Methoxycarbonyl Shifts in Diels–Alder Adducts of Methoxycarbonyl-1,4-benzoquinones

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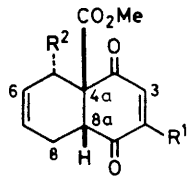
Treatment of 4a,5,8,8a-tetrahydro-4a-methoxycarbonyl-1,4-naphthaquinone with acetic anhydride gives the $\Delta^{8a,1}$ enol acetate, which in the presence of sodium acetate yields 1,4-diacetoxy-5,8-dihydro-6-methoxycarbonylnaphthalene; the 2- and the 5-methyl, and the 2,5-dimethyl homologues behave analogously.

Regiospecific [1,5]-migrations of acyl groups from the 4a-position of Diels–Alder adducts between acyl-1,4-benzoquinones and acyclic 1,3-dienes occur readily in the presence of acetic anhyride.[1] Because of the much lower sigmatropic



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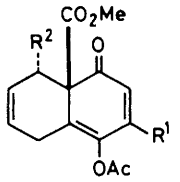

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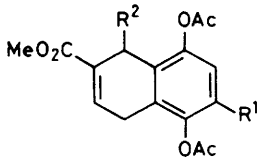

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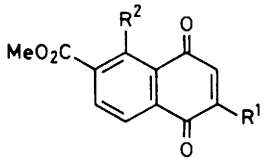

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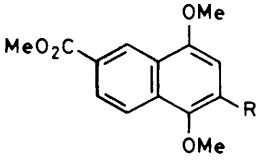
	R^1	R^2
a;	H	H
b;	Me	H
c;	H	Me
d;	Me	Me



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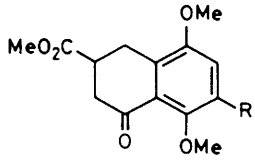

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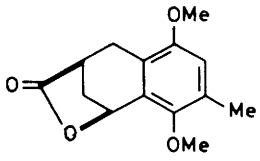

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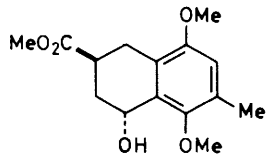

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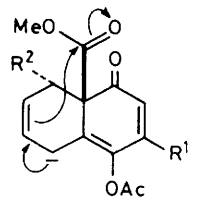
migratory aptitude of the methoxycarbonyl group,[2] treatment of the adduct† (**1a**) with acetic anhydride (140 °C, 48 h) affords only the enol acetate‡[3] (**2a**) [δ ($CDCl_3$, 60 MHz) 6.02 (dd, $J_{2,3}$ 10, $J_{3,8}$ 1 Hz, 3-H) and 6.87 (d, *J* 10 Hz, 2-H)]. However, when (**1a**) or (**2a**) are heated (140 °C, 4 h) in acetic anhydride containing 2% of anhydrous sodium acetate, the methoxycarbonyl group migrates to C-6, giving (**3a**) [m.p. 160.5—161.5 °C; δ ($CDCl_3$, 60 MHz) 2.31 (s, Ac), 2.34 (s, Ac), 3.42 (m, 5-H_2 + 8-H_2), 3.78 (s, CO_2Me), 6.94 (s, 2-H + 3-H), and 7.07 (m, 7-H)] in 51% yield; the methyl homologue (**1b**) similarly affords (**3b**) (m.p. 179—180 °C) in 46% yield.

Selective cleavage (aq. 5% H_2SO_4–MeOH, reflux; 63% yield) of the acetoxy-groups in (**3a**) followed by dehydrogenation (MnO_2[4]–Et_2O, 25 °C, 1 h; 71% yield) gives the 1,4-naphthaquinone (**4a**) [yellow, m.p. 97—98 °C; δ ($CDCl_3$, 60 MHz) 8.13 (dd, J_1 8, J_2 1.5 Hz, 7-H), 8.35 (d, *J* 8 Hz, 8-H),

† All compounds were racemic; only one enantiomer is depicted.

‡ All compounds described have analytical and spectroscopic data in accord with the structures assigned to them. Yields are of isolated products.



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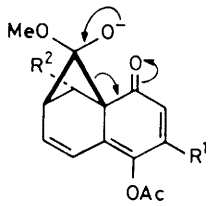

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and 8.68 (d, *J* 1.5 Hz, 5-H)]. Similarly, the methyl homologue (**3b**) gives (**4b**) (yellow, m.p. 149—152 °C).

