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Photochemical formation of [4.4.4](1,3,5)cyclophanes from 1,3,5-tris(3-phenylpropenoyl)benzenes

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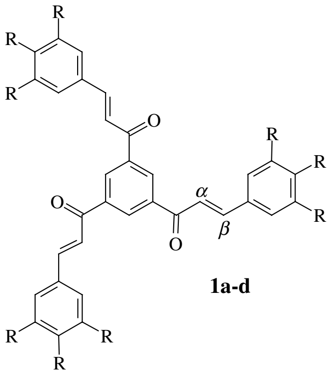
Abstract—Irradiation of 1,3,5-tris(3-phenylpropenoyl)benzene (**1a**) yields in solution a dimer **2a** by a threefold head-to-head/*anti* [2π+2π]cycloaddition. The stereochemistry of this [4.4.4](1,3,5)cyclophane was determined by ^{1}H and ^{13}C NMR studies including NOE measurements and a calculation of the AA′MM′ spin pattern of the methine protons. In contrast to the solution photochemistry, which is presumably controlled by the arrangement of an excimer, the irradiation in the crystalline state leads by a topochemical control to a dimer **3a**, which contains a single four-membered ring.

Cyclodimerization processes of chalcones (1,3-diphenylpropen-1-ones) belong to the best known photoreactions since the work of Stobbe in the 20's of the previous century.[1,2] Numerous cyclobutanes with two aryl and two aroyl substituents have been prepared on this route.[3–20] The regio- and stereoselectivities of the involved [2π+2π]cycloadditions depend on the reaction conditions; the process has been studied in solution, in the molten and in the crystalline state.

We report here on the photochemistry of 1,3,5-tris(3-phenylpropenoyl)benzenes (**1a–d**), which afford a simple preparative entry to [4.4.4](1,3,5)cyclophanes. The starting compounds **1a–d** can be prepared by threefold condensation reactions of 1,3,5-triacetylbenzene with the corresponding benzaldehydes (Scheme 1).[21] This process seems to be facile; however, insoluble polycondensation products are often the major products—particularly, when the electrophilicity of the aldehydes is lowered by electron-releasing substituents. According to NOE measurements, the cisoid conformations of (*E*,*E*,*E*)-**1a–d** are preferred.

The parent compound **1a** ($\lambda_{max} = 326$ nm) shows fast photochemical *E*/*Z* isomerization reactions, which lead to a photostationary state of four stereoisomers. According to the ^{1}H NMR signals, the ratio obtained for a 2.9×10^{-2} M solution of **1a** in CD_2Cl_2 irradiated with a Hanovia—450 W middle-pressure mercury lamp with Pyrexfilter ($\lambda \geqslant 290$ nm) amounted to (*E*,*E*,*E*):(*E*,*E*,*Z*):(*E*,*Z*,*Z*):(*Z*,*Z*,*Z*) = 2:4:8:5 (Scheme 2). Protonation of the isomeric mixture induces the reverse reaction, in which the *all*-(*E*) configuration is so enriched that the other isomers are below the detection limit in the ^{1}H NMR spectrum.



1a-d

1	R	Yield[%]	M.p. [°C]
a[21]	H	51	179
b	OCH_3	3	208
c	OC_6H_{13}	18	173
d	$OC_{12}H_{25}$	30	wax

Scheme 1. 1,3,5-Tris(3-phenylpropenoyl)benzenes **1a–d**.[22]

Keywords: Cyclophanes; Photodimerization; Photoisomerization.

