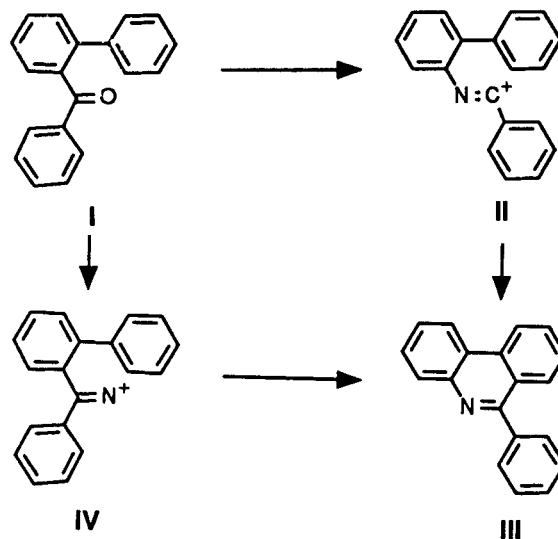
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[10] Compare this value with that of 66.4 ppm for the carbinol carbon of α -methyl-3-pyridinemethanol (ref [12]).

[11] This compound is numbered according to the acridine ring numbering system, in which the ring nitrogen is the 10-position, not the 5-position.

[12] Sadtler Research Laboratories, Standard Spectra, Carbon-13 Collection, Spectrum No. 20015.