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Regioselectivity of the Diels-Alder Reactions of 2,5,8(1*H*)-Quinolinetriones

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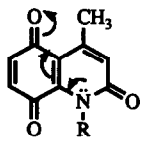
Abstract.- Diels-Alder reactions of 2,5,8(1*H*)-quinolinetriones were completely regioselective for all the unsymmetrical dienes tested, except in the case of isoprene. This corresponds to a level of regioselectivity higher than the one found by previous workers for 5,8-quinolinequinone.

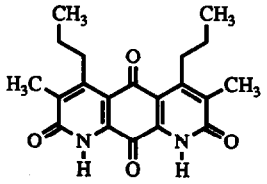
A number of studies are available on the regioselectivity of the Diels-Alder reactions of 1,4-naphthoquinones,[1] and 1,4-anthraquinones,[2] many of them prompted by synthetic work in the field of the anthracyclines and related antibiotics.[3] In contrast, the regiochemistry of the Diels-Alder cycloadditions between heterocyclic quinones and unsymmetrical aliphatic dienes has received very little attention. In the case of quinolinequinones, Potts and coworkers[4] have shown that the electron distribution in 5,8-quinolinequinone provides complete control of the cycloaddition of electron-rich dienes, such as 1-methoxy-1,3-cyclohexadiene and 1-methoxy-3-trimethylsilyloxy-1,3-butadiene (Danishefsky's diene). These reactions are regulated by the electron-withdrawing effect of the nitrogen atom of the heterocyclic dienophile, which causes the C_8 carbonyl group to be more electron-defficient and directs the attack of the more negative end of the diene to its conjugated position C_6. However, less polarized dienes like isoprene and piperylene give mixtures of both possible regioisomers.[5]

The electron-releasing nitrogen atom of 2,5,8-(1*H*)-quinolinetriones (**1**) should also exert some control on the regiochemistry of Diels-Alder cycloadditions, since its conjugation with the C_5=O group (structure **1**, arrows) leaves the C_6=C_7-C_8=O portion of the molecule as an isolated system, which should react at C_6 with the negative end of the diene. This idea is supported by the complete regioselectivity found in the reactions between **1** and activated 1-azadienes,[6] although this result is not necessarily applicable to the case of carbodienes.

Due to our interest[6] in the synthesis of antitumour analogs of the antibiotic diazaquinomycin A (**2**), we have studied the preparation of deaza analogues of the parent structure through Diels-Alder reactions of quinones (**1a**) (R = H) and (**1b**) (R = CH_3) with unsymmetrical dienes. To our knowledge, only one example of a Diels-Alder reaction of a derivative of the 2,5,8-(1*H*)-quinolinetrione system, involving a symmetrical diene, was known prior to our work.[7]



1a R = H
1b R = CH_3



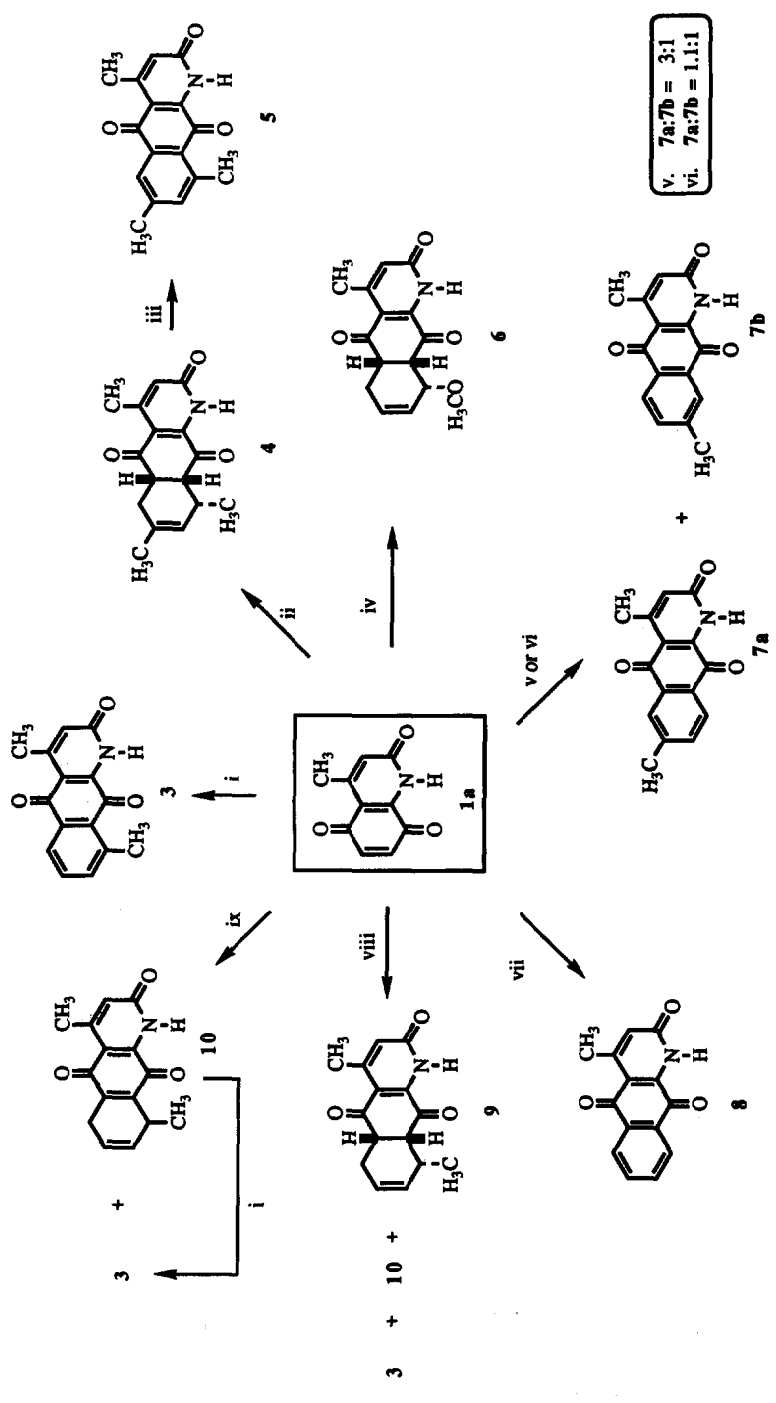
2 (Diazaquinomycin)

