Regioselective Reductive 2-Oxoalkylation of *N*-methylquinolinium and -isoquinolinium Iodides under Sonochemical Activation

Faïza Diaba, Ifan Lewis, Micheline Grignon-Dubois,* and Sébastien Navarre

Laboratoire de Chimie Organique et Organométallique, CNRS URA 35, Université Bordeaux I, 351, Cours de la Libération, F-33405 Talence-Cedex, France

Received September 27, 1995

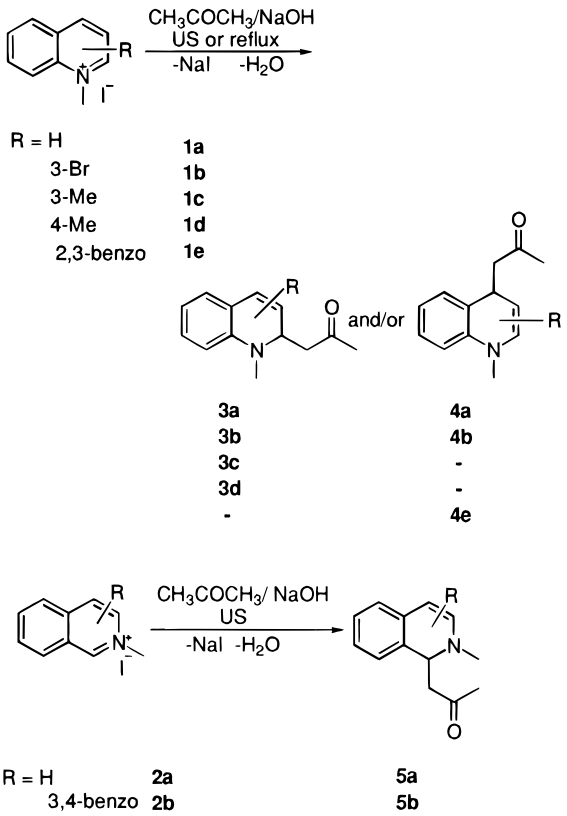
Introduction

Nucleophilic addition to quinolinium salts is well known for the functionalization of the quinoline ring.[1] However, the regiochemistry of the addition is reported to be dependent on substituent effects as well as on the nature of the nucleophilic reagent, leading to a competition between C-2 and C-4 additions.[1,2] We have recently demonstrated that sonochemical activation allows regiospecific C-2 addition of trichloromethyl anion to quinolinium iodides in good to quantitative yields.[3] An ultrasound-promoted synthesis of 2-quinolones by reacting quinolinium iodides with potassium *tert*-butylate has also been proposed.[4] As part of our continuing interest in the development of new synthetic methods in heterocyclic chemistry, we have investigated the oxoalkylation of a series of quinoline and isoquinoline methiodides. Recent attempts to synthesize acetonylquinolines and -isoquinolines have been reported to be difficult,[5] and the products were only observed by NMR. In contrast, berberine salts have been known for a long time to react with acetone in the presence of alkali to afford 8-acetonylberberine.[6] Moreover, 6-acetonyl-5,6-dihydro-5-alkylphenanthridines have been obtained from alkylphenanthridinium iodides by Dostal *et al.*[7] by reaction with K_2CO_3/acetone, and by us,[3] when using CCl_3COONa/acetone. However, these two reactions led to a mixture of products. We describe here an efficient regioselective synthesis of 1-methyl-2-(2-oxoalkyl)-1,2-dihydroquinolines and 2-methyl-1-(2-oxoalkyl)-1,2-dihydroisoquinolines using NaOH/ketone reagents under sonochemical activation.

