

Synthesis and Reactivity of Michael Adducts of Lithiated 2,5-Dimethoxy-*N*-pivaloylanilines and Arylidenemalonates.

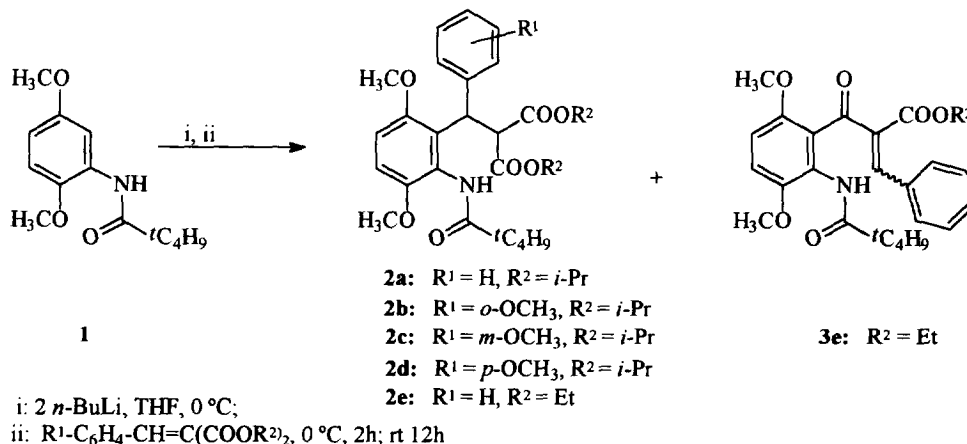
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Abstract: Michael addition of lithiated 2,5-dimethoxypivaloylaniline to diisopropyl arylidenemalonates, followed by acid cyclization, affords 5,8-dimethoxy-4-aryl-3,4-dihydro-2(1*H*)quinolinones (**5**). These compounds are very inert to the 3,4-dehydrogenation, but were easily transformed to 4-aryl-3,4-dihydro-(1*H*)quinoline-2,5,8-triones (**10**) which, through Diels-Alder heterocyclization, gave 4-aryl-3,4-dihydro-1,8-diazanthracene-2,9,10-triones (**16**).
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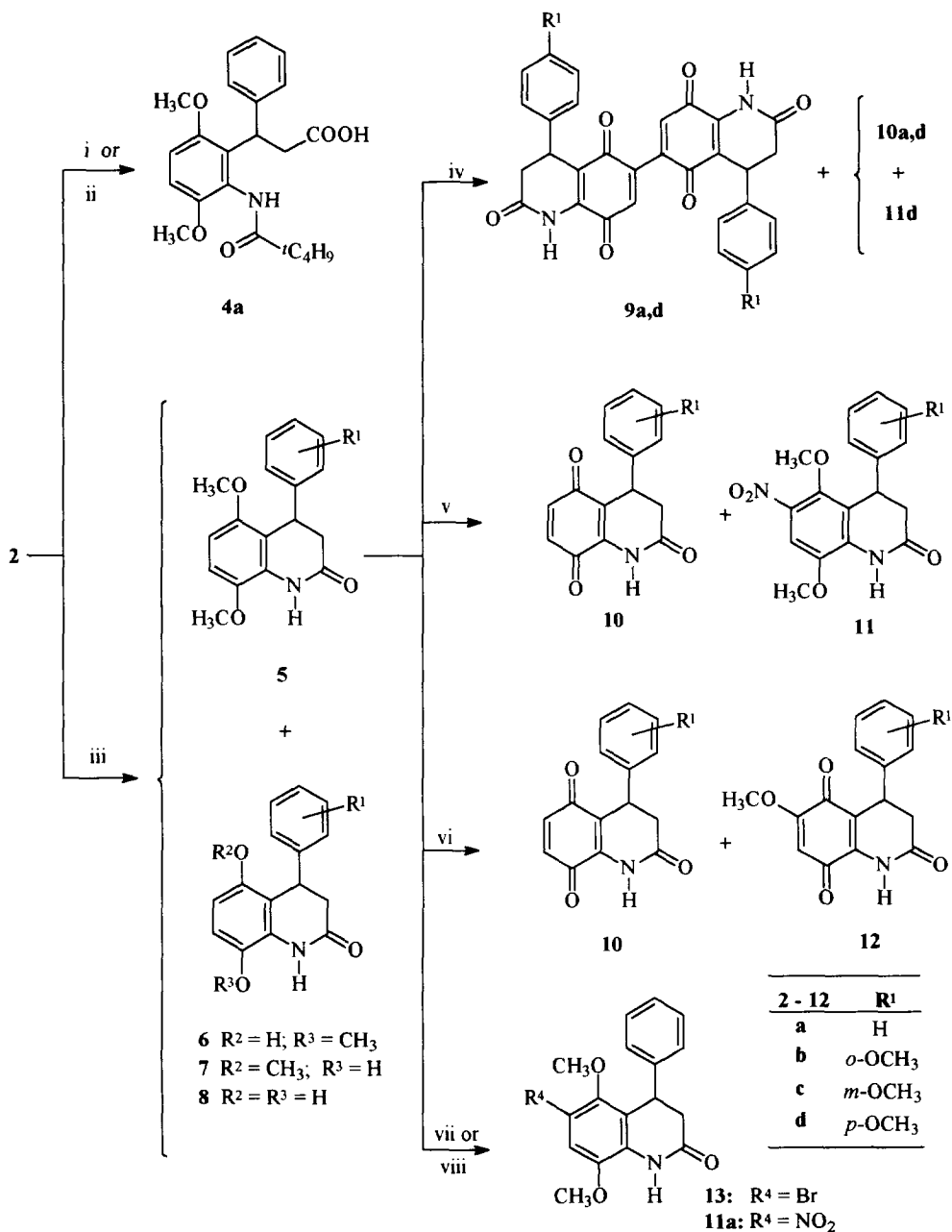
In the last years our work has been directed to the synthesis of antitumor Diazaquinomycin A analogues. In this context, we have developed several strategies to prepare 3- and/or 4-substituted (1*H*)-quinoline-2,5,8-triones, which have been used as dienophiles with carbodienes or activated 1-azadienes.¹ We report here a short and efficient route to prepare 4-aryl-3,4-dihydro derivatives, via Michael addition of 2,5-dimethoxypivaloylaniline to isopropylarylidene malonates. This strategy overcomes other alternative procedures such as that proposed by Tamura and coworkers, which implies catalytic hydrogenation of 3,4-unsaturated 2(1*H*)quinolinones.²

Synthetic methods of 2(1*H*)quinolinones using anilines as starting compounds, generally imply Knorr,^{3a} Pommeranz-Fritsch,^{3b} or related reactions,^{3c-3f} in which a first *N*-acylation to anilides is followed by a Friedel-Crafts cyclization. In other cases, the intermediate anilides are used to perform on them chemical transformations such as Vilsmeier-Haack^{3g} or Wittig^{3hi} reactions, before the final cyclization. In some cases both C₄-C_{4a} and NH-CO bonds



Scheme 1

are formed in a one-pot procedure, as it occurs in the reaction of 3-amino-2-cyclohexenone with acrylates or

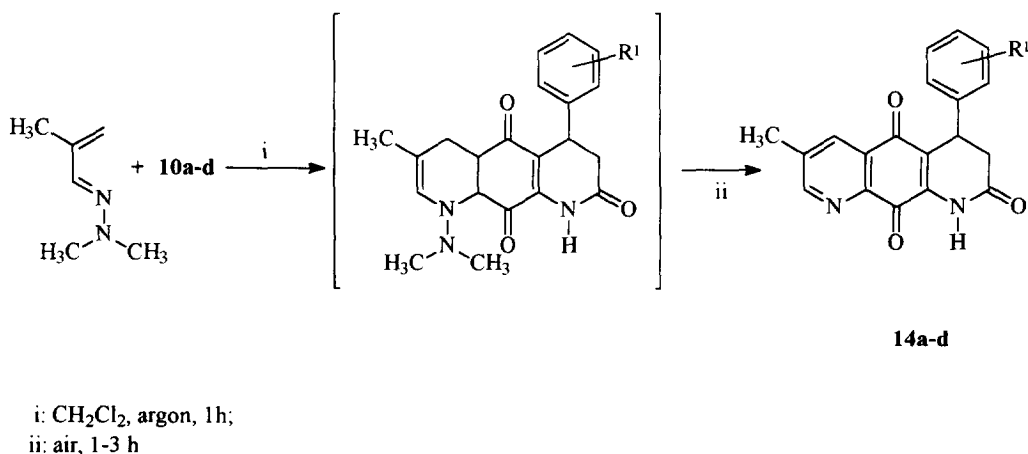


Scheme 2

propiolates,^{3j} or when an *ortho*-alkylation is followed by the intramolecular acylation, as it occurs in Heck reaction between *o*-haloanilides and α,β -unsaturated carboxylic acids.^{3k} It has been shown that some of these methods, when applied to 2,5-dimethoxyanilines, in order to obtain (1*H*)-2,5,8-quinolinetriones after oxidative demethylation, are affected by steric interactions between substituents at C-4 and C-5 of the quinoline system.^{3i,4}

Taking this considerations into account, we explored the reaction of lithiated 2,5-dimethoxy-*N*-pivaloylaniline **1** with diethylbenzylidenemalonate. It is well known that organolithium reagents give 1,2-additions with α,β unsaturated carboxylic esters,⁵ and that the use of organocuprates as well as the presence of bulky substituents in the substrate or in the reagent favour the 1,4-conjugate addition.⁶ In our case, the reaction favoured chemoselectively the Michael adduct **2e** over the 1,2-addition product **3e** (**2e**:**3e**=5:1). By using the corresponding diisopropyl ester the 1,4-addition compound **2a** was exclusively obtained. Compounds **2b-2d** were similarly prepared as the only reaction products from diisopropyl methoxybenzylidenemalonates in 40 - 50 % yields (Scheme 1). As it was expected, alkaline hydrolysis of **2e** took place at the ester functions leading exclusively to the propionic acid **4a**, but in acid media (1:1 HCl/ HOAc, 140°C, 6h) the expected hydrolysis of the pivaloyl amide was performed, giving directly the intramolecular condensation product **5a** and a very small amount of **4a** (Scheme 2). The maintenance of the external temperature in the acid hydrolysis is very critical. For instance, at 90°C, acids **4** are mainly formed. The isopropyl esters **2a-2d** required longer reaction times (up to 12 hours). In these conditions, traces of mono- and dihydroxylated quinolines **6 - 8** were also obtained (Scheme 2).

