Experimental Section

General. Reactions were carried out in an inert atmosphere using predried (sodium benzophenone ketyl) and distilled THF. Haloalkanes were obtained commercially. Product mixtures were separated to obtain analytical data by medium-pressure chromatography using an EM Lobar Si 60 column with 10% diethyl ether–90% ligroin (60–80 °C) as eluent. Quantitative analysis of the reaction mixtures was accomplished on a Waters 6000 HPLC using an IBM silica column with 15% diethyl ether–85% ligroin (60–80 °C). The UV detector was calibrated on known product mixtures. NMR spectra were obtained using a Varian EM-390 spectrometer.

General Alkylation Procedure. One millimole each of the sulfone and base were added to 7–15 mL of THF and allowed to stir for 1 h at 0 °C. One millimole of the alkylating agent was added at that same temperature, and the mixture was allowed to stir at room temperature for 5 h. Addition of 5 mL of water, ether extraction, drying with $MgSO_4$, and removal of the solvent via a rotary evaporator provided the product mixture.

Kinetic Reactions. Six millimoles of the appropriate sulfone in THF and of butyllithium were mixed at 0 °C. After 1 h the slurry was brought to room temperature, and then 6 mmol of bromoalkane was added. Alliquots (1 mL) were removed and quenched with water at specific times. The samples were recovered as above and analyzed by HPLC.

Equilibration–Deuterium Quench. An equimolar mixture of butyllithium, sulfone 1, and sulfone **4a** were stirred for 1 h at 0 °C in 7 mL of THF. Deuterium oxide was added to the mixture, and the products were recovered as above, separated by medium-pressure chromatography, and analyzed for deuterium content by NMR spectroscopy.

Deuterium Quench. An equimolar mixture of 1 and butyllithium were stirred in 7 mL of THF at 0 °C for 1 h. Deuteriosulfuric acid (1 M) was added, and the product was recovered as above and analyzed for deuterium content by NMR spectroscopy.

Methyl phenyl sulfone (1): via oxidation of methyl phenyl sulfide with 30% hydrogen peroxide in acetic acid;[18] 91%; mp 87.4–89.6 °C (lit.[18b] mp 86–88 °C); ^{1}H NMR ($CDCl_3$) δ 3.0 (s, 3), 7.5–7.8 (m, 5).

Butyl phenyl sulfone (4a): ^{1}H NMR (CCl_4) δ 0.9 (t, 3, J = 6 Hz), 1.1–1.9 (m, 4), 3.0 (t, 2, J = 6 Hz), 7.3–7.9 (m, 5). Anal. Calcd for $C_{10}H_{14}O_2S$: C, 60.58; H, 7.12. Found: C, 60.71; H, 7.20.

4-Heptyl phenyl sulfone (5a): ^{1}H NMR (CCl_4) δ 0.9 (t, 6, J = 6 Hz), 1.1–1.9 (m, 8), 2.6–2.9 (m, 1), 7.2–7.9 (m, 5). Anal. Calcd for $C_{13}H_{20}O_2S$: C, 64.96; H, 8.39. Found: C, 64.79; H, 8.07.

4-(4-Propylheptyl) phenyl sulfone (6a): ^{1}H NMR ($CDCl_3$) δ 0.8 (t, 9, J = 6 Hz), 1.2–1.8 (m, 12), 7.3–7.8 (m, 5). Anal. Calcd for $C_{16}H_{26}O_2S$: C, 68.04; H, 9.27. Found: C, 67.93; h, 9.29.

Pentyl phenyl sulfone (4b): ^{1}H NMR (CCl_4) δ 0.8 (t, 3, J = 6 Hz), 1.0–1.9 (m, 6), 2.8–3.1 (m, 2), 7.3–8.0 (m, 5). Anal. Calcd for $C_{11}H_{16}O_2S$: C, 62.23; H, 7.60. Found: C, 62.18; H, 7.64.

5-Nonyl phenyl sulfone (5b): ^{1}H NMR (CCl_4) δ 0.8 (6 t, J = 6 Hz), 1.0–2.0 (m, 12), 2.6–2.8 (m, 1), 7.4 (m, 3), 7.8 (m, 2). Anal. Calcd for $C_{15}H_{24}O_2S$: C, 67.12; H, 9.01. Found: C, 67.31; H, 8.83.

5-(5-Butylnonyl) phenyl sulfone (6b): ^{1}H NMR ($CDCl_3$) δ 0.7–1.8 (m, 27), 7.3–7.8 (m, 5). Anal. Calcd for $C_{19}H_{32}O_2S$: C, 70.32; H, 9.93. Found: C, 70.23; H, 9.94.

4-Pentenyl phenyl sulfone (4c): ^{1}H NMR (CCl_4) δ 1.5–2.4 (m, 4), 2.8–3.1 (m, 2), 4.8–5.1 (m, 2), 5.4–5.9 (m, 1), 7.4–7.9 (m, 5). Anal. Calcd for $C_{11}H_{14}O_2S$: C, 62.83; H, 6.71. Found: C, 62.82; H, 6.63.

5-(1,8-Nonadienyl) phenyl sulfone (5c): ^{1}H NMR (CCl_4) δ 1.4–2.4 (m, 8), 2.7–2.9 (m, 1), 4.7–5.1 (m, 4), 5.3–5.8 (m, 2), 7.4–7.8 (m, 5). Anal. Calcd for $C_{15}H_{20}O_2S$: C, 68.14; H, 7.62. Found: C, 68.26; H, 7.70.