Results and Discussion

Sonication of quinolinium and isoquinolinium methiodides **1** and **2** with sodium hydroxide in acetone solution afforded the acetonyl products in good to quantitative yields (Scheme 1, Table 1). The reaction was regiospecific with all quinolines, leading to the C-2 adducts **3a**−**d** as the only product. The 1-methyl-3-bromoquinolinium iodide (**1b)** constituted the only exception and led, as previously observed in the trichloromethylation reactions,[3] to a 83:17 mixture of the C-2 and C-4 adducts, **3b/4b.** A simple steric effect cannot be invoked in this case. Indeed, the nucleophilic addition was perfectly regiospecific in the case of the 3-methyl derivative **1c,** despite the larger interference radius of the methyl group compared to bromine (200 and 195 pm, respectively).[8] The efficiency of the procedure is well demonstrated by obtaining **4e** from the acridine methiodide, **1e**. Indeed, **4e** had been previously isolated as an oil by Bunting *et al.*,[5] but no yield was reported. Our process allowed us to obtain **4e** as an analytically pure solid in 81% yield. As expected**,** the isoquinolinium iodides **2a,b** led to the C-1 adducts in good yields (Table 1). However, in the case of phenanthridine methiodide, the acetonyl derivative **5b** (75% yield) was obtained in mixture with *N*-methylphenanthridone (**6**; 24% yield). This side reaction was probably due to the competition between the hydroxyl anion abstracting a proton from acetone and its direct addition to the methiodide. We had previously obtained **5b** (45% yield) in mixture with the 5-trichloromethyl derivative (9%) when reacting sodium trichloroacetate and phenanthridine methiodide in acetone medium.[3] Under these conditions, no trace of phenanthridone was observed. We tried without success to improve the yield of **5b** by increasing the quantity of acetone used (160 mL per mol instead of 80). This procedure was also applied to 1,2-dimethylquinolinium

Scheme 1



(1) For reviews, see: Sidgewick, N. Y.; Sidgewick, F. R. S. *The Organic Chemistry of Nitrogen*; Clarendon: Oxford, 1966; p 718. Dyke, S. F. *Adv. Heterocycl. Chem.* **1972**, *14*, 279. Gurnos, J. *Quinolines*; Wiley: New York, 1982.

(2) See, for example: Leonard, N. J.; Foster, R. L. *J. Am. Chem. Soc.* **1951**, *73*, 3325; *ibid.* **1952**, *74*, 2110. Metzgzer, J.; Larivé, H.; Vincent, E.-J.; Dennilauler, R.; Baralle, R.; Gaurat, C. *Bull. Soc. Chim. Fr.* **1967**, 30. Metzgzer, J.; Larivé, H.; Vincent, E.-J.; Dennilauler, R. *Bull. Soc. Chim. Fr.* **1967**, 46. Pilygun, G. T.; Gutsulyak, B. M. *Russ. Chem. Rev.* **1963**, *32*, 167. Bunting, J. W.; Meathrel, W. G. *Tetrahedron Lett.* **1971**, 133. Fukuzumi, S.; Noura, S. *J. Chem. Soc., Chem. Commun.* **1994**, *287*. Maeda, M. *Chem. Pharm. Bull.* **1990**, *38*, 2577.

(3) Grignon-Dubois, M.; Diaba, F.; Grelier-Marly, M.-C. *Synthesis* **1994**, 800.

(4) Grignon-Dubois, M.; Meola, A. *Synth. Commun.* **1995,** *25*, 2999.

(5) Chen, T.-K.; Bradsher, C. K. *Tetrahedron* **1973**, *29*, 2951. Bunting, J. W.; Fu, C.; Tam, J. W. *Can. J. Chem.* **1990**, *68*, 1762.

(6) Schmidt, E.; Gaze, R. *Arch. Pharm.* **1890**, *228*, 604.

(7) Dostal, J.; Potacek, M.; Nechvatal, M. *Collect. Chem. Commun.* **1993,** *58*, 395.

(8) Pauling, L. In *The Nature of Chemical Bond*; Verlag Chemie: Weinheim; 1962, p 242. Seebach, D. *Angew. Chem., Int. Engl.* **1990**, *29*, 1320.

