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An Unconventional Approach to Structure Determination of Isomeric Cage Compounds

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Contribution from the Department of Chemistry, Tel-Aviv University, Ramat-Aviv, Tel-Aviv, Israel. Received March 15, 1978

Abstract: After the failure of conventional chemical and physical attempts for structural differentiation between C_{2v} and D_{2h} symmetries in the bishomocubane dione cage compounds of photochemical origin (**4** and **5**), this was achieved using an approach which combines mass spectrometry with isotopic labeling techniques and symmetry considerations. The isomeric cages of C_2 symmetry (**3**) exhibit also interesting characteristic fragmentation patterns, under electron impact, which are inter alia of diagnostic value.

We are, for some time now, engaged in a study of a versatile and interesting class of compounds, namely, cyclopentadienones (**1**) and their dimers (**2**).[1-4] In the course of an investigation of the photochemical behavior of the substituted
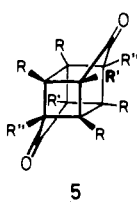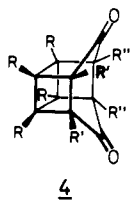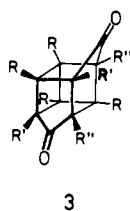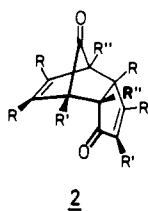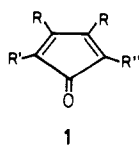
*	a	b	c	e	f
R	H	Ph	Ph	Ph-d_5	Ph-d_5
R'	H	Me	Me	Me-d_3	Me-d_3
R''	H	Me	H	Me-d_3	H

*Notation used throughout the paper (in text and formulas)

dimer (**2b**)[2] we were faced with a structural problem seemingly simple to deal with, based on our experience with the unsubstituted dimer (**2a**).[4]

Irradiation of **2b** provides two photoproducts, in temperature-, phase-, and wavelength-dependent yields.[2] Both are isomeric with the starting material and we list in Table I the spectroscopic properties that one could use for structure determination. Thus, UV and IR spectroscopic data evidently point to the absence of conjugated phenyl groups and to the presence of only saturated, strained carbonyls. This indicates that we deal with cage compounds of three possible structures, **3b**, **4b**, and **5b**. The one having structure **3b** was given away by its NMR spectrum in which two methyl-proton resonances occur, one for each equivalent pair of methyls in **3b** as expected for a dissymmetric structure (point symmetry C_2). The second photoproduct exhibits only one singlet for all 12 methyl protons indicating a symmetric structure but not discriminating between **4b** of point symmetry C_{2v} and the centrosymmetric form **5b**, of symmetry D_{2h}.

Unfortunately, the symmetric product is a high-melting compound of extremely low solubility in all organic solvents and exceedingly inert to chemical agents, although thermally unstable above ca. 100 °C when it reverts to **2b**.[2] This behavior is understandably due to its high molecular weight and symmetry as well as steric crowding around potential chemical reaction centers. Thus, it withstood all nucleophilic attack as attempted with various reagents and the only reaction that could be carried out was reduction by LiAlH$_4$ in boiling tetrahydrofuran to give a diol, which also resisted derivatization and hence structural assignment.[2] Moreover, even an x-ray diffraction analysis could not be attempted because no proper crystals could be grown owing to the low solubility of both these compounds.

Table I. Spectroscopic Data of Cage Compounds

Compd	IR ν_{CO}^{KBr}, cm^{-1}	UV $\lambda^{dioxane}$, nm (ϵ)	NMR δ^{CDCl_3} (s)^a
2b^{b,c}	1765, 1690	223 (34 600) 280 (24 500)	0.6 (3 H), 1.25 (3 H) 1.65 (3 H), 2.25 (3 H)
3b^c	1750	220 (23 200)	0.5 (6 H), 1.85 (6 H)
4b^{c,d}	1750	220 (24 500)	1.2 (12 H)^e
5c^{d,f}	1750	g	0.92 (6 H), 4.97 (2 H)

^{a} Only singlets representing saturated protons are relevant and given here. ^{b} Included here for the sake of comparison. ^{c} Cf. ref 2. ^{d} For the sake of clarity we list here already the correct structure, out of the two possible ones, as proven below. ^{e} Measured in hot chlorobenzene. ^{f} Cf. ref 3. ^{g} This electronic spectrum is left out since it is obscured by highly absorbing impurities.

