Efficient Preparation of Substituted 5,6,7,8-Tetrahydroquinolines and Octahydroacridine Derivatives

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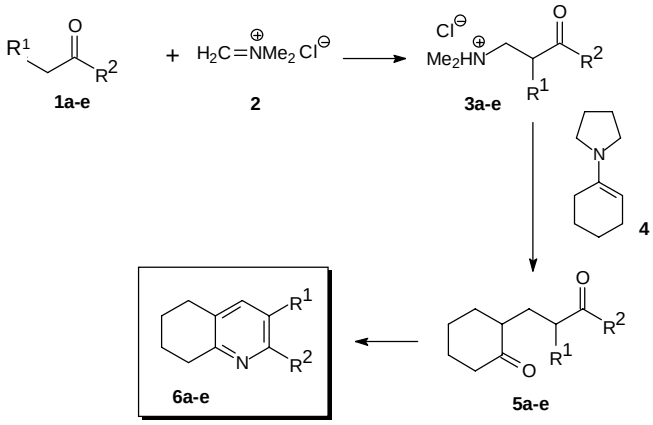
Abstract. The reaction of the enamine **4** with different β-amino ketone hydrochlorides **3a**–**e** affords the diketones **5a**–**e** which can be cyclized to the corresponding mono- and disubstituted tetrahydroquinolines **6a**–**e**. Furthermore the preparation of the octahydroacridines **8f** and **8g** by using a straightforward multi step sequence is described.

Quinolines and their derivatives, especially the tetrahydroquinolines, occur in numerous natural products [1, 2]. Many tetrahydroquinoline derivatives show interesting physiological activities and have found attractive applications as pharmaceuticals and agrochemicals as well as being general synthetic building blocks [2]. Chiral 5,6,7,8-tetrahydroquinolines [3] are the most convenient starting points for the synthesis of the corresponding optically active 2,2'-bipyridines and 1,10-phenanthrolines [4, 5]. Furthermore tetrahydroquinolines and partially hydrogenated acridine derivatives have been prepared and studied with regard to their possible activity as acetylcholinesterase inhibitors [6] and their effects on the memory improvement of Alzheimer patients. In the last few years interest has been focused on 5,6,7,8-tetrahydroquinolin-8-one derivatives since they play an important role as starting material for the synthesis of oligopyridines. Oligopyridines bearing 2,2'-bipyridine, 2,2':6',2''-terpyridine or 1,10-phenanthroline subunits are extremely versatile building blocks for the construction of metallo-supramolecular systems. Different syntheses have been developed for these heterocycles, but due to their great importance, the development of novel synthetic methods remains an active research area [7]. For this reason we were interested in simple approaches towards 5,6,7,8-tetrahydroquinoline derivatives [8].

Our studies in the field of ternary iminium salts led to the development of one pot reactions yielding a wide range of functionalized pyridines, bipyridines and terpyridines [9]. All these reactions are based on the ability of Mannich bases to form α,β-unsaturated ketones by thermally induced amine elimination. It is known that enamines as well as ketones are easily alkylated by these Michael acceptors to form 1,5-diketones [10] which can be converted to the corresponding pyridine derivatives by treatment with ammonia. We chose to prepare several substituted 5,6,7,8-tetrahydroquinolines by treating the β-amino ketone hydrochlorides **3a**–**e** [11] with the pyrrolidine enamine of cyclohexanone **4**. Heating a solution of the hydrochlorides **3a**–**e** in the presence of enamine **4** afforded the expected 1,5-diketones **5a**–**e** which can be isolated in good to moderate yields.