S0022-3263(95)01766-X CCC: $12.00

Table 1. Oxoalkylation of Compounds 1 and 2 under Sonochemical Activation

substrate	reagent	product(s) (ratio)	total yield (%)
1a	acetone	**3a/4a** (100:0)	97
1b	acetone	**3b/4b** (83:17)	98
1c	acetone	**3c/4c** (100:0)	98
1d	acetone	**3d/4d** (100:0)	91
1e	acetone	**4e**	81
2a	acetone	**5a**	95
2b	acetone	**5b**	75
1a	butanone	**7**	40,[a] 70[b]
1a	2-pentanone	**8**	72,[a] 82[b]
1a	butanone	**9**	54,[a] 80[b]
2a	2-pentanone	**10**	67[a] 72[b]

[a] Isolated yields using the typical procedure. [b] isolated yields when reactions are conducted in acetonitrile (see Experimental Section for details).

iodide, for which the acetonyl addition failed when using the NaOH/acetone reagent. Indeed, in this case sonochemical activation did not prevent the hydroxyl anion abstracting a proton from the C-2 methyl group. These attempts were unsuccessful and only led to the trichloromethyl C-2 adduct (35% yield).

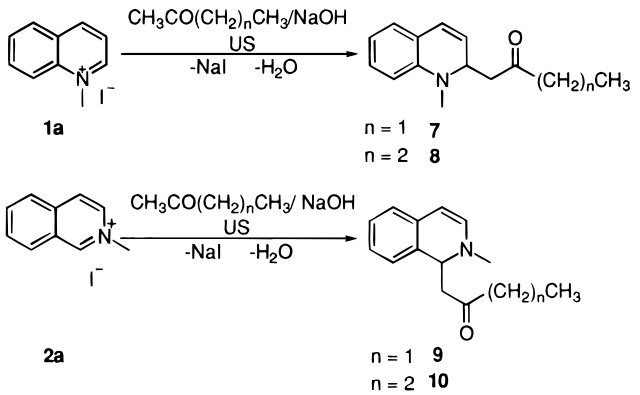
In the case of **1a**, the reaction has also been conducted under mechanical stirring. We obtained a **3a**/**4a** mixture (56:44; 95% yield) after 5 h at reflux instead of 1.5 h at 0 °C under ultrasound, and a 75:25 mixture of **3a**/**4a** in only 14% yield after 17 h at rt. These results demonstrate the efficiency of ultrasonic waves upon the regioselectivity and the reaction rate.

It is worth noting that the reaction outcome is more sensitive to temperature with acridine and phenanthridine methiodides than with the other substrates. In these two cases, it is necessary to carefully maintain the bath temperature between 0−5 °C during the sonication. An increase of temperature resulted in the formation of the corresponding quinolones along with the acetonyl derivatives.

From a mechanistic point of view, these results are consistent with the addition of the enolate ion of acetone to the ortho position versus nitrogen. As previously observed for trichloromethylation,[3] sonochemical activation allowed kinetic control of the nucleophilic addition, and the mild experimental conditions prevented the isomerization of the C-2 adduct to its C-4 regioisomer. In the case of dissymmetric ketones, the question arises regarding the regiochemistry of the enolate formation under sonochemical activation. For this purpose, we also studied the reaction of **1a** and **2a** with butanone and 2-pentanone. In the conditions used for acetone, the C-2 or C-1 (2-oxoalkyl) adducts **7**−**10** were, respectively, obtained as the only product, but in lower yields than with acetone (Scheme 2, Table 1). Improvements in the yields were achieved when the reaction was carried out in acetonitrile solution (Table 1, see Experimental Section for details). These results show that sonochemical activation allows both the enolate formation and its addition to the methiodide to be regiospecific. The systematic formation of the less-subtituted enolate is in good agreement with a kinetically controlled deprotonation process.[9]

In conclusion, this new procedure provides a facile and very clean method for the regioselective synthesis of

Scheme 2



1-methyl-2-(2-oxoalkyl)-1,2-dihydroquinolines and 2-methyl-1-(2-oxoalkyl)-1,2-dihydroisoquinolines under very mild and inexpensive conditions.

Experimental Section

Melting points were uncorrected. ^{1}H and ^{13}C NMR spectra were recorded at 250 and 63 MHz, respectively, with TMS as internal standard. Elemental analyses were performed by Service Central D'analyses du CNRS (F-69390 Vernaison).

Flash column chromatography techniques (30 cm × 2 cm column) were employed to purify crude product using 70−230 mesh alumina (activity II−III, CH_2Cl_2) under positive air pressure. Ultrasound-promoted reactions were carried out in a common ultrasonic laboratory cleaner filled with thermostated water at 0−5 °C. The reaction flask was partially submerged in the sonicator water bath in a place that produced maximum agitation.

