JOC*Note*

Electrosynthesis of 3-Chloro-1,4-disubstituted-2(1*H*)-quinolinones and 3,3-Dichloro-4-hydroxy-1,4-disubstituted-3,4-dihydro-2(1*H*)-quinolinones, as Well as a New Convenient Process to Dioxindoles†

Belén Batanero and Fructuoso Barba*

Department of Organic Chemistry, University of Alcalá, 28871 Alcalá de Henares (Madrid), Spain

fructuoso.barba@uah.es

Received November 20, 2002

Abstract: Cathodic reduction of *N*-(2-acyl(or aroyl)phenyl)-2,2,2,-trichloro-*N*-alkylacetamide at −1.2 V (vs SCE) under aprotic conditions yields 3-chloro-1,4-disubstituted-2(1*H*)-quinolinones (**1**) as the major product. When the reaction is carried out at −0.8 V (vs SCE), 3,3-dichloro-4-hydroxy-1,4-disubstituted-3,4-dihydro-2(1*H*)-quinolinones (**2**) and 1,4-disubstituted-1,4-dihydro-quinoline-2,3-dione (**3**) are formed. Ring contraction of **2** and **3** in aqueous sodium hydroxide resulted in the formation of 3-hydroxy-1,3-dihydroindol-2-ones (**5**). The most plausible reaction mechanisms are proposed.

Cathodic reduction of α-halocarbonyl substrates has been demonstrated to be a useful procedure to synthesize heterocyclic compounds.[1]

Quinolin-2-one derivatives have been paid considerable attention in organic chemistry due to their use as antiinflammatories, antihypertensives, and analgesics[2] or in the preparation of antipsychotic agents.[3] 3-Halo-2(1*H*)-quinolinones have been used as cardiac stimulants[4] and as herbicides.[5] The 3,3-dihalo-3,4-dihydroquinolin-2,4-diones have shown antiinflamatory activity[6] and *N*-substituted 3-arylquinolin-2,4-diones are natural alkaloid precursors;[7] in addition 3-aryl-4-hydroxyquinolin-2(1*H*)-ones have recently been found[8] to serve as key intermediates in the synthesis of non-peptide GnRH receptor antagonists.

Some described synthetic procedures to produce 3-chloro-1,4-dialkyl-2(1*H*)-quinolones involve halocarbene intermediates.[9,10] However, 3-halo-*N*-substituted-2(1*H*)-quinolinones have been prepared by using the Vilsmaier reagent,[11−13] and 3,3-dichloro-4-aryl-*N*-substituted-3,4-dihydro-2(1*H*)-quinolone synthesis involves cyclization of *β*-keto amides in H_2SO_4.[14]

Dioxindoles are recognized antihypoxic compounds but their biological activity has been evaluated only as racemates.[15] Dioxindol derivatives are encountered in nature and were isolated from the culture of a marine Streptomyces species.[16] Dioxindoles can be obtained by Grignard reaction on isatines[17] and by oxidation of 1,3-disubstituted-2-indolinones.[18] Enantiomerically pure dioxindoles can be obtained via catalytic hydrogenations of isatine derivatives.[19]

In the present paper an easy methodology to prepare 1-alkyl-4-alkyl(or phenyl)-3-chloro-2(1*H*)-quinolinones and 1-alkyl-4-alkyl(or phenyl)-3,3-dichloro-4-hydroxy-3,4-dihydro-2(1*H*)-quinolinones, as well as a simple process to dioxindole derivatives by using *N*-alkyl-acetamides as starting material, is described.

The electroactive substrates were obtained by *N*-alkylations of 2-aminophenones prior to acylations with trichloroacetic acid chloride.[20] Methyl, ethyl, and isopropyl iodides were used as alkylating agents.

Cyclic voltammograms (scan rate: 0.1 V/s) of *N*-(2-acyl-(or aroyl)phenyl)-*N*-alkylacetamides exhibit two irreversible $1e^-$ (−0.8 V) and $2e^-$ (−0.9 V vs SCE) peaks. Cathodic reduction of these substrates, in dry acetonitrile/$LiClO_4$ with mercury as a cathode at a constant potential of −1.2 V vs SCE, affords 1-alkyl-3-chloro-4-methyl(or phenyl)-1*H*-quinolin-2-ones (**1**) in good yield (70−82%). Coulommetry under these potential conditions confirms a $3e^-$ process.

Preparative scale electrolyses at the first peak potential were performed. However, due to the vicinity of the second peak, the charge consumption at the end of the

† Dedicated to Prof. Hans J. Schäfer on the occasion of his 65th birthday.

