JOC*Note*

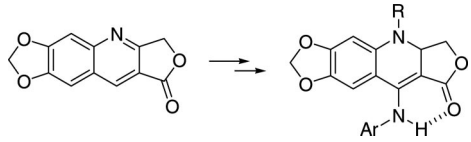
Design and Effective Synthesis of the First 4-Aza-2,3-didehydropodophyllotoxin Rigid Aminologue: A *N*-Methyl-4-[(3,4,5-trimethoxyphenyl)amino)]-1,2-dihydroquinoline-lactone

Raphaël Labruère, Philippe Helissey, Stéphanie Desbène-Finck, and Sylviane Giorgi-Renault*

Laboratoire de Chimie Thérapeutique, UMR CNRS No. 8638, Université Paris Descartes, Faculté des Sciences Pharmaceutiques et Biologiques, 4 avenue de l'Observatoire, 75270 Paris Cedex 06, France

sylviane.giorgi-renault@univ-paris5.fr

Received January 22, 2008



The first *N1*-alkyl-4-amino-1,2-dihydroquinoline-lactone has been prepared by a five-step sequence in a 51% overall yield via the corresponding furo[3,4-*b*]quinolin-1(3*H*)-one. A new practical synthesis of this intermediate was carried out using versatile, commercially available starting materials and constitutes the shortest and highest yielding route. These synthetic pathways could be widened with a view toward the preparation of different substituted derivatives, which could be considered as rigid aminologues of 4-aza-2,3-didehydropodophyllotoxins.

We have previously described and patented a three-component one-pot synthesis of 4-aza-2,3-didehydropodophyllotoxins **2**,[1,2] aza-analogues of podophyllotoxin (**1**) (Figure 1), which is a cytotoxic plant lignan. The 1,4-dihydroquinoline-lactones **2** present very interesting antitumor properties.[2]

Podophyllotoxin (**1**) works by acting in the colchicine binding site of tubulin, resulting into depolymerization of microtubules.[3,4] The colchicine binding mode was recently confirmed by the determination of an X-ray structure of α-*β* tubulin complexed with DAMA-colchicine.[3] Colchicine and podophyllotoxin bind to *β*-tubulin at its interface with α-tubulin, the trimethoxyphenyl nucleus being hidden into the *β*-subunit.[3] Furthermore, dynamic

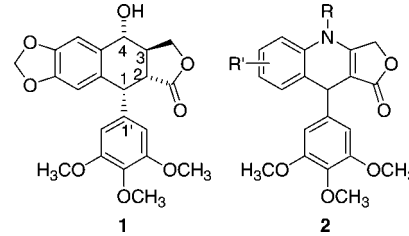


FIGURE 1. Structures of podophyllotoxin and 4-aza-2,3-didehydropodophyllotoxins.

NMR and X-ray studies show that podophyllotoxin adopts, in solution, a single conformation in which the trimethoxy phenyl ring is in a quasi-axial position and nearly perpendicular to the tricyclic moiety, and this conformation seems to be important for the binding of the molecule to the colchicine binding site in tubulin.[4] We have not yet investigated this point in the 4-aza-2,3-didehydropodophyllotoxin series.

As part of a program directed at developing new antitumor drugs, the great interest revealed by this category of biologically relevant molecules prompted us to synthesize a rigid analogue of 4-aza-2,3-didehydropodophyllotoxins (**2**). In this context, we designed the aminologue **3** in which the rotation between the tetracycle and the aryl ring is blocked by creation of an additional pseudocycle. The central heterocyclic moiety of **3** is constituted by a 4-amino-1,2-dihydroquinoline nucleus.

It is noteworthy that *N*-substituted dihydroquinolines can potentially exist in two tautomeric forms, the 1,4-dihydroquinoline being generally more stable than the 1,2-dihydro tautomer. 4-Aminodihydroquinolines are an exception when they are substituted at position 3 by an acyl or a carboxylate function. Hydrogen bonding between the NH and the CO could explain the stabilization of the 1,2-dihydro structure, and the two types of derivatives can be isolated depending on the synthetic method. 4-Amino-1,4-dihydroquinolines were obtained by addition of an amine to a quinolinium salt,[5] and the 1,2-dihydroanalogues were usually prepared by reduction of the corresponding imines.[5e,6]

Consequently, two routes were designed for the synthesis of the desired *N*-methyl-4-anilino-1,2-dihydroquinoline lactone **3** from the quinoline-lactone **7** via the imine **4**. Route A would involve a Michaël addition of the aniline to the quinolinium salt **6** and subsequent oxidation of the resulting *N*-methyl-4-amino-1,4-dihydroquinoline **5** into **4**. In route B, the 4-anilino group would be introduced on the aromatic heterocyclic skeleton before quaternarization and the imine **4** would be obtained by deprotonation of the 4-anilinoquinolinium salt **8** (Scheme 1).