5-[5-(3-Butenyl)-1,8-nonadienyl] phenyl sulfone (6c): ^{1}H NMR (CCl_4) δ 1.5–1.8 (m, 6), 1.9–2.3 (m, 6), 4.7–5.1 (m, 6), 5.4–5.8 (m, 3), 7.3–7.8 (m, 5). Anal. Calcd for $C_{19}H_{26}O_2S$: C, 71.66; H, 8.23. Found: C, 71.36; H, 8.29.

3-Butenyl phenyl sulfone (4d): ^{1}H NMR (CCl_4) δ 2.1–2.5 (m, 2), 2.8–3.1 (m, 2), 4.8–5.1 (m, 2), 5.3–5.8 (m, 1), 7.2–7.9 (m, 5). Anal. Calcd for $C_9H_{10}O_2S$: C, 61.20; H, 6.16. Found: C, 61.13; H, 6.23.

4-(1,6-Heptadienyl) phenyl sulfone (5d): ^{1}H NMR (CCl_4) δ 2.1–2.7 (m, 4), 2.8–3.2 (m, 1), 4.8–5.2 (m, 4), 5.4–6.0 (m, 2), 7.3–8.0 (m, 5). Anal. Calcd for $C_{13}H_{16}O_2S$: C, 66.07; H, 6.82. Found: C, 66.18; H, 6.75.

4-[4-(2-Propenyl)-1,6-heptadienyl] phenyl sulfone (6d): ^{1}H NMR (CCl_4) δ 2.4 (d, 6, J = 9 Hz), 4.8–5.2 (m, 6), 5.5–6.1 (m, 3), 7.3–7.9 (m, 5). Anal. Calcd for $C_{16}H_{20}O_2S$: C, 69.53; H, 7.29. Found: C, 69.41; H, 7.24.

2-Phenylethyl phenyl sulfone (4e): ^{1}H NMR (CCl_4) δ 2.7–3.3 (m, 4), 7.0 (s, 5), 7.2–7.9 (m, 5). Anal. Calcd for $C_{14}H_{14}O_2S$: C, 68.27; H, 5.73. Found: C, 68.33; H, 5.35.

2-(1,3-Diphenylpropyl) phenyl sulfone (5e): ^{1}H NMR ($CDCl_3$) δ 2.5–3.4 (m, 5), 6.6–7.8 (m, 15). Anal. Calcd for $C_{21}H_{20}O_2S$: C, 74.97; H, 5.99. Found: C, 74.92; H, 6.03.

2-Benzyl-1,3-diphenylpropyl phenyl sulfone (6e): ^{1}H NMR ($CDCl_3$) δ 3.2 (s, 6), 7.2 (s, 20). Anal. Calcd for $C_{28}H_{26}O_2S$: C, 78.84; H, 6.14. Found: C, 78.74; H, 6.24.

Registry No. 1, 3112-85-4; **3a**, 106-94-5; **3b**, 109-65-9; **3c**, 5162-44-7; **3d**, 106-95-6; **3e**, 100-39-0; **4a**, 16823-62-4; **4b**, 34009-04-6; **4c**, 41795-36-2; **4d**, 67100-44-1; **4e**, 27846-25-9; **5a**, 124992-95-6; **5b**, 105494-88-0; **5c**, 125023-16-7; **5d**, 124992-96-7; **5e**, 124992-97-8; **6a**, 124992-98-9; **6b**, 124992-99-0; **6c**, 124993-00-6; **6d**, 124993-01-7; **6e**, 124993-02-8; MeSPh, 100-68-5.

(18) (a) Cram, D. J.; Scott, D. A.; Nielson, W. D. *J. Am. Chem. Soc.* **1961**, *83*, 3696. (b) Field, L.; Clark, R. D. *J. Org. Chem.* **1957**, *22*, 1129.

Synthesis of 2-Octalones from Quinaldine

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The addition of a methyl vinyl ketone unit to a cyclic ketone to form a new carbocyclic ring (the Robinson annulation[1]) has found many applications in the synthesis of organic compounds.[2] Since the reaction in its original form suffers from low yields and only moderate regiochemical control, synthetic chemists have developed various alternatives, many of which have been applied to the total synthesis of natural products.[3] In this connection, heterocycles in which lie "hidden" or "masked" ketones or enols have proven especially fruitful.[4]

We have developed a synthetic method by which one can efficiently convert 2-alkylquinolines into 2-octalones, which are important intermediates in many steroid and terpenoid total syntheses.[2] Such a transformation is of significant potential importance in view of the commercial availability of a variety of quinolines and tetrahydroquinolines,[5] as well as the many heterocycle syntheses by which virtually any substituted quinoline may be prepared.[6]

In this paper we report the conversion of the tar distillate product quinaldine (1) into 2-octalone **3**. We then demonstrate that quinaldine may be functionalized by alkylation and subsequently converted into 1-substituted-2-octalones.

