Synthesis, Structure, and Properties of the [7]Paracyclophane Ring System[1]

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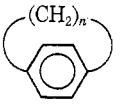
Abstract: The 3-carboxy derivative of [7]paracyclophane was prepared from the corresponding [8]paracyclophane in a number of steps, of which the key was the Wolff rearrangement for ring contraction. The ultraviolet spectrum shows a general red shift, in line with expectations. One proton in the nmr is forced into the π electrons of the benzene ring and is observed at -1.4 ppm. The structure was determined by X-ray crystallography, but because of disorder in the crystal it was of limited accuracy. However, it was observed that the para carbons of the benzene ring were approximately 17° out of the plane of the other four benzene carbons, while the benzyl carbons were 24° from that same plane.

Preparation and studies of strained molecules have long intrigued organic chemists. The [*n*]paracyclophanes (**1**) which contain a benzene ring connected



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by an aliphatic chain at the para positions are no exception.[3]

The [*n*]paracyclophane ring system is known for most values of *n* from 16 down to 8, the [8]paracyclophane ring system having been first reported in 1961.[4-6] For 11 years the [7]paracyclophane system remained unknown and has now been prepared by two completely unrelated syntheses.[7]

As *n* decreases in the series of [*n*]paracyclophanes, the benzene ring becomes more and more boat shaped.[8] This is reflected in the ultraviolet spectrum by an increasing red shift of the benzene absorption. From theoretical studies, estimates of the deviation from planarity of the benzene ring and the strain energies of the [*n*]paracyclophanes have been made.[4c]

The nmr spectra of the [*n*]paracyclophanes are quite characteristic. The protons connected to the aliphatic carbons over the benzene ring are substantially shielded. This shielding is attributed to the immersion of these protons into the shielding cone generated by the aromatic ring current.[9]

The present paper reports the details of the preparation of the [7]paracyclophane ring system, an X-ray crystal structure study of the [7]paracyclophane ring, and preliminary attempts to construct the [6]paracyclophane ring system.

Synthesis

Since attempts to form the [8]paracyclophane ring by the acyloin reaction were unsuccessful,[5a] it was presumed such approaches to the smaller ring would also be, so the synthetic approach to the formation of the [7]paracyclophane ring required either a new ring-forming reaction or a ring contraction.[10] Our method of choice was the latter, which had been very successful in forming the [8]paracyclophane ring.[8] Furthermore, with the latter route it seemed possible to carry out a synthetic sequence using known, high-yield reactions.

Two ring contraction reactions were considered: the Wolff and Favorski rearrangements. The former requires an α-diazo ketone and was used in the formation of the [8]paracyclophane ring.[8] This reaction has the advantage that the enthalpy of the products is favored by the formation of the very stable nitrogen molecule, and the entropy of the reaction is favored by the formation of two molecules from one. This was the reaction of choice. The alternative reaction requires an α-halo ketone and has also been used to form strained molecules.

Thus, starting with 4-carboxy[8]paracyclophane (**2**) whose synthesis has been previously described,[8] the ketone **3** was logically the next goal, followed by the diazo ketones **4a** and/or **4b**. See Scheme I.

Initial attempts to form ketone **3** from the acid **2** employed the traditional Barbier–Wieland procedure. 4-Carboxy[8]paracyclophane was converted to 4-carbomethoxy[8]paracyclophane with diazomethane and subsequently, to the diphenyl alcohol **5** with phenylmagnesium bromide. Elimination of water from **5** in aqueous acetic acid produced 4-diphenylmethylene[8]-paracyclophane (**6**).

The task of cleaving the olefin **6** to ketone **3** proved most difficult and was finally abandoned. Unsuccessful attempts included treatment of 4-diphenylmethylene-[8]paracyclophane with: (1) a catalytic amount of osmium tetroxide and an excess of sodium metaperiodate; (2) a full equivalent of osmium tetroxide;

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(2) National Science Foundation Trainee, 1971–1972.

(3) For reviews, see (a) D. J. Cram and J. M. Cram, *Accounts Chem. Res.*, **4**, 204 (1971); (b) B. H. Smith, "Bridged Aromatic Compounds," Academic Press, New York, N. Y., 1964.

(4) (a) D. J. Cram and G. R. Knox, *J. Amer. Chem. Soc.*, **83**, 2204 (1961); (b) N. L. Allinger and L. A. Freiberg, *J. Org. Chem.*, **27**, 1490 (1962); (c) N. L. Allinger, L. A. Freiberg, R. B. Hermann, and M. A. Miller, *J. Amer. Chem. Soc.*, **85**, 1171 (1963); (d) D. J. Cram, C. S. Montgomery, and G. R. Knox, *ibid.*, **88**, 515 (1966); (e) T. Tsuji and S. Nishida, *ibid.*, **95**, 7519 (1973).

(5) For some key references for the preparation and studies of the [12]-, [10]-, and [9]paracyclophane ring respectively see (a) D. J. Cram, N. L. Allinger, and H. Steinberg, *J. Amer. Chem. Soc.*, **76**, 6132 (1954); (b) D. J. Cram and H. U. Daeniker, *ibid.*, **76**, 2743 (1954); (c) D. J. Cram and M. F. Antar, *ibid.*, **80**, 3109 (1958).

(6) For additional references, see ref 3b.

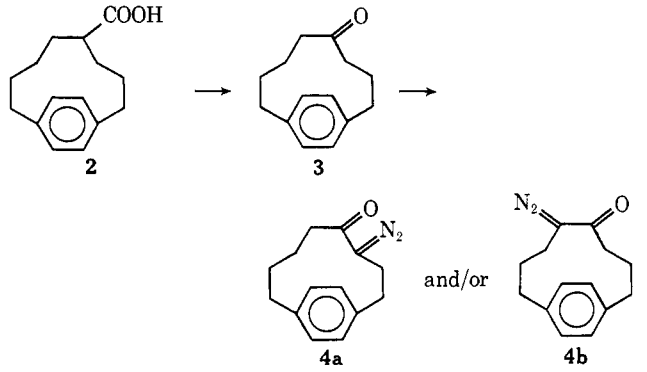
(7) (a) N. L. Allinger and T. J. Walter, *J. Amer. Chem. Soc.*, **94**, 9267 (1972); (b) A. D. Wolf, V. V. Kane, R. H. Levin, and M. Jones, Jr., *ibid.*, **95**, 1680 (1973).

(8) For an X-ray crystal structure study of 4-carboxy[8]paracyclophane, see M. G. Newton, T. J. Walter, and N. L. Allinger, *J. Amer. Chem. Soc.*, **95**, 5652 (1973).

(9) Reference 3b, pp 415–416.

(10) The new ring formation approach was that used in ref 7b.

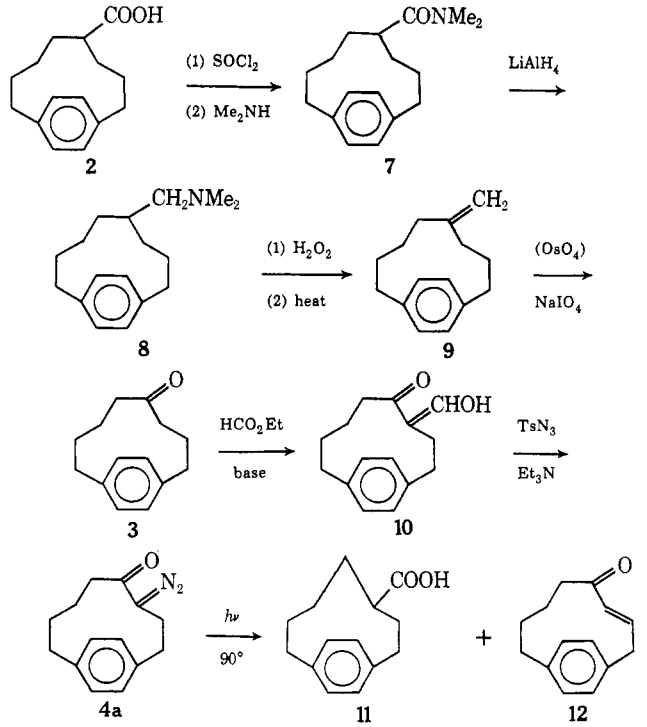
Scheme I. Synthetic Plan for the Preparation of the [7]Paracyclophane Ring



and (3) ozonolysis. It is felt that the steric bulk of the tetrasubstituted olefin is largely responsible for the poor results.

At this point the strategy dictated the formation of a less sterically congested olefin which could be more easily cleaved. Furthermore, it was felt that an intramolecular elimination would be most successful in removing the rather inaccessible proton that was located between the aliphatic chain and the benzene ring. These ideas were successfully utilized as shown in Scheme II.

Scheme II. Conversion of 4-Carboxy[8]paracyclophane to 3-Carboxy[7]paracyclophane[a]



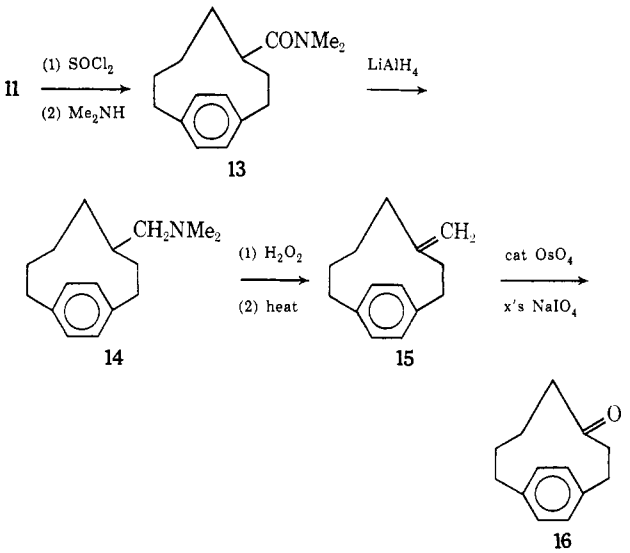
[a] The *Z* or *E* isomer should not be implied from structure **12** as written.