In agreement with the reasoning outlined above, our results show that Diels-Alder reactions of 4-methyl-2,5,8-(1*H*)-quinolinetrione (**1a**)[8] are more regioselective than those of 5,8-quinolinequinones (Scheme 1). Thus, **1a** reacted with piperylene to give a single aromatic regioisomer (**3**), while quinolinequinone is known to give a ~ 1:1 mixture of both possible reaction products.[5,9] Complete regioselectivity was similarly observed with 2-methyl-1,3-pentadiene and 1-methoxy-1,3-butadiene, which gave adducts (**4**) and (**6**), respectively. Isoprene was the only diene that afforded an inseparable mixture of regioisomers (**7a**:**7b** = 3:1) after cycloaddition and aromatization (the comparable reaction of quinolinequinone lacked any regioselectivity[5,9]). Selectivity dropped to **7a**:**7b** = 1.1:1 when the reaction was performed in the presence of one equivalent of boron trifluoride, which can be attributed to coordination of the Lewis acid with the more nucleophillic carbonyl oxygen atom (C_5) and the consequent increase in the electrophillic character of C_7. The *cis* and *endo* stereochemical assignments of the Diels-Alder adducts (**4**) and (**6**) were based on NOE difference spectra of compound (**6**); particularly significant enhancements were those of C_{8a}-H on irradiation of either C_{10a}-H or C_8-H. The assignments were also consistent with the multiplicities of the angular protons C_{8a}-H and C_{10a}-H (triplets, J *ca.* 6 Hz).

The oxidation level of the Diels-Alder adducts could be controlled in some cases by modifications in the solvent, temperature and reaction time. Isolation of the initial Diels-Alder adduct was feasible under mild reaction conditions, and thus adducts (**4**) and (**6**) were obtained after reaction at 120 °C for 2 h in a sealed tube or at room temperature for 16 h, respectively. While **4** can be aromatized to **5** by air oxidation, the related 8-methoxy derivative was not isolated, since **6** invariably lost the methoxy group on aromatization, leading to **8**.[10] The reactions with piperylene show that longer reaction times lead to mixtures of the initial Diels-Alder adduct (compound **9**), the partially oxidized dehydro derivative (**10**) and the aromatic system (**3**). In any case, these intermediates can be easily aromatized by air oxidation.

Regiochemical assignment of the aromatic cycloadducts (**3**), (**5**) and (**7**) was based upon the chemical shift of C_5-H and C_8-H. The ^{1}H-nmr spectrum of the mixture of the isoprene adducts (**7a**) and (**7b**) showed a small but significant displacement of the doublets that correspond to the *ortho* coupled protons (δ = 8.12 for the major product and 8.05 for the minor one). Since the higher δ must correspond to the proton adjacent to the more electrophillic C_9 carbonyl group the data above are consistent with the structure **7a** for the major product and **7b** for the minor one. A similar argument can be applied to the singlets assigned to C_5-H and C_8-H (δ = 7.93 in **7a** and 8.03 in **7b**, respectively). The chemical shifts found for the C_5 and C_8 protons of other aromatic adducts were also in agreement with the proposed structures.

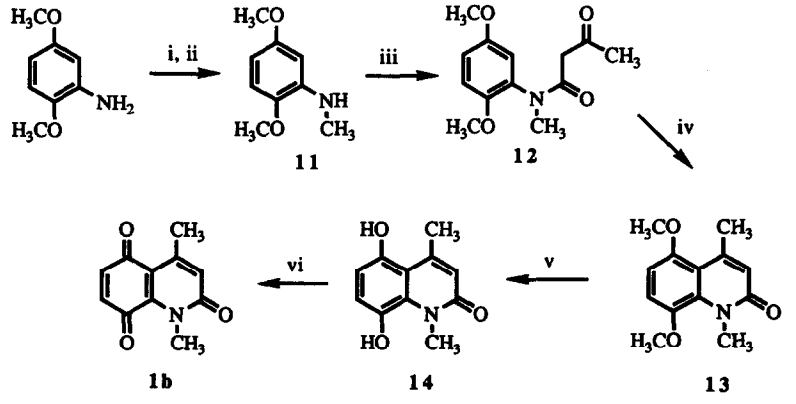
Finally, the regioselectivity of the Diels-Alder reactions of two silylated dienes, namely 1-trimethylsilyloxy-1,3-butadiene and 1-methoxy-3-trimethylsilyloxy-1,3-butadiene (Danishefsky's diene) was examined on the *N*-methylated quinone (**1b**), which was synthesized through a route consisting of acetoacetylation of *N*-methyl-2,5-dimethoxyaniline (**11**) by 2,2,6-trimethyl-4*H*-1,3-dioxin-4-one,[11] followed by Knorr cyclization of the acetoacetamide (**12**) to the carbostyril (**13**), demethylation and oxidation (Scheme 2).