* To whom correspondence may be addressed. Tel: 33 (0)1 53 73 96 98. Fax: 33 (0)1 43 29 14 03.

(1) Tratrat, C.; Giorgi-Renault, S.; Husson, H.-P. *Org. Lett.* **2002**, *4*, 3187–3189.

(2) Husson, H.-P.; Giorgi-Renault, S.; Tratrat, C.; Atassi, G.; Pierré, A.; Renard, P.; Pfeiffer, B. Eur. Pat. Appl. EP 1.103.554, 2000. *Chem. Abstr.* **2001**, *135*, P5535u.

(3) Ravelli, R. B. G.; Gigant, B.; Curmi, P. A.; Jourdain, I.; Lachkar, S.; Sobel, A.; Knossow, M. *Nature* **2004**, *428*, 192–202.

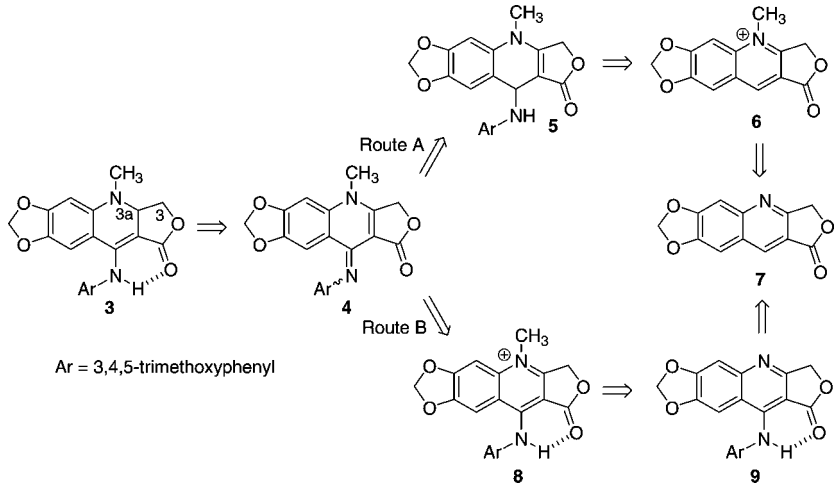
(4) Desbène, S.; Giorgi-Renault, S. *Curr. Med. Chem.*−*Anti-Cancer Agents* **2002**, *2*, 71–90, and references therein.

(5) (a) Gündel, W.-H.; Berenbold, H. *Liebigs. Ann. Chem.* **1978**, 188–190. (b) Gündel, W.-H.; Bohnert, S. *Liebigs. Ann. Chem.* **1986**, 395–401. (c) Gündel, W.-H.; Bohnert, S. *Liebigs. Ann. Chem.* **1986**, 1127–1130. (d) Bohnert, S.; Gündel, W.-H. *Z. Naturforsch.* **1987**, *42b*, 1159–1166. (e) Gündel, W.-H.; Bohnert, S. *Z. Naturforsch.* **1988**, *43b*, 769–777. (f) Gündel, W.-H.; Bohnert, S. *Liebigs. Ann. Chem.* **1988**, 611–614. (g) Duchstein, H.-J.; Fenner, H.; Franck, P.; Bauch, W. *Arch. Pharm.* **1990**, *323*, 67–72. (h) Leleu, S.; Papamicaël, C.; Marsais, F.; Dupas, G.; Levacher, V. *Tetrahedron: Asymmetry* **2004**, *15*, 3919–3928. (i) Leleu, S.; Penhoat, M.; Bouet, A.; Dupas, G.; Papamicaël, C.; Marsais, F.; Levacher, V. *J. Am. Chem. Soc.* **2005**, *127*, 15668–15669.

