A Simple Multistep Conversion of 1,2-Dihydro-1,1-dimethoxynaphthalen-2-ones to (3,4-Dihydro-3,4-dioxonaphthalen-2-yl)acetates

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Dedicated to Professor *Chun-Chen Liao* (NTHU, Hsinchu, Taiwan) on the occasion of his 65th birthday

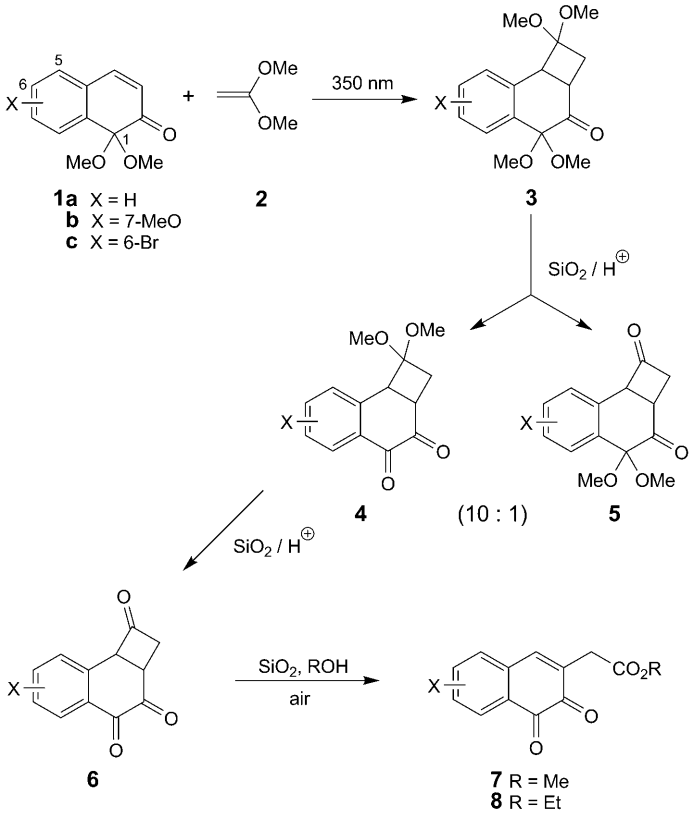
On irradiation ($\lambda = 350$ nm) in the presence of 1,1-dimethoxyethene, naphthalene-1,2-dionemonoacetals **1** regioselectively afford 1,1,4,4-tetramethoxycyclobuta[*a*]naphthalen-3-ones **3**. Sequential deprotection of these bis-acetals first lead to 1,1-dimethoxycyclobuta[*a*]naphthalene-3,4-diones **4** and then to cyclobuta[*a*]naphthalene-1,3,4-triones **6**, which, in turn, are converted into (3,4-dihydro-3,4-dioxonaphthalen-2-yl)acetates **7** by treatment with SiO_2/MeOH/air.

Introduction. – Several 3-alkylnaphthalene-1,2-diones, *e.g.*, *mansonone D*, *hibiscoquinones A–D*, *azanzone A*, or *saprortoquinone*, have been isolated from plants. As direct C,C-linkages at C(3) of a naphthalene-1,2-dione are difficult to achieve, the synthesis of such compounds most often involves the introduction of the alkyl group at C(3) on a (reduced) precursor, usually either a α-tetralone, a naphthalen-1-ol, or a naphthalen-2-ol, followed by oxidation with, *e.g.*, SeO_2, *Fremy*'s salt or Ce^{IV} salts [1]. In contrast, naphthalene-1,2-diols undergo oxidation to naphthalene-1,2-diones already by exposure to air [2], but here again alkylation at C(3) of the parent naphthalene-1,2-diol is unprecedented. We have recently reported that naphthalene-1,2-dione monoacetals **1** undergo efficient [2+2] photocyclodimerization to dibenzobiphenylenediones, which can then be deprotected to afford the corresponding photocyclodimers of naphthalene-1,2-dione itself [3]. Here, we report that compounds **1** undergo regioselective [2+2] photocycloaddition to 1,1-dimethoxyethene, and that the resulting photocycloadducts can be converted into 3-[(methoxycarbonyl)alkyl]naphthalene-1,2-diones under very mild reaction conditions.