In contrast with our previous experiences,^{3a} attempts to perform the demethylation of **5a** with CAN (cerium ammonium nitrate) gave the dimer **9a** together with the expected quinolinetrione **10a** in a 2:1 ratio. In the case of **5d**, besides the dimer **9d** and very small amounts of the quinolinetrione **10d**, the 6-nitro-5,8-dimethoxy-2-quinolinone **11d** was isolated. The use of AgO in HNO₃ (6N; dioxane, r.t., 20 min) led to the expected quinones **10** (45 - 63%) and notable amounts of the 6-nitro-5,8-dimethoxy-2-quinolinones **11** (10-28%), which were very difficult to separate by chromatography. The great reactivity of position-6 in compounds **5** required the use of AgO/pyridine-2,6-dicarboxylic acid-*N*-oxide⁷ to obtain the pure quinones **10** in satisfactory yields (62-82%) together with traces of the easily separable 6-methoxyderivatives **12**. Compounds **10**, after Diels-Alder heterocyclisation with 1-dimethylamino-3-methyl-1-azadiene⁸ under argon, followed by air oxidation, gave the aromatized adducts **14a-d** (Scheme 3). The



Scheme 3

regioselectivity of this cycloaddition reaction was also observed for other 2,5,8-quinolinetriones,⁹ and can be attributed to the relative electron deficiencies of the carbonyl groups in the dienophile.¹⁰

Attempts to aromatize compound **5a**, following reported successful methodologies for 4-phenyl-3,4-dihydro-2(1*H*)quinolinone,¹¹ 5-hydroxy-3,4-dihydro-2(1*H*)quinolinone,³¹ or others such as oxidation with DDQ,¹² only allowed the recovery of unchanged **5a** (see Scheme 2). These results clearly indicate that the steric interaction between the C4-phenyl and the C5-methoxy groups destabilises the conjugated product. On the other hand, attempts to achieve the C3-halogenation with NBS¹³ or I₂/CAN¹⁴ followed by dehydrohalogenation also failed, taking place instead the electrophilic substitution at C6 (see compounds **13** and **11a**, respectively, in experimental). These results showed that the reactivity towards electrophiles of the C6 position in compounds **5** is significantly greater than in related C3,C4-unsaturated analogues.^{1,3}

ACKNOWLEDGEMENTS

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EXPERIMENTAL

All melting points were obtained using a Reichart hot-stage microscope and are uncorrected. Infrared spectra were recorded on a Perkin-Elmer Paragon 1000 spectrometer. ¹H-NMR and ¹³C-NMR spectra were recorded on a Bruker AC-250 spectrometer (Servicio de RMN, UCM). Elemental analyses were determined on a Perkin-Elmer 2400 CHN microanalyser (Servicio de Microanálisis, UCM). Reactions were monitored by thin layer chromatography: silica gel 60 F254. Separations by column chromatography were performed on silica gel (SDS 60 ACC, 230-440 mesh).

Diethyl and Diisopropyl 1-(3,6-Dimethoxy-2-pivaloylaminophenyl)-1-phenylmethyl-malonates (2a, 2b) and Ethyl 2-(3,6-Dimethoxy-2-pivaloylaminobenzoyl)cinnamate (3e).

General Procedure:

To a stirred solution of 2,5-dimethoxy-N-pivaloylaniline^{4b} (4.75 g, 20 mmol) in anhydrous THF (60 ml) at 0°C was added dropwise 24 ml (60 mmol) of *n*-BuLi (2.5 M in hexane) under argon. After 2 h a solution of 20 mmol of the appropriate diethyl or diisopropyl benzylidenemalonate in 12 ml THF was added slowly. The resultant solution was stirred at 0°C for 3 h followed by 8 h at room temp. The reaction mixture was quenched with ice water (10 ml) and diluted with brine (50 ml). The organic phase was separated, and the aqueous phase was extracted with THF (3 x 50 ml). The combined organic extracts were dried (MgSO₄), concentrated *in vacuo*, and the crude product was treated with EtOAc (5-10 ml). Filtration of the white precipitate formed, provided pure **2a - e**, which were recrystallized from ethyl acetate. In the case of **2e**, the concentrated filtration liquids were subjected to flash column chromatography on silica gel (petroleum ether / ethyl acetate, 9:1) to afford 1.2 g (14 %) of **3e**.

Diisopropyl 1-(3,6-Dimethoxy-2-pivaloylaminophenyl)-1-phenylmethyl-malonate (2a).

Yield: 45%. Mp: 165-167°C. IR (KBr) ν : 3414, 1745, 1677, 1496, 1264, 1247 cm⁻¹. ¹H-NMR (CDCl₃) δ : 0.83 (3H, d, *J* = 6.2 Hz, CH₃); 0.98 (3H, d, *J* = 6.2 Hz, CH₃); 1.10 (3H, d, *J* = 6.2 Hz, CH₃); 1.14 (3H, d, *J* = 6.2 Hz, CH₃); 1.42 (9H, s, 3-CH₃); 3.41 (3H, s, OCH₃); 3.73 (3H, s, OCH₃); 4.73 (1H, d, *J* = 12.2 Hz, CH(COOR)₂); 4.79 (1H, sep, *J* = 6.2 Hz, CH(CH₃)₂); 4.93 (1H, sep, *J* = 6.2 Hz, CH(CH₃)₂); 5.15 (1H, d, *J* = 12.2 Hz, CH(Ar)₂); 6.60 (1H, d, *J* = 9 Hz, H-5'); 6.71 (1H, d, *J* = 9.0 Hz, H-4'); 7.17 (5H, m, Ph); 7.76 (1H, s, NH) ppm. ¹³C-NMR (CDCl₃) δ : 177.2 (CONH); 169.3 (COOR); 167.5 (COOR); 152.3 (C-6'); 150.4 (C-3'); 139.6 (C-1''); 128.6 (C-1'); 128.1

(C-3" y 5"); 127.6 (C-2" y 6"); 125.9 (C-2'); 125.8 (C-4"); 111.5 (C-5'); 111.3 (C-4'); 69.1 ($\underline{\text{CH}}(\text{CH}_3)_2$); 68.9 ($\underline{\text{CH}}(\text{CH}_3)_2$); 56.7 (OCH_3); 55.8 (OCH_3); 53.9 ($\text{CH}(\text{COOR})_2$); 42.3 (CHAr_2); 39.2 (C- α *t*-Bu); 27.8 (3- CH_3 *t*-Bu); 21.5 (CH_3); 21.3 (CH_3); 21.2 (CH_3); 21.1 (CH_3) ppm. Analysis calc. for $\text{C}_{29}\text{H}_{39}\text{NO}_7$: C, 67.82; H, 7.65; N, 2.73. Found: C, 67.51; H, 7.43; N, 2.63.

Diisopropyl 1-(3,6-Dimethoxy-2-pivaloylaminophenyl)-1-(2-methoxyphenyl)-malonate (2b).

