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LETTERS TO THE EDITOR

The Mannich Bases of Naphthalene Series in the Synthesis of 14*H*-Dibenzo[*a*,*j*]xanthenes

V. A. Osyanin, M. R. Demidov, and Yu. N. Klimochkin

Samara State Technical University, ul. Molodogvardeyskaya 244, Samara, 443100 Russia
e-mail: VOsyanin@mail.ru

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14*H*-Dibenzo[*a*,*j*]xanthenes attracted attention of researchers due to their antitumor activity [1–3]. Numerous examples of the synthesis of such compounds are described mainly by pseudo three-component condensation of 2-naphthol and aromatic aldehydes in the presence of various catalysts [4–7]. However, the conversion of Mannich bases, 2-naphthol derivatives, into 14*H*-dibenzo[*a*,*j*]xanthenes, except for one example involving 1-[(dimethylamino)(phenyl)-methyl]-2-naphthol [8], was not performed. We found that Mannich bases of naphthalene series **Ia–Ie** transformed into dibenzoxanthenes **IIa–IIe** in yields of 36–50% under reflux in acetic acid (Scheme 1).

The mechanism of dibenzoxanthenes formation can be represented as follows. In an acid medium a part of the Mannich base underwent a retro-Mannich reaction to form 2-naphthol. Another part of the Mannich base generated quinone methides [9–12], which underwent the Michael addition with 2-naphthol. A moderate products yields indicated that the two processes occurred to dissimilar degree. The subsequent cyclodehydration led to the formation of dibenzoxanthenes.

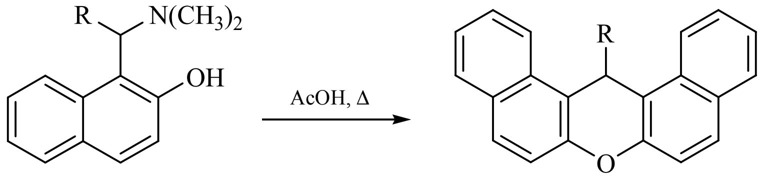
This reaction has no advantages over the previously developed methods of obtaining 14*H*-dibenzo[*a*,*j*]-xanthenes. However, the possibility of its occurrence should be considered when using the Mannich base derived from 2-naphthol under acid conditions [13].

Note that dibenzoxanthenes can be obtained in higher yield by heating in acetic acid an equimolar mixture of 2-naphthol and the Mannich base of naphthalene series. In the case of xanthene **IIb** the yields reached 87%.

In the ^{1}H NMR spectra of the obtained compounds the proton H^{14} resonated as a singlet in the range of 6.49–6.83 ppm. The signals of aromatic protons appeared at 6.65–8.63 ppm. In the ^{13}C NMR spectra the signal of C^{14} atom was observed at 32.4–38.1 ppm. The absence of the proton signals in the areas of >9 ppm in the ^{1}H NMR spectra and absorption bands in the region of the stretching vibrations of the hydroxy group in the IR spectra also confirmed the cyclic structure of the compounds obtained (Scheme 2).

The Mannich bases **Ia–Ie** were prepared according to the known methods [9, 14, 15].

