Quinoneimines in the Nenitzescu reaction

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The Nenitzescu reaction involving quinoneimines was studied; new 5-aminoindole, 5-aminobenzofuran, and 9-aminochromenopyridine derivatives were synthesized.

Key words: quinoneimines, Nenitzescu reaction, 5-aminoindoles, 5-aminobenzofurans.

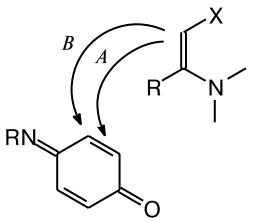
The Nenitzescu reaction possesses a large synthetic potential due to the possibility of broad variation of the structures of the initial compounds: quinones and enamines.[1—3] The major products of the Nenitzescu reaction, 5- or 6-hydroxyindoles and 5-hydroxybenzofurans, are often difficult to synthesize by other methods. Meanwhile, the synthesis of amino analogs of these indoles and benzofurans, *i.e.*, 5-aminoindoles and 5-aminobenzofurans, by the Nenitzescu reaction has not been adequately studied. Usually, these compounds are prepared by multistep procedures, whose last step is the replacement of the functional group present in the benzene ring, most often a nitro group, by an amino group.[4]

The purpose of the present work is to study the reactions of some quinoneimines with various enamines such as enamino esters, enamino ketones, enamino amides, and nitroenamines.

Limited published data are available on the reactions of enamines with arylsulfonylimino benzoquinone analogs. These quinoneimines were also shown to enter into the Nenitzescu reaction. The reaction of arylsulfonylquinoneimine derivatives with tertiary enamines affords cyclic adducts, which are converted into 5-aminobenzofuran derivatives on heating in hydrochloric acid.[5] The reactions of quinoneimines with 3-alkyl- or cycloalkylaminocrotonamides yielded acyclic hydroquinone adducts, which were further converted, depending on the reaction conditions, into 5-aminobenzofuran derivatives or cyclic enaminolactones.[6]

The starting quinoneimines we used in this study included 4-methyl-*N*-(4-oxo-2,5-cyclohexadienylidene)benzenesulfonamide (**1**), 4-[(2,4-dinitrophenyl)imino]-2,5-cyclohexadien-1-one (**2**) and 4-[(4-methoxyphenyl)imino]-2,5-cyclohexadien-1-one (**3**). Using a series of quinoneimines and a broad range of enamines, one can, first, solve the synthetic problems related to the synthesis of 5-aminoindole and 5-aminobenzofuran derivatives and, second, discuss the theoretical problems concerning the mechanism of the Nenitzescu reaction that have not been considered earlier. First, this is the path of condensation of enamines with quinoneimines, because the latter are asymmetric structures able to react with enamines along two basically different paths *A* and *B* (Scheme 1).

Scheme 1



The studies cited above[5,6] do not give unambiguous evidence indicating that processes go along only one path; however, only path *A* is discussed. Analysis of the probable transition states (Scheme 2) formed upon condensation of quinoneimine **1** with enamines attests in favor of this reaction route.

The above structures of the probable transition states (see Scheme 2) indicate that their energy is largely determined by stabilization of the anionic centers; since the acidities of sulfonylimines and phenols do not differ much, the rates of processes along paths *A* and *B* should also be similar. However, the results of our study indicate that the reaction follows path *A* almost exclusively to give tosylamino derivatives of indole and/or benzofuran (Scheme 3).

This suggests that the ultimate outcome of the reaction of enamines with iminoquinones may be determined

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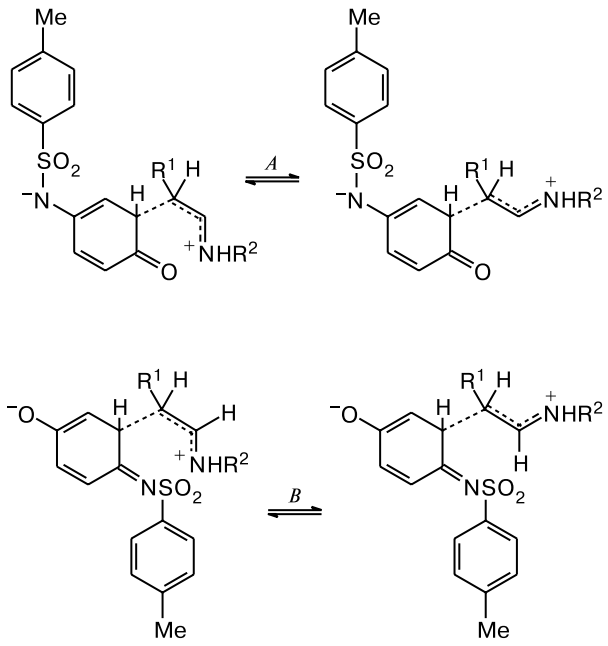
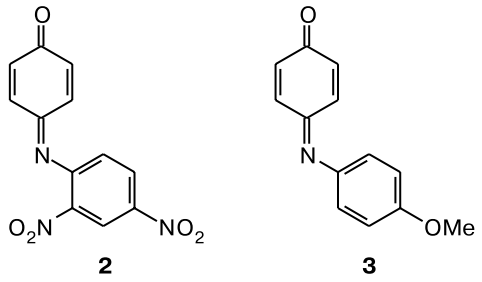
Scheme 2



by not only (and probably not so much) electronic but largely steric factors. As can be seen from Scheme 2, the steric requirements that arise in path *B* are much more pronounced than those in path *A*. Probably, this accounts for the unambiguity of the outcome of condensation of iminoquinone **1** with enamines.

The results of the reaction of enamines with iminoquinones **2** and **3** can be examined to verify the above considerations.

The dinitrophenyl fragment in quinone **2** is a strong electron acceptor, whereas a *p*-methoxyphenyl group in quinone **3** has a relatively low negative inductive effect. Nevertheless, further account of the experimental data will show that in this cases, too, the attack by the electron-excessive β-position of enamine is directed to the *ortho*-position with respect to the carbonyl fragment of



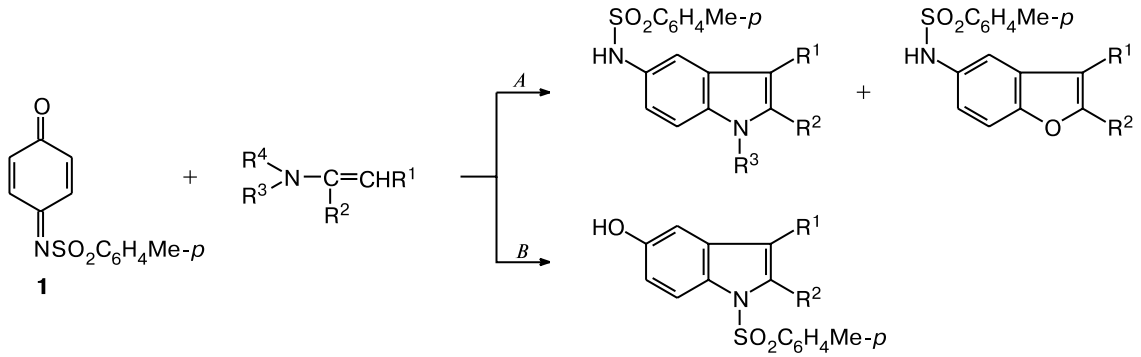
quinoneimine, *i.e.*, path *A* predominates. This regioselectivity of condensation can be interpreted as a stereocontrolled process mainly depending on steric factors.