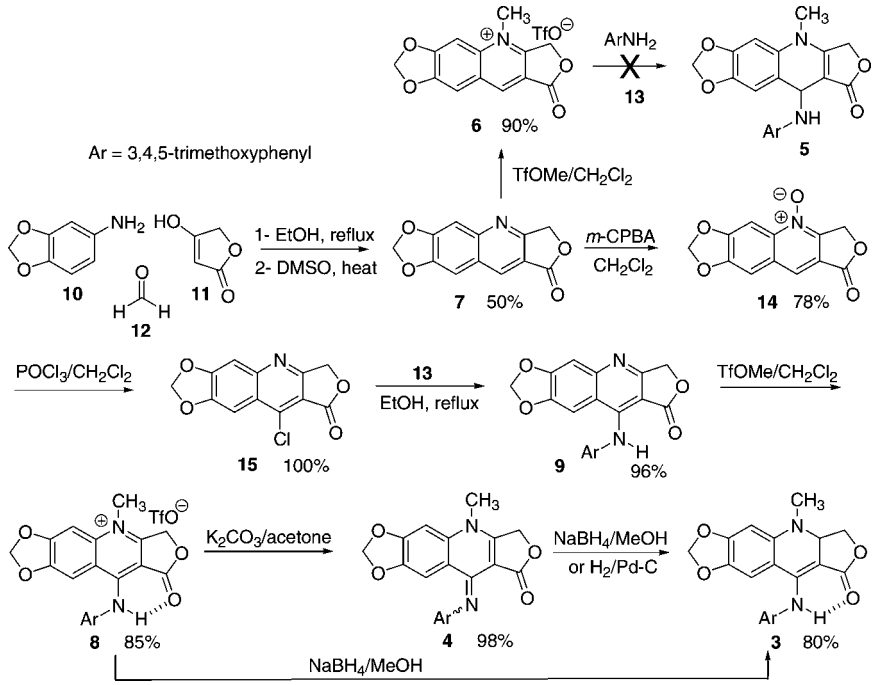
(6) (a) Blurton, P.; Brickwood, A.; Dhanak, D. *Heterocycles* **1997**, *45*, 2395–2403. (b) Van Es, T.; Staskun, B. *S. Afr. J. Chem.* **1998**, *51*, 121–126.; *Chem. Abstr.* **1999**, *130*, 52311z.

10.1021/jo800166b CCC: $40.75
Published on Web 04/02/2008

SCHEME 1. Retrosynthesis Plans for the Synthesis of the Aminologue 3



SCHEME 2. Synthesis of the Aminologue 3



In the literature, two syntheses of the key synthon **7** have been described starting from 6-nitropiperonal, in 4 steps and 41% overall yield for the first one,[7] and in 2 steps but only 34% yield for the second one.[8] To circumvent the preparation of the unstable aminobenzaldehyde, we have elaborated a new synthetic pathway by adaptation of the one-pot synthesis of 4-aza-2,3-didehydropodophyllotoxins[1] to an aliphatic aldehyde. Thus, the quinoline-lactone **7** was readily obtained in 50% yield by refluxing in ethanol a mixture of 3,4-methylenedioxyaniline (**10**), tetronic acid (**11**), and formaldehyde (**12**) and then, after filtration of the resulting solid, subsequent oxidation of the dihydroquinoline intermediate in warmed DMSO (Scheme 2). Another interesting feature of this method is the possibility of changing the substituent pattern on the quinolinic nucleus by using various commercially available anilines.

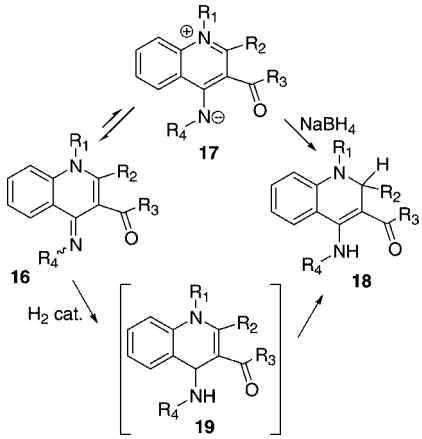
Quaternarization of the quinoline-lactone **7** needs the use of very reactive alkylating agents such as trifluoromethyl sulfonate. The poor nucleophilicity of this quinoline could be explained by the vinylamide character of the nitrogen. Unfortunately, treatment of the resulting salt **6** with aniline **13** in neutral medium or in the presence of NaH was unsuccessful, probably because of the instability of **6** in solution. For this reason, compound **6** was not characterized.