Materials. Synthesis grade acetone (Aldrich) was used as received. Commercial sodium hydroxide pellets (Aldrich, reagent ACS) were pulverized prior to use. Methiodides were prepared according to literature procedures[10] by alkylation of the appropriate quinoline with methyl iodide in acetone (**1a-d**, **2a**) or methylene chloride solution (**1e, 2b**). The mixture was maintained at rt until the substrate had completely reacted, as monitored by TLC (SiO_2; Et_2O/CH_2Cl_2, 30:70 v/v). The precipitated salts were filtered and recrystallized. All data for these compounds are identical to literature data.[10]

Typical Procedure for Acetonylation. To a sonicated suspension of methiodide (22 mmol) in acetone (20 mL), 1.0 g of pulverized sodium hydroxide (27 mmol) was added over 5 min. The reaction was complete within 90 min, as monitored by TLC (Al_2O_3; CH_2Cl_2). The reaction mixture was filtered through Celite, and the filtrate was evaporated to dryness. The residue was taken up with cyclohexane (40 mL), and insoluble materials, if present, were removed by filtration and analyzed separately. The cyclohexane solution was evaporated to dryness leading to the analytically pure acetonyl derivatives as the only product, except in the case of phenanthridine, for which it was obtained in mixture with *N*-methylphenanthridone and chromatographed on alumina (CH_2Cl_2). **5b** was eluted first and then **6**. The same procedure was applied to purify the **3b**/**4b** mixture of isomers leading first to **3b** then **4b**.

1-Methyl-2-acetonyl-1,2-dihydroquinoline (3a): 4.29 g isolated as a pale yellow liquid (97%); ^{1}H NMR ($CDCl_3$) δ 2.1 (3H, s), 2.8 (3H, s), 2.6 (1H, dd, J = 15.8, 7.6 Hz), 2.7 (1H, dd, J = 15.8, 5.5 Hz), 4.4 (1H, ddd, J = 7.6, 5.5 Hz), 5.8 (1H, dd, J = 9.7, 5.5 Hz), 6.4 (1H, d, J = 9.7 Hz), 6.5 (1H, d, J = 8.1 Hz), 6.6 (1H, dd, J = 7.3 Hz), 6.9 (1H, dd, J = 7.3, 1.3 Hz), 7.1 (1H, ddd, J = 8.1, 7.3, 1.3 Hz); ^{13}C NMR ($CDCl_3$) δ 31.1, 36.5, 46.2, 56.5, 111.1, 117.2, 122.2, 124.8, 125.9, 126.9, 129.2, 144.3, 207.3; MS, *m*/*z* (%) 201 (M^+, 3.7), 144 (100); IR (NaCl) 1710 cm^{-1}. Anal.

(9) Evans, D. A. In *Asymmetric Synthesis;* Morrison, J. D., Ed.; Academic Press: New York, 1984; Vol. 3, p 1 and ref therein. D'Angelo, J. *Tetrahedron* **1976**, *32*, 2979 and ref therein.

(10) Doebner, O.; Miller, W. *Ber*, **1883,** *16*, 2464. Duffin, C. F. *Adv. Heterocycl. Chem*. **1964**, *3*, 1. Marchwald, W.; Meijer, E. *Ber*. **1884**, *33*, 1990. Gurevitch, A. I.; Sheinker, Yu. N. *Zhur. Fiz. Chim*. **1959**, *33*, 883; *Chem. Abstr*. **1960**, *4*, 8285b. Zanker, V.; Cnobloch, H. *Z. Naturforsch. B Chem. Sci*. **1962**, *17*, 819.

Calcd for $C_{13}H_{15}NO$: C, 77.58; H, 7.51; N, 6.96; O, 7.95. Found: C, 77.22; H, 7.41; N, 7.01; O, 8.25.

