Synthesis of 3-Substituted 2-Hydroxybenz[*f*]indolequinones and Benz[*f*]isatinquinone - A New π-Acceptor System

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Starting from 2,3-dichloro-1,4-naphthaquinone a series of 2-hydroxy-1-methylbenz[*f*]indolequinones bearing benzyl-, amino- and hydroxy substituents in position 3, and benz[*f*]isatinquinone have been synthesised and their reactions have been studied.

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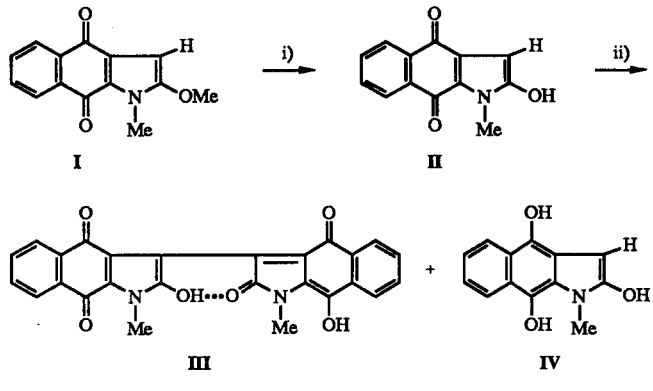
In the previous communication [1] we have reported the synthesis of unstable biradicaloid [2] 1-methyl-2-hydroxybenz[*f*]indole-4,7-quinone (**II**) by demethylation of corresponding 2-methoxy derivative **I**. Oxindolequinone **II** spontaneously dimerizes and disproportionates to yield 3,3'-dimer **III** and 1-methyl-2,4,9-trihydroxybenz[*f*]indole (**IV**) (Chart 1). According to the scheme reported in [1] the absence of a substitutent in 3-position of the hydroxypyrrole ring was hold responsible for dimerisation. It was therefore intriguing to obtain -3-substituted 2-hydroxybenz[*f*]indolequinones in order to study their ability for spontaneous dimersiation. Another goal was to prepare a new polycarbonyl π-acceptor system -benz[*f*]isatinquinone starting from 2-hydroxybenzindolequinone with an easily oxidizeable 3-substituent.

Chart 1

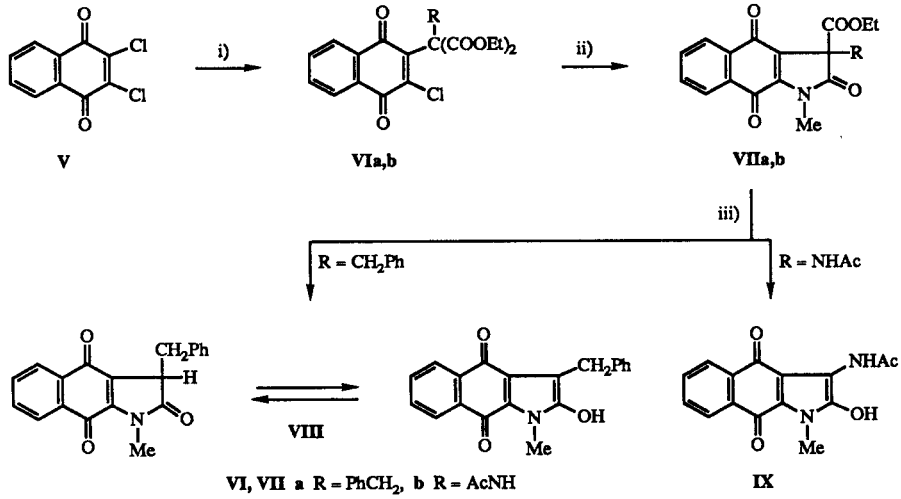


i) BBr_3/CH_2Cl_2, -80°; ii) spontaneously

Sodium salts of diethyl benzylmalonate and diethyl acetamidomalonate, obtained from corresponding esters by treatment with sodium hydride in tetrahydrofuran, react with 2,3-dichloro-1,4-naphthaquinone (**V**) to give 2-substituted-3-chloro-1,4-naphthaquinones **VIa,b**, which cyclize to lactams **VIIa,b** upon treatment with 2 mole of methylamine. Treated with potassium hydroxide or excess of methylamine these lactams eliminate carbethoxy groups to form 3-substituted 2-hydroxybenz[*f*]indolequinones **VIII,IX** (Chart 2).

A keto form and two enol tautomeric forms (2- and 9-hydroxy) are possible for compounds **VIII** and **IX** (Chart 3). 3-Benzyloxindolequinone **VIII** in chloroform solution exists exclusively in the keto form, as can be confirmed by its pmr spectrum, where the 3-proton of the pyrrole ring ap-

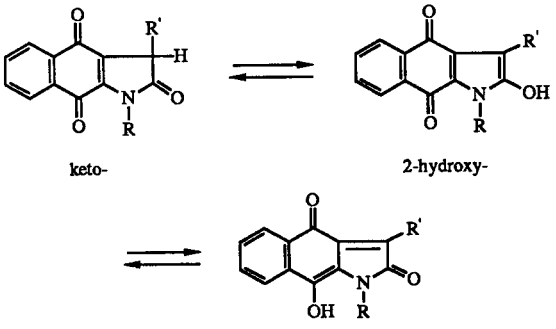
Chart 2



i) $PhCH_2CH(COOEt)_2$ or $AcNHCH(COOEt)_2$ + NaH in THF; ii) 2 moles $MeNH_2$ in EtOH; iii) excess $MeNH_2$ in EtOH or KOH then HCl