In light of these results, route B was investigated. The 4-chloroquinoline-lactone **15** was prepared in near quantitative yield by reaction of $POCl_3$ on the quinoline-*N*-oxide **14**, which is easily obtained by *m*-CPBA oxidation of the key synthon **7**. Then an aromatic nucleophilic substitution by the aniline **13** provided the phenylaminoquinoline-lactone **9**, which was quaternarized as before with trifluoromethyl sulfonate to afford the quinolinium salt **8** in good yield (85%). Deprotonation of **8** was

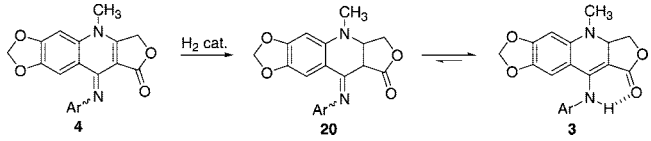
(7) (a) Kurihara, T.; Sano, H.; Hirano, H. *Chem. Pharm. Bull.* **1975**, *23*, 1155–1157. (b) Kurihara, T.; Michida, T.; Hirano, H. *Chem. Pharm. Bull.* **1975**, *23*, 2451–2453.

(8) (a) Smith, D. G.; Seemuth, P. D.; Zimmer, H. *J. Org. Chem.* **1983**, *48*, 1914–1916. (b) Pendrak, I.; Wittrock, R.; Kingsbury, W. D. *J. Org. Chem.* **1995**, *60*, 2912–2915.

SCHEME 3. Mechanisms Proposed in the Literature for the Reduction of 16 into 18



SCHEME 4. New Mechanism Hypothesized for the Catalytic Hydrogenation of 4 into 3



accomplished by a weak base in heterogeneous medium; the resulting imine **4** could be regioselectively reduced into the aminologue **3** either by $NaBH_4$ or by catalytic hydrogenation. Surprisingly, the quinolinium **8** could be reduced into the aminologue **3** in one step by treatment with $NaBH_4$ without preliminary formation of the imine. To our knowledge, this is the first example of a 4-amino-1,2-dihydro-3-quinolinecarboxylate reduction. In both cases, the reduced derivative exists only under the 1,2-dihydroquinoline form. HMBC spectrum of compound **3** showed clearly ^3J correlation between the proton of *N*-methyl group (δ 2.68 ppm) and C-3a (δ 57.10 ppm) and ^2J correlation between C-3a and both H3 of the lactone (δ 4.30 and 4.66 ppm) (see Supporting Information).

Two different mechanisms have been proposed for the transformation of 4-iminoquinoline-3-carboxyles **16** into 4-amino-1,2-dihydroquinolines **18** (Scheme 3). According to the literature, hydride reduction proceeds by reaction on the N1−C2 iminium double bound of the zwitterion **17**, a minor mesomeric form of **16**[5e] whereas catalytic hydrogenation of the N−C4 imine function of **16** leads to the formation of the 1,4-dihydro intermediate **19** which is spontaneously isomerized into **18**.[6a]

In our case, the reactivity of the quinolinium salt **8** (Scheme 2), which can be explained by addition of $NaBH_4$ on the N^+−C double bond, corroborates the mechanism described in the literature for hydride reduction of the imines **16**. Concerning the mechanism envisaged for the catalytic hydrogenation,[6a] we proposed another hypothesis. Indeed, the transformation of the 1,4-dihydro isomer into the 1,2-dihydro derivative has never been described for 4-aminoquinoline-3-carboxylates and both forms can be obtained according to the synthetic method.[5,6] Consequently, it seems reasonable to hypothesize a regioselective reduction of the C2−C3 double bond of **4** into the 4-imino-2,3-dihydroquinoline **20**, which was isolated in the more stable tautomeric form **3** (Scheme 4).

In conclusion, the first potentially bioactive *N*-methyl-4-amino-1,2-dihydroquinoline-lactone **3**, which could be considered as a rigid aminologue of 4-aza-2,3-didehydropodophyllotoxins, has been prepared via a five-step sequence in a 51% overall yield from the quinoline-lactone **7**. Furthermore, a new practical synthesis of the previously described derivative **7** was carried using versatile commercially available starting materials and constitutes the shortest and highest yielding route. These synthetic pathways could be widened with a view toward the preparation of different substituted aminologues of 4-aza-2,3-didehydropodophyllotoxins. Biological activities of the aminologues will be reported in due course.