Entry	R^1	R^2	Yield **5**	Yield **6**
a	H	C_6H_5	39	42 [a]
b	H	4-BrC_6H_4	62	45
c	H	t-C_4H_9	77	76
d	Me	C_6H_5	46	33
e	C_6H_5	C_6H_5	67	54

[a] The overall yield can be increased to 40% if the diketone **5a** is not purified

Scheme 1 Preparation of diketones **5a**–**e** and tetrahydroquinolines **6a**–**e**

The final cyclization is achieved by refluxing the dicarbonyl compound **5** in the presence of an ammonia source (*e.g.* hydroxylammonium hydrochloride). The

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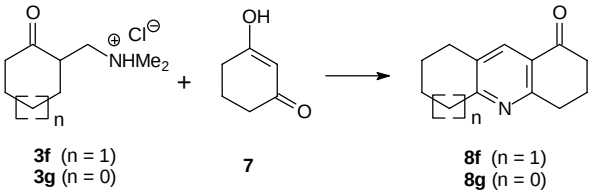
isolation of the intermediate 1,5-diketone **5** is not necessary, and the cyclization of **5** can be carried out without further purification of the crude product. This procedure provides higher yields of the tetrahydroquinoline **6**.

These results prompted us to develop a similar reaction sequence for the preparation of acridine derivatives. Instead of employing the enamine **4** we used the very reactive 1,3-cyclohexanedione **7** (see scheme 2). The reaction between Mannich base **3f** and **3g**, respectively, and **7** was carried out in the presence of ammonium acetate so that the 1,5-diketone is cyclized *in situ* to the 1,4-dihydropyridine and octahydroacridine derivative, respectively. After workup small amounts of 1,4-dihydropyridine are present which can be converted to the corresponding octahydroacridine derivative by stirring a solution of the crude product with SiO_2 under an oxygen atmosphere. This simple procedure allows us to prepare the octahydroacridine **8f** in 76% and **8g** in 42% yield.



3f (n = 1)
3g (n = 0)

7

8f (n = 1)
8g (n = 0)

Scheme 2 Preparation of octahydroacridine derivatives **8f** and **8g**

Our method is distinguished by its simplicity and high yields in comparison with known literature procedures [12]. It is noteworthy that the acridine derivative **8** is quite similar to known pharmacologically interesting acridine compounds [6]. Considerable attention has been focused on these heterocycles, because of their bactericidal, central stimulating [13], coronary dilating [14], antifibrillatory, spasmolytic and antihypertensive activity [15].

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Experimental

All reactions were conducted under argon atmosphere unless otherwise indicated. Anhydrous solvents were distilled as follows: $CHCl_3$, CH_3CN were destilled from P_4O_{10}; EtOH was distilled from Na. Melting points are uncorrected. ^1H and ^{13}C NMR spectra were recorded on a Bruker ARX 200 spectrometer, using TMS as internal standard. Infrared frequencies are reported in units of cm^{-1}. MS data were obtained from a VG Fisons MD 800.

Preparation of the β-amino ketone hydrochlorides (3a–g)

The Mannich bases are synthesized according to the method described by Tietze/Kinast [11].

3-Dimethylamino-1-phenyl-propane-1-one hydrochloride (**3a**)

Prepared from 4.32 g (22.0 mmol) of acetophenone (**1a**) and 2.0 g (22.0 mmol) of *N,N*-dimethylmethylene ammonium chloride (**2**). Yield 4.54 g of colourless crystals (73%), *m.p.* 152 °C [16]. – ^1H NMR (200 MHz, $CDCl_3$) δ/ppm = 12.43 (bs, 1H), 7.96 (m_c, 2H), 7.62–7.41 (m, 3H), 3.74 (m_c, 2H), 3.60 (m_c, 2H), 2.86 (s, 6H). – ^{13}C NMR (50 MHz, $CDCl_3$) δ/ppm = 196.2 (s), 135.8 (s), 134.52 (d), 129.30 (d), 128.7 (d), 53.1 (t), 43.7 (q), 34.2 (t). – IR (KBr) ν/cm^{-1} = 2 541, 2 433, 1 688, 1 470, 1 445, 1 336, 1 217, 959, 757, 700.