(1)] (a) Barba, F.; Batanero, B. *J. Org. Chem.* **1993**, *58*, 6889. (b) Barba, F.; de la Fuente, J. L. *J. Org. Chem.* **1996**, *61*, 8662−8663. (c) Batanero, B.; Vago, M.; Barba, F. *Heterocycles* **2000**, *53*, 1337−1342. (d) Batanero, B.; Barba, F. *Electrochem. Commun.* **2001**, *3*, 595−598.

(2)] Setoguchi, N.; Takano, Y. Ch. Kitami. Jpn. Kokai Tokkyo Koho: JP 01006269A2, Jan 1989.

(3)] Howard, H. R. Eur. Pat. Appl. EP 409,435 (Cl. C07D403 14).

(4)] Roberts, D. A.; Campbell, S. F. Faming Zhuanli Shenqing Gongkai Shuomingshu CN 85,100,796 (Cl. C07D401/04), 1986.

(5)] Theodoridis, G. US 4,909,829 (Cl.71-92; A01N43/64), Appl. 138,-981, 1987.

(6)] Faber, K.; Steininger, H.; Kappe, Th. *J. Heterocycl. Chem.* **1985**, *22*, 1081.

(7)] Ji, R. Y. *Med. Chem. Res.* **1995**, *5*, 587.

(8)] DeVita, R. J.; Hollings, D. D.; Goulet, M. T.; Wyvratt, M. J.; Fisher, M. H.; Lo, J.-L.; Yang, Y. T.; Cheng, K.; Smith, R. G. *Bioorg. Med. Chem. Lett.* **1999**, *9*, 2615.

(9)] Rees, C. W.; Smithen, C. E. *J. Chem. Soc.* **1984**, 938.

(10)] De Angelis, F.; Inesi, A.; Feroci, M.; Nicoletti, R. *J. Org. Chem.* **1995**, *60*, 445.

(11)] Chupp, J. P.; Metz, S. *J. Heterocycl. Chem.* **1979**, *16*, 65.

(12)] Hayes, R.; Meth-Cohn, O.; Tarnowski, B. *J. Chem. Res. Synop.* **1980**, 414.

(13)] Andreani, A.; Bonazzi, D.; Rambaldi, M. *Boll. Chim. Farm.* **1976**, *115*, 732.

(14)] Staskun, B. *J. Org. Chem.* **1980**, *45*, 2482. Marais, J. L. C.; Staskun, B. *J. Org. Chem.* **1985**, *50*, 4652.

(15)] Mazhilis, L. I.; Garalene, V. N.; Stankyavichyus, A. P.; Risyalis, S. P. *Khim. Farmat. Zh.* **1985**, *19*, 960.

(16)] Tang, Y.-Q.; Sattler, I.; Thiericke, R.; Grabley, S.; Feng, X.-Z. *Eur. J. Org. Chem.* **2001**, 261−267. Balk-Bindseil, W.; Helmke, E.; Weyland, H.; Laatsch, H. *Liebigs Ann. Chem.* **1995**, 1291−1294.

(17)] Ogata, M.; Matsumoto, H.; Tawara, K. *Eur. J. Med. Chem. Chim. Ther.* **1981**, *16*, 373−379. Wierenga, W.; Griffin, J.; Warpehoski, M. A. *Tetrahedron Lett.* **1983**, *24*, 2437−2440.

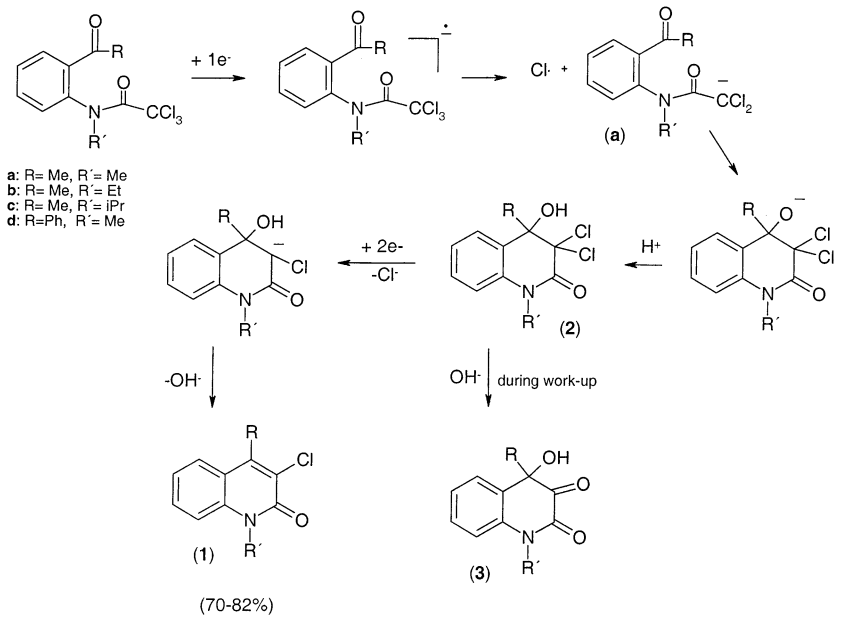
(18)] Nishio, T. *J. Chem. Soc., Perkin Trans. 1* **1991**, 1717−1720.