As shown in Scheme I, quinaldine was hydrogenated in neat trifluoroacetic acid (TFA) as described by Vierhapper and Eliel.[7] The methiodide **2** was formed by allowing the above compound to stir in iodomethane followed by recrystallization from 2-propanol/ether. This material was not very hygroscopic and was easy to handle when prepared in this way. Birch reduction and hydrolysis provided

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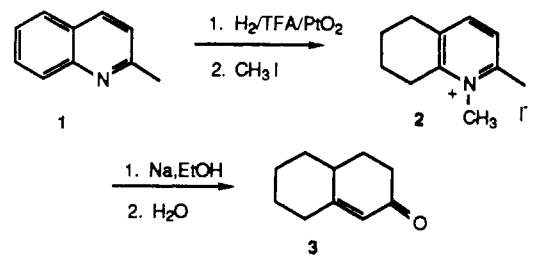
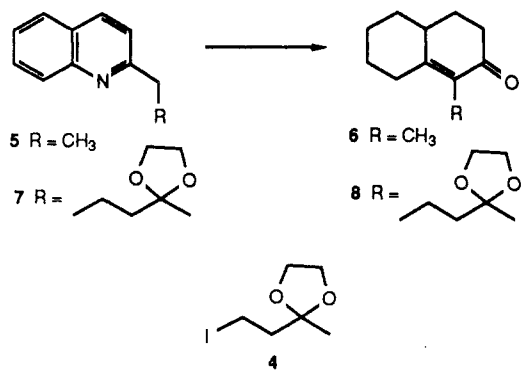
Scheme I



Scheme II

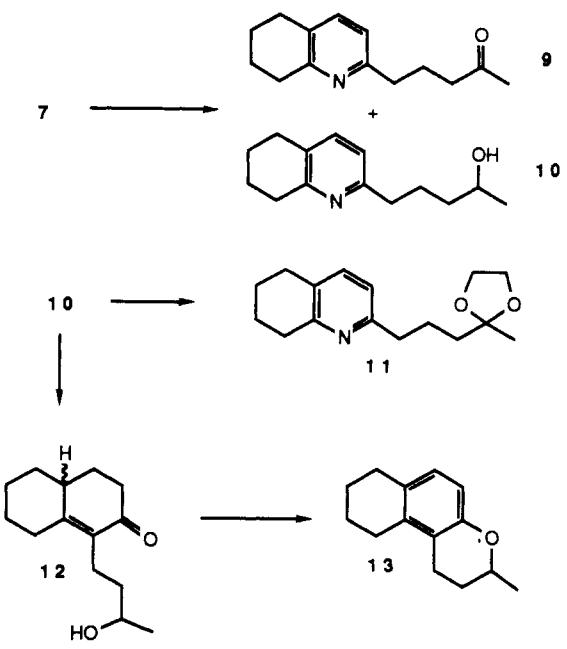


2-octalone[8] in 75–85% overall yield. This last step was inspired by the work of Danishefsky and co-workers,[9] who worked with derivatives of 2-methyl-6-vinylpyridine. In our case, the Birch reduction and subsequent hydrolysis proceeds much more efficiently when carried out on the pyridinium methiodide than on the simple pyridine.[10]

In a second study, 2-ethylquinoline (**5**), which we either purchased or made by deprotonation with *n*-butyllithium in tetrahydrofuran and alkylation[11] with iodomethane, was similarly converted into 1-methyl-2-octalone (**6**) (Scheme II). We found that slightly longer reaction times were required for the methiodide formation and for the final hydrolysis, but that the overall yield of **6** was still 75–85%.

Finally, we wished to append a substituent to the quinaldine that could later be elaborated into an additional carbocyclic ring. The target we choose was compound **8**, the corresponding diketone of which is an intermediate in the preparation of a tricyclic dienone.[12] Thus, compound

Scheme III



7 was prepared by deprotonation of quinaldine[13] and alkylation with the iodo ketal **4**.[14] Although the hydrogenation in concentrated acid did not proceed cleanly, we found that if the reaction was stopped at 40% conversion to the tetrahydro product, the yield of the ketone was 92%, with very little alcohol being formed. The partially hydrogenated and unhydrogenated materials were readily separable by flash chromatography so that the 2-(4-oxopentyl)quinoline could be recycled. Alternatively, if much longer hydrogenation times were utilized, pure **10** was isolated (90% yield) after Kugelrohr distillation and could be subjected to Swern oxidation to provide ketone **9**. Ketal **11** was formed from **9** and ethylene glycol in the presence of *p*-toluenesulfonic acid in 76% yield. Quaternization of compound **11** followed by reduction and cyclization provided enone **8** in pure form (76% yield) after bulb-to-bulb distillation.

In an attempt to bypass the oxidation and reketalization steps, compound **12** was prepared from the alcohol **10** (Scheme III). However, the mixture of diastereomers that was obtained could not be adequately characterized and several attempts at oxidation produced mainly compound **13**. Compound **12** apparently exists partially in the cyclic hemiketal state.

In summation, we have developed an efficient and convenient synthesis of 2-octalone and 1-alkyl-2-octalones. The synthesis begins with cheap starting materials, is readily adaptable to the preparation of analogues, and produces cyclic enones in excellent yield. It shows great promise as a versatile tool for the synthesis of natural products.

Experimental Section

***N*,2-Dimethyl-5,6,7,8-tetrahydroquinolinium Iodide (2).** Tetrahydroquinaldine (9.0 g, 62.8 mmol) was dissolved in iodomethane (35 mL) and stirred at room temperature overnight. The iodomethane was removed by distillation and the yellow residue immediately recrystallized from dry 2-propanol/diethyl ether.