1-(4-Bromo-phenyl)-3-dimethylamino-propan-1-one hydrochloride (**3b**)

Prepared from 10.4 g (52.0 mmol) 4-bromoacetophenone (**1b**) and 4.65 g (52.0 mmol) of *N,N*-dimethylmethylene ammonium chloride (**2**). Yield 11.5g of colourless crystals (76%), *m.p.* 193 °C [17]. – ^1H NMR (200 MHz, $CDCl_3$) δ/ppm = 12.6 (bs, 1H), 7.91 (d, ^3J = 8.6 Hz, 2H), 7.68 (d, ^3J = 8.6 Hz, 2H), 3.78 (t, ^3J = 7.1 Hz, 2H), 3.54 (t, ^3J = 7.1 Hz, 2H), 2.89 (s, 3H). – IR (KBr) ν/cm^{-1} = 2 993, 2 547, 2 433, 1 688, 1 579, 1 398, 1 222, 1 067, 964.

1-Dimethylamino-4,4-dimethyl-pentan-3-one hydrochloride (**3c**)

Prepared from 19.8 g (0.20 mol) of 3,3-dimethyl-2-butanone (**1c**) and 18.0 g (0.19 mol) of *N,N*-dimethylmethylene ammonium chloride (**2**). Yield 27.1 g of colourless crystals (76%), *m.p.* 175 °C [18]. – ^1H NMR (200 MHz, $CDCl_3$) δ/ppm = 12.65 (bs, 1H), 3.25 (m_c, 4H), 2.81 (s, 3H), 2.78 (s, 3H), 1.14 (s, 9H). – ^{13}C NMR (50 MHz, $CDCl_3$) δ/ppm = 212.5 (s), 53.2 (t), 43.6 (q), 32.3 (t), 26.74 (q). – IR (KBr) ν/cm^{-1} = 2 977, 2 577, 2 474, 1 703, 1 465, 1 383, 1 093, 964.

3-Dimethylamino-2-methyl-1-phenyl-propane-1-one hydrochloride (**3d**)

Prepared from 2.7 g (20.0 mmol) propiophenone (**1d**) and 4.65 g (22.0 mmol) of *N,N*-dimethylmethylene ammonium chloride (**2**). Yield 3.7 g of colourless crystals (74%), *m.p.* 165 °C [19]. – ^1H NMR (200 MHz, $CDCl_3$) δ/ppm =12.43 (bs, 1H), 8.09 (m_c, 2H), 7.49 (m_c, 3H), 4.50 (m_c, 1H), 3.83 (m_c, 1H), 3.17 (m_c, 1H), 2.88 (s, 3H), 2.60 (s, 3H), 1.32 (d, ^3J = 7.3 Hz, 3H). – ^{13}C NMR (50 MHz, $CDCl_3$) δ/ppm = 201.3 (s), 134.7 (s), 134.7 (d), 129.6 (d), 129.3 (d), 59.2 (t), 45.6 (q), 42.5 (q), 38.0 (d), 18.9 (q). – IR (KBr) ν/cm^{-1} = 2 929, 2 686, 2 619, 1 688, 1 465, 1 222, 979, 700.

3-Dimethylamino-1,2-diphenyl-propan-1-one hydrochloride (**3e**)

Prepared from 4.32 g (22.0 mmol) of benzylphenylketone (**1e**) and 2.0 g (22.0 mmol) of *N,N*-dimethylmethylene ammonium chloride (**2**). Yield 4.54 g of a white solid (72%), *m.p.* 168 °C [9a]. – ^1H NMR (200 MHz, $CDCl_3$) δ/ppm = 12.75 (bs, 1H), 8.05 (d, ^3J = 7.4 Hz, 2H), 7.53–7.25 (m, 8H), 5.89 (dd, ^3J = 7.8 Hz, ^4J = 3.5 Hz, 1H), 4.12 (dd, ^2J = 12.7 Hz, ^3J = 7.8 Hz, 1H), 3.34 (dd, ^2J = 12.7 Hz, ^3J = 3.5 Hz, 1H), 2.73 (s, 6H). – ^{13}C NMR (50 MHz, $CDCl_3$) δ/ppm = 197.4