(19)] Carpentier, J.-F.; Mortreux, A. *Tetrahedron*: *Asymmetry* **1997**, *8*, 1083−1099.

(20)] Cathodic reduction of *N*-(2-acetylphenyl)-2,2,2-trichloroacetamide yields *N*-(2-acetylphenyl)-2,2-dichloroacetamide as the only product. This reaction involves protonation of the electrogenerated anion. For this reason to protect the nitrogen atom, 2-aminophenone (10 mmol) was refluxed in toluene for 3−6 h in the presence of the corresponding alkyl iodide (20 mmol) to get *N*-alkyl-2-aminophenones in very good yield. Subsequent acylation of them (10 mmol) with commercially available trichloroacetic acid chloride (12 mmol) added dropwise and refluxing in toluene afforded quantitatively *N*-(2-acyl-(or aroyl)phenyl)-2,2,2-trichloro-*N*-alkylacetamides. These electroactive acetamides have been used after purification in silica gel chromatography with $CHCl_3$/EtOH(100/1) as eluent.

10.1021/jo0267403 CCC: $25.00
Published on Web 03/29/2003

SCHEME 1



electrolysis was slighly higher than expected for a 1e$^-$ process. The reaction products were isolated and identified as 1-alkyl-3,3-dichloro-4-hydroxy-4-methyl-3,4-dihydro-1*H*-quinolin-2-one (**2**) (as major product) and 1-alkyl-3-chloro-4-methyl(or phenyl)-1*H*-quinolin-2-one (**1**) and 1-alkyl-4-hydroxy-4-methyl(or phenyl)-1,4-dihydroquinoline-2,3-dione (**3**) as side products.

The formation of these compounds is explained as follows: reduction of *N*-alkylacetamides at −0.8 V (vs SCE), by uptake of 1e$^-$, affords the corresponding radical anion, which further decomposes to chlorine radical and the anion **a** (Scheme 1).

As confirmed by our previous studies,[1d] the unusual fragmentation of the radical anion is supported by formation of anion **a**, which is highly stabilized by the inductive effect of chlorine atoms and the resonance effect of the adjacent carbonyl group. Subsequent intramolecular attack of the carbanion to the acyl (or aroyl) group gives compound **2** as the major product.

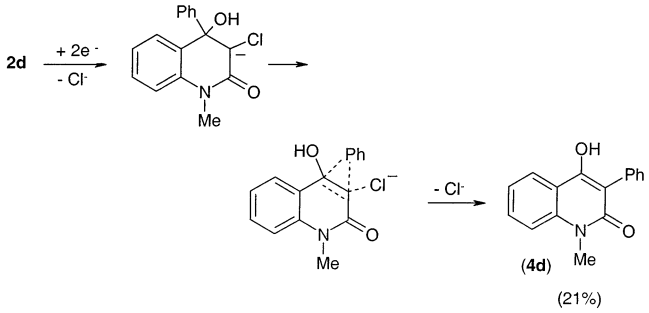
As expected, 1-alkyl-4-hydroxy-4-methyl(or phenyl)-1,4-dihydroquinoline-2,3-dione (**3**) is formed, due to the basic medium of the catholyte, during workup (see the Experimental Section), through a substitution of chlorine by OH.

The selective reduction of *N*-(2-acetyl(or benzoyl)-phenyl)-*N*-alkylacetamides to **2**, without further reduction of **2** to 1-alkyl-3-chloro-4-methyl(or phenyl)-1*H*-quinolin-2-one (**1**), is difficult due to the vicinity of the two reduction peaks.

The product **1** arises from the electrochemical reduction of **2**. It was confirmed when **2**, previously isolated and purified, was electrolized at −1.2 V. In this case, the only obtained product was 1-alkyl-3-chloro-4-methyl(or phenyl)-1*H*-quinolin-2-one (**1**), with an experimental charge consumption corresponding to a 2e$^-$ process.

