The Photocyclodimers of 2,3-Dihydro-2,2-dimethyl-4*H*-pyran-4-one

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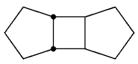
Dedicated to Professor *Heinz Heimgartner* on the occasion of his 65th birthday

On irradiation (350 nm) in benzene solution, dihydropyranone **3** affords predominantly (75%) the *cis-anti-cis HH*-dimer **4**, but in smaller amounts (12%) also dimer **5**, wherein one of the six-membered rings is *trans*-fused to the (central) cyclobutane ring. The constitution and configuration of **5** was fully elucidated by NMR-analysis. On contact with SiO_2, **5** isomerizes quantitatively to the *cis-anti-cis HT*-dimer **7**, the structure of which was established by X-ray crystal-structure determination.

1. Introduction. – Sesquiterpenes display a large variety of substructures. Some of them contain a cyclobutane ring, *e.g.*, those bearing the (bicyclic) *caryophillane*, or the (tricyclic) *tritomarane*, *protoilludane*, *panasinsane*, and *bourbonane* skeletons [1]. While the latter skeleton type contains a tricyclo[5.3.0.0^{2,6}]decane structural unit, there are no examples of naturally occuring compounds exhibiting the homologous tricyclo[6.4.0.0^{2,7}]dodecane substructure. Formally, these tricycles result from [2+2] cyclodimerization of two cyclopentene or cyclohexene units, respectively. Whereas the C_{10} parent hydrocarbon **1** occurs in only two diastereoisomeric forms, *i.e.*, **1a** and **1b**, there are five possible diastereoisomers, *i.e.*, **2a**–**2e**, for the C_{12} parent hydrocarbon **2**. Among them, the doubly *trans*-fused dimers **2c** and **2d** are of special interest with respect to the strain incorporated in such molecules [2][3]. Interestingly, the *trans-anti-trans* dimer **2c** is a major product in the sensitized photocyclodimerization of cyclohexene, whereas the *trans-syn-trans* dimer **2d** remains unknown [4][5].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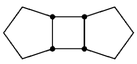
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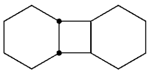
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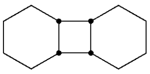
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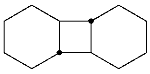
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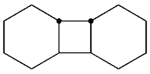
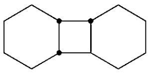
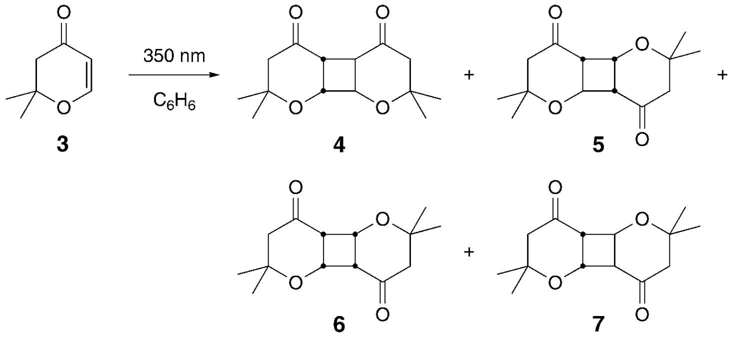

2d


2e

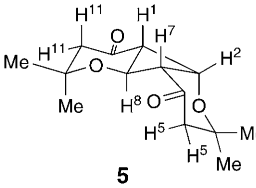
Insertion of a trigonal planar C-atom into the six-membered ring leads to a slight increase in strain energy, *e.g.*, 2.1 kcal/mol for cyclohexanone as compared to cyclohexane [6]. It is, therefore, not surprising that, in the photocyclodimerization of cyclohex-2-enones, *cis*-fused tricyclic dimers are formed predominantly. Nevertheless, a *trans* ring fusion has been assigned to a minor dimer of the (parent) cyclohex-2-enone, as it showed twelve distinct peaks in its ^{13}C-NMR spectrum, although its structure was not assigned [7]. Similarly, it has been reported that a minor dimer of 4,4- dimethylcyclohex-2-enone isomerized to a – now – *cis*-fused tricyclic dimer, and, therefore, it was tentatively concluded, that it may be a *trans*-fused dimer [8]. Here, we now report on the first full spectroscopic characterization (^{1}H- and ^{13}C-NMR) of such a *trans*-fused tricyclo[6.4.0.0^{2,7}]dodecanedione.