4-Carboxy[8]paracyclophane was treated with thionyl chloride to form the acid chloride, which was allowed to react with anhydrous dimethylamine in benzene to produce 4-*N*,*N*-dimethylcarboxamido[8]paracyclophane (**7**). The crude amide **7** was treated with lithium aluminum hydride to produce 4-(*N*,*N*-dimethylamino)-methyl[8]paracyclophane (**8**). Treatment of the crude amine **8** with hydrogen peroxide followed by pyrolysis of the *N*-oxide at 140° produced 4-methylene[8]paracyclophane (**9**). The product was purified by distillation, bp 86.5–88.0° (0.6 mm), and isolated in 79% yield over-all from 4-carboxy[8]paracyclophane.

Compound **9** was allowed to react with a catalytic amount of osmium tetroxide and an excess of sodium metaperiodate to produce 4-keto[8]paracyclophane (**3**). Purification by sublimation yielded the pure ketone, mp 44.5–46.0°, in 83% yield from the olefin **9** and in 65% yield from 4-carboxy[8]paracyclophane.

Conversion of 4-keto[8]paracyclophane (**3**) to 3-diazo-4-keto[8]paracyclophane (**4a**) is illustrated in Scheme III. At the outset it was not known whether formyla-

Scheme III. Conversion of 3-Carboxy[7]paracyclophane to 3-Keto[7]paracyclophane



tion would produce 3-hydroxymethylene-4-keto[8]paracyclophane (**10**), the 5-hydroxymethylene isomer, or a mixture of the two. Subsequent identification of the photolysis product required that **10** was formed.

Formylation of 4-keto[8]paracyclophane in ether with ethyl formate, sodium, and a catalytic amount of ethanol produced a crude solid whose ir 1730, 1705, and 1625 cm^{-1} was consistent with an α-hydroxy methylene ketone. Since these compounds tend to polymerize, no further purification was attempted. Treatment of crude **10** with triethylamine and *p*-toluenesulfonyl azide in methylene chloride produced an orange oil whose ir spectrum, 2080 (C=N_2) and 1625 cm^{-1} (C=O), was consistent with an α-diazo ketone. The Wolff rearrangement (see Scheme III) of diazo ketone **4a** produced a 50% yield of 3-carboxy[7]paracyclophane. The crude product was purified by preparative tlc and recrystallized from hexane. Identification was made from the following data: mp 130.5–132.5°; ir 3500–2300 (broad, OH) and 1705 cm^{-1} (C=O); nmr δ 11.2 (s, 1, COOH), 7.15 (d, J = 12 Hz, 4, aromatic), 2.95 (m, 2, benzylic), 2.45 (m, 2, benzylic), 2.1–0.0 (m, 8, aliphatic), and −1.4 ppm (2 doublets, J = 11 and 15 Hz, 1, highly shielded proton); mass spectrum, M^+ = 218, calcd 218; uv_{max} (95% EtOH), 292 sh (ϵ 298), 284 (ϵ 364), 237 (ϵ 7140), and 207 nm (ϵ 22,700); and elemental analysis.

It should be noted that the Wolff rearrangement of 5-diazo-4-keto[8]paracyclophane would have produced 4-keto[7]paracyclophane. The isolated product was identified as 3-carboxy[7]paracyclophane from the nmr spectra of the product acid **11** and its alcohol 3-hydroxymethyl[7]paracyclophane as previously described.[7a] This isomer assignment has been further substantiated

by the X-ray crystal structure study of **11** which is discussed in this paper.

The organic fraction from the Wolff rearrangement was purified by preparative tlc followed by recrystallization from hexane to produce white crystals, mp 85.5–87.0°, in 25% yield from diazo ketone **4a**. The product was identified as 4-keto-2-[8]paracyclophene (**12**) from the following evidence. It decolorizes bromine in carbon tetrachloride; ir 1690 (α,β-unsaturated C=O), 1610 cm^{-1} (C=C); nmr δ 6.95 (m, 4, aromatic), 5.50 (m, 2, vinylic), 3.35 (m, 2, C_1 protons), 2.65 (t, J = 6 Hz, 2, C_8 protons), 1.35 (m, 4, methylene), and 0.90 ppm (t, J = 5 Hz, 2, methylene); mass spectrum, M^+ = 200; and elemental analysis. Hydrogenation of **12** with 10% palladium on carbon produced white crystals, of which the ir spectrum, melting point, and mixed melting point were identical with those of 4-keto[8]paracyclophane.

In attempts to prepare suitable derivatives for X-ray crystal study the anilide of 3-carboxy[7]paracyclophane, mp 196–198.5°, was prepared by treating the acid chloride with aniline.

Discussion of Results

Some aspects of the successful synthetic sequence merit elaboration. The reaction series for the conversion of 4-carboxy[8]paracyclophane to 4-keto[8]paracyclophane is noteworthy (see Scheme II). Although a number of transformations are required, the reactions all proceed cleanly and in high yield. This, then, represents a high-yield general synthetic transformation of a carboxylic acid to a ketone of one less carbon under mild conditions, offering an excellent alternative to the traditional Barbier–Wieland procedure.

Products from 3-diazo-4-keto[8]paracyclophane (**4a**) were 3-carboxy[7]paracyclophane (**11**) in 50% yield and 4-keto-2-[8]paracyclophene (**12**) in 25% yield. These products can be rationalized in terms of the generally accepted keto–carbene intermediate.[11] A 1,2 shift of C_5 would produce **11** while a 1,2-hydride shift of a C_2 hydrogen would yield **12**.

Considering these results, it is interesting to speculate what would happen if a diazoketo[7]paracyclophane were photolyzed. One must first consider whether or not the [6]paracyclophane ring system is stable enough to exist. If so, then could the ring contraction by the Wolff rearrangement be successful? Only a small reduction in yield, from 65 to 50%, was observed in the preparation of the [8]-[8] and [7]paracyclophane rings, respectively, but would the competing hydride shift dominate? Our current estimate is that the [6]paracyclophane would have a strain energy of approximately 30 kcal/mol, compared with 20 kcal/mol for the [7]paracyclophane. The latter appears to be quite stable upon standing in the laboratory. The former may tend to show properties more characteristic of a polyene, since the release in strain possible upon a 1,4-addition reaction (for example) is of the same magnitude as the resonance energy of the benzene ring. Thus the thermodynamic stability of the compound, though maybe not very great, should be sufficient for it to be isolable. The synthetic route needed to obtain the compound is less clear, however. It could well be that hydride shift will predominate over ring contraction in this case, but the large driving force associated with the Wolff rearrangement should offer an excellent chance of obtaining at least a small yield of the desired product.

The ultraviolet and nmr spectra of the [n]paracyclophanes are very characteristic. Considering first the ultraviolet spectra, it has been known for some time[4c,12] that as n decreases in the series of [n]paracyclophanes, there is a red shift in the absorption of the benzene chromophore, with a loss of fine structure. This has been attributed to the deviation from planarity of the

Table I. Ultraviolet Spectra of the [n]Paracyclophanes (λ_{max}; log ϵ)

p-Diethylbenzene	193 (4)	193 (4)	214 (3)	265 (2)
[10]Paracyclophane			223 (3)	268 (2)
[9]Paracyclophane			224 (3)	271 (3)
[8]Paracyclophane[a]	200 (4)	205 (4)	230 (3)	275 (2)
[7]Paracyclophane (found)[a]		207 (4)	237 (4)	284 (2)
[7]Paracyclophane (found)[b]			237 (4)	284 (2)
[7]Paracyclophane (found)[c]		216 (4)	245 (4)	283 (3)
[7]Paracyclophane (predicted)[d]	196 (4)	210 (4)	247 (3)	288 (2)

[a] A carboxy derivative. [b] 3-Hydroxymethyl derivative. [c] Reference 7b. [d] Reference 4c.

Table II. Nmr Data for Some [n]Paracyclophanes

	Shielded protons ppm, multiplicity, no. of protons	Aromatic protons ppm, multiplicity, no. of protons
[10]Paracyclophane[a]	+0.7, m	7, s
[9]Paracyclophane[a]	+0.4, m, 4	7, s
4-Carboxy[8]paracyclophane (**2**)[b]	−0.25, m, 1	7.15, m, 4
4-Carbomethoxy[8]-paracyclophane[b]	−0.25 m, 1	7.15 m, 4
4-Diphenylhydroxymethyl[8]-paracyclophane (**5**)	−0.85, m, 1	7.6–6.9, m, 14
4-Diphenylmethylene[8]-paracyclophane (**6**)	+0.75, m, 4	7.15, m, 14
4-*N*,*N*-Dimethylcarboxamido[8]paracyclophane (**7**)	−0.45, m, 1	7.10, m, 4
4-(*N*,*N*-Dimethylamino)-methyl[8]paracyclophane (**8**)	−0.55, m, 1	7.05, m, 4
4-Methylene[8]-paracyclophane (**9**)	+0.20, t, 2	6.90 s, 4
4-Keto[8]paracyclophane (**3**)	+2.15–0.95, m, 10	6.95, m, 4
4-Keto-2-[8]paracyclophane (**12**)	0.90, t, 2	6.95, m, 4
3-Carboxy[7]paracyclophane (**11**)	−1.4, 2 doublets, 1	7.15, d, 4
3-Hydroxymethyl[7]-paracyclophane	−1.4, 2 doublets, 1	7.20, m, 4
Anilide of 3-carboxy[7]-paracyclophane	−1.35, 2 doublets, 1	7.6–6.9, m, 9
3-*N*,*N*-Dimethylcarboxamido[7]paracyclophane (**13**)	−1.60, m, 1	7.10, d, 4
3-(*N*,*N*-Dimethylamino)-methyl[7]paracyclophane (**14**)	−1.45, 2 doublets, 1	7.05, d, 4
3-Methylene[7]-paracyclophane (**15**)	+0.20, m, 2	7.05, s, 4
3-Keto[7]paracyclophane (**16**)	+1.40–0.80, m, 6	7.00, s, 4

[a] D. J. Cram and M. Goldstein, *J. Amer. Chem. Soc.*, **85**, 1063 (1963). [b] Reference 8.