Controlled potential (−1.2 V vs SCE) reduction of *N*-(2-benzoylphenyl)-2,2,2-trichloroacetamide affords 3-chloro-1-methyl-4-phenyl-1*H*-quinolin-2-one (**1d**) (70%) and 1-methyl-3-phenyl-1*H*-quinolin-2,4-dione (**4d**) (21%). The formation of **4d** is summarized in Scheme 2.

SCHEME 2



Once **2d** is formed, electrochemical C−Cl cleavage takes place immediately in a 2e$^-$ process to give the corresponding anion, which yields **1d** by subsequent elimination of OH$^-$ whereas **4d** is formed by migration of the phenyl group to the carbene center, generated after elimination of Cl$^-$ (Scheme 2). The participation of the phenyl group in this migration is clear because when other groups are employed the rearrangement is only negligible.

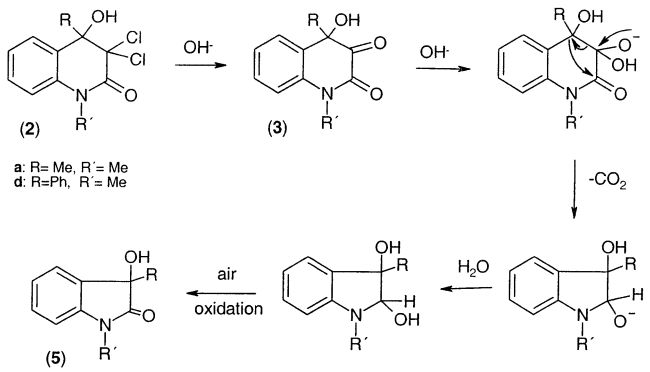
On the other hand, **2** can be converted quantitatively into 3-hydroxy-3-alkyl(or aryl)-1-methyl-2(1*H*)-indolinone (**5**) by alkali (5% NaOH water solution) in 30 min at room temperature in the presence of air (Scheme 3). In the last step, the air oxidation is a facile reaction of indole-2,3-dihydrodiols, which has already been reported.[21] The process takes place through the formation of **3**, which leads to dioxindol **5** under the same alkaline conditions.

Experimental Section

General Electrochemical Procedure. The electrochemical reductions were performed under potentiostatic conditions in a concentric cell with two compartments separated by a porous (D3) glass diaphragm and equipped with a magnetic stirrer. A mercury pool (20 cm^2) was used as the cathode, a platinum plate as the anode, and a saturated calomel electrode as the reference.

(21)] Kafka, S.; Klasek, A.; Kosmrlj, J. *J. Org. Chem.* **2001**, *66*, 6394.

SCHEME 3



The solvent-supporting electrolyte system (SSE) was nominally anhydrous acetonitrile containing 0.05 M lithium perchlorate. Anhydrous potassium carbonate was added to the anodic compartment for "in situ" neutralization of the generated perchloric acid.

A solution of the electroactive *N*-(2-acyl(or aroyl)phenyl)-2,2,2-trichloro-*N*-alkylacetamide (5.0 mmol in 30 mL of SSE) was electrolyzed at a constant potential of −0.8 V and −1.2 V (versus SCE). The initial current was 200 or 300 mA, respectively, depending on the applied potential. When the current fell almost to zero, the reduction was finished and the solvent in the cathodic solution was removed under reduced pressure. The residue was extracted with ether/water and the organic phase dried over Na_2SO_4 and concentrated by evaporation. The resulting solid or oil was chromatographed on a silica gel (18 × 3 cm) column, using toluene/MeOH (80/1) as eluent. Spectroscopical description of all the compounds is given below.

***N*-(2-Acetylphenyl)-2,2,2,-trichloro-*N*-methylacetamide:** Mp 58 °C. IR (KBr) ν 3069, 2973, 1730, 1685, 1601, 1364, 1250, 839, 763, 661 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.57 (s, 3H), 3.68 (br s, 3H), 7.2−7.3 (m, 1H), 7.4−7.62 (m, 2H), 7.7−7.8 (m, 1H). ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 28.4, 41.8, 92.6, 127.6, 128, 129, 132.6, 135.5, 141.7, 159.5, 198.6. MS *m/e* (rel intensity) EI 293 (M^+, 1), 250 (32), 215 (10), 182 (61), 176 (100), 148 (68), 134 (72), 104 (28), 91 (36), 77 (69), 51 (32).