(s), 136.1 (s), 135.2 (s), 134.4 (d), 130.1 (d), 129.7 (d), 129.3 (d), 129.1 (d), 128.8 (d), 128.7 (d), 60.1 (t), 49.7 (d), 43.7 (q). – IR (KBr) ν/cm^{-1} = 2 950, 2 660, 1 678, 1 460, 1 383, 1 238, 1 145, 938, 767, 694.

2-Dimethylaminomethyl-cyclohexanone hydrochoride (**3f**)
Prepared from 2.0 g (20.0 mmol) cyclohexanone and 1.86 g (20.0 mmol) of *N*,*N*-dimethylmethylene ammonium chloride (**2**). Yield 3.0 g of colourless crystals (83%), *m.p*. 159 °C [20]. – ^{1}H NMR (200 MHz, $CDCl_3$) δ/ppm = 3.69 (m_c, 1H), 3.15 (m_c, 2H), 2.93 (s, 3H), 2.86 (s, 3H), 2.34 (m_c, 2H), 2.06 (m_c, 2H), 1.92–1.70 (m, 2H). – ^{13}C NMR (50 MHz, $CDCl_3$) δ/ppm = 210.2 (s), 57.4 (t), 47.3 (q), 45.6 (q), 42.7 (d), 42.4 (t), 34.5 (t), 28.3 (t), 25.3 (t).

2-Dimethylaminomethyl-cyclopentanone hydrochloride (**3g**)
Prepared from 1.49 g (20.0 mmol) cyclopentanone and 1.87 g (20.0 mmol) of *N*,*N*-dimethylmethylene ammonium chloride (**2**). Yield 2.84 g of colourless crystals (89%), *m.p*. 150 °C [9b]. – ^{1}H NMR (200 MHz, $CDCl_3$) δ/ppm = 3.41 (m_c, 1H), 3.02 (m_c, 1H), 2.86 (t, ^3J = 4.43 Hz, 6H), 2.76 (m_c, 2H), 2.38 (m_c, 1H), 2.10 (m_c, 2H), 1.83 (m_c, 2H). – IR (KBr) ν/cm^{-1} = 3 015, 2 963, 2 853, 2 672, 2 595, 2 479, 1 732, 1 474, 1 408, 1 159, 1 115, 1 009, 964, 926, 824.

Preparation of the 1,5-Diketones (5a–e) (General Procedure)

The reactions were carried out by refluxing 0.1 mol of the pyrrolidine enamine **4** [21] with 0.1 mole of the Mannich base in 100 mL of dioxane for 16 h. After addition of 30 mL of water, the reaction mixture was refluxed for 1 h. The solution was cooled to room temperature, and additional 100 mL of water were added. The reaction mixture was extracted with CH_2Cl_2 (4 × 40 mL). The organic layer was washed with 20 mL of dilute HCl, 20 mL of water and dried over Na_2SO_4. Rotary evaporation yielded brown oils which were purified either by Kugelrohr distillation or chromatography.

2-(3-Oxo-3-phenyl-propyl)-cyclohexanone (**5a**)
Prepared from 3.4 g (16.0 mmol) of Mannich base **3a** and 2.4 g (16.0 mmol) of enamine **4**. Yield 1.43 g (39%) of an oil after chromatography on SiO_2, petroleum ether/EtOAc, 9:1. – ^{1}H NMR (200 MHz, $CDCl_3$) δ/ppm = 7.96 (dd, ^3J = 7.0 Hz, ^4J = 1.3 Hz, 2H), 7.48 (m_c, 3H), 3.03 (m_c, 2H), 2.34 (m_c, 3H), 2.08 (m_c, 2H), 1.85 (m_c, 2H), 1.66 (m_c, 2H), 1.39 (m_c, 2H). – ^{13}C NMR (50 MHz, $CDCl_3$) δ/ppm = 213.6 (s), 200.6 (s), 137.2 (s), 133.4 (d), 128.9 (d), 128.5 (d), 50.3 (d), 48.1 (t), 36.7 (t), 35.0 (t), 28.5 (t), 25.5 (t), 24.9 (t). – IR(KBr) ν/cm^{-1} = 2 935, 2 852, 1 698, 1 678, 1 595, 1 585, 1 445, 1 367, 1 316, 1 274, 1 222, 741, 685.