(11) J. March, "Advanced Organic Chemistry: Reactions, Mechanisms, and Structure," McGraw-Hill, New York, N. Y., 1968, p 809.

(12) Reference 3b, pp 359–384.

Table III. Summary of Crystallographic Data

Molecular formula	$C_{14}H_{18}O_2$
Molecular weight	218.3
Linear absorption coefficient	6.29 cm^{-1} (Cu Kα)
Observed density (flotation in aq $ZnCl_2$)	1.19 g/cm^3
Calculated density	1.20 g/cm^3
Crystal dimensions	0.3 × 0.3 × 0.8 mm
Space group	$P2_1/c$
Cell constants	a = 12.38, b = 7.80, c = 12.72 Å, β = 99.25, Z = 4, V = 1213 Å

benzene ring.[4c] In fact the spectra of the [7]paracyclophane ring were well predicted from theoretical studies.[4c]

A summary of the experimental and predicted spectra is found in Table I.

Considering the nmr spectra of the [n]paracyclophanes, the protons over the aromatic ring are substantially shielded. This shielding is attributed to the aromatic ring current.[13] Another region of the nmr spectrum that might be characteristic is that of the aromatic protons. Conceivably, if the benzene ring is bent enough, the chemical shifts of aromatic protons would become more vinylic. These data are summarized in Table II.

Examination of Table II reveals the increased shielding of the most shielded protons in [n]paracyclophanes as n decreases from 10 to 7. If one assumes a normal chemical shift for methylene protons to be 1.4 ppm,[14] then the proton at −1.4 ppm in 3-carboxy[7]paracyclophane is shielded by 2.8 ppm. There does not appear to be any noticeable trend in the chemical shifts of the aromatic protons.

X-Ray Structure

A great deal of effort was expended in trying to obtain an accurate structural analysis for the [7]paracyclophane ring system. (See the Experimental Section.) The structure of the 3-carboxy[7]paracyclophane was solved; however, it would refine only to R = 0.167. Data obtained from a second crystal of the same compound refined to R = 0.163. Data were also collected on a crystal of 3-hydroxymethyl[7]paracyclophane and the anilide of 3-carboxy[7]paracyclophane, but the structures were not solved. The information reported in this paper is that obtained from the first 3-carboxy[7]-paracyclophane crystal and, although less accurate than desired, provides chemically meaningful results.

A summary of crystallographic data is recorded in Table III. Positional coordinates, temperature factors, bond lengths, and bond angles are tabulated in Tables IV–VI, respectively. The bond lengths are normal (to within the large experimental error). Examination of nonbonded distances between aliphatic bridge carbons and aromatic carbons reveals many interactions on the repulsive portion of the van der Waals curve. These are denoted by an asterisk in Table VII. C_4 is less than the sum of its van der Waals

Table IV. Positional Coordinates and Temperature Factors[a] for 3-Carboxy[7]paracyclophane

Atom	x	y	z	β_{11}	β_{22}	β_{33}	β_{12}	β_{13}	β_{23}
C_1	0.3392 (9)	−0.1298 (11)	0.3247 (9)	0.0204 (12)	0.0167 (16)	0.0142 (10)	0.0014 (23)	−0.0141 (18)	0.0011 (19)
C_2	0.4112 (7)	0.0351 (10)	0.3330 (7)	0.0132 (8)	0.0157 (13)	0.0104 (7)	0.0065 (17)	−0.0098 (12)	−0.0044 (15)
C_3	0.3462 (5)	0.2051 (8)	0.3379 (5)	0.0093 (6)	0.0150 (11)	0.0055 (5)	0.0007 (13)	−0.0036 (8)	−0.0025 (11)
C_4	0.3095 (6)	0.2825 (9)	0.2242 (5)	0.0094 (6)	0.0168 (12)	0.0056 (4)	−0.0009 (14)	−0.0020 (8)	−0.0000 (12)
C_5	0.2065 (8)	0.3964 (10)	0.2081 (6)	0.0150 (8)	0.0165 (13)	0.0087 (6)	0.0079 (17)	−0.0087 (12)	−0.0041 (15)
C_6	0.1570 (8)	0.3985 (12)	0.0857 (7)	0.0146 (9)	0.0244 (18)	0.0100 (7)	0.0068 (21)	−0.0118 (13)	0.0010 (18)
C_7	0.0625 (8)	0.2615 (13)	0.0514 (8)	0.0157 (10)	0.0252 (19)	0.0124 (9)	−0.0088 (23)	−0.0122 (15)	0.0077 (21)
C_8	0.1016 (8)	0.0976 (12)	0.1004 (9)	0.0116 (8)	0.0263 (20)	0.0123 (9)	0.0021 (21)	−0.0108 (14)	0.0081 (22)
C_9	0.1746 (7)	−0.0069 (11)	0.0614 (7)	0.0108 (7)	0.0225 (17)	0.0110 (8)	−0.0026 (18)	−0.0062 (12)	0.0124 (17)
C_{10}	0.2492 (8)	−0.1086 (11)	0.1318 (8)	0.0160 (10)	0.0200 (17)	0.0122 (9)	−0.0010 (20)	−0.0078 (15)	0.0122 (19)
C_{11}	0.2433 (10)	−0.1057 (11)	0.2407 (8)	0.0188 (12)	0.0138 (14)	0.0114 (9)	0.0053 (21)	−0.0101 (16)	−0.0001 (16)
C_{12}	0.1442 (12)	−0.0395 (15)	0.2728 (8)	0.0188 (13)	0.0293 (24)	0.0122 (10)	−0.0254 (32)	−0.0042 (19)	−0.0015 (26)
C_{13}	0.0744 (10)	0.0595 (15)	0.2037 (11)	0.0150 (10)	0.0307 (24)	0.0140 (11)	0.0118 (26)	−0.0059 (18)	0.0065 (27)
C_{14}	0.4168 (6)	0.3339 (8)	0.4071 (5)	0.0103 (6)	0.0136 (11)	0.0058 (5)	0.0009 (13)	−0.0036 (8)	−0.0008 (12)
O_{15}	0.4436 (8)	0.2890 (10)	0.5045 (6)	0.0315 (12)	0.0282 (16)	0.0134 (7)	−0.0151 (23)	−0.0216 (15)	0.0048 (16)
O_{16}	0.4379 (9)	0.4743 (9)	0.3799 (6)	0.0344 (14)	0.0258 (15)	0.0099 (6)	−0.0206 (24)	−0.0171 (14)	0.0044 (14)

[a] Anisotropic temperature factors (β_{ij}) have the form $h^2\beta_{11} + k^2\beta_{22} + l^2\beta_{33} + hk\beta_{12} + hl\beta_{13} + kl\beta_{23}$.

Table V. Distances between Bonded Atoms in 3-Carboxy[7]paracyclophane

Atoms	Distance, Å[a]	Atoms	Distance, Å[a]
C_1–C_2	1.56 (1)	C_8–C_9	1.37 (1)
C_1–C_{11}	1.48 (2)	C_8–C_{13}	1.44 (2)
C_2–C_3	1.56 (1)	C_9–C_{10}	1.42 (1)
C_3–C_4	1.57 (1)	C_{10}–C_{11}	1.40 (1)
C_3–C_{14}	1.52 (1)	C_{11}–C_{12}	1.45 (2)
C_4–C_5	1.54 (1)	C_{12}–C_{13}	1.37 (2)
C_5–C_6	1.58 (1)	C_{14}–O_{15}	1.28 (1)
C_6–C_7	1.59 (1)	C_{14}–O_{16}	1.19 (1)
C_7–C_8	1.47 (1)		

[a] The estimated standard deviations given in parentheses do not contain cell constant errors and bond lengths have not been corrected for thermal motion.

Table VI. Angles between Bonded Atoms in 3-Carboxy[7]paracyclophane

Atoms	Angle, deg	Atoms	Angle, deg
C_2–C_1–C_{11}	109 (1)	C_9–C_8–C_{13}	118 (1)
C_1–C_2–C_3	114 (1)	C_8–C_9–C_{10}	120 (1)
C_2–C_3–C_4	112 (1)	C_9–C_{10}–C_{11}	119 (1)
C_2–C_3–C_{14}	110 (1)	C_1–C_{11}–C_{10}	123 (1)
C_4–C_3–C_{14}	110 (1)	C_1–C_{11}–C_{12}	117 (1)
C_3–C_4–C_5	117 (1)	C_{10}–C_{11}–C_{12}	118 (1)
C_4–C_5–C_6	109 (1)	C_{11}–C_{12}–C_{13}	120 (1)
C_5–C_6–C_7	114 (1)	C_8–C_{13}–C_{12}	119 (1)
C_6–C_7–C_8	107 (1)	C_3–C_{14}–O_{15}	115 (1)
C_7–C_8–C_9	124 (1)	C_3–C_{14}–O_{16}	125 (1)
C_7–C_8–C_{13}	117 (1)	O_{15}–C_{14}–O_{16}	120 (1)

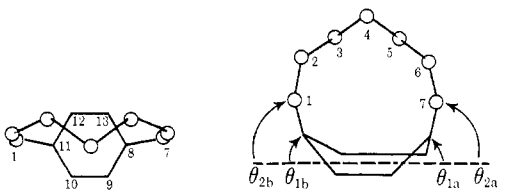
(13) Reference 3b, pp 407–422.
(14) D. H. Williams and I. Fleming, "Spectroscopic Methods in Organic Chemistry," McGraw-Hill, New York, N. Y., 1966, p 126.