Scheme I
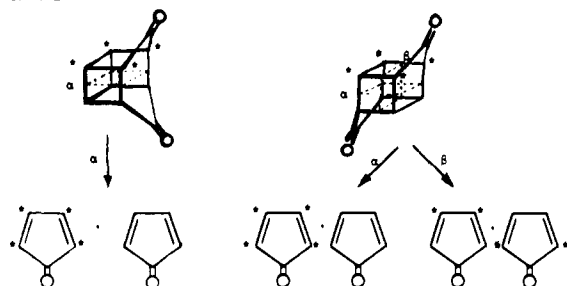
Since the matter was of considerable mechanistic importance in our photochemical study[1,2] we deemed it necessary to seek a way out of this impasse, even if it meant having to resort to unconventional methods, and we designed such a one. This was based on the fact (Table II) that the most abundant fragment ion in the product's mass spectrum is M/2$^+$ (m/e 260), i.e., that of the monomeric unit (**1b**). We reasoned that since **4b** can have only one possible half-splitting mode while **5b** could have two, statistically equivalent, available modes (Scheme I) the problem reduces itself to find a way of *half-labeling* the molecule: a type **4** cage would split under electron impact into *two* unequal monomeric fragments whereas **5** would exhibit *four* such structurally identical but isotopically different halves in its mass spectrum.

After considering group or isotopic labeling we settled on the latter and the procedure was based on the long-known synthesis of substituted cyclopentadienones[5,6] (Scheme II). Thus, benzil-d_{10} (**6**) (R = C$_6$D$_5$) readily underwent base-catalyzed condensation with diethyl-*1,1,1,5,5,5-d$_6$* ketone (**7**, R' = R'' = CD$_3$),[7] to give the hydroxycyclopentenone (**8e**). This was then subjected to acid-catalyzed elimination of water to give **1e** which, owing to its substitution pattern,[5,6] is in temperature-dependent equilibrium with its dimer (**2e**). The latter property plays a crucial role in our plan, since now reflux of a benzene solution of equimolar amounts of **2b** with **2e** provided an isotopically mixed product (**2b** + **2e**) which contains the desired half-labeled dimer (**2b-d_{16}**) albeit in an inseparable mixture with its precursors, in the expected statistical ratio as shown (Scheme III), viz., **2b**:**2b-d_{16}**:**2e** 1:2:1. This was proven by the mass spectrum of the crystalline dimer isolated from the above reaction mixture (Figure 1a and Table II).

Scheme II
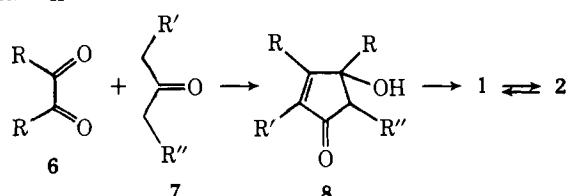
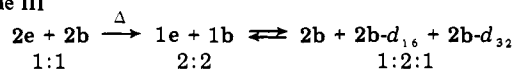**Table II.** Mass Spectrometric Data, m/e (Rel Abundance, %)

Compd	M^{+b}	(M/2)$^{+b}$
2b^s	520 (<1)	260 (100)
2e^a	552 (<1)	276 (100)
2b + **e**^{a,c}	520 (<1), 536 (1), 552 (<1)	260 (100), 266 (<1),^{d} 270 (<1),^{d} 276 (86)
3b	520 (5)	260 (51) [322 (100), 198 (22)]^h
3e	552 (6)	276 (51)[340 (100), 212 (15)]^h
3c	492 (40)	246 (10)[322 (30), 170 (58), 308 (18), 184 (14)]^h
4b	520 (4)	260 (100)
4e	552 (2)	276 (100)
4b + **e**^{e}	520 (1), 536 (2), 552 (1)	260 (100), 266 (<1), 270 (2), 276 (81)
9c^a	492 (21)	246 (100)
9f^a	518 (22)	259 (100)
9c + **f**^{a,f}	492 (22), 505 (44), 518 (21)	246 (96), 249 (2),^{d} 256 (3),^{d} 259 (100)
5c	492 (70)	246 (100)
5f	518 (66)	259 (100)
5c + **f**^{g}	518 (57), 505 (100), 492 (50)	246 (50), 249 (20), 256 (20), 259 (52)

^{a} Included here for the sake of comparison with their respective photoproducts under scrutiny. ^{b} All other fragmentations, e.g., loss of CO and CH$_3$ from the molecular ion or from the monomeric fragment as well as the occurrence of acetylene ions from the latter,[8] were observed but are expected and irrelevant to our issue. ^{c} Cf. Figure 1a. ^{d} This comes to emphasize the clean background at these mass numbers. ^{e} Cf. Figure 1b, Scheme 1, and discussion. ^{f} Cf. Figure 2a. ^{g} Cf. Figure 2b, Scheme 1, and discussion. ^{h} Regular data represent M/2 ions from mode "α" fragmentation; data in brackets represent ions from modes "β" and "γ"; cf. Scheme V and discussion.