Results. – Irradiation of 1,1-dimethoxy-1,2-dihydronaphthalen-2-one (**1a**) in the presence of a tenfold molar excess of 1,1-dimethoxyethene (**2**) regioselectively affords [2+2] photocycloadduct **3a**. On contact for 1 h with slightly acidified SiO_2 [4], the acetal function at the six-membered ring of **3a** is selectively deprotected to afford monoacetal **4a**, with only minor amounts (5–10% rel.) of the isomeric monoacetal **5a** being detectable. Whereas the latter (mono)acetal is not hydrolyzed further, **4a**, on prolongued stirring (8 h), is quantitatively converted to trione **6a**. Finally, **6a**, upon stirring over, now neutral, SiO_2 in the presence of MeOH and air, is converted to

methyl (3,4-dihydro-3,4-dioxonaphthalen-2-yl)acetate (**7a**). The now 1:10 mixture **5a**/**7a** is then easily separated by chromatography, with the overall yield of **7a** from **1a** being 42%. Similarly, **1b** or **1c** can be transformed to **7b** and **7c** in 41 and 35% overall yield, respectively (*Scheme 1*). Finally, ethyl ester **8a** is obtained in similar yields from **6a** by replacing MeOH by EtOH in the second (alcoholysis) step.

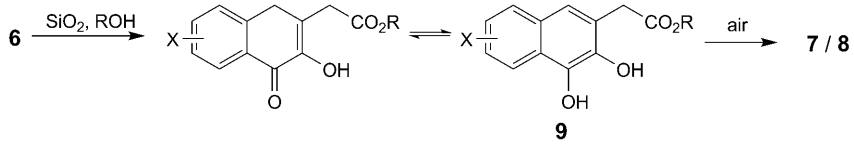
Scheme 1



Discussion. – The regioselective formation of **3** from triplet-excited **1** and (ground state) **2** is typical for cyclohex-2-enones, in general [5], and for naphthalen-2-ones, in particular [6]. In contrast, the chemoselective SiO_2/H^+ deprotection of the acetal function in the six-membered ring (as compared to that on the cyclobutane ring) in photoadducts **3** is surprising, as this acetal group, both in the photocyclodimers of **1** and also in compounds **5**, is stable under these reaction conditions. A synergistic effect between the two acetal functions in compounds **3** could be the reason for this chemoselectivity. The subsequent – slower – conversion of 1,1-dimethoxycyclobutanes **4** to triones **6** by this same reagent is again typical for such cycloadducts of cyclohexenones to **2** [5]. Whereas simple cyclobutanones usually only react with

alcohols to give open-chain esters in the presence of rhodium(I)-phosphine catalysts, ring opening and ester formation promoted by acids have been reported for some cyclobutanones bearing substituents like phenyl or acyl, which apparently facilitate the – first – ring-opening step [7]. It can thus be assumed that triones **6** undergo ring opening and alcoholysis by SiO_2/alcohol to afford the dihydro precursor **9**, which is then readily oxidized to **7** or **8** on contact with air (*Scheme 2*). In conclusion, we have developed an attractive simple method for the synthesis of esters **7** or **8**, which only employs light as energy source, SiO_2 as acid catalyst, and air as oxidant.

Scheme 2



Experimental Part

1. *General.* Dione acetals **1** were synthesized from the corresponding commercially available naphthalen-2-ols according to [8]. 1,1-Dimethoxyethene (**2**) was generously provided by *Wacker Chemie AG* (Munich).

Photolyses were conducted in a *Rayonet RPR-100* photoreactor equipped with (16) 350-nm lamps and solvents of spectrophotometric grade. Column chromatography (CC): silica gel *60* (*Merck*; 230–400 mesh). ^{1}H- and ^{13}C-NMR spectra (including 2D plots): *Bruker WM-500* instrument at 500.13 and 125.8 MHz, resp., in $CDCl_3$, δ in ppm, J in Hz.

