23. Chemistry of Succinyl Succinic Acid Derivatives. Part IV[1]) On the Hydrogenation of Diethyl Succinyl Succinate

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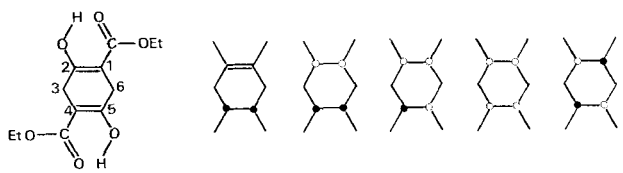
Summary

The preparation of 2 new tetrasubstituted cyclohexane isomers by hydrogenation of diethyl succinyl succinate is reported. A route for their formation is postulated.

Introduction. – Diethyl succinyl succinate (DESS) exists in the crystal in its enol form [2]. This reacts in the solid in a photochemical [2+2]-cycloaddition, proving the 1,4-cyclohexadiene character of the molecule [3]. The reactivity of the unsaturated moiety of succinyl succinate in its ground state has now been investigated by hydrogenation of DESS in solution[2]).

Results and discussion. – DESS was hydrogenated in solution in the presence of *Raney*-nickel or -cobalt, giving 3 main products. Upon absorption of 1 equiv. H_2 a product of Rf 0.55[3]) was obtained, showing a UV. absorption at $\lambda_{max}^{EtOH} = 250$ nm ($\varepsilon = 9500$). As DESS absorbs in the same region with $\varepsilon = 20{,}000$ [3], this hydrogenation product must have lost half of the original light-absorbing chromophores. By IR., NMR. and mass spectra analyses the product showed to be ethyl 2,5-dihydroxy-

Scheme 1. *DESS and stereoisomers of its hydrogenation products*



DESS 1 2 3 4 5

[1]) Part III, s. [1].

[2]) Earlier work has mentioned a single hydrogenation product of undefined configuration [4]. The planar structure of DESS permitted, however, 2 isomers at least to be expected.

[3]) See experimental part.

Table 1. *^{1}H-NMR. absorptions of the cyclohexane moieties of tetrahydro-DESS-isomers* (Scheme 2) (270 MHz in $CDCl_3$ + TMS)

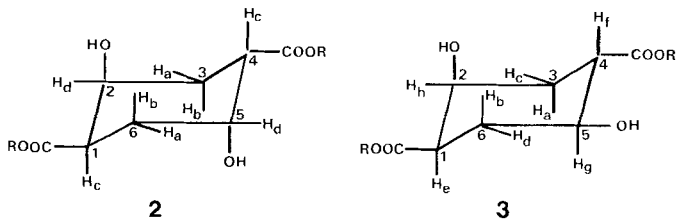
Isomer	Proton	ppm	Multiplicity	Coupling constants in Hz
2	a	1.85	$d \times t$	Ha, Hb – 13.5; Ha, Hc 4.0; Ha, Hd 3.5
	b	2.45	$d \times d \times d$	Ha, Hb – 13.5; Hb, Hc 8.0; Hb, Hd 4.0
	c	2.65	$d \times t$	Hc, Hb 8.0; Hc, Ha 4.0; Hc, Hd 4.0
	d	3.95	br. *s*	Hd, Ha 3.5; Hd, Hb 4.0; Hd, Hc 4.0
3	a	1.51	$t \times d$	Ha, Hc – 13.5; Ha, Hf 13.0; Ha, Hh 2.5
	b	1.92	*qa*	Hb, Hd – 12.8; Hb, He 12.5; Hb, Hg 10.0
	c	2.26	$d \times t$	Ha, Hc – 13.5; Hc, Hf 3.75; Hc, Hh 3.25
	d	2.14	$d \times t$	Hb, Hd – 12.8; Hd, He 4.0; Hd, Hg 5.0
	e	2.48	$d \times qa$	Hb, He – 12.5; He, Hd 4.0; He, Hh 2.0
	f	2.81	$t \times d$	Ha, Hf 13.0; Hf, Hg 10.0; Hf, Hc 3.75
	g	3.84	$t \times d$	Hf, Hg 10.0; Hb, Hg 10.0; Hg, Hd 5.0
	h	4.27	br. *s*	Hh, Hc 3.25; Hh, He 2.0; Hh, Ha 2.5

cyclohex-1-ene-1,4-dicarboxylate (**1**, *Scheme 1*), in accord with the hydrogenation of one double bond of DESS.