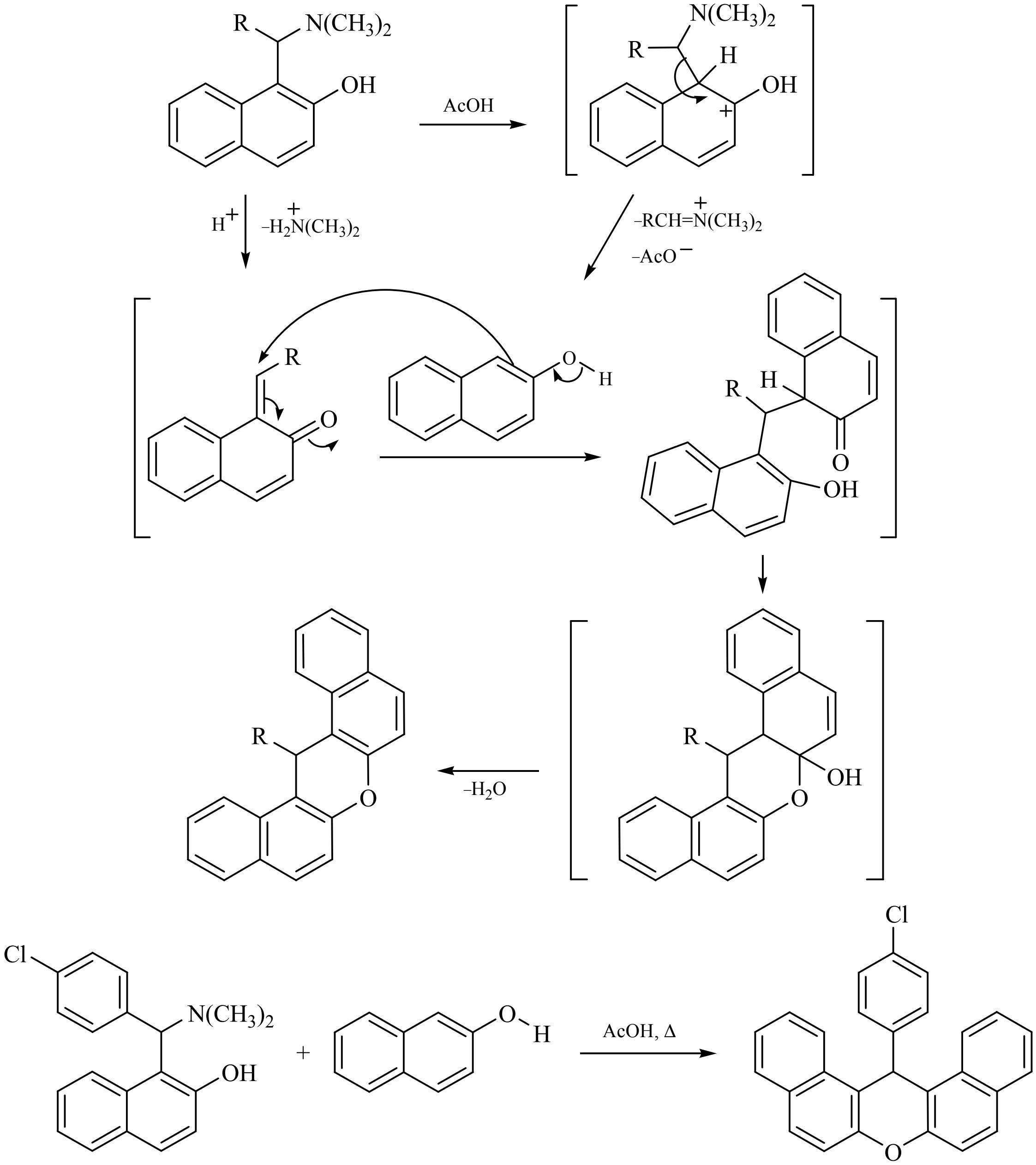
Scheme 1.



Ia–Ie **IIa–IIe**

R = Ph (**a**), 4-$CH_3OC_6H_4$ (**b**), 4-ClC_6H_4 (**c**), 3-$NO_2C_6H_4$ (**d**), 2-thienyl (**e**).

Scheme 2.



Ic **IIc**

General procedure for the preparation of 14*H*-dibenzo[*a*,*j*]xanthenes (IIa–IId). A solution of 2.0 g (6.4 mmol) of the naphthalene-derived Mannich base in 10 mL of acetic acid was heated at reflux for 6 h. The precipitate was filtered off, washed with acetic acid, and purified by recrystallization.

