Found: C, 76.57; H, 6.67; N, 4.58; S, 11.02.

Cyclohexanespiro-5′-(2′-*o*-biphenylylthiazoline) (3g): 484 mg, 79%; mp 121–122 °C (toluene–hexane); NMR ($CDCl_3$) δ 1.2–2.2 (10 H, m, cyclohexyl), 4.05 (2 H, s, CH_2), 7.2–8.1 (9 H, m, Ar); IR ($CDCl_3$, cm^{-1}) 2845, 1650, 1320, 980. Anal. Calcd for $C_{20}H_{21}NS$: C, 78.14; H, 6.89; N, 4.56; S, 10.41. Found: C, 77.88; H, 6.62; N, 4.31; S, 10.25.

Cyclohexanespiro-5′-(2′-benzylthiazoline) (3h): 395 mg, 81%; mp 146 °C (toluene–heptane); NMR ($CDCl_3$) δ 1.1–2.1 (10 H, m, cyclohexyl), 3.7 (2 H, s, CH_2Ph), 4.16 (2 H, s, CH_2), 7.4 (5 H, m, Ar); IR ($CDCl_3$, cm^{-1}) 3010, 2800, 1640, 1320. Anal. Calcd for $C_{15}H_{19}NS$: C, 73.44; H, 7.81; N, 5.71; S, 13.04. Found: C, 73.11; H, 7.63; N, 5.55; S, 12.86.

Registry No. **1a**, 5202-81-3; **1b**, 88425-11-0; **1c**, 88413-28-9; **1d**, 88413-29-0; **1e**, 88413-30-3; **1f**, 88413-31-4; **1g**, 88413-32-5; **1h**, 88413-33-6; **2a**, 88413-34-7; **2b**, 88413-35-8; **2c**, 88413-36-9; **2d**, 88413-37-0; **2e**, 88413-38-1; **2f**, 88413-39-2; **2g**, 88413-40-5; **2h**, 88413-41-6; **3a**, 37950-61-1; **3b**, 88413-42-7; **3c**, 88413-43-8; **3d**, 88413-44-9; **3e**, 88413-45-0; **3f**, 88413-46-1; **3g**, 88413-47-2; **3h**, 88413-48-3; phenylcarboxamide, 55-21-0; α-naphthylcarboxamide, 2243-81-4; *o*-biphenylylcarboxamide, 13234-79-2; β-naphthylcarboxamide, 2243-82-5; phenylacetamide, 103-81-1; isobutyraldehyde, 78-84-2; cyclohexanecarboxaldehyde, 2043-61-0.

Use of [2,3]-Sigmatropic Rearrangements in a One-Step Conversion of Tetrahydroquinoline to Substituted 1,2,5,6-Tetrahydro-4*H*-pyrrolo[3,2,1-*ij*]quinolin-2-one and 5,6-Dihydro-4*H*-pyrrolo[3,2,1-*ij*]quinoline

Paul G. Gassman,* Jodi J. Roos,[1] and Sung J. Lee

Department of Chemistry, University of Minnesota, Minneapolis, Minnesota 55455

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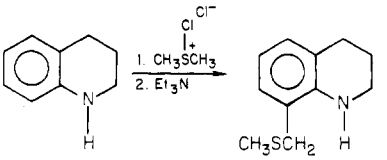
The 1,2,5,6-tetrahydro-4*H*-pyrrolo[3,2,1-*ij*]quinoline ring system has been of interest to a variety of investigators[2] because of the physiological effects of certain of its derivatives[3] and because it represents the basic ring system of the lilolidines.[4] The synthetic paths into this system have relied heavily on the Fischer indole synthesis or on Friedel–Crafts-type substitution of the aromatic ring. Since these reactions have limited applicability to systems bearing a wide variety of electron-withdrawing substituents, we decided to apply our oxindole[5] and indole[6] syntheses to the preparation of the 1,2,5,6-tetrahydro-4*H*-pyrrolo[3,2,1-*ij*]quinolin-2-one and 5,6-dihydro-4*H*-pyrrolo[3,2,1-*ij*]quinoline skeletons. Our process, which involves a [2,3]-sigmatropic rearrangement of intermediate azasulfonium ylides, results in negligible charge buildup on the aromatic ring, and as a result, proceeds readily in the presence of a wide range of electron-donating and electron-withdrawing groups.[7]