The first stage of investigation included the condensation of quinoneimine **1** with enamines containing ethoxycarbonyl, acetyl, benzoyl, or nitro group in the β-position (**4—9**) and with α-oxocaprolactam enamine **10** (Schemes 4 and 5).

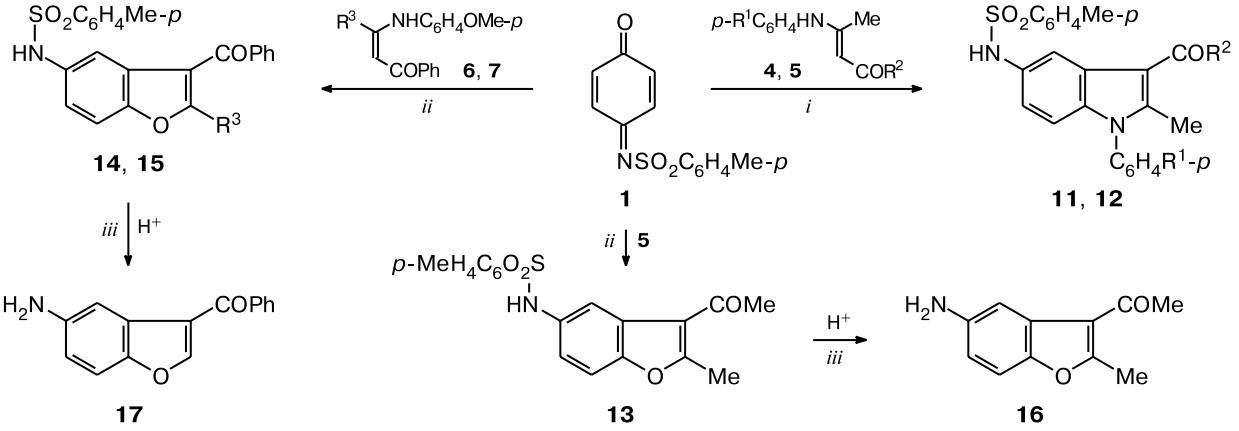
The condensation of quinoneimine **1** with enamine **4**, a derivative of aminocrotonic ester, in acetone and with acetylacetone enamine **5** in chloroform gave 5-tosylaminoindole derivatives **11** and **12**, respectively, in high yields. Quinoneimine **1** reacts with enamine **5** in acetic acid giving rise to 5-tosylaminobenzofuran derivative **13**. Benzofuran derivatives **14** and **15** were also the major products in the condensation of quinoneimine **1** with β-benzoylenamines **6** and **7** in acetic acid (see Scheme 4). In these cases, the formation of benzofuran rather than indole derivatives is quite natural for a number of reasons: the use of acetic acid as the solvent and the presence of a strong acceptor (COPh) in the β-position of enamine.[1—3]

The product structures were confirmed by ^{1}H NMR (see Experimental). However, in compounds **13—15**, it was impossible to distinguish unambiguously between benzofuran and indole structures (path *A* or *B*, see Scheme 3) on the basis of ^{1}H NMR spectra alone. Therefore, taking compounds **11** and **13** as examples, we carried out acid hydrolysis of the sulfamide group and obtained compounds **16** and **17**, containing a free amino group, which would be impossible for compounds produced along path *B*.

Scheme 3



Scheme 4



R^1 = OMe (**4**, **11**), Me (**5**, **12**); R^2 = OEt (**4**, **11**), Me (**5**, **12**); R^3 = Me (**6**, **14**), H (**7**, **15**)

Reagents and conditions: *i*. acetone (for **5**, chloroform), 20 °C, 24 h; *ii*. AcOH, 20 °C, 24 h (for **7**, 2 h); *iii*. 75% H_2SO_4, 80 °C, 30 min.

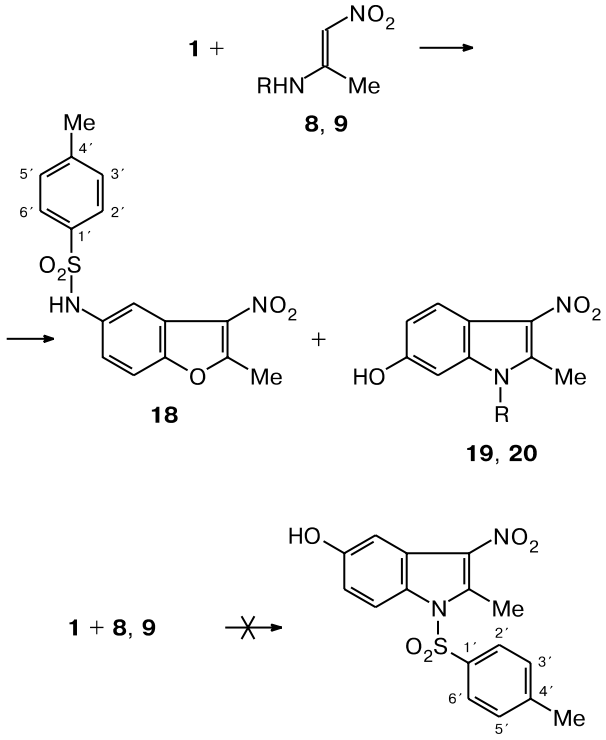
The ^{1}H NMR spectra of derivatives **16** and **17** exhibit singlets with δ 4.82 and 4.86, respectively, for the amino-group protons.

Previously,[7] it was found that β-nitroenamines react with *p*-benzoquinone to give a mixture of 6-hydroxy-indoles and 5-hydroxybenzofurans, the product ratio changing toward 6-hydroxyindoles on passing from *N*-alkyl- to *N*-arylenamines.

An attempted reaction of quinoneimine **1** in acetic acid as described previously[7] resulted in resinification of the reaction mixture. We carried out condensation of quinoneimine **1** with *N*-benzyl- (**8**) and *N*-isopropyl-nitroenamine (**9**) in acetone in the presence of *p*-toluene-sulfonic acid. The reaction of quinoneimine **1** with enamine **8** afforded a product mixture; according to ^{1}H NMR, this was a mixture of 5-aminobenzofuran derivative **18** and 6-hydroxyindole derivative **19** (see Scheme 5). The ratio of **18** and **19** estimated from the integral intensities of signals for the NH protons (δ 10.21) (**18**) and the CH_2 group (δ 5.45) (**19**) in the ^{1}H NMR spectrum of the mixture was ~85 : 15. In this case, the yield of indole **19** was only 2.2%. *N*-Benzyl-6-hydroxy-2-methyl-3-nitroindole (**19**) has been obtained in a good yield in our previous study[7] from *p*-benzoquinone and enamine **8**. A similar mixture (benzofuran **18** and indole **20**) was formed upon condensation of quinone **1** with enamine **9**. The mixtures were separated by column chromatography. The yield of compound **18** was 34% in the former case and 52% in the latter case.