pears as doublet of doublets at 3.916 ppm, the splitting being due to the interaction with diastereotopic α-methylene protons of benzyl substituent ($J_{3,\alpha}$ = 4.24 Hz, $J_{3,\alpha'}$ = 5.47 Hz) together with the signals of these α-methylene protons at 3.503 and 3.599 ppm. Each of these signals appears also as doublet of doublets ($J_{\alpha,\alpha'}$ = 13.3 Hz, $J_{3,\alpha}$ = 4.24 Hz, $J_{3,\alpha'}$ = 5.47 Hz). The presence of lactam carbonyl group is confirmed by the presence of lactam carbonyl band at 1730 cm^{-1} in ir spectrum of compound **VIII** in chloroform solution. The absorption spectrum of **VIII** in chloroform is similar to the spectrum of carbethoxy lactam **VIIa** fixed in the keto form. In dimethyl sulfoxide ketone **VIII** enolizes completely: there is no signal of the 3-proton, and the signals of benzylic methylene protons coalesce into a singlet at 4.11 ppm. The absorption spectra of quinone **VIII** in dimethyl sulfoxide or ethanol are similar to the spectrum of enol ether **I**.

Chart 3



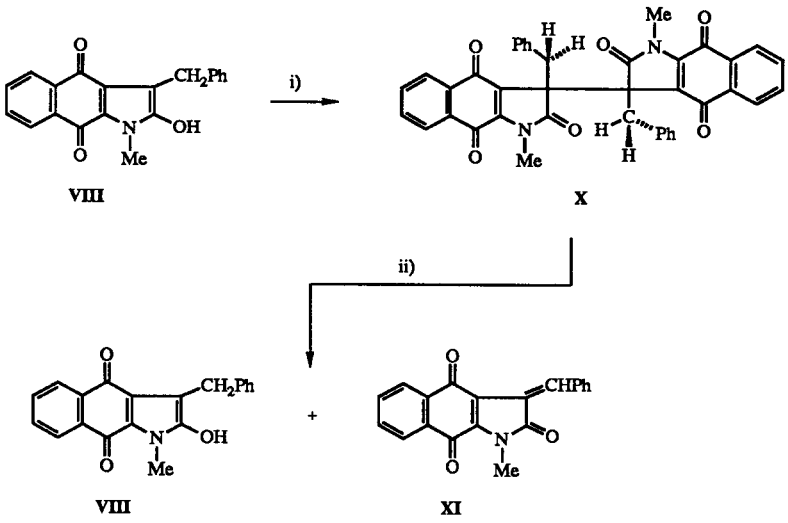
Contrary to unsubstituted 2-hydroxybenz[*f*]indolequinone **II**, 3-benzyl-2-hydroxybenz[**f**]indolequinone **VIII** does not undergo spontaneous disproportionation with dimerisation, but upon oxidation with 1 mole of potassium ferricyanide at *p*H 13 forms a mixture of diastereomeric 3,3'-dimers (**X**, *dl* + *meso*) in more than 80% yield (Chart 4). The nmr spectrum of **X** is consistent with the proposed structure; there are signals of two *N*-methyl groups (from *dl* and *meso*-form), two pairs of diastereotopic α-benzyl protons (δ = 3.764 and 4.390 ppm, J = 13 Hz, δ = 4.105 and 4.174 ppm, J = 13 Hz). According to the pmr data the ratio of **X** diastereomers is about 1.4:1. The absorption spectrum of dimer **X** is almost identical with the spectrum of the keto form **VIII**.

The dimer **X** structure is confirmed by the results of thermal degradation (toluene, reflux), which gives a mixture of 1 mole of 3-benzylidene-1-methyl-2,4,9-trioxobenz-[*f*]indole **XI**, and of 1 mole of 3-benzyl-1-methyl-2-hydroxybenz[*f*]indolequinone **VIII**. The spectral data of quinone **XI** are consistent with the proposed structure.

Spontaneous dimerisation of the unsubstituted 2-hydroxybenzindolequinone **II** in the presence of the 3-benzyl derivative **VIII** as a possible radical intermediate acceptor, does not yield a mixed dimer, but dimer **III** only. The recovery of **VIII** is quantitative.

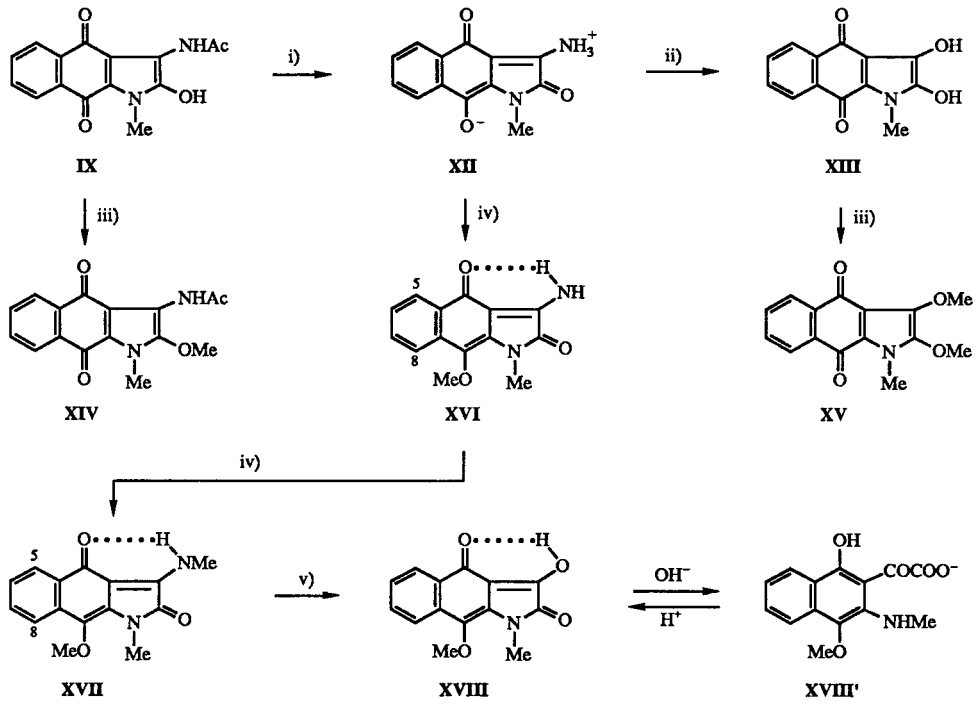
The study of 3-acetamidoquinone **IX** shows that contrary to quinones **II** and **VIII** it exists exclusively in the form of the 2-hydroxy-tautomer. There is pronounced difference between the absorption spectrum of **IX** and the oxindolequinone **VIII** spectrum in chloroform on one hand, and its similarity to the spectrum of the latter in ethanol - on the other. Contrary to the spectra of compounds **II** and **VIII**, the form and location of compound **IX** of the absorption bands are not affected by the nature of the solvent (chloroform, DMSO, ethanol). To assume that **IX** exists in the 9-hydroxy form is inconsistent with the absence of the characteristic lactam carbonyl group band at 1700-1758 cm^{-1} [3] in the ir spectrum of **IX**. Similar to other 2-hydroxybenzindolequinones, compound **IX** readily dissolves in alkaline solutions to give a navy