14-Phenyl-14*H*-dibenzo[*a*,*j*]xanthene (IIa). Yield 36%, colorless crystals, mp 183–185°C (AcOH) (mp 184–185°C [16]). IR spectrum (KBr), ν, cm^{-1}: 3073, 3019, 1620, 1593, 1510, 1456, 1400, 1252, 1078, 958, 825, 740, 697. ^1H NMR spectrum ($CDCl_3$), δ, ppm: 6.49 s (1H, H^{14}), 7.00 t.t (1H, H^4_{Ph}, *J* 7.3, 1.4 Hz), 7.16 t.t (2H, H_{Ar}, *J* 7.3, 1.4 Hz), 7.41 d.d.d (2H, H_{Ar}, *J* 8.2, 6.9, 1.4 Hz), 7.49 d (2H, H_{Ar}, *J* 8.7 Hz), 7.55 d.d (2H, H_{Ar}, *J* 8.2, 1.4 Hz), 7.59 d.d.d (2H, H_{Ar}, *J* 8.2, 6.9, 1.4 Hz), 7.79 d (2H, H_{Ar}, *J* 8.7 Hz), 7.82 d (2H, H_{Ar}, *J* 8.2 Hz), 8.40 d (2H, H_{Ar}, *J* 8.2 Hz). ^{13}C NMR spectrum ($CDCl_3$), δ_C, ppm: 38.1 ($C^{14}H$), 117.4 (C), 118.1 (CH), 122.8 (CH), 124.3 (CH), 126.5 (CH), 126.9 (CH), 128.4 (CH), 128.6 (CH), 128.89 (CH), 128.95 (CH), 131.1 (C), 131.5 (C), 145.1 (C), 148.8 (C). Found, %: C 90.46; H 5.11. $C_{27}H_{18}O$. Calculated, %: C 90.47; H 5.06.

14-(4-Methoxyphenyl)-14*H*-dibenzo[*a,j*]xanthene (IIb). Yield 41%, colorless crystals, mp 202–204°C (EtOH) (mp 204–205°C [16]). IR spectrum (KBr), ν, cm^{-1}: 1620, 1593, 1508, 1458, 1433, 1402. 1252, 1179, 1030, 962, 839, 824, 812, 748. ^{1}H NMR spectrum (DMSO-*d*$_6$), δ, ppm: 3.50 s (3H, CH_3O), 6.62 s (1H, H^{14}), 6.65 d (2H, $H^{3',5'}$, *J* 8.7 Hz), 7.42 d.d.d (2H, H_{Ar}, *J* 7.8, 6.9, 0.9 Hz), 7.48 d (2H, $H^{2',6'}$, *J* 8.7 Hz), 7.51 d (2H, H_{Ar}, *J* 8.7 Hz), 7.59 d.d.d (2H, H_{Ar}, *J* 8.2, 6.9, 1.2 Hz), 7.86–7.90 m (4H, H_{Ar}), 8.63 d (2H, H_{Ar}, *J* 8.5 Hz). ^{13}C NMR spectrum (DMSO-*d*$_6$), δ_C, ppm: 36.2 ($C^{14}H$), 55.4 (CH_3), 114.3 (CH), 118.2 (CH, C), 124.0 (CH), 125.0 (CH), 127.4 (CH), 129.1 (CH), 129.36 (CH), 129.45 (CH), 131.2 (C), 131.4 (C), 138.3 (C), 148.4 (C), 158.0 (C). Found, %: C 86.51; H 5.16. $C_{28}H_{20}O_2$. Calculated, %: C 86.57; H 5.19.

14-(4-Chlorophenyl)-14*H*-dibenzo[*a,j*]xanthene (IIc). Yield 50%, pale yellow crystals, mp 287–289°C (AcOH) (mp 290–292°C [16]). IR spectrum (KBr), ν, cm^{-1}: 3071 (CH_{Ar}), 1622, 1593, 1516, 1485, 1458, 1431, 1400, 1354, 1242, 1084, 1015, 961, 833, 806, 741, 709. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 6.72 s (1H, H^{14}), 7.17 d (2H, H_{Ar}, *J* 8.5 Hz), 7.43 t (2H, H_{Ar}, *J* 7.4 Hz), 7.52 d (2H, H_{Ar}, *J* 8.9 Hz), 7.57–7.62 m (4H, H_{Ar}), 7.90 d (4H, H_{Ar}, *J* 8.7 Hz), 8.63 d (2H, H_{Ar}, *J* 8.5 Hz). ^{13}C NMR spectrum ($CDCl_3$), δ_C, ppm: 36.3 ($C^{14}H$), 117.5 (C), 118.2 (CH), 123.9 (CH), 125.2 (CH), 127.6 (CH), 128.9 (CH), 129.2 (CH), 129.8 (CH), 130.2 (CH), 131.2 (C), 131.3 (C), 131.4 (C), 145.0 (C), 148.5 (C). Found, %: C 82.62; H 4.33. $C_{27}H_{17}ClO$. Calculated, %: C 82.54; H 4.36.

