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POLYSUBSTITUTED NAPHTHALENES FROM PHTHALIDE ORTHO ESTERS AND DIENOPHILES

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Several new approaches to the preparation of polysubstituted naphthalenes have appeared recently in the literature, three by Hauser and Rhee (1,2,3) and one by Broom and Sammes (4). Two of these methods (3,4) involve the use of phthalides as key intermediates as does this work. We have found that dienophiles react over a period of six hours in a sealed glass tube in chloroform solution at 140-150° with ortho esters **1**, derived from phthalide or substituted phthalides (5,6). The reaction is considered to take place through the intervention of transient isobenzofuran intermediates **2** generated *in situ* as outlined in Scheme 1 for the reaction with dimethyl acetylenedicarboxylate **3**. Although there is no direct evidence for the generation of intermediates, **2** or **4**, the products, **5a** and **5b**, derived from the reaction **1a** and **1b**, respectively, with **3**, are clearly naphthalenes of the structure shown. Their properties are:

5a; m.p. 85-86°C; IR: $\nu_{max}^{CHCl_3}$ 1735, 1670 cm^{-1}; ^{1}HMR ($CDCl_3$); δ 1.50 (t, 3H, $OCH_2\underline{CH_3}$, J = 6 Hz), 3.95 (s, 6H, 2 x OCH_3), 4.16 (q, 2H, $O\underline{CH_2}CH_3$, J = 6 Hz), 7.40-8.60 (m, 4H, aromatic), and 12.17 (s, 1H, ArOH).

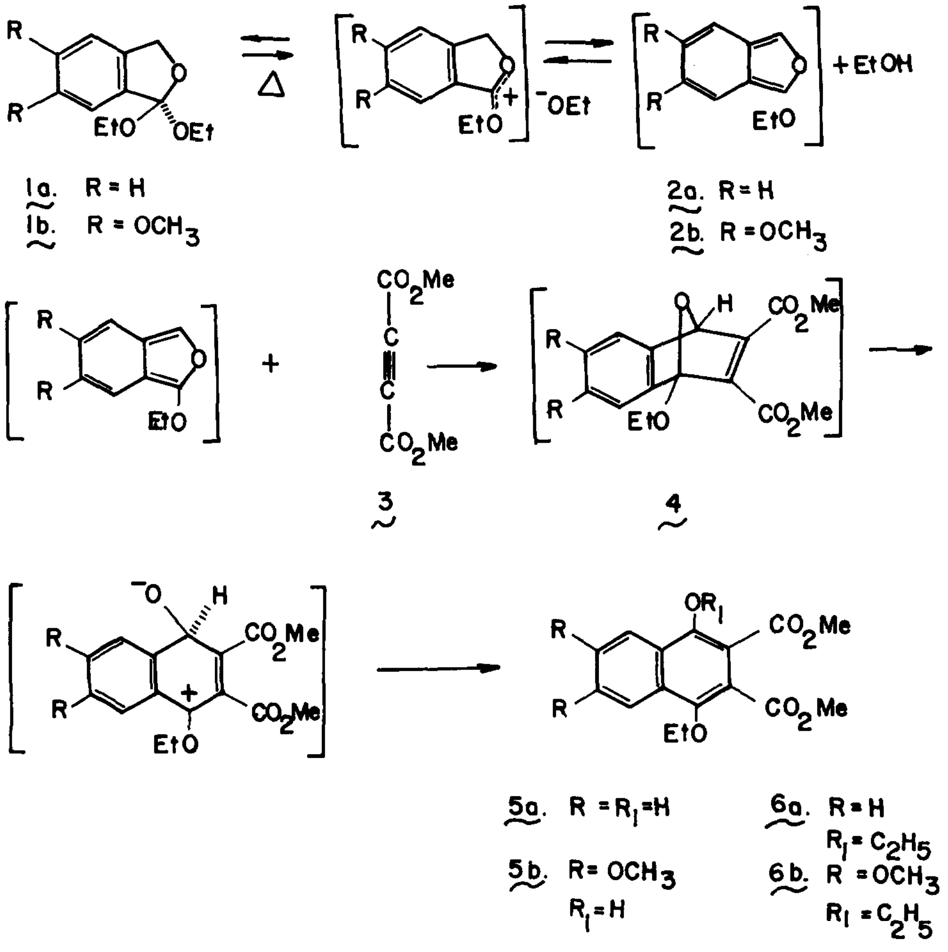
5b; m.p. 149-151°C; IR: $\nu_{max}^{CHCl_3}$: 1735, 1670 cm^{-1}; ^{1}HMR ($CDCl_3$) δ 1.45 (t, 3H, $OCH_2\underline{CH_3}$, J = 6 Hz), 3.98 (s, 2H, 2 x OCH_3), 4.03 (s, 6H, 2 x OCH_3), 4.10 (q, 2H, $O\underline{CH_2}CH_3$, J = 6 Hz), 7.28 (s, 1H, aromatic), 7.66 (s, 1H, aromatic), and 12.10 (s, 1H, ArO$\underline{H}$).