Chart 4



i) $K_3Fe(CN)_6$ + KOH; ii) PhMe, reflux

Chart 5



IX XII XIII XIV XVI XV XVII XVIII XVIII'

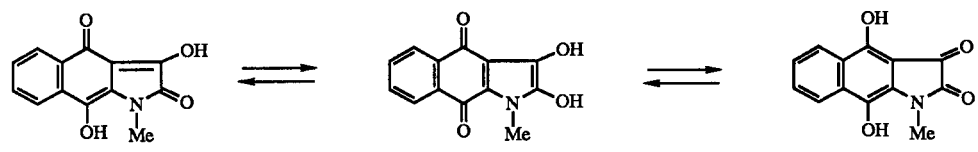
i) 2% HCl in MeOH, reflux; ii) 15% HCl in EtOH, reflux; iii) CH_2N_2 in ether; iv) MeI/K_2CO_3 in acetone; v) HBr in AcOH

blue anion and is regenerated on acidification. (In our previous work [4] the pK_a of the 2-hydroxy group in benz[*f*]indolequinones was found to be about 3.5). The molecular mass determination by means of mass spectrometry confirms the monomeric structure of quinone **IX**. The first fragmentation step according to the mass spectrum is the characteristic loss of ketene for arylacetamides. Oxidation of acetamidoquinone **IX** with potassium ferricyanide gives an unseparable mixture of water-soluble products.

Quinone **IX** desacetylates under mild conditions (2% hydrochloric acid in methanol) to form aminoquinone **XII** (Chart 5). Since there are three bands in the visible part of the absorption spectrum of **XII**, it is likely to exist as a mixture of tautomers. Because of its poor solubility in common solvents we failed to determine which of the tautomers prevails. Aminoquinone **XII** is depicted as a 3-ammonio-9-olate because of a) the presence of a strong wide band of the NH_3^+-group oscillations (ν = 2500 - 3300 cm^{-1}) in its ir spectrum, b) high acidity of the enol group in indolequinones, as was mentioned above, and c) formation of the 9-methoxy derivative as a sole methylation product (s.u.).

Hydrolysis of acetamidoquinone **IX** or betaine **XII** under more drastic conditions (15% of hydrochloric acid in 70% ethanol, reflux) yields dioxindolequinone **XIII**, for which three tautomeric hydroxy forms **XIIIa-c** are possible (Charts 5,6). In order to fix the tautomeric forms of compounds **IX** and **XIII** they were subjected to methylation with diazomethane to form only 4,7-indolequinone derivatives **XIV** and **XV** respectively in a 100% yield. All the spectral data for compounds **XIV** and **XV** unambiguously confirm their structure. Betaine **XII** is methylated in a different way: when treated with 1 mole of methyl iodide in the presence of potassium carbonate in acetone, it quickly yields the 9-methoxy derivative **XVI**. Methylation of **XII** with excess of the reagent or methylation of **XVI** under the same conditions gives only the 3-aminomethyl-9-methoxy derivative **XVII**. No 3-dimethylamino compound was detected, possibly because of a strong intramolecular hydrogen bond between the 3-amino group and the 4-carbonyl group in the molecule of **XVII**. The nmr spectra of **XVI** and **XVII** confirm, that methylation

Chart 6



XIIIa XIIIb XIIIc

occurs in the 9-position: the symmetry of molecules in their quinoid ring site is distorted. The difference in chemical shifts between the 5- and 8-protons reaches 0.5-0.6 ppm, while for quinones **I, VIII, IX** it does not exceed 0.1 ppm. Further evidence of 9-substitution is the presence of a lactam carbonyl band in the ir spectra of **XVI** and **XVII**. When **XVII** is treated with hydrobromic acid, no *O*-demethylation occurs; instead the exocyclic C-N bond undergoes hydrolytic cleavage to form the 3-hydroxy-9-methoxy derivative **XVIII**. Its nmr spectrum also develops the lack of symmetry of the quinoid site. Compound **XVIII** readily dissolves in alkaline solution, giving *yellow* isatoic acid salts **XVIII'**, this fact being additional evidence of the 2(9)-hydroxy group blocking, because all 2-hydroxybenzindolequinones give *blue* salts. Upon acidification **XVIII** is fully recovered.