Reagents and conditions: i. 1,3-pentadiene, AcOEt, sealed tube, 120 °C, 14 h. ii. 2-methyl-1,3-pentadiene, AcOEt, sealed tube, 120 °C, 1 h. iii. Xylene, air, 140 °C, 36 h. iv. 1-Methoxy-1,3-butadiene, $CHCl_3$, r.t., 16 h. v. 2-Methyl-1,3-butadiene, AcOEt, sealed tube, 120 °C, 24 h. vi. 2-Methyl-1,3-butadiene, AcOEt, sealed tube, BF_3-Et_2O (1 eq.), 100 °C, 4h. vii. 1-Methoxy-1,3-butadiene, $CHCl_3$, sealed tube, 95 °C, 2 h. viii. 1,3-Pentadiene, AcOEt, sealed tube, 100 °C, 14 h. ix. 1,3-Pentadiene, $CHCl_3$, sealed tube, 100 °C, 49 h.

Scheme 1

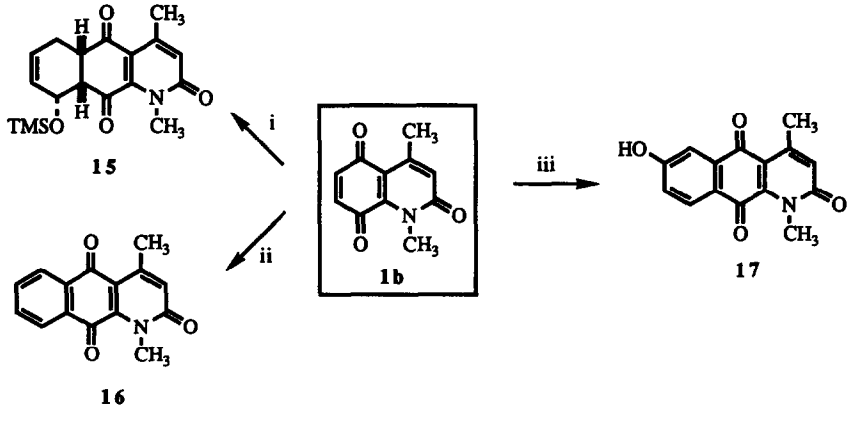
Preparation of compound (**13**) through an alternative route has been reported during the synthesis of Nybomycin analogues, but none of the intermediates has been fully characterized.[12]



Reagents and conditions: i. HCO_2H, $^iPr_2O$, 80 °C, 90 min. ii. $LiAlH_4$, Et_2O, r.t., 4 h. iii. 2,2,6-trimethyl-1,3-dioxin-4-one, xylene, 120 °C, 90 min. iv. 96 % H_2SO_4, r.t., 30 min. v. 48 % HBr, reflux, 48 h. vi. $K_2Cr_2O_7$, H_2O, 96 % H_2SO_4, 0 °C, 10 min.

Scheme 2

The Diels-Alder reactions of quinone (**1b**) with silyl dienes were completely regioselective (Scheme 3). In the reaction involving 1-trimethylsilyloxy-1,3-butadiene, the adduct (**15**) was easily isolated but aromatization



Reagents and conditions: i. 1-trimethylsilyloxy-1,3-butadiene, $CHCl_3$, sealed tube, 100 °C, 2 h. ii. i. 1-trimethylsilyloxy-1,3-butadiene, $CHCl_3$, sealed tube, 100 °C, 24 h. iii. 1-methoxy-3-trimethylsilyloxy-1,3-butadiene, $CHCl_3$, sealed tube, 100 °C, 18 h.

Scheme 3

resulted in the loss of the trimethylsilyl group, affording compound (**16**). In the case of Danishefsky's diene, isolation of the initial Diels-Alder adduct was not possible and the only product observed was phenol (**17**), after reaction at 100 °C for 18 h in a sealed tube, followed by silica gel column chromatography. Loss of the methoxy group has been previously reported for the reaction between Danishefsky's diene and quinolinequinone.[4]

In conclusion, Diels-Alder reactions of 2,5,8(1*H*)-quinolinetriones are regioselective in most of the cases studied. The adducts are currently being evaluated as antitumour agents, and the results obtained in these studies will be reported in due course.