2-(3-Oxo-3-(4-brom-phenyl)-propyl)-cyclohexanone (**5b**)
Prepared from 2.6 g (8.9 mmol) of Mannich base **3b** and 1.34 g (8.9 mmol) of enamine **4**. Yield 1.7 g (62%) of an oil after flash chromatography on SiO_2, petroleum ether/EtOAc, 3:1. – ^{1}H NMR (200 MHz, $CDCl_3$) δ/ppm = 7.86 (d, ^3J = 8.2 Hz, 2H), 7.60 (d, ^3J = 8.2 Hz, 2H), 3.02 (m_c, 2H), 2.40 (m_c, 2H), 2.10 (m_c, 3H), 1.83 (m_c, 2H), 1.65 (m_c, 2H), 1.47 (m_c, 2H). – ^{13}C NMR (50 MHz, $CDCl_3$) δ/ppm = 212.6 (s), 199.6 (s), 135.9 (s), 132.2 (d), 130.2 (d), 128.5 (s), 50.34 8d), 42.7 (t), 36.8 (t). 35.1 t), 28.5 (t), 25.5 (t), 24.9 (t). – IR (KBr) ν/cm^{-1} = 2 924, 2 551, 1 703, 1 683, 1 590, 1 460, 1 398, 1 072. 1 005, 824.

2-(3-Oxo-3-(tert-butyl)-propyl)-cyclohexanone (**5c**)
Prepared from 25.2 g (0.14 mol) of Mannich base **3c** and 21.0 g (0.14 mol) of enamine **4**. Yield 21.3 g (77%) of an oil after distillation, *b.p*. 175° C/0,9 mbar. – ^{1}H NMR (200 MHz, $CDCl_3$) δ/ppm = 2.52 (m_c, 2H), 2.41–2.19 (m, 3H), 2.19–1.97 (m, 2H), 1.97–1.71 (m, 2H), 1.71–1.48 (m, 2H), 1.48–1.24 (m, 2 H) 1.10 (s, 9H). – ^{13}C NMR (50 MHz, $CDCl_3$) δ/ppm = 216.5 (s), 213.7 (s), 50.7 (d), 44.5 (s), 42.6 (t). 35.0 (d), 34.5 (t), 28.5 (d), 26.8 (q), 25.9 (t), 24.6 (t). – IR (KBr) ν/cm^{-1} = 2 935, 2 862, 1 713, 1 481, 1 445, 1 367, 1 305, 1 129, 1 062, 985.

2-(2-Methyl-3-oxo-3-phenyl-propyl)-cyclohexanone (**5d**)
Prepared from 2.4 g (10.6 mmol) of Mannich base **3d** and 1.51 g (10 mmol) of enamine **4**. Yield 1.1 g (46%) of an oil after distillation, *b.p*. 190 °C/0.8 mbar.