The mere fact of formation of compounds **19** and **20**, even in these low yields, indicates that the steric requirements are somewhat softened upon the replacement of an aryl substituent at the nitrogen atom by the benzyl (as in enamine **8**) or an alkyl group (as in enamine **9**) and in the presence of the relatively small nitro group in the β-position of enamines and, hence, the attack on the carbon atom bonded to the sulfonylimino group becomes possible (Scheme 6). The structure of compound **18** was determined by an NMR NOESY procedure. The correla-

Scheme 5

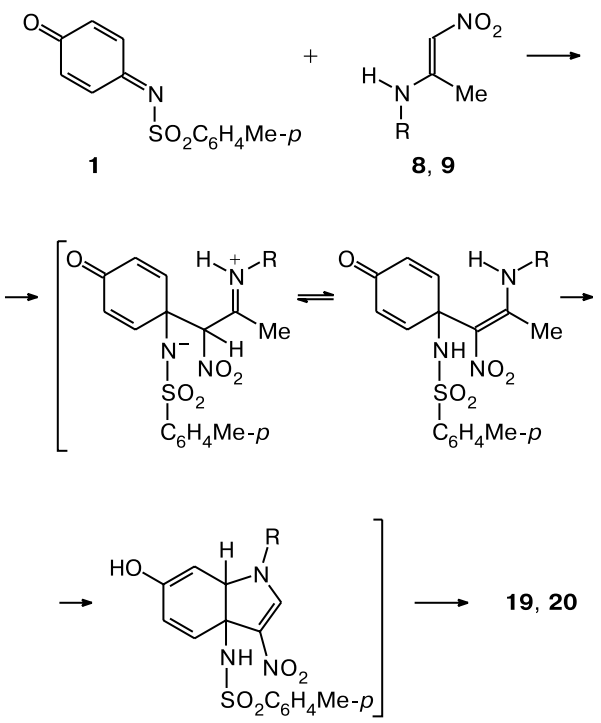


R = CH_2Ph (**8**, **19**), $CHMe_2$ (**9**, **20**)

Reagents and conditions: acetone, TsOH, 20 °C, 4 h, chromatography on a column with SiO_2.

tion peak δ 10.36/7.63 (NH/H(2′),H(6″)) present in the spectrum attests to spatial proximity of the NH-group protons and the *o*-protons of the benzene ring of the arylsulfamide group, which is possible only for the benzofuran structure. For a structural isomer of benzofuran **18**, *viz.*, the indole formed along path *B* (see Schemes 3 and 5), one would expect a H(7)/H(2′),H(6′) correlation peak in the NOESY spectrum due to the spatial proximity of the arylsulfamide group and the proton in position 7.

Scheme 6

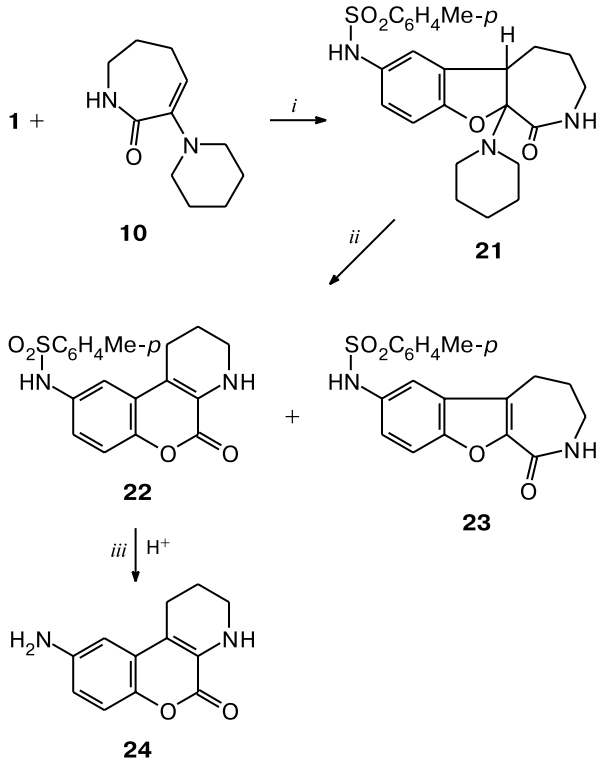


The structure of 6-hydroxyindole **19** has been proven previously.[7] In the ^{1}H NMR spectra of compounds **19** and **20**, the chemical shifts of signals for the same groups either differ little or coincide; this implies that indole **20** is also a 6-hydroxy derivative.

Recently, we have found an unusual Nenitzescu reaction route, namely, the formation of chromenopyridine derivatives upon the condensation of *p*-benzoquinones with α-oxocaprolactam enamine.[8] We studied this reaction with quinoneimines.

Quinoneimine **1** reacts with piperidinic α-oxocaprolactam enamine **10** in the same way as *p*-benzoquinone, giving cyclic adduct **21** in a high yield; **21** can be regarded as the amino analog of the adduct obtained previously in the reaction of enamine **10** with *p*-benzoquinone.[8] Under the conditions described[8] for the *p*-benzoquinone with enamine **10**, adduct **21** was converted into a 9-tosylaminochromenopyridine derivative **22**. 7-Tosylaminobenzofuroazepine derivative **23** was isolated as the side product (Scheme 7). The structures of derivatives **21—23** were confirmed by ^{1}H NMR spectra. In addition, acid hydrolysis of compound **22** gave 9-aminochromenopyridine **24**. The ^{1}H NMR spectrum of this compound exhibits a signal for two amino group protons with δ 4.76.

Scheme 7

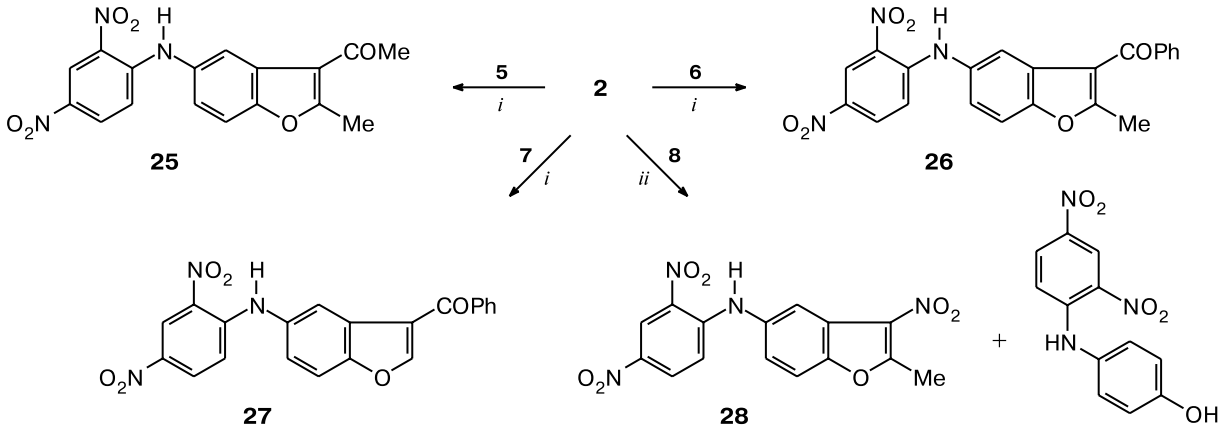


Reagents and conditions: *i*. acetone, 20 °C, 3 h; *ii*. AcOH, refluxing, 3 h, chromatography on a SiO_2 column; *iii*. 75% H_2SO_4, 80 °C, 3.5 h.