ACKNOWLEDGEMENT

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EXPERIMENTAL

Infrared spectra were recorded on Perkin-Elmer 577 and Buck Scientific 500 spectrophotometers, with all compounds compressed into KBr pellets. NMR spectra were obtained on Bruker AC-250 (250 MHz for ^{1}H, 63 MHz for ^{13}C) and Varian VXR-300 (300 MHz for ^{1}H, 75 MHz for ^{13}C) spectrometers; $CDCl_3$, DMSO-d_6 and pyridine-d_5 were used as solvents, and TMS was added in all cases as an internal standard. ^{1}H-NMR spectra were assigned with the aid of COSY-45 experiments, and ^{13}C-NMR spectra were assigned with the aid of DEPT experiments, when necessary. Elemental analyses were determined by the Servicio de Microanálisis, Universidad Complutense, on a Perkin-Elmer 2400 CHN microanalyzer. Melting points were measured in open capillary tubes using a Büchi inmersion apparatus, and are uncorrected. Reactions were monitored by thin layer chromatography, on aluminium plates coated with silica gel with fluorescent indicator (Scharlau Cf 530). Separations by flash chromatography were performed on silica gel (SDS 60 ACC, 230-400 mesh and Scharlau Ge 048). All reagents were of commercial quality (Aldrich, Merck, SDS, Probus) and were used as received. The expression "petroleum ether" refers to the fraction boiling at 40-60 °C.

4,8-Dimethyl-2,9,10(2*H*)-1-azaanthracenetrione (3).

A solution of **1a** (440 mg, 2.3 mmol) and 1,3-pentadiene (190 mg, 2.7 mmol) in ethyl acetate (150 ml), placed in a sealed tube, was heated in an oven at 120 °C for 14 h. The cooled solution was evaporated and the residue was chromatographed on silica gel, eluting with dichloromethane-ethyl acetate (7:3), to yield 350 mg (60 %) of compound (**3**). Melting point, 245-248 °C (ethyl acetate). IR (KBr): 3280-3010 (N-H); 1640 (C=O) cm^{-1}. ^{1}H-NMR (300 MHz, DMSO-d_6) δ: 10.10 (br. s, 1H, NH); 7.98 (dd, 1H, J = 7.8 and 1.2 Hz, H-5); 7.75 (t, 1H, J = 7.8 Hz, H-6); 7.64 (dd, 1H. J = 7.8 and 1.2 Hz, H-7); 6.58 (d, 1H, J = 1.2 Hz, H-3); 2.70 (s, 3H, C_8-CH_3); 2.55 (d, 3H, J = 1.2 Hz, C_4-CH_3) ppm. Analysis calc. for $C_{15}H_{11}NO_3$: C, 71.14; H, 4.34; N, 5.53. Found: C, 70.44; H, 4.19; N, 5.53.

4,6,8-Trimethyl-5,8,8a,10a-tetrahydro-2,9,10(2*H*)-1-azaanthracenetrione (4).

A solution of **1a** (100 mg, 0.53 mmol) and 2-methyl-1,3-pentadiene (47 mg, 0.58 mmol) in ethyl acetate (150 ml), placed in a sealed tube, was heated at 120 °C for 1 h. Evaporation of the solvent and recrystallization from ethyl acetate afforded 124 mg (87 %) of compound (**4**). Melting point, 241-243 °C (ethyl acetate). IR (KBr): 3415 (N-H); 1655 (C=O) cm^{-1}. ^{1}H-NMR (250 MHz, $CDCl_3$) δ: 9.55 (br. s, 1H, NH); 6.62 (s, 1H, H-

3); 5.39 (s, 1H, H-7); 3.43 (t, 1H, J = 6.0 Hz, H-8a); 3.35 (m, 1H, H-10a); 2.63 (m, 2H, H-8 and H-5_{eq}); 2.52 (s, 3H, C_4-CH_3); 2.14 (dd, 1H, J = 16.5 and 6.0 Hz, H-5_{ax}); 1.74 (s, 3H, C_6-CH_3); 0.86 (d, 3H, J = 7.3 Hz, C_8-CH_3) ppm. ^{13}C-NMR (63 MHz, $CDCl_3$) δ: 195.75 (C-9); 193.98 (C-10); 160.66 (C-2); 151.45 (C-4); 140.89 (C-9a); 131.14 (C-6); 127.87 (C-3); 124.76 (C-7); 118.51 (C-4a); 49.14 (C-10a); 46.26 (C-8a); 32.56 (C-8); 27.41 (C-5); 23.34 (C_6-CH_3); 21.85 (C_4-CH_3); 18.26 (C_8-CH_3) ppm. Analysis calc. for $C_{16}H_{17}NO_3$. $CH_3CO_2C_2H_5$: C, 66.85; H, 6.96; N, 3.89. Found: C, 66.49; H, 6.62; N, 4.20.

4,6,8-Trimethyl-2,9,10(2*H*)-1-azaanthracenetrione (5).

A solution of **4** (75 mg, 0.39 mmol) in xylene (100 ml) was heated at 140 °C for 36 h, with simultaneous bubbling of air and periodical additions of fresh xylene. After evaporation of the solvent and recrystallization from petroleum ether-ethyl ether, a yield of 60 mg (57 %) of **5** was obtained. Melting point, 272-275 °C (AcOEt). IR (KBr): 3180 (NH), 1680, 1650 (C=O) cm^{-1}. ^{1}H-NMR (250 MHz, $CDCl_3$) δ: 9.84 (br. s, 1H, NH); 7.94 (s, 1H, H-5); 7.35 (s, 1H, H-7); 6.63 (s, 1H, H-3); 2.76 (s, 3H, C_8-CH_3); 2.68 (s, 3H, C_6-CH_3); 2.48 (s, 3H, C_4-CH_3) ppm. ^{13}C-NMR (63 MHz, $CDCl_3$) δ: 181.91 (C-10); 178.48 (C-9); 160.81 (C-2); 152.18 (C-4); 146.37 (C-6); 142.78 (C-9a); 140.65 (C-8); 138.09 (C-7); 134.81 (C-8a); 127.02 (C-3); 126.88 (C-5); 125.46 (C-10a); 115.27 (C-4a); 23.00, 22.77 and 22.07 (3 CH_3) ppm. Analysis calc. for $C_{16}H_{13}NO_3$: C, 71.91; H, 4.87; N, 5.24. Found: C, 71.57; H, 4.49; N, 4.90.