(1) Rapson, W. S.; Robinson, R. *J. Chem. Soc.* **1935**, 1285–1288.
(2) (a) Jung, M. E. *Tetrahedron* **1976**, *32*, 3–31. (b) Gawley, R. E. *Synthesis* **1976**, 777–794.
(3) (a) Danishefsky, S.; Cavanaugh, R. *J. Am. Chem. Soc.* **1968**, *90*, 520–521. (b) Stork, G. *Pure Appl. Chem.* **1964**, *9*, 131–144.
(4) (a) Stork, G.; Danishefsky, S.; Ohashi, M. *J. Am. Chem. Soc.* **1967**, *89*, 5459. (b) Stork, G.; McMurry, J. E. *J. Am. Chem. Soc.* **1967**, *89*, 5463–5465. (c) Kametani, T.; Nemoto, H. *Heterocycles* **1978**, *10*, 349–390. (d) Scott, J. W.; Saucy, G. *J. Org. Chem.* **1972**, *37*, 1652–1658, 1659–1663. (e) Yamamoto, M.; Iwasa, S. Takatsuki, K.; Yamada, K. *J. Org. Chem.* **1986**, *51*, 346–349.
(5) Besche, B. *Aldrichimica Acta* **1978**, *11*, 13–16.
(6) (a) Claret, P. A.; Osborne, A. G. In *Heterocyclic Compounds*; Jones, G., Ed.; John Wiley & Sons: New York, 1982; Vol. 32, Part 2, pp 1–352. (b) Jones, G. In *Heterocyclic Compounds*; Jones, G., Ed.; John Wiley & Sons: New York, 1977; Vol. 32, Part 1, pp 93–318.
(7) Vierhapper, F. W.; Eliel, E. L. *J. Org. Chem.* **1975**, *40*, 2729–2734.
(8) Augustine, R. L.; Caputo, J. A. *Organic Syntheses*; Baumgarten, H. E., Ed., John Wiley & Sons: New York, 1973, Collect. Vol. V, p 869.
(9) (a) Danishefsky, S.; Cain, P.; Nagel, A. *J. Am. Chem. Soc.* **1975**, *97*, 380–387. (b) Danishefsky, S.; Cain, P. *J. Am. Chem. Soc.* **1976**, *98*, 4975–4980. (c) Danishefsky, S.; Zimmer, A. *J. Org. Chem.* **1976**, *41*, 4059–4064.
(10) de Koning, A. J.; Budzelaar, P. H. M.; Brandsma, L.; de Bie, M. J. A.; Boersma, J. *Tetrahedron Let.* **1980**, *21*, 2105–2108.
(11) (a) Bergstrom, F. W. *J. Am. Chem. Soc.* **1931**, *53*, 3027–3039. (b) Ayer, W. A.; Dame, R.; Eisner, R. A.; Furuichi, K. *Can. J. Chem.* **1976**, *54*, 473–481.
(12) Tsuji, J.; Shimizu, I.; Suzuki, H.; Naito, Y. *J. Am. Chem. Soc.* **1979**, *101*, 5070–5072.
(13) We originally attempted alkylation of 2-methyl-5,6,7,8-tetrahydroquinoline using alkyllithium reagents or LDA in THF at low temperatures, but poor selectivity was obtained, and the product mixtures were difficult to separate.
(14) Francis, R. F.; Howell, H. M.; Fetzer, D. T. *J. Org. Chem.* **1981**, *46*, 2213–2215.

Light brown needles (14.7 g, 51.5 mmol, 82%) were thus obtained, which were only slightly hygroscopic and could be stored in a desiccator for weeks: mp 128–129 °C (lit.[15] mp 125–128 °C); IR (neat film) 3020, 1609, 1582, 1491, 1413 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 7.95 (d, J = 8 Hz, 1 H, Ar-H), 7.62 (d, J = 8 Hz, 1 H, Ar-H), 4.20 (s, 3 H, NCH_3), 3.18 (t, J = 6.6 Hz, 2 H, ArCH_2), 2.93–2.89 (m, 5 H, overlapping frequencies), 2.18–1.97 (m, 2 H, CH_2), 1.90–1.78 (m, 2 H, CH_2); ^{13}C NMR (22.5 MHz, $CDCl_3$) δ 154.0, 152.6, 144.0, 136.0, 125.9, 40.9, 28.6, 28.0, 22.4, 20.9, 19.4.

4,4a,5,6,7,8-Hexahydro-2(3*H*)-naphthalenone (3). Pyridinium methiodide **2** (4.80 g, 16.8 mmol) was added to 100 mL of liquid ammonia (freshly distilled from sodium) along with 4.5 mL of dry methanol and 20 mL of dry diethyl ether. Sodium metal (0.775 g, 33.7 mmol) was added in small chunks. The ammonia was evaporated and 150 mL of a 2:1 methanol/water solution (degassed with nitrogen) was added. The solution was heated at 50 °C for 3 h. The green solution was cooled, acidified with 2 N HCl, and concentrated. Distilled water (40 mL) was added to the residue and extractive isolation was carried out with ether. The combined organic layers were washed with brine, dried over Na_2SO_4, and concentrated. Filtration of the resulting oil through Florisil yielded the product (2.31 g, 15.4 mmol, 92%), which appeared to be homogeneous by TLC (silica, 2:1 hexane/ethyl acetate, R_f = 0.3), although a slight yellow color could be removed by distillation (bp 76–80 °C, 0.5 Torr; lit.[16] bp 101–102 °C, 2–3 Torr): UV (CH_3CN) λ_{max} = 234.0 nm (lit[16] 234.5 nm); semicarbazone mp 211–212 °C (lit.[16] mp 215 °C).