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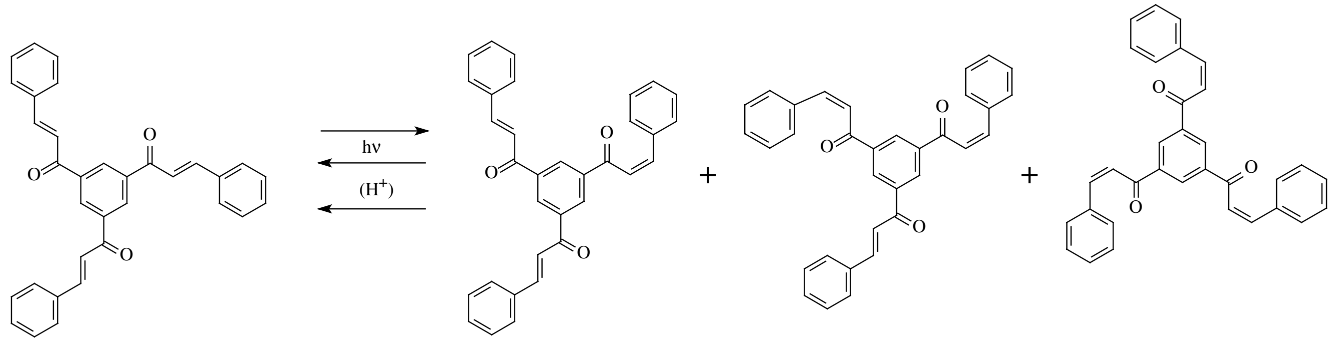


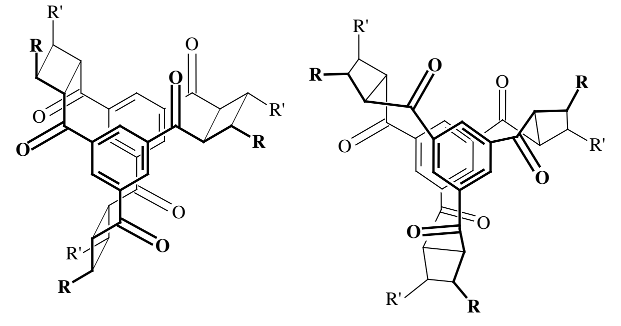
(E,E,E)-**1a** *(E,E,Z)*-**1a** *(E,Z,Z)*-**1a** *(Z,Z,Z)*-**1a**

Scheme 2. Photoisomerization of **1a**.

Table 1. Possible threefold photodimerizations of **1a**/**1a**′

Variant	Involved conformers	Regioselectivity	Stereoselectivity of the two heads	Point group of the product	Spin system of 4-ring protons
A	**1a**′+**1a**′	Head-to-head	*syn*	C_{3h}	AA′MM′
B	**1a**′+**1a**′	Head-to-tail	*syn*	D_3	A_2M_2
C	**1a**+**1a**′	Head-to-tail	*syn*	C_{3h}	ABM_2/A_2M_2[a]
D	**1a**+**1a**	Head-to-head	*syn*	C_{3h}	AA′MM′
E	**1a**+**1a**	Head-to-head	*anti*	D_3	AA′MM′

[a] Molecular dynamics, which are fast in terms of the NMR time scale would transfer the ABM_2 spin pattern into an A_2M_2.



D E

Scheme 3. Structure D (head-to-head/*syn* dimer with C_{3h} symmetry, **2a**: R = R′ = C_6H_5) and structure E (head-to-head/*anti* dimer with D_3 symmetry, **2a**: R = R′ = C_6H_5).

Irradiation of **1a** in more concentrated solutions (1.4×10^{-1} M in CH_2Cl_2) yields a selective dimerization of (*E*,*E*,*E*)-**1a**. The product **2a** (81%) contains three four-membered rings in a C_3 arrangement. Although the carbonyl groups and the phenyl substituents of each arm of (*E*,*E*,*E*)-**1a** are in **2a** still in *trans* position, there are several possible structures for **2a**. The *regiochemistry* of the cyclodimerization can be *head-to-head* or *head-to-tail*, and the orientation of the two heads can be *syn* or *anti*. Table 1 summarizes the possible processes, whereby extremely strained structures were omitted. Apart from the fact that the photodimerization is a stepwise process, the dimeric structures can be rationalized on the basis of the *all-cisoid* conformation (*E*,*E*,*E*)-**1a** or the *all-transoid* conformation (*E*,*E*,*E*)-**1a**′ or both together. The ^{1}H NMR spectrum of **2a** reveals that the two head-to-tail dimers B and C with D_3 and C_{3h} symmetry, respectively, can be excluded.

The head-to-head adduct A can be ruled out, since the NOE measurement by irradiation into the singlet of the protons on the central ring reveals an effect for the protons in α-position and not in β-position to the carbonyl group. Thus, the dimer corresponds to the *all-cisoid* conformation shown in Scheme 3 (for the enone moieties). Finally, the two isomers, namely the achiral structure D and the chiral structure E remain.

