177. Synthesis of 2,3,4,6,7,8-Hexahydro-5*H*-1-benzopyran-5-ones and 3-(6-Oxo-1-cyclohexenyl)alkanoic Acids by Reduction of 4,6,7,8-Tetrahydro-2*H*-1-benzopyran-2,5(3*H*)-diones

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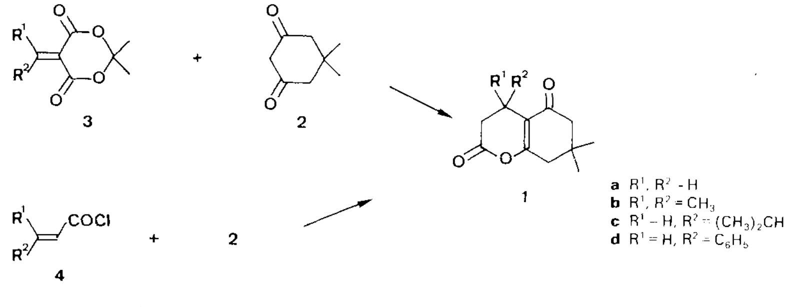
Comparative results on the reduction of 4,6,7,8-tetrahydro-7,7-dimethyl-2*H*-1-benzopyran-2,5(3*H*)-diones **1** are reported. Hydride reduction ($LiAlH_4$ in Et_2O or $NaBH_4$ in i-PrOH) affords 2,3,4,6,7,8-hexahydro-5*H*-1-benzopyran-5-ones **5** in 30–60% isolated yield. Photochemical reduction of **1b** and **1d** (direct irradiation at λ = 300 or 254 nm in i-PrOH, or sensitized irradiation in acetone/i-PrOH or benzene/i-PrOH) gives 3-(6-oxo-1-cyclohexenyl)alkanoic acids **6** in 50–80%, while **1c** affords the isomeric 3-(4,4-dimethyl-6-oxo-1-cyclohexenyl)-4-methyl-4-pentenoic acid (**9**) in 73% isolated yield. Electrochemical reduction (Hg, CH_3CN, $Bu_4N^+ClO_4^-$, −2.6 V *vs.* Ag/Ag^+) requires more than 4 Farad/mol for the consumption of **1** without any major product being detected.

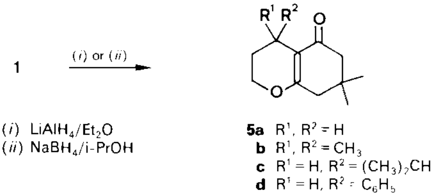
In the course of our investigations on the photochemistry and electrochemistry of 2-cycloalkenones substituted with anionic leaving groups, we have communicated results on the reductive cleavage of the C-halogen bond in several fluoro-, chloro-, and bromo-2-cyclohexenones [1–5]. Here we report results on the reduction of 4,6,7,8-tetrahydro-2*H*-1-benzopyran-2,5(3*H*)-diones **1** which are easily synthesized from dimedone (**2**) and either alkylidene-substituted *Meldrum*'s acids **3** [6] or acryloyl chlorides **4** [7] [8] and represent suitable model compounds for 3-acyloxy-2-cyclohexenones (*Scheme 1*).

Scheme 1



We first studied the reaction of **1a–d** with $LiAlH_4$ and $NaBH_4$. Both hydrides, the first in either Et_2O or THF and the second in i-PrOH afford 2,3,4,6,7,8-hexahydro-5*H*-1-benzopyran-5-ones **5** selectively in reasonable to good yields (*Scheme 2*). This method thus represents an efficient way for the synthesis of compounds **5** which up to now were only accessible in moderate yields, *e.g.* **5a** from dimedone and 1,3-diiodopropane [9] or

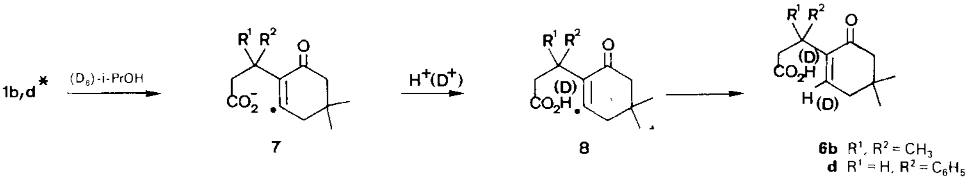
Scheme 2



2,4-diphenyl-substituted compounds by catalytic reduction of 4,6,7,8-tetrahydro-5*H*-benzopyran-5-ones [10] albeit the products were only characterized by elemental analysis. Reduction of the parent 4,6,7,8-tetrahydro-2*H*-1-benzopyran-2,5(3*H*)-dione with Zn/Hg is reported to give octahydrocoumarine [11].