1-Methyl-2-acetonyl-3-bromo-1,2-dihydroquinoline (3b): 4.99 g isolated as a pale yellow liquid (81%); ^{1}H NMR ($CDCl_3$) δ 2.1 (3H, s), 2.8 (3H, s), 2.6 (1H, dd, J = 16.2, 4.0 Hz), 2.8 (1H, dd, J = 16.2, 7.0 Hz), 4.7 (1H, dd, J = 7.0, 4.0 Hz), 6.7 (1H, s), 6.5 (1H, d, J = 8.2 Hz), 6.7 (1H, dd, J = 7.4, 7.3 Hz), 6.9 (1H, dd, J = 7.4, 1.5 Hz), 7.1(1H, ddd, J = 8.2, 7.3, 1.5 Hz); ^{13}C NMR ($CDCl_3$) δ 31.0, 37.6, 44.9, 63.2, 112.1, 116.7, 117.9, 122.0, 126.5, 128.2, 129.6, 142.0, 206.3; MS, *m*/*z* (%) 279 (M^+, 2.2), 224 (100); IR (NaCl) 1720 cm^{-1}. Anal. Calcd for $C_{13}H_{14}BrNO$: C, 55.73; H, 5.04; N, 5.0; O, 5.71. Found: C, 55.76; H, 4.99; N, 4.87; O, 5.86.

1,3-Dimethyl-2-acetonyl-1,2-dihydroquinoline (3c): 4.64 g isolated as a pale yellow liquid (98%); ^{1}H NMR ($CDCl_3$) δ 1.8 (3H, d, J = 1.3 Hz), 2.1 (3H, s), 2.8 (3H, s), 2.4 (1H, dd, J = 15.9, 4.9 Hz), 2.7 (1H, dd, J = 15.9, 6.4 Hz), 4.3 (1H, dd, J = 6.4, 4.9 Hz), 6.2 (1H, d, J = 1.3 Hz), 6.5 (1H, dd, J = 8.1, 0.9 Hz), 6.7 (1H, ddd, J = 7.3, 0.9 Hz), 6.9 (1H, dd, J = 7.3, 1.5 Hz), 7.1 (1H, ddd, J = 8.1, 7.3, 1.5 Hz); ^{13}C NMR ($CDCl_3$) δ 20.8, 31.0, 37.0, 44.7, 60.6, 111.2, 117.5, 121.8, 123.2, 126.0, 128.2, 133.6, 142.6, 207.5; MS, *m*/*z* (%) 215 (M^+, 3.1), 158 (100); IR (NaCl) 1711 cm^{-1}. Anal. Calcd for $C_{14}H_{17}NO$: C, 78.10; H, 7.96; N, 6.51; O, 7.43. Found: C, 77.81; H, 8.08; N, 6.40; O, 7.52.

1,4-Dimethyl-2-acetonyl-1,2-dihydroquinoline (3d): 4.30 g isolated as a pale yellow liquid (91%); ^{1}H NMR ($CDCl_3$) δ 2.0 (3H, d, J = 1.3 Hz), 2.1 (3H, s), 2.9 (3H, s), 2.6 (1H, dd, J = 15.9, 7.9 Hz), 2.7 (1H, dd, J = 15.9, 5.2 Hz), 4.4 (1H, ddd, J = 7.9, 5.8, 5.2 Hz), 5.7 (1H, dd, J = 5.8, 1.3 Hz), 6.5 (1H, dd, J = 8.2, 1.2 Hz), 6.7 (1H, ddd, J = 7.6, 1.2 Hz), 7.1 (1H, dd, J = 7.6, 1.5 Hz), 7.1 (1H, ddd, J = 8.2, 7.6, 1.5 Hz); ^{13}C NMR ($CDCl_3$) δ 18.8, 27.0, 36.8, 45.9, 56.4, 111.2, 117.0, 122.3, 123.5, 123.8, 129.0, 130.7, 144.3, 207.6; MS, *m*/*z* (%) 215 (M^+ , 2.7), 158 (100); IR (NaCl) 1709 cm^{-1}. Anal. Calcd for $C_{14}H_{17}NO$: C, 78.10; H, 7.96; N, 6.51; O, 7.43. Found: C, 78.0; H, 8.14; N, 6.72; O, 7.08.

1-Methyl-4-acetonyl-1,4-dihydroquinoline (**4a**). The reaction was conducted under mechanical stirring at reflux for 5 h leading to 4.32 g of a crude mixture. It produced after flash chromatography (alumina, CH_2Cl_2), in order of elution, 2.35 g of **3a** (53%) and 1.85 g of **4a** (42%) both as slightly-colored liquid.