In the next stage of our study, we carried out condensation of enamines with other quinoneimines, **2** and **3**, which had not been involved previously in the Nenitzescu reaction. The reactions of quinoneimine **2** with enamino ketones **5—7** or with nitroenamine **8** afforded 5-arylaminobenzofuran derivatives **25—28**, respectively. A small amount of *p*-arylaminophenol, resulting from reduction of the initial quinoneimine, was also isolated upon the reaction with enamine **8**. This indicates that the Nenitzescu reaction with quinoneimines follows the same pattern as that with usual quinones, *i.e.*, involves the intermediate formation of acyclic hydroquinone adducts[1—3] (Scheme 8).

The structures of compounds **26** and **28** were determined using NMR NOESY experiments. As in the case of benzofuran **18**, in addition to the NH/H(4) and NH/H(6) correlation peaks, the spectra of these compounds exhibit NH/H(6″) peaks: δ 10.15/7.00 and 10.19/7.06, respec-

Scheme 8



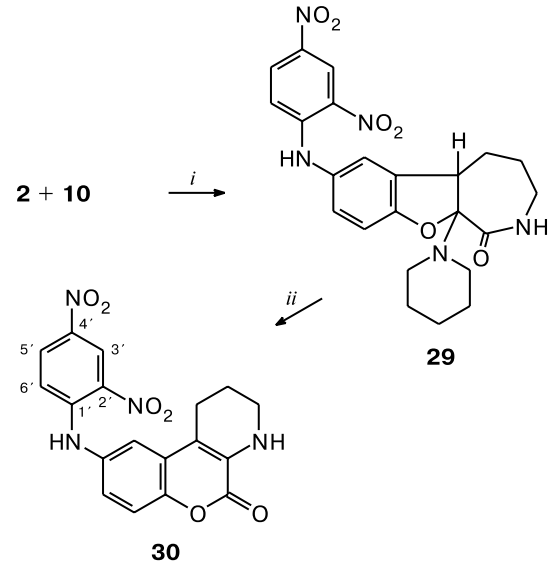
Reagents and conditions: *i*. AcOH, 1 drop of Ac_2O, 20 °C, 24 h; *ii*. AcOH, TsOH, 20 °C, 30 min.

tively, which confirm the spatial proximity of the NH and 2,4-dinitrophenyl groups.

Comparison of the signal positions in the ^{1}H NMR spectra of compounds **25**, **27** and **26**, **28**, in particular, the signals of the NH protons (δ 10.15—10.20), leads to the conclusion that compounds **25** and **27** also have a benzofuran structure.

α-Oxocarolactam enamine **10** reacts with quinoneimine **2** in acetone to furnish cyclic adduct **29**, which was then converted into chromenopyridine derivative **30** (Scheme 9).

Scheme 9

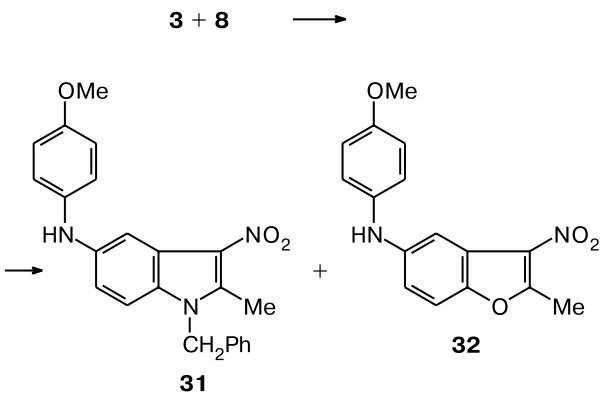


Reagents and conditions: *i*. acetone 20 °C, 3 h; *ii*. AcOH, refluxing, 3 h.

The NMR NOESY spectrum of compound **30**, like the spectra of **26**, **28**, exhibits a correlation peak with δ 10.13/7.10 (NH/H(6′)). This implies that the *N*-aryl substituent is located in the benzene ring.

Quinoneimine **3**, containing *p*-methoxyphenyl substituent at nitrogen, reacts with enamine **8** at position 3 of quinoneimine, like quinones **1** and **2**, to give 5-aminoindole derivative **31** and 5-aminobenzofuran derivative **32** (Scheme 10). The structure of indole **31** was also proven using a NMR NOESY experiment: the signal with δ 5.55, due to the protons of the methylene group of the benzyl substituent, has a correlation peak with the signal at δ 7.47 (d, H(7), J = 8.8 Hz).