4,6-Dimethyl-2,9,10(2*H*)-1-azaanthracenetrione (7a) and 4,7-dimethyl-2,9,10(2*H*)-1-azaanthracenetrione (7b).

Method A. A solution of **1a** (250 mg, 1.32 mmol) and 2-methyl-1,3-butadiene (108 mg, 1.59 mmol) in ethyl acetate (150 ml) was heated in a sealed tube at 120 °C for 24 h. The solution was evaporated and the residue was purified by chromatography on silica gel, eluting with dichloromethane-ethyl acetate (6:4), yielding 189 mg (64 %) of an inseparable mixture of **7a** and **7b** (**7a**:**7b** = 3:1 by ^{1}H-NMR).

Method B. A solution of **1a** (50 mg, 0.26 mmol), 20 mg of 2-methyl-1,3-butadiene (29 mmol) and boron trifluoride-ethyl ether complex (41 mg, 29 mmol of BF_3) in chloroform (125 ml) was heated in a sealed tube at 100 °C for 4 h. The solution was evaporated and the residue was chromatographed on silica gel, eluting with a gradient from net dichloromethane to 1:1 dichloromethane-ethyl acetate, yielding 50 mg (60 %) of an inseparable mixture of compounds **7a** and **7b** (**7a**:**7b** = 1.1:1 by ^{1}H-NMR). Analysis calc. for $C_{15}H_{11}NO_3$: C, 71.15; H, 4.35; N, 5.53. Found: C, 70.90; H, 4.61; N, 5.29.

Data for **7a**: ^{1}H-NMR (250 MHz, $CDCl_3$) δ: 9.55 (br. s, 1H, NH); 8.12 (d, 1H, J = 7.8 Hz, H-8); 7.94 (br. s, 1H, H-5); 7.64 (br. d, 1H, J = 7.8 Hz, H-7); 6.68 (s, 1H, H-3); 2.69 (s, 3H, C_6-CH_3); 2.52 (s, 3H, C_4-CH_3) ppm.

Data for **7b**: ^{1}H-NMR (250 MHz, $CDCl_3$) δ: 9.55 (br. s, 1H, NH); 8.03 (d, 1H, J = 7.7 Hz, H-5); 8.00 (br. s, 1H, H-8); 7.56 (br. d, 1H, J = 7.8 Hz, H-7); 6.68 (s, 1H, H-3); 2.69 (s, 3H, C_6-CH_3); 2.54 (s, 3H, C_4-CH_3) ppm.

4-Methyl-8-methoxy-5,8,8a,10a-tetrahydro-2,9,10(2*H*)-1-azaanthracenetrione (6).

A solution of **1a** (100 mg, 0.53 mmol) and 1-methoxy-1,3-butadiene (48 mg, 0.58 mmol) in chloroform (50 ml) was stirred at room temperature for 16 h. The reaction mixture was evaporated and the residue was washed with chloroform, yielding 103 mg (76 %) of (**6**), as a white solid. An analytical sample was obtained by recrystallization from ethyl acetate. Melting point: decomposes at 185 °C. IR (KBr): 3150 (N-H); 1700, 1655 (C=O), 1085 (C-O) cm^{-1}. ^{1}H-NMR (250 MHz, DMSO-d_6) δ: 11.54 (NH); 6.50 (d, 1H, J = 1.2 Hz, H-3); 5.97 (m, 2H, H-6,7); 3.92 (t, 1H, J = 3.5 Hz, H-8); 3.55 (t, 1H, J = 5.9 Hz, H-8a); 3.35 (m, 1H, H-10a; signal

partially hidden by the water resonance); 2.98 (*s*, 3H, OCH_3); 2.84 (*d*, 1H, *J* = 16.3 Hz, H-5_{eq}); 2.37 (*s*, 3H, C_4-CH_3); 1.99 (dd, 1H, *J* = 16.3 and 5.9 Hz, H-5_{ax}) ppm. ^{1}H-NMR (250 MHz, $CDCl_3$) δ: 9.80 (NH); 6.60 (s, 1H, H-3); 5.98 (m, 2H, H-6,7); 4.00 (t, 1H, *J* = 3.3 Hz, H-8); 3.38 (t, 1H, *J* = 5.9 Hz, H-8a); 3.29 (t, 1H, *J* = 6.4 Hz, H-10a); 3.12 (dd, 1H, *J* = 1.5 Hz, H-5_{eq}; the other coupling was hidden by the methoxyl resonance); 3.07 (s, 3H, OCH_3); 2.51 (s, 3H, C_4-CH_3); 2.10 (dd, 1H, *J* = 19.9 and 6.98 Hz, H-5_{ax}) ppm. ^{13}C-NMR (63 MHz, $CDCl_3$) δ: 193.50 (C-9); 192.63 (C-10); 161.22 (C-2); 151.15 (C-4); 141.35 (C-9a); 130.73 (C-6); 127.13 (C-3); 123.13 (C-7); 121.90 (C-4a); 72.55 (C-8); 56.57 (OCH_3); 50.11 (C-10a); 42.55 (C-8a); 21.95 (C-5); 21.60 (C_4-CH_3) ppm. Analysis calc. for $C_{15}H_{15}NO_4$: C, 65.92 ; H,5.53 ; N,5.12. Found: C, 66.01; H, 5.55; N, 5.46.