Experimental Section

Melting points are uncorrected. ^1H and ^{13}C NMR experiments were performed at 300 and 75 MHz, respectively, using a 300 MHz instrument. $^1H-^{13}C$ HSQC and $^1H-^{13}C$ HMBC NMR experiments were performed at 400 MHz.

6,7-(Methylenedioxy)furo[3,4-*b*]quinolin-1(3*H*)-one (7). A mixture of tetronic acid (**11**) (300 mg, 3 mmol), a 37% solution of formaldehyde **12** (730 μL, 9 mmol), and 3,4-methylenedioxyaniline (**10**) (411 mg, 3 mmol) in EtOH (30 mL) was refluxed for 0.5 h. The resulting white precipitate was filtered off and then dissolved in DMSO (15 mL). The solution was stirred at 105 °C for 1 h. After addition of water (150 mL), the resulting precipitate was collected and recrystallized from EtOH to give **7** as a white powder (345 mg, 50%): mp = 281–282 °C (lit.,[8a] mp = 284–285 °C). The analytical data are in agreement with literature values.[8a] ^1H NMR (400 MHz, $CDCl_3$) δ 8.50 (s, 1H), 7.45 (s, 1H), 7.25 (s, 1H), 6.20 (s, 2H,), 5.40 (s, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 165.2 (C=O), 158.3 (Cq), 149.7 (Cq), 146.7 (Cq), 144.8 (Cq), 129.6 (CH), 120.8 (Cq), 111.4 (Cq), 101.5 (CH), 100.0 (CH), 98.5 (CH_2), 66.4 (CH_2).

4-Methyl-6,7-(methylenedioxy)-1-oxo-1,3-dihydrofuro[3,4-*b*]quinolin-4-ium trifluoromethanesulfonyl (6). To a solution of quinoline **7** (300 mg, 1.31 mmol) in CH_2Cl_2 (60 mL) was added a large excess of methyl triflate (1 mL). After 48 h of stirring at rt, the resulting solid was filtered off to afford quite pure **6** as a yellow powder (463 mg, 90%) that is unstable in solution and was used without further purification in the next step.

6,7-(Methylenedioxy)-4-oxyfuro[3,4-*b*]quinolin-1(3*H*)-one (14). To a solution of quinoline **7** (1.15 g, 5.0 mmol) in CH_2Cl_2 (300 mL) was added *m*-CPBA (70% of purity) (1.8 g, 7.5 mmol). After 10 h of stirring at rt, the solvent was eliminated under reduced pressure, and the residue was recrystallized from EtOAc to give **14** as a white powder (960 mg, 78%): mp = 285–287 °C; ^1H NMR (300 MHz, DMSO-d_6) δ 8.35 (s, 1H), 7.93 (s, 1H), 7.70 (s, 1H), 6.37 (s, 2H), 5.51 (s, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 168.4 (C=O), 154.4 (Cq), 150.1 (Cq), 147.4 (Cq), 142.2 (Cq), 128.1 (Cq), 122.6 (CH), 118.9 (Cq), 105.7 (CH), 104.2 (CH_2), 95.8 (CH), 67.5 (CH_2); Anal. Calcd for $C_{12}H_7NO_5 \cdot 0.5\ H_2O$: C, 56.70; H, 3.17; N, 5.51. Found: C, 56.85; H, 3.44; N, 5.72.

9-Chloro-6,7-(methylenedioxy)furo[3,4-*b*]quinolin-1(3*H*)-one (15). To a solution of quinoline *N*-oxide **14** (960 mg g, 3.92 mmol) in CH_2Cl_2 (300 mL) was added $POCl_3$ (4 mL). After refluxing for 10 h, water (150 mL) and then a saturated aqueous solution of $NaHCO_3$ were added until a pH of 9 was reached. After extraction of the aqueous layer with CH_2Cl_2 (3 × 50 mL), the organic phases were dried over Na_2SO_4, filtered, and then the solvent was eliminated under reduced pressure. The solid residue was recrystallized from EtOAc to give **15** as a white powder (1.03 g, 100%): mp = 310–312 °C; ^1H NMR (300 MHz, DMSO-d_6) δ 7.71 (s, 1H), 7.56 (s, 1H), 6.38 (s, 2H), 5.42 (s, 2H); ^{13}C NMR (75 MHz, DMSO-*d6*) δ 167.0 (C=O), 163.8 (Cq), 154.6 (Cq), 151.2 (Cq), 150.3 (Cq), 140.2 (Cq), 123.1 (Cq), 112.7 (Cq), 105.6 (CH), 104.1 (CH_2), 100.1 (CH), 69.6 (CH_2); Anal. Calcd for $C_{12}H_6ClNO_4$: C, 54.67; H, 2.29; N, 5.31. Found: C, 54.99; H, 2.09; N, 5.22.