2-(3-Oxo-2,3-diphenyl-propyl)-cyclohexanone (**5e**)
Prepared from 2.14 g (7.4 mmol) of Mannich base **3e** and 1.12 g (7.4 mmol) of enamine **4**. Yield 1.5 g (67%) of an oil which slowly crystallizes after distillation, *b.p*. 200 °C/0.8 mbar. – ^{1}H NMR (200 MHz, $CDCl_3$) δ/ppm = 8.03 (m_c, 2H), 7.63–7.20 (m, 8H), 4.94 (m_c, 1H), 2.54–1.31 (m, 9H). – ^{13}C NMR (50 MHz, $CDCl_3$) δ/ppm = 214.1 (s), 213.9 (s), 200.4 (s), 198.1 (s), 140.6 (s), 138.5 (s), 136.6 (s), 137.0 (s), 135.0 (s), 133.6 (d), 133.4 (d), 133.3 (s), 129.9 (d), 129.4 (d), 129.3 (d), 129.2 (d), 129.1 (d), 129.1 (d), 129.0 (d), 128.4 (d) 127.6 (d), 127.4 (d), 127.3 (d), 51.6 (d), 51.0 (d). 49.3 (d), 48.1 (d), 45.8 (t), 42.8 (t), 35.8 (t), 35.3 (t), 34.4 (t), 35.6 (t), 28.7 (t), 28.6 (t), 25.5 (t).

Preparation of the 5,6,7,8-Tetrahydroquinolines (6a–e) (General Procedure)

The diketone (10.0 mol) and hydroxylammonium hydrochloride (10.0 mol) were refluxed in 10 mL of ethanol for 3 h. The reaction mixture was neutralized with Na_2CO_3. After addition of 50 mL of water the solution was extracted with CH_2Cl_2 (4 × 30 mL). The combined organic layers were dried over Na_2SO_4. Rotary evaporation yielded the crude products which were purified either by Kugelrohr distillation or chromatography.

2-Phenyl-5,6,7,8-tetrahydroquinoline (**6a**)
Prepared from 1.43 g (6.3 mmol) of diketone **5a** and 0.44 g (6.3 mmol) of hydroxyl-ammonium hydrochloride. Yield 0.55 g (42%) of an oil after distillation, *b.p*. 150–160 °C/0.3 mbar [10a]. – ^{1}H NMR (200 MHz, $CDCl_3$) δ/ppm = 7.95 (mc, 2H), 7.38 (m_c, 5H), 3.00 (t, ^3J = 6.2 Hz, 2H), 2.77 (t, ^3J = 6.2 Hz, 2H), 1.88 (m_c, 4H). – ^{13}C NMR (50 MHz, $CDCl_3$) δ/ppm = 157.7 (s), 155.1 (s), 140.4 (s), 137.9 (d), 131.2 (s), 129.1 (d), 127.8 (d), 127.3 (d), 118.4 (d), 33.3 (t), 29.0 (t), 23.7 (t), 23.3 (t). – IR (KBr) ν/cm^{-1} = 2 929, 2 862, 1 594, 1 564, 1 455, 1 253, 1 253, 1 129, 1 031, 772, 736, 695. – MS (EI/70 eV) *m/z* (%) = 208 (100) [M$^+$], 195 (11), 181 (30), 154 (3), 141 (6), 115 (10), 77 (9).

2-(4-Brom-phenyl)-5,6,7,8-tetrahydroquinoline (**6b**)
Prepared from 1.66 g (5.4 mmol) of diketone **5b** and 0.38 g (5.4 mmol) of hydroxylammonium hydrochloride. Yield

0.70 g (45%) of a white solid after chromatography on SiO_2, petroleum ether/Et_2O, 5:1, *m.p.* 109 °C. – ^{1}H NMR (200 MHz, $CDCl_3$) δ/ppm = 7.87 (m_c, 2H), 7.59 (m_c, 2H), 7.45 (s, 2H), 3.02 (t, ^3J = 6.2 Hz, 2H), 2.83 (t, ^3J = 6.2 Hz, 2H), 1.92 (m_c, 4H, CH_2). – ^{13}C NMR (50 MHz, $CDCl_3$) δ/ppm = 157.9 (s), 153.0 (s), 139.2 (s), 137.9 (d), 132.1 (d), 131.6 (s), 128.8 (d), 123.1 (s), 118.0 (d), 32.2 (t), 29.0 (t), 23.6 (t), 23.2 (t). – IR (KBr) ν/cm^{-1} = 2 940, 1 579, 1 455, 1 072, 1 005, 813.