Upon further hydrogenation **1** disappeared and 2 additional products were formed. One, of Rf 0.46, corresponded with ethyl, dihydroxycyclohexane dicarboxylate, resulting from reduction of both double bonds of DESS. Assuming a chair configuration for the molecule [5], axial-axial and axial-equatorial interactions evident in the ^{1}H-NMR. spectrum *(Table 1)* were in accord with a symmetric *cis-trans-cis* cyclohexane isomer. Centrosymmetry was also evident from the ^{13}C-NMR. spectrum, which gave 3 signals for the 6 cyclohexane carbon atoms *(Table 2)*. The slight deviation of the coupling constants from the perfect chair form may, however, point to a flattening of the cyclohexane ring due to residual hydrogen bonding between hydroxyl and adjacent carbonyl group. Hence the final structure assignment for the product as ethyl 2-*c*,5-*t*-dihydroxycyclohexane-1-*r*-4-*t*-dicarboxylate (**2**, *Scheme 2*).

The other product obtained by exhaustive hydrogenation of the cyclohexadiene moiety had an Rf of 0.40 and it differed from **2** in its NMR. spectra. The ^{1}H-NMR. was in good agreement with the chair form of a 1,2-*cis* 4,5-*trans* substituted DESS, as evident from the coupling constants in *Table 1*. The ^{13}C-NMR. showed 6 lines for the various cyclohexane carbon atoms *(Table 2)*, as required for an asymmetric isomer. Additional spectroscopic and elemental evidence permitted its characterization as ethyl 2-*c*,5-*c*-dihydroxycyclohexane-1-*r*-4-*t*-dicarboxylate (**3**, *Scheme 2*).

Scheme 2. *Chair configurations of tetrahydro-DESS-isomers* **2** *and* **3**



2 **3**

Table 2. *^{13}C-NMR. chemical shifts of the cyclohexane moiety of tetrahydro-DESS-isomers* (Scheme 2) (ppm at 25.2 MHz in $CDCl_3$)

Carbon atom	1	2	3	4	5	6
2	44.0	67.2	30.6	44.0	67.2	30.6
3	45.2	64.4	32.9	44.4	69.9	29.9

The lower Rf values of the hydrogenation products relative to that of DESS (Rf 0.75), is attributed to the increase of the polarity due to the deminution of the hydrogen bonding between the hydroxyl and the adjacent ester group[4]).

The catalytic reduction of the stabilized cyclohexadiene moiety of DESS was expected to proceed by *cis*-addition of hydrogen to the enolic double bonds, as far as they were chemically available. Whereas compounds **1** and **2** were indeed produced *(Scheme 1)*, lack of detectable amounts of an all-*cis* isomer **4** is most likely due to prohibitive steric hindrance required for such configuration. The isomer **3** actually arose from isomer **2**. Thus, when pure isomer **2** was subjected to the same hydrogenation conditions, a mixture containing both **2** and **3** was obtained, whereas similar treatment of the isomer **3** did not lead to isomer **2**. A reduction scheme is therefore anticipated in which DESS is hydrogenated in a *cis* manner, leading *via* **1** to isomer **2**. By a reversible hydrogen atom abstraction on the surface of the catalyst [7] the production of a planar sp^2 free radical is assumed, whose further protonation leads to the thermodynamically preferred *cis-trans-trans* isomer **3**.