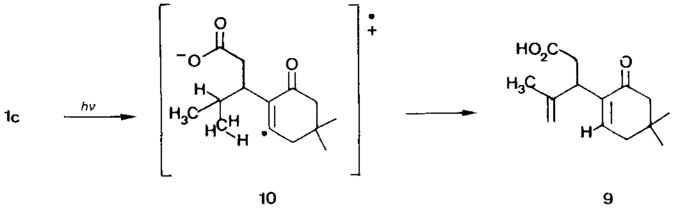
We next investigated the behaviour of compounds **1** on irradiation (λ = 254 or 300 nm) in i-PrOH. At both wavelengths, compounds **1b** and **1d** afford 3-(6-oxo-1-cyclohexen-1-yl)alkanoic acids **6** in good yields. The same products **6** are obtained in sensitized irradiations using acetone (λ = 300 nm) or benzene (λ = 254 nm) indicating that the reduction proceeds from the T_1-state of **1**. No major product(s) are obtained from **1a** under all these reaction conditions, although the rate of photodecomposition of **1a** corresponds to the rate of photoreduction of **1b** and **1d**. Irradiation in (D_8)-i-PrOH gives compounds **6** with the deuterium label on C(β) of the 2-cyclohexenone. Most probably, the reaction path **1**→**6** consists in electron transfer from i-PrOH to excited **1** [12] to give the ring-open anion radical **7** followed by proton transfer (formation of radical **8**) and subsequent disproportionation of the radical pair (*Scheme 3*). Direct H-abstraction by excited **1** at C(β) [13] would give an acyloxy radical, a species known to loose CO_2 very rapidly [14].

Scheme 3



In contrast, irradiation of **1c** under all conditions mentioned above, also in (D_8)-i-PrOH, gives only the isomeric carboxylic acid **9** in 73% yield. The same product **9** is again obtained selectively in various other solvents. This intramolecular rearrangement **1c**→**9** can be explained by the sequence in *Scheme 4*, wherein excitation leads to intermediate **10** which then gives **9** *via* proton and H-atom transfer. No competition by intermolecular reduction is observed.

Scheme 4



Finally, we examined the cathodic behaviour of compounds **1**. Cyclic voltammetry (Hg, CH_3CN, $Bu_4N^+ClO_4^-$) shows the electron transfer to **1** to be irreversible at scan rates up to 2000 mV/s, indicating the C–O bond cleavage to be a very fast process. In contrast, in the voltammograms of **5**, an anodic peak is observed at scan rates above 100 mV/s which is consistent with the expected much longer lifetime of the anion radical of **5** as compared to **1**. Preparative electrolyses of **1a-d** with a Hg pool as cathode and a Pt wire as anode in a divided cell at – 2.6 V *vs.* Ag/Ag^+ led to slow decomposition of starting material without formation of low molecular weight products. Coulometry shows that more than 4 Farad/mol are required to consume 80–90% of starting material. As 2-cyclohexenones are known to be reduced at less cathodic potentials ($E_{1/2} \approx -2.2$ V *vs.* the same reference electrode [15]), a plausible explanation for these findings is that **1** is reduced to a product containing a 2-cyclohexenone ring, eventually **6**, which is immediately further reduced to give only polymeric material. The spectroscopic data of the products are summarized in *Table 1* and the electroanalytical data in *Table 2*.

Table 1. *Spectroscopic Data of Reduction Products* **5**, **6**, *and* **9**

Compound[a])	IR (CCl_4)	^{1}H-NMR ($CDCl_3$)	^{13}C-NMR ($CDCl_3$)	MS
5a	1660, 1630	4.10 (*m*, 2 H); 2.23 (*m*, 6 H); 1.86 (*m*, 2 H); 1.01 (*s*, 6 H)	196.8, 169.1, 110.0, 67.2, 50.5, 42.4, 31.8, 28.3, 21.5, 17.3	180 ($M^{+\cdot}$), 124
5b	[b]) 1680, 1660	4.01 (*m*, 2 H); 2.18 (*s*, 2 H); 2.16 (*s*, 2 H); 1.54 (*m*, 2 H); 1.23 (*s*, 6 H); 0.96 (*s*, 6 H)	197.1, 168.8, 118.2, 64.1, 52.2, 42.9, 34.4, 31.0, 29.2, 28.1, 27.6	208 ($M^{+\cdot}$), 193
5c	[b]) 1640, 1620	4.14 (*m*, 2 H); 2.53 (*m*, 1 H); 2.29 (*s*, 2 H); 2.25 (*s*, 2 H); 1.89 (*m*, 2 H); 1.70 (*m*, 1 H); 1.07 (*s*, 6 H); 0.89 (*d*, 6 H)	197.2, 169.1, 113.5, 64.7, 51.1, 42.8, 32.2, 31.6, 30.7, 28.6, 28.2, 23.4, 20.9, 19.6	222 ($M^{+\cdot}$), 179
5d	[c]) 1660, 1625	7.23 (*m*, 5 H); 4.14 (*ddd*, *J* = 11.2, 4.0, 2.4); 4.00 (*m*, C_6H_5CH); 3.88 (*ddd*, *J* = 13.0, 11.2, 2.4); 2.40, 2.26 (*AB*, *J* = 17.0); 2.28, 2.20 (*AB*, *J* = 16.2); 2.10 (*m*, 1 H); 1.83 (*m*, 1 H); 1.10 (*s*, 3 H); 1.02 (*s*, 3 H)		256 ($M^{+\cdot}$), 241
6b	1710, 1685	6.57 (*t*, *J* = 4.2); 2.82 (*s*, 2 H); 2.28 (*d*, *J* = 4.2, 2 H); 2.24 (*s*, 2 H); 1.24 (*s*, 6 H); 1.02 (*s*, 6 H)		224 ($M^{+\cdot}$), 122
6d	[c]) 1715, 1680	7.22 (*m*, 5 H); 6.58 (*t*, *J* = 5.1); 4.47 (*t*, *J* = 7.0); 2.94 (*dd*, *J* = 17.0, 8.3); 2.82 (*dd*, *J* = 17.0, 8.3); 2.26 (*s*, 2 H); 2.25 (*d*, *J* = 5.1, 2 H); 1.03 (*s*, 6 H)		272 ($M^{+\cdot}$), 83
9	1710, 1675	6.62 (*t*, *J* = 4.0); 4.89 (*s*); 4.80 (*s*); 3.83 (*t*, *J* = 8.0); 2.61 (*d*, *J* = 8.0, 2 H); 2.30 (*s*, 2 H); 2.30 (*s*, 2 H); 1.68 (*s*, 3 H); 1.02 (*s*, 6 H)		236 ($M^{+\cdot}$), 41

