Organic and Biological Chemistry

Macro Rings. XXXIV. A Ring Expansion Route to the Higher Paracyclophanes, and Spectra–Structure Correlations of Their Derived Ketones[1]

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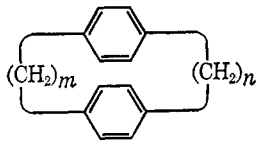
Abstract: Four-step syntheses of [3.3]-, [3.4]-, and [4.4]paracyclophanes from [2.2]paracyclophane are reported in which the critical ring enlarging step involves treatment of either 1,7- or 1,8-diketo[2.2]paracyclophane with appropriate amounts of diazomethane. The yield pattern of homologous ketones suggests that the smaller the ring system of the reacting ketone, the faster is the ring expanding step. The best over-all yield (23%) of [3.3]paracyclophane was obtained when the ring expansion was uncatalyzed by methanol, whereas the best over-all yield (25%) of [4.4]-paracyclophane involved methanol catalysis. No epoxide was observed as by-product. Similarly, 1-keto[2.2]paracyclophane when tested with diazomethane produced [2.3]- and [2.4]paracyclophane monoketones. Each of the ten ketones prepared exhibited a unique nuclear magnetic resonance (nmr) spectrum that allowed an unambiguous structural assignment to be made. The nmr spectra of the smaller [*m.n*]paracyclophanes are reported.

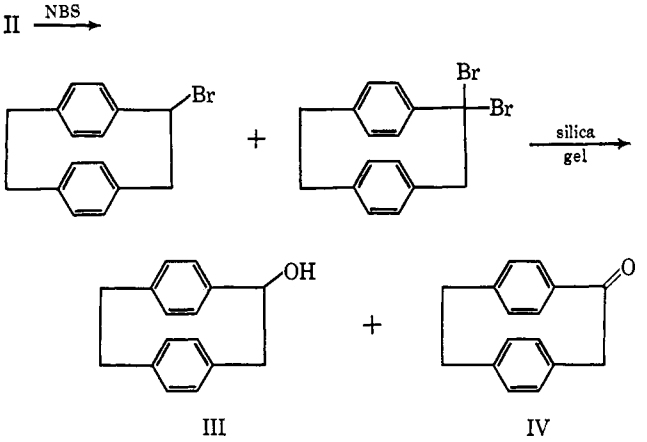
Although classical synthetic methods produced the lower members of the [*m.n*]paracyclophane (I) homologous series,[2] some of the most interesting members were unavailable for other than characterization purposes because of the numbers of steps and low yields involved in the synthetic sequences. Because of its peculiar molecular structure,[3a] the chemistry of [3.3]paracyclophane promises to be particularly interesting, and yet only 0.020 g of the compound had ever been prepared. A torturous synthetic route was employed that involved ten troublesome steps, and a miniscule over-all yield.[3] This paper reports a practical synthesis of this substance, some of its homologs, as well as derived ketones, whose structures and physical properties are interesting in their own right.



I

Syntheses

[2.3]- and [2.4]Paracyclophanes. Expansion of only one of the two bridges of [2.2]paracyclophane (II) was first studied. Bromination of II with N-bromosuccinimide (NBS) gave a mixture of mono-, *gem*-di- and tribromo derivatives, which when chromatographed on silica gel gave 1-hydroxy[2.2]paracyclophane (III), 1-keto[2.2]paracyclophane (IV), and unhydrolyzed bromides. Alternatively, the *gem*-dibromide was converted to ketone IV with silver acetate in acetic acid and water. A Wolff–Kishner reduction of IV produced a mixture of 60% II and 40% *p,p'*-dimethylbibenzyl.