2. *Photolyses.* Ar-Degassed solns. of **1** (1 mmol) and **2** (880 mg, 10 mmol) in benzene (5 ml) were irradiated for 18 h up to a total conversion of **1**. After evaporation of the solvent and excess alkene, the crude bis-acetal **3** can either be purified by recrystallization from hexane or directly converted further (*cf.* below).

*1,2,3,4-Tetrahydro-1,1,4,4-tetramethoxy-2a*H,*8b*H-*cyclobuta[*a*]naphthalen-3-one* (**3a**). M.p. 101–104°. ^{1}H-NMR: 7.68 (*d*, J = 8.2, H–C(5)); 7.27 (*m*, H–C(6), H–C(7), H–C(8)); 4.27 (*d*, J = 10.1, H–C(8b)); 3.52 (*s*, Me); 3.50 (*ddd*, J = 5.8, 9.9, 10.1, H–C(2a)); 3.37, 3.02, 2.96 (3*s*, 3 Me); 2.58 (*dd*, J = 5.8, 12.8, H_{endo}–C(2)); 2.28 (*dd*, J = 9.9, 12.8, H_{exo}–C(2)). ^{13}C-NMR: 206.0 (*s*, C(3)); 135.5 (*s*, C(4a)); 133.5 (*s*, C(8a)); 129.4 (*d*, C(7)); 128.4 (*d*, C(6)); 127.1 (*d*, C(5)); 126.1 (*d*, C(8)); 102.0 (*s*, C(1)); 99.0 (*s*, C(4)); 51.2 (*d*, C(8b)); 51.1, 50.2, 50.1, 49.3 (*q*); 34.5 (*d*, C(2a)); 31.7 (*t*, C(2)).

*1,2,3,4-Tetrahydro-1,1,4,4,6-pentamethoxy-2a*H,*8b*H-*cyclobuta[*a*]naphthalen-3-one* (**3b**). M.p. 46–49°. ^{1}H-NMR: 7.22 (*m*, H–C(5), H–C(8)); 6.90 (*d*, J = 8.2, H–C(7)); 4.20 (*d*, J = 10.0, H–C(8b)); 3.81, 3.52 (2 *s*, 2 Me); 3.45 (*ddd*, J = 5.9, 9.9, 10.0, H–C(2a)); 3.35, 3.01, 2.97 (3*s*, 3 Me); 2.53 (*dd*, J = 5.9, 12.5, H_{endo}–C(2)); 2.27 (*dd*, J = 9.9, 12.5, H_{exo}–C(2)). ^{13}C-NMR: 206.0 (*s*, C(3)); 159.2 (*s*, C(6)); 138.1 (*s*, C(4a)); 130.8 (*d*, C(8)); 126.5 (*s*, C(8a)); 115.3 (*d*, C(7)); 111.1 (*d*, C(5)); 102.0 (*s*, C(1)); 99.0 (*s*, C(4)); 54.9 (*q*); 50.8 (*d*, C(8b)); 50.5, 50.2, 49.8, 49.3 (*q*); 34.0 (*d*, C(2a)); 30.9 (*t*, C(2)).

*7-Bromo-1,2,3,4-tetrahydro-1,1,4,4-tetramethoxy-2a*H,*8b*H-*cyclobuta[*a*]naphthalen-3-one* (**3c**). M.p. 77–81°. ^{1}H-NMR: 7.56 (*d*, J = 8.2, H–C(5)); 7.44 (*s*, H–C(8)); 7.41 (*d*, J = 8.2, H–C(6)); 4.20 (*d*, J = 10.0, H–C(8b)); 3.50 (*s*, Me); 3.46 (*ddd*, J = 5.8, 9.9, 10.0, H–C(2a)); 3.35, 3.05, 2.95 (3*s*, 3 Me); 2.52 (*dd*, J = 5.8, 12.8, H_{endo}–C(2)); 2.30 (*dd*, J = 9.9, 12.8, H_{exo}–C(2)). ^{13}C-NMR: 205.8 (*s*, C(3)); 135.9 (*s*, C(4a)); 135.5 (*s*, C(8a)); 133.0 (*s*, C(7)); 132.0 (*d*, C(8)); 129.1 (*d*, C(6)); 128.1 (*d*, C(5)); 102.0 (*s*, C(1)); 99.0 (*s*, C(4)); 50.9 (*d*, C(8b)); 50.8, 50.2, 50.1, 49.3 (4*q*); 34.1 (*d*, C(2a)); 32.1 (*t*, C(2)).