Both **5a** and **5b** were isolated in approximately 50% yield. Ethylation of **5a** and **5b** gave the symmetrical compounds, **6a** and **6b**, respectively. Their properties are:

6a; m.p. 87-89°C; IR $\nu_{max}^{CHCl_3}$; 1735 cm^{-1}; ^{1}HMR ($CDCl_3$): δ 1.40 (t, 6H, 2 x $OCH_2\underline{CH_3}$, J = 6 Hz), 3.88 (s, 6H, 2 x $O\underline{CH_3}$), 4.15 (m, 4H, 2 x $O\underline{CH_2}CH_3$, J = 6 Hz), 7.66 (m, 4H, AA'BB' centred at 7.60 and 8.16.

6b; m.p. 152-153°C; IR $\nu_{max}^{CHCl_3}$: 1735 cm^{-1}; ^{1}HMR: δ 1.45 (t, 6H, $CH_2\underline{CH_3}$, J = 6 Hz), 3.90 (s, 6H, 2 x $O\underline{CH_3}$), 4.01 (s, 6H, 2 x $O\underline{CH_3}$), 4.16 (q, 4H, 2 x $O\underline{CH_2}CH_3$, J = 6 Hz) and 7.47 (s, 2H, aromatic).

In a second series of experiments diethyl maleate **7** was used as dienophile. Two products, **8** and **9**, separated by chromatography, were formed in approximately 10% and 30% yields, respectively, in the reaction between **1a** and **7** in $CHCl_3$ at 170° for 72 hours in a sealed glass tube. A proposal for their formation, based upon the isobenzofuran intermediate, **2a** is given in Scheme 2. Again a tricyclic intermediate is postulated. It is written in the endo form in keeping with the observed predominance of endo isomers in the reaction of isobenzofuran itself with dienophiles (7,8,9). Compound 8 has been converted by ethylation into 9. A multi-step synthesis (10) of 8 has been reported but it was not obtained before in crystalline form. In another study the dimethyl ester of 1-hydroxy-2,3-naphthalenedicarboxylic acid was prepared (11,12). Its spectroscopic properties are very similar to those of 8. The properties of the compounds are:



1a. R = H
1b. R = OCH_3

2a. R = H
2b. R = OCH_3

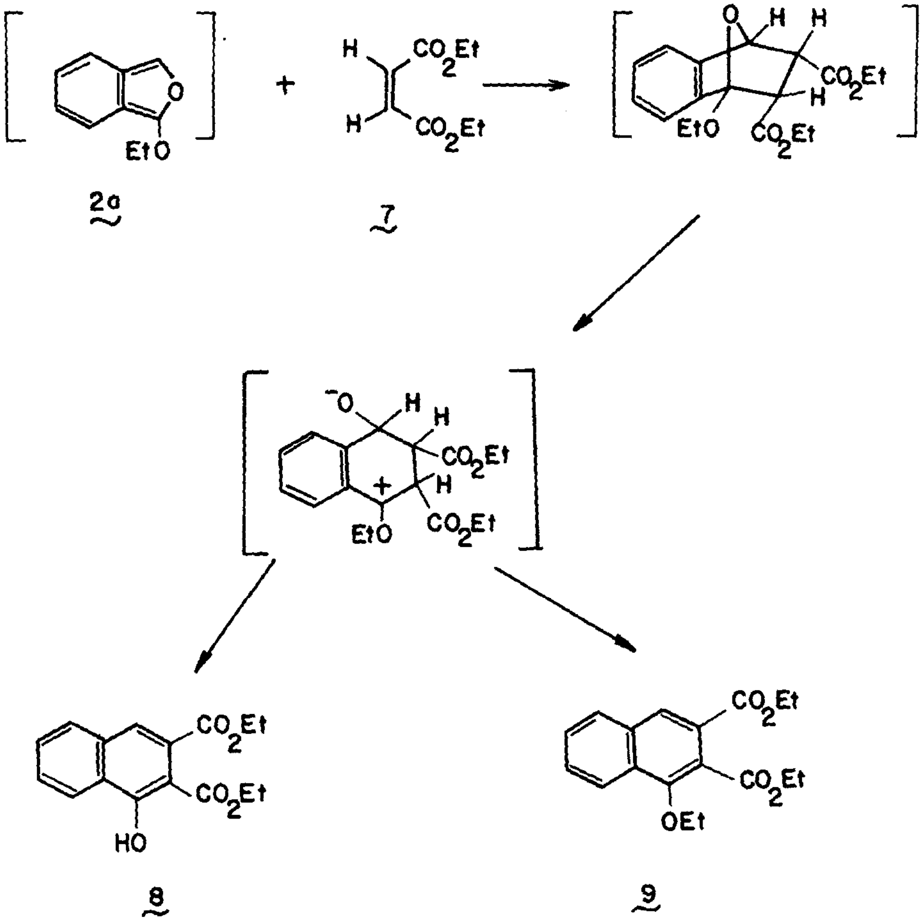
3

4

5a. R = R_1 = H
5b. R = OCH_3, R_1 = H

6a. R = H, R_1 = C_2H_5
6b. R = OCH_3, R_1 = C_2H_5

SCHEME 1



SCHEME 2

$\underset{\sim}{8}$; m.p. 52-54°C; IR: $\nu_{max}^{CHCl_3}$: 1730, 1665 cm^{-1}; ^{1}HMR δ 1.48 (t, 6H, 2 x OCH$_2\underline{CH_3}$, J = 6.0 Hz); 4.40 (q, 2H, -O$\underline{CH_2}$CH$_3$), 4.49 (q, 2H, -O$\underline{CH_2}$CH$_3$), 7.50-8.55 (m, 4H, aromatic $\underline{H}$-5 to H-8), 7.48 (s, 1H, aromatic $\underline{H}$-4), 12.10 (s, 1H, Ar$\underline{OH}$).

$\underset{\sim}{9}$; yellow oil; IR: $\nu_{max}^{CHCl_3}$; 1720 cm^{-1}; ^{1}HMR δ 1.35-1.65 (m, 9H, 3 x OCH$_2\underline{CH_3}$), 4.12-4.70 (m, 6H, 3 x O$\underline{CH_2}$CH$_3$), 7.45-8.25 (m, 4H, aromatic H-5 to H-8), and 8.38 (s, $\underline{1H}$, aromatic H-4).

The scope of this reaction in the synthesis of naphthalenes and other aromatic systems is under active investigation.

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12. The compositions of all compounds were established by high resolution mass spectrometry or by elemental analysis or both.