9-[(3,4,5-Trimethoxyphenyl)amino]-6,7-(methylenedioxy)furo[3,4-*b*]quinolin-1(3*H*)-one (9). A mixture of chloroquinoline **15** (1.00 g, 3.80 mmol) and 3,4,5-trimethoxyaniline (**13**) (1.40 g ; 7.60 mmol) in EtOH (500 mL) was refluxed for 6 h. The resulting precipitate

was filtered off, washed with EtOH, and then recrystallized from EtOAc to give **9** as a pale-yellow powder (1.50 g, 96%): mp = 297–299 °C; ^{1}H NMR (300 MHz, DMSO-d_6) δ 9.08 (br s, 1H), 7.32 (s, 2H), 6.50 (s, 2H), 6.22 (s, 2H), 5.28 (s, 2H), 3.67 (s, 6H), 3.65 (s, 3H); ^{13}C NMR (75 MHz, DMSO-d_6) δ 169.5 (C═O), 165.0 (Cq), 153.4 (2 × Cq), 152.6 (Cq), 151.4 (Cq), 147.6 (Cq), 146.8 (Cq), 138.1 (Cq), 134.9 (Cq), 115.1 (Cq), 106.1 (CH), 103.1 (CH_2), 100.9 (CH), 100.8 (Cq), 100.3 (2xCH), 69.8 (CH_2), 60.1 (CH_3), 56.4 (2 × CH_3); Anal. Calcd for $C_{21}H_{18}N_2O_7 \cdot 0.5\ H_2O$: C, 60.14; H, 4.57; N, 6.58. Found: C, 60.31; H, 4.63; N, 6.56.

4-Methyl-6,7-(methylenedioxy)-1-oxo-9-[(3,4,5-trimethoxyphenyl)amino]-1,3-dihydrofuro[3,4-*b*]quinolin-4-ium trifluoromethanesulfonyl (8). To a solution of aminoquinoline **9** (560 mg, 1.37 mmol) in CH_2Cl_2 (100 mL) was added a large excess of methyl triflate (1 mL). After 4 h of stirring at rt, the solvent was eliminated under reduced pressure, and the residue was recrystallized from EtOH to give **8** as a dark-yellow powder (665 mg, 85%): mp = 272–274 °C; ^{1}H NMR (300 MHz, DMSO-d_6) δ 10.69 (s, 1H), 7.87 (s, 1H), 7.82 (s, 1H), 6.70 (s, 2H), 6.42 (s, 2H), 5.63 (s, 2H), 3.97 (s, 3H), 3.70 (s, 6H), 3.68 (s, 3H);^{13}C NMR (75 MHz, DMSO-d_6) δ 165.9 (C═O) 164.0 (2 × Cq), 155.7 (CF_3), 153.6 (2 × Cq), 151.0 (Cq), 148.6 (Cq), 140.0 (Cq), 136.9 (Cq), 136.0 (Cq), 115.5 (Cq), 105.1 (CH), 102.4 (CH_2), 102.2 (2 × CH), 100.7 (Cq), 98.0 (CH), 67.3 (CH_2), 60.7 (CH_3), 56.7 (2 × CH_3), 38.6 (CH_3); Anal. Calcd for $C_{23}H_{21}F_3N_2O_{10}S \cdot 0.5\ H_2O$: C, 47.34; H, 3.80; N, 4.80. Found: C, 47.30; H, 3.58; N, 4.50.