2. Results. – Long time ago, we had reported [9] that irradiation of 2,3-dihydro-2,2-dimethyl-4*H*-pyran-4-one (**3**) in either MeCN or hexane affords the *cis-anti-cis* dimer **4** selectively (> 95%). We have now repeated the same experiment in benzene at different enone concentrations and found that, on irradiation (350 nm) of a 1M solution of **3** in this solvent, the relative amount of **4** formed was reduced to 75%, while three other tricyclic dimers **5**–**7** were formed in appreciable amounts of 12, 9, and 4%, respectively (*Scheme*).

Scheme



The structure elucidation of dimers **5**–**7** was facilitated by the fact that dimer **4** was only slightly soluble in Et_2O. Trituration of the original dimer mixture with this solvent allowed the separation of *ca.* 2/3 of **4** by filtration, affording a new mixture with the (relative) composition 40 : 27 : 22 : 11 of the same four dimers. Attempted separation of this mixture by column chromatography on SiO_2 afforded fractions which contained mixtures of **4**, **6**, and **7** without any clue of dimer **5**. Indeed, stirring of this mixture over SiO_2, both in the absence or presence of traces of Et_3N, altered the composition of the mixture to 40 : 0 : 22 : 38 without any loss of material, indicating that **5** was quantitatively converted to **7** under these conditions. From this mixture, both dimers **6** and **7** were successfully isolated by column chromatography on SiO_2 with CH_2Cl_2/MeOH 99 : 1 as eluent, whereby **7** exhibited a just slightly higher R_f value than **4**, while the R_f value of **6** was distinctly lower. The structure assignment for dimers **4**, **6**, and **7** was confirmed by X-ray crystal-structure determinations, whereas the assignment of a *trans*-ring fusion in **5** (*Figure*) resulted from both the observation of its isomerization to **7** and its NMR data.



5

Figure. *Selected NMR data of* **5**. ^{1}H-NMR Coupling constants J in Hz: $H^1,H^2 = 4.3$, $H^2,H^7 = 4.5$, $H^7,H^8 = 8.2$, $H^1,H^8 = 10.9$, $H^5,H^5 = 14.8$, $H^{11},H^{11} = 13.5$. ^{13}C-NMR Chemical shifts in $CDCl_3$ in ppm: C(1) 56.1, C(2) 71.1, C(4) 78.1, C(5) 52.2, C(6) 205.5, C(7) 53.1, C(8) 76.2, C(10) 82.1, C(11) 54.2, C(12) 199.2.

3. Discussion. – Usually, the variation of the (isotropic) solvent in enone photocyclodimerization reactions only moderately affects the regio- and stereochemical outcome of such reactions, whereas zeolites have been shown to exert a more significant influence [7]. It is, thus, noteworthy that the substitution of, *e.g.*, hexane by benzene induces a quite important change in the photocyclodimerization product ratio of oxaenone **3**, as the dielectric constants of these two solvents are quite similar. A plausible explanation for the differing product distribution in these bimolecular reactions could be related to the difference in viscosities, $\eta = 0.313$ cp for hexane and 0.649 cp for benzene. The advantage of using oxaenone **3** as a 'model' cyclohex-2-enone is straightforward, regarding the simplicity of the first order ^{1}H-NMR spectra of the photodimers. Identification of the H-atoms adjacent to both the O-atom and the C=O group in the six-membered rings is unambiguous, and subsequent C,H-correlation spectra then allow a full assignment of the their constitution and (relative) configuration. Nonetheless, the structures of **4**, **6**, and **7** have been additionally confirmed by X-ray crystal-structure determination. The ^{1}H-NMR data of the two six-membered rings in dimer **5** reflect the expected differences between a *trans*- and a *cis*-fused bicyclo[4.2.0]octan-2-one [10]. Indeed, the vicinal coupling constant for the H-atoms at the fusion site is larger, and the magnitude of the geminal coupling constant of the CH_2 H-atoms vicinal to the C=O group is smaller in the *trans*-fused moiety. Similarly, the ^{13}C-NMR data support this assignment, as all tetrahedral C-atoms in the *trans*-fused moiety resonate at lower field than the corresponding C-atoms in the *cis*-fused moiety, whereas the opposite is observed for the C=O C-atoms [10]. In conclusion, we have, for the first time, identified and fully characterized spectroscopically a *trans-cis*-fused tricyclic cyclohexenone photodimer. Isolation of such compounds by conventional column chromatography is totally hampered by the ease of isomerization to a (less strained) *cis-cis*-fused diastereoisomer. We are, therefore, now studying the photodimerization of the analogous thia-enone, 2,3-dihydro-2,2-dimethyl-4*H*-thiopyran-4-one, hoping that the corresponding – more flexible – *trans*-fused six-membered thia-cyclic moiety will be more resistant towards isomerization under these conditions.