4-Methyl-2,9,10 (2*H*)-1-azaanthracenetrione (8).

A solution of **1a** (100 mg, 0.53 mmol) and 1-methoxy-1,3-butadiene (66 mg, 0.79 mmol) in dry chloroform (50 ml), placed in a sealed tube, was heated at 95 °C for 2 h. The solution was evaporated and the residue was recrystallized from methanol, yielding 75 mg (54 %) of compound (**8**). Melting point, > 300 °C. Lit.[10], > 300 °C.

4,8-Dimethyl-5,8,8a,10a-tetrahydro-2,9,10 (2*H*)-1-azaanthracenetrione (9) and 4,8-Dimethyl-5,8-dihydro-2,9,10 (2*H*)-1-azaanthracenetrione (10).

A solution of **1a** (210 mg, 1.1 mmol) and 1,3-pentadiene (80 mg, 1.2 mmol) in ethyl acetate (75 ml) at 100 °C for 14 h, 157 mg (56 %) of a mixture of the tetrahydro derivative (**9**), the dihydro derivative (**10**) and the aromatic compound (**3**) was obtained (**9**:**10**:**3** = 1.4:1.7:1, as shown by ^{1}H-NMR analysis of the mixture), after the same purification described for the synthesis of **3** When the same reaction was performed in dry chloroform (130 ml), placed in a sealed tube at 100 °C for 49 h, 223 mg (79 %) of an inseparable mixture of the dihydro derivative (**10**) and compound (**3**) (**10**:**3** = 1:1.6, as shown by NMR analysis of the mixture) was obtained.

Data for **9** : ^{1}H-NMR (250 MHz, $CDCl_3$) δ: 6.62 (d, 1H, *J* = 1.0 Hz, H-3); 5.71 (m, 2H, H-6,7); 3.52 (m, 2H, H-8a, 10a); 2.54 (d, 3H, *J* = 1.0 Hz, C_4-CH_3); 2.80 (m, 1H, H-5_{eq}); 2.70 (m, 1H, H-8); 2.20 (dd, 1H, *J* = 18.7 and 7.8 Hz, H-5_{ax}) ; 0.93 (d, 3H, *J* = 7.3 Hz, C_8-CH_3) ppm.

Data for **10**: ^{1}H-NMR (250 MHz, $CDCl_3$) δ: 10.32 (br. s, 1H, NH); 6.63 (s, 1H, H-3); 5.80 (m, 2H, H-6 and H-7); 3.51 (m, 1H, H-8); 3.23 (m, 1H, H-5_{ax}); 3.09 (m, 1H, H-5_{eq}); 2.59 (s, 3H, C_4-CH_3); 1.23 (d, 3H, *J* = 8.3 Hz, C_8-CH_3) ppm.

N-Methyl-2,5-dimethoxyaniline (11).

A suspension of 2,5-dimethoxyaniline (10 g, 65 mmol) in dry isopropyl ether (200 ml) was heated at 60 °C until complete dissolution. Formic acid (11.5 g, 0.25 mol) was added and the solution was heated at 80 °C for 90 min. Evaporation of the reaction mixture left a residue that was purified by column chromatography on silica gel, eluting with dichloromethane-ethyl acetate (8:2) to yield 11.04 g (94 %) of N-(2,5-dimethoxyphenyl)formamide, Melting point, 78 °C (petroleum ether-ethyl ether), lit.[13], 78 °C. A solution of this amide (2 g, 11 mmol) in dry ethyl ether (50 ml) was added dropwise to a cooled (0 °C) suspension of lithium aluminium hydride (2.1 g, 55 mmol) in dry ethyl ether (100 ml). The reaction mixture was stirred 4 h at room temperature and then worked up by addition of ethyl acetate (10 ml), wet ethyl ether (5 ml), water (0.5 ml) and solid sodium bicarbonate (30 g). The solid was filtered and washed with ether (3 x 100 ml). The combined organic phases were evaporated and the residue was chromatographed on silica gel, eluting with ethyl ether-petroleum ether (1:1), yielding 1.62 g (88 %) of (**1**). bp 40 °C (0.01 torr), lit.[14], 70 °C (0.00018 torr). IR (KBr): 3420 (N-H), 1220 (O-CH_3) cm^{-1}. ^{1}H-NMR (250 MHz, $CDCl_3$) δ: 6.65 (d, 1H, *J* = 8.5 Hz, H-3); 6.20

(d, 1H, J = 2.9 Hz); 6.14 (dd, 1H, J = 8.5 and 2.9 Hz, H-4); 3.79 and 3.72 (2 s, 6H, 2 OCH_3); 2.83 (s, 3H, N-CH_3); 1.82 (s, 1H, NH) ppm.

N-(2',5'-Dimethoxyphenyl)-3-oxobutanamide (12).