2-(tert-Butyl)-5,6,7,8-tetrahydroquinoline (**6c**)

Prepared from 21.3 g (0.11 mol) of diketone **5c** and 7.3 g (0.11 mol) of hydroxylammonium hydrochloride. Yield 15.0 g (76%) of a liquid after distillation, *b.p.* 97 °C 1 mbar [22]. – ^{1}H NMR (200 MHz, $CDCl_3$) δ/ppm = 7.31 (d, ^3J = 8.0 Hz, 1H), 7.11 (d, ^3J = 8.0 Hz, 1H), 2.95 (t, ^3J = 6.3 Hz, 2H), 2.77 (t, ^3J = 6.3 Hz, 2H), 1.89 (m_c, 4H), 1.39 (s, 9H). – ^{13}C NMR (50 MHz, $CDCl_3$) δ/ppm) = 166.5 (s), 156.2 (s), 137.2 (d), 129.1 (s), 116.5 (d), 37.4 (s), 33.3 (t), 30.8 (q), 28.9 (t), 23.8 (t), 23.3 (t). – IR (KBr) ν/cm^{-1} = 2 952, 2 852, 1 595, 1 568, 1 488, 1 468, 1 350, 1 132, 823.

2-Phenyl-3-methyl-5,6,7,8-tetrahydroquinoline (**6d**)

Prepared from 1.0 g (4.6 mmol) of diketone **5d** and 0.88 g (4.6 mmol) of hydroxylammonium hydrochloride. Yield 0.34 g (33%) of an oil after chromatography on SiO_2, petroleum ether/Et_2O, 2:1. – ^{1}H NMR (200 MHz, $CDCl_3$) δ/ppm = 7.39 (m_c, 5H), 7.23 (s, 1H), 2.94 (t, ^3J = 6.2 Hz, 2H), 2.76 (t, ^3J = 6.2 Hz, 2H), 2.24 (s, 3H). – ^{13}C NMR (50 MHz, $CDCl_3$) δ/ppm = 156.2 (s), 154.8 (s), 14.1 (s), 139.6 (d), 131 (s), 129.4 (d), 128.6 (d), 128.1 (s), 127.0 (d), 32.7 (t), 28.8 (t), 23.8 (d), 23.3 (d), 19.9 (q). – IR (KBr) ν/cm^{-1} = 2 929, 2 852, 1 564, 1 435, 1 429, 1 248, 1 021, 783, 741, 705.

2,3-Diphenyl-5,6,7,8-tetrahydroquinoline (**6e**)

Prepared from 1.5 g (5.0 mmol) of diketone **5e** and 0.36 g (5.0 mmol) of hydroxylammonium hydrochloride. Yield 0.5 g (54%) of white crystals after chromatography on SiO_2, petroleum ether/Et_2O, 10:1, *m.p.* 105 °C [23]. – ^{1}H NMR (200 MHz, $CDCl_3$) δ/ppm = 7.38 (s, 1H), 7.33 (m_c, 2H), 7.20 (m_c, 8H), 3.03 (t, ^3J = 6.3 Hz, 2H), 2.83 (t, ^3J = 6.3 Hz, 2H), 1.80 (m_c, 4H). – ^{13}C NMR (50 MHz, $CDCl_3$) δ/ppm = 156.6 (s), 154.7 (s), 140.9 (s), 140.6 (s), 139.6 (d), 133.8 (s), 131.2 (s), 130.4 (d), 130.0 (d), 128.6 (d), 128.3 (d), 127.8 (d), 127.3 (d), 33.0 (t), 28.9 (t), 23.7 (t), 23.3 (t). – IR (KBr) ν/cm^{-1} = 2 924, 2 857, 1 543, 1 445, 1 424, 1 248, 1 070, 990, 767, 700. – MS (EI/70 eV) *m/z* (%) = 285 (100) [M$^+$], 256 (13), 215 (5), 165 (3), 133 (6), 127 (10), 114 (6), 77 (4).