III IV

The uncatalyzed and methanol-catalyzed reactions of ketone IV with ether-distilled diazomethane were studied at 0°. The three ketonic products (V, VI, and VII) were isolated by preparative vpc, and the results are recorded in Table I. No epoxide or re-

Table I. Yields of 1- and 2-Keto[3.3]paracyclophane (V and VI) and 2-Keto[4.2]paracyclophane (VII) by Ring Expansion of 1-Keto[2.2]paracyclophane (IV)

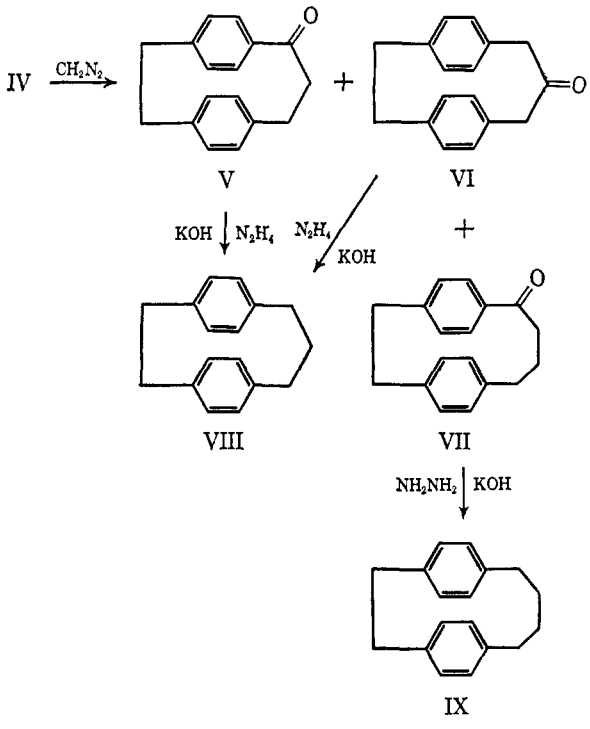
Run no.	Time, hr	Solvent	IV	V	VI	VII
1	20	Chloroform–ether	34	25	16	0
2	20	Benzene–ether	24	29	13	0
3	0.17	Chloroform–ether–methanol	17	21	26	11
4	0.75	Chloroform–ether–methanol	0	19	38	25
5	3	Chloroform–ether–methanol	0	5	32	32
6	5	Chloroform–ether–methanol	0	0	28	33

(1) The authors wish to thank the National Science Foundation for a grant used in support of this research.

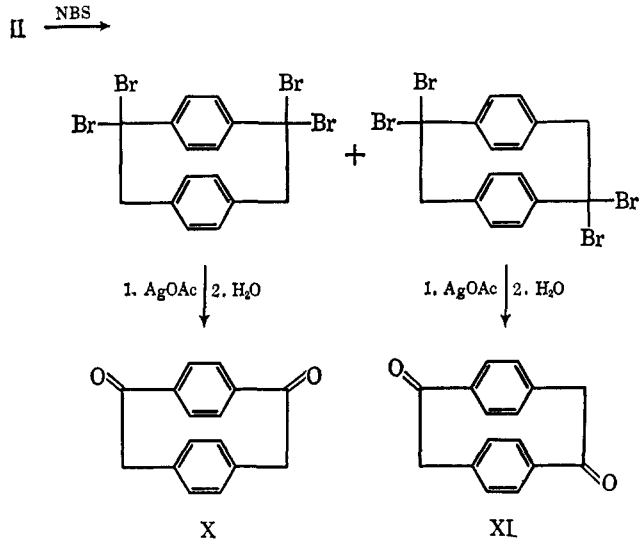
(2) (a) D. J. Cram and H. Steinberg, *J. Am. Chem. Soc.*, 73, 5691 (1951); (b) D. J. Cram and N. L. Allinger, *ibid.*, 76, 726 (1954); (c) N. L. Allinger and D. J. Cram, *ibid.*, 76, 2362 (1954); (d) D. J. Cram, N. L. Allinger, and H. Steinberg, *ibid.*, 76, 6132 (1954); (e) D. J. Cram and R. W. Kierstead, *ibid.*, 77, 1186 (1955).

(3) (a) P. K. Gantzel and K. N. Trueblood, *Acta Cryst.*, 18, 958 (1965); (b) D. A. Bekoe and K. N. Trueblood, private communication; (c) C. J. Brown, *J. Chem. Soc.*, 3265 (1953).