It was interesting to oxidize dioxindolequinone **XIII** to the corresponding isatinquinone. Nitrous acid in acetic acid media proved to be the most appropriate oxidizer. The reaction products were isatin quinone (**XIX**) together with α-ketocarbonic acid (**XX**) - the product of isatin ring hydrolytic cleavage (Chart 7). The ir spectrum of isatinquinone **XIX** contains quinone carbonyl absorption bands together with two carbonyl bands at 1732 and 1763 cm^{-1}, corresponding to the 2- and 3-carbonyl groups of isatin [3]. The characteristic feature of the isatinquinone **XIX** mass spectrum is the presence of four very intensive peaks at M-28, M-56, M-84 and M-112, corresponding to 1, 2, 3 and (possibly) 4 carbonyl group extrusions. Solutions of isatinquinone in anhydrous solvents are stable, but in the presence of traces of water rapid hydrolysis takes

Table 1

Absorption Spectra of Compounds I-XX

Compound	(Solvent)	λ max. (log ε), nM
I	(EtOH)	236 (4.07), 274 (4.48), 334 (3.75), 454 (3.61)
II	(EtOH)	240 (4.14), 278 (4.51), 330 (3.60), 480 (3.52)
VIa	(EtOH)	250 (4.14), 256 (4.17), 277 (4.07), 340 (3.46)
VIb	(MeCN)	249 (4.11), 255 (4.12), 271 (3.95), 339 (3.41)
VIIa	(EtOH)	260 (4.32), 305 (3.91), 343 (sh, 3.46), 430 (3.18)
VIIb	(MeCN)	260 (4.33), 304 (3.94), 341 (sh, 3.48), 436 (3.31)
VIII	(EtOH)	244 (415), 285 (4.38), 345 (3.62), 4.90 (3.57)
VIII	($CHCl_3$)	266 (4.19), 290 (sh, 4.03), 340 (sh, 3.58), 460 (3.49)
IX	(MeCN)	247 (4.29), 283 (4.23), 344 (sh, 3.53), 514 (3.61)
X	(MeCN)	259 (4.27), 299 (3.90), 338 (sh, 3.51), 439 (3.24)
XI	(MeCN)	272 (4.36), 350 (4.37), 505 (3.80)
XII	(EtOH)	248 (4.35), 280 (4.23), 392 (3.65), 400 (3.63), 410 (3.64), 495 (3.89)
XIII	(EtOH)	243 (4.56), 298 (3.81), 360 (3.38), 503 (3.27)
XIV	(MeCN)	242 (4.22), 276 (4.40), 337 (3.59), 455 (3.59)
XV	(MeCN)	242 (4.31), 278 (4.41), 340 (3.57), 463 (3.64)
XVI	(EtOH)	246 (4.36), 275 (4.35), 417 (3.80), 4.72 (3.95)
XVII	(EtOH)	249 (4.38), 280 (4.35), 443 (3.87), 490 (4.04)
XVIII	(EtOH)	242 (4.61), 289 (4.24), 357 (3.70), 474 (3.55)
XIX	(MeCN)	239 (4.40), 298 (3.81), 360 (3.38), 503 (3.27)
XX	(EtOH)	237 (4.32), 293 (4.19), 420 (3.56)

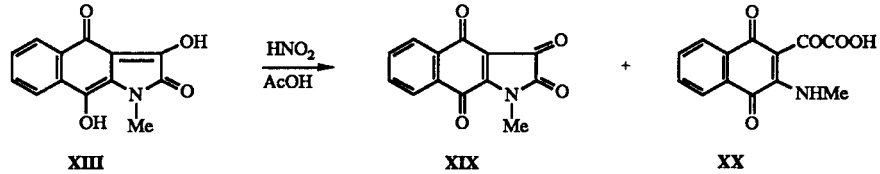
Table 2

Analytical Data of Compounds VI-XX

Compound Number	Mol Formula (Mol Weight)	Analysis, % Calcd./(Found) C	H	N	Mass Spectrum M^+, m/e
VIa	$C_{24}H_{21}ClO_6$ (440.86)	65.38 (65.25)	4.80 (4.91)	– –	[a]
VIb	$C_{19}H_{18}ClNO_7$ (407.79)	55.96 (55.85)	4.45 (4.21)	3.44 (3.52)	[a]
VIIa	$C_{23}H_{19}NO_5$ (389.39)	70.94 (70.82)	4.92 (4.71)	3.60 (3.55)	[a]
VIIb	$C_{18}H_{16}N_2O_6$ (356.33)	60.67 (60.62)	4.53 (4.70)	7.86 (7.69)	[a]
VIII	$C_{20}H_{15}NO_3$ (317.33)	75.70 (75.68)	4.76 (4.71)	4.41 (4.11)	317
IX	$C_{15}H_{12}N_2O_4$ (284.26)	63.38 (63.22)	4.26 (4.11)	9.86 (9.80)	284
X	$C_{40}H_{28}N_2O_6$ (632.63)	75.94 (76.15)	4.46 (4.25)	4.43 (4.11)	[b]
XI	$C_{20}H_{13}NO_3$ (315.31)	76.18 (76.01)	4.15 (4.10)	4.44 (4.51)	315
XII	$C_{13}H_{10}N_2O_3$ (242.23)	64.46 (64.29)	4.16 (4.34)	11.57 (11.43)	242
XIII	$C_{13}H_9NO_4$ (243.21)	64.20 (64.43)	3.73 (3.70)	5.76 (5.66)	243
XIV	$C_{16}H_{14}N_2O_4$ (298.29)	64.42 (64.33)	4.73 (4.61)	9.39 (9.30)	298
XV	$C_{15}H_{13}NO_4$ (271.26)	66.41 (66.50)	4.83 (4.71)	5.16 (5.02)	271
XVI	$C_{14}H_{12}N_2O_3$ (256.25)	65.61 (65.48)	4.72 (4.60)	10.93 (10.82)	256
XVII	$C_{15}H_{14}N_2O_3$ (270.27)	66.66 (66.60)	5.23 (5.11)	10.37 (10.22)	270
XVIII	$C_{14}H_{11}NO_4$ (257.25)	65.36 (65.06)	4.31 (4.44)	5.45 (5.25)	257
XIX	$C_{13}H_7NO_4$ (241.24)	64.73 (64.55)	2.93 (3.02)	5.81 (5.59)	241
XX	$C_{13}H_9NO_5$ (259.26)	60.22 (60.34)	3.50 (3.55)	5.40 (5.51)	259