Irradiation of this isotopic mixture in dioxane at λ > 300 nm gave a minute quantity of the dissymmetric cage compound of type **3** along with the major, symmetric product, both of isotopic composition identical with that of the starting material, as shown by their molecular ions (cf. Figure 1b). To recapitulate: (1) The molecular ions (M$^+$), i.e., the -d_0, -d_{16}, and -d_{32} isotopic isomers, are expected to be m/e 520, 536, and 552, respectively, of relative abundance 1:2:1. (2) The half-molecular fragment ions (M/2$^+$) stemming from the -d_0 and -d_{32} cages are obviously m/e 260 and 276, respectively, but the M/2$^+$ ions of the -d_{16} (half-labeled) cage depend on the latter's structure and hence splitting modes (cf. Scheme I): **4b-d_{16}** should exhibit m/e 260 and 276 fragments in ratio 1:1 whereas **5b-d_{16}** should split equally well in both possible modes giving fragments m/e 260, 266, 270, and 276 in ratio 1:1:1:1. Altogether, the expected abundance ratio of M/2$^+$ fragments of the entire isotopic mixture is m/e 260:276 = 1:1 for **4b** + **4e** and m/e 260:266:270:276 = 3:1:1:3 for **5b** + **5e**. The results, as reproduced in Figure 1b and Table II, clearly show the former pattern indicating unequivocally that the second, symmetric irradiation product of **2b** is of symmetry C_{2v}, i.e., **4b**.

Notwithstanding this successful attainment of our immediate goal, viz., structural proof of **4b**, we felt that a similar accomplishment involving a type **5** structure would help in establishing the general validity of the approach. Luckily, such a case was there, waiting to be dealt with. While investigating the photochemical behavior of the dimer **2c** (Scheme IV) we had observed that further irradiation of the photodimer **9c** gave, besides the starting dimer **2c**, a new, isomeric compound,
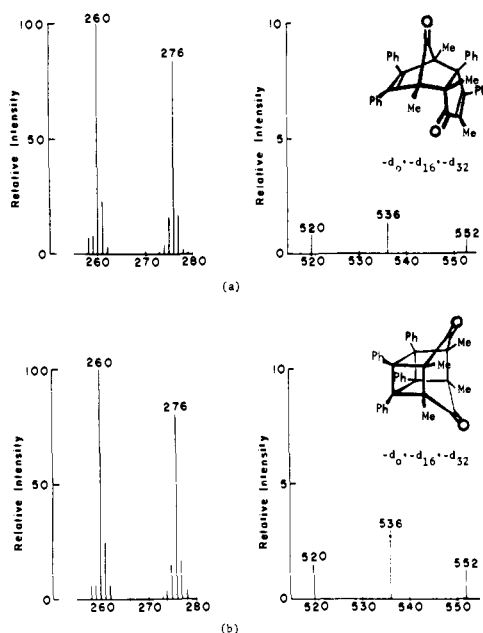
Scheme III

$$\begin{array}{c} 2e + 2b \xrightarrow{\Delta} 1e + 1b \rightleftarrows 2b + 2b\text{-}d_{16} + 2b\text{-}d_{32} \\ \quad 1:1 \qquad\qquad 2:2 \qquad\qquad 1:2:1 \end{array}$$