In order to test our approach for the use of [2,3]-sigmatropic rearrangements for the specific functionalization of the 8-position of tetrahydroquinoline (1), we first examined the (methylthio)methylation of this position.[7] Treatment of 1 with dimethylchlorosulfonium chloride[7] at −78 °C, followed by addition of triethylamine and workup, gave a 46% yield of 8-[(methylthio)methyl]-tetrahydroquinoline (2). In a similar fashion, chlorine was added to ethyl methylthioacetate to give the corresponding chlorosulfonium chloride, 3, which was added dropwise to



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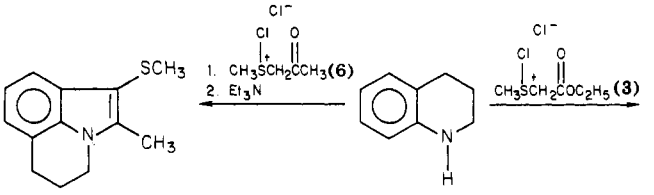
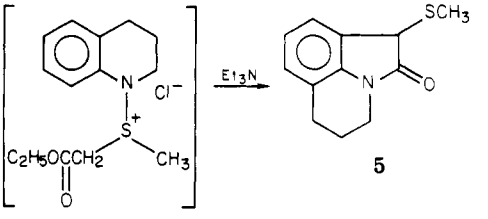


7 1



4 5

1 at −78 °C. Treatment of the intermediate azasulfonium salt 4 with triethylamine gave **5** in 53% yield. When 1 was treated with the chlorosulfonium chloride salt **6**, derived from 1-(methylthio)propan-2-one, and subsequently with triethylamine at −70 °C, a 39% yield of 1-(methylthio)-2-methyl-5,6-dihydro-4*H*-pyrrolo[3,2,1-*ij*]quinoline (**7**) was obtained.

Overall, we have demonstrated that the use of [2,3]-sigmatropic rearrangements of ylides generated from tetrahydroquinoline-derived azasulfonium salts provides a one-pot procedure for the synthesis of derivatives of the 5,6-dihydro-4*H*-pyrrolo[3,2,1-*ij*]quinoline system.

Experimental Section

8-[(Methylthio)methyl]tetrahydroquinoline (2). Chlorine (2.0 mL, 44 mmol) was condensed into a dry ice–acetone-cooled (jacketed) addition funnel at −78 °C. The chlorine was added dropwise to 120 mL of dry methylene chloride at −78 °C. To the resultant pale yellow solution, under a static nitrogen pressure,

(1) Undergraduate research participant, 1982–1983.

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was added 4.0 mL (3.3 g, 53 mmol) of dimethyl sulfide. On completion of the addition the yellow color disappeared. After being stirred for 10 min, a solution of 2.66 g (20 mmol) of tetrahydroquinoline (1) and 2.02 g (20 mmol) of triethylamine in 6 mL of dry methylene chloride was added dropwise. The reaction mixture was stirred for 4 h at −70 °C, and an additional 20 mL of triethylamine was added to the reaction mixture. After being stirred at −70 °C for 1 h, the reaction mixture was allowed to warm to room temperature (23 °C) over a 10-h period. The reaction mixture was washed with dilute sodium hydroxide solution, dried over anhydrous sodium carbonate, filtered, and concentrated to yield an oil. Chromatography of this material on a Waters Prep 500 liquid chromatograph using a silica gel column with 10% ethyl acetate–90% hexane gave 1.76 g (46%) of **2**. Distillation of this material gave 1.50 g (39%) of **2**: bp 95–98 °C (0.1 mm); IR (neat) 3350 (mw), 3040 (vw), 3010 (vw), 2910 (m), 2830 (mw), 1595 (m), 1495 (ms), 1470 (ms), 1440 (m), 1430 (m), 1355 (mw), 1330 (w), 1310 (ms), 1270 (ms), 1225 (w), 1190 (w), 1175 (w), 1150 (vw), 1105 (mw) cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.72–2.15 (m, 2 H), 1.92 (s, 3 H), 2.60–2.90 (m, 2 H), 3.18–3.46 (m, 2 H), 3.55 (s, 2 H), 4.35 (s, 1 H), 6.32–7.02 (cm, 3 H); ^{13}C NMR ($CDCl_3$) δ 14.43 (q), 21.68 (t), 27.18 (t), 35.28 (t), 41.88 (t), 115.84 (d), 119.85 (s), 121.99 (s), 128.29 (d), 128.64 (d), 142.98 (s); exact mass m/e 193.0935 (calcd for $C_{11}H_{15}NS$ 193.0924).