Yield: 38%. Mp: 143°C. IR (KBr) ν : 3397, 1752, 1684, 1492, 1248 cm^{-1} . $^1\text{H-NMR}$ (CDCl_3) δ : 0.74 (3H, d, $J = 6.3$ Hz, CH_3); 0.91 (3H, d, $J = 6.3$ Hz, CH_3); 1.10 (6H, d, $J = 6.3$ Hz, CH_3); 1.42 (9H, s, 3 CH_3); 3.48 (3H, s, OCH_3); 3.67 (3H, s, OCH_3); 3.73 (3H, s, OCH_3); 4.73 (1H, d, $J = 12.4$ Hz, $\text{CH}(\text{COOR})_2$); 4.78 (1H, sep, $J = 6.3$ Hz, $\text{CH}(\text{CH}_3)_2$); 4.86 (1H, sep, $J = 6.3$ Hz, $\text{CH}(\text{CH}_3)_2$); 5.32 (1H, d, $J = 12.4$ Hz, $\text{CH}(\text{Ar})_2$); 6.56 (1H, d, $J = 9$ Hz, H-5'); 6.71 (1H, d, $J = 8.1$ Hz, H-3"); 6.72 (1H, d, $J = 9$ Hz, H-4"); 6.81 (1H, "t", $J = 7.1$ Hz, H-5"); 7.07 (1H, "t", $J = 7.3$ Hz, $J = 1.5$ Hz, H-4"); 7.40 (1H, d, $J = 8.1$ Hz, H-6"); 8.18 (1H, s, NH). $^{13}\text{C-NMR}$ (CDCl_3) δ : 175.6 (CONH); 169.6 (COOR); 167.6 (COOR); 157.6 (C-2"); 153.2 (C-6'); 150.2 (C-3'); 128.8* (C-6"); 127.5 (C-1"); 127.4* (C-4"); 126.9 (C-1"); 125.4 (C-2"); 119.1 (C-5"); 111.9 (C-3"); 110.5 (C-5'); 110.1 (C-4'); 69.3 ($\underline{\text{CH}}(\text{CH}_3)_2$); 68.7 ($\underline{\text{CH}}(\text{CH}_3)_2$); 56.8 (OCH_3); 56.0 (OCH_3); 55.3 (OCH_3); 54.2 ($\underline{\text{CH}}(\text{COOR})_2$); 39.3 (C- α *t*-Bu); 37.0 ($\underline{\text{CH}}\text{-Ar}$); 28.0 (3 CH_3 *t*-Bu); 21.6 (CH_3); 21.5 (CH_3); 21.3 (CH_3); 21.1 (CH_3) ppm. Analysis calc. for $\text{C}_{30}\text{H}_{41}\text{NO}_8$: C, 66.27; H, 7.60; N, 2.57. Found: C, 66.23; H, 7.50; N, 2.42.

Diisopropyl 1-(3,6-Dimethoxy-2-pivaloylaminophenyl)-1-(3-methoxyphenyl)-malonate (2c).

Yield: 50.8%. Mp: 118–20°C. IR (KBr) ν : 3402, 1743, 1673, 1600, 1494, 1252 cm^{-1} . $^1\text{H-NMR}$ (CDCl_3) δ : 0.85 (3H, d, $J = 6.1$ Hz, CH_3); 1.02 (3H, d, $J = 6.1$ Hz, CH_3); 1.11 (3H, d, $J = 6.1$ Hz, CH_3); 1.16 (3H, d, $J = 6.1$ Hz, CH_3); 1.43 (9H, s, 3 CH_3); 3.47 (3H, s, OCH_3); 3.69 (3H, s, OCH_3); 3.73 (3H, s, OCH_3); 4.74 (1H, d, $J = 12.2$ Hz, $\text{CH}(\text{COOR})_2$); 4.80 (1H, sep, $J = 6.1$ Hz, $\text{CH}(\text{CH}_3)_2$); 4.95 (1H, sep, $J = 6.1$ Hz, $\text{CH}(\text{CH}_3)_2$); 5.14 (1H, d, $J = 12.2$ Hz, $\text{CH}(\text{Ar})_2$); 6.6 (1H, d, $J = 9$ Hz, H-5"); 6.6 (1H, dd, $J = 8$ Hz, $J = 2.2$ Hz, H-4"); 6.72 (1H, d, $J = 9$ Hz, H-4"); 6.75 (1H, m, H-2"); 6.79 (1H, d, $J = 8$ Hz, H-6"); 7.05 (1H, t, $J = 8$ Hz, H-5"); 7.75 (1H, s, NH). $^{13}\text{C-NMR}$ (CDCl_3) δ : 177.6 (CONH); 169.3 (COOR); 167.7 (COOR); 159.2 (C-3"); 152.4 (C-6"); 150.6 (C-3'); 128.8 (C-1"); 128.4 (C-5"); 125.9 (C-2"); 120.1 (C-6"); 113.6 (C-2"); 112.9 (C-4"); 111.4 (C-5' y 4"); 69.2 ($\underline{\text{CH}}(\text{CH}_3)_2$); 69.1 ($\underline{\text{CH}}(\text{CH}_3)_2$); 56.7 (OCH_3); 56.0 (OCH_3); 55.3 (OCH_3); 54.0 ($\underline{\text{CH}}(\text{COOR})_2$); 39.3 (C- α *t*-Bu); 37.0 ($\underline{\text{CH}}\text{-Ar}$); 27.9 (3 CH_3 *t*-Bu); 21.6 (CH_3); 21.4 (2- CH_3); 21.3 (CH_3) ppm. Analysis calc. for $\text{C}_{30}\text{H}_{41}\text{NO}_8$: C, 66.27; H, 7.60; N, 2.57. Found: C, 66.14; H, 7.47; N, 2.38.

Diisopropyl 1-(3,6-Dimethoxy-2-pivaloylaminophenyl)-1-(4-methoxyphenyl)-malonate (2d).

Yield: 48%. Mp: 166°C. IR (KBr) ν : 3419, 1750, 1713, 1677 cm^{-1} . $^1\text{H-NMR}$ (CDCl_3) δ : 0.83 (3H, d, $J = 6.3$ Hz, CH_3); 0.99 (3H, d, $J = 6.3$ Hz, CH_3); 1.09 (3H, d, $J = 6.3$ Hz, CH_3); 1.14 (3H, d, $J = 6.3$ Hz, CH_3); 1.42 (9H, s, 3 CH_3); 3.45 (3H, s, OCH_3); 3.68 (3H, s, OCH_3); 3.72 (3H, s, OCH_3); 4.67 (1H, d, $J = 12.3$ Hz, $\text{CH}(\text{COOR})_2$); 4.78 (1H, sep, $J = 6.3$ Hz, $\underline{\text{CH}}(\text{CH}_3)_2$); 4.92 (1H, sep, $J = 6.3$ Hz, $\underline{\text{CH}}(\text{CH}_3)_2$); 5.07 (1H, d, $J = 12.3$ Hz, $\text{CH}(\text{Ar})_2$); 6.57 (1H, d, $J = 9.1$ Hz, H-5"); 6.69 (1H, d, $J = 9.1$ Hz, H-4"); 6.69 (2H, d, $J = 8.7$ Hz, H-3" y 5"); 7.11 (2H, d, $J = 8.7$ Hz, H-2" y 6"); 7.75 (1H, s, NH). $^{13}\text{C-NMR}$ (CDCl_3) δ : 177.4 (CONH); 169.4 (COOR); 167.7 (COOR); 157.7 (C-4"); 152.4 (C-6"); 150.5 (C-3'); 131.8 (C-1"); 129.4 (C-3" y 5"); 128.9 (C-1"); 125.9 (C-2"); 113.0 (C-2" y 6"); 111.4 (C-5'); 111.3 (C-4"); 69.2 ($\underline{\text{CH}}(\text{CH}_3)_2$); 69.0 ($\underline{\text{CH}}(\text{CH}_3)_2$); 56.8 (OCH_3); 56.0 (OCH_3); 55.2 (OCH_3); 54.3 ($\underline{\text{CH}}(\text{COOR})_2$); 41.9 (CH-Ar); 39.3 (C- α *t*-Bu); 27.9 (3 CH_3 *t*-Bu); 21.7 (CH_3); 21.4 (2 CH_3); 21.3 (CH_3) ppm. Analysis calc. for $\text{C}_{30}\text{H}_{41}\text{NO}_8$: C, 66.27; H, 7.60; N, 2.57. Found: C, 66.05; H, 7.41; N, 2.40.

Diethyl 1-(3,6-Dimethoxy-2-pivaloylaminophenyl)-1-phenylmethylmalonate (2e).

Yield: 45%. Mp: 168–170°C. IR ν : 3406, 1745, 1717, 1677, 1493, 1247 cm^{-1} . $^1\text{H-NMR}$ (CDCl_3) δ : 0.96 (3H, t, $J = 7.1$ Hz, CH_3); 1.10 (3H, t, $J = 7.1$ Hz, CH_3); 1.42 (9H, s, CH_3); 3.42 (3H, s, OCH_3); 3.74 (3H, s, OCH_3); 3.96

(2H, q, $J = 7.1$ Hz, CH₂); 4.08 (2H, m, CH₂); 4.80 (1H, d, $J = 12.2$ Hz, CH(COOR)₂); 5.16 (1H, d, $J = 12.2$ Hz, CHAr₂); 6.60 (1H, d, $J = 9$ Hz, H-5'); 6.73 (1H, d, $J = 9$ Hz, H-4'); 7.03-7.2 (5H, m, Ar-H); 7.72 (1H, s, NH). ¹³C-NMR (CDCl₃) δ : 177.4 (CONH); 169.8 (COOR); 168.2 (COOR); 152.3 (C-6'); 150.5 (C-3'); 139.7 (C-1''); 128.8 (C-1'); 128.2 (C-3" y 5"); 127.8 (C-2" y 6"); 126.0 (C-2' y 4"); 111.6 (C-5'); 111.5 (C-4'); 61.8 (CH₂); 61.7 (CH₂); 56.7 (OCH₃); 55.9 (OCH₃); 53.7 (CH(COOR)₂); 42.5 (CHAr₂); 39.3 (C- α *t*-Bu); 27.9 (3 CH₃ *t*-Bu); 14.0 (CH₃); 13.8 (CH₃) ppm. Analysis calc. for C₂₇H₃₃NO₇: C, 66.79; H, 7.27; N, 2.88. Found: C, 66.73; H, 7.16; N, 2.77.