[a]) All new compounds gave satisfactory elemental analyses.
[b]) Liquid film.
[c]) In KBr.

Table 2. *Cyclovoltammetric Data of* **1** *and* **5**a)

	1a	**1b**	**1c**	**1d**	**5a**	**5b**	**5c**	**5d**
E_{Pc}	−2.54	−2.59	−2.52	−2.54	−3.01	−3.06	−3.04	−3.05
E_{Pa}						−2.94	−2.90	
i_{Pa}/i_{Pc}						0.15	0.10	

a) Measured in CH_3CN with $Bu_4N^+ClO_4^-$ ($5 \cdot 10^{-1}$ M) as electrolyte *vs.* Ag/Ag^+ (10^{-1} M), sweep rate 100 mV/s; peak potentials in V.

Experimental Part

General. See [2]. Benzopyrandiones **1a** [8], **1b** [7], **1c** and **1d** [6] were synthesized according to the literature. Solvents used for photolyses were of spectral grade. (D_8)-i-PrOH was purchased from *Aldrich*. Irradiations were performed with Ar-degassed solns. in a *Rayonet RPR-100* photoreactor using either 254-nm or 300-nm lamps.

*5*H-*1-Benzopyran-5-ones* **5**. *a) With* $LiAlH_4$. A mixture of $5 \cdot 10^{-3}$ mol of **1** and $5 \cdot 10^{-3}$ mol of $LiAlH_4$ in 80 ml of Et_2O is refluxed for 2 h. After addition of 250 ml of 5% HCl, separation of the Et_2O phase, 3 further extractions with 50 ml of Et_2O, washing of the combined org. phases with aq. NaCl soln., drying over $MgSO_4$, and evaporation, the residue is purified by chromatography (SiO_2, CH_2Cl_2) to give *2,3,4,6,7,8-hexahydro-7,7-dimethyl-5*H-*1-benzopyran-5-on* (**5a**, 30%), *2,3,4,6,7,8-hexahydro-4,4,7,7-tetramethyl-5*H-*1-benzopyran-5-one* (**5b**, 50%), and *2,3,4,6,7,8-hexahydro-4-isopropyl-7,7-dimethyl-5*H-*1-benzopyran-5-one* (**5c**, 53%; all liquids) or by recrystallization from Et_2O to give *2,3,4,6,7-hexahydro-7,7-dimethyl-4-phenyl-5*H-*1-benzopyran-5-one* (**5d**, 65%; m.p. 83–84°).

b) With $NaBH_4$. A soln. of $5 \cdot 10^{-3}$ mol of **1** and $5 \cdot 10^{-3}$ mol of $NaBH_4$ in 100 ml of i-PrOH is refluxed for 2 h. After addition of 200 ml of 10% HCl soln. and extraction with CH_2Cl_2, workup as above affords **5** in slightly lower yields (30–50%).

Acids **6b** *and* **6d**. A soln. of 10^{-3} mol of **1b** or **1d** in 2 ml of i-PrOH is irradiated ($\lambda = 254$ nm) for 48 h. After evaporation, chromatography (SiO_2, CH_2Cl_2/MeOH 99:1→95:5) affords *3-(4,4-dimethyl-6-oxo-1-cyclohexenyl)-3-methylbutyric acid* (**6b**, 70%, m.p. 90–92°) and *3-(4,4-dimethyl-6-oxo-1-cyclohexenyl)-3-phenylpropionic acid* (**6d**, 49%, oil), respectively.

3-(4,4-Dimethyl-6-oxo-1-cyclohexenyl)-4-methyl-4-pentenoic Acid **9**. From **1c**, as above, yield 73%, m.p. 94–96°.

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