Anal. Calcd for $C_{11}H_{15}NS$: C, 68.35; H, 7.82; N, 7.25. Found: C, 68.25; H, 7.87; N, 7.31.

1-(Methylthio)-1,2,5,6-tetrahydro-4*H*-pyrrolo[3,2,1-*ij*]-quinolin-2-one (5). Chlorine (2.0 mL, 44 mmol) was condensed into a dry ice–acetone-cooled addition funnel at −78 °C. The chlorine was added dropwise to 100 mL of dry methylene chloride at −78 °C. To the resultant pale yellow solution, under a static nitrogen pressure, was added 6.5 g (48.5 mmol) of ethyl methylthioacetate in 15 mL of dry methylene chloride. The mixture was stirred at −78 °C for 25 min, and 11.72 g (88 mmol) of tetrahydroquinoline in 15 mL of dry methylene chloride was added dropwise. The reaction mixture was stirred for 4 h at −78 °C, followed by the addition of 20 mL of triethylamine. After being stirred for 1 h at −78 °C, the reaction mixture was allowed to warm to ambient temperature. To the reaction mixture was added 50 mL of 6 *N* hydrochloric acid, and the reaction mixture was stirred for 10 h. The organic layer was separated, dried over anhydrous sodium carbonate, filtered, and concentrated to give an oil, which was chromatographed on a Waters Prep 500 liquid chromatograph using a silica gel column with 20% ethyl acetate–80% hexane to yield 6.6 g (68%) of a solid, which was recrystallized from ether–hexane to give 5.1 g (53%) of **5**: mp 71.5–73.5 °C; IR ($CDCl_3$) 3060 (vw), 2490 (w), 2880 (w), 2840 (vw), 1635 (s), 1625 (m), 1600 (m), 1480 (m), 1435 (vw), 1380 (w) 1350 (ms), 1330 (w), 1295 (w), 1240 (w), 1195 (w), 1170 (w), 1155 (w), cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.80–2.20 (m, 2 H), 2.01 (s, 3 H), 2.60–2.90 (m, 2 H), 3.55–3.86 (m, 2 H), 4.17 (s, 1 H), 6.85–7.27 (cm, 3 H); ^{13}C NMR ($CDCl_3$) δ 11.99 (q), 20.73 (t), 23.92 (t), 38.50 (t), 46.31 (d), 119.70 (s), 121.34 (d), 122.16 (d), 123.83 (s), 127.30 (d), 139.48 (s) 173.44 (s); exact mass m/e 219.0713 (calcd for $C_{12}H_{13}NOS$ 219.0716).

Anal. Calcd for $C_{12}H_{13}NOS$: C, 65.72; H, 5.97; N, 6.39. Found: C, 65.79; H, 6.05; N, 6.41.