Ethyl 2-(3,6-Dimethoxy-2-pivaloylaminobenzoyl)cinnamate (3e).

Yield: 8%. Mp: 145-147 °C. IR ν : 1730, 1700, 1494, 1262 cm⁻¹. ¹H-NMR (CDCl₃) δ : 1.07 (3H, t, $J = 7.2$ Hz, CH₃); 1.38 (9H, br s, 3 CH₃); 3.69 (3H, s, OCH₃); 3.74 (3H, s, OCH₃); 4.07 (2H, m, $J = 7.2$ Hz, CH₂-CH₃); 5.07 and 5.09 (1H, 2s, =CH); 6.63 (1H, d, $J = 9$ Hz, H-5); 6.80 (1H, d, $J = 9$ Hz, H-4); 7.21 (5H, m, Ph). ¹³C-NMR (CDCl₃) δ : 188.7; 167.8; 165.8; 151.1; 142.7; 138.6; 129.4; 128.8; 127.4; 127.2; 118.3; 111.7; 107.7; 61.1; 60.3; 56.1; 44.4; 39.8; 27.9; 14.1 ppm. Analysis calc. for C₂₅H₂₉O₆N: C, 68.32; H, 6.65; N, 3.19. Found: C, 68.23; H, 6.80; N, 3.24.

4-Aryl-3,4-dihydro-5,8-dimethoxy-2(1H)-quinolinones (5).

A suspension (3.6 mmol) of **2a - e** in 140 ml glacial acetic acid / conc. HCl (1 : 1) was heated at reflux under argon in a 130 °C bath during 6 (**2e**) or 12 h (**2a - d**). The reaction mixture was filtered, concentrated *in vacuo*, and the residue chromatographed on silica gel using ethyl acetate / petroleum ether (1 : 1) as eluent. The first fraction corresponded to **5**, followed by traces of mono- and dihydroxylated products.

3,4-Dihydro-5,8-dimethoxy-4-phenyl-2(1H)-quinolinone (5a).

Yield: 44% from **2e** and 33% from **2a**. Mp 153-155°C (chloroform / ethyl acetate). IR ν : 3223, 1684, 1502, 1258 cm⁻¹. ¹H-NMR (CDCl₃) δ ppm= 2.83 (1H, ddd, $J = 16.4$ Hz, $J = 2$ Hz, $J = 1$ Hz, H-3 ec); 2.96 (1H, dd, $J = 16.4$ Hz, $J = 7.2$ Hz, H-3 ax); 3.71 (3H, s, OCH₃); 3.82 (3H, s, OCH₃); 4.62 (1H, dd, $J = 7.2$ Hz, $J = 2$ Hz, H-4 ec); 6.48 (1H, d, $J = 8.9$ Hz, H-6); 6.73 (1H, d, $J = 8.9$ Hz, H-7); 7.15 (5H, m, Ph); 7.82 (1H, br s, NH). ¹³C-NMR (CDCl₃) δ : 169.2 (C-2); 150.9 (C-5); 142 (C-1'); 140.5 (C-8); 128.7 (C3',5'); 127.3 (C-8a); 127 (C2',6'); 126.9 (C-4'); 115 (C-4a); 109.7 (C-7); 104.5 (C-6); 56.2 (OCH₃); 55.9 (OCH₃); 37.8 (C-3); 35.5 (C-4) ppm. Analysis calc. for C₁₇H₁₇NO₃: C, 72.07; H, 6.05; N, 4.94. Found: C, 71.82; H, 5.90; N, 4.63.

3,4-Dihydro-5,8-dimethoxy-4-(*o*-methoxyphenyl)-2(1H)-quinolinone (5b).

Yield: 44%. Mp 185-18°C (ethyl acetate / petroleum ether). IR ν : 3213, 1676, 1602 cm⁻¹. ¹H-NMR (CDCl₃) δ : 2.86 (2H, m, H-3); 3.64 (3H, s, OCH₃); 3.85 (3H, s, OCH₃); 3.87 (3H, s, OCH₃); 4.94 (1H, t, H-4); 6.48 (1H, d, $J = 8.9$ Hz, H-6); 6.57 (1H, dd, $J = 7.6$ Hz, $J = 1.6$ Hz, H-3'); 6.70 (1H, "t" d, $J = 7.5$ Hz, $J = 1$ Hz, H-5'); 6.77 (1H, d, $J = 8.9$ Hz, H-7); 6.83 (1H, dd, $J = 8.2$ Hz, $J = 0.8$ Hz, H-6'); 7.14 (1H, "t" d, $J = 7.6$ Hz, $J = 1.6$ Hz, H-4'); 7.81 (1H, br s, NH). ¹³C-NMR (CDCl₃) δ : 169.7 (C-2); 156.9 (C-2'); 151 (C-5); 129.4* (C-8); 128.5* (C-1'); 128 (C-6'); 127.5 (C-4'); 120.4 (C-5'); 114.3 (C-4a); 110.6 (C-3'); 109.7 (C-7); 104.5 (C-6); 56.2 (OCH₃); 56 (OCH₃); 55.4 (OCH₃); 36.5 (C-3); 30.4 (C-4). Analysis calc. for C₁₈H₁₉NO₄: C, 68.99; H, 6.11; N, 4.47. Found: C, 68.56; H, 6.09; N, 4.27.

3,4-Dihydro-5,8-dimethoxy-4-(*m*-methoxyphenyl)-2(1H)-quinolinones (5c).

Yield: 51%. Mp 140-142°C (ethyl acetate / petroleum ether). IR ν : 3230, 1677, 1607 cm⁻¹. ¹H-NMR (CDCl₃) δ : 2.85 (1H, ddd, $J = 16.4$ Hz, $J = 1.8$ Hz, $J = 0.8$ Hz, H-3 eq); 2.91 (1H, dd, $J = 16.4$ Hz, $J = 7.1$ Hz, H-3 ax); 3.70 (3H, s, OCH₃); 3.71 (3H, s, OCH₃); 3.80 (3H, s, OCH₃); 4.59 (1H, dd, $J = 7.1$ Hz, $J = 1.8$ Hz, H-4 eq); 6.47 (1H, d, $J = 8.9$ Hz, H-6); 6.68 (1H, d, $J = 8.9$ Hz, H-7); 6.70 (3H, m, H-2', 4', y 6'); 7.12 (1H, dd, $J = 8.9$ Hz, $J = 7.7$ Hz, H-5'); 7.82 (1H, s a, NH) ppm. ¹³C-NMR (CDCl₃) δ : 169.2 (C-2); 159.7 (C-3'); 150.9 (C-5); 143.9 (C-1'); 140.5 (C-8); 129.7 (C-5'); 127.4 (C-8a); 119.3 (C-6'); 114.8* (C-4a); 113.4* (C-4'); 111.6 (C-2'); 109.7 (C-7);

104.5 (C-6); 56.2 (OCH₃); 55.9 (OCH₃); 55.1 (OCH₃); 37.8 (C-3); 35.6 (C-4) ppm. Analysis calc. for C₁₈H₁₉NO₄: C, 68.99; H, 6.11; N, 4.47. Found: C, 68.65; H 6.10; N 4.57.

3,4-Dihydro-5,8-dimethoxy-4-(*p*-methoxyphenyl)-2(1*H*)-quinolinones (5d).

Yield: 59%. Mp 174-176°C (ethyl acetate / petroleum ether). IR ν : 3211, 1677, 1601, 1503, 1261 cm⁻¹. ¹H-NMR (CDCl₃) δ : 2.78 (1H, ddd, J = 16.4 Hz, J = 1.5 Hz, J_w = 1 Hz, H-3eq.); 2.92 (1H, dd, J = 16.4 Hz, J = 7 Hz, H-3ax); 3.69 (3H, s, OCH₃); 3.70 (3H, s, OCH₃); 3.79 (3H, s, OCH₃); 4.57 (1H, dd, J = 7 Hz, J = 1.5 Hz, H-4 eq.); 6.47 (1H, d, J = 8.9 Hz, H-6); 6.71 (1H, d, J = 8.9 Hz, H-7); 6.72 (2H, d, J = 8.6 Hz, H-3' y 5'); 7.06 (2H, dd, J = 8.6 Hz, J = 0.6 Hz, H-2' y 6'); 7.89 (1H, sa, NH). ¹³C-NMR (CDCl₃) δ : 169.4 (C-2); 158.4 (C-4'); 150.8 (C-5); 140.5 (C-8); 134.4 (C-1'); 128 (C-2', 6'); 127.1 (C-8a); 115.4 (C-4a); 114.1 (C-3', 5'); 109.6 (C-7); 104.6 (C-6); 56.2 (OCH₃); 55.9 (OCH₃); 55.3 (OCH₃); 37.9 (C-3); 34.7 (C-4) ppm. Analysis calc. for: C₁₈H₁₉NO₄: C, 68.99; H, 6.11; N, 4.47. Found: C, 68.57; H, 6.11; N, 4.25.

3-(3,6-Dimethoxyphenyl)-2-pivaloylphenyl-3-phenylpropionic acid (4a).