Dehydrogenation (DDQ–PhH, 80 °C, and MnO_2–PhH, 20 °C, respectively) (DDQ = dichlorodicyanobenzoquinone) of (**3a**) and (**3b**) followed by hydrolysis–methylation (aq. NaOH–Me_2SO_4–dioxan–N_2) affords the corresponding naphthalenes (**5**; R = H) and (**5**; R = Me), identical with materials synthesised as described below.

Stobbe condensation (Bu^tOK–Bu^tOH) of 2,5-dimethoxybenzaldehyde with dimethyl succinate, hydrogenation (Pd–C, MeOH) of the olefinic double bond, and cyclisation (P_2O_5–H_3PO_4, 85 °C, 2.5 h; 75% yield) gave the tetralone (**6**; R = H) (m.p. 132—133 °C). Hydrogenolysis (Pd–C, aq. HCl–MeOH; 51% yield) of the keto-group followed by dehydrogenation (DDQ–PhH, 80 °C; 46% yield) gave the naphthalene (**5**; R = H) [m.p. 115—117 °C; δ ($CDCl_3$, 90 MHz) 8.04 (dd, J_1 9, J_2 2 Hz, 7-H), 8.24 (d, *J* 9 Hz, 8-H), and 8.98 (d, *J* 2 Hz, 5-H)].

A similar sequence starting with 2,5-dimethoxy-4-methylbenzaldehyde gave the tetralone (**6**; R = Me), but attempted hydrogenolysis of the keto-group failed. However, reduction ($NaBH_4$–aq. MeOH) gave a mixture[5] containing, *inter alia*, the lactone (**7**) [21% yield, m.p. 111—113.5 °C; ν_{max} (CCl_4) 1790 cm^{-1}] and the alcohol (**8**) (17% yield, m.p. 111—114 °C). Dehydration (TsOH–PhH, 80 °C; 70% yield) (Ts = tosyl) of (**8**) followed by dehydrogenation (MnO_2–PhH, 20 °C; 77% yield) gave the naphthalene (**5**; R = Me) [m.p. 98—100 °C; δ (C_6D_6, 80 MHz) 8.08 (d, *J* 9 Hz, 8-H), 8.32 (dd, J_1 9, J_2 2 Hz, 7-H), and 9.45 (d, *J* 2 Hz, 5-H)]. Opening (TsOH–PhH, 80 °C) of the lactone (**7**) and methylation (CH_2N_2–Et_2O) of the resulting β,γ-unsaturated carboxylic acid gave the ester, identical with that obtained by dehydration of (**8**).

The (*E*)-penta-1,3-diene adducts (**1c**) and (**1d**) give (**3c**) (85% yield, m.p. 126—128 °C) and (**3d**) (60% yield, m.p. 44—46 °C), respectively, when refluxed with sodium acetate in acetic anhydride. The structure of (**3c**) was determined by *X*-ray crystallographic techniques.[6]

The enol acetate (**2a**) is unchanged after being refluxed in acetic anhydride containing *O*-deuterioacetic acid, but in the presence of sodium acetate the rearrangement product (**3a**) is formed with some incorporation (m.s.) of deuterium. Deuterium is not incorporated into 1,4-diacetoxy-5,8-dihydronaphthalene under similar conditions, suggesting that the more acidic 8-H in the enol acetates is involved in the rearrangements. Thus internal nucleophilic addition of the 8-anion to the methoxycarbonyl group, as (**9**), followed by collapse, as shown, of the intermediate (**10**) with concomitant aromatisation of the dienone ring and subsequent *O*-acetylation and prototropic shift of the olefinic double bond into conjugation with the ester function[7] accounts for the observed products (**3**). The 'abnormal Michael reaction'[8] provides a precedent for the migration step.

Diels–Alder reactions between acyl-1,4-benzoquinones and acylic 1,3-dienes afford tetrahydro-1,4-naphthaquinones [as (**1**)] in which the 4a-acyl groups (formyl, acetyl, benzoyl, and methoxycarbonyl) can now be induced[1,3,9,10] to migrate regiospecifically to the 2-, 3-, and 6-positions, thus providing inter-

mediates for the synthesis of anthracyclines. A 4a-cyano-group will also migrate to C-6.

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