Experimental Part

1. *General.* Photolyses were run 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 two-dimensional plots): in $CDCl_3$ at 500.13 and 125.8 MHz, resp., δ in ppm, J in Hz. GC/EI-MS: at 70 eV; 30-m *SE-30* cap. column. X-Ray analyses were run on an *Bruker APEX CCD* three-circle diffractometer at 153 K with MoK_α radiation ($\lambda = 0.71073$ Å).

2. *Starting Materials. 2,3-Dihydro-2,2-dimethyl-4*H*-pyran-4-one* (**3**) was synthesized according to [11].

3. *Prep. Photolysis.* An Ar-degassed soln. of **3** (504 mg, 4 mmol) in benzene (5 ml) was irradiated for 72 h up to 90% conversion. After evaporation of the solvent, ^{1}H-NMR analysis of the residue (504 mg, mixture *A*) indicated the formation of four products **4**–**7** in a 75:12:9:4 ratio. The residue was stirred at r.t. in Et_2O (5 ml) for 10 min and then filtered to afford 252 mg (50%) pure *1α,2β,7β,8α-4,4,11,11-tetramethyl-3,12-dioxatricyclo[6.4.0.0*^{2,7}*]dodecane-6,9-dione* (**4**). M.p. 134–136°. ^{1}H-NMR: 4.36, 3.26 (*AA'XX'*, $J_{AX}=5.2$, $J_{AA'}=8.4$, $J_{AX'}=-1.1$, $J_{XX'}=-0.5$, 4 H); 2.57, 2.34 (*AB*, $J=15.9$, 4 H); 1.37, 1.23 (2*s*, 4 Me). ^{13}C-NMR: 206.5 (*s*); 77.1 (*s*); 74.2 (*d*); 51.2 (*t*); 47.2 (*d*); 31.1, 25.0 (*q*, Me). MS: 252 (0.05, M^+), 127 (30), 111 (40), 82 (55), 71 (60), 41 (100).

^{1}H-NMR Analysis of the filtrate (mixture *B*) after evaporation of the solvent (148 mg) indicated a 40:27:22:11 composition ratio of products **4**–**7**. This residue was redissolved in CH_2Cl_2 (5 ml), and SiO_2 (800 mg) was added, and the mixture was stirred at r.t. for 4 h. ^{1}H-NMR Analysis of the residue (mixture *C*) after filtration and evaporation of the solvent indicated a 40:0:22:38 composition, *i.e.*, **5** was quantitatively converted to **7**. The following spectroscopic data for *1α,2α,7α,8β-4,4,10,10-tetramethyl-3,9-dioxatricyclo[6.4.0.0*^{2,7}*]dodecane-6,12-dione* (**5**) were directly from product mixture *B*. ^{1}H-NMR: 4.80 (*dd*, $J=4.3$, 4.5); 4.62 (*dd*, $J=8.2$, 10.9); 2.94 (*dd*, $J=4.5$, 8.2); 2.87 (*dd*, $J=4.3$, 10.9); 2.62 (*d*, $J=14.8$); 2.38 (*d*, $J=13.5$, 2.29 (*d*, $J=14.8$); 2.29 (*d*, $J=13.5$); 1.42, 1.412, 1.38, 1.17 (4*s*, 4 Me). ^{13}C-NMR: 205.5 (*s*); 199.2 (*s*); 82.1 (*s*); 78,1 (*s*); 76.2 (*d*); 71.1 (*d*); 56.1 (*d*); 54.2 (*t*); 53.1 (*d*); 52.2 (*t*); 31.5, 30.5, 25.2, 24.3 (4*q*, 4 Me). MS: 252 (25, M^+), 155 (90), 99 (75), 43 (100).