Preparation of the Hexahydroacridinones (8f–g) (General Procedure)

A suspension of 5 mmol of the appropiate carbonyl compound, 5 mmol of the β-amino ketone hydrochloride and 15 mmol of ammonium acetate (anhydrous) in 25–30 mL of absolute ethanol were refluxed for 3–4 h under argon. After cooling to room temperature, the ethanol was removed *in vacuo*. The crude product was dissolved in a mixture of 35–40 mL CH_2Cl_2, 15–20 mL of H_2O and 5 mL of 25% ammonia solution. The organic layer was separated, and the residual aqueous layer was extracted with CH_2Cl_2 (3 × 15 mL). The combined organic layers were washed with H_2O and dried with Na_2SO_4. After removal of the solvent, the residue was dissolved in 25 ml of CH_2Cl_2, and circa 2 g of SiO_2 are added. The mixture was stirred under an oxygen atmosphere over night and then filtered. The filter cake was washed thoroughly with CH_2Cl_2/MeOH, 10:1. The solvent was removed in vacuo, and the residue was purified by flash chromatography on Al_2O_3, CH_2Cl_2.

3,4,5,6,7,8-Hexahydro-2H-acridin-1-one (**8f**)

Prepared from 5.0 g (21.6 mmol) of Mannich base **3f**, 2.42 g (21.6 mmol) of 1,3-cyclohexandione (**7**) and 4.99 g (64.8 mmol) of NH_4OAc. Yield 3.56 g (76%) of a yellow solid after flash chromatography on Al_2O_3, CH_2Cl_2, *m.p.* 96 °C [12a]. – ^{1}H NMR (200 MHz, $CDCl_3$) δ/ppm = 7.98 (s, 1H), 3.10 (t, ^3J = 6.1 Hz, 2H), 2.97 (t, ^3J = 6.1 Hz, 2H), 2.83 (t, ^3J = 6.1 Hz, 2H), 2.68 (m_c, 2H), 2.19 (m_c, 2H), 1.91 (m_c, 4H). – ^{13}C NMR (50 MHz, $CDCl_3$) δ/ppm = 198.7 (s), 162.9 (s), 160.9 (s), 135.6 (d), 131.5 (s), 126.3 (s), 39.0 (t), 33.5 (t), 32.6 (t), 28.7 (t), 23.2 (t), 22.9 (t), 22.5 (t). – IR (KBr) ν/cm^{-1} = 3 021, 2 999, 2 941, 2 876, 2 557, 1 998, 1 693, 1 635, 1 556, 1 425, 1 363, 1 332, 1 284, 801.

1,2,3,5,6,7-Hexahydro-cyclopenta[b]quinolin-8-one (**8g**)

Prepared from 680 mg (3.84 mmol) of Mannich base **3g**, 430 mg (3.84 mmol) of 1,3-cyclohexandione (**6**) and 887 mg (11.52 mmol) of NH_4OAc. Yield 304 mg (42%) of a white solid after flash chromatography on Al_2O_3, CH_2Cl_2, *m.p.* 59 °C [12a]. – ^{1}H NMR (200 MHz, $CDCl_3$) δ/ppm = 8.63 (s, 1H), 2.88 (mc, 6H), 2.51 (t, ^3J = 6.1 Hz, 2H), 2.02 (m_c, 4H). – ^{13}C NMR (50 MHz, $CDCl_3$) δ/ppm = 198.4 (s), 171.1 (s), 162.4 (s), 136.1 (s), 130.6 (d). 126.4 (s), 38.9 (t), 35.0 (t), 32.8 (t), 30.5 (t), 23.3 (t), 22.4 (t). – IR (KBr) ν/cm^{-1} = 2939, 1690, 1602, 1408, 1360, 1210, 924.

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