2-Ethyl-*N*-methyl-5,6,7,8-tetrahydroquinolinium Iodide. Freshly distilled 2-ethyl-5,6,7,8-tetrahydroquinoline was treated as described for the preparation of **2** with the exception that the iodomethane solution was stirred for 24 h. Light brown crystals were obtained (16.0 g, 52.8 mmol, 80%) after recrystallization: mp 109–110 °C; IR (KBr) 3020, 2932, 1605, 1578, 1050 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 7.94 (d, J = 8.3 Hz, Ar-H), 7.57 (d, J = 8.3 Hz, 1 H, Ar-H), 4.15 (s, 3 H, NCH_3), 3.14–3.08 (m, 4 H, Ar-CH_2), 2.89–2.83 (m, 2 H, Ar-CH_2), 2.0–1.8 (m, 2 H, CH_2), 1.80–1.75 (m, 2 H, CH_2), 1.33 (t, J = 7.3 Hz, 3 H, CH_2CH_3); ^{13}C NMR (22.5 MHz, $CDCl_3$) δ 158.8, 155.9, 145.5, 136.9, 125.0, 40.1, 29.5, 28.9, 22.4, 20.9, 12.3, 7.0.

4,4a,5,6,7,8-Hexahydro-1-methyl-2(3*H*)-naphthalenone (6). Dry 2-ethyl-*N*-methyl-5,6,7,8-tetrahydroquinolinium iodide (1.74 g, 6.11 mmol) was added to a solution of liquid NH_3 (70 mL, freshly distilled from Na), THF (7 mL), and methanol (14 mL). Sodium (0.296 g, 12.6 mmol) was added in small chunks. The ammonia was evaporated and 60 mL of a 50% aqueous ethanol solution (degassed with N_2) was added. The reaction mixture was brought to reflux for 3 h. After cooling, it was acidified with 2 N HCl. Extractive isolation with CH_2Cl_2 yielded 0.930 g (5.66 mmol, 93%) of **6** which appeared to be homogeneous by ^1H NMR and TLC (silica, 1:3 ethyl acetate/hexane, R_f = 0.48) and had identical spectral characteristics with a sample prepared by established methods:[17] UV (ethanol) λ_{max} = 245.5 nm (lit.[17] 246 nm); IR (neat film) 1663, 1612 (lit.[17] 1670, 1605) cm^{-1}.

2-[3-(2-Methyl-1,3-dioxolan-2-yl)propyl]quinoline (7). Quinaldine (2.50 g, 17.5 mmol) was dissolved in dry THF (35 mL). The reaction vessel was cooled to −78 °C and *n*-butyllithium in hexanes (10.9 mL, 17.5 mmol) was added. After 30 min, the iodide **4** (5.57 g, 23.0 mmol) was added via syringe. The mixture was allowed to gradually warm to room temperature while being stirred overnight. The resulting light yellow solution was concentrated, diluted with water (75 mL) and brine (25 mL), and extracted thrice with 75-mL portions of CH_2Cl_2. The combined organic layers were dried over Na_2SO_4. After concentration, flash chromatography on silica (2:1 hexane/ethyl acetate, R_f = 0.28) yielded compound **7** (3.96 g, 15.4 mmol, 88%) as a slightly yellow oil: IR (neat film) 3040, 2940, 1615, 1595, 1050 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 8.08–7.97 (m, 2 H, Ar-H), 7.76–7.62 (m, 2 H, Ar-H), 7.45 (t, J = 8.5 Hz, 1 H, Ar-H), 7.38 (d, J = 8.5 Hz, 1 H, Ar-H), 3.88 (s, 4 H, OCH_2), 2.98 (t, J = 8.5 Hz, 2 H, CH_2), 2.13–1.61 (m, 4 H, CH_2), 1.39 (s, 3 H, CH_3); MS (200 °C, 70 eV) m/e 257 (5.4), 212 (46.2), 170 (26.7), 143 (88.9), 87 (100.0); high resolution MS (200 °C, 70 eV) calcd for $C_{16}H_{19}NO_2$ m/e 257.1417, found 257.1410.