[a] Not measured. [b] Rapid decomposition in the ion source of mass spectrometer; only the superposition of mass spectra of compounds VIII and XI has been obtained (see text).

Chart 7



XIII XIX XX

place. Lactamisation of acid **XX** is achieved by action of acetic anhydride or even (partly) by crystallisation from anhydrous ethyl acetate.

Studies of isatinquinone as a starting material for various heterocyclisations are now in progress.

EXPERIMENTAL

Melting points were determined on a Kofler hot stage apparatus and are uncorrected. The ir spectra were recorded on a Specord M80 spectrophotometer in potassium bromide disks or in chloroform solutions; wavenumbers are given in cm^{-1}. Absorption spectra were taken on a Specord M40 spectrophotometer. Proton nmr spectra were run in deuteriochloroform (if no other solvent mentioned) with Jeol FX-90Q (90 MHz) and Bruker WM 250 (250 MHz) spectrometers, chemical shifts are given in ppm downfield to TMS. Mass spectra were obtained with Varian MAT 311A mass spectrometer. Analytical tlc's were done on aluminium foil precoated with silica gel (Silufol, developing with benzene or benzene-ethyl acetate 1:1). Microanalyses were performed with a Perkin-Elmer 240 C instrument.

3-Chloro-2-(2-phenyl-1,1-bis(carbethoxy))-1,4-naphthoquinone (**VIa**).

Diethyl benzylmalonate (12.5 g, 50 mmoles) was added to the stirred suspension of sodium hydride (1.2 g, 50 mmoles) in 250 ml of dry THF and the mixture was stirred until the evolution of hydrogen ceased (about 2 hours). Then 2,3-dichloro-1,4-naphthoquinone **V** (6.81 g, 30 mmoles) was added, and the stirring was continued until tlc showed the absence of **V** (about 4 hours). The reaction mixture was acidified with hydrochloric acid. The precipitated sodium chloride was removed by filtration, and the filtrate was evaporated *in vacuo*. Crystallisation of the residue from methanol gave 9.93 g (75%) of **VIa**, light-yellow crystals with mp 121-122°; ir (potassium bromide): 1672, 1692 (quinone CO), 1745 (COOEt); ^{1}H nmr: 1.21 (6H, t, C-CH_3), 3.72 (2H, s, C-CH_2-C), 4.05 (4H, q, O-CH_2-C), 6.81-7.23 (5H, m, C_6H_5), 7.45-8.00 (4H, m, C_6H_4.

3-Chloro-2-(acetamidobis(carbethoxy)methyl)-1,4-naphthoquinone (**VIb**).

Quinone **VIb** was obtained in a similar way from diethyl acetamidomalonate (50 mmoles), sodium hydride (50 mmoles) and dichloronaphthoquinone (30 mmoles), yield 8.9 g (73%), light-yellow crystals with mp 137-139° (methanol); ir (potassium bromide): 1660, 1677, 1685 (quinone CO), 1735, 1770 (COOEt), 3350 (NH).

3-Benzyl-3-carbethoxy-1-methyl-2,3,4,9-tetrahydro-2,4,9-trioxo-1*H*-benz[*f*]indole (**VIIa**).

A methanolic solution of methylamine (0.78 g, 25 mmoles) was added dropwise to the stirred suspension of naphthoquinone **VIa** (4.6 g, 11 mmoles) in 100 ml of methanol with cooling to 0°. After stirring for 30 minutes at this temperature the reaction mixture was evaporated *in vacuo* to dryness, the residue was dissolved in chloroform and filtered through aluminium oxide. The filtrate was evaporated to a minimal volume and diluted with hexane. Quinone **VIIa** precipitated as yellow needles, yield 2.61 g (61%), mp 107-109°; ir (potassium bromide): 1662, 1685 (quinone CO), 1732 (lactam CO), 1775 (COOEt); ^{1}H nmr: 1.1 (3H, t, C-CH_3), 3.15 (3H, s, N-CH_3), 3.58 (2H, s, C-CH_2-C), 4.10 (2H, q, O-CH_2), 6.85 (5H, m, C_6H_5), 7.79-8.08 (4H, m, C_6H_4).

3-Acetamido-3-carbethoxy-1-methyl-2,3,4,9-tetrahydro-2,4,9-trioxo-1*H*-benz[*f*]indole (**VIIb**).

Indolequinone **VIIb** was obtained in the same manner as quinone **VIIa** using compound **VIb** as a starting material, yield 80%, yellow crystals with mp 208-211° (methanol); ir (potassium bromide): 1650, 1675 (quinone CO), 1750 (lactam CO), 1760 (COOEt); ^{1}H nmr: 1.19 (3H, s, C-CH_3), 2.05 (3H, s, CH_3-CO), 3.61 (3H, s, N-CH_3), 4.26 (2H, q, CH_3-CH_2), 7.21 (1H, br s, N-H), 7.72 (1H, td, J = 7.5, 1.33 Hz, 6- or 7-H), 7.76 (1H, td, J = 7.5, 1.33 Hz, 7- or 6-H), 8.03 (1H, dd, J = 7.5, 1.33 Hz, 5- or 8-H), 8.11 (1H, dd, J = 7.5, 1.33 Hz, 8- or 5-H).