The kinetically favoured isomer **2** and the thermodynamically favoured isomer **3** were the only hydrogenation end-products isolated, no evidence having been found for the production of isomer **5**. These, however, together with dihydro-DESS **1** obtained under deficient hydrogen conditions, proved the availability of the enol double bonds in alkyl succinyl succinates for chemical reaction in the ground state.

Experimental Part

A 0.2M solution of DESS[5]) in ethanol was pressurized with H_2 at 120 at. and 100° in the presence of 15 weight% of *Raney*-cobalt. The catalyst was filtered off and the solution evaporated under reduced pressure, to give a viscuous oil which solidified upon standing. The mixture was separated by column chromatography on silica gel H with acetone/petroleum ether and could be followed by TLC. on silica gel with acetone/petroleum ether 3:2.

First, compound **2** was eluted, (3 parts), m.p. 64–67, which had no maxima in the UV. and showed IR. absorptions at 3420 (OH) and at 1710 cm^{-1} (ester), and the following mass fragmentation pattern (CH 7, 10eV, 300 μ Amp., sample temperature 20°)[6]): 261 (16, MH^+ H), 242 (57, $M-H_2O$). 232 (14, $M-C_2H_4$), 224 (9, $M-2\ H_2O$), 214 (61, $242-C_2H_4$ or $M-C_2H_5OH$), 197 (54, $242-C_2H_5O$), 196 (53,

[4]) Elimination of the unsaturation brings the hydroxyl away from the transesterification axis of the neighbouring ester group. In contrast to DESS, its hydrogenation products can therefore undergo polycondensation [6]. Whereas isomers **2** and **3** are expected to give cross-linked polyesters, dihydro-DESS **1** should lead to a linear polyester with chelating properties.

[5]) Diethyl succinyl succinate was kindly donated by *Lonza AG*.

[6]) Data given are mass numbers, relative intensities and tentative assignments of principal fragments.

242 – C_2H_5OH or 214 – H_2O), 168 (62, 214 – C_2H_5OH or 196 – C_2H_4)[7]), 150 (53, 168 – H_2O), 122 (60, 150 – CO or 150 – C_2H_4), 117 (67), 113 (59), 101 (99), 73 (100). – The compound had a molecular weight, by vapour phase osmometry, of 260.

$C_{12}H_{20}O_6$ (260.29) Calc. C 55.50 H 7.70% Found C 55.58 H 7.76%

Next, compound **3** was eluted (1 part). Its IR. and mass spectra were similar to those of isomer **2**. The elemental analysis gave C 55.64 H 7.79%.

By stopping the hydrogenation at 50% H_2 uptake, the reaction mixture contained, in addition to the unconverted DESS and isomers **2** and **3**, also dihydro-DESS **1**.

This substance had m.p. 56° and an IR. absorption band at 3420 cm^{-1} (OH). The ^{1}H-NMR. (100 MHz, in $CDCl_3$ + TMS) gave 2*t* at 1.3 ppm (CH_3–CH_2, 6 H), a *m* at 2.1–3.0 (cyclohexane methylenes and C*H*–COOR, 5 H), a broad absorption at 3.1 (OH, 1 H), a *m* at 3.5–3.9 (C*H*–OH, 1 H) a *qa* at 4.1 (OCH_2CH_3, 4 H) and an absorption at 12.2 ppm (enol). – Its mass spectrum (CH 7, 70 eV, 300 μAmp., sample temperature 90°) showed the following fragmentation pattern[6]): 259 (6, MH^+), 258 (2, M^+), 240 (38, $M - H_2O$), 213 (20, $M - {}^{\cdot}OC_2H_5$), 194 (22, 240 – HOC_2H_5), 167 (88, 240 – ${}^{\cdot}COOC_2H_5$), 121 (100, 167 – HOC_2H_5).

Hydrogenation in presence of *Raney*-nickel as catalyst gave the same results as with *Raney*-cobalt. Use of Pd/C or Pt/C at 1–4 at. and at 50–70° produced the same isomers, but with conversions of about 10% as compared with quantitative conversions found for the former conditions.

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