A suspension of 100 mg (0.2 mmol) **2e** in 7 ml 30 % ethanolic KOH are sonicated during 24 h (*method A*) or refluxed during 24 h (*method B*). Neutralization with 15 % HCl gave 65 mg (82%) (*method A*) or 70 mg (88%) (*method B*) of **4a**, as a white precipitate. Mp 241 - 243 °C (acetic acid). IR ν : 3360, 2960, 1718, 1635, 1508, 1490, 1261 cm⁻¹. ¹H-NMR (DMSO-*d*₆) δ : 1.24 (9H, s, 3 CH₃); 2.66 (1H, dd, J = 16.7 Hz, J = 4.1 Hz, H-2); 3.38 (1H, dd, J = 16.7 Hz, J = 10.6 Hz, H-2); 3.38 (3H, s, OCH₃); 3.66 (3H, s, OCH₃); 4.67 (1H, dd, J = 10.7 Hz, J = 4.1 Hz, H-3); 6.74* (1H, d, J = 9 Hz, H-4'); 6.82* (1H, d, J = 9 Hz, H-5'); 7.07 (5H, m, Ph); 8.75 (1H, s, NH); 12.05 (1H, br s, COOH) ppm. ¹³C-NMR (DMSO-*d*₆) δ : 177.3 (CONH); 173.7 (COOH); 151.7 (C-6'); 149.7 (C-3'); 142.8 (C-1'); 132.8 (C-2'); 127.5* (C-2', 6'); 127.2* (C-3', 6'); 125.7 (C-1'); 125.1 (C-4'); 111.2* (C-5'); 110* (C-4'); 56 (OCH₃); 55.6 (OCH₃); 39.6 (C₃); 37.8 (C-3); 35.2 (C-2); 27.4 (3 CH₃) ppm. Analysis calc. for C₂₃H₂₇NO₅: C, 69.50; H, 6.85; N, 3.52. Found: C, 69.78; H, 6.56; N, 3.48.

5-Hydroxy-8-methoxy-4-phenyl-3,4-dihydro-2(1*H*)-quinolinone (6a).

Yield: 16% (from **2a**); 2nd fraction. ¹H-NMR (CDCl₃/CD₃OD) δ : 2.63 (1H, dd, J = 16.1 Hz, J = 1.7 Hz, H-3_{eq}); 2.82 (1H, dd, J = 16.1 Hz, J = 7.3 Hz, H-3_{ax}); 3.66 (3H, s, OCH₃); 4.47 (1H, dd, J = 7.3 Hz, J = 1.7 Hz, H-4_{eq}); 6.33 (1H, d, J = 8.8 Hz, H-6); 6.52 (1H, d, J = 8.8 Hz, H-7); 7.02 (5H, m, Ph) ppm. ¹³C-NMR (CDCl₃/CD₃OD) δ : 170.4 (C-2); 148.1 (C-5); 141.9* (C-8); 139.7* (C-1'); 128.5 (C-3', 5'); 126.8 (C-2', 6'); 126.7 (C-4'); 126.4 (C-8a); 113.7 (C-4a); 110.4 (C-6); 109.3 (C-7); 56 (OCH₃); 37.5 (C-3); 35.1 (C-4) ppm.

8-Hydroxy-5-methoxy-4-phenyl-3,4-dihydro-2(1*H*)-quinolinone (7a).

Yield: 15% (from **2a**); 3rd fraction. ¹H-NMR (CDCl₃/CD₃OD) δ : 2.67 (1H, dd, J = 16.4 Hz, J = 1.8 Hz, H-3_{eq}); 2.86 (1H, dd, J = 16.4 Hz, J = 7.3 Hz, H-3_{ax}); 3.57 (3H, s, OCH₃); 4.5 (1H, dd, J = 7.3 Hz, J = 1.8 Hz, H-4_{eq}); 6.33 (1H, d, J = 8.8 Hz, H-6); 6.59 (1H, d, J = 8.8 Hz, H-7); 7.08 (5H, m, Ph) ppm. ¹³C-NMR (CDCl₃/CD₃OD) δ : 170.3 (C-2); 149.9 (C-5); 142.2 (C-8); 137.9 (C-1'); 128.6 (C-3', 5'); 127.5 (C-8a); 126.8 (C-2', 6'); 125.6 (C-4'); 114.9 (C-4a); 113.9 (C-6); 105.7 (C-4); 55.8 (OCH₃); 37.8 (C-3); 35.4 (C-4) ppm.

5,8-Dihydroxy-4-phenyl-3,4-dihydro-2(1*H*)-quinolinone (8a).

Yield: 5% (from **2a**); 4th fraction. ¹H-NMR (CD₃OD) δ : 2.81 (1H, dd, J = 16.2 Hz, J = 1.7 Hz, H-3_{eq}); 3.06 (1H, dd, J = 16.2 Hz, J = 6.2 Hz, H-3_{ax}); 4.68 (1H, dd, J = 6.2 Hz, J = 1.7 Hz, H-4_{eq}); 6.47 (1H, d, J = 8.7 Hz, H-6); 6.71 (1H, d, J = 8.7 Hz, H-7); 7.23 (5H, m, Ph) ppm. ¹³C-NMR (CD₃OD) δ : 172.4 (C-2); 148.9 (C-5); 144.1 (C-8); 138.9 (C-1'); 129.8 (C-3', 5'); 128.4 (C-4'); 127.5 (C-8a); 115.7 (C-6); 115.5 (C-4a); 11.2 (C-7); 39.5 (C-3); 37.1 (C-4) ppm.

Oxidation reactions of 4-Aryl-3,4-dihydro-5,8-dimethoxy-2(1*H*)-quinolinones (5).

Method A: CAN (Cerium ammonium nitrate) (2.2 equivalents) was added portionwise to a solution of 100 mg

(0.33 mmol) of the suitable compound **5a,d** in 10 ml acetonitrile / water (3 : 1). The reaction mixture was stirred at room temperature for 30 min, was then diluted with water (30 ml) and extracted with dichloromethane (3 x 30 ml). The extracts were dried (sodium sulfate) and evaporated, and the residue was purified by chromatography (petroleum ether / ethyl acetate, 1 : 1) on silica gel, affording firstly the nitroderivatives **11d** (22 %), followed by the quinone **10** (**10a**: 17 %, **10d**: 4 %) and finally the dimer **9** (**9a**: 34 %, **9d**: 28 %).

Method B: To a suspension of 0.33 mmol of the suitable compound **5** and 200 mg (1.5 mmol) silver(II) oxide (AgO) in 20 ml dioxane were added 2 ml of HNO₃ 6N with stirring. After 20 min. 20 ml chloroform / water (3 : 2) were added. The organic layer was separated and the aqueous phase was extracted with chloroform (3 x 50 ml). The organic extracts were dried (sodium sulfate) and evaporated, and the residue was purified by chromatography on silica gel, affording **11** and **10**.

Method C: To a stirred, ice cooled suspension of 0.33 mmol of the suitable compound **5** and 360 mg (2 mmol) of pyridine-2,6-dicarboxylic acid *N*-oxide¹⁵ in 18 ml acetonitrile / water (7 : 1), was added 250 mg (2 mmol) of AgO and the reaction was maintained in the icebath during 40 min. Water (20 ml) was added, the reaction mixture was filtered and the liquids extracted with dichloromethane (3 x 15 ml). The organic layers were dried (magnesium sulfate) and concentrated, and the residue was purified by chromatography on silica gel, affording the quinones **10** and very small amounts of the 6-methoxy derivative **12**.

4,4'-Diphenyl-3,3',4,4'-tetrahydro-6,6'-biquinolyl-2,2',5,5',8,8'-hexaone (9a).

Yield: 34% (Method A). ¹H-NMR (CDCl₃) δ: 2.85 (2H, dd, *J* = 16.9 Hz, *J* = 1.8 Hz, H-3,3'_{eq}); 2.98 (2H, dd, *J* = 16.9 Hz, *J* = 7.4 Hz, H-3,3'_{ax}); 4.45 (2H, dd, *J* = 7.4 Hz, *J* = 1.8 Hz, H-4,4'_{eq}); 6.72 (2H, s, H-7); 6.75 (2H, s, H-7'); 7.23 (10H, m, 2 Ph); 7.95 (2H, br s, 2 NH). ¹³C-NMR (CDCl₃) δ: 182.1 (C-8,8'); 180.1 (C-5,5'); 169.5 (C-2,2'); 140.7 (C-6,6'); 137.9 (C-1 Ph,Ph'); 136.4 (C-4a,4a'); 133.3 (C-7,7'); 129.1 (C-3,5 Ph,Ph'); 127.6 (C-4 Ph,Ph'); 126.6 (C-2,6 Ph,Ph'); 120.1 (C-8a,8a'); 36.9 (C-3,3'); 35 (C-4,4') ppm.

4,4'-Bis(*p*-methoxyphenyl)-3,3',4,4'-tetrahydro-6,6'-biquinolyl-2,2',5,5',8,8'-hexaone (9d).