4-Methyl-6,7-(methylenedioxy)-9-[(3,4,5-trimethoxyphenyl)imino]4,9-dihydrofuro[3,4-*b*]quinolin-1(3*H*)-one (4). To a solution of aminoquinolinium **8** (300 mg, 0.52 mmol) in dry acetone (50 mL) was added K_2CO_3 (72 mg, 0.52 mmol). After 3 h of stirring at rt, the resulting solid was filtered off and recrystallized from EtOH to afford **4** as a yellow powder (217 mg, 98%): mp = 284–286 °C; ^{1}H NMR (300 MHz, DMSO-d_6) δ 7.85 (s, 1H), 7.31 (s, 1H), 6.19 (s, 2H), 6.02 (s, 2H), 5.21 (s, 2H), 3.66 (s, 6H), 3.60 (s, 3H), 3.52 (s, 3H);^{13}C NMR (75 MHz, DMSO-d_6) δ 167.1 (C═O), 164.4 (Cq), 153.0 (Cq), 151.2 (Cq), 149.8 (2 × Cq), 146.4 (Cq), 146.1 (Cq), 136.0 (Cq), 132.7 (Cq), 122.6 (Cq), 104.1 (CH), 102.9 (CH_2), 97.7 (2 × CH, Cq), 96.9 (CH), 65.4 (CH_2), 60.5 (CH_3), 56.1 (2 × CH_3), 35.6 (CH_3); Anal. Calcd for $C_{22}H_{20}N_2O_7 \cdot 0.5\ H_2O$: C, 60,97; H, 4.88; N, 6.46. Found: C, 61.08; H, 4.52; N, 6.84.

(3a*RS*)-4-Methyl-6,7-(methylenedioxy)-9-[(3,4,5-trimethoxyphenyl)amino]-3a,4-dihydrofuro[3,4-*b*]quinolin-1(3*H*)-one (3), Prepared from 4. A. A solution of iminoquinoline **4** (100 mg, 0.24 mmol) in dry MeOH (50 mL) was hydrogenated for 4 h at rt in the presence of 10% Pd/C (20 mg) and under a pressure of 10 bar. After filtration through a pad of Celite, the solvent was eliminated under reduced pressure and the residue was recrystallized from EtOH to give **3** as an orange-yellow powder (82 mg, 80%). **B.** To a solution of iminoquinoline **4** (100 mg, 0.24 mmol) in dry MeOH (50 mL) was added $NaBH_4$ (46 mg, 1.20 mmol). After 10 h of stirring at rt, the resulting solid was filtered off and recrystallized to afford **3** (82 mg, 80%): mp = 220 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.34 (s, 1H), 6.64 (s, 1H), 6.41 (s, 1H), 6.12 (s, 2H), 5.90 (s, 2H), 4.66 (m, 1H), 4.30 (m, 2H), 3.81 (s, 3H), 3.71 (s, 6H), 2.68 (s, 3H);^{13}C NMR (75 MHz, $CDCl_3$) δ 170.5 (C═O), 153.4 (2 × Cq), 151.2 (Cq), 147.4 (Cq), 146.7 (Cq), 140.0 (Cq), 137.2 (Cq), 134.6 (Cq), 110.3 (Cq), 108.1 (CH), 101.5 (CH_2), 100.2 (2 × CH), 95.4 (CH), 94.0 (Cq), 71.9 (CH_2), 61.0 (CH_3), 57.1 (CH), 56.1 (2 × CH_3), 35.3 (CH_3); Anal. Calcd for $C_{22}H_{22}N_2O_7$: C, 61,97; H, 5.20; N, 6.57. Found: C, 62.05; H, 5.42; N, 6.29.

(3a*RS*)-4-Methyl-6,7-(methylenedioxy)-9-[(3,4,5-trimethoxyphenyl)amino]-3a,4-dihydrofuro[3,4-*b*]quinolin-1(3*H*)-one (3), Prepared from 8. The same procedure as previously was used starting from the aminoquinolinium **8** (120 mg, 0.21 mmol) in dry MeOH (50 mL) and $NaBH_4$ (40 mg, 1.05 mmol) to afford **3** (72 mg, 80%). The analytical data were identical to those described for **3** prepared from **4**.

Acknowledgment. R. Labruère was supported by a fellowship from MNSER.

Supporting Information Available: Copies of ^{1}H NMR spectrum and proton-decoupled ^{13}C NMR spectrum for each new compound, along with two-dimensional ^{1}H−^{13}C HSQC ^1J correlation for compound **4** and ^{1}H−^{13}C HSQC ^1J correlation and HMBC ^3J correlation for compound **3**. Complete IR peak listings for all new compounds. This material is available free of charge via the Internet at http://pubs.acs.

JO800166B