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An Unusual Stereoelectronically-dictated, Quinone-mediated Dehydrogenation Implicated in Dienediaminoketone Nenitzescu Reactions

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For the first time dienediaminoketones (1-benzoyl-2-arylamino-4-dimethylaminobuta-1,3-dienes) have been used in a reaction with benzoquinone and as a result 2-dimethylamino-3-(1′-aryl-3′-benzoyl-5′-hydroxyindol-2′-yl)-5-hydroxybenzofurans have been synthesized.

The interaction of enaminoketones and *p*-benzoquinone with the formation of 5-hydroxy-benzofurans and -indoles (Nenitzescu reaction) has already been examined in detail.[1,2] However, there are no data in the literature on the use of dienediaminoketones as the 'enamine' component in the Nenitzescu reaction. The synthesis and some properties of these compounds have been described by us recently,[3] and their application in the Nenitzescu reaction is of undoubted interest since the course of their reactions with quinone is not evident – electrophilic attack can proceed on either the β- or the δ-position of the dienediamine system.

In the present work 1-benzoyl-2-arylamino-4-dimethylaminobuta-1,3-dienes **1a,b** were chosen as the starting compounds. These compounds **1a,b** react smoothly with benzoquinone **2** in acetic acid. It has been established experimentally that the reaction proceeds optimally when the ratio of reagents is 1:2 (in an equimolar ratio yields diminish and in the ratio 1:3 tar formation takes place).

2-Dimethylamino-3-(1′-aryl-3′-benzoyl-5′-hydroxyindol-2′-yl)-5-hydroxybenzofurans **3a,b**[†] were obtained as a result of the reaction between **1a,b** and **2**, Scheme 1: **3a**, yield 17%, m.p. 284–286 °C (AcOH);[‡] **3b**, yield 28%, m.p. 274–276 °C (AcOH).[§] In the EI mass spectra of **3a,b** intense molecular ion peaks are observed (see Table 1). The basic fragmentation of molecular ions proceeds according to a common scheme (Scheme 2) with elimination of NMe_2, COPh groups and

Table 1 Characteristic ion peaks in the spectra of compounds studied, *m/z* (relative intensity).[a]

Ion	Compound			
	3a	**3b**	**6**	**10**
M^+	488(100)	518(100)	546(100)	532(100)
$[M^+ - Me_2N]^+$	444(58)	474(60)	502(30)	488(66)
$[M - COPh]^+$	383(25)	413(20)	441(15)	427(18)
A	326(60)	356(58)	370(77)	370(78)
B	196(35)	226(30)	240(24)	240(24)
$PhCO^+$	105(25)	105(25)	105(55)	105(31)
Ph^+	77(20)	77(20)	77(38)	77(20)
M^{2+}	244(16)	259(18)	273(30)	–

[a] The mass spectra of **3a,b** and **6** were recorded with a Finnigan SSQ-710 mass spectrometer using a direct inlet with ionizing potential 70 eV. The mass spectrum of **10** was obtained using a Finnigan MAT 112 instrument (50 eV).