Yield: 28% (Method A). Mp 178-80°C. ¹H-NMR (CDCl₃) δ: 2.84 (2H, d, *J* = 17.1 Hz, H-3,3'_{eq}); 2.96 (2H, dd, *J* = 17.1 Hz, *J* = 7.9 Hz, H-3,3'_{ax}); 3.71 (3H, s, OCH₃); 3.73 (3H, s, OCH₃); 4.37 (2H, d, *J* = 7.9 Hz, H-4,4'_{eq}); 6.71 (1H, s, H-7); 6.73 (1H, s, H-7'); 6.78 (2H, d, *J* = 8.7 Hz, H-3,5 Ph); 6.80 (2H, d, *J* = 8.7 Hz, H-3,5 Ph'); 7.09 (4H, d, *J* = 8.7 Hz, H-2,6 Ph,Ph); 8.01 (2H, br s, 2 NH). ¹³C-NMR (CDCl₃) δ: 182.1, 182 (C-8,8'); 180.1, 180 (C-5,5'); 168.5 (C-2,2'); 159.2 (C-4 Ph,Ph'); 140.6, 140.5 (C-6,6'); 136.6 (C-4a,4a'); 133.3, 133.2 (C-7,7'); 132.4, 132.1 (C-1 Ph,Ph'); 128.1, 128 (C-2,6 Ph,Ph'); 12.5, 120.4 (C-8a,8a'); 114.5 (C-3,5 Ph,Ph'); 55.3 (2 OCH₃); 36.9 (C-3,3'); 34.7, 34.5 (C-4,4') ppm. Analysis calc. for C₃₂H₂₄N₂O₈: C, 68.08; H, 4.28; N, 4.96. Found: C, 67.74; H, 4.49; N, 4.69.

4-Phenyl-3,4-dihydro-2,5,8(1*H*)-quinolinetriene (10a).

Yield: 17% (Method A); 51% (Method B); 82% (Method C). Mp 130-132°C. IR ν: 3336, 1709, 1639, 1590, 1462 cm⁻¹. ¹H-NMR (CDCl₃) δ: 2.87 (1H, ddd, *J* = 17.1 Hz, *J* = 7.7 Hz, *J*_w = 0.8 Hz, H-3_{eq}); 2.98 (1H, dd, *J* = 17.1 Hz, *J* = 7.7 Hz, H-3_{ax}); 4.43 (1H, dd, *J* = 7.7 Hz, *J* = 2.1 Hz, H-4_{eq}); 6.69* (1H, d, *J* = 10.2 Hz, H-6); 6.74* (1H, d, *J* = 10.2 Hz, H-7); 7.23 (5H, m, Ph); 7.94 (1H, br s, NH). ¹³C-NMR (CDCl₃) δ: 184.4 (C-8); 181.1 (C-5); 168.4 (C-2); 140.2 (C-1'); 137.9 (C-6); 136.4 (C-4a); 133.1 (C-7); 129.1 (C-3', 5'); 127.6 (C-4'); 126.7 (C-2',6'); 119.9 (C-8a); 36.7 (C-3); 34.8 (C-4) ppm. Analysis calc. for C₁₅H₁₁NO₃: C, 71.14; H, 4.38; N, 5.53. Found: C, 70.78; H, 4.57; N, 5.54.

4-(*o*-Methoxy)phenyl-3,4-dihydro-2,5,8(1*H*)-quinolinetriene (10b).

Yield: 45% (Method B); 62% (Method C). Mp 173-175°C. IR ν: 3446, 1700, 1639, 1464 cm⁻¹. ¹H-NMR (CDCl₃) δ: 2.74 (1H, ddd, *J* = 17.5 Hz, *J* = 1.5 Hz, *J*_w = 1 Hz, H-3_{eq}); 2.91 (1H, dd, *J* = 17.5 Hz, *J* = 9.4 Hz, H-3_{ax});

3.76 (3H, s, OCH₃); 4.58 (1H, dd, $J = 9.4$ Hz, $J = 1.5$ Hz, H-4); 6.69* (1H, d, $J = 10.3$ Hz, H-6); 6.73* (1H, d, $J = 10.3$ Hz, H-7); 6.84 (1H, d"t", $J = 7.7$ Hz, $J = 1.1$ Hz, H-5'); 6.84 (1H, dd, $J = 8.2$ Hz, $J = 1.1$ Hz, H-3') 7.12 (1H, dd, $J = 7.7$ Hz, $J = 1.8$ Hz, H-6'); 7.19 (1H, ddd, $J = 8.2$ Hz, $J = 7.7$ Hz, $J = 1.8$ Hz, H-4'); 7.83 (1H, br s, NH). ¹³C-NMR (CDCl₃) δ : 184.6 (C-8); 181.5 (C-5); 168.5 (C-2); 157.1 (C-2'); 138.4 (C-6); 137.3 (C-4a); 133.1 (C-7); 129 (C-6',4'); 128.3 (C-1'); 120.7 (C-5'); 117.9 (C-8a); 111 (C-3'); 54.9 (OCH₃); 36 (C-3); 32.5 (C-4) ppm. Analysis calc. for C₁₆H₁₃NO₄: C, 67.84; H, 4.63; N, 4.94. Found: C, 67.56; H, 4.68; N, 4.83.

4-(*m*-Methoxy)phenyl-3,4-dihydro-2,5,8(1*H*)-quinolinetrioxone (10c).

Yield: 60% (Method B); 78% (Method C). Mp 175°C. IR ν : 3445, 1702, 1637, 1592, 1457 cm⁻¹. ¹H-NMR (CDCl₃) δ : 2.86 (1H, ddd, $J = 17.1$ Hz, $J = 2.2$ Hz, $J_w = 0.8$ Hz, H-3_{eq}); 2.97 (1H, dd, $J = 17.1$ Hz, $J = 7.6$ Hz, H-3_{ax}); 3.74 (3H, s, OCH₃); 4.4 (1H, dd, $J = 7.6$ Hz, $J = 2.2$ Hz, H-4_{eq}); 6.73 (2H, 2d, $J = 10$ Hz, H-6,7); 6.76 (3H, m, Ph); 7.2 (1H, dd, $J = 9$ Hz, $J = 7.6$ Hz, H-5') 7.83 (1H, br s, NH). ¹³C-NMR (CDCl₃) δ : 184.4 (C-8); 181.1 (C-5); 168.2 (C-2); 159.8 (C-3'); 141.1 (C-1'); 137.9 (C-6); 136.5 (C-4a); 133 (C-7); 130.1 (C-5'); 119.6 (C-8a); 118.7 (C-6'); 112.9 (C-4'); 112.5 (C-2'); 55.3 (OCH₃); 36.8 (C-3); 34.9 (C-4) ppm. Analysis calc. for C₁₆H₁₃NO₄: C, 67.84; H, 4.63; N, 4.94. Found: C, 67.43; H, 4.68; N, 5.18.

4-(*p*-Methoxy)phenyl-3,4-dihydro-2,5,8(1*H*)-quinolinetrioxone (10d).

Yield: 4% (Method A); 63% (Method B); 80% (Method C). Mp 180-182°C. IR ν : 3238, 1653, 1608, 1511, 1248 cm⁻¹. ¹H-NMR (CDCl₃) δ : 2.83 (1H, ddd, $J = 17$ Hz, $J = 2$ Hz, $J_w = 0.7$ Hz, H-3_{eq}); 2.96 (1H, dd, $J = 17$ Hz, $J = 7.7$ Hz, H-3_{ax}); 3.68 (3H, s, OCH₃); 4.37 (1H, dd, $J = 7.7$ Hz, $J = 2$ Hz, H-4_{eq}); 6.68* (1H, d, $J = 10$ Hz, H-6); 6.72* (1H, d, $J = 10$ Hz, H-7); 6.78 (2H, d, $J = 8.8$ Hz, H-3',5'); 7.11 (2H, d, $J = 8.8$ Hz, H-2',6'); 7.95 (1H, br s, NH). ¹³C-NMR (CDCl₃) δ : 184.4 (C-8); 181.3 (C-5); 168.7 (C-2); 159.1 (C-4'); 137.9 (C-6); 136.3 (C-4a); 133.2 (C-7); 132.4 (C-1'); 128 (C-2',6'); 120.4 (C-8a); 114.5 (C-3',5'); 55.4 (OCH₃); 36.9 (C-3); 34.2 (C-4) ppm. Analysis calc. for C₁₆H₁₃NO₄: C, 67.84; H, 4.63; N, 4.94. Found: C, 68.07; H, 4.93; N, 4.97.

5,8-Dimethoxy-6-nitro-4-phenyl-3,4-dihydro-2(1*H*)-quinolinone (11a).

Yield: 14% (Method B). Mp 182°C (EtOH). IR ν : 3225, 1693, 1587, 1525, 1327 cm⁻¹. ¹H-NMR (CDCl₃) δ : 2.87 (1H, ddd, $J = 16.5$ Hz, $J = 2$ Hz, $J_w = 0.7$ Hz, H-3_{eq}); 2.98 (1H, dd, $J = 16.5$ Hz, $J = 6.9$ Hz, H-3_{ax}); 3.54 (3H, s, OCH₃); 3.93 (3H, s, OCH₃); 4.72 (1H, dd, $J = 6.9$ Hz, $J = 2$ Hz, H-4_{eq}); 7.08 (2H, m, Ph); 7.2 (3H, m, Ph); 7.49 (1H, s, H-7); 8.09 (1H, br s, NH). ¹³C-NMR (CDCl₃) δ : 168.5 (C-2); 147.3 (C-5); 141.5 (C-1'); 141.2 (C-8); 137.3* (C-4a); 133* (C-8a); 129.2 (C-3', 5'); 127.6 (C-4'); 126.9 (C-2',6'); 121.5 (C-6); 107.2 (C-7); 62.9 (OCH₃(5)); 56.6 (OCH₃); 38 (C-3); 36.4 (C-4) ppm. Analysis calc. for C₁₇H₁₆N₂O₅: C, 62.19; H, 4.91; N, 8.53. Found: C, 61.98; H, 4.95; N, 8.78.