Figure 1. Mass spectrum (M^+ and $M/2^+$) of the isotopic mixtures (-d_0 + -d_{16} + -d_{32}) (1:2:1) of (a) **2b** + **c** and (b) **4b** + **e**; cf. Table II.
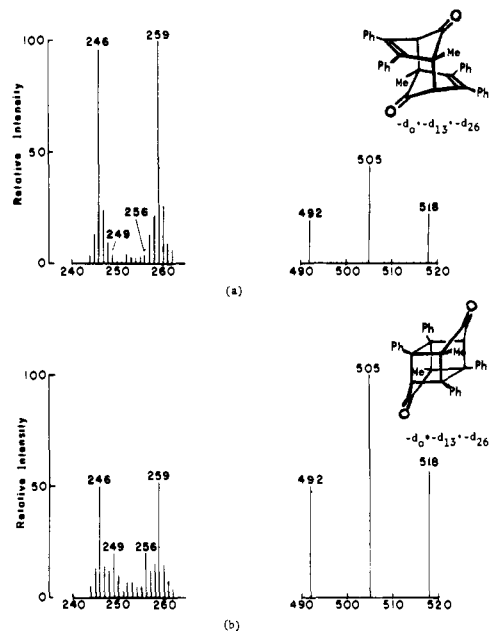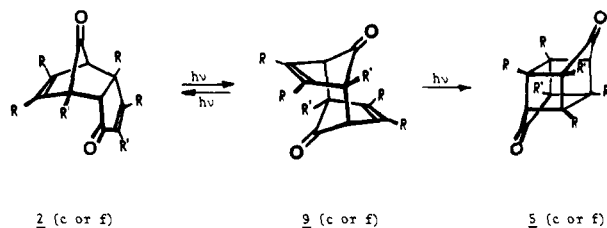

Figure 2. Mass spectrum (M^+ and $M/2^+$) of the isotopic mixtures (-d_0 + -d_{13} + -d_{26})(1:2:1) of (a) **9c** + **f** and (b) **5c** + **f**; cf. Table II.

Scheme IV

**2** (c or f)   **9** (c or f)   **5** (c or f)

Scheme V

which was tentatively assigned structure **5c**.[2c,3] The proof was, though, still to come.

Following an analogous procedure to that described above (Scheme II),[5,6] benzil-d_{10} (**6**) was condensed with methyl ethyl ketone-*4,4,4*-d_3 (**7**, R′ = Me; R″ = H)[7] to give **8f**. At this stage, however, we had to change our tactics, since dehydration of this trisubstituted hydroxycyclopentenone (**8f**) gives a corresponding cyclopentadienone (**1f**) of fleeting existence, which undergoes *irreversible* dimerization to **2f**.

Therefore, an equimolar mixture of the hydroxycyclopentenones **8f** and **8c**[5,6] was dehydrated to an isotopic mixture of dimers **2c**, **2f**, and **2c**-d_{13} shown, by mass spectrometric measurements, to have *m/e* 492, 505, and 518 in ratio 1:2:1, respectively. Irradiation of this mixture gave a photodimer (**9**) of the same isotopic composition as one can see in Figure 2a and Table II, the half-molecular ions *m/e* 246 and 259 being also shown. Further irradiation of **9** still of this isotopic composition yielded the mentioned cage product, which was subjected to careful mass spectrometry. Again (cf. Scheme I), structure **4c**-d_{13} would give in this case $M/2^+$ fragments *m/e* 246 and 259 while structure **5c**-d_{13} is bound to undergo both modes of splitting in half to *m/e* 246, 249, 256, and 259 in ratio 1:1:1:1. The theoretical ratio of these fragment ions in the mass spectrum of the whole isotopic mixture should then be in the latter case 3:1:1:3 and this was indeed found in reality (Figure 2b and Table II). Structure **5c** is, hence, also unequivocally proven as is the reliability of the method.

We would like to top off this story with an additional interesting, if not exciting, case of mass spectrometric probe for structure determination. This concerns the dissymmetric cages of type **3** and needs no labeling device.
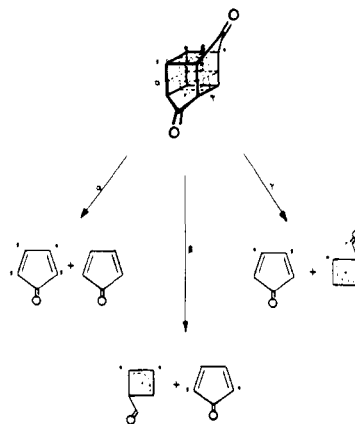
Judging from the behavior of the various cyclopentadienone dimers of type **2** and their photoproducts of type **4, 5**, and **9**[1b] (Table II), one might be tempted to conclude that *all* such dimeric compounds split into half under electron impact such that their monomeric units are formed as the most abundant ions in the spectrum. Indeed their mass spectra show below $M/2^+$ the characteristic fragmentation pattern of cyclopentadienones analogous to that reported by Bursey et al.[8] for tetracyclones. A careful analysis of the mass spectra of the cages of type **3** (Table II) reveals, however, a lower relative abundance of these monomeric units. Instead, new type of fragments are formed, indicating an additional and characteristic fragmentation mode available to these cages (**3**) (Scheme V). Interestingly, these are also $M/2^+$ fragments of a sort and they split accordingly.[8] This can be considered, hence, a useful tool for structural assignment of such dissymmetric cage compounds (**3**).