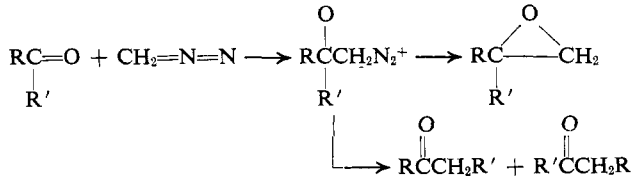
arrangement products of epoxides were observed when either vpc or nmr techniques were applied to the reaction mixtures. Reduction of these ketones with hydrazine and base gave [2.3]paracyclophane (VIII) and [2.4]paracyclophane (IX), identified by comparisons with authentic samples.[2a] These reactions coupled with their nmr spectra (see later section) serve to establish the structures of ketones V, VI, and VII.



[3.3]-, [3.4]-, and [4.4]Paracyclophanes. Exhaustive bromination of [2.2]paracyclophane with NBS produced as the main products two tetrabromides, hydrolysis of which gave diketones X and XI.[4a] Ring expansion of diketone XI in the uncatalyzed reaction gave the diketones formulated which were reduced to [3.3]- and [3.4]paracyclophane (XVIII and XIX). These diketones were identified by their spectral properties (see later sections), and the hydrocarbons by comparison of their physical and spectral properties with those of authentic samples.[2d,e] The reaction conditions were adjusted to obtain maximum yields of the [3.3]paracyclophane diketones. When II was submitted to the four-step reaction sequence without separation of the isomeric intermediates, XVIII was isolated in 19% and XIX in 4% over-all yield. When diketone XI was homologated in the presence of methanol and the resulting ketones reduced, a 25% yield of XX and 12% yield of XIX was obtained. Hydrocarbon XX was identified by comparison with an authentic sample.



Ring Expansion Step. The reaction of diazomethane with ketones has been formulated as a nucleophilic addition to the carbonyl group to give an adduct that decomposes with loss of nitrogen to give either an epoxide or the product of a 1,2 rearrangement.[5] The use of methanol, water, or various Lewis acids has been found to catalyze the reaction and to increase the amount of ketonic product.[6] The absence of epoxide products from the smaller paracyclophane ketones is attributed to a faster than usual rate of the 1,2 rearrangement, a reaction in which π–π aryl repulsions are decreased. Thus, ketone IV was 80% consumed in 10 min at 0°, whereas acetophenone underwent only 44% reaction in 4 days at room temperature.[6] The strain energy of [2.2]paracyclophane was found to be 31.3 kcal/mole, and that of [2.3]paracyclophane is undoubtedly considerably less.[7]



House and co-workers[6] determined the relative migratory aptitudes of several aryl and alkyl groups in the methanol-catalyzed reaction of diazomethane and several ketones: benzyl, 1; methyl, 1.5; phenyl, 25. In the methanol-catalyzed ring expansion of ketone IV (see Table I), the relative amounts of phenyl and benzyl migration were about equal (run 4). Conversely, the methanol-catalyzed reaction of ketone V produced only VII (phenyl migration only), as can be seen by the results of runs 3–6. In the noncatalyzed reaction, benzyl migrates in slight preference to phenyl (runs 1 and 2 Table I). These relative yields clearly reflect a composite of conformational, strain, and electrical effects which are not identifiable with the scant data at hand. Methanol has been reported to enhance phenyl migration at the expense of hydrogen in reaction of a substituted benzaldehyde with diazomethane.[8]

Wolff–Kishner Reduction. Reduction of the ketones whose two-carbon bridge contained the carbonyl group produced varying amounts of open-chain hydrocarbons, whereas those with carbonyls on the three- and four-carbon bridges gave good yields of cyclic hydrocarbons. The ring-opening process is only partially associated with the degree of strain since the [3.3]paracyclophane ketones only reduced, whereas some of the [2.4]paracyclophane ketones underwent ring opening. Probably the ring-opening reaction occurs through a