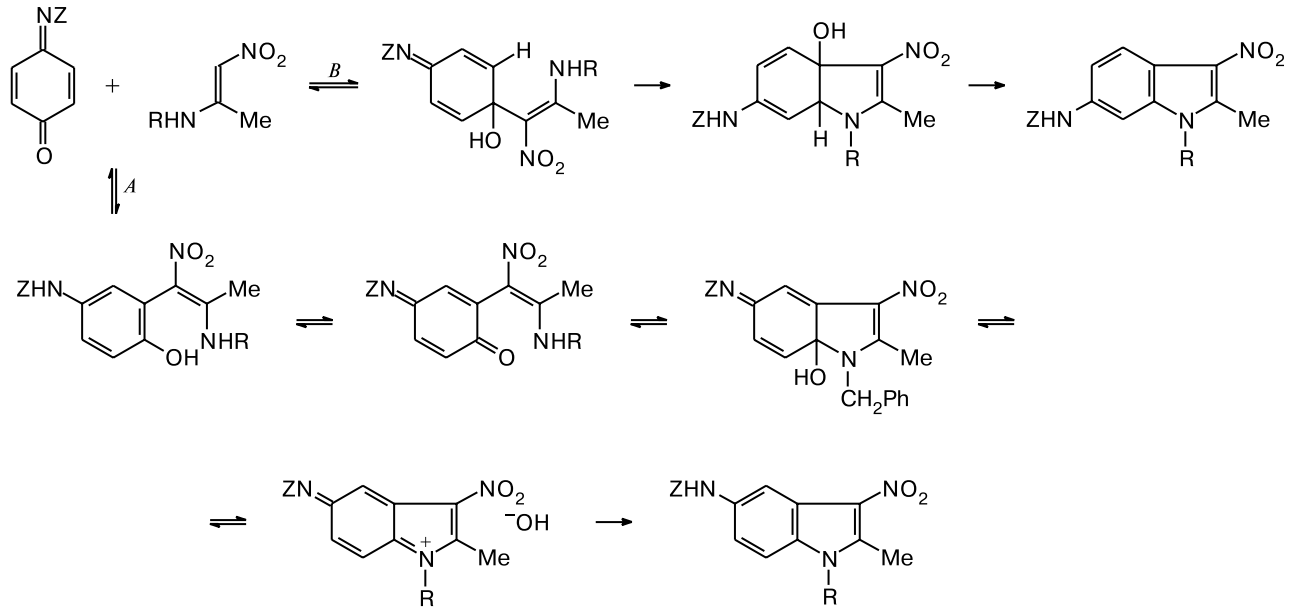
Scheme 10



Reagents and conditions: AcOH, TsOH, 20 °C, 1 h, chromatography on a SiO_2 column.

Note that this reaction yields 5- rather than 6-arylaminoindoles, whereas condensation of nitroenamines with *p*-benzoquinone gives most often 6-hydroxyindoles.[7]

Scheme 11



Z = C_6H_4OMe-*p*

In our opinion, this outcome, unusual for nitroenamines, could be interpreted in terms of the specific features of processes that lead to 5- or 6-substituted indoles (Scheme 11).

The reaction of quinoneimine with nitroenamines resulting in 5-arylaminoindoles proceeds through the initial formation of an adduct, similar to the hydroquinone adducts formed with *p*-benzoquinone.[1—3] To be converted into the indole derivative, this adduct should be further oxidized and then, after cyclization, reduced (path *A*). Conversely, path *B* directed at 6-arylaminoindoles does not involve redox processes; in this case, the transformation into indole requires dehydration. When comparing quinoneimine **3** with *p*-benzoquinone, one may note that the former is a much weaker oxidant: the redox potentials E^0 are 0.553 and 0.71 V, respectively.[9,10] Thus, the electron-withdrawing effect of the *p*-methoxyphenylimino group is much lower than that of the quinone carbonyl. The electron density deficiency on the carbon atom of the second carbonyl group of *p*-benzoquinone is much more pronounced than that in quinoneimine **3**. As a result, the attack of nitroenamine on the quinoneimine carbonyl is hampered compared to the attack on the *p*-benzoquinone carbonyl, and the process leading to 6-arylimino derivatives is retarded.

The reduction of hydroxide-immonium is the final step in the synthesis of 5-arylaminoindoles (see Scheme 11, path *A*). The active reducing agents functioning in these reactions are adducts, which are stronger oxidants, judging from the redox potentials, than hydroquinone adducts formed when *p*-benzoquinone is used. All steps preceding the reduction are apparently reversible. Upon the reduction, the equilibrium shifts to 5-arylaminoindole, which accelerates the process along this route. Both of these factors act in the same direction, ensuring different positions of the substituent in the benzene ring upon the condensation of nitroenamines with *p*-benzoquinone (the formation of 6-hydroxyindoles) and quinoneimine **3** (the formation of 5-arylaminoindoles).

Experimental

Mass spectra were recorded on a Finnigan SSQ-710 mass spectrometer with direct sample injection into the ion source. ^{1}H NMR spectra were recorded on a Bruker AC-200 spectrometer in DMSO-d_6 and DMSO-d_6/CCl_4, the NOESY experiments were carried out on a Bruker DRX-500 spectrometer in DMSO-d_6 using standard commercial procedures. The reactions were monitored and the product purity was checked on Silufol UV-254 plates in a benzene—methanol mixture, 9 : 1, and in chloroform (UV visualization). The yields, elemental analysis data, and physocochemical characteristics of the compounds are summarized in Tables 1—5.

3-Ethoxycarbonyl-1-(4-methoxyphenyl)-2-methyl-5-tosylaminoindole (11). Enamine **4** (0.4 g, 1.7 mmol) was added at 20 °C to a stirred solution of quinoneimine **1** (0.4 g, 1.5 mmol) [11] in acetone (7.5 mL). The stirring was continued for 24 h. The reaction mixture was concentrated and the residue was recrystallized from isopropyl alcohol to give 0.35 g of compound **11**.

3-Acetyl-2-methyl-3-ethoxycarbonyl-1-(4-tolyl)-5-tosylaminoindole (12) was prepared similarly to compound **11** but in chloroform. The reaction of compound **1** (0.4 g, 1.5 mmol) and enamine **5** (0.34 g, 1.8 mmol) gave 0.1 g of compound **12**.

Table 1. Yields, melting points, elemental analysis data, and mass spectrometric data for compounds **11—18** and **20—32**