Heating of 1 g (3.2 mmol) of the Mannich base **Ic** and 0.46 g (3.2 mmol) of 2-naphthol in 10 mL of acetic acid for 6 h afforded dibenzoxanthene **IIc** in a yield of 1.09 g (87%).

14-(3-Nitrophenyl)-14*H*-dibenzo[*a,j*]xanthene (IId). Yield 44%, yellow crystals, mp 212–213°C (AcOH) (mp 213–215°C [16]). IR spectrum (KBr), ν, cm^{-1}: 3070 (CH_{Ar}), 1619, 1590, 1525 (NO_2), 1499, 1350 (NO_2), 1248, 812, 750. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 6.58 s (1H, H^{14}), 7.27 d.d (1H, $H^{5'}$, *J* 8.2, 7.3 Hz), 7.43 t (2H, H_{Ar}, *J* 7.3 Hz), 7.50 d (2H, H_{Ar}, *J* 8.7 Hz), 7.61 t (2H, H_{Ar}, *J* 7.3 Hz), 7.78–7.89 m (6H, H_{Ar}), 8.29 d (2H, H_{Ar}, *J* 8.7 Hz), 8.41 s (1H, $H^{2'}$). ^{13}C NMR spectrum ($CDCl_3$), δ_C, ppm: 37.8 ($C^{14}H$), 116.0, 118.2, 121.8, 122.1, 122.8, 124.7, 127.3, 129.1, 129.59, 129.64, 131.1, 134.3, 147.0, 148.3, 148.9. Found, %: C 80.23; H 4.28; N 3.52. $C_{27}H_{17}NO_3$. Calculated, %: C 80.38; H 4.25; N 3.47.

14-(2-Thienyl)-14*H*-dibenzo[*a,j*]xanthene (IIe). A solution of 1.0 g (3.5 mmol) of 1-[(dimethylamino)(2-thienyl)methyl]-2-naphthol **Ie** in 10 mL of acetic acid was refluxed for 6 h. The reaction mixture was poured into water, the formed precipitate was filtered off and purified by column chromatography (eluent $CHCl_3$) followed by recrystallization from ethanol. Yield 0.58 g (45%) orange crystals, mp 179–181°C. IR spectrum (KBr), ν, cm^{-1}: 3071 (CH_{Ar}), 1624, 1593, 1516, 1458, 1431, 1400, 1354, 1249, 1029, 960, 813, 744, 705, 609. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 6.69 d.d (1H, H_{thien}, *J* 5.0, 3.7 Hz), 6.79 d (1H, H_{thien}, *J* 3.7 Hz), 6.83 s (1H, H^{14}), 6.94 d.d (1H, H_{thien}, *J* 5.0, 0.9 Hz), 7.43–7.51 m (4H, H_{Ar}), 7.63 d.d.d (2H, H_{Ar}, *J* 8.2, 6.9, 0.9 Hz), 7.82 d (2H, H_{Ar}, *J* 9.2 Hz), 7.87 d (2H, H_{Ar}, *J* 8.2 Hz), 8.39 d (2H, H_{Ar}, *J* 8.2 Hz). ^{13}C NMR spectrum ($CDCl_3$), δ_C, ppm: 32.4 ($C^{14}H$), 116.7 (C), 118.1 (CH), 122.7 (CH), 124.1 (CH), 124.5 (CH), 124.9 (CH), 126.4 (CH), 127.0 (CH), 128.9 (CH), 129.2 (CH), 131.1 (C), 131.3 (C), 148.5 (C), 149.1 (C). Found, %: C 82.44; H 4.37; S 8.70. $C_{25}H_{16}OS$. Calculated, %: C 82.39; H 4.42; S 8.80.

Mass spectra were recorded on a Thermo Finnigan Trace DSQ instrument at the direct input of the sample into the ion source, energy of ionizing electrons 70 eV. ^{1}H, ^{13}C NMR and DEPT spectra were obtained on a JEOL JNM-ECX400 spectrometer (400 and 100 MHz, respectively) in $CDCl_3$ or DMSO-*d*$_6$, internal reference TMS. IR spectra were recorded on a Shimadzu FTIR-8400S spectrometer from KBr pellets. Elemental analysis was performed on a CHNS EuroVector EA-3000 automatic analyzer. Melting points were determined by the capillary method on a PTP-M apparatus.

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