2-(4-Hydroxypentyl)-5,6,7,8-tetrahydroquinoline (10). Ketal **7** (1.37 g, 5.32 mmol) was placed in a pressure bottle with 40 mL of fresh trifluoroacetic acid and 0.2 g of PtO_2. The reaction mixture was placed at 60 psi on a Parr hydrogenation apparatus. The reaction was complete after 14 h (NMR spectrum of the reaction mixture). The mixture was then filtered through Celite to remove the catalyst, diluted with 50 mL of water, and finally made basic with 6 N NaOH. Extractive isolation of the product with diethyl ether followed by bulb-to-bulb distillation afforded a clear viscous oil (1.06 g, 4.81 mmol, 90%): IR (neat film) 3600–3000, 1592, 1569, 1467, 1120 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 7.19 (d, J = 8 Hz, 1 H, Ar-H), 6.82 (d, J = 8 Hz, 1 H, Ar-H), 3.77 (q, J = 6, 1 H, CHOH), 3.49 (br s, 1 H, OH), 2.82 (t, J = 6 Hz, 2 H, CH_2), 2.7–2.5 (m, 4 H, CH_2), 2.0–1.7 (m, 6 H), 1.7–1.5 (m, 2 H, CH_2), 1.12 (d, J = 6 Hz, 3 H, CH_2); ^{13}C NMR (22.5 MHz, $CDCl_3$) δ 158.7, 156.2, 137.1, 129.2, 119.8, 67.0, 38.6, 37.2, 32.2, 28.3, 25.8, 23.4, 23.0, 22.6; MS (180 °C, 70 eV) m/e 219 (M^+, 1.1), 204 (3.1), 174 (25.5), 160 (21.7), 147 (100.0); high resolution MS (200 °C, 70 eV) calcd for $C_{14}H_{21}NO$ m/e 219.1624, found 219.1623. Anal. Calcd: C, 76.67; H, 9.65. Found: C, 76.60; H, 9.66.

2-(4-Oxopentyl)-5,6,7,8-tetrahydroquinoline (9) (From Oxidation of **10**). Oxalyl chloride (0.425 g, 3.35 mmol) was dissolved in dry CH_2Cl_2 (75 mL) and cooled to −78 °C. A solution of DMSO (0.52 mL, 7.3 mmol) in 1.5 mL of CH_2Cl_2 was added dropwise by syringe. Ten minutes later, alcohol **10** (0.668 g, 3.05 mmol) was also added by syringe. After 15 min, triethylamine (1.9 mL) was added over 2–3 min. The mixture was allowed to slowly warm to room temperature, and 90 mL of water was added. The solution was then concentrated, aqueous NaOH (10 mL of a 6 N solution) and 25 mL of H_2O were added, and the mixture was extracted with three 50-mL portions of ether. The combined organic layers were washed with brine, dried over Na_2SO_4, and concentrated. Silica chromatography of the product utilizing ethyl acetate as eluant (R_f = 0.4) provided **9** as a clear oil (0.4499 g, 2.07 mmol, 68%): IR (neat film) 2920, 1705, 1587, 1564, 1460 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 7.28 (d, J = 8 Hz, 1 H, Ar-H), 6.86 (d, J = 8 Hz, 1 H, Ar-H), 2.88 (t, J = 5 Hz, 2 H, CH_2), 2.75 (t, J = 7 Hz, 2 H, CH_2), 2.47 (t, J = 7 Hz, 2 H, CH_2), 2.12 (s, 3 H, CH_3), 1.97–1.75 (m, 8 H, CH_2); ^{13}C NMR (22.5 MHz, $CDCl_3$) δ 207.6, 157.4, 155.8, 136.5, 128.7, 119,2, 42.3, 36.5, 32.0, 29.2, 27.8, 23.5, 22.5, 22.2; MS (180 °C, 70 eV) m/e 217 (M^+, 6.8), 174 (37.8), 160 (44.6), 147 (100.0); high resolution MS (200 °C, 70 eV) calcd for $C_{14}H_{19}NO$ m/e 217.1467, found 217.1465. Anal. Calcd: C, 77.38; H, 8.81. Found: C, 77.43; H, 8.85.

2-(4-Oxopentyl)-5,6,7,8-tetrahydroquinoline (9) (Directly from Quinaldine without Isolating Any Intermediates). Quinaldine (4.00 g, 0.9279 mmol) was dissolved in 70 mL of dry THF. The mixture was cooled to −78 °C and 11.6 mL of *n*-butyllithium (2.4 M, 27.8 mmol) was added. The mixture was allowed to warm to about 0 °C for 5 min and then cooled to −78 °C again. Iodo ketal **4** was then added via syringe, and the solution was allowed to slowly warm to ambient temperature. The reaction was quenched after 14–16 h by the addition of 40 mL of 2 N HCl. The mixture was concentrated and washed with two 40-mL portions of diethyl ether. The aqueous layer was then made basic with concentrated NaOH solution, extracted with three 40-mL portions of ether which were combined, washed with brine, dried over Na_2SO_4, and concentrated. This produced about 7 g of a brown oil, which was dissolved in 50 mL of fresh TFA. The catalyst PtO_2 (0.1 g) was added and the mixture placed in a pressure bottle and shaken under 50 psi H_2 for 6 h, after which time another 0.05 g of PtO_2 was added. Twelve hours later, the bottle was removed and the solution was filtered through Celite and concentrated. The concentrate was made basic with 6 N NaOH while cooling with ice and then extracted with three 40-mL portions of diethyl ether. These were dried over Na_2SO_4 and concentrated. Flash chromatography (silica, 50% ethyl acetate/hexane) gave 2.38 g (11.3 mmol) of deprotected starting material and 2.29 g (10.5 mmol) of ketopyridine **9** (37.8% conversion, 92.8% yield).