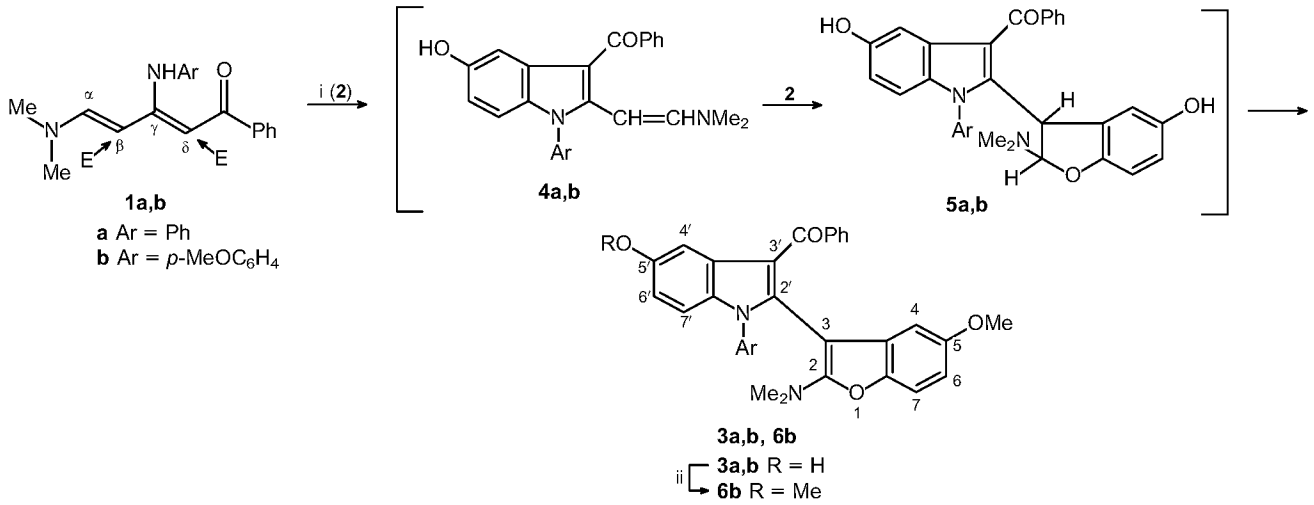
cleavage of the C(2′)–C(3) bond between the indole and benzofuran rings. This cleavage is accompanied by migration of the CH_2 group from the NMe_2 group to the indole ring with quinolinium cation **A** formation. The latter fragmentation is connected with the elimination of a PhCOC≡C group to form ion **B**. It is also possible to observe in the spectra peaks due to dicharged ions.

The Scheme 1 for **3a,b** formation shows that the Nenitzescu reaction proceeds unusually in this case and that cyclization to benzofuran derivatives is accompanied by dehydrogenation of C(2)–C(3) bonds with conservation of the Me_2N group at position 2. It is necessary to note that the reaction of **2** with enaminoketones usually proceeds with cleavage of the dimethylamine group resulting in formation of benzofuran without an amine-containing substituent at position 2.[1,2] The above Scheme 1, in which quinone firstly

[†] All new compounds gave the expected IR, ^1H NMR and mass spectra and satisfactory elemental analysis data.

[‡] *Spectroscopic data for* **3a**: ^1H NMR ($[^2H_6]Me_2SO$) δ 2.63 (s, 6H, NMe_2), 8.76 (s, 1H, OH), 9.16 (s, 1H, OH), 6.14–7.42 (m, 16H, arom. protons).

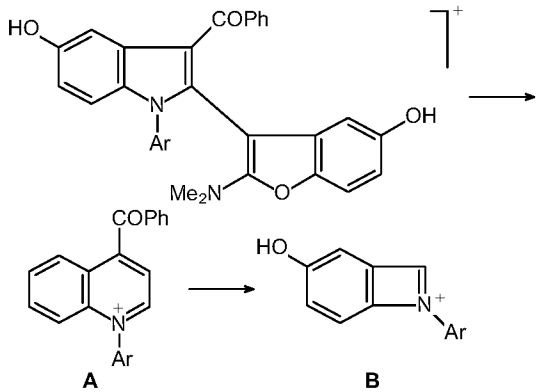
[§] *Spectroscopic data for* **3b**: ^1H NMR ($[^2H_6]Me_2SO$) δ 2.67 (s, 6H, NMe_2), 3.75 (s, 3H, OMe), 6.20–7.48 (m, 15H, arom. protons), 8.81 (s, 1H, OH), 9.17 (s, 1H, OH).



Scheme 1 *Reagents and conditions*: i, **1a,b** and **2**, AcOH, 15 h, 20 °C; ii, combination of Me_2SO_4:NaOH:triethylbenzylammonium chloride (TEBAC):**3a,b** = 6:3:0.2:2, CH_2Cl_2, H_2O, 4 h, 20 °C.

attacks the δ-position of the enamine, is based on results[4] obtained from the reaction of **2** with nitrodienediamines in which the reaction proceeds at the δ-position. However, the interaction of nitrodienediamines with quinone leads to benzofuran (not to indole) derivatives. The reason for this difference is probably the stronger electron-withdrawing effect of the NO_2 group, which facilitates benzofuran cyclization (nucleophilic attack on the β-position relative to the nitro group) and hinders electophilic attack of the second quinone molecule on the dimethylaminovinyl fragment of the 3-nitrobenzofuran derivative obtained.