Both structures give calculated ^{1}H NMR spectra, which agree very well with the measured ^{1}H NMR spectrum (Fig. 1).

A differentiation between D and E could be achieved by NOE measurements of the mixed addition product **2ab** with R = C_6H_5 and R′ = 3,4,5-$(OCH_3)_3C_6H_2$. A 2:1 mixture of **1a** and **1b** yielded on irradiation **2b** the dimer of **1b** and the mixed dimer **2ab** in a ratio of about 1:4; the dimer of **1a** was only formed in traces, what proves a somewhat higher dimerization tendency of **1b**. NOE experiments with the mixture **2ab**/**2b** proved that irradiation into the singlet of the protons on the trimethoxybenzene ring ($\delta = 6.63$) caused a positive effect for the β methine protons of the four-membered rings ($\delta = 4.37$ and $\delta = 4.49$). Thus a *cis* arrangement of R and R′ could be ruled out and therefore structure E was assigned to the obtained cyclophanes **2**.

Irradiation ($\lambda \geqslant 290$ nm) of **1a** in the crystalline state however, afforded a dimer **3a** (80%), which contains only one four-membered ring and has the head-to-tail/*anti* structure shown in Scheme 4. The structure determination was based on 1- and 2-dimensional ^{1}H and ^{13}C

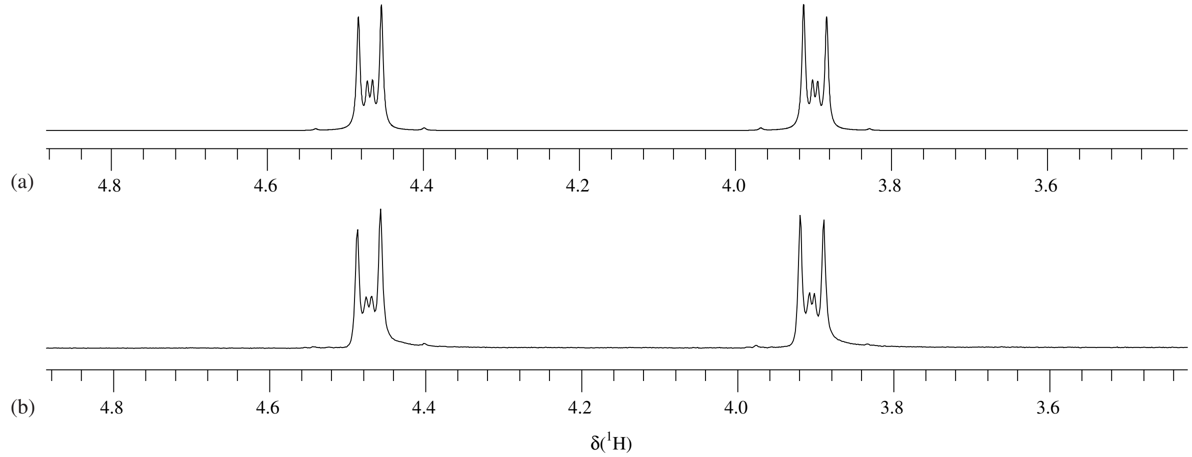
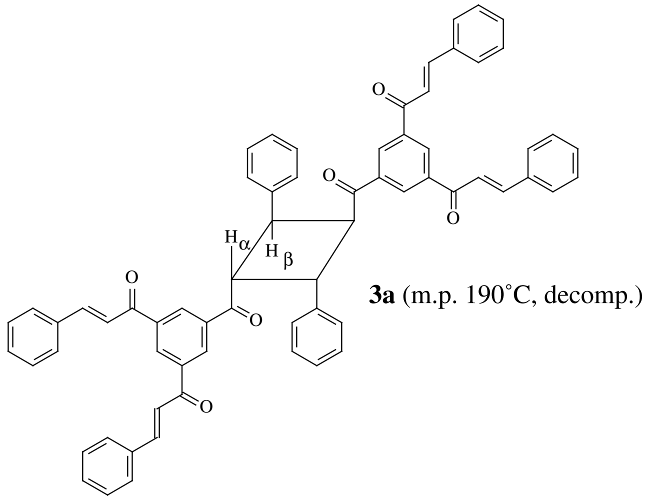