3-Benzyl-1-methyl-2-hydroxy-4,9-dihydro-4,9-dioxo-1*H*-benz[*f*]indole (**VIII**).

The solution of sodium hydroxyde (2 g, 50 mmoles) was added to the boiling solution of quinone ester **VIIa** (3.9 g, 10 mmoles) in 50 ml of methanol, and the blue solution was refluxed for 10 minutes. After cooling to room temperature the solution of the enolate was acidified with concentrated hydrochloric acid and the precipitate of oxindolequinone **VIII** was collected by filtration, washed with acidified water and oven dried. The yield after recrystallisation from chloroform-methanol mixture was about 2.6 g (81%), dark red crystals with mp 162-165°; ir (potassium bromide): 1650, 1670 (quinone CO), 3430 (OH); ir (chloroform): 1644, 1678 (quinone CO), 1730 (lactam CO); ^{1}H nmr (in DMSO-d_6): 3.76 (3H, s, N-CH_3), 4.12 (2H, s, C-CH_2-Ph), 7.20 (5H, m, C_6H_5), 7.63 (2H, m, 6 and 7-H), 7.87 (2H, m, 5 and 8-H); ^{1}H nmr (deuteriochloroform): 3.328 (3H, s, N-CH_3), 3.503 (1H, dd, α-H, J = 13.3, 4.24 Hz), 3.599 (1H, dd, α'-H, J = 13.3, 5.47 Hz), 3.916 (1H, dd, 3-H, J = 4.24, 5.47 Hz), 7.000-7.107 (5H, m, C_6H_5), 7.690 (1H, td, J = 7.5, 1.43 Hz, 6- or 7-H), 7.773 (1H, td, J = 7.5, 1.43 Hz, 7- or 6-H), 8.001 (1H, dd, J = 7.5, 1.43 Hz, 5- or 8-H), 8.136 (1H, dd, J = 7.5, 1.43 Hz, 8- or 5-H).

3-Acetamido-2-hydroxy-1-methyl-4,9-dihydro-4,9-dioxo-1*H*-benz[*f*]indole (**IX**).

Aqueous methylamine solution (30% w/w, 5 ml) was added with stirring to a mixture of quinone **VIb** or **VIIb** (15 mmoles) and 50 ml of methanol. The color of the mixture changed immediately from yellow to blue, and the stirring was continued for 3 hours at room temperature. After tlc checking of starting material absence the mixture was cooled to 0°, acidified with 10% hydrochloric acid and the red precipitate of acetamidoquinone **IX** was immediately collected by filtration and washed several times with cold methanol. The product was recrystallised from chloroform-methanol mixture to give 3.83 g (90%) of **IX** as red needles with mp 243-244°; ir (chloroform): 1640 (CO), 3340 (OH, NH); ^{1}H nmr: 2.263 (3H, s, CO-CH_3), 3.852 (3H, s, N-CH_3), 7.586 (1H, td, J = 7.61, 1.66 Hz, 6- or 7-H), 7.665 (1H, td, J = 7.61, 1.66 Hz, 7- or 6-H), 7.981 (1H, dd, J = 7.61, 1.66 Hz, 5- or 8-H), 8.085 (1H, dd, J = 7.61, 1.66 Hz, 8- or 5-H), 9.337 (1H, br s, N-H), 12.562 (1H, s, OH).

3,3'-Bis(3-benzyl-1-methyl-2,3,4,9-tetrahydro-2,4,9-trioxo-1*H*-benz[*f*]indole (**X**).

Oxindolequinone **VIII** (370 mg, 1.17 mmoles) was dissolved in 60 ml of 0.1 *N* potassium hydroxide. Twelve milliliters of 0.1 *M* potassium ferricyanide were added dropwise with stirring to the resulting deep blue solution. A rapid reaction occurred and the reaction mixture changed color to greenish-yellow. It was acidified with hydrochloric acid to *p*H 2-3 and extracted with two portions of chloroform (total 50 ml). The extract was dried over calcium chloride and evaporated *in vacuo* to dryness. The residue

was treated several times with boiling hexane. The combined hexane extracts gave after cooling dimer **X**, yield 0.3 g, (80-82%), which was recrystallised from hexane, and then from methanol, orange powder, decomposing when heated to 90-100°; ir (chloroform): 1640, 1670 (quinone CO), 1730 (lactam CO); ^{1}H nmr: (*dl* + *meso* mixture) 3.050 (3H, s, N-CH_3 (isomer 1)), 3.200 (3H, s, N-CH_3 (isomer 2)), 3.764 (1H, d, J = 13 Hz, α-H (isomer 2)), 4.105 (1H, d, J = 13 Hz, α-H (isomer 1)), 4.174 (1H, d, J = 13 Hz, α'-H (isomer 1)), 4.390 (1H, d, J = 13 Hz, α'-H (isomer 2)), 6.952 (5H + 5H, m, $2C_6H_5$ (1 + 2)), 7.701 (2H + 2H, m, 4H-6,7 (1 + 2)), 7.954 (2H + 2H, m, 4H,5,8 (1 + 2)). Isomer 1:isomer 2 ratio is approximately 1.4:1.

Thermolysis of dimer **X**: Formation of 3-Benzylidene-1-methyl-2,3,4,9-tetrahydro-2,4,9-trioxo-1*H*-benz[*f*]indole (**XI**) and 3-Benzyl-1-methyl-2-hydroxy-4,9-dihydro-4,9-dioxo-1*H*-benz[*f*]indole (**VIII**).