Compound	Yield (%)	M.p./°C (solvent)	Found / Calculated (%)				Molecular formula	MS, m/z (I_{rel} (%))
			C	H	N	S		
11	50	165—167 (Pr^iOH)	65.68 65.25	5.33 5.48	5.80 5.85	6.71 6.70	$C_{26}H_{26}N_2SO_5$	478 $[M]^+$ (36), 432 $[M - C_2H_5OH]^+$ (4), 323 $[M - SO_2C_6H_4Me\text{-}p]^+$ (100)
12	61	225—226 (hexane—benzene)	70.00 69.42	5.29 5.59	6.05 6.48	—	$C_{25}H_{24}N_2SO_3$	432 $[M]^+$ (12), 277 $[M - SO_2C_6H_4Me\text{-}p]^+$ (100)
13	67	226—228 (AcOH)	62.70 62.96	5.17 4.99	4.07 4.08	9.52 9.34	$C_{18}H_{17}NSO_4$	343 $[M]^+$ (87), 188 $[M - SO_2C_6H_4Me\text{-}p]^+$ (100)
14	75	177—178 (AcOH)	67.86 68.13	4.89 4.72	3.33 3.45	—	$C_{23}H_{19}NSO_4$	405 $[M]^+$ (86), 250 $[M - SO_2C_6H_4Me\text{-}p]^+$ (100)
15	77	139—140 (EtOH)	67.77 67.50	4.72 4.38	3.56 3.58	8.38 8.19	$C_{22}H_{17}NSO_4$	391 $[M]^+$ (98), 236 $[M - SO_2C_6H_4Me\text{-}p]^+$ (100)
16	32	156—158 (acetone)	69.40 69.82	5.86 5.86	7.35 7.40	—	$C_{11}H_{11}NO_2$	189 $[M]^+$ (100), 174 $[M - NH]^+$ (97), 146 $[M - COMe]^+$ (77)
17	53	225—226 (hexane—benzene)	75.51 75.94	5.04 4.67	5.86 5.90	—	$C_{15}H_{11}NO_2$	237 $[M]^+$ (100), 132 $[M - COPh]^+$ (23)
18	35 (*A*) 52 (*B*)	202—205 (EtOH)	55.33 55.48	4.04 4.07	8.09 8.09	—	$C_{16}H_{17}N_2SO_5$	346 $[M]^+$ (59), 191 $[M - SO_2C_6H_4Me\text{-}p]^+$ (100), 175 $[M - HNSO_2C_6H_4Me\text{-}p]^+$ (12)
20	17	227—230 (benzene)	61.03 61.52	6.18 6.02	11.90 11.96		$C_{12}H_{14}N_2O_3$	234 $[M]^+$ (100), 217 $[M - OH]^+$ (41)
21	75	225—227 (acetone)	63.38 63.27	6.50 6.42	9.21 9.22	—	$C_{24}H_{25}N_3SO_4$	455 $[M]^+$ (6), 370 $[M - C_5H_{10}N]^+$ (9), 300 $[M - SO_2C_6H_4Me\text{-}p]^+$ (100)
22	86	182—183 (ethyl acetate)	61.63 61.60	5.20 4.90	7.26 7.56	8.78 8.66	$C_{19}H_{18}N_2SO_4$	370 $[M]^+$ (36), 215 $[M - SO_2C_6H_4Me\text{-}p]^+$ (100)
23	4.3	243—245 (EtOH)	61.62 61.60	4.99 4.90	7.55 7.56	8.49 8.66	$C_{19}H_{18}N_2SO_4$	370 $[M]^+$ (36), 215 $[M - SO_2C_6H_4Me\text{-}p]^+$ (100)
24	97	198—199 (EtOH)	66.60 66.66	5.68 5.59	12.92 12.95	—	$C_{12}H_{12}N_2O_2$	216 $[M]^+$ (100), 199 $[M - NH_2]^+$ (9)
25	28	189—190 (AcOH)	57.16 57.47	3.62 3.69	11.68 11.83	—	$C_{17}H_{13}N_3O_6$	355$[M]^+$ (100), 220 $[M - C_6H_3(NO_2)_2]^+$ (34), 204 $[M - HNC_6H_3(NO_2)_2]^+$ (14)
26	25	193—194 (AcOH)	63.19 63.31	4.18 3.62	10.05 10.07	—	$C_{22}H_{15}N_3O_6$	417 $[M]^+$ (100)
27	23	177—178 (AcOH)	62.25 62.53	3.33 3.25	10.30 10.42	—	$C_{21}H_{13}N_3O_6$	403 $[M]^+$ (100), 221 $[M - C_6H_3(NO_2)_2]^+$ (11)
28	85.5	241—243 (DCE)	50.15 50.28	2.92 2.81	15.48 15.64	—	$C_{15}H_{10}N_4O_7$	358 $[M]^+$ (100), 191 $[M - C_6H_3(NO_2)_2]^+$ (29)
29	48	196—199	58.50 59.09	5.88 5.39	14.50 14.98	—	$C_{23}H_{25}N_5O_6$	467 $[M]^+$ (28), 382 $[M - C_5H_{10}N]^+$ (100)
30	77	256—258 (DMF)	56.68 56.54	3.55 3.69	14.66 14.65	—	$C_{18}H_{14}N_4O_6$	382 $[M]^+$ (100)
31	12.4	164—165 (EtOH)	70.96 71.30	5.46 5.46	10.79 10.85	—	$C_{23}H_{21}N_3O_3$	387 $[M]^+$ (100), 296 $[M - CH_2Ph]^+$ (18), 279 $[M - C_6H_4OMe\text{-}p]^+$ (40), 264 $[M - HNC_6H_4OMe\text{-}p]^+$ (32)
32	7.4	170—171 (EtOH)	64.22 64.42	4.70 4.73	9.05 9.39	—	$C_{16}H_{14}N_2O_4$	298 $[M]^+$ (100), 283 $[M - Me]^+$ (88), 251 $[M - NO_2]^+$ (24)

Table 2. ^{1}H NMR spectra of compounds **11**, **12**, **19**, **20**, **31**

Compound	δ (*J*/Hz)						
	H(4) H(7) (d, 1 H)*	H(5) H(6) (dd, 1 H)*	C(2)Me (s, 3 H)	Substituents at the atoms			
				N(1)	C(3)	C(5)	C(6)
11	7.82 6.80	— 6.92	2.44	3.84 (s, 3 H, Me); 7.13, 7.32 (both m, 2 H each, C_6H_4)	1.35 (t, 3 H, Me, J_o = 7.0); 4.27 (q, 2 H, CH_2)	2.31 (s, 3 H, Me); 7.31, 7.62 (both m, 2 H each, C_6H_4); 9.97 (br.s, 1 H, NH)	—
12	7.77 6.76	— 6.89	2.47	2.48 (s, 3 H, Me); 7.22, 7.39 (both m, 2 H each, C_6H_4)	2.50 (s, 3 H, COMe)	2.35 (s, 3 H, Me); 7.25, 7.61 (both m, 2 H each, C_6H_4); 9.75 (br.s, 1 H, NH)	—
19	7.92 6.84	6.81 —	2.78	5.45 (s, 2 H, CH_2); 7.09 (2 H), 7.28 (3 H) (both m, Ph)	—	—	9.25 (br.s, 1 H, OH)
20	7.91 7.02	6.79 —	2.86	1.62 (d, 6 H, 2 Me, J_o = 7.0); 4.86 (m, 1 H, CH)	—	—	9.22 (br.s, 1 H, OH)
31	7.75 7.47	— 6.94	2.79	5.54 (s, 2 H, CH_2); 7.13 (d, 2 H, Ph); 7.28 (t, 1 H, Ph); 7.34 (d, 2 H, Ph), J_o = 7.5	—	3.72 (s, 3 H, OMe); 6.88, 7.07 (both m, 2 H each, C_6H_4); 7.93 (br.s, 1 H, NH)	—

* J_o = 8.4—8.8 Hz, J_m = 1.6–2.0 Hz.