3. *Stepwise Deprotection of* **3a**. To a suspension of SiO_2 (150 mg) in CH_2Cl_2 (1 ml) was added 10% aq. H_2SO_4 (15 µl), and the mixture was stirred for 5 min. Then, a soln. of **3a** (14.6 mg, 5.10^{-5} mol) in

CH_2Cl_2 (1 ml) was added, and the mixture was stirred for 50 min. After filtration of the SiO_2 and evaporation of the solvent, the semi-solid residue was triturated with Et_2O (1 ml). The now solid residue (10.5 mg) contained a 12:1 mixture **4a**/**5a** (from ^{1}H-NMR).

*1,2,3,4-Tetrahydro-1,1-dimethoxy-2a*H*,8b*H*-cyclobuta[*a*]naphthalene-3,4-dione* (**4a**). ^{1}H-NMR: 8.14 (*d*, *J* = 8.2, H–C(5)); 7.62 (*t*, *J* = 8.2, H–C(7)); 7.45 (*m*, H–C(6), H–C(8)); 4.07 (*d*, *J* = 8.2, H–C(8b)); 3.28 (*s*, Me); 3.26 (*ddd*, *J* = 2.2, 8.2, 9.8, H–C(2a)); 2.91 (*s*, Me); 2.59 (*dd*, *J* = 2.2, 12.0, H_{endo}–C(2)); 2.57 (*dd*, *J* = 9.8, 12.0, H_{exo}–C(2)). ^{13}C-NMR: 197.2 (*s*, C(3)); 181.1 (*s*, C(4)); 141.1 (*s*, C(8a)); 137.2 (*s*, C(4a)); 134.1 (*d*, C(7)); 130.1 (*d*, C(5)); 129.2 (*d*, C(6)); 128.3 (*d*, C(8)); 102.1 (*s*, C(1)); 50.3, 50.2 (2*q*); 50.1 (*d*, C(8b)); 49.1 (*d*, C(2a)); 37.1 (*t*, C(2)).

When the same reaction was run for 8 h and worked up as before, a 10:1 mixture (7.9 mg) **6a**/**5a** was obtained.

*2a,8b-Dihydrocyclobuta[*a*]naphthalene-1,3,4(2*H*)-trione* (**6a**). ^{1}H-NMR: 8.15 (*d*, *J* = 8.2, H–C(5)); 7.75 (*t*, *J* = 8.2, H–C(7)); 7.50 (*t*, *J* = 8.2, H–C(6)); 7.48 (*d*, *J* = 8.2, H–C(8)); 4.97 (*ddd*, *J* = 2.8, 3.1, 9.0, H–C(8b)); 3.83 (*ddd*, *J* = 6.3, 9.0, 11.0, H–C(2a)); 3.77 (*ddd*, *J* = 3.1, 11.0, 18.3, H_{exo}–C(2)); 3.51 (*ddd*, *J* = 2.8, 6.3, 18.3, H_{endo}–C(2)). ^{13}C-NMR: 202.1 (*s*, C(1)); 197.1 (*s*, C(3)); 180.9 (*s*, C(4)); 137.1 (*s*, C(8a)); 137.0 (*d*, C(7)); 136.5 (*s*, C(4a)); 131.1 (*d*, C(5)); 130.2 (*d*, C(8)); 130.1 (*d*, C(6)); 64.1 (*d*, C(8b)); 50.1 (*t*, C(2)); 36.4 (*d*, C(2a)).