2,2,6-Trimethyl-1,3-dioxin-4-one (1.96 g, 13.7 mmol) was added to a magnetically stirred solution of aniline (**11**) (2.3 g, 13.7 mmol) in xylene (10 ml) heated at 120 °C, and stirring at this temperature was maintained for 90 min. The solution was evaporated and the residue was recrystallized from petroleum ether, yielding 2.73 g (79 %) of (**12**). Melting point, 69 °C (petroleum ether). lit.[11], 69 °C. IR (KBr): 1725 (C_3=O), 1660 (C_1=O) cm^{-1}. ^{1}H-NMR (300 MHz, $CDCl_3$) δ: 6.88 (m, 2H, H-3 and H-6); 6.75 (m, 1H, H-4); 3.78 and 3.76 (2 s, 3H, 2 OCH_3); 3.21 (s, 5H, N-CH_3 and H-2); 2.18 (s, 3H, H-4) ppm. ^{13}C-NMR (75 MHz, $CDCl_3$) δ: 202.54 (C-3); 167.47 (C-1); 153.68 (C-5'); 148.84 (C-2'); 132.09 (C-1'); 114.73 (C-6'); 114.39 (C-3'); 112.61 (C-4'); 56.13 (C-2); 55.77 and 55.72 (2 OCH_3); 49.71 (N-CH_3); 36.12 (C-4) ppm.

1,4-Dimethyl-5,8-dimethoxy-2(1*H*)quinolinone (13).

A solution of the acetoacetamide (**12**) (2.73 g, 10.8 mmol) in 96 % sulfuric acid (13.6 ml) was stirred at room temperature for 30 min. The reaction mixture was poured on ice (5 g) and basified with 22 % aqueous ammonia (34 ml). The aqueous solution was extracted with chloroform (3 x 50 ml), which was dried (sodium sulfate) and evaporated. The residue was chromatographed on silica gel, eluting with petroleum ether-ethyl ether (3:1), affording 2.04 g (80 %) of (**13**). Melting point, 122 °C, lit.[11], 122.5-123.5 °C. IR (KBr): 1650 (C=O) cm^{-1}. ^{1}H-NMR (300 MHz, $CDCl_3$) δ: 7.02 (d, 1H, J = 9.0 Hz, H-7); 6.62 (d, 1H, J = 9.0 Hz, H-6); 6.45 (s, 1H, H-3); 3.84 and 3.83 (2 s, 6H, 2 OCH_3); 3.81 (s, 3H, N-CH_3); 2.59 (s, 3H, C_4-CH_3) ppm. ^{13}C-NMR (75 MHz, $CDCl_3$) δ: 163.34 (C-2); 152.89 (C-5); 147.46 (C-8); 143.08 (C-4); 133.86 (C-8a); 121.86 (C-3); 115.36 (C-7); 114.50 (C-4a); 104.03 (C-6); 55.75 and 55.71 (2 OCH_3); 36.07 (N-CH_3); 25.14 (C_4-CH_3) ppm.

5,8-Dihydroxy-1,4-dimethyl-2(1*H*)quinolinone (14).

A suspension of the carbostyril (**13**) (2.0 g, 8.58 mmol) in 48 % hydrobromic acid (23 ml) was heated at 145 °C for 48 h, while magnetically stirred. The solution was poured on water (15 ml) and cooled. The precipitate was filtered, yielding 1.73 g (99 %) of pure (**14**). An analytical sample was obtained by column chromatography on silica gel, eluting with ethyl ether-petroleum ether (2:1). Melting point, 276-278 °C. IR (KBr): 3240 (O-H), 1630 (C=O) cm^{-1}. ^{1}H-NMR (300 MHz, DMSO-d_6) δ: 9.50 (br. s, 1H, NH); 6.85 (d, 1H, J = 8.6 Hz, H-7); 6.51 (d, 1H, J = 8.6 Hz, H-6); 6.22 (s, 1H, H-3); 5.12 (br. s, 2H, 2 OH); 3.71 (s, 3H, N-CH_3); 2.55 (s, 3H, C_4-CH_3) ppm. ^{13}C-NMR (63 MHz, DMSO-d_6) δ: 162.19 (C-2); 149.45 (C-5); 147.83 (C-4); 138.49 (C-8); 131.31 (C-8a); 120.02 (C-3); 118.69 (C-7); 112.56 (C-6); 109.06 (C-4a); 35.33 (N-CH_3); 24.85 (C_4-CH_3) ppm. Analysis calc. for $C_{11}H_{11}NO_3$: C, 64.38; H, 5.40; N, 6.82. Found: C, 64.10; H, 5.20; N, 6.61.

1,4-Dimethyl-2,5,8(1*H*)quinolinetrione (1b).