Alternative synthesis: A mixture of **5a** (280 mg, 1 mmol), iodine (127 mg, 0.5 mmol), and CAN (275 mg, 0.5 mmol) in methanol (10 ml) was stirred at 50 °C for 6h. The reaction mixture was poured into water and extracted with ether. The ethereal solution was washed with aqueous NaHCO₃ and water, dried, and concentrated. The residue was purified by chromatography (ethyl acetate/petroleum ether 1 : 1) to afford **14** (300 mg, 79 %): mp 180 - 82 °C. C₁₇H₁₆N₂O₅: C, 62.19; H, 4.91; N, 8.53. Found: C, 62.12; H, 5.03; N, 8.13.

5,8-Dimethoxy-4-(*o*-methoxy)phenyl-6-nitro-3,4-dihydro-2(1*H*)-quinolinone (11b).

Yield: 12% (Method B). Mp 160-162°C (EtOH). ¹H-NMR (CDCl₃) δ : 2.87 (2H, m, H-3); 3.48 (3H, s, OCH₃); 3.88 (3H, s, OCH₃); 3.94 (3H, s, OCH₃); 5.08 (1H, d, $J = 5.8$ Hz, H-4); 6.57 (1H, dd, $J = 7.6$ Hz, $J = 1.8$ Hz, H-6'); 6.73 (1H, d"t", $J = 7.5$ Hz, $J = 1.2$ Hz, H-5'); 6.87 (1H, dd, $J = 8$ Hz, $J = 1.1$ Hz, H-3') 7.18 (1H, ddd, $J = 8.3$ Hz, $J = 7.5$ Hz, $J = 1.8$ Hz, H-4'); 7.50 (1H, s, H-7); 8.04 (1H, br s, NH) ppm. ¹³C-NMR (CDCl₃) δ : 169.1 (C-2); 156.5 (C-2'); 147.3 (C-5); 141.3 (C-8); 137.4 (C-4a); 133.8 (C-8a); 128.8 (C-6'); 128.7 (C-1'); 127.3 (C-4'); 121.5 (C-6); 120.7 (C-5'); 110.9 (C-3'); 106.9 (C-7); 62.7 (OCH₃); 56.6 (OCH₃); 56.4 (OCH₃); 36.8 (C-3); 30.8 (C-4) ppm.

Analysis calc. for $C_{18}H_{18}N_2O_6$: C, 60.33; H, 5.06; N, 7.82. Found: C, 60.77; H, 5.00; N, 8.03.

5,8-Dimethoxy-4-(*m*-methoxy)phenyl-6-nitro-3,4-dihydro-2(1*H*)-quinolinone (11c).

Yield: 28% (Method B). Mp 144–146°C (EtOH). 1H -NMR ($CDCl_3$) δ : 2.86 (1H, ddd, $J = 16.5$ Hz, $J = 2.1$ Hz, $J_w = 0.9$ Hz, H-3_{eq}); 2.97 (1H, dd, $J = 16.5$ Hz, $J = 7$ Hz, H-3_{ax}); 3.56 (3H, s, OCH₃); 3.73 (3H, s, OCH₃); 3.94 (3H, s, OCH₃); 4.7 (1H, dd, $J = 7$ Hz, $J = 2.1$ Hz, H-4_{eq}); 6.60 (1H, "t", $J = 2.1$ Hz, H-2'); 6.63 (1H, d, $J = 8$ Hz, H-4'); 6.70 (1H, d, $J = 8$ Hz, H-6'); 7.15 (1H, "t", $J = 8$ Hz, H-5'); 7.47 (1H, s, H-7); 8.15 (1H, br s, NH) ppm. ^{13}C -NMR ($CDCl_3$) δ : 168.1 (C-2); 160.35 (C-3'); 147.3 (C-5); 142.8 (C-1'); 141.4 (C-8); 137.1 (C-4a); 133 (C-8a); 130.3 (C-5'); 121.3 (C-6); 119.1 (C-6'); 112 (C-2'); 107.1 (C-7); 62.9 (OCH₃); 56.5 (OCH₃); 55.5 (OCH₃); 38.1 (C-3); 36.4 (C-4) ppm. Analysis calc. for $C_{18}H_{18}N_2O_6$: C, 60.33; H, 5.06; N, 7.82. Found: C, 60.26; H, 5.41; N, 7.66.

5,8-Dimethoxy-4-(*p*-methoxy)phenyl-6-nitro-3,4-dihydro-2(1*H*)-quinolinone (11d).

Yield: 22% (Method A); 6% (Method B). Mp 176–178°C (EtOH). IR ν : 3230, 1686, 1591, 1526, 1500, 1490, 1329 cm^{-1} . 1H -NMR ($CDCl_3$) δ : 2.85 (1H, ddd, $J = 16.4$ Hz, $J = 2.3$ Hz, $J_w = 0.9$ Hz, H-3_{eq}); 2.95 (1H, dd, $J = 16.4$ Hz, $J = 6.7$ Hz, H-3_{ax}); 3.57 (3H, s, OCH₃); 3.72 (3H, s, OCH₃); 3.93 (3H, s, OCH₃); 4.68 (1H, dd, $J = 6.7$ Hz, $J = 2.3$ Hz, H-4_{eq}); 6.76 (2H, d, $J = 8.8$ Hz, H-3',5'); 7.0 (2H, d, $J = 8.8$ Hz, H-2',6'); 7.49 (1H, s, H-7); 8.02 (1H, br s, NH) ppm. ^{13}C -NMR ($CDCl_3$) δ : 168.6 (C-2); 158.9 (C-4'); 147.2 (C-5); 141.5 (C-8); 137.3 (C-4a); 133.1 (C-8a); 132.8 (C-1'); 127.9 (C-2',6'); 121.9 (C-6); 114.5 (C-3',5'); 106.9 (C-7); 62.99 (OCH₃); 56.3 (OCH₃); 55.3 (OCH₃); 38.2 (C-3); 35.6 (C-4) ppm. Analysis calc. for $C_{18}H_{18}N_2O_6$: C, 60.33; H, 5.06; N, 7.82. Found: C, 60.26; H, 5.39; N, 7.57.

6-Methoxy-4-(*p*-methoxy)phenyl-3,4-dihydro-2,5,8(1*H*)-quinolinetrione (12d).

Yield: 15% (Method C). Mp 201–203°C. IR ν : 3249, 1707, 1652, 1588, 1458, 1225 cm^{-1} . 1H -NMR ($CDCl_3$) δ : 2.85 (1H, ddd, $J = 17$ Hz, $J = 2.4$ Hz, $J_w = 0.6$ Hz, H-3_{eq}); 2.95 (1H, dd, $J = 17$ Hz, $J = 7.2$ Hz, H-3_{ax}); 3.72 (3H, s, OCH₃); 3.90 (3H, s, OCH₃); 4.41 (1H, dd, $J = 7.2$ Hz, $J = 2.4$ Hz, H-4_{eq}); 5.73 (1H, s, H-7); 6.76 (2H, d, $J = 8.7$ Hz, H-3',5'); 7.12 (2H, d, $J = 8.7$ Hz, H-2',6'); 8.08 (1H, s, NH). ^{13}C -NMR ($CDCl_3$) δ : 178.3* (C-8); 176.3* (C-5); 169.4 (C-2); 160.9 (C-6); 159 (C-4'); 140.3 (C-4a); 132.4 (C-1'); 127.9 (C-2',6'); 116.5 (C-8a); 114.5 (C-3',5'); 102.9 (C-7); 57.5 (OCH₃); 55.4 (OCH₃); 36.8 (C-3); 33.6 (C-4) ppm. Analysis calc. for $C_{17}H_{15}NO_5$: C, 65.17; H, 4.83; N, 4.47. Found: C, 64.93; H, 4.94; N, 4.45.

6-Bromo-5,8-dimethoxy-4-phenyl-3,4-dihydro-2(1*H*)-quinolinone (13).