Dimer **X** (1.63 g, 1 mmole) was dissolved in 15 ml of toluene and the resulting orange solution was refluxed for 15 minutes. After tlc checking for the absence of starting material, the solution was evaporated to dryness *in vacuo*. The residue was dissolved in 50 ml of chloroform, and extracted 3 times with 50 ml of 0.2 *M* potassium carbonate solution. The combined blue alkaline extracts (potassium salt of **VIII**) were washed with ether, acidified with hydrochloric acid, and the precipitated **VIII** was collected by filtration, yield 273 mg (86%). The chloroform solution was evaporated to a minimal volume and diluted with methanol; 3-benzylidenequinone **XI** (267 mg, 85%) was obtained, crimson needles with mp 190-192°; ir (chloroform): 1660 (quinone CO), 1700 (lactam CO); ^{1}H nmr: 3.64 (3H, s, N-CH_3), 7.52 + 7.73 (2H + 3H, m, C_6H_5), 8.11 (2H, m, 6 and 7-H), 8.45 (2H, m, 5 and 8-H), 8.90 (1H, s, =CHPh).

3-Ammonio-1-methyl-2,4-dihydro-2,4-dioxo-1*H*-benz[*f*]indol-9-olat (**XII**).

The mixture of acetamidoquinone **IX** (1.5 g, 5.3 mmoles), 2.5 ml of 36% hydrochloric acid and 150 ml of methanol was refluxed with stirring for approximately 1.5 hours. The hot reaction mixture was filtered, and the precipitate on the filter was thoroughly washed with methanol, then with chloroform to remove **IX** (betaine **XII** is insoluble in chloroform). The obtained betaine **XII** is pure and does not require recrystallisation, yield 770 mg (60%), yellowish-brown needles with mp 255-258°; ir (potassium bromide): 1660, 1695 (CO), 2500-3300 (NH_3^+, very intensive band).

2,9-Dihydroxy-1-methyl-2,4-dihydro-2,4-dioxo-1*H*-benz[*f*]indole (**XIII**).

The mixture of acetamidoquinone **IX** (3.5 g, 12.3 mmoles), 150 ml of ethanol, 25 ml of water and 25 ml of 36% hydrochloric acid was refluxed for 4-5 hours, cooled to 0° and the precipitated dioxindolequinone was collected by filtration and recrystallised from acetone to give 1.06 g (85%) of **XIII** as dark red crystals with mp 232-238° dec; the compound is readily soluble in alkaline solutions with a blue color and can be regenerated by acidification; ir (potassium bromide): 1650, 1665, 1700, 1705 (CO), 3390 (OH), 3510 (OH); ^{1}H nmr (acetone-d_6): 3.60 (1H, s, N-CH_3), 7.48 (1H, t, J = 8 Hz, 6- or 7-H), 7.71 (1H, t, J = 8 Hz, 7- or 6-H), 7.91 (1H, br s, OH), 8.12 (1H, d, J = 8 Hz, 5- or 8-H), 8.24 (1H, d, J = 8 Hz, 8- or 5-H).

3-Acetamido-2-methoxy-1-methyl-4,9-dihydro-4,9-dioxo-1*H*-benz[*f*]indole (**XIV**).

The large excess of etherial diazomethane solution was added to the mixture of acetamidooxindolequinone **IX** (284 mg, 1 mmole) and 50 ml of ether. After standing overnight at room temperature the resulting yellow solution was evaporated to give 295 mg (100%) of pure methoxy derivative **XIV** as yellow crystals with mp 239-240°; ir (potassium bromide): 1645 (CO), 1660, 1669 (quinone CO), 3270 (NH); ^{1}H nmr: 2.25 (3H, s, CO-CH_3), 3.90 (3H, s, N-CH_3), 4.05 (3H, s, O-CH_3), 7.63 (1H, td, J = 7.5, 2.0 Hz, 6- or 7-H), 7.67 (1H, td, J = 7.5, 2.0 Hz, 7- or 6-H), 8.04 (1H, dd, J = 7.5, 2.0 Hz, 5- or 8-H), 7.99 (1H, br s, N-H), 8.11 (1H, dd, J = 7.5, 2.0 Hz, 8- or 5-H).

2,3-Dimethoxy-1-methyl-4,9-dihydro-4,9-dioxo-1*H*-benz[*f*]indole (**XV**).

This compound is obtained with quantitative yield in the same manner as the previous one by methylation of dioxindolequinone **XIII** by diazomethane, orange needles, mp 128-130° (from methanol); ir (potassium bromide): 1650, 1660 (quinone CO); ^{1}H nmr: 3.75 (3H, s, N-CH_3), 4.02 (3H, s, 2-O-CH_3), 4.19 (3H, s, 3-O-CH_3), 7.61 (1H, td, J = 7.5, 2.0 Hz, 6- or 7-H), 7.65 (1H, td, J = 7.5, 2.0 Hz, 7- or 6-H), 8.08 (1H, dd, J = 7.5, 2.0 Hz, 5- or 8-H), 8.12 (1H, dd, J = 7.5, 2.0 Hz, 8- or 5-H).

3-Amino-1-methyl-9-methoxy-2,4-dihydro-2,4-dioxo-1*H*-benz[*f*]indole (**XVI**).

