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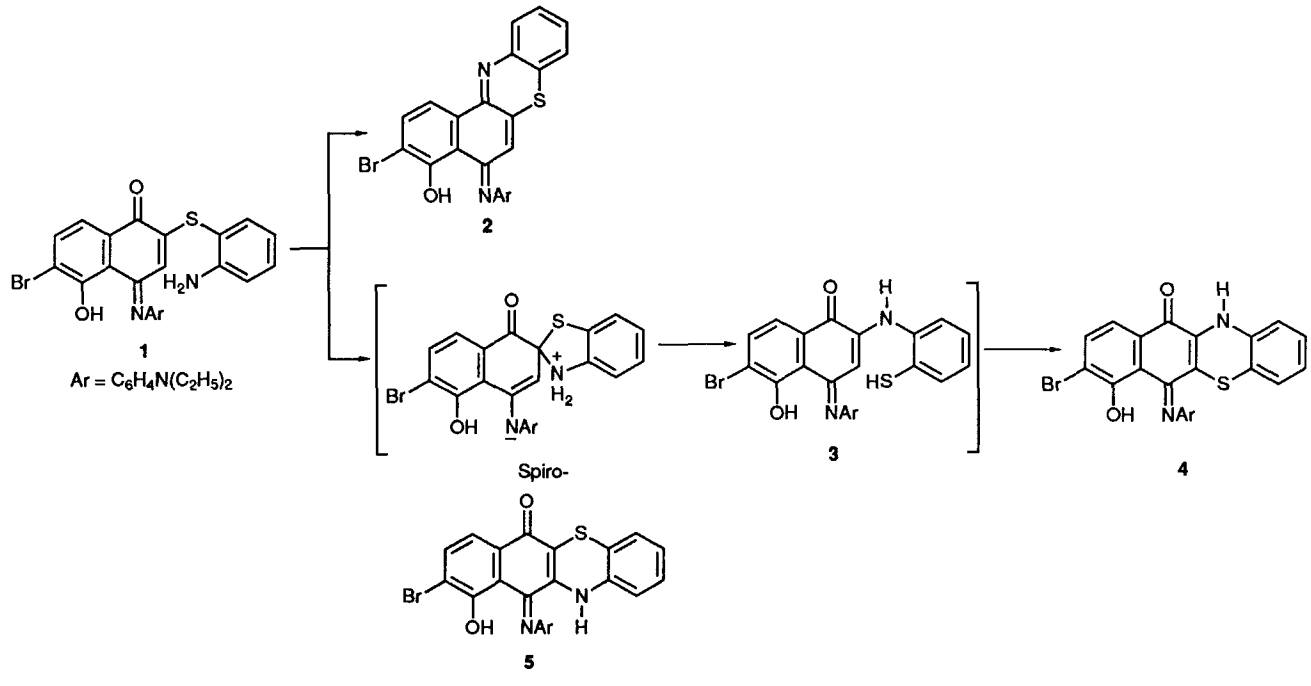
A Smiles Rearrangement as an Intermediate Step in the Formation of 8-Bromo-7-hydroxy-*N*-(4′-*N*,*N*-diethylaminophenyl)-12*H*-benzo[*b*]phenothiazine-6,11-quinone 6-Imine from 2-(2′-Aminophenylthio)-6-bromo-5-hydroxy-*N*-(4′-*N*,*N*-diethylaminophenyl)-1,4-naphthoquinone 4-Imine

Larisa V. Ektova* and Fedor A. Zhuravlev

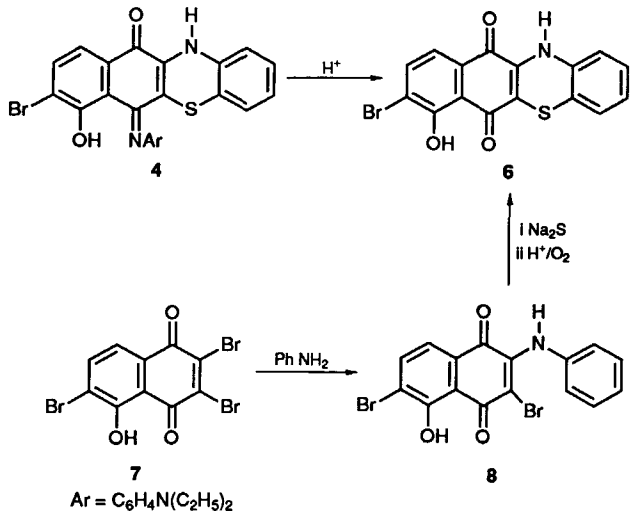
Novosibirsk Institute of Organic Chemistry, Siberian Branch of the Russian Academy of Sciences, 630090 Novosibirsk, Russian Federation. Fax: +7 383 235 4752

Heating 2-(2′-aminophenylthio)-6-bromo-5-hydroxy-*N*-(4′-*N*,*N*-diethylaminophenyl)-1,4-naphthoquinone **1** in DMF–Py leads, along with the product of cyclization at the carbonyl group, to formation of 8-bromo-7-hydroxy-*N*-(4′-*N*,*N*-diethylaminophenyl)-12*H*-benzo[*b*]phenothiazine-6,11-quinone 6-imine **4** *via* a Smiles rearrangement in the starting quinone imine and subsequent cyclization.