4a: ^{1}H NMR ($CDCl_3$) δ 2.0 (3H, s), 3.0 (3H, s), 2.5 (1H, dd, J = 16.2, 5.1 Hz), 2.7 (1H, dd, J = 16.2, 8.4 Hz), 6.0 (1H, d, J = 7.8 Hz), 4.6 (1H, dd, J = 7.8, 5.0 Hz), 4.0 (1H, ddd, J = 8.4, 5.1, 5.0 Hz), 6.6 (1H, dd, J = 7.6, 1.1 Hz), 6.8 (1H, ddd, J = 7.5, 1.1 Hz), 7.0 (1H, d, J = 7.5 Hz), 7.1 (1H, dd, J = 7.6, 7.5 Hz); ^{13}C NMR ($CDCl_3$) δ 31.0, 35.5, 37.9, 54.8, 99.3, 111.2, 121.0, 124.1, 127.2, 128.7, 133.0, 141.3, 207.7; MS, *m*/*z* (%) 201 (M^+ , 3.7), 144 (100); IR (NaCl) 1705 cm^{-1}. Anal. Calcd for $C_{13}H_{15}NO$: C, 77.58; H, 7.51; N, 6.96; O, 7.95. Found: C, 77.62; H, 7.53; N, 7.16; O, 7.60.

1-Methyl-3-bromo-4-acetonyl-1,4-dihydroquinoline (4b): 1.02 g isolated as a pale yellow liquid (17%); ^{1}H NMR (C_6D_6) δ 1.6 (3H, s), 2.4 (3H, s), 2.5 (1H, dd, J = 16.4, 7.6 Hz), 2.7 (1H, dd, J = 16.4, 4.0 Hz), 6.0 (1H, s), 4.6 (1H, dd, J = 7.6, 4.0 Hz), 6.4 (1H, dd, J = 8.2, 1.1 Hz), 6.8 (1H, ddd, J = 7.5, 1.1 Hz), 7.2 (1H, dd, J = 7.5, 1.6 Hz), 7.0 (1H, ddd, J = 8.2, 7.5, 1.6 Hz); ^{13}C NMR (C_6D_6) δ 30.5, 41.9, 51.3, 63.2, 94.9, 111.7, 121.9, 124.0, 128.4, 129.4, 133.8, 140.0, 207.0; MS, *m*/*z* (%): 279 (M^+, 1.5), 222 (100); IR (NaCl) 1715 cm^{-1}. Anal. Calcd for $C_{13}H_{14}BrNO$: C, 55.73; H, 5.04; N, 5.0; O, 5.71. Found: C, 56.01; H, 5.20; N, 5.0; O, 5.68.

9-Acetonyl-10-methyl-9,10-dihydroacridine (4e): 4.47 g isolated as a solid (81%); mp 127 °C; ^{1}H NMR ($CDCl_3$) δ 1.9 (3H, s), 3.4 (3H, s), 2.7 (2H, d, J = 7.0 Hz), 4.6 (1H, t, J = 7.0 Hz), 7.0 (4H, m), 7.3 (4H, m); ^{13}C NMR ($CDCl_3$) δ 31.3, 33.1, 50.4, 39.6, 112.3, 121.0, 127.3, 128.2, 126.9, 142.7, 207.5; MS, *m*/*z* (%) 251 (M^+ , 6.9), 194 (100); IR (NaCl) 1712 cm^{-1}. Anal. Calcd for $C_{17}H_{17}NO$: C, 81.24; H, 6.82; N, 5.57; O, 6.37. Found: C, 81.08; H, 6.68; N, 5.78; O, 6.18.