Table 3. ^{1}H NMR spectra of compounds **13—18**, **25—28**, and **32**

Compound	δ (*J*/Hz)						
	H(2) (s, 1 H)	H(4) (d, 1 H)[a]	H(6) (dd, 1 H)[a]	H(7) (d, 1 H)[a]	C(2)Me (s, 3 H)	Substituents at the atoms	
						C(3)	C(5)
13	—	7.69	7.05	7.29	2.72	2.51 (s, 3 H, COMe)	2.35 (s, 3 H, Me); 7.24, 7.50 (both m, 2 H each, C_6H_4); 9.91 (br.s, 1 H, NH);
14	—	7.20	7.05	7.34	2.42	2.36 (s, 3 H, Me); 7.26 (d, 2 H, H(3′), H(5′), J_o = 8.8); 7.49—7.73 (m, 7 H, H(2′), H(6′), COPh); 9.88 (br.s, 1 H, N(5)H)	
15	8.44	7.91	7.21	7.46	—	2.35 (s, 3 H, Me); 7.26 (d, 2 H, H(3′), H(5′), J_o = 8.8); 7.50—7.89 (m, 7 H, H(2′), H(6′), COPh); 10.04 (br.s, N(5)H)	
16	—	7.17	6.59	7.20	2.69	2.53 (s, 3 H, COMe)	4.82 (br.s, 2 H, NH_2)
17	8.25	7.32	6.69	7.26		7.56 (m, 3 H, H(3′), H(4′), H(5′)); 7.84 (d, 2 H, H(2′), H(6′), J_o = 7.0)	4.86 (br.s, 2 H, NH_2)
18	—	7.76	7.19	7.57	2.81	—	2.29 (s, 3 H, Me); 7.31, 7.63 (both m, 2 H each, C_6H_4); 10.36 (br.s, 1 H, NH)
25	—	7.98	7.29	7.63	2.82	2.58 (s, 3 H, COMe)	7.04 (d, 1 H, H(6′))[b]; 8.13 (dd, 1 H, H(5′))[b]; 8.94 (d, 1 H, H(3′))[b]; 10.20 (br.s, 1 H, NH)
26	—	7.43	7.33	7.77	2.50	7.55 (t, 2 H, H(3′), H(5′), J_o = 7.0); 7.66 (t, 1 H, H(4′); 7.77 (d, 2 H, H(2′), H(6′))	7.00 (d, 1 H, H(6″))[b]; 8.16 (d, 1 H, H(5″))[b]; 8.84 (d, 1 H, H(3″))[b]; 10.15 (br.s, 1 H, NH)
27	8.64	8.16	7.44	7.79	—	7.59 (m, 3 H, Ph); 7.92 (m, 2 H, Ph)	7.11 (d, 1 H, H(6′))[b]; 8.16 (dd, 1 H, H(5′))[b]; 8.97 (d, 1 H, H(3′))[b]; 10.20 (br.s, 1 H, NH)
28	—	7.98	7.49	7.84	2.92	—	7.06 (d, 1 H, H(6′))[b]; 8.17 (d, 1 H, H(5′))[b]; 8.87 (d, 1 H, H(3′))[b]; 10.19 (br.s, 1 H, NH)
32	—	7.52	7.01	7.49	2.85	—	3.74 (s, 3 H, OMe); 6.90, 7.08 (both m, 2 H each, C_6H_4); 7.93 (br.s, 1 H, NH)

[a] J_o = 8.4—8.8 Hz, J_m = 1.8—2.6 Hz.
[b] J_o = 9.6 Hz, J_m = 2.7 Hz.

Table 4. ^{1}H NMR spectra of compounds **22**, **24**, and **30**

Compound	δ (*J*/Hz)							
	H(1) (t, 2 H)[a]	H(2) (qt, 2 H)[a]	H(3) (m, 2 H)	N(4)H (br.s, 1 H)	H(7) (d, 1 H)[b]	H(8) (dd, 1 H)	H(10) (d, 1 H)[b]	RC(9)
22[c]	—	1.88	—	5.90	7.13	6.93	7.11	2.33 (s, 3 H, Me); 7.33, 7.64 (both m, 2 H each, C_6H_4); 10.07 (br.s, 1 H, NH)
24	2.61	1.95	3.27	5.50	6.90	6.46—6.54 (m, 2 H)		4.76 (br.s, 2 H, NH_2)
30	2.64	1.89	3.27	6.12	7.38	7.23	7.42	7.10 (d, 1 H, H(6′), J_o = 9.6); 8.17 (dd, 1 H, H (5′), J_o = 9.6, J_m = 2.7); 8.85 (d, 1 H, H (3′), J_m = 2.7); 10.13 (br.s, 1 H, NH)

[a] J_o = 6.4 Hz.
[b] J_o = 8.4—8.8 Hz, J_m = 2.4—2.6 Hz.
[c] The signals of the H(1), H(2) atoms of the methylene groups are superimposed by signals of admixtures of undeuterated DMSO and water δ 2.50 and δ 3.20.

Table 5. ^{1}H NMR spectra of compounds **21** and **29**

Compound	δ (*J*/Hz)								
	N(2)H	H(3) (m, 1 H)	H(4), H(5), H(3″)—H(5″) (all m, 10 H)	H(5a) (d, 1 H)	H(2″), H(6″), H(3′) (all m, 5 H)	H(6) (d, 1 H)*	H(8) (dd, 1 H)*	H (9) (d, 1 H)*	RC(7)
21	—	3.91	1.34—1.80	3.29 (J = 11.8)	2.39, 2.60, 3.04	6.81	6.73	6.58	2.33 (s, 3 H, Me); 7.29, 7.51 (both m, 2 H each, C_6H_4); 9.30 (br.s, 1 H, NH)
29	7.60 (t, 1 H, J_o = 6.8)	3.98	1.43—1.91, 2.05	3.45 (J = 11.6)	2.52, 2.71, 2.99	7.19	7.11	6.88	7.01 (d, 1 H, H(6′′′), J_o = 9.6); 8.18 (dd, 1H, H(5′′′), J_o = 9.6, J_m = 2.2); 8.88 (d, 1 H, H (3′′′), J_m = 2.2); 9.97 (br.s, 1 H, NH)

* J_o = 8.4 Hz, J_m = 2.2 Hz.

3-Acetyl-2-methyl-5-tosylaminobenzofuran (13) Two drops of acetic anhydride and then enamine **5** (0.42 g, 2.2 mmol) were added at 20 °C to a stirred suspension of quinone **1** (0.52 g, 2 mmol) in AcOH (6 mL). The stirring was continued for 24 h. The precipitate was filtered off, washed with AcOH and ethanol, and dried to give 0.4 g of compound **13**.

3-Benzoyl-2-methyl-5-tosylaminobenzofuran (14) was prepared similarly to compound **13**. The reaction of compound **1** (0.4 g, 1.5 mmol) and enamine **6** (0.54 g, 2 mmol) gave 0.3 g of compound **14**.

3-Benzoyl-5-tosylaminobenzofuran (15) was prepared similarly to compound **13** but for 2 h instead of 24 h. The reaction of compound **1** (2 g, 7 mmol) with enamine **7** (1.6 g, 9 mmol) gave 1 g of compound **15**.

3-Acetyl-5-amino-2-methylbenzofuran (16). A suspension of compound **13** (0.85 g, 2.5 mmol) in 20 mL of 75% H_2SO_4 was stirred for 30 min at 75—80 °C. The reaction mixture was poured onto ice, the precipitate was filtered off, washed with water, and suspended in 15 mL of 2 *N* NaOH, and the mixture was stirred for 3 h at 20 °C. The precipitate was filtered off, washed with water, and dried to give 0.2 g of compound **16**.

5-Amino-3-benzoylbenzofuran (17) was prepared similarly to compound **16**. Compound **15** (0.3 g, 0.8 mmol) was converted into 0.15 g of **17**.