4. *One-Step Conversion of* **1** *into* **7** (and **5**). The crude bis-acetal **3** obtained by irradiation of **1** (1 mmol; *cf.* above) in CH_2Cl_2 (20 ml) was added to a suspension of SiO_2 (4.0 g) and 10% aq. H_2SO_4 (0.4 ml) in CH_2Cl_2 (20 ml), and the mixture was stirred at r.t. for 9 h. After filtration from the SiO_2, the solvent was evaporated, and the residue was redissolved in CH_2Cl_2 (15 ml) containing SiO_2 (1.5 g) and MeOH (1.5 ml), and the mixture was stirred at r.t. for 20 h. After filtration from SiO_2 and evaporation of the solvent, the residue was purified by CC (CH_2Cl_2/MeOH 99:1) to afford as first fraction traces of **5** and thereafter methyl ester **7** as main product. 1,2,3,4-Tetrahydro-4,4-dimethoxy-2a*H*,8b*H*-cyclobuta[*a*]-naphthalene-1,3-diones **5**, which eluted first, were obtained as light yellow semisolid oils in quantities between 5 and 8 mg (2–3% overall yield) and characterized by NMR (signals for aromatic H- and C-atoms omitted).

Data of **5a**: ^{1}H-NMR: 4.50 (*d*, *J* = 9.9, H–C(8b)); 3.65 (*ddd*, *J* = 6.5, 9.9, 10.0, H–C(2a)); 3.37 (*dd*, *J* = 9.9, 18.2, H_{exo}–C(2)); 3.36 (*dd*, *J* = 6.5, 18.2, H_{endo}–C(2)); 3.35, 3.19 (2*s*, 2 Me). ^{13}C-NMR: 203.1 (*s*, C(1)); 202.9 (*s*, C(3)); 99.1 (*s*, C(4)); 65.5 (*d*, C(8b)); 50.8, 50.2 (2*q*); 47.1 (*t*, C(2)); 33.5 (*d*, C(2a)).

Data of **5b**: ^{1}H-NMR: 4.28 (*d*, *J* = 9.9, H–C(8b)); 3.81 (*s*, Me); 3.62 (*ddd*, *J* = 6.5, 9.9, 10.0, H–C(2a)); 3.37 (*dd*, *J* = 9.9, 18.2, H_{exo}–C(2)); 3.36 (*dd*, *J* = 6.5, 18.2, H_{endo}–C(2)); 3.35, 3.19 (2*s*, 2 Me). ^{13}C-NMR: 203.1 (*s*, C(1)); 202.9 (*s*, C(3)); 99.1 (*s*, C(4)); 65.5 (*d*, C(8b)); 50.8, 50.2 (2*q*); 47.1 (*t*, C(2)); 33.5 (*d*, C(2a)).

Data of **5c**: ^{1}H-NMR: 4.82 (*d*, *J* = 9.8, H–C(8b)); 3.68 (*ddd*, *J* = 6.5, 9.9, 10.0, H–C(2a)); 3 3.39 (*dd*, *J* = 9.9, 18.2, H_{exo}–C(2)); 3.36 (*dd*, *J* = 6.5, 18.2, H_{endo}–C(2)); 3.34, 3.17 (*s*, Me). ^{13}C-NMR: 202.9 (*s*, C(1)); 202.1 (*s*, C(3)); 99.1 (*s*, C(4)); 64.6 (*d*, C(8b)); 50.8, 50.2 (2*q*); 47.1 (*t*, C(2)); 33.5 (*d*, C(2a)).

Methyl (3,4-Dihydro-3,4-dioxonaphthalen-2-yl)acetate (**7a**). Orange solid (97 mg, 42%). M.p. 128–130°. UV (MeCN): λ_{max} 410 nm. ^{1}H-NMR: 8.08 (*d*, *J* = 8.2, H–C(5)); 7.64 (*t*, *J* = 8.2, H–C(7)); 7.48 (*t*, *J* = 8.2, H–C(6)); 7.38 (*s*, H–C(1)); 7.32 (*d*, *J* = 8.2, H–C(8)); 3.72 (*s*, Me); 3.49 (*s*, 2 H). ^{13}C-NMR: 181.0 (*s*, C(3)); 179.1 (*s*, C(4)); 171.1 (*s*, CO_2); 144.1 (*d*, C(1)); 136.1 (*d*, C(7)); 135.1 (*s*, C(4a)); 134.3 (*s*, C(8a)); 133.2 (*s*, C(2)); 130.7 (*d*, C(5)); 130.6 (*d*, C(6)); 129.2 (*d*, C(8)); 52.2 (*q*); 34.1 (*t*).