5,6,7,8-Tetrahydro-2-[3-(2-methyl-1,3-dioxolan-2-yl)-propyl]quinoline (11). Pyridyl ketone **9** (1.25 g, 5.25 mmol) was dissolved in benzene (50 mL). Toluenesulfonic acid (0.11 g) was added and the solution was brought to reflux for 24 h. Saturated

(15) Giam, C. S.; Abbott, S. D. *J. Am. Chem. Soc.* **1971**, *93*, 1294–1296.
(16) (a) du Feu, E. C.; McQuillin, F. J.; Robinson, R. *J. Chem. Soc.* **1937**, 53–60. (b) Birch, A. J. *J. Chem. Soc.* **1944**, 430–436.
(17) Stork, G.; Brizzolara, A.; Landesman, H.; Szmuszkovicz, J.; Terrell, R. *J. Am. Chem. Soc.* **1963**, *85*, 207–222.

aqueous $NaHCO_3$ (20 mL) solution and water (25 mL) were added and the layers were separated. The aqueous phase was further extracted with two 25-mL portions of diethyl ether. The combined organic fractions were dried over Na_2SO_4 and concentrated. The remaining yellow oil was purified by flash chromatography (silica, ethyl acetate, R_f = 0.3), affording 1.83 g (3.41 mmol, 59%) of the product as a clear oil: IR (neat film) 2905, 1590, 1565, 1460, 1050 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 7.26 (d, J = 8 Hz, 1 H, Ar-*H*), 6.88 (d, J = 8 Hz, 1 H, Ar-*H*), 3.91 (s, 4 H, OCH_2), 2.89 (t, J = 6 Hz, 2 H, $arCH_2$), 2.76–2.68 (m, 4 H, CH_2), 1.93–1.63 (m, 8 H), 1.31 (s, 3 H, CH_3); ^{13}C NMR (22.5 MHz, $CDCl_3$) δ 142.1, 140.2, 124.8, 118.4, 110.8, 103.0, 66.7 (double intensity), 46.1, 45.6, 41.2, 37.8, 34.9, 34.3, 33.9, 33.6; MS (170 °C, 70 eV) m/e 261 (M^+, 20.1), 246 (23.1), 216 (72.1), 174 (71.2), 160 (31.9), 147 (86.4), 87 (88.8); high resolution MS (150 °C, 70 eV) calcd for $C_{16}H_{23}NO_2$ m/e 261.1730, found 261.1729. Anal. Calcd: C, 73.53; H, 8.87. Found: C, 73.63; H, 8.84.

4,4a,5,6,7,8-Hexahydro-1-[3-(2-methyl-1,3-dioxolan-2-yl)-propyl]-2(3*H*)-naphthalenone (8). Pyrido ketal 11 (0.851 g, 3.26 mmol) was dissolved in 10 mL of iodomethane and stirred overnight. The iodomethane was concentrated at reduced pressure, leaving a dark oil. This was dried at high vacuum (10^{-4} Torr) overnight to remove traces of solvent. The oil was rinsed with ethanol (0.75 mL) and THF (3.7 mL) into condensed ammonia (40 mL), which had been distilled from sodium. To this solution was added 0.15 g (6.5 mmol) of sodium metal in small portions. The ammonia was then removed and a degassed equivolume solution of ethanol and water (30 mL) was added. The mixture was brought to reflux for 1 h. The solution was concentrated and diluted with 20 mL of water. Extractive isolation with CH_2Cl_2 followed by bulb-to-bulb distillation afforded 0.657 g (2.48 mmol, 76%) of a clear oil: UV (ethanol) λ_{max} = 248.1 nm; IR (neat film) 2909, 1603, 1610, 1445, 1360, 1050 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 3.93 (s, 4 H, OCH_2), 2.91–1.81 (m, 1 H, C_3CH), 2.46–1.22 (m, 19 H, overlapping frequencies); ^{13}C NMR (22.5 MHz, $CDCl_3$) δ 198.6, 159.7, 132.7, 109.6, 64.4 (double intensity), 38.6, 38.2, 36.2, 34.8, 30.8, 28.5, 27.0, 25.4, 23.3, 19.5; MS (170 °C, 70 eV) m/e 264 (M^+, 3.0), 249 (4.7), 204 (6.2), 105 (4.3), 91 (9.0), 87 (100.0), 43 (43.3); high resolution MS (200 °C, 70 eV) calcd for $C_{16}H_{24}O_3$ m/e 264.1726, found 264.1726. Anal. Calcd: C, 72.69; H, 9.15. Found: C, 72.65; H, 9.12.

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Registry No. 1, 91-63-4; 2, 56826-62-1; 3, 1196-55-0; 4, 53750-51-9; 5, 1613-34-9; 6, 5164-37-4; 7, 124992-61-6; 8, 124992-62-7; 9, 124992-63-8; 10, 124992-64-9; 11, 124992-65-0; 12 (isomer 1), 124992-66-1; 12 (isomer 2), 124992-68-3; 13, 75608-57-0; 5,6,7,8-tetrahydroquinaldine, 2617-98-3; 2-ethyl-*N*-methyl-5,6,7,8-tetrahydroquinolinium iodide, 124992-67-2; 2-ethyl-5,6,7,8-tetrahydroquinoline, 56717-33-0; 2-(4-oxopentyl)quinoline, 92247-61-5.