***N*-(2-Acetylphenyl)-2,2,2,-trichloro-*N*-ethylacetamide:** Mp 65−67 °C. IR (NaCl) ν 3071, 2979, 1736, 1683, 1596, 1250, 841, 765, 669 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.17 (br s, 3H), 2.6 (s, 3H), 4.31 (br s, 2H), 7.2−7.9 (m, 4H). ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 12.6, 28.6, 47.5, 92.7, 128.3, 129.2, 129.5, 130.0, 132.4, 135.7, 162.7, 200.2. MS *m/e* (rel intensity) EI 274 ($M^+ + 2 - Cl$, 4), 272 ($M^+ - Cl$, 6), 268 (3), 266 (9), 230 (4), 190 (27), 162 (100), 146 (29), 144 (66), 116 (26), 105 (9), 91 (13), 77 (20), 51 (6).

***N*-(2-Acetylphenyl)-2,2,2,-trichloro-*N*-isopropylacetamide:** Mp 69−71 °C. IR (KBr) ν 3071, 2977, 1735, 1689, 1596, 1247, 836, 758, 667 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.91 (br s, 3H), 1.24 (d, 3H, J = 6.4 Hz), 2.51 (s, 3H), 5.08 (br s, 1H), 7.1−7.4 (m, 1H), 7.4−7.57 (m, 2H), 7.77 (br s, 1H). ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 19.1, 20.9, 28.4, 53.4, 94, 128.8, 129.5, 130.1, 131.7, 132.3, 132.9, 160, 198.2. MS *m/e* (rel intensity) EI 288 ($M^+ + 2 - Cl$, 16), 286 ($M^+ - Cl$, 25), 238 (5), 236 (5), 204 (8), 176 (48), 162 (100), 144 (71), 116 (31), 91 (21), 77 (15), 63 (7), 51 (6).

***N*-(2-Benzoylphenyl)-2,2,2,-trichloro-*N*-methylacetamide:** Mp 67 °C. IR (NaCl) ν 3064, 1663, 1598, 1377, 1275, 840, 750 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.63 (s, 3H), 7.3−7.6 (m, 7H), 7.75−7.85 (m, 2H). ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 42.6, 93.1, 128.0, 128.4, 128.6, 130.7, 130.9, 132.3, 133.6, 136.8, 137.0, 142.8, 160.1, 195.5. MS *m/e* (rel intensity) EI 357 ($M^+ + 2$, 0.3), 355 (M^+, 0.2), 322 ($M^+ + 2 - Cl$, 2), 320 ($M^+ - Cl$, 3), 284 (3), 252 (8), 250 (9), 238 (22), 210 (1), 180 (15), 152 (10), 132 (8), 105 (100), 91 (17), 77 (68), 51 (18).

Electrochemical Reduction at −1.2 V (vs SCE). 3-Chloro-1,4-dimethyl-1*H*-quinolin-2-one (1a): 797 mg, 77% yield. Mp 180 °C [lit.[9] mp 187 °C]. IR (KBr) ν 2924, 1648, 1596, 1081, 963, 814, 749 cm^{-1}. ^{1}H NMR [10] (300 MHz, $CDCl_3$) δ 2.65 (s, 3H), 3.8 (s, 3H), 7.3 (t, 1H, J = 7.1 Hz), 7.38 (d, 1H, J = 8.3 Hz), 7.6 (t, 1H, J = 7.1 Hz), 7.76 (d, 1H, J = 8.3 Hz). ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 16.6, 31, 114.7, 120.8, 122.8, 123.1, 125.6, 130.6, 139.8, 142.7, 158.2. MS *m/e* (rel intensity) EI 209 ($M^+ + 2$, 33), 207 (M^+, 100), 178 (32), 164 (16), 144 (45), 128 (23), 115 (27), 102 (15), 81 (19), 69 (36), 51 (14).

3-Chloro-1-ethyl-4-methyl-1*H*-quinolin-2-one (1b): 862 mg, 78% yield. Mp 110−112 °C. IR (KBr) ν 3087, 2978, 1643, 1597, 1093, 993, 821, 748 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.34 (t, 3H, J = 7.1 Hz), 2.6 (s, 3H), 4.37 (q, 2H, J = 7.1 Hz), 7.25 (t, 1H, J = 7.5 Hz), 7.37 (d, 1H, J = 8.4 Hz), 7.55 (t, 1H, J = 7.1 Hz), 7.72 (dd, 1H, J_1 = 8.1 Hz, J_2 = 1.3 Hz). ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 12.5, 16.4, 38.5, 114.2, 120.7, 122.3, 125.5, 126.1, 130.3, 136.7, 142.3, 157.3. MS *m/e* (rel intensity) EI 223 ($M^+ + 2$, 23), 221 (M^+, 69), 220 ($M^+ - 1$, 68), 195 (34), 193 (100), 164 (23), 143 (19), 130 (38), 128 (29), 115 (19), 101 (16), 89 (8), 77 (20), 63 (13), 51 (14). Anal. Calcd for $C_{12}ClH_{12}NO$: C, 65.01; H, 5.42; N, 6.32. Found: C, 64.77; H, 5.62; N, 6.29.