Methyl (3,4-Dihydro-6-methoxy-3,4-dioxonaphthalen-2-yl)acetate (**7b**). Dark red solid (107 mg, 41%). M.p. 147–149°. UV (MeCN): λ_{max} 471 nm. ^{1}H-NMR: 7.58 (*d*, *J* = 1.5, H–C(5)); 7.31 (*s*, H–C(1)); 7.23 (*d*, *J* = 8.2, H–C(8)); 7.12 (*dd*, *J* = 1.5, 8.2, H–C(7)); 3.90, 3.72 (2*s*, 2 Me); 3.44 (*s*, 2 H). ^{13}C-NMR: 180.5 (*s*, C(3)); 179.2 (*s*, C(4)); 170.2 (*s*, CO_2); 161.2 (*s*, C(6)); 144.1 (*d*, C(1)); 133.1 (*s*, C(4a)); 131.5 (*d*, C(8)); 131.1 (*s*, C(2)); 128.1 (*s*, C(8a)); 121.5 (*d*, C(7)); 114.8 (*d*, C(5)); 55.3, 52.1 (2*q*); 34.8 (*t*).

Methyl 7-Bromo-(3,4-dihydro-3,4-dioxonaphthalen-2-yl)acetate (**7c**). Dark yellow solid (108 mg, 35%). M.p. 135–138°. UV (MeCN): λ_{max} 401 nm. ^{1}H-NMR: 7.94 (*d*, *J* = 8.2, H–C(5)); 7.63 (*d*, *J* = 8.2, H–C(6)); 7.51 (*s*, H–C(8)); 7.32 (*s*, H–C(1)); 3.73 (*s*, Me); 3.48 (*s*, 2 H). ^{13}C-NMR: 180.1 (*s*, C(3)); 178.7 (*s*, C(4)); 171.1 (*s*, CO_2); 142.1 (*d*, C(1)); 136.0 (*s*, C(4a)); 134.5 (*s*, C(2)); 133.1 (*d*, C(6)); 132.1 (*d*, C(8)); 131.8 (*d*, C(5)); 131.1 (*s*, C(8a)); 129.5 (*s*, C(7)); 51.5 (*q*); 33.5 (*t*).

5. *One-Step Conversion of* **1a** *to* **8a**. As described above, but replacing MeOH by EtOH both in the alcoholysis step and in the eluent mixture. CC afforded first **5a** (6 mg), and then *ethyl (3,4-dihydro-3,4-*

dioxonaphthalen-2-yl)acetate (**8a**; 92 mg, 39%). Orange solid. M.p. 81–83° (80–81° according to [9]). UV (MeCN): λ_{max} 411 nm. ^{1}H-NMR: 8.08 (*d*, *J* = 8.2, H–C(5)); 7.64 (*t*, *J* = 8.2, H–C(7)); 7.48 (*t*, *J* = 8.2, H–C(6)); 7.38 (*s*, H–C(1)); 7.32 (*d*, *J* = 8.2, H–C(8)); 4.23 (*q*, 2 H); 3.48 (*s*, 2 H); 1.29 (*t*, Me). ^{13}C-NMR: 181.0 (*s*, C(3)); 179.1 (*s*, C(4)); 171.1 (*s*, CO_2); 144.1 (*d*, C(1)); 136.1 (*d*, C(7)); 135.1 (*s*, C(4a)); 134.3 (*s*, C(8a)); 133.2 (*s*, C(2)); 130.7 (*d*, C(5)); 130.6 (*d*, C(6)); 129.2 (*d*, C(8)); 62.1 (*t*); 34.1 (*t*); 14.5 (*q*).

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Received April 23, 2008