The mixture of betaine **XII** (242 mg, 1 mmole), 500 mg of anhydrous potassium carbonate, 186 mg (1.3 mmoles) of methyl iodide and 10 ml of anhydrous acetone was stirred for 3 hours at room temperature. The potassium salts and unreacted starting material were removed by filtration and the filtrate was evaporated *in vacuo* to dryness. The residue was recrystallised from ethanol to give 160 mg (63%) of methoxy derivative **XVI** as orange needles with mp 252-253°; ir (chloroform): 1670 (CO), 1705 (lactam CO), 3360 (NH); nmr: 3.534 (3H, s, N-CH_3), 3.887 (3H, s, O-CH_3), 6.158 (1H, br s, N-H), 7.340 (1H, td, J = 7.35, 1.70 Hz, 6- or 7-H), 7.567 (1H, td, J = 7.35, 1.70 Hz, 7- or 6-H), 7.630 (1H, dd, J = 7.35, 1.70 Hz, 5- or 8-H), 8.184 (1H, dd, J = 7.35, 1.70 Hz, 8- or 5-H).

3-Methylamino-1-methyl-9-methoxy-2,4-dihydro-2,4-dioxo-1*H*-benz[*f*]indole (**XVII**).

The mixture of **XII** or **XVI** (1 mmole, 242 or 256 mg respectively), methyl iodide (3.5 g, 25 mmoles), anhydrous potassium carbonate (3 g) and 50 ml of dry acetone was refluxed for 3 hours. After tlc checking of the starting material for its absence, the potassium salts were removed by filtration and the filtrate was evaporated to dryness. Crystallisation of the residue from methanol gave 240 mg (90%) of dimethyl derivative **XVII** as dark red prisms with mp 193-196° dec; ir (chloroform): 1655 (CO), 1705 (lactam CO); nmr: 3.472 (3H, s, N-CH_3), 3.531 (3H, s, N-CH_3), 3.844 (3H, s, O-CH_3), 7.314 (1H, td, J = 7.55, 1.42 Hz, 6- or 7-H), 7.536 (1H, td, J = 7.55, 1.42 Hz, 7- or 6-H), 7.622 (1H, dd, J = 7.55, 1.42 Hz, 5- or 8-H), 8.184 (1H, dd, J = 7.55, 1.42 Hz, 8- or 5-H), 9.00 (1H, br s, N-H).

3-Hydroxy-1-methyl-9-methoxy-2,4-dihydro-2,4-dioxo-1*H*-benz[*f*]indole (**XVIII**).

A hydrobromic acid solution (0.5 ml, 48%) was added to the solution of compound **XVII** (135 mg, 0.5 mmole) in 5 ml of glacial actic acid, and the mixture was refluxed for 10 minutes, then it was cooled to 0° and diluted with equal volume of cold water. The hydroxy derivative **XVIII** precipitated as long yellow-

ish-brown needles, yield 36 mg (30%), mp 248-250° (sublimation at 230°); ir (chloroform): 1658 (CO), 1712 (CO), 1730 (CO), 3410 (OH), 3630 (OH); ^{1}H nmr: 3.61 (3H, s, N-CH_3), 3.93 (3H, s, O-CH_3), 6.60 (1H, br s, OH), 7.45 (1H, td, J = 7.5, 2 Hz, 6- or 7-H), 7.69 (1H, td, J = 7.5, 2 Hz, 7- or 6-H), 7.91 (1H, dd, J = 7.5, 2 Hz, 5- or 8-H), 8.24 (1H, dd, J = 7.5, 2 Hz, 8- or 5-H).

1-Methyl-2,3,4,9-tetrahydro-2,3,4,9-tetraoxo-1*H*-benz[*f*]indole (**XIX**) and 2-Methylamino-3-oxocarboxy-1,4-naphthoquinone (**XX**).

Powdered sodium nitrite (1.04 g, 15 mmoles) was added in small portions to the stirred suspension of dioxindolequinone **XIII** (1.22 g, 15 mmoles) in 30 ml of glacial acetic acid during a period of 2 hours, and the stirring was continued for additional 3 hours. The color of the solution changed from red to yellow and the isatinquinone **XIX** precipitated. It was collected by filtration, recrystallised from anhydrous acetonitrile and dried *in vacuo*, yield 500 mg (50%), dark red prisms with mp 251-254° dec; ir (potassium bromide): 1648, 1695 (CO), 1735 (CO), 1763 (CO); ^{1}H nmr: 3.60 (3H, s, N-CH_3), 7.79 (1H, td, J = 7.5, 1.6 Hz, 6- or 7-H), 7.88 (1H, td, J = 7.5, 1.6 Hz, 7- or 6-H), 8.13 (1H, dd, J = 7.5, 1.6 Hz, 5- or 8-H), 8.19 (1H, dd, J = 7.5, 1.6 Hz, 8- or 5-H); ms: m/e (relative abundance %) 241 (M, 100), 213 (M-CO, 15.1), 185 (M-2CO, 28), 184 (10.5), 157 (M-3CO, 18), 141 (10), 129 (M-4CO(?), 23), 117 (12), 114 (12), 104 (28).

The yellow filtrate, containing acid **XX**, was diluted with an equal volume of water and cooled to 0°. The precipitated yellow crystals of acid (130 mg, 10%) were collected by filtration, recrystallised from acetone, containing several drops of water to prevent lactamisation, and dried at room temperature in the dark, mp 165-170° with full decomposition and strong gas evolution; ir (potassium bromide): 1630, 1700, 1747 (CO), 3000-3200 (broad band, OH and NH); ^{1}H nmr (acetone-d_6): 3.63 (3H, d, J = 5 Hz, NH-CH_3), 7.84 (1H, t, J = 7.5 Hz, 6- or 7-H), 7.92 (1H, t, J = 7.5 Hz, 7- or 6-H), 8.09 (1H, d, J = 7.5 Hz, 5- or 8-H), 8.13 (1H, d, J = 7.5 Hz, 8- or 5-H), 11.9 (1H, s, COOH). If the oxidation of dioxindolequinone **XIII** was performed in acetic acid, containing 10-20% of acetic anhydride, isatinquinone **XIX** was the sole product with the yield about 70-75%.

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