Table VII. Nonbonded Distances between Aliphatic Bridge Carbons and Aromatic Carbons[a]

	C_8	C_9	C_{10}	C_{11}	C_{12}	C_{13}	Av dist from all 6 aromatic carbons
C_3	4.01 (1)	4.15 (1)	3.65 (1)	2.92 (1)*	3.15 (2)*	3.70 (2)	3.60
C_4	3.14 (1)*	3.33 (1)*	3.31 (1)*	3.15 (1)*	3.36 (2)*	3.36 (2)*	3.28
C_5	2.90 (1)*	3.65 (1)	4.11 (1)	3.96 (1)	3.61 (2)	3.09 (2)*	3.55

[a] An * denotes C–C distance less than the sum of the van der Waals radii.[15]

radii[15] from all six benzene carbons. The average distance of C_3, C_4, and C_5 from all six aromatic carbon atoms is 3.60, 3.28, and 3.55 Å, respectively. This is substantially less than that observed in 4-carboxy[8]-paracyclophane.[8,16]



θ_{1a} 18.3° θ_{2a} 24.0°
θ_{1b} 15.2° θ_{2b} 23.0°

The data in Table VII reveal that the [7]paracyclophane ring (excluding the carboxyl group) possesses approximate C_s symmetry. This is better illustrated in the sketch, which is a projection looking down the line drawn from C_4 to the center of the benzene ring.

The most interesting structural feature for the [7]paracyclophane ring system is, of course, the distortion in the benzene ring brought about by the short length of the side chain which is bridging the para positions. The para carbons of the benzene ring are lifted out of the plane of the other four benzene carbons by 17° (average value), while the benzyl carbon is out of the benzene plane by 23.5°. These numbers may be compared with the values 9 and 15°, respectively, found with the [8]paracyclophane. It is also anticipated, and found, that certain of the angles in the side chain are widened out to unusually large values. Thus the angle $C_3C_4C_5$ has the value 117°, and the angle $C_1C_2C_3$ has the (average) value of 115°. The latter widens out in an effort to separate the side chain from the benzene ring, while the former widens out in an effort to lengthen the side chain and facilitate bridging. The angle $C_2C_3C_4$ is normal (111°), suggesting that widening here would not contribute much to either of these methods of relieving strain. It is interesting to note that the angle $C_7C_8C_9$ is open to a value of 124°, with a consequent compression of the $C_7C_8C_{13}$ angle to 117°, as the position of the benzene ring is offset sideways with respect to the side chain.

A packing diagram is shown in Figure 1. The molecules form racemic dimers related by the inversion center of the space group, and the $O_{15}\cdots O_{16}$ intermolecular distance of 2.65 Å is quite similar to the corresponding value in 4-carboxy[8]paracyclophane.[8] Only four other intermolecular distances are <3.5 Å: $C_1\cdots O_{16}$, 3.35 Å (x, 1 + y, z); $C_1\cdots O_{15}$, 3.41 Å (1 − x, $-y$, 1 − z); $C_{14}\cdots O_{16}$, 3.35 Å (1 − x, 1 − y, 1 − z); and $O_{16}\cdots O_{16}$, 3.21 Å (1 − x, 1 − y, 1 − z).

(15) The sum of the van der Waals radii for C_{sp^2}–C_{sp^3} is taken to be 3.50 Å; N. L. Allinger and J. T. Sprague, *J. Amer. Chem. Soc.*, **94**, 5734 (1972).

(16) The average distances of C_3, C_4, C_5, and C_6 from all the aromatic carbon atoms in 4-carboxy[8]paracyclophane are 3.76, 3.63, 3.58, and 3.80, respectively.

Attempts to Prepare the [6]Paracyclophane Ring

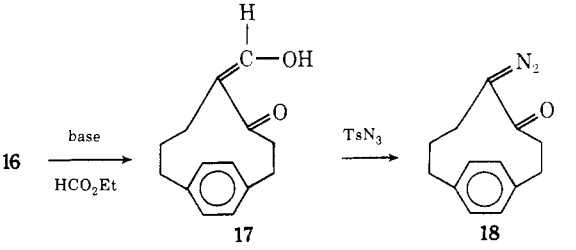
Having successfully completed the transformation of a carboxy[8]paracyclophane to a carboxy[7]paracyclophane, it seemed quite reasonable to extend the synthesis to the preparation of a carboxy[6]paracyclophane. The first goal molecule for this sequence, 3-keto[7]paracyclophane (**16**), was successfully prepared as illustrated in Scheme III.

3-Carboxy[7]paracyclophane (**11**) was converted *via* the acid chloride to 3-*N*,*N*-dimethylcarboxamido[7]-paracyclophane (**13**). The crude amide **13** was reduced with lithium aluminum hydride to form 3-(*N*,*N*-dimethylamino)methyl[7]paracyclophane (**14**), which was converted to the *N*-oxide with hydrogen peroxide. Subsequent pyrolysis produced 3-methylene[7]paracyclophane (**15**). Partial purification was effected by column chromatography. A portion was distilled, bp 75–76° (0.3 mm), for characterization. The ir and nmr spectra and elemental analysis are consistent with the assigned structure.

The olefin **15** was treated with a catalytic amount of osmium tetroxide and excess sodium metaperiodate to produce 3-keto[7]paracyclophane (**16**) in 29% yield from 3-carboxy[7]paracyclophane. The ketone was characterized as follows: white crystals, mp 82.5–84.5°; ir 1705 cm^{-1} (C=O); nmr δ 7.0 (s, 4, aromatic), 2.90 (t, J = 7 Hz, 2, benzylic), 2.60 (t, J = 6 Hz, 2, benzylic), 2.00 (t, J = 7 Hz, 2, C_2 methylene), 1.4–0.8 ppm (m, 6, C_4, C_5, and C_6 methylene); and elemental analysis.

The plan for forming the diazo ketone **18** required formylation followed by treatment with *p*-toluenesulfonyl azide as previously described and illustrated in Scheme IV. Examination of molecular models reveals

Scheme IV. Plan for the Conversion of 3-Keto[7]paracyclophane into a [7]Paracyclophane Diazo Ketone



16 17 18

that it is reasonable to expect formation of only the Δ^3 enolate which would produce the 4-hydroxymethylene derivative (**17**). This formylation, however, proved to be an insurmountable task.

Using the previously described formylation procedure, treatment of 3-keto[7]paracyclophane with sodium, ethyl formate, and a catalytic amount of ethanol

in ether produced a small amount (estimated to be less than 40 mg) of desired product, ir 3600–3100 broad and 1710 cm^{-1} broad. The major portion of the starting ketone **16** was recovered.

Subsequent formylation attempts included substitution of sodium hydride for sodium; use of potassium *tert*-butoxide with dicyclohexyl-18-crown-6 (**19**), sodium hydride, and ethyl formate in benzene; and use of excess sodium and excess ethyl formate with a 1 week reaction time. All these attempts were unsuccessful in that no evidence for a diazo ketone was found after treatment with *p*-toluenesulfonyl azide.

The small amount of formylated product from the first formylation was treated with *p*-toluenesulfonyl azide to produce a diazo ketone, ir 2070 ($C{=}N_2$) and 1690 cm^{-1} (C=O), contaminated with an approximate threefold excess of *p*-toluenesulfonyl azide, ir 2120 cm^{-1} (N_3). Since no obvious separation technique seemed available, the mixture was photolyzed.

Work-up of the photolysis mixture failed to produce any carboxylic acid or any compound whose uv spectrum corresponded to that expected of a [6]paracyclophane. A fraction whose ir corresponded to a sulfonamide was isolated. At this point the supply of 3-carboxy[7]paracyclophane was exhausted. The possibility of preparing the [6]paracyclophane ring in this way remains. There is good evidence that a diazoketo-[7]paracyclophane was prepared on one occasion; however, we were unable to reproduce these results. Different formylation procedures, different routes to a diazoketo[7]paracyclophane, and different ring contraction schemes are available.

Experimental Section

Physical Methods. Ir spectra were taken on a Perkin-Elmer Model PE-257 or PE-621 grating spectrophotometer. Nmr were recorded on a Varian Model HA-100 by C. Pape. Since many of the compounds studied have absorptions near tetramethylsilane (TMS), the following procedure was used. A preliminary spectrum was taken on a Varian Model T-60 without an internal reference. If protons were found closer than 0.6 ppm from TMS and no absorptions were found in the region 6.3–4.3 ppm, then methylene chloride with protons at 5.3 ppm was used as a lock and internal reference. If protons were no closer to TMS than 0.6 ppm, then TMS was used as a lock and internal reference. All spectra were recorded under one of these two situations. Spectra are reported in the standard manner, in parts per million from TMS. Ultraviolet spectra were recorded on a Cary 15. Mass spectra were recorded on a Hitachi Model RMU-6. Melting points were recorded on an Eimer and Amend melting point block and were uncorrected. Analyses were by Atlantic Microlab, Inc., Atlanta, Georgia 30308. Preparative thin layer chromatography plates were prepared using a 50:50 mixture of silica gel H and silica gel HF. Plates were spread 1.25-mm thick and spots were detected with uv light.

4-Carbomethoxy[8]paracyclophane. The preparation is described in ref 8.

4-Diphenylhydroxymethyl[8]paracyclophane (5). Phenylmagnesium bromide was generated by slowly adding 6.55 g of bromobenzene to 0.99 g of magnesium turnings in dry THF under a nitrogen atmosphere. The solution was refluxed for 1 hr to ensure completion of the reaction. The solution was cooled and 1.00 g of 4-carbomethoxy[8]paracyclophane in 25 ml of dry THF was added. The solution was refluxed for 40 hr and then cooled. Approximately 20 ml of saturated ammonium chloride was added (until the THF layer became clear). The THF layer was decanted and the magnesium salts were washed thoroughly with ether. The combined THF and ether extracts were dried and the solvent was evaporated leaving a brownish semisolid. This was chromatographed on a florisil column, eluting first with low boiling petroleum ether to remove biphenyl. The portion eluted with benzene–ether 50:50 until the yellow band was ready to come off the column was saved and the solvent was evaporated. The resulting white solid was recrystallized from hexane to produce 1.25 g (83%) of white crystals: mp 123.0–124.5°; ir (CCl_4) 3610 cm^{-1} (OH); nmr (CH_2Cl_2) δ 7.6–6.9 (m, 14, aromatic), 2.75 (m, 2, benzylic), 2.20 (m, 2, benzylic), 1.95 (s, 1, OH), 1.80 (m, 1, aliphatic proton), 1.35 (m, 4, aliphatic protons), 1.0–0.0 (m, 5, partially shielded protons), and −0.85 ppm (m, 1, highly shielded protons). On treatment with D_2O the peak at 1.95 ppm disappeared.