Interaction of naphthoquinone with 2-aminothiophenol is known to lead to 2-(2′-aminophenylthio)naphthoquinones which are readily cyclized at the carbonyl group to form angularly condensed benzo[*a*]phenothiazinones.[1,2] To investigate the reactivity of naphthoquinone imines in reactions with *S*-nucleophiles and to synthesize phenothiazinequinone imines we have obtained 2-(2′-aminophenylthio)-6-bromo-5-hydroxy-*N*-(4′-*N*,*N*-diethylaminophenyl)-1,4-naphthoquinone 4-imine **1** by the reaction of 5-hydroxy-2,6-dibromo-*N*-(4′-*N*,*N*-diethylaminophenyl)-1,4-naphthoquinone 4-imine[3] with the zinc salt of 2-aminothiophenol under conditions similar to those described in ref. 2. Compound **1**† was heated in DMF–Py (dimethyl formamide–pyridine) (1:3), (4 h, 125°C), the reaction mixture was poured into water and the precipitate was dried and chromatographed (TLC, SiO_2, benzene). Along with

† Compound **1** m.p. 226–227°C, ^{1}H NMR ($CDCl_3$) δ 1.19 (t, 6H, $1CH_2CH_3$), 3.37 (q, 4H, $2CH_2CH_3$), 4.32 (s, 2H, NH_2), 6.46–7.71 (m, 11H, arom. H) and 16.90 (s, 1H, OH); IR ($CHCl_3$) ν/cm^{-1} 3500, 3380 (NH_2), 1630 (C=O) and 1600 (C=C, C=N); UV λ_{max}/nm (lg ε), ($CHCl_3$) 641 (4.33); *m*/*z* Found/calc. 521.0759/521.0773, yield 88%.



4 6 7 8

2‡ corresponding to the "classical" route (condensation at the carbonyl group) we have isolated in 15% yield a compound that may be identified by spectral data as either structure **4** or **5**. Compound **5** may result from nucleophilic addition of the amino group at the 3- position of the quinonoid ring whereas formation of **4** should be preceded by the Smiles rearrangement in the starting quinone imine **1** (Scheme 1). To identify the structure of the isolated product the latter was hydrolysed to the corresponding quinone. An alternative synthesis of compound **6**§ was carried out using 2,3,6-tribromojuglone **7** as a starting compound (Scheme 2). The reaction of **7** with aniline has been previously[4,5] reported to give 2-anilino-3,6-dibromojuglone **8**. Interaction of **8** with Na_2S in ethanol according to a standard procedure[6] leads to the mercapto derivative **6** whose melting point and IR spectrum are identical to those for the product obtained in hydrolysis. All new compounds gave satisfactory elemental analyses.

The route to **4**¶ seems to involve the Smiles rearrangement of **1** to **3** and subsequent cyclization. Our attempts to isolate **3** were unsuccessful. Formation of phenothiazines accompanied by the Smiles rearrangement is known for *o*-amino- and *o*-acylaminodiaryl sulfides activated to nucleophilic substitution by the presence of electron-withdrawing substituents in the aromatic ring.[7] In our case the Smiles rearrangement is made possible by the clear-cut π-electronic deficiency of the quinone imine nucleus of compound **1**.

The transformation reported in this communication is the first example of the formation of phenothiazine derivatives accompanied by the Smiles rearrangement where the migrant is the quinone imine residue. The scope of the Smiles rearrangment of the quinone imines will be reported later.

References

1 J. A. Van Allan and G. A. Reynolds, *J. Org. Chem.*, 1963, **28**, 1019.
2 K. Hasegawa, M. Sakakibara, T. Ishida and Y. Ueno, *Bull. Chem. Soc. Jpn.*, 1990, **63**, 1467.
3 L. V. Ektova and A. D. Bukhtoyarova, *Sib. Khim. Zh.*, in press (in Russian).
4 R. H. Thomson, *J. Org. Chem.*, 1948, **13**, 870.
5 A. S. Wheeler and J. W. Scott, *J. Am. Chem. Soc.*, 1919, **41**, 833.
6 K. Fries and F. Kerkow, *Liebigs Ann. Chem.*, 1922, **427**, 281.
7 W. E. Truce, E. M. Kreider and W. W. Brand, *Organic Reactions*, J. Wiley, New York, 1970, vol. 18, p. 99.

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‡ Compound **2** m.p. 231–232°C, ^{1}H NMR ($CDCl_3$) δ 1.19 (t, 6H, $2CH_2CH_3$), 3.38 (q, 4H, $2CH_2CH_3$), 6.64–7.93 (m, 11H, arom. H) and 17.85 (s, 1H, OH); IR (KBr) ν/cm^{-1} 1610 (C=C, C=N); UV λ_{max}/nm (lg ε), ($CHCl_3$) 261 (4.17) and 616 (3.81); *m/z* Found/calc. 503.0649/503.0667, yield 60%.

§ Compound **6** {m.p. 313–315°C, ^{1}H NMR ([$^2H_6$]DMSO) δ 6.28–7.94 (m, 6H, arom. H), 9.44 (s, 1H, NH) and 12.92 (s, 1H, OH); IR ($CHCl_3$) ν/cm^{-1} 3310 (NH), 1670 (C=O) and 1610 (C=C, C=N); UV λ_{max}/nm (lg ε), (DMF) 321 (4.36) and 744 (0.346); *m/z* Found/calc. 372.9398/372.9409} prepared by hydrolysis of **4** (48 h, 25°C) in HCl–EtOH (3:1), yield 60%.

¶ Compound **4** m.p. 205–207°C, ^{1}H NMR ($CDCl_3$) δ 1.22 (t, 6H, $2CH_2CH_3$), 3.40 (q, 4H, $2CH_2CH_3$), 7.21 (s, 1H, NH), 6.64–7.70 (m, 10H, arom. H) and 17.23 (s, 1H, OH); IR ($CHCl_3$) ν/cm^{-1} 3360 (NH), 1640 (C=O) and 1600 (C=C, C=N); UV λ_{max}/nm (lg ε), ($CHCl_3$) 258 (4.23), 334 (4.18) and 698 (4.14); *m/z* Found/calc. 519.0592/519.0617.