1-Acetonyl-2-methyl-1,2-dihydroisoquinoline (5a): 4.20 g isolated as a pale yellow liquid (95%); ^{1}H NMR ($CDCl_3$) δ 1.9 (3H, s), 2.9 (3H, s), 2.8 (2H, m), 4.8 (1H, ddd, J = 7.0, 6.7, 1.2 Hz), 5.3 (1H, d, J = 7.3 Hz), 6.0 (1H, dd, J = 7.3, 1.2 Hz), 6.9 (H, dd, J = 7.3, 1.5 Hz), 6.9 (1H, dd, J = 7.3, 1.8 Hz), 7.0 (1H, ddd, J = 7.3, 1.5 Hz), 7.1 (1H, ddd, J = 7.3, 1.8 Hz); ^{13}C NMR ($CDCl_3$) δ 31.7, 40.5, 44.7, 58.2, 97.5, 122.7, 124.8, 125.7, 127.5, 128.5, 132.5, 136.5, 208.0; MS, *m*/*z* (%) 201 (M^+, 7.9), 144 (100); IR (NaCl) 1707 cm^{-1}. Anal. Calcd for $C_{13}H_{15}NO$: C, 77.58; H, 7.51; N, 6.96; O, 7.95. Found: C, 77.65; H, 7.43; N, 7.12; O, 7.68.

5-Methyl-6-acetonyl-5,6-dihydrophenanthridine (5b). The typical procedure led to 5.30 g of a crude mixture. It produced after flash chromatography (alumina, CH_2Cl_2), in order of elution, 4.14 g of **5b** as a pale yellow liquid (75%) and 1.10 g of **6** (24%), which was identical to literature data.[3,4]

5b: ^{1}H NMR ($CDCl_3$) δ 1.9 (3H, s), 3.0 (3H, s), 2.6 (1H, dd, J = 15.6, 7.7 Hz), 2.7 (1H, dd, J = 15.6, 5.4 Hz), 4.9 (1H, dd, J = 7.7, 5.4 Hz), 6.7−7.8 (8H, m); ^{13}C NMR ($CDCl_3$) δ 31.6, 37.4, 44.5, 59.8, 113.4, 118.4, 122.7, 123.0, 123.4, 126.1, 127.3, 127.9, 129.4 130.6, 135.6, 144.4, 207.7; IR (NaCl) 1710 cm^{-1}.

Reactions with butanone and 2-pentanone were performed according to the typical procedure using 22 mmol of methiodide and 0.6 mol of ketone (procedure a), and also in acetonitrile solution (10 mL), using the same conditions (procedure b).

1-Methyl-2-(2-oxobutyl)-1,2-dihydroquinoline (7). Isolated as a pale yellow liquid: 1.89 g (40%) using procedure a; 3.30 g (70%) using procedure b; ^{1}H NMR ($CDCl_3$) δ 1.0 (3H, t, J = 7.3 Hz), 2.4 (2H, dq, J = 7.3, 2.8 Hz), 2.5 (1H, dd, J = 15.6, 7.5 Hz), 2.7 (1H, dd, J = 15.6, 5.3 Hz), 2.8 (3H, s), 4.5 (1H, ddd, J = 7.5, 5.7, 5.3 Hz), 5.8 (1H, dd, J = 9.7, 5.7 Hz), 6.4 (1H, d, J = 9.7 Hz), 6.6 (1H, dd, J = 8.3, 1.0 Hz), 6.7 (1H, ddd, J = 7.6, 7.3, 1.0 Hz), 6.9 (1H, dd, J = 7.3, 1.5 Hz), 7.1 (1H, ddd, J = 8.3, 7.6, 1.5 Hz); ^{13}C NMR ($CDCl_3$) δ 7.7, 36.5, 37.4, 44.9, 56.7, 111.0, 117.1, 122.0, 124.9, 125.9, 126.9, 129.2, 144.3, 210.0; MS, *m*/*z* (%) 215 (M^+, 3), 144 (100); IR (NaCl) 1702 cm^{-1}. Anal. Calcd for $C_{14}H_{17}NO$: C, 78.10; H, 7.96; N, 6.51; O, 7.43. Found: C, 78.28; H, 7.82; N, 6.49; O, 7.29.