Anal. Calcd for $C_{27}H_{30}O$: C, 87.52; H, 8.16. Found: C, 87.14; H, 8.27.

4-Diphenylmethylene[8]paracyclophane (6). To a solution of 80 ml of glacial acetic acid and 17 ml of water was added 920 mg of 4-diphenylhydroxymethyl[8]paracyclophane. The solution was refluxed for 3 hr, cooled, and diluted with 50 ml of water. The solution was extracted with ether. The ether extracts were washed with water, dilute sodium bicarbonate, and water, dried, and evaporated, leaving a brownish solid. This product was chromatographed on a silica gel column, eluting with low boiling petroleum ether. The third through fifth column volumes were combined to give 660 mg (76%) of a white solid. Recrystallization from hexane produced white crystals: mp 122.5–123.5°; ir (CCl_4) 1665 cm^{-1} (C=C); nmr (CH_2Cl_2) δ 7.15 (m, 14, aromatic), 2.55 (m, 4, benzylic), 1.35 (m, 6, methylene), and 0.75 ppm (m, 4, methylene).

Anal. Calcd for $C_{27}H_{28}$: C, 91.99; H, 8.01. Found: C, 91.96; H, 8.01.

4-*N*,*N*-Dimethylcarboxamido[8]paracyclophane (7).[17] To 3.00 g of 4-carboxy[8]paracyclophane was added 2.3 g of distilled thionyl chloride. The solution was kept at 130° for 30 min, after which the ir of an aliquot of the solution showed the absence of carboxylic acid and showed absorption at 1790 cm^{-1}, consistent with an acid chloride carbonyl. The solution was cooled and 6 ml of anhydrous benzene was added. The benzene and thionyl chloride were distilled (until the temperature of the vapors reached 90°). A second 6-ml portion of benzene was added and the process was repeated.

A benzene solution of the crude acid chloride was added to 3.5 g (38.8 mmol) of a cold 50% anhydrous dimethylamine–benzene solution. The ice–salt bath was removed and the solution was stirred overnight at room temperature. Water was added and the layers were separated. The aqueous layer was washed with ether and the combined ether–benzene extracts were washed with water and dried. The solvent was evaporated, leaving 3.91 g (116%) of a dark brown oil. A small portion was distilled to give a thick yellowish oil, bp 148–150° (0.1 mm). This oil was subjected to a molecular distillation (bath temperature 100–120°, pressure <0.01 mm). The resulting clear viscous oil had the following properties: ir (neat) 1640 cm^{-1} (C=O); nmr (CCl_4) δ 7.10 (m, 4, aromatic), 2.80 (m, 8, N-(CH_3)$_2$ and benzylic), 2.35 (m, 2, benzylic) 1.9–0.1 (m, 10, aliphatic protons), and −0.45 ppm (m, 1, highly shielded proton).

Anal. Calcd for $C_{17}H_{25}NO$: C, 78.72; H, 9.72. Found: C, 78.50, 78.44; H, 9.85, 9.81.

4-(*N*,*N*-Dimethylamino)methyl[8]paracyclophane (8).[18] An ether solution of the crude brown 4-*N*,*N*-dimethylcarboxamido[8]paracyclophane (3.91 g) from the previous step was slowly added to a stirred suspension of 0.780 g of lithium aluminum hydride in ether under a nitrogen atmosphere. The solution was refluxed for 20 hr and then cooled. Water (0.8 ml) was slowly added, followed by 0.8 ml of 15% sodium hydroxide. The solution was stirred for 20 min. Water (2.4 ml) was added, causing crystallization of the aluminum salts. The aluminum salts were thoroughly washed with ether and then extracted for 20 hr with ether in a Soxhlet. The combined ether layers were washed with water and then extracted with dilute hydrochloric acid. Sodium hydroxide pellets were added to the aqueous extracts until the solution was basic. The basic solution was extracted with ether. The ether extracts were washed with water and dried. The solvent was evaporated leaving a nearly clear oil (2.9 g, 91% from 4-carboxy[8]paracyclophane). A portion of this oil was taken up in anhydrous ether, and dry hydrogen chloride gas was bubbled through the solution. The resulting very hygroscopic amine hydrochloride, mp 178–180°, was not characterized further. The crude amine has the following spectral properties: ir (neat) 2805 and 2760 cm^{-1} (Bohlmann Bands); nmr (CCl_4) δ 7.05 (m, 4, aromatic), 2.80 (m, 2, benzylic), 2.5–1.9 (m, 8, benzylic and N-(CH_3)$_2$), 1.9–0.8 (m, 8, aliphatic protons), 0.7–0.0 (m, 4, shielded aliphatic protons), and −0.55 ppm (m, 1, highly shielded protons).

4-Methylene[8]paracyclophane (9).[19] In an erlenmeyer flask were

(17) A. C. Cope and E. Ciganek, "Organic Syntheses," Collect Vol. IV, Wiley, New York, N. Y., 1963, p 339.
(18) Reference 17, p 340.
(19) Reference 17, p 612.

placed 2.9 g of crude 4-*N*,*N*-(dimethylamino)methyl[8]paracyclophane and 7 ml of methanol. Three 1.34-g portions of 30% hydrogen peroxide were added at 0, 4, and 12 hr from the beginning of the reaction. The flask was covered with a watch glass and kept at room temperature. After 36 hr the excess peroxide was destroyed by swirling with a small amount of aqueous platinum black.[20] After evolution of gas had ceased, the solution was filtered. As much solvent as possible was removed on the rotary evaporator at room temperature. The flask was equipped with a stirring bar and attached to a still head which was attached to a trap submerged in a bath at −78°. The pressure was reduced to 1 mm, and the flask was kept at room temperature until the contents of the flask solidified. The temperature was then raised to 140° and kept there for 30 min. Elimination appeared to begin at a bath temperature of 110°. The system was cooled and the flask and trap were washed with ether. The resulting ether solution was washed with water and dried. The solvent was evaporated leaving a slightly brownish oil which was distilled to produce 2.05 g (79% from 4-carboxy[8]paracyclophane) of a clear oil: bp 86.5–88.0° (0.6 mm); ir (neat) 3070 (C–H vinyl stretch), 1640 (C=C), and 875 cm^{-1} (vinyl out of plane C–H deformation); nmr (CCl_4) δ 6.90 (s, 4, aromatic), 4.30 (d, J = 14 Hz, 2, vinylic), 2.60 (t, J = 6 Hz, 4, benzylic), 2.0–0.9 (m, 8, methylene), and 0.20 ppm (t, J = 7 Hz, 2, shielded allylic protons).

Anal. Calcd for $C_{15}H_{20}$: C, 89.94; H, 10.06. Found: C, 89.75, 89.75; H, 10.11, 10.16.

4-Keto[8]paracyclophane (3).[21] To a stirred solution at room temperature of 2.05 g of 4-methylene[8]paracyclophane in 50 ml of *p*-dioxane (distilled from lithium aluminum hydride) and 16 ml of water was added approximately 40 mg of osmium tetroxide. The solution turned black within a few minutes. Finely ground sodium metaperiodate, 6.5 g, was added in portions over a 1-hr period. At this point the solution was heavily laden with salts, so an additional 25 ml of *p*-dioxane and 8 ml of water were added. The solution was stirred for 11 hr. Ether was added along with enough water to dissolve the iodate and periodate salts. The ether layer was separated and the aqueous layer was washed with ether. The combined ether layers were washed with 10% aqueous sodium sulfide (to remove osmium tetroxide) until the aqueous layer remained clear. The ether layer was then washed with water and dried. The solvent was evaporated leaving a brownish solid which was sublimed at 40° (1 mm) to produce 1.70 g (83% from olefin **9**, 65% from 4-carboxy[8]paracyclophane) of 4-keto[8]paracyclophane: mp 44.5–46.0°; ir (CCl_4) 1710 cm^{-1} (C=O); nmr (CCl_4) δ 6.95 (m, 4, aromatic), 2.60 (t, J = 6.5 Hz, 4, benzylic), and 2.15–0.95 ppm (m, 10, methylene); mass spectrum (70 eV) M^+ 202 (calcd 202).

Anal. Calcd for $C_{14}H_{18}O$: C, 83.12; H, 8.97; Found: C, 83.04; H, 8.85.