2,2-Dichlorovinyl Chloroformate

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Many members of modern generations of insecticides continue to take advantage of the toxicity to insects of particular patterns of halogens in the molecule but now they also contain functionalities guaranteeing ready degradation by environmental agents. Examples include the 2,2-dichlorovinyl group in Dichlorvos (1) and similar 2,2-dihalovinyl units in pyrethrin analogues.[2] In an obscure report, activity as pesticides and as synergists for increasing the toxicity of insecticides also is attributed to *O*-(2,2-dichlorovinyl) carbonates and carbamates.[3] However, real progress in this area has been stifled because 2,2-dihalovinyl chloroformates (2) are unknown. If available, the reagents 2 also might be attractive monomers and acid-stable/base-labile hydroxyl masking agents.

$Cl_2C{=}CHOP(=O)(OMe)_2$ (1) $\qquad$ $X_2C{=}CHOC(=O)Cl$ (2)

Among related compounds, only vinyl chloroformate itself [$H_2C{=}CHOC(=O)Cl$] and a few simple enol chloroformates have been made previously. While these reagents are tedious to prepare,[4] they have proved useful in alcohol and amine protection,[5] as N-dealkylation agents,[6] and as monomers in polymer chemistry.[7] In this paper, we describe a simple and quite surprising synthesis of 2 (X = Cl or Br).

In a continuing collaboration between SNPE and this laboratory, a rapid and economical synthesis of α-chloroalkyl chloroformates by treatment of aldehydes with phosgene in the presence of a reusable "naked Cl^-" catalyst, preferably benzyltributylammonium chloride (BTBAC), has been described.[8] When this reaction is applied with chloral as the aldehyde component, the tetrachloroethyl chloroformate **3a** is obtained in 65% yield. The bromal reaction is slower (2 days vs 1 h) and the chloroformate **3b** yield is lower (33%). If the chloroformates 3 could be induced to undergo a Boord elimination of halogen, the desired products 2 would be available from a simple two-step process.

$$X_3CCHO + COCl_2 \rightarrow X_3CCH(Cl)OC(=O)Cl \rightarrow X_2C{=}CHOC(=O)Cl$$

3a: X = Cl; **3b**: X = Br; **2a**: X = Cl; **2b**: X = Br

However, several excellent precedents would seem to negate a favorable outcome for such a scheme. First, when Favorskii treated 2,2,2-trichloroethyl acetate with zinc in 1899, he not only discovered the first synthesis of 1,1-dichloroethylene but also found that the process was dramatically exothermic.[9] Since chloroformate anion is a better leaving group than acetate,[10] it should compete with

(1) Adapted and condensed from the Ph.D. Dissertation of M. P. Bowman, The Pennsylvania State University, University Park, PA, 1986.

(2) Worthing, C. R., Ed. *The Pesticide Manual*, 7th ed.; British Crop Protection Council, 1983. Ware, G. W. *The Pesticide Book*; Freeman: San Francisco, 1978; p 47.

(3) Kay, I. T.; Punja, N. Brit. Pat. 1,221,205, 1971; *Chem. Abstr.* **1971**, *74*, 141037g.

(4) Kung, F. E. U.S. Pat. 2,377,085, 1945. Lee, L. H. *J. Org. Chem.* **1965**, *30*, 3943. Olofson, R. A.; Bauman, B. A.; Wancowicz, D. J. *Ibid.* **1978**, *43*, 752. Lecolier, S.; Malfroot, T.; Piteau, M.; Senet, J.-P. Eur. Pat. 2973, 1979; *Chem. Abstr.* **1980**, *92*, P6698e. Malfroot, T.; Piteau, M. Fr. Pat. 2,421,866, 1979; *Chem. Abstr.* **1980**, *93*, P7667b.

(5) Olofson, R. A.; Schnur, R. C. *Tetrahedron Lett.* **1977**, 1571. Olofson, R. A.; Yamamoto, Y. S.; Wancowicz, D. J. *Ibid.* 1563.

(6) Olofson, R. A.; Schnur, R. C.; Bunes, L.; Pepe, J. P. *Tetrahedron Lett.* **1977**, 1567. Olofson, R. A.; Pepe, J. P. *Ibid.* 1575; U.S. Pat 4,141,897, 1979; 4,161,597, 1979, and references therein. For newer, better method see: Olofson, R. A.; Martz, J. T.; Senet, J.-P.; Piteau, M.; Malfroot, T. *J. Org. Chem.* **1984**, *49*, 2081.

(7) Meunier, G.; Hemery, P.; Senet, J.-P.; Boileau, S. *Polym. Bull.* **1981**, *4*, 705. Boivin, S.; Chettouf, A.; Hemery, P.; Boileau, S. *Ibid.* **1983**, *9*, 114. Meunier, G; Hemery, P.; Boileau, S.; Senet, J.-P.; Cheradame, H. *Polymer* **1982**, *23*, 849; Meunier, G.; Boivin, S.; Hemery, P.; Boileau, S.; Senet, J.-P. *Ibid.* **1982**, *23*, 861. Boileau, S.; Kassir, F.; Boivin, S.; Cheradame, H.; Wooden, G. P.; Olofson, R. A. *Ibid.* **1985**, *26*, 443 and references therein.

(8) Cagnon, G.; Piteau, M.; Senet, J.-P.; Olofson, R. A.; Martz, J. T. Eur. Pat. 40153, **1981**; *Chem. Abstr.* **1982**, *96*, 142281y; U. S. Pat. 4,592,874, 1986.

(9) Favorskii, A. *Chem. Zentralblatt* **1899**, 778.

0022-3263/90/1955-2240$02.50/0