A solution of potassium dichromate (1.07 g, 3.64 mmol) in water (15 ml) was added to a solution of the hydroquinone (**14**) (700 mg, 3.41 mmol) in water (20 ml) and 96 % aqueous sulfuric acid (2.5 ml) placed in an ice bath. The mixture was stirred at 0 °C for 10 min and extracted with chloroform (3 x 15 ml). The organic layer was dried over sodium sulfate and evaporated, and the residue was purified by rapid chromatography on silica gel, eluting with ethyl ether-petroleum ether (2:1), yielding 510 mg (74 %) of quinone (**1b**). Melting point, 107-109 °C. IR (KBr): 1660 (C=O) cm^{-1}. ^{1}H-NMR (300 MHz, $CDCl_3$) δ: 6.79 (d, 1H, J = 7.5 Hz, H-7); 6.73 (d, 1H, J = 7.5 Hz, H-6); 6.65 (s, 1H, H-3); 3.83 (s, 3H, N-CH_3); 2.55 (s, 3H, C_4-CH_3) ppm. ^{13}C-NMR (63 MHz, DMSO-d_6) δ: 184.36 (C-8); 182.30 (C-5); 161.77 (C-2); 149.22 (C-4); 141.68 (C-8a); 137.43 (C-6);

135.43 (C-7); 125.86 (C-3); 117.27 (C-4a); 34.12 (N-CH_3); 22.73 (C_4-CH_3) ppm. Analysis calc. for $C_{11}H_9NO_3$: C, 65.02; H, 4.43; N, 6.89. Found: C, 64.84; H, 4.46; N, 6.85.

1,4- Dimethyl- 8- trimethylsilyloxy -5,8,8a,10a-tetrahydro-2,9,10(2*H*)-1-azaanthracenetrione (15).

A solution of **1b** (100 mg, 0.49 mmol) and 1-trimethylsilyloxy-1,3-butadiene (270 mg, 1.33 mmol) in dry chloroform (50 ml), placed in a sealed tube, was heated at 100 °C for 2 h. The reaction mixture was evaporated and the residue was recrystallized from petroleum ether, yielding 98 mg (58 %) of compound (**15**). Melting point, 75-78 °C (AcOEt). IR (KBr): 1680 (C=O) cm^{-1}. ^{1}H-NMR (300 MHz, $CDCl_3$) δ: 6.62 (s, 1H, H-3); 5.78 (m, 2H, H-6,7); 4.46 (br. s, 1H, H-8); 3.79 (s, 3H, N-CH_3); 3.30 (m, 2H, H-8a,10a); 3.05 (dd, 1H, J = 18.6 and 3.5 Hz, H-5_{eq}); 2.50 (s, 3H, C_4-CH_3); 2.10 (dd, 1H, J = 18.6 and 6.7 Hz, H-5_{ax}) ppm. ^{13}C-NMR (63 MHz, $CDCl_3$) δ: 194.79 (C-9); 193.61 (C-10); 161.80 (C-2); 148.64 (C-5); 145.49 (C-9a); 128.61 (C-6); 126.42 (C-3); 125.10 (C-7); 123.02 (C-4a); 64.89 (C-8); 53.22 (C-10a); 42.56 (C-8a); 22.05 (C-5); 22.00 (C_4-CH_3); -0.38 ($Si(CH_3)_3$) ppm. Analysis calc. for $C_{18}H_{23}NO_4Si$: C, 62.60; H, 6.66; N, 4.05. Found: C, 62.64; H, 6.36; N, 3.97.

1,4-Dimethyl-2,9,10(2*H*)-1-azaanthracenetrione (16).

A solution of **1b** (100 mg, 0.49 mmol) and 1-trimethylsilyloxy-1,3-butadiene (105 mg, 0.73 mmol) in dry chloroform (10 ml), placed in a sealed tube, was heated at 100 °C for 24 h. The reaction mixture was recrystallized from petroleum ether, yielding 100 mg (81 %) of compound (**15**). Melting point, 184-187 °C (petroleum ether). IR (KBr): 1675, 1670 cm^{-1}. ^{1}H-NMR (250 MHz, $CDCl_3$) δ: 8.07 (m, 2H, H-5,8); 7.76 (m, 2H, H-6,7); 3.88 (s, 3H, N-CH_3); 2.55 (s, 3H, C_4-CH_3) ppm. ^{13}C-NMR (63 MHz, $CDCl_3$) δ: 182.19 (C-9); 180.98 (C-10); 161.99 (C-2); 149.83 (C-4); 144.25 (C-9a); 134.63 (C-6); 133.62 (C-7); 132.12 (C-10a); 132.08 (C-10a); 126.55 (C-3); 126.37 (C-5); 126.07 (C-8); 119.03 (C-4a); 34.81 (N-CH_3); 23.34 (C_4-CH_3) ppm. Analysis calc. for $C_{15}H_{11}NO_3$: C, 71.15; H, 4.35; N, 5.53. Found: C, 68.93; H, 4.52; N, 5.14.

6-Hydroxy-1,4-dimethyl-2,9,10(2*H*)-1-azaanthracenetrione (17).

A solution of **1b** (100 mg, 0.49 mmol) and 1-methoxy-3-trimethylsilyloxy-1,3-butadiene (127 mg, 0.74 mmol) in dry chloroform (50 ml), placed in a sealed tube, was heated at 100 °C for 18 h. The solution was evaporated and the residue was chromatographed on silica gel, eluting with dichloromethane-ethyl acetate (1:1), to yield 95 mg (62 %) of compound (**17**). Melting point > 300 °C. IR (KBr): 3460 (O-H), 1660 (C=O) cm^{-1}. ^{1}H-NMR (300 MHz, pyridine-d_5) δ: 12.50 (br. s, 1H, OH); 8.21 (d, 1H, J = 8.4 Hz, H-8); 7.90 (d, 1H, J = 2.1 Hz, H-5); 7.45 (dd, 1H. J = 8.4 and 2.1 Hz, H-7); 6.80 (s, 1H, H-3); 4.09 (s, 1H, N-CH_3); 2.67 (s, 3H, C_4-CH_3) ppm.

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