A mixture of **5a** (280 mg, 1 mmol), NBS (4.4 g, 2.4 mmol), and benzoyl peroxide (72 mg) in CCl_4 (30 ml) was stirred for 5 h under reflux. The mixture was concentrated, dissolved in ether, washed with 5% Na_2CO_3 and water, and dried over $MgSO_4$. The solvent was removed and the residue was purified by chromatography (ethyl acetate/petroleum ether, 1 : 1) to afford **13** (240 mg, 72 %): mp 160–62 °C. IR ν : 3212, 1700, 1486, 1215 cm^{-1} . 1H -NMR ($CDCl_3$) δ : 2.65 (1H, dd, $J = 16.1$ Hz, $J = 1.5$ Hz, H-3_{eq}); 2.92 (1H, dd, $J = 16.1$ Hz, $J = 7.1$ Hz, H-3_{ax}); 3.5 (3H, s, OCH₃); 3.85 (3H, s, OCH₃); 4.65 (1H, dd, $J = 7.1$ Hz, $J = 1.5$ Hz, H-4_{eq}); 6.9 (1H, s, H-7); 7.1 (5H, m, Ph); 7.75 (1H, s, NH). ^{13}C -NMR ($CDCl_3$) δ : 168.5 (C-2); 148.4 (C-5); 142.9 (C-8); 141.7 (C-1'); 129 (C-3', 5'); 127.3 (C-8a); 127 (C-2',6'); 126.7 (C-4'); 121.3 (C-4a); 114.2 (C-7); 109.8 (C-6); 61.4 (OCH₃); 56.6 (OCH₃); 38.3 (C-3); 37.1 (C-4) ppm. Analysis calc. for $C_{17}H_{16}NO_3Br$: C, 56.37; H, 4.45; N, 3.87. Found: C, 56.35; H, 4.39; N, 3.67.

4-Aryl-3,4-dihydro-7-methyl-1(1*H*)-1,8-diazaanthracene-2,9,10-trione (14).

To a solution of the quinone **10** (0.6 mmol) in dry acetonitrile (50 ml) was added 3-methyl-1-dimethylamino-1-aza-1,3-butadiene⁸ (66 mg, 0.6 mmol) in 10 ml of acetonitrile. The reaction mixture was stirred at room temperature for 1 h under argon obtaining a dark green solution, which became colourless after stirring further 3 h under air. After evaporation of the solvent under reduced pressure, the reaction mixture was purified dissolving in 15 ml diluted HCl

(10%), washing with ether (10 ml), neutralizing with ammonium hydroxide (14%) and extracting with CH_2Cl_2 (3 x 15 ml). The residue obtained after evaporation of the dried (Na_2SO_4) dichloromethane phase was recrystallized from acetonitrile or purified as hydrochloride salt.

4-Phenyl-3,4-dihydro-7-methyl-(1*H*)-1,8-diazaanthracene-2,9,10-trione (14a).

Yield: 48 %. Mp: 185°C. IR ν : 3220, 1721, 1684, 1652, 1628 cm^{-1} . $^1\text{H-NMR}$ (CDCl_3) δ : 2.90 (3H, "t", J = 0.6 Hz, CH_3); 3.36 (1H, dd, J = 17.1 Hz, J = 1.9 Hz, H-3); 3.46 (1H, dd, J = 17.1 Hz, J = 7.9 Hz, H-3); 5.05 (1H, dd, J = 7.9 Hz, J = 1.9 Hz, H-4); 7.66 (5H, m, Ph); 8.57 (1H, dd, J = 2.2 Hz, J = 0.6 Hz, H-7); 8.69 (1H, s, NH); 9.19 (1H, dd, J = 2.2 Hz, J = 0.6 Hz, H-5). $^{13}\text{C-NMR}$ (CDCl_3) δ : 181.6 (C-10); 177.8 (C-9); 168.5 (C-2); 154.9 (C-7); 144.4 (C-8a); 140.3 (C-1'); 139.9 (C-4a); 139.0 (C-10a); 134.6 (C-5); 129.3 (C-3' y C-5'); 129.2 (C-6); 127.9 (C-4'); 126.9 (C-2' y C-6'); 121.9 (C-9a); 36.7 (C-3); 35.4 (C-4); 19.2 (CH_3). Analysis calc. for $\text{C}_{19}\text{H}_{14}\text{N}_2\text{O}_3$: C, 71.69; H, 4.43; N, 8.80. Found: C, 71.49; H, 4.68; N, 8.63.

4-*o*-Methoxyphenyl-3,4-dihydro-7-methyl-(1*H*)-1,8-diazaanthracene-2,9,10-trione (14b).

Yield: 59 %. Mp: 217-218 °C. IR ν : 3150, 1686, 1638, 1630 cm^{-1} . $^1\text{H-NMR}$: (CDCl_3) δ : 2.47 (3H, s, CH_3); 2.77 (1H, dd, J = 17.2 Hz, J = 1.4 Hz, H-3 eq); 2.98 (1H, dd, J = 17.2 Hz, J = 9.5 Hz, H-3 ax); 3.76 (3H, s, OCH_3); 4.77 (1H, dd, J = 9.5 Hz, J = 1.4 Hz, H-4 eq); 6.83 (2H, m, H-2' y H-5'); 7.20 (2H, m, H-4' y H-6'); 8.10 (1H, d, J = 1.9 Hz, H-7); 8.25 (1H, sa, NH); 8.76 (1H, d, J = 1.9 Hz, H-5). $^{13}\text{C-NMR}$ (CDCl_3) δ ppm= 181.6 (C-10); 178.0 (C-9); 168.5 (C-2); 157.1 (C-2'); 154.7 (C-7); 144.4 (C-8a); 139.5 (C-4a y C-10a); 134.3 (C-5); 129.1 (C-1'); 129.0 (C-6); 128.8* (C-6'); 128.1* (C-4'); 120.6 (C-5'); 119.6 (C-9a); 110.8 (C-3'); 54.9 (OCH_3); 35.8 (C-3); 33.1 (C-4); 19.1 (CH_3). Analysis calc. for: $\text{C}_{20}\text{H}_{16}\text{N}_2\text{O}_4$. HCl: C, 62.42; H, 4.45; N, 7.28. Found: C, 62.10; H, 4.77; N, 7.89.

4-*m*-Methoxyphenyl-3,4-dihydro-7-methyl-(1*H*)-1,8-diazaanthracene-2,9,10-trione (14c).

Yield: 52 %. Mp: 199-201 °C. IR ν : 3363, 1710, 1690, 1636 cm^{-1} . $^1\text{H-NMR}$ (CDCl_3) δ : 2.50 (3H, s, CH_3); 2.92 (1H, dd, J = 17.1 Hz, J = 2 Hz, H-3 eq); 3.03 (1H, dd, J = 17.1 Hz, J = 7.7 Hz, H-3 ax); 3.73 (3H, s, OCH_3); 4.61 (1H, dd, J = 7.7 Hz, J = 2 Hz, H-4 eq); 6.81 (1H, t, J = 1.8 Hz, H-2'); 6.88 (2H, m, H-4' y H-6'); 7.18 (1H, "t", J = 7.9 Hz, H-5'); 8.17 (1H, dd, J = 2.2 Hz, J = 0.7 Hz, H-7); 8.24 (1H, sa, NH); 8.78 (1H, dd, J = 2.2 Hz, J = 0.7 Hz, H-5). $^{13}\text{C-NMR}$ (CDCl_3) δ : 181.6 (C-10); 177.7 (C-9); 168.3 (C-2); 160.2 (C-3'); 154.9 (C-7); 144.4 (C-8a); 141.8 (C-1'); 139.9 (C-4a); 139.0 (C-10a); 134.6 (C-5); 130.4 (C-5'); 129.3 (C-6); 121.7 (C-9a); 119.0 (C-6'); 113.3 (C-4'); 112.8 (C-2'); 55.3 (OCH_3); 36.8 (C-3); 35.4 (C-4); 19.2 (CH_3).

Analysis calc. for: $\text{C}_{20}\text{H}_{16}\text{N}_2\text{O}_4$. HCl: C, 62.42; H, 4.45; N, 7.28. Found: C, 62.53; H, 4.59; N, 7.39.

4-*p*-Methoxyphenyl-3,4-dihydro-7-methyl-(1*H*)-1,8-diazaanthracene-2,9,10-trione (14d).

Yield: 58%. Mp: 203 - 205 °C. IR ν : 3150, 1717, 1684, 1653, 1627 cm^{-1} . $^1\text{H-NMR}$ (CDCl_3) δ : 2.49 (3H, s, CH_3); 2.90 (1H, dd, J = 17 Hz, J = 1.8 Hz, H-3 eq.); 3.03 (1H, dd, J = 17 Hz, J = 7.9 Hz, H-3 ax.); 3.72 (3H, s, OCH_3); 4.59 (1H, dd, J = 7.9 Hz, J = 1.8 Hz, H-4 eq.); 6.78 (2H, d, J = 8.7 Hz, H-3' y 5'); 7.17 (1H, d, J = 8.7 Hz, H-2' y 6'); 8.16 (1H, d, J = 2 Hz, H-7); 8.25 (1H, sa, NH); 8.78 (1H, d, J = 2 Hz, H-5) ppm. $^{13}\text{C-NMR}$ (CDCl_3) δ : 181.6 (C-10); 177.8 (C-9); 168.6 (C-2); 159.2 (C-4'); 154.8 (C-7); 144.4 (C-8a); 139.8 (C-4a); 138.6 (C-10a); 134.6 (C-5); 132.4 (C-1'); 129.2 (C-6); 128.1 (C-2' y 6'); 122.2 (C-9a); 114.6 (C-3' y 5'); 55.4 (OCH_3); 36.9 (C-3); 34.6 (C-4); 19.2 (CH_3) ppm. Analysis calc. for: $\text{C}_{20}\text{H}_{16}\text{N}_2\text{O}_4$: C, 68.43; H, 4.63; N, 8.04. Found: C, 68.32; H, 4.53; N, 7.99.

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