2-Methyl-3-nitro-5-tosylaminobenzofuran (18) (*A*) and 1-benzyl-6-hydroxy-2-methyl-3-nitroindole (19). *p*-Toluenesulfonic acid (0.76 g, 4.4 mmol) and enamine **8** (0.84 g, 4.4 mmol) were added successively at 20 °C to a stirred solution of quinone **1** (1.05 g, 4 mmol) in acetone (20 mL). The stirring was continued for 4 h. The reaction mixture was concentrated, the residue was triturated with ethanol, and the precipitate was filtered off, washed with water, dried, and recrystallized from alcohol to give 0.48 g of compound **18**. The ethanol mother liquor was concentrated and the residue was chromatographed on a column with silica gel. Elution with chloroform gave 0.25 g (2.2%) of compound **19**. According to ^{1}H NMR spectrum, the melting point, and TLC, the product was identical to that obtained previously.[7]

2-Methyl-3-nitro-5-tosylaminobenzofuran (18) (*B*) and 6-hydroxy-1-isopropyl-2-methyl-3-nitroindole (20). *p*-Toluenesulfonic acid (0.91 g, 5.3 mmol) and then enamine **9** (0.7 g, 5.3 mmol) were added successively at 20 °C to a stirred solution

of quinone **1** (1.25 g, 4.8 mmol) in acetone (25 mL). The stirring was continued for 4 h. The precipitate was filtered off, washed with water, and dried to give 0.3 g of compound **18**. The acetone mother liquor was concentrated and the residue was triturated with ethanol. The precipitate was filtered off and recrystallized from ethanol to give additionally 0.57 g of compound **18**. The ethanol mother liquor was concentrated and the residue was chromatographed on a column with silica gel. Elution with chloroform gave 0.19 g of compound **20**.

10a-Piperidino-7-tosylamino-2,3,5,5a,10a-hexahydrobenzofuro[2,3-c]azepin-1(1*H*)-one (21). Enamine **10** (1.14 g, 5.9 mmol) was added at 20 °C to a stirred solution of quinone **1** (1.53 g, 5.9 mmol) in acetone (12 mL). The stirring was continued for 3 h. The precipitate was filtered off, washed with hot acetone, and dried to give 2.0 g of compound **21**.

9-Tosylamino-1,2,3,4-tetrahydro-5*H*-chromeno[3,4-*b*]pyridine-5-one (22) and 7-tosylamino-2,3,4,5-tetrahydro-1*H*[1]benzofuro[2,3-*c*]azepin-1-one (23). A suspension of compound **21** (3.16 g, 6.9 mmol) in AcOH (45 mL) was stirred for 20 min at 17—18 °C and refluxed for 2.5 h. The reaction mixture was cooled to 20 °C and diluted with water (400 mL). The precipitate was filtered off, washed with water, dried, and chromatographed on a column with silica gel. Elution with ethyl acetate gave 2.2 g of compound **22** and 0.11 g of compound **23**.

Compound 23. ^{1}H NMR (DMSO-d_6), δ: 2.01 (m, 2 H, H(4)); 2.87 (t, 2 H, H(5), $J_1 = J_2 = 6.4$ Hz); 3.26 (m, 2 H, H(3), $J_1 = J_2 = 6.4$ Hz, $J_3 = 4.8$ Hz); 7.12 (dd, 1 H, H(8)), $J_o = 8.4$ Hz, $J_m = 1.8$ Hz); 7.31, 7.61 (both m, 2 H each, C_6H_4); 7.35 (d, 1 H, H(6), $J_m = 1.8$ Hz); 7.47 (d, 1 H, H(9), $J_o = 8.4$ Hz); 8.02 (t, 1 H, N(2)H, $J_o = 4.8$ Hz); 10.05 (br.s, 1 H, NH(C(7)).

9-Amino-1,2,3,4-tetrahydro-5*H*-chromeno[3,4-*b*]pyridin-5-one (24). A suspension of compound **20** (1.1 g, 3 mmol) in 75% H_2SO_4 (20 mL) was stirred for 3.5 h at 75—80 °C. The reaction mixture was poured onto ice, filtered, and cooled to 10—15 °C. A solution of ammonia was added to pH ~8. The precipitate was filtered off, washed with water, and dried to give 0.63 g of compound **24**.

3-Acetyl-5-(2,4-dinitrophenylamino)-2-methylbenzofurans (25) was prepared similarly to compound **13**. The reaction of quinone **2** (0.54 g, 2 mmol) [11] with enamine **5** (0.56 g, 2.2 mmol) gave 0.2 g of benzofuran **25**.

3-Benzoyl-5-(2,4-dinitrophenylamino)-2-methylbenzofuran (26) was prepared similarly to compound **13**. The reaction of quinone **2** (0.27 g, 1 mmol) with enamine **6** (0.28 g, 1.1 mmol) gave 0.08 g of benzofuran **26**.

3-Benzoyl-5-(2,4-dinitrophenylamino)benzofuran (27) was prepared similarly to compound **13**. The reaction of compound (0.5 g, 2 mmol) **2** with enamine **7** (0.38 g, 2.2 mmol) gave 0.17 g of benzofuran **27**.

5-(2,4-Dinitrophenyl)amino-2-methyl-3-nitrobenzofuran (28). *p*-Toluenesulfonic acid (0.17 g, 1 mmol) and enamine **8** (0.21 g, 1.1 mmol) were added successively at 20 °C to a stirred suspension of quinone **2** (0.27 g, 1 mmol) in AcOH (3 mL). The stirring was continued for 30 min. The precipitate was filtered off, washed with AcOH and water, and dried to give 0.31 g of compound **28**.

7-(2,4-Dinitrophenyl)amino-10a-piperidino-2,3,5,5a,10a-hexahydrobenzofuro[2,3-*c*]azepin-1(1*H*)-one (29) was prepared similarly to compound **21**. The reaction of quinone **2** (2.18 g, 8 mmol) with enamine **10** (1.55 g, 2.2 mmol) gave 1.8 g of compound **29**.

9-(2,4-Dinitrophenyl)amino-1,2,3,4-tetrahydro-5*H*-chromeno[3,4-*b*]pyridin-5-one (30). A suspension of compound **29** (1.8 g, 3.8 mmol) in AcOH (35 mL) was stirred for 20 min at 17—18 °C and refluxed for 3 h. The reaction mixture was cooled to 20 °C and stirred for 2 h. The precipitate was filtered off, washed with AcOH and water, and dried to give 1.13 g of compound **30**.

1-Benzyl-5-(4-methoxyphenyl)amino-2-methyl-3-nitroindole (31) and 5-(4-methoxyphenyl)amino-2-methyl-3-nitrobenzofuran (32). *p*-Toluenesulfonic acid (0.17 g, 1 mmol) and enamine **8** (0.21 g, 1.1 mmol) were added successively at 20 °C to a stirred solution of quinone **3** (0.213 g, 1 mmol) [12] in AcOH (3 mL). The stirring was continued for 1 h. The reaction mixture was diluted with water (30 mL) and the precipitate was filtered off, washed with water, dried, and chromatographed on a column with silica gel. Elution with benzene gave 0.022 g of indole **31** and 0.038 g of benzofuran **32**.

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