3-Hydroxymethylene-4-keto[8]paracyclophane (10).[22,23] In a flask under a nitrogen atmosphere was placed 20 ml of dry ether, 224 mg of freshly cut sodium, 2.00 g of 4-keto[8]paracyclophane, and 1.10 g of ethyl formate which had been dried over anhydrous potassium carbonate and distilled from phosphorous pentoxide. The reaction was initiated with 0.048 ml of absolute ethanol and placed in an ice bath with continued stirring for 9 hr (until the sodium had dissolved). The flask was then allowed to stand for 12 hr at room temperature. Absolute ethanol (0.24 ml) was added and the reaction mixture was stirred for 1 hr. Water was added and the layers were separated. The ether fraction was washed with water and the aqueous fractions were acidified with 1.68 ml of 6.0 *N* hydrochloric acid and extracted with ether. The ether extracts were washed with water and dried. The solvent was evaporated leaving a light brownish oil, 1.68 g (74%, 87% based on recovered starting material) of which could be solidified by cooling. Because of potential polymerization, no further purification was attempted: ir (neat) 1730, 1705, and 1625 cm^{-1} (α-hydroxy methylene ketone). The organic fraction was dried and the solvent was evaporated. The remaining solid was sublimed to produce 298 mg of starting ketone, mp 41–44°. Yields for subsequent steps in this synthesis are based on the unrecovered starting material.

p-**Toluenesulfonyl Azide.**[24] *p*-Toluenesulfonyl chloride, purified according to ref 25, was allowed to react with sodium azide as described in ref 24. *Note of caution:* *p*-toluenesulfonyl azide is reported to be shock sensitive.[26]

3-Diazo-4-keto[8]paracyclophane (4a).[22,27] In a flask with a stirrer was placed 1.68 g of crude 3-hydroxymethylene-4-keto[8]-paracyclophane, 6 ml of freshly distilled methylene chloride, and 1.48 g of freshly distilled triethylamine. The flask was cooled in an ice–salt bath and 1.17 g of *p*-toluenesulfonyl azide was added over a 1 hr period. The amount of *p*-toluenesulfonyl azide added was based on an estimated 60% yield of hydroxy methylene ketone (**10**) from 4-keto-[8]paracyclophane. This corresponded to the yield obtained from the model compound, cyclohexanone. Stirring was continued for 2 hr while the ice melted. A solution of 510 mg of potassium hydroxide in 6 ml of water was added and the solution was stirred for 15 min. The layers were separated and the aqueous layer was washed twice with methylene chloride. The combined methylene chloride extracts were washed with 2.8 ml of a 1.4% potassium hydroxide solution, washed with water, and dried. The solvent was removed on the rotary evaporator at 35° until a constant weight of the orange oil was obtained, 1.36 g (101% based on the *p*-toluenesulfonyl azide used): ir (neat) 2080 (C=N_2) and 1625 cm^{-1} (C=O). No azide absorption at 2120 cm^{-1} was observed when this amount of *p*-toluenesulfonyl azide was used.

3-Carboxy[7]paracyclophane (11). To a Pyrex round-bottom flask was added 1.36 g of crude 3-diazo-4-keto[8]paracyclophane, 75 ml of *p*-dioxane (distilled from lithium aluminum hydride), 35 ml of water, and 1.00 g of sodium bicarbonate. The solution was irradiated with a Sears 275 W sunlamp for 4 hr while being immersed in an oil bath at 90°. The solution was cooled, some ether was added, and the layers were separated. The ether layer was extracted with 10% sodium hydroxide. The combined aqueous extracts (note that the ether extracts were worked up as described under 4-keto-2-[8]paracyclophene (**12**)) were washed with ether and acidified with hydrochloric acid. The solution was extracted with ether. The ether extracts were washed with water and dried. The solvent was evaporated leaving 790 mg (61% from crude diazo ketone **4a**) of yellowish semisolid. The product was purified by preparative thin layer chromatography using silica gel and hexane–ethyl acetate 1:1. Despite tailing, good results were obtained. The band R_f 0.8–0.5 yielded 3-carboxy[7]paracyclophane, 641 mg (49% from diazo ketone **4a**, 35% from 4-keto[8]paracyclophane). Recrystallization from hexane produced white crystals which were characterized as follows: mp 130.5–132.5°; ir (CCl_4) 3500–2300 (broad, OH), 1705 cm^{-1} (C=O); nmr (CCl_4) δ 11.2 (s, 1, COOH), 7.15 (d, J = 12 Hz, 4, aromatic), 2.95 (m, 2, benzylic), 2.45 (m, 2, benzylic), 2.1–0.0 (m, 8, aliphatic protons), and −1.4 ppm (2 doublets, J = 11 and 15 Hz, 1, highly shielded protons); uv_{max} (95% EtOH), 292 sh (ε 298), 284 (ε 364), 237 (ε 7140), and 207 nm (ε 22,700); mass spectrum (70 eV) M^+ 218 (calcd 218).

Anal. Calcd for $C_{13}H_{18}O$: C, 77.03; H, 8.31. Found: C, 77.06, 77.09; H, 8.33, 8.36.

4-Keto-2-[8]paracyclophene (12). The ether layer from the first extraction reported under 3-carboxy[7]paracyclophane (**11**) was washed with water and dried. The solvent was evaporated to leave 467 mg of a dark yellow solid. This was separated by preparative thin layer chromatography using silica gel and hexane–ethyl acetate 1:1. The band with R_f 0.50–0.75 was eluted with ether to yield 300 mg (25% from crude diazo ketone **4a**) of a slightly yellowish solid. Treatment with decolorizing carbon and recrystallization from hexane left 184 mg of white crystals, mp 85.5–87.0°. The structure 4-keto-2-[8]paracyclophene was assigned on the basis of the following evidence: it decolorized bromine in carbon tetrachloride; ir (CCl_4) 1690 (α,β-unsaturated C=O), 1610 cm^{-1} (C=C); nmr (CCl_4) δ 6.95 (m, 4, aromatic), 5.50 (m, 2, vinylic), 3.35 (m, 2, C_1 benzylic), 2.65 (t, J = 6 Hz, 2, C_8 benzylic), 1.35 (m, 4, methylene), and 0.90 ppm (t, J = 5 Hz, 2, methylene); mass spectrum (70 eV) M^+ 200 (calcd 200); uv_{max} (95% EtOH), 280 (ε 460, with a tail extending to 330 nm), 272 (ε 530), and 225 nm sh (ε 7600).

Anal. Calcd for $C_{14}H_{16}O$: C, 83.96; H, 8.05. Found: C, 83.60, 83.68; H, 8.21, 8.23.

(20) R. Feulgen, *Chem. Ber.*, **54**, 360 (1921).

(21) R. Pappo, D. S. Allen, Jr., R. U. Lemieux, and W. S. Johnson, *J. Org. Chem.*, **21**, 478 (1956).

(22) Since the isolated product of photolysis of the diazo ketone prepared from this product was subsequently shown to be 3-carboxy[7]-paracyclophane and not 4-carboxy[7]paracyclophane, this formylation must have produced the 3-hydroxymethylene product rather than the 4-hydroxymethylene product.

(23) C. Ainsworth, "Organic Syntheses," Collect. Vol. IV, Wiley, New York, N. Y., 1963, p 536.

(24) M. Regitz, J. Hocker, and A. Liedhegener, "Organic Syntheses," Collect. Vol. 48, Wiley, New York, N. Y., 1968, p 36.

(25) S. W. Pelletier, *Chem. Ind. (London)*, 1034 (1953).

(26) (a) L. F. Fieser and M. Fieser, "Reagents for Organic Synthesis," Vol. 2, Wiley-Interscience, New York, N. Y., 1969, p 468; (b) Eastman Kodak Co., Rochester, N. Y., personal communication.

(27) M. Regitz, J. Ruter, and A. Liedhegener, "Organic Syntheses," Collect. Vol. 51, Wiley, New York, N. Y., 1971, p 86.

3-Hydroxymethyl[7]paracyclophane. To a flask under a nitrogen atmosphere was added 300 mg of sodium bis(2-methoxyethoxy)-aluminum hydride (70% in benzene) and 0.55 ml of anhydrous benzene. A solution of 80 mg of 3-carboxy[7]paracyclophane in 0.40 ml of benzene was slowly added. The solution was refluxed for 1 hr and cooled, and 0.23 ml of 6.0 *N* hydrochloric acid in 1 ml of water was slowly added. The benzene layer was separated and saved. The aqueous layer was acidified to pH 4 and extracted with benzene. The combined benzene extracts were washed with 10% sodium hydroxide and water and dried. The solvent was evaporated to produce 63 mg (84%) of white solid. The product was recrystallized from hexane to give white crystals: mp 74.5–75.5°; ir (CCl_4) 3640 and 3560–3200 cm^{-1} (OH); nmr (CCl_4) δ 6.20 (m, 4, aromatic), 2.95 (m, 4, benzylic and CH_2OH), 2.40 (m, 2, benzylic), 2.15 (s, 1, OH), 1.55 (m, 3, aliphatic protons), 1.0 to −0.1 (m, 5, aliphatic protons), and −1.4 ppm (2 doublets, J = 11 and 15 Hz, 1, highly shielded protons); uv_{max} (95% EtOH), 292 (ϵ 330), 284 (ϵ 401), and 237 nm (ϵ 7580).

Anal. Calcd for $C_{14}H_{20}O$: C, 82.30; H, 9.87. Found: C, 82.15; H, 9.99.

Hydrogenation of 4-Keto-2-[8]paracyclophene (12). A mixture of 25 mg of 10% palladium on carbon, 111 mg of 4-keto-2-[8]paracyclophene, and 2 ml of methanol was stirred under an atmosphere of hydrogen at room temperature and atmospheric pressure. After 25 min absorption of hydrogen ceased. At this time approximately 1 equiv of hydrogen had been taken up. The solution was filtered and the solvent was evaporated to produce 99 mg (88%) of white solid, mp 44.0–45.5°. The product was identified as 4-keto[8]paracyclophane on the basis of the ir, which was identical with that of the previously prepared 4-keto-[8]paracyclophane, the melting point which was identical with 4-keto-[8]paracyclophane, and the mixed melting point which was 44.5–46.0°.

Anilide of 3-Carboxy[7]paracyclophane. The acid chloride of 100 mg of 3-carboxy[7]paracyclophane was prepared as described under the preparation of 3-*N*,*N*-dimethylcarboxamido[7]paracyclophane (**13**). The acid chloride was added to a solution of 130 mg of freshly distilled aniline and stirred overnight at room temperature. Water was added and the layers were separated. The benzene layer was washed with dilute hydrochloric acid, washed with water, and dried. The solvent was evaporated leaving 150 mg (112%) of off-white product. Treatment with decolorizing carbon followed by recrystallization from methanol produced white crystals: mp 196.0–198.5°; ir (Nujol) 3290 and 3250 (N–H stretch), 1660 (amide I, C=O) and 1540 cm^{-1} (amide II, C=O); nmr ($CDCl_3$) δ 7.6–6.9 (m, 9, aromatic), 2.95 (m, 2, benzylic), 2.35 (m, 2, benzylic), 2.0–0.0 (m, 9, N–H and aliphatic protons), and −1.35 ppm (2 doublets, J = 11 and 15 Hz, 1, highly shielded protons).