1-Methyl-2-(2-oxopentyl)-1,2-dihydroquinoline (**8**)**.** Isolated as a pale yellow liquid: 3.63 g (72%) using procedure a; 4.13 g (82%) using procedure b; ^{1}H NMR ($CDCl_3$) δ 0.9 (3H, t, J = 7.4 Hz), 1.5(2H, sextet, J = 7.4 Hz), 2.3 (2H, t, J = 7.4 Hz), 2.6 (1H, dd, J = 15.6, 7.5 Hz), 2.7 (H, dd, J = 15.6, 5.5 Hz), 2.9 (3H, s), 4.5 (1H, ddd, J = 7.5, 5.7, 5.5 Hz), 5.8 (1H, dd, J = 9.7, 5.7 Hz), 6.4 (1H, d, J = 9.7 Hz), 6.5 (1H, dd, J = 8.1, 0.9 Hz), 6.7 (1H, ddd, J = 7.4, 7.7, 0.9 Hz), 6.9 (1H, dd, J = 7.4, 1.5 Hz), 7.1 (1H, ddd, J = 8.1, 7.7, 1.5 Hz); ^{13}C NMR ($CDCl_3$) δ 11.0, 13.7, 17.1, 36.5, 45.2, 46.2, 56.6, 117.1, 122.0, 124.9, 125.8, 126.9, 129.1, 144.3, 210.0; MS, *m*/*z* (%) 229 (M^+, 4.9), 144 (100); IR (NaCl) 1705 cm^{-1}. Anal. Calcd for $C_{15}H_{19}NO$: C, 78.56; H, 8.35; N, 6.11; O, 6.98. Found: C, 78.70; H, 8.26; N, 6.30; O, 6.65.

2-Methyl-1-(2-oxobutyl)-1,2-dihydroisoquinoline (**9**)**.** Isolated as a pale yellow liquid: 2.55 g (54%) using procedure a; 3.78 g (80 %) using procedure b; ^{1}H NMR ($CDCl_3$) δ 0.9 (3H, t, J = 7.2 Hz), 2.0 (1H, dq, J = 18.0, 7.2 Hz), 2.2 (1H, dq, J = 18.0, 7.2 Hz), 2.7 (2H, d, J = 6.4 Hz), 2.9 (3H, s), 4.8 (1H, t, J = 6.4 Hz), 5.3 (1H, d, J = 7.2 Hz), 6.0 (1H, dd, J = 7.2, 1.0 Hz), 6.7−7.4 (4H, m); ^{13}C NMR ($CDCl_3$) δ 7.6, 37.9, 40.5, 43.3, 58.6, 97.5, 122.7, 124.7, 125.6, 127.5, 128.5, 132.5, 136.5, 210.5; MS, *m*/*z* (%) 215 (M^+, 4.1), 144 (100); IR (NaCl) 1706 cm^{-1}. Anal. Calcd for $C_{14}H_{17}NO$: C, 78.10; H, 7.96; N, 6.51; O, 7.43. Found: C, 78.16; H, 8.02; N, 6.48; O, 7.10.

2-Methyl-1-(2-oxopentyl)-1,2-dihydroisoquinoline (**10**)**.** Isolated as a pale yellow liquid: 3.37 g (67%) using procedure a; 3.62 g (72%) using procedure b; ^{1}H NMR ($CDCl_3$) δ 0.9 (3H, t, J = 7.4 Hz), 1.5 (2H, sextet, J = 7.4 Hz), 2.0 (1H, td, J = 17.1, 7.4 Hz), 2.1 (1H, td, J = 17.1, 7.4 Hz), 2.7 (2H, d, J = 6.4 Hz), 2.9 (s, 3H), 4.8 (1H, t, J = 6.5 Hz), 5.3 (1H, d, J = 7.1 Hz), 6.0 (1H, d, J = 7.1 Hz), 6.8 (1H, d, J = 7.3 Hz), 6.8 (1H, d, J = 7.3 Hz), 6.9 (1H, ddd, J = 7.3, 1.2 Hz), 7.0 (1H, ddd, J = 7.3, 1.5 Hz); ^{13}C NMR ($CDCl_3$) δ 11.0, 13.7, 17.1, 36.5, 45.2, 46.2, 56.6, 117.1, 122.0, 124.9, 125.8, 126.9, 129.1, 144.3, 210.0; MS, *m*/*z* (%) 229 (M^+ , 4.9), 144 (100); IR (NaCl) 1707 cm^{-1} . Anal. Calcd for $C_{15}H_{19}NO$: C, 78.56; H, 8.35; N, 6.11; O, 6.98. Found: C, 78.22; H, 8.04; N, 6.39; O, 7.20.

JO951766Y