The unusual (for the Nenitzescu reaction) conservation of the Me_2N group in the benzofuran ring is due to stereoelectronic factors: the protons at position 3 and the Me_2N group at position 2 in the intermediates **5a,b** are in an *S-syn*-position (according to Dreiding models). This hinders the cleavage of Me_2NH but facilitates the dehydrogenation stage (*S-anti* position of 2,3-protons), which probably proceeds by action of quinone **2**. The methylation of **3b** under phase-transfer catalysis[5] conditions yields 74% of dimethoxy derivative **6b**, m.p. 180–181 °C (Pr^iOH).¶ The final confirmation of the structures **3a,b** and **6b** is afforded by a supplementary synthesis: the methylation of 1-(*p*-methoxyphenyl)-2-methyl-5-hydroindole **7**[6] gives 5-methoxy derivative **8**, yield 75%, m.p. 102–103 °C (heptane). Condensation of the latter with DMF diethylacetal yields 78% of indolyl enamine **9**, m.p. 147–149 °C (Pr^iOH). Enamine **9** undergoes the Nenitzescu reaction with the formation of indolylbenzofuran **10**, yield 35%, m.p. 228–230 °C.* The methylation of **10** yields 87% of **6b**, which is identical with the sample from **3b** (see above).



Scheme 2

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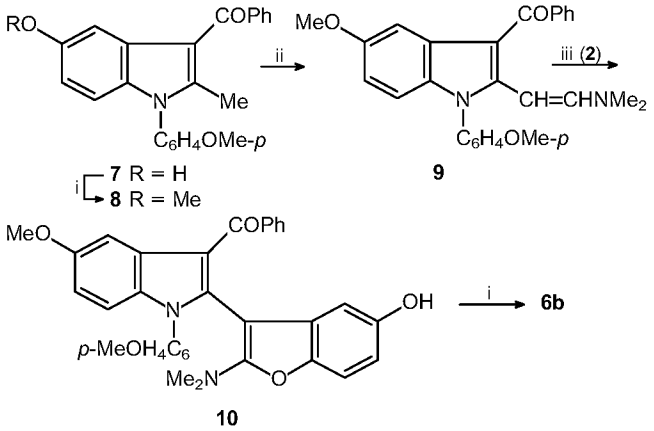

Scheme 3 *Reagents and conditions*: i, combination of Me_2SO_4:NaOH:TEBAC:**7**,**10** = 3:1.5:0.1:1, CH_2Cl_2, H_2O, 4 h, 20 °C; ii, $Me_2NCH(OEt)_2$, DMF, reflux for 25 h; iii, **9** and **2**, AcOH, 15 h, 20 °C.

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¶ *Spectroscopic data for* **6b**: ^1H NMR ($[^2H_6]Me_2SO$) δ 2.66 (s, 6H, NMe_2), 3.63, 3.72 and 3.79 (three s on 3H, OMe groups), 6.35 (q, 1H, 6-CH), 6.40 (d, 1H, 4-CH), 7.11 (d, 1H, 7′-CH), 7.58 (d, 1H, 4′-CH), 6.85–7.30 (m, 11H, N–C_6H_4, COPh, 7-CH, 6′-CH), mass spectra, see Table 1.

* *Spectroscopic data for* **10**: ^1H NMR ($[^2H_6]Me_2SO$) δ 2.65 (s, 6H, NMe_2), 3.73 and 3.78 (two s on 3H, OMe groups), 6.93–7.31 (m, 9H, C_6H_4 and COPh), 6.23 (q, 1H, 6-CH), 6.26 (d, 1H, 4-CH), 6.77 (d, 1H, 7-CH), 6.89 (q, 1H, 6′-CH), 7.08 (d, 1H, 7′-CH), 7.58 (d, 1H, 4′-CH), mass spectra, see Table 1.