Anal. Calcd for $C_{20}H_{23}NO$: C, 81.87; H, 7.90. Found: C, 81.97; H, 7.9.

3-*N*,*N*-Dimethylcarboxamido[7]paracyclophane (13). 3-Carboxy-[7]paracyclophane (1.20 g) was treated with 0.98 g (0.60 ml) of thionyl chloride as described in the preparation of 4-*N*,*N*-dimethylcarboxamido[8]paracyclophane. The solution was heated for 30 min at 120°. The benzene and excess thionyl chloride were distilled under aspirator pressure. An ir of an aliquot showed the absence of a carboxylic acid and the presence of an acid chloride carbonyl, 1790 cm^{-1}. The acid chloride was added to 750 mg (16.5 mmol of dimethylamine) of a 50% solution of anhydrous dimethylamine in benzene as described above. After work-up, 1.31 g (97%) of crude amide was isolated. A portion was subjected to a molecular distillation (bath temperature 100°, pressure <0.01 mm) to produce a clear oil: ir (neat) 1640 cm^{-1} (C=O); nmr (CCl_4) δ 7.10 (d, J = 16 Hz, 4, aromatic), 3.1–2.0 (m, 10, *N*-methyl and benzylic), 1.9–0.4 (m, 7, aliphatic protons), 0.10 (m, 1, shielded protons), and −1.60 ppm (m, 1, highly shielded protons).

Anal. Calcd for $C_{16}H_{23}NO$: C, 78.32; H, 9.45. Found: C, 78.08; H, 9.66.

3-(*N*,*N*-Dimethylamino)methyl[7]paracyclophane (14). Crude 3-*N*,*N*-dimethylcarboxamido[7]paracyclophane (1.35 g) was added to a suspension of 460 mg of lithium aluminum hydride in ether as described in the preparation of 4-(*N*,*N*-dimethylamino)methyl[8]-paracyclophane. A brownish oil of the crude amine (1.18 g, 93% from 3-carboxy[7]paracyclophane) was obtained: ir (neat) 2810 and 2755 cm^{-1} (Bohlmann Bands); nmr (CCl_4) δ 7.05 (d, J = 14 Hz, 4, aromatic), 2.85 (m, 2, benzylic), 2.50–1.90 (m, 8, *N*-methyl and benzylic), 1.8 to −0.3 (m, 10, aliphatic protons), and −1.45 ppm (2 doublets, J = 13 and 14 Hz, 1, highly shielded protons).

3-Methylene[7]paracyclophane (15). The crude 3-(*N*,*N*-dimethylaminomethyl[7]paracyclophane (1.18 g) was treated with a total of 1.45 g of 30% hydrogen peroxide as described in the preparation of 4-methylene[8]paracyclophane. After the pyrolysis the contents of the flask and trap were taken up in ether, washed twice with water, and dried over anhydrous sodium sulfate. The solvent was evaporated to produce 1.16 g of crude brownish olefin. The crude olefin was chromatographed on an alumina (activity II, 75 g) column using pentane. The first four column volumes were collected to produce 960 mg (101% from 3-carboxy[7]paracyclophane) of clear oil contaminated with stopcock grease. A portion was distilled, bp 75–76° (0.3 mm), to give the following spectra: ir (neat) 3070 (vinyl C–H stretch), 1640 (C=C), 885 cm^{-1} (vinyl C–H out of plane deformation); nmr (CCl_4) δ 7.05 (s, 4, aromatic), 4.45 (m, 2, vinylic), 2.70 (m, 4, benzylic), 2.00–0.9 (m, 6, methylene), and 0.2 ppm (m, 2, highly shielded protons).

Anal. Calcd for $C_{14}H_{18}$: C, 90.26; H, 9.74. Found: C, 90.00; H, 9.95.

3-Keto[7]paracyclophane (16). The 3-methylene[7]paracyclophane prepared above (970 mg) was treated with approximately 30 mg of osmium tetroxide and 3.27 g of sodium metaperiodate as described in the preparation of 4-keto[8]paracyclophane. After 24 hr tlc showed the absence of starting material. Work-up produced 298 mg (29% from 3-carboxy[7]paracyclophane) of 3-keto[7]paracyclophane. A portion was sublimed to produce white crystals, mp 82.5–84.5°, which gave the following spectra: ir (dioxane) 1705 cm^{-1} (C=O); nmr (CCl_4) δ 7.0 (s, 4, aromatic), 2.90 (t, J = 7 Hz, 2, benzylic), 2.60 (t, J = 6 Hz, 2, benzylic), 2.00 (t, J = 7 Hz, 2, C_2 methylene), 1.4–0.8 ppm (m, 6, C_4, C_5, and C_6 methylene).

Anal. Calcd for $C_{13}H_{16}O$: C, 82.94; H, 8.57. Found: C, 82.89; H, 8.62.[28]

The crude ketone could also be separated from impurities by preparative thin layer chromatography (silica gel, hexane–ethyl acetate 2:1, R_f 0.45). Despite extensive efforts to isolate additional aromatic products, none were found.

4-Hydroxymethylene-3-keto[7]paracyclophane (17). Using the procedure for the preparation of 3-hydroxymethylene-4-keto[8]-paracyclophane, 345 mg of 3-keto[7]paracyclophane, 42 mg of sodium, 204 mg of ethyl formate (dried over anhydrous potassium carbonate and distilled from phosphorous pentoxide), and 0.009 ml of absolute ethanol in anhydrous ether were combined. The reaction was stirred at room temperature for 24 hr and then allowed to stand an additional 12 hr. Work-up as previously described produced 135 mg (34%) of crude viscous yellowish oil, ir 3600–3100 broad and 1710 cm^{-1} broad.

4-Diazo-3-keto[7]paracyclophane (18). The crude product (**17**) from the previous step (135 mg) was treated with 126 mg of freshly distilled triethylamine and 111 mg of *p*-toluenesulfonyl azide using the procedure for the preparation of 3-diazo-4-keto[8]paracyclophane. After work-up 120 mg of viscous orange oil contaminated with *p*-toluenesulfonyl azide was isolated: ir 2070 ($C{=}N_2$), 1690 (C=O), and 2120 cm^{-1} (N_3). The ratio of azide absorption to diazo absorption was approximately 3:1.

Photolysis of the Crude 4-Diazo-3-keto[7]paracyclophane (18). The crude diazo ketone-*p*-toluenesulfonyl azide oil was taken up in 60 ml of *p*-dioxane (distilled from lithium aluminum hydride) and 30 ml of water and 100 mg of sodium bicarbonate was added. The mixture was photolyzed as described in the preparation of 3-carboxy[7]paracyclophane. Some ether was added and the solution was extracted first with dilute bicarbonate and then with 10% sodium hydroxide. After acidification, extraction, drying, and evaporation of solvent, 27 mg of yellowish brown semisolid was isolated from the bicarbonate fraction. The ir 3300 and 1710 cm^{-1} did not clearly indicate the presence of a carboxylic acid. The uv shows a gradually increasing absorption without shoulders from 345 to beyond 260 nm, inconsistent with the desired carboxy[6]-paracyclophane. The 27-mg sample was separated by preparative thin layer chromatography (silica gel, hexane–ethyl acetate 1:1) to produce five fractions ranging from 7 mg to a trace. None of these fractions had an ir or uv consistent with a carboxy[6]paracyclophane. Acidification of the 10% sodium hydroxide fraction followed by extraction, drying, and evaporation of solvent produced a white solid whose ir corresponded to a sulfonamide.

X-Ray Structure

Crystals of 3-carboxy[7]paracyclophane were grown in hexane. A crystalline sample suitable for collection

(28) The ketone turns brown upon standing in the light at room temperature over a period of weeks. No visual evidence for decomposition was noted when stored in the dark, under nitrogen, in the refrigerator.

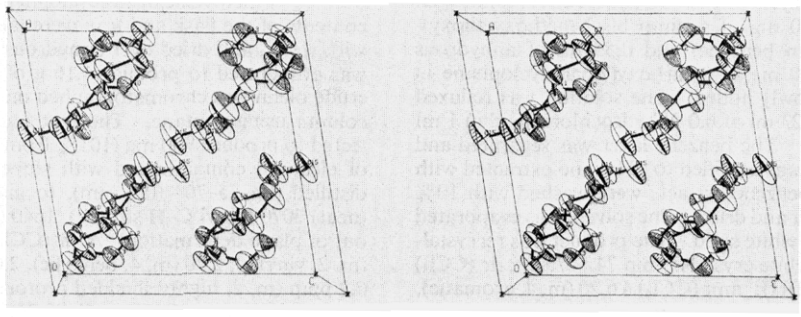


Figure 1. Stereoprojection of 3-carboxy[7]paracyclophane.

of intensity data was cut from a larger needle crystal. Precession photographs revealed a monoclinic system mounted along the c axis, and systematic absences unambiguously identified the space group as $P2_1/c$. A summary of crystal data is provided in Table III.

The crystal was transferred to an Enraf-Nonius CAD-4 diffractometer. The orientation matrix and cell dimensions were calculated using 13 accurately centered reflections near $\theta = 25°$. Intensity data were collected to a maximum θ of 75° using Cu Kα radiation and a graphite monochromator. In all, 2638 reflections were measured and recorded. Rejection of reflections less than $2\sigma_I$ gave 1606 unique nonzero diffraction maxima which were used in solution and refinement of the structure.

Three control reflections (135, $\bar{6}\bar{1}3$, $\bar{5}22$) monitered after each block of 50 reflections indicated a significant decomposition of the sample. The average percentage decrease in control reflection intensity was 12% over the period of the data collection. A correction for sample decomposition was applied by multiplying each reflection in a block by an appropriate linear correction factor obtained from the control reflection. These data were corrected for Lorentz-polarization effects[29] and reduced to an absolute scale by the method of Wilson[30] utilizing program FAME.[31] The statistical distribution of E's was in close agreement with that theoretically expected for a centrosymmetric space group.