3-Chloro-1-isopropyl-4-methyl-1*H*-quinolin-2-one (1c): 963 mg, 82% yield. Mp 64−66 °C. IR (KBr) ν 2970, 2933, 1652, 1600, 1380, 1365, 1302, 1025, 749 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.34 (d, 6H, J = 7.0 Hz), 2.62 (s, 3H), 5.42 (br s, 1H), 7.22−7.3 (t, 1H, J = 7.6 Hz), 7.5−7.6 (m, 2H), 7.74 (d, 1H, J = 8.3 Hz). ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 16.7, 19.9, 48.8, 115.2, 121.5, 122.4, 125.9, 127.1, 129.9, 137.4, 142.2, 158.2. MS *m/e* (rel intensity) EI 237 ($M^+ + 2$, 8), 235 (M^+, 25), 234 ($M^+ - 1$, 13), 195 (34), 193 (100), 176 (4), 164 (15), 130 (22), 128 (15), 103 (7), 77 (8). Anal. Calcd for $C_{13}ClH_{14}NO$: C, 66.24; H, 5.94; N, 5.94. Found: C, 65.97; H, 5.77; N, 6.11.

3-Chloro-1-methyl-4-phenyl-1*H*-quinolin-2-one (1d): 942 mg, 70% yield. Mp 163−165 °C. IR (KBr) ν 2925, 1650, 1597, 1080, 754, 701 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.85 (s, 3H), 7.1−7.2 (m, 2H), 7.27 (d, 2H, J = 7.3 Hz), 7.38−7.42 (d, 1H, J = 7.7 Hz), 7.45−7.6 (m, 4H). ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 31.2, 114.5, 121.2, 122.7, 128.3, 128.8, 129, 130.8, 135.4, 138.6, 147.4, 158.6. MS *m/e* (rel intensity) EI 271 ($M^+ + 2$, 34), 269 (M^+, 100), 243 (11), 241 (31), 234 (18), 204 (14), 190 (16), 176 (9), 165 (13), 152 (4), 117 (6), 102 (6), 63 (5), 51 (8). Anal. Calcd for $C_{16}ClH_{12}NO$: C, 71.24; H, 4.45; N, 5.19. Found: C, 71.22; H, 4.67; N, 5.04.

Electrochemical Reduction at −0.8 V (vs SCE). 3,3-Dichloro-4-hydroxy-1,4-dimethyl-3,4-dihydro-1*H*-quinolin-2-one (2a): 660 mg, 51% yield. Mp 158−160 °C. IR (KBr) ν 3411, 2988, 1671, 1600, 1370, 1183, 768 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.55 (br s, 3H), 2.8 (br s, 1H), 3.5 (s, 3H), 7.07 (d, 1H, J = 8.1 Hz), 7.22 (t, 1H, J = 7.6 Hz), 7.39 (t, 1H, J = 8.1 Hz), 7.7 (br s, 1H). ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 24.3, 29.3, 31.2, 76.9, 114.8, 124.4, 128.1, 129.0, 130.0, 135.6, 161.5. MS *m/e* (rel intensity) EI 261 ($M^+ + 2$, 10), 259 (M^+, 16), 218 (9), 216 (14), 182 (5), 180 (12), 149 (100), 134 (59), 117 (5), 91 (6), 77 (15), 51 (5). Anal. Calcd for $C_{11}Cl_2H_{11}NO_2$: C, 50.77; H, 4.23; N, 5.38. Found: C, 51.02; H, 4.20; N, 5.23.