Figure 1. (a) Calculated[23] AA′MM′ pattern for the protons on the four-membered rings $\delta_\alpha(\mathrm{A}) = 3.898$ ppm, $\delta_\beta(\mathrm{M}) = 4.468$ ppm, $^3J(\mathrm{A,A'}) = {}^3J(\mathrm{M,M'}) = 9.95$ Hz, $^3J(\mathrm{AM}) = {}^3J(\mathrm{A'M'}) = 8.95$ Hz, $|^4J(\mathrm{AM'})| = |^4J(\mathrm{A'M})| = 0.25$ Hz; (b) measured spectrum of **2a** in $CDCl_3$.



3a (m.p. 190°C, decomp.)

Scheme 4. Photodimer of **1a** obtained in the crystalline state.

NMR studies including NOE measurements and calculations of the corresponding AA′BB′ spin patterns.

Whereas dimer **3a** is generated by a topochemical control,[24] we assume that dimer **2a** (structure E) corresponds to the preferred geometry of an excimer, in which the π stacking is realized in a way, that the oxygen atoms of the carbonyl groups avoid a close interaction of their electron clouds. The ^{1}H and ^{13}C NMR data of **2a** and **3a** are listed in Refs. 25, 26, respectively.

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22. ^{1}H NMR ($CDCl_3$) of **1a**–**d**: $\delta = 7.43$–7.67 (d, $^3J = 15.7$ Hz, 3H, α-H), 7.74–7.95 (d, $^3J = 15.7$ Hz, 3H, β-H); ^{13}C NMR ($CDCl_3$) of **1a**–**d**: $\delta = 121.1$–129.8 (d, α-C), 145.8–147.2 (d, β-C), 188.4–189.3 (s, CO).

23. Software: MestRe—C 2.3a.
24. Irradiation of an amorphous phase of **1a** did not lead to **2a**.
25. **2a**: ^{1}H NMR ($CDCl_3$): $\delta = 3.90$ (AA′ part of AA′MM′, 6H, α-H), 4.47 (MM′, 6H, β-H), 7.20–7.40 (AA′BB′C, 30H, phenyl), 7.81 (s, 3H, central benzene ring); ^{13}C NMR ($CDCl_3$): $\delta = 41.7$ (β-C), 52.9 (α-C), 127.0 (*o*-CH, phenyl), 128.9 (*m*-CH, phenyl), 127.4 (*p*-CH, phenyl), 131.4 (CH, central ring), 140.4, 140.6 (*i*-C, phenyl, and C_q, central ring), 197.8 (CO).
26. **3a**: ^{1}H NMR ($CDCl_3$): $\delta = 4.94$ (AA′ part of AA′BB′, 2H, α-H, 4-ring), 5.16 (BB′, 2H, β-H, 4-ring), 7.01 (m, 2H, *p*-H, phenyl), 7.12 (m, 4H, *m*-H, phenyl), 7.30 (m, 4H, *o*-H, phenyl), 7.45 (m, 12H, aromat. H of cinnamoyl), 7.52 (d, $^3J = 15.8$ Hz, 4H, olefin. H), 7.68 (m, 8H, aromat. H of cinnamoyl), 7.87 (d, $^3J = 15.8$ Hz, 4H, olefin. H), 8.46 (d, $^4J = 15.8$ Hz, 4H, aromat. H, benzoyl), 8.67 (t, 2H, aromat. H, benyl); ^{13}C NMR ($CDCl_3$): $\delta = 42.3$ (β-CH, 4-ring), 51.2 (α-CH, 4-ring), 120.9 (α-CH, olefin. CH), 127.4 (*p*-CH, phenyl), 128.2 (*o*-CH, phenyl), 128.5 (*m*-CH, phenyl), 128.7 (*o*-CH, cinnamoyl), 129.0 (*m*-CH, cinnamoyl), 131.1 (*p*-CH, cinnamoyl), 131.4 (*o*-CH, benzoyl), 131.7 (*p*-CH, benzoyl), 134.4 (C_q, cinnamoyl), 137.4 (C_q, phenyl), 138.4 (C_q, benzoyl), 138.6 (C_q, benzoyl), 146.3 (β-CH, olefin. CH), 188.6 (CO, cinnamoyl), 197.7 (CO, benzoyl).