The structure was solved by direct methods using MULTAN[32] although some difficulty was encountered at this stage. Using E's $\geq$ 1.5, MULTAN produced several almost equally consistent phase sets with ABSFOM $\approx$ 0.8, none of which produced a chemically meaningful E map. A similar result was obtained by using E's $\geq$ 2.0. A successful solution was obtained using E's $\geq$ 1.83 which gave only one reasonably consistent phase set with ABSFOM = 0.92. This phase set produced an E map[33] which gave starting positions for all carbon and oxygen atoms. Isotropic refinement[34] of the carbon and oxygen skeleton using unit weights reduced R to 0.308. Several cycles of anisotropic refinement employing weights of $(1/\sigma_{Fo})$[35] reduced the R to a final value of only 0.167.

Because of the poor refinement at this stage, another crystal was grown in cyclohexane. The cell constants were essentially unchanged, a = 12.36, b = 7.81, c = 12.74 Å, β = 99.19°, V = 1215 Å^3. The crystal was somewhat larger, 0.4 × 0.3 × 0.8; as a result, 1847 unique nonzero diffraction maxima were obtained after rejecting those reflections which were less than $2\sigma_{F_o}$. These data were also corrected for decomposition. Using the coordinates obtained from the first crystal, isotropic refinement produced an R of 0.321. Anisotropic refinement employing weights of $(1/\sigma_{Fo})$ gave an R value of 0.163, essentially the same final R value as the first crystal.

Several attempts were made to adjust the structure model to obtain a better refinement. One odd feature of the structure is the nearly equal x and z values of C_1, C_3, C_5, C_7, C_8, C_{11}, and C_{14} which means, in effect, that a sizable portion of the atoms in the structure lie in the $\bar{1}01$ diagonal plane (see Figure 1). This feature is also indicated by the enormity of the $\bar{2}02$ reflection which has an F value more than twice as large as any other reflection. A disordered model was envisioned which involved random packing of enantiomeric molecules; *i.e.*, because a major portion of the nonbenzene carbon atoms of the molecules occupy the diagonal plane, a molecule or its enantiomer could conceivably pack in the same positions with only C_2, C_4, and C_6 not in register in the isomers. A difference map, however, does not provide evidence of a disorder of the kind described and suggests a more profound disorder. Pairs of peaks are associated with each of the 16 reported atomic positions and are approximately equidistant on either side of the $\bar{1}01$ crystal plane passing through the original atomic coordinates. The difference map appears as though large anisotropic thermal motions perpendicular to the $\bar{1}01$ plane have not been accounted for, although the difference map was generated by data obtained from an anisotropic refinement. Another disordered model was composed by placing atoms of $^1/_2$ weight in each relevant position located in the difference map. Upon refinement, the $^1/_2$ atoms moved back to positions very close to those of the original model.

Because the bond lengths and angles are quite reasonable chemically and because there are no unusually short intermolecular distances, we believe the reported structure is an essentially correct one even though the

(29) Corrections were made using program DATRED, a PL-1 program for the IBM-360: M. G. Newton and C. J. Finder, University of Georgia, Athens, Ga.

(30) A. J. C. Wilson, *Nature (London)*, **150**, 152 (1942).

(31) The computer program FAME was written by R. A. Dewar, A. Stone, and E. B. Fleischer, The University of Chicago, Chicago, Ill.

(32) The computer program MULTAN was written by P. Main and M. M. Woolfson, University of York, York, England and G. Germain, Universite de Louvain, Leuven, Belgium.

(33) The Fourier program used is FORDAP written by A. Zalkin, Lawrence Radiation Lab., Livermore, Calif.

(34) The full-matrix, least-squares program (UCLALS) used in refinement was written by P. K. Gantzel, R. A. Sparks, and K. N. Trueblood and modified by M. G. Newton for the IBM-360.

(35) σ_{F_o} values were estimated for each reflection from counting statistics. See ref 8 for details.

nature of the probable disorder is unknown. Likely, in view of the above, the disorder is only a partial one.

Supplementary Material Available. Listings of h, k, l, F_o, and F_c will appear following these pages in the microfilm edition of this volume of the journal. Photocopies of the supplementary material from this paper only or microfiche (105 × 148 mm, 24× reduction, negatives) containing all of the supplementary material for the papers in this issue may be obtained from the Journals Department, American Chemical Society, 1155 16th St., N.W., Washington, D. C. 20036. Remit check or money order for $4.00 for photocopy or $2.00 for microfiche, referring to code number JACS-74-4588.

One Stage Synthesis of Bicyclo[3.2.2]nona-6,8-dien-3-ones. The Silver Trifluoroacetate Induced Reaction of 2-Methoxyallyl Bromide with Arenes

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Abstract: The 2-methoxyallyl cation has been generated from 2-methoxyallyl bromide and silver trifluoroacetate in the presence of sodium carbonate and shown to react with benzene, toluene, *p*-xylene, and mesitylene. On acidic work-up 1-aryl-2-propanones and bicyclo[3.2.2]nona-6,8-dien-3-ones were isolated, whereas nonaqueous work-up gave further products including arylated enol ethers, a simple acyclic hemiketal, namely 2-hydroxy-2-methoxy-1-phenylpropane, possibly bicyclo[3.2.2]nona-2,6,8-trienes and bromine containing by-products. Bicyclo[4.3.0]nona-6,8-dien-3-ones (dihydroindanones), which are the potential products of a 3 + 2 cycloaddition of the 2-methoxyallyl cation to the arene, were not formed. Bicyclo[3.2.2]nona-6,8-dien-3-ones are sensitive to acid and heat, yielding 1-aryl-2-propanones under fairly mild conditions. It is suggested that formation of the bicyclics involves two-pronged electrophilic attack of silver ion and the 2-methoxyallyl cation on opposite faces of the aromatic molecule.

In studying the silver salt promoted formation of allyl cations from allyl halides we noticed several years ago the utility of benzene as a solvent[1a] and considered that benzene-separated ion pairs are formed, which are stabilized by virtue of the favorable interaction of the lowest unoccupied molecular orbital (LUMO) of the cation and the appropriate highest occupied molecular orbital (HOMO) of benzene (Figure 1a).[1b] There arose the intriguing question whether the aromatic sextet might actually be sacrificed under conditions which favored formation of a bicyclic carbocation (Figure 1b). Accordingly, we have investigated the behavior of arenes toward the 2-methoxyallyl cation (Figure 1b, R = OCH_3), which was generated from 2-methoxyallyl bromide and silver trifluoroacetate, and we now report our results in detail.[2] Throughout this paper, compounds **1a–g** refer to the series of products from the reaction with benzene, **2a**, etc., to those from toluene, **3** from *p*-xylene and **4** from mesitylene, while **5a–d** are bromine-containing by-products.

Identification of Products. Basically, the reaction was carried out as described previously,[3] an arene being used instead of the cyclic diene. In order to gain further mechanistic insight, the products were worked up in two ways. In the most simple case (mode of isolation A), the reaction mixture was treated with dilute nitric acid and then extracted with chloroform to yield the known bicyclo[3.2.2]nona-6,8-dien-3-one[4] (**1b**) and 1-phenyl-2-propanone (**1c**) (see Table I and Scheme I, arene = benzene).

Table I. Products from the Reaction with Benzene

Mode of isolation	Retention time R_t	Composition %	Assignment	Formula no.
A. Work-up with dilute HNO_3	1.25	23	Bicyclo[3.2.2]nona-6,8-dien-3-one	**1b**
	≡1.00	77	$PhCH_2COCH_3$	**1c**
B1. Non-aqueous work-up of mother liquor	1.30	24	Bicyclo[3.2.2]nona-6,8-dien-3-one[a]	**1b**
	−1.25			
	1.00	32	$PhCH_2COCH_3$	**1c**
	0.92	~24	$PhCH_2COH(OCH_3)CH_3$	**1g**
	0.86	Trace	$CH_2BrC(OCH_3)_2CH_2Br$	**5b**
	0.85	8	2-Methoxy-1-phenyl-1-propene[b]	**1e**
	0.73	3	$CH_3C(OCH_3)_2CHBr_2$	**5a**
	0.58	7	2-Methoxy-1-phenyl-1-propene[c]	**1f**
	0.49	2	Benzaldehyde	
B2. Acid treated residue	1.30	71	Bicyclo[3.2.2]nona-6,8-dien-3-one	**1b**
	1.00	26	$PhCH_2COCH_3$	**1c**
	0.92	3	Unknown	

[a] The bicyclic dienone so isolated contained another compound of similar retention time which was possibly 3-methoxybicyclo-[3.2.2]nona-2,6,8-triene (**1a**). [b] The phenyl and methyl groups are probably trans to each other; see text. [c] Probably the cis isomer.

On work-up under milder, nonaqueous conditions (mode of isolation B) it became clear that **1b** and **1c** arose from a sequence of sensitive precursors, the identification of which was not trivial, since they were formed in small and changing amounts and tended to be ill-resolved on glc. By using mainly combined glc–ms and

(1) (a) H. M. R. Hoffmann and D. R. Joy, *J. Chem. Soc. B*, 1182 (1968); (b) D. R. Joy, Ph.D. Thesis, University of London, 1968.
(2) Preliminary account: H. M. R. Hoffmann and A. E. Hill, *Angew. Chem., Int. Ed. Engl.*, **13**, 136 (1974).
(3) A. E. Hill, G. Greenwood, and H. M. R. Hoffmann, *J. Amer. Chem. Soc.*, **95**, 1338 (1973).
(4) A. J. Baker, A. M. Chalmers, W. W. Flood, D. D. MacNicol, A. B. Penrose, and R. A. Raphael, *Chem. Commun.*, 166 (1970).