3,3-Dichloro-1-ethyl-4-hydroxy-4-methyl-3,4-dihydro-1*H*-quinolin-2-one (2b): 737 mg, 54% yield. Mp 98−100 °C. IR (KBr) ν 3436, 2981, 1682, 1604, 1385, 954, 842, 757 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.28 (t, 3H, J = 7.2 Hz), 1.51 (br s, 3H), 3.0 (br s, 1H), 4.1 (br s, 2H), 7.1 (d, 1H, J = 8.2 Hz), 7.2 (t, 1H, J = 7.6 Hz), 7.36 (t, 1H, J = 7.6 Hz), 7.67 (br s, 1H). ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 12.3, 24.9, 30.0, 39.6, 77.4, 115.2, 124.9, 125.2, 129.5, 132, 134.8, 161.6. MS *m/e* (rel intensity) EI 275 ($M^+ + 2$, 24), 273 (M^+, 36), 232 (18), 230 (19), 194 (21), 163 (100), 148 (85), 130 (28), 105 (4), 77 (19). Anal. Calcd for $C_{12}Cl_2H_{13}NO_2$: C, 52.55; H, 4.74; N, 5.11. Found: C, 52.42; H, 4.94; N, 4.99.

3,3-Dichloro-4-hydroxy-1-isopropyl-4-methyl-3,4-dihydro-1*H*-quinolin-2-one (2c): 832 mg, 58% yield. Mp 133−134 °C. IR (KBr) ν 3470, 2970, 2934, 1685, 1601, 1365, 1342, 837, 758 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.5−1.61 (m, 9H), 2.75 (br s, 1H), 4.6 (sept, 1H, J = 6.8 Hz), 7.15 (d, 1H, J = 8.2 Hz), 7.21 (d, 1H, J = 7.5 Hz), 7.35 (t, 1H, J = 8.2 Hz), 7.65 (br s, 1H). ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 19.0, 20.3, 24.2, 29.4, 51.7, 77.4, 116.6, 124.9, 125.9, 129.2, 132.3, 136.2, 161.3. MS *m/e* (rel intensity) EI 289 ($M^+ + 2$, 12), 287 (M^+, 18), 254 (5), 252 (12), 244 (11), 210 (5), 194 (8), 177 (22), 162 (48), 135 (100), 120 (39), 102 (9),

83 (15), 77 (16), 51 (8). Anal. Calcd for $C_{13}Cl_2H_{15}NO_2$: C, 54.17; H, 5.21; N, 4.86. Found: C, 54.07; H, 4.93; N, 5.01.

4-Hydroxy-1,4-dimethyl-1,4-dihydroquinoline-2,3-dione (3a): 205 mg, 20% yield. Mp 147−149 °C. IR (KBr) ν 3384, 2928, 1711, 1676, 1603, 1372, 1100, 758 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) δ 1.62 (s, 3H), 3.5 (s, 3H), 7.1−7.2 (m, 2H), 7.67 (td, 1H, $J_1 = 1.6$ Hz, $J_2 = 7.7$ Hz), 8.0 (dd, 1H, $J_1 = 1.6$ Hz, $J_2 = 7.7$ Hz). ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 28.5, 29.3, 30, 114.7, 123.4, 125.2, 127.9, 135.9, 142.2, 172.5, 194.6. MS *m/e* (rel intensity) EI 206 ($M^+ + 1$, 4), 205 (M^+, 26), 163 (29), 162 (100), 149 (25), 134 (45), 116 (9), 106 (13), 91 (11), 77 (29), 63 (8), 51 (11). Anal. Calcd for $C_{11}H_{11}NO_3$: C, 64.39; H, 5.37; N, 6.83. Found: C, 64.25; H, 5.48; N, 6.73.

1-Ethyl-4-hydroxy-4-methyl-1,4-dihydroquinoline-2,3-dione (3b): 230 mg, 21% yield. Mp 142−143 °C. IR (KBr) ν 3400, 2989, 1712, 1677, 1601, 1382, 1198, 1108, 759 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) δ 1.25 (t, 3H, $J = 7.1$ Hz), 1.57 (s, 3H), 3.97 (br s, 1H), 4.08 (m, 2H), 7.12−7.2 (m, 2H), 7.63 (td, 1H, $J_1 = 1.8$ Hz, $J_2 = 7.9$ Hz), 7.95 (dd, 1H, $J_1 = 1.6$ Hz, $J_2 = 7.7$ Hz). ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 12.5, 28.9, 38.2, 79.5, 115.2, 120.6, 123.8, 128.7, 136.5, 141.5, 172.8, 195.4. MS *m/e* (rel intensity) EI 219 (M^+, 26), 177 (48), 176 (100), 162 (10), 148 (68), 130 (18), 120 (11), 104 (7), 77 (18), 65 (6), 51 (5). Anal. Calcd for $C_{12}H_{13}NO_3$: C, 65.75; H, 5.94; N, 6.39. Found: C, 65.65; H, 5.97; N, 6.5.