Experimental Section

The preparation and physical properties of the cage compounds have been described elsewhere.[2,3] The deuterated derivatives were prepared along the same lines.

Mass spectrometric measurements were performed using instruments as follows: Du Pont 21-491 B, Hitachi Perkin-Elmer RMU-6, Atlas CH-4 (courtesy of Dr. A. Mandelbaum) and MS-9 (courtesy

of Dr. D. Rosenthal), such that mass spectra were reproduced on at least two different instruments.

Acknowledgment. We are grateful to Professors A. Mandelbaum (Israel Institute of Technology) and D. Rosenthal (Research Triangle Institute) for agreeing to measure some of the mass spectra on their instruments in order to check the reproducibility of our results. Mrs. Sarah Weinman provided valuable technical assistance.

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Photoreduction of Tetraphenylporphyrins by Amines in the Visible. Photochemical Syntheses of Reduced Tetraphenylporphyrins and the Mechanism of Photoreduction

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Contribution from the Department of Plastics Research, The Weizmann Institute of Science, Rehovot, Israel. Received June 24, 1977

Abstract: Irradiation of meso tetraphenylporphyrins with visible light in the presence of aliphatic amines leads to their photoreduction and chlorins and isobacteriochlorins are formed. 7-H,8-Amino substituted tetraphenylchlorins are obtained on photoreduction by tertiary amine, and the nonsubstituted tetraphenylchlorin and tetraphenylisobacteriochlorin are obtained on photoreduction by pyrrolidine. A hydroxy substituted chlorin, 7-hydro-8-hydroxytetraphenylchlorin, is obtained on chromatography of the amino-substituted chlorins. The photochemical syntheses of the compounds and some of their physical properties are described. ^{1}H NMR data indicate a gradual decrease in ring current in the order $H_2TPP > H_2TPC > H_2TPB > H_2TP\text{-}i\text{-}B$. The mechanism of the photoreduction is elucidated by the use of EPR and photochemical techniques. Porphyrin free radicals are formed in the primary photochemical reaction with all the amines used. The different stable reaction end products are formed in subsequent dark reactions.

Introduction

Synthetic porphyrin macrocycles and their metallo complexes are useful model compounds in physical–chemical studies vital to the understanding of the biological function of the natural porphyrins. Over a decade meso tetraphenylporphyrins (TPP) and octaethylporphyrins (OEP) have been popular model compounds in such studies owing to their relatively easy synthesis.[1]

Synthetically reduced porphyrins, i.e., chlorins and bacteriochlorins, more related to the chlorophylls and bacteriochlorophylls received less attention because of the difficulties encountered in their synthesis. The only synthetic procedure described in the literature for the preparation of the reduced derivatives of the porphyrin ring system is based on chemical reduction by the diimide precursor *p*-toluenesulfonylhydrazine.[2] This procedure has its own limitations: (a) in the synthesis of tetraphenylchlorin the final mixture contains a relative large amount (~38%) of tetraphenylbacteriochlorin and additional dehydrogenation with *o*-chloranil and selective extraction with phosphoric acid are required in order to improve the yield and purity of the product. (b) Free base isobacteriochlorin cannot be made directly by this method and has to be synthesized by way of the zinc complex.

An alternative and attractive route, the photoreduction of parent porphyrins, has been the subject of many studies, few of which proved to be of synthetic value. Photoreduction of water-soluble free base porphyrins with EDTA as reducing agent results in the production of the isomeric, less stable, phlorins[3] whereas photoreduction of ZnTPP by benzoin proceeds only with light absorbed by the benzoin, to a mixture of products.[4] Similar results have been reported on the photoreduction of Zn porphine,[5] and of protochlorophyll and some of its derivatives with ascorbic acid.[6] In these studies it was indicated that addition of amines to the reaction mixture causes a catalytic effect on the reaction rate.

Some success was obtained in the photoreduction of Sn(IV) and Ge(IV) OEP to the corresponding isobacteriochlorins with EDTA in acetic acid[7] and with $SnCl_2 \cdot H_2O$ in pyridine.[8]

In recent years it has been found that many aromatic carbonyl compounds with low-lying π,π^* and charge-transfer triplet states which are not photoreduced by alcohols or hydrocarbons are photoreduced efficiently by amines which contain α hydrogen.[9,10] The proposed mechanism involves a rapid charge transfer interaction between the carbonyl compound excited state and the ground-state amine. More recently it was found that aromatic macrocycles having π-π^* configurations—unreactive in photoreduction processes via radi-