1-(Methylthio)-2-methyl-5,6-dihydro-4*H*-pyrrolo[3,2,1-*ij*]quinoline (7). Chlorine (2.0 mL, 44 mmol) was condensed into a dry ice–acetone-cooled additional funnel at −78 °C and then added dropwise to 150 mL of dry methylene chloride at −78 °C under a static nitrogen atmosphere. To this pale yellow solution was added 5.0 g (48 mmol) of 1-(methylthio)propan-2-one in 15 mL of dry methylene chloride. An off-white precipitate formed. After the reaction mixture had been stirred for 35 min, a solution of 11.72 g (88 mmol) of tetrahydroquinoline in 12 mL of dry methylene chloride was added dropwise. The reaction mixture was stirred for 2 h at −70 °C, followed by the addition of 25 mL of triethylamine. After being stirred for an additional hour at −70 °C, the reaction mixture was allowed to warm to ambient temperature over a 10-h period. The reaction mixture was extracted with dilute aqueous sodium hydroxide solution, dried over anhydrous sodium carbonate, filtered, and concentrated to give an oil. Chromatography of this oil on a Waters Prep 500 liquid chromatograph using a silica gel column with 5% ethyl acetate–95% hexane yielded 3.70 g (39%) of **7**. Recrystallization of **7** from hexane gave 3.10 g (32%) of analytically pure material: mp 91.5–93.5 °C; IR ($CDCl_3$) 3060 (w), 2940 (m), 2920 (m), 2860 (w), 2840 (vw), 1615 (vw), 1515 (w), 1490 (w), 1440 (m), 1395 (ms), 1375 (w), 1355 (w), 1330 (m), 1255 (m), 1180 (w), 1170 (m), 1050 (w) cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.0–2.40 (m, 2 H), 2.19 (s, 3 H), 2.42 (s, 3 H), 2.91 (t, 2 H), 3.94 (t, 2 H), 6.59–7.59 (cm, 3 H); ^{13}C NMR ($CDCl_3$) δ 9.82 (q), 19.97 (q), 22.56 (t), 24.42 (t), 41.78 (t), 102.29 (s), 115.67 (d), 118.19 (d), 119.75 (d), 121.09 (s), 127.32 (s), 133.68 (s), 139.00 (s); exact mass m/e 217.0926 (calcd for $C_{13}H_{15}NS$ 217.0924).

Anal. Calcd for $C_{13}H_{15}NS$: C, 71.84; N, 6.96; N, 6.44. Found: C, 71.76; H, 6.97; N, 6.35.

Acknowledgment. We are indebted to the National Institutes of Health for Grant GM-22346 which supported this investigation.

Registry No. **1**, 635-46-1; **2**, 88426-28-2; **3**, 50450-25-4; **4**, 88426-29-3; **5**, 88426-30-6; **6**, 50450-24-3; **7**, 88426-31-7; dimethylchlorosulfonium chloride, 23372-58-9; chlorine, 7782-50-5; ethyl methylthioacetate, 4455-13-4; 1-(methylthio)propan-2-one, 14109-72-9; dimethyl sulfide, 75-18-3.

Friedel–Crafts Chemistry: A New Synthetic Route for Polynuclear Compounds

Shashi B. Mahato,*[1a] Nirup B. Mandal,[1b] Anil K. Pal,[1b] and Swapan K. Maitra[1b]

Indian Institute of Chemical Biology, Jadavpur, Calcutta-700032, India, and Central Public Health & Drugs Laboratory, Calcutta-700015, India

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Friedel–Crafts reaction is one of the most useful reactions in organic chemistry. It has widely been used for the preparation of diverse types of products by alkylation, acylation, cycliacylation, and other miscellaneous types of reactions.[2] Although literature is scanty, haloacylation of organic compounds in Friedel–Crafts conditions has also been described.[2-4] Diacylaton of naphthalene derivatives by the use of excess of Friedel–Crafts reagents has been reported by Gore et al.[5-7] Haloacylation of anisole (1) and phenetole (2) (Chart I) using dichloroacetyl chloride has been reported long ago,[8] and as expected dichloroacylation took place in the para-position with respect to the ether group. In our efforts to prepare polynuclear derivatives by newer synthetic techniques, it was observed that Friedel–Crafts conditions may conveniently be adopted for preparation of such compounds by varying the temperature and proportions of the substrate and the catalyst. Aromatic ethers, e.g., anisole (1) and phenetole (2) were used as model substrates, dichloroacetyl chloride as the reactant, and the versatile anhydrous $AlCl_3$ as the catalyst. The products that were obtained are reported in this paper.

Results and Discussion

It is well-known that when substrates are employed in unimolar proportions in Friedel–Crafts reaction normal

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