4-Hydroxy-1-isopropyl-4-methyl-1,4-dihydroquinoline-2,3-dione (3c): 245 mg, 21% yield; oil. IR (KBr) ν 3430, 2974, 2932, 1721, 1655, 1598, 1370, 1340, 1195, 1109, 754 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) δ 1.54 (s, 3H), 1.58 (s, 6H), 3.94 (br s, 1H), 4.92 (h, 1H, $J = 6.9$ Hz), 7.12−7.24 (m, 2H), 7.62 (t, 1H, $J = 7.7$ Hz), 7.96 (d, 1H, $J = 7.7$ Hz). ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 19.0, 20.3, 28.4, 43.7, 48.5, 115.7, 121.8, 123.4, 128.4, 130.5, 135.6, 172.9, 195.2. MS *m/e* (rel intensity) EI 234 ($M^+ + 1$, 3), 233 (M^+, 21), 191 (45), 190 (57), 149 (42), 148 (100), 130 (8), 120 (9), 104 (4), 92 (10), 77 (14), 65 (7). Anal. Calcd for $C_{13}H_{15}NO_3$: C, 66.95; H, 6.44; N, 6.01. Found: C, 67.16; H, 6.41; N, 6.14.

4-Hydroxy-1-methyl-4-phenyl-1,4-dihydroquinoline-2,3-dione (3d): 227 mg, 17% yield. Mp 161−162 °C. IR (KBr) ν 3423, 3071, 1708, 1667, 1602, 1361, 1098, 757 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) δ 3.57 (s, 3H), 4.4 (s, 1H), 7.1−7.4 (m, 7H), 7.6 (t, 1H, $J = 7.8$ Hz), 7.9 (d, 1H, $J = 7.8$ Hz). ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 30.6, 115.3, 121.3, 124.2, 125.9, 128.6, 129.2, 129.5, 136.5, 138.1, 142.6, 171.3, 192.8. MS *m/e* (rel intensity) EI 267 (M^+, 16), 251 (15), 250 (20), 210 (8), 162 (60), 134 (8), 105 (100), 77 (61), 63 (7), 51 (19). Anal. Calcd for $C_{16}H_{13}NO_3$: C, 71.91; H, 4.87; N, 5.24. Found: C, 72.10; H, 4.60; N, 5.42.

4-Hydroxy-1-methyl-3-phenyl-1*H*-quinolin-2-one (4d): 262 mg, 21% yield. Mp 222−224 °C [lit.[22] mp 225 °C]. IR (KBr) ν 3261, 2924, 1623, 1393, 1271, 752 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) δ 3.9 (s, 3H), 7.14 (br s, 1H), 7.19 (t, 1H, $J = 7.3$ Hz), 7.35−7.6 (m, 8H). ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 31.1, 114.4, 122.3, 123.3, 123.5, 126.4, 127.5, 128.4, 128.8, 130.1, 133.1, 134.6, 140.9, 159.1. MS *m/e* (rel intensity) EI 251 ($M^+ + 1$, 90), 250 (M^+, 100), 235 (5), 223 (4), 179 (5), 165 (14), 152 (11), 77 (9), 63 (7).

3-Hydroxy-1,3-dimethyl-1,3-dihydro-2*H*-indol-2-one (5a): mp 139−140 °C [lit.[23] mp 140−142 °C]. Spectroscopic data (IR, NMR, and MS) are coincident with those described in the literature.[23]

3-Hydroxy-1-methyl-3-phenyl-1,3-dihydro-2*H*-indol-2-one (5d): mp 141 °C [lit.[21] mp 141−143 °C]. MS *m/e* (rel intensity) EI 240 ($M^+ + 1$, 13), 239 (M^+, 72), 211 (63), 210 (100), 195 (18), 194 (69), 181 (7), 165 (13), 152 (15), 134 (24), 105 (32), 91 (15), 77 (96), 63 (16), 51 (45). Spectroscopic data (IR and NMR) are coincident with those described in the literature.[21]

Acknowledgment. This study was financed by the spanish Ministry of Science and Technology (BQU2001-1083). B. Batanero thanks to this Ministry for the "*Ramon y Cajal*" financiation.

JO0267403

(22)] Stadlbauer, W.; Schmut, O.; Kappe, Th. *Monatsh. Chem*. **1980**, *111*, 1005.

(23)] Alvarez, R. G.; Hunter, I. S.; Suckling, C. J.; Thomas, M.; Vitinius, U. *Tetrahedron* **2001**, *57*, 8581.