Mixture *C* (148 mg) was subjected to CC (2.5 × 60-cm column; CH_2Cl_2/MeOH 99:1). The first fraction (12 mg, 2.4%) contained pure *1α,2β,7β,8α-4,4,10,10-tetramethyl-3,9-dioxatricyclo[6.4.0.0*^{2,7}*]-dodecane-6,12-dione* (**7**). M.p. 144–146°. ^{1}H-NMR: 4.86, 3.01 (*AA'XX'*, $J_{AX}=6.3$, $J_{AA'}=0.0$, $J_{AX'}=4.1$, $J_{XX'}=0.0$, 4 H); 2.45, 2.38 (*AB*, $J=16.4$, 4 H); 1.34, 1.28 (2*s*, 4 Me). ^{13}C-NMR: 207.5 (*s*); 77.1 (*s*); 71.7 (*d*); 52.2 (*t*); 52.1 (*d*); 30.5, 26.1 (2*q*, 4 Me). MS: 252 (0.05, M^+), 127 (80), 71 (100).

The second fraction (101 mg, 20%) consisted of a 2:3 mixture of **7** and **4**. The third fraction (15 mg, 3%) contained pure *1α,2α,7α,8α-4,4,10,10-tetramethyl-3,9-dioxatricyclo[6.4.0.0*^{2,7}*]dodecane-6,12-dione* (**6**). M.p. 154–156°. ^{1}H-NMR: 4.76, 3.09 (*AA'XX'*, $J_{AX}=5.6$, $J_{AA'}=0.0$, $J_{AX''}=5.7$, $J_{XX'}=0.0$, 4 H); 2.57, 2.35 (*AB*, $J=16.1$, 4 H); 1.33, 1.13 (2*s*, 4 Me). ^{13}C-NMR: 206.2 (*s*); 76.2 (*s*); 71.2 (*d*); 54.1 (*t*); 47.2 (*d*); 30.5, 25.1 (2*q*, 4 Me). MS: 252 (0.05, M^+), 127 (35), 126 (40), 111 (45), 71 (100).

X-Ray Crystal-Structure Determination of **4**1). Pale colorless needles (0.38 × 0.07 × 0.05 mm) from Et_2O, $C_{14}H_{20}O_4$, M_r 252.30: monoclinic, space group *C*2/*c*, $Z=4$, $a=11.687(5)$, $b=19.846(8)$, $c=6.440(3)$ Å, $\beta=117.699(7)°$; $V=1322.5(9)$ Å^3, $D_x=1.267$ g cm^{-3}.

X-Ray Crystal-Structure Determination of **6**1). Pale colorless blocks (0.45 × 0.25 × 0.20 mm) from Et_2O, $C_{14}H_{20}O_4$, M_r 252.30: monoclinic, space group $P2_1/c$, $Z=4$, $a=10.363(3)$, $b=8.067(2)$, $c=16.340(4)$ Å, $\beta=98.415(5)°$; $V=1351.3(6)$ Å^3, $D_x=1.240$ g cm^{-3}.

X-Ray Crystal-Structure Determination of **7**1). Pale colorless blocks (0.19 × 0.17 × 0.05 mm) from Et_2O, $C_{14}H_{20}O_4$, M_r 252.30: monoclinic, space group $P2_1/c$, $Z=4$, $a=11.078(2)$, $b=10.904(2)$, $c=12.427(2)$ Å, $\beta=118.826(11)°$; $V=1315.1(4)$ Å^3, $D_x=1.274$ g cm^{-3}.

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1) CCDC-613920, CCDC-613921, and CCDC-613922 contain the supplementary crystallographic data for **4**, **6**, and **7**, respectively. This data can be obtained free of charge *via* www.ccdc.cam.ac.uk/data_request/cif.

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