= 11 Hz, OCH_3), 4.42 (s, 3 H, NCH_3), 5.38 (d, 2 H, J = 8 Hz, CH_2); 7.97-8.80 (m, 3 H, 3-, 4-, 5-H), 9.02 (d, 1 H, J = 6 Hz, 6-H).

The rates of disappearance of 1 were determined by measuring the decrease in the integrated area of the methylene doublet for the substrate (5.08 ppm) relative to the total integrated area for the methylene signals involved. All reactions were followed to 61-81% conversion. The values of k_1 and k_2 were calculated as slopes of the plots of the values of ln $(a_o/a_o - x_t)$ or x_t/a_o $(a_o - x_t)$ vs time.

Quantitatively meaningful integrals of ^{13}C signals were obtained by using 40° pulses, followed with a 6-8-s pulse delay, during which time the BB decoupler was gated off. In this way all ^{13}C signals except C-2 of the pyridine ring, yielded quantitative integrals to within ±5%. Typically 10^3 transients were collected, taking <1.8 h.

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Registry No. 1, 99668-67-4; 2, 99668-68-5; $(MeO)_2P(o)Cl$, 813-77-4; sodium 2-pyridylmethoxide, 99668-69-6.

The Conversion of Tetrahydroquinoline into Derivatives of 8*H*-Pyrido[3,2,1-*jk*][1,3]benzodiazepines via [2,3]-Sigmatropic Rearrangements

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Although pyridobenzodiazepines have been previously reported in the literature,[1] the pyrido[3,2,1-*jk*][1,3]-benzodiazepine ring system does not appear to be known. Recently, we described the use of tetrahydroquinoline as a starting material for the synthesis of derivatives of 4*H*-pyrrolo[3,2,1-*ij*]quinoline.[2] This transformation, which is exemplified by the conversion of **1** into **2**, utilized the general concept of [2,3]-sigmatropic rearrangements of ylides derived from aza sulfonium salts.[3] These rearrangements, which we have exploited in the synthesis of indoles[4] and oxindoles,[5] are widely applicable to a variety of ring systems bearing both electron-donating and electron-withdrawing substituents. Thus, it seemed reasonable that we should be able to apply this same methodology in the synthesis of the 8*H*-pyrido[3,2,1-*jk*][1,3]benzodiazepines, a class of compounds which is attractive because of its close relationship to pharmaceutically intriguing structures.[1]

Treatment of 2-(methylthio)-*N*-methylacetamide[6] with 0.95 equiv of chlorine at -78 °C gave the chlorosulfonium chloride salt **3**. Dropwise addition of **1** to a methylene chloride solution of **3**, followed by ylide formation using triethylamine as base, afforded a 71% yield of **4**. Raney nickel reduction of **4** produced **5** in 85% yield. When a benzene solution of **5** was refluxed with paraformaldehyde for 12 h, the cyclization product, 2-methyl-1,2,9,10-tetrahydro-8*H*-pyrido[3,2,1-*jk*][1,3]benzodiazepin-3(4*H*)-one (**6**) was obtained in 76% yield.

Reduction of **5** with lithium aluminum hydride gave an 84% yield (71% based on **4**) of **7** as an oil. When **7** was refluxed in benzene with 1 equiv of paraformaldehyde, a 91% yield of 1,2,3,4,9,10-hexahydro-2-methyl-8*H*-pyrido-[3,2,1-*jk*][1,3]benzodiazepine (**8**) was isolated. Refluxing **7** in tetrahydrofuran with 1 equiv of 1,1′-carbonyldiimidazole produced a 56% yield of the cyclic urea **9**.

The investigation outlined above makes the 8*H*-pyrido[3,2,1-*jk*][1,3]benzodiazepines readily available for the first time.

Experimental Section

α-(Methylthio)-α-(1,2,3,4-tetrahydroquinolin-8-yl)-*N*-methylacetamide (4). Chlorine (4.0 mL, 88 mmol) was con-

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densed into a dry ice–acetone-cooled (jacketed) addition funnel at −78 °C. The chlorine was added dropwise to 250 mL of dry methylene chloride at −78 °C. To the resultant pale yellow solution, under a static nitrogen pressure, was added 11.0 g (92 mmol) of 2-(methylthio)-*N*-methylacetamide[6] in 10 mL of dry methylene chloride. A white precipitate formed. After the reaction mixture had been stirred for 20 min, a solution of 23.44 g (176 mmol) of 1,2,3,4-tetrahydroquinoline (1) in 25 mL of dry methylene chloride was added dropwise. The reaction mixture was stirred for 3 h at −70 °C, followed by addition of 40 mL of triethylamine. After being stirred for an additional hour at −70 °C, the reaction mixture was allowed to warm to ambient temperature (overnight). The organic mixture was washed with aqueous sodium carbonate solution, dried over anhydrous sodium carbonate, filtered, and concentrated to give a solid. This solid was recrystallized from ether–hexane to give 15.7 g (62.8 mmol, 71%) of white crystalline product: mp 137–139 °C; IR ($CDCl_3$) 3380 (w), 2940 (w), 2850 (vw), 1670 (s), 1610 (w), 1520 (m), 1450 (w), 1410 (w), 1380 (vw), 1310 (m), 1190 (w), 1115 (w) cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.11–2.13 (m, 2 H), 2.03 (s, 3 H), 2.57–2.92 (m, 5 H), 3.16–3.48 (m, 2 H), 4.47 (s, 1 H), 5.03 (br s, 1 H), 6.36–7.10 (complex m, 3 H); ^{13}C NMR ($CDCl_3$) δ 15.27 (q), 21.40 (t), 26.44 (q), 27.44 (t), 41.95 (t), 53.16 (d), 116.18 (d), 119.75 (s), 122.69 (s), 125.89 (d), 129.14 (d), 143.02 (s), 170.66 (s); exact mass, *m/e* 250.1143 (calcd for $C_{13}H_{18}N_2OS$, *m/e* 250.1139).

Anal. Calcd for $C_{13}H_{18}N_2OS$: C, 62.37; H, 7.25; N, 11.19. Found: C, 62.43; H, 7.27; N, 11.16.

2-(1,2,3,4-Tetrahydroquinolin-8-yl)-*N*-methylacetamide (5). To 7.5 g (30 mmol) of α-(methylthio)-α-(1,2,3,4-tetrahydroquinolin-8-yl)-*N*-methylacetamide (4) in a mixture of 100 mL of acetone and 100 mL of denatured ethanol was added 10 level teaspoons (approximately 30 g) of activated Raney nickel, and the reaction mixture was stirred for 30 min. The reaction mixture was filtered through a fritted glass funnel. The spent catalyst was washed with 50 mL of acetone. The combined filtrates were concentrated in vacuo. The resulting residue was taken up in 100 mL of methylene chloride and dried over anhydrous magnesium sulfate. Filtration and concentration gave 5.8 g (28.2 mmol, 94%) of product. Distillation gave 5.2 g (25.5 mmol, 85%) of pure 5: bp 175–190 °C (0.2 mm); IR ($CDCl_3$) 3420 (w), 3310 (vw), 2930 (w), 2850 (w), 1670 (s), 1610 (w), 1530 (m), 1415 (w), 1310 (w), 1280 (w) cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.69–2.12 (m, 2 H), 2.58–2.90 (m, 5 H), 3.34 (s, 2 H), 3.18–3.47 (m, 2 H), 4.78 (br s, 1 H), 6.09 (br s, 1 H), 6.35–7.06 (complex m, 3 H); ^{13}C NMR ($CDCl_3$) δ 21.47 (t), 26.11 (q), 27.2 (t), 40.30 (t), 41.83 (t), 116.13 (d), 118.85 (s), 122.01 (s), 128.26 (d), 128.61 (d), 143.39 (s), 171.91 (s); exact mass, *m/e* 204.1260 (calcd for $C_{12}H_{16}N_2O$, *m/e* 204.1262).

Anal. Calcd for $C_{12}H_{16}N_2O$: C, 70.56; H, 7.90; N, 13.72. Found: C, 70.58; H, 7.87; N, 13.58.

2-Methyl-1,2,9,10-tetrahydro-8*H*-pyrido[3,2,1-*jk*][1,3]-benzodiazepin-3(4*H*)-one (6). To 2.04 g (10 mmol) of 2-(1,2,3,4-tetrahydroquinolin-8-yl)-*N*-methylacetamide (5) in 25 mL of benzene was added 0.30 g (10 mmol) of paraformaldehyde, and the reaction mixture was refluxed overnight. The reaction mixture was concentrated to give a syrup, which was distilled to give 2.01 g (9.3 mmol, 93%) [bp 155–170 °C (0.2 mm)] of a syrup that gradually crystallized. Recrystallization from ether–hexane gave 1.65 g (7.6 mmol, 76%) of 6 as crystals: mp 92.0–93.5 °C; IR ($CDCl_3$) 2950 (w), 1670 (s), 1600 (w), 1480 (m), 1460 (m), 1400 (w), 1370 (w), 1330 (w), 1270 (w), 1210 (w), 1180 (w), 1110 (w) cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.78 (quintet, 2 H), 2.63 (t, 2 H), 3.06 (s, 3 H), 3.78 (t, 2 H), 3.93 (s, 2 H), 4.73 (s, 2 H), 6.40–6.98 (complex m, 3 H); ^{13}C NMR ($CDCl_3$) δ 23.28 (t), 27.27 (t), 34.37 (q), 43.29 (t), 50.35 (t), 67.41 (t), 117.79 (s), 118.59 (d), 127.19 (s), 127.42 (d), 130.00 (d), 143.04 (s), 171.94 (s); exact mass, *m/e* 216.1265 (calcd for $C_{13}H_{16}N_2O$, *m/e* 216.1261).

Anal. Calcd for $C_{13}H_{16}N_2O$: C, 72.19; H, 7.46; N, 12.95. Found: C, 72.18; H, 7.49; N, 12.93.

8-[2-(Methylamino)ethyl]-1,2,3,4-tetrahydroquinoline (7). α-(Methylthio)-α-(1,2,3,4-tetrahydroquinolin-8-yl)-*N*-methylacetamide (4) (7.5 g, 30 mmol) was desulfurized with activated Raney nickel as described for the preparation of 5 (vide supra). The resulting undistilled product was dissolved in 200 mL of dry tetrahydrofuran, and 2.0 g (52.7 mmol) of lithium aluminum hydride was added. The reaction mixture was refluxed for 4 h and hydrolyzed by adding, in sequence (slowly), 2 mL of water, 2 mL of 15% sodium hydroxide solution, and 6 mL of water. The resulting mixture was filtered through a fritted glass funnel, and the filtrate was concentrated to give an oil. Distillation of the oil gave 4.07 g (21.4 mmol, 71%) of 7: bp 106–112 °C (0.2 mm); IR (neat) 3300 (w), 2920 (m), 2830 (m), 1595 (m), 1500 (m), 1450 (m), 1350 (w), 1315 (m), 1280 (m), 1190 (w), 1115 (w) cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.70–2.17 (m, 2 H), 2.38 (s, 3 H), 2.54–2.98 (m, 6 H), 3.16–3.44 (m, 2 H), 6.33–7.02 (complex m, 3 H); ^{13}C NMR ($CDCl_3$) δ 21.86 (t), 27.36 (t), 31.62 (t), 36.37 (q), 41.01 (t), 51.34 (t), 116.17 (d), 121.28 (s), 123.5 (s), 127.41 (d), 127.64 (d), 142.80 (s); exact mass, *m/e* 190.1476 (calcd for $C_{12}H_{18}N_2$, *m/e* 190.1470).

Anal. Calcd for $C_{12}H_{18}N_2$: C, 75.74; H, 9.53; N, 14.72. Found: C, 75.45; H, 9.54; N, 14.60.

1,2,3,4,9,10-Hexahydro-2-methyl-8*H*-pyrido[3,2,1-*jk*][1,3]-benzodiazepine (8). To 0.95 g (5 mmol) of 8-[2-(methylamino)ethyl]-1,2,3,4-tetrahydroquinoline (7) in 20 mL of benzene was added 0.15 g (5 mmol) of paraformaldehyde, and the reaction mixture was refluxed overnight. Concentration of the reaction mixture gave an oil, which was distilled to give 0.92 g (4.55 mmol, 91%) of 8: bp 100–102 °C (0.2 mm); IR (neat) 2960 (m), 2840 (w), 1605 (w), 1500 (m), 1370 (w), 1320 (m), 1300 (m), 1260 (w), 1220 (w), 1200 (w), 1120 (m), 1080 (w), 1060 (w) cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.56–2.05 (m, 2 H), 2.47 (s, 3 H), 2.58–3.00 (m, 6 H), 3.12–3.43 (m, 2 H), 3.90 (s, 2 H), 6.49–7.02 (complex m, 3 H); ^{13}C NMR ($CDCl_3$) δ 21.29 (t), 27.84 (t), 32.59 (t), 39.60 (q), 53.03 (t, 2 C), 77.86 (t), 119.35 (d), 126.03 (s), 126.89 (d), 128.13 (d), 131.80 (s), 147,72 (s); exact mass, *m/e* 202.1471 (calcd for $C_{13}H_{18}N_2$, *m/e* 202.1470).

Anal. Calcd for $C_{13}H_{18}N_2$: C, 77.18; H, 8.97; N, 13.85. Found: C, 77.10; H, 9.03; N, 13.99.

2-Methyl-3,4,9,10-tetrahydro-8*H*-pyrido[3,2,1-*jk*][1,3]-benzodiazepin-1(2*H*)-one (9). To 0.95 g (5 mmol) of 8-[2-(methylamino)ethyl]-1,2,3,4-tetrahydroquinoline (7) in 50 mL of dry tetrahydrofuran was added 0.81 g (5 mmol) of 1,1′-carbonyldiimidazole, and the reaction mixture was refluxed for 1 h. To this reaction mixture was added 2.25 g (20 mmol) of potassium *tert*-butoxide, and the reaction mixture was refluxed for 2 h. The reaction mixture was concentrated, and 100 mL of methylene chloride was added. The mixture was washed with water, dried over anhydrous sodium carbonate, filtered, and concentrated to give a solid. This solid was recrystallized from ether–hexane to give 0.61 g (2.8 mmol, 56%) of 9: mp 121–123 °C; IR ($CDCl_3$) 2940 (w), 1620 (ms), 1490 (m), 1440 (m), 1400 (w), 1350 (w), 1330 (w), 1310 (w), 1250 (w), 1180 (w), 1060 (w) cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.72–2.13 (m, 2 H), 2.76 (s, 3 H), 2.63–3.12 (m, 4 H), 3.20–3.85 (m, 4 H), 6.99 (s, 3 H); ^{13}C NMR ($CDCl_3$) δ 22.53 (t), 26.67 (t), 30.34 (t), 38.31 (q), 44.51 (t), 56.61 (t), 123.81 (d), 124.95 (d), 127.70 (d), 129.46 (s), 133.57 (s), 140.76 (s), 158.44 (s); exact mass, *m/e* 216.1260 (calcd for $C_{13}H_{16}N_2O$, *m/e* 216.1261).

Anal. Calcd for $C_{13}H_{16}N_2O$: C, 72.19; H, 7.46; N, 12.95. Found: C, 72.16; H, 7.54; N, 12.93.

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A Short Synthesis of Elasnin

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Elasnin (1) is a complex trisubstituted 4-hydroxy-2-pyrone that has been isolated from culture broths of *Streptomyces norboritoensis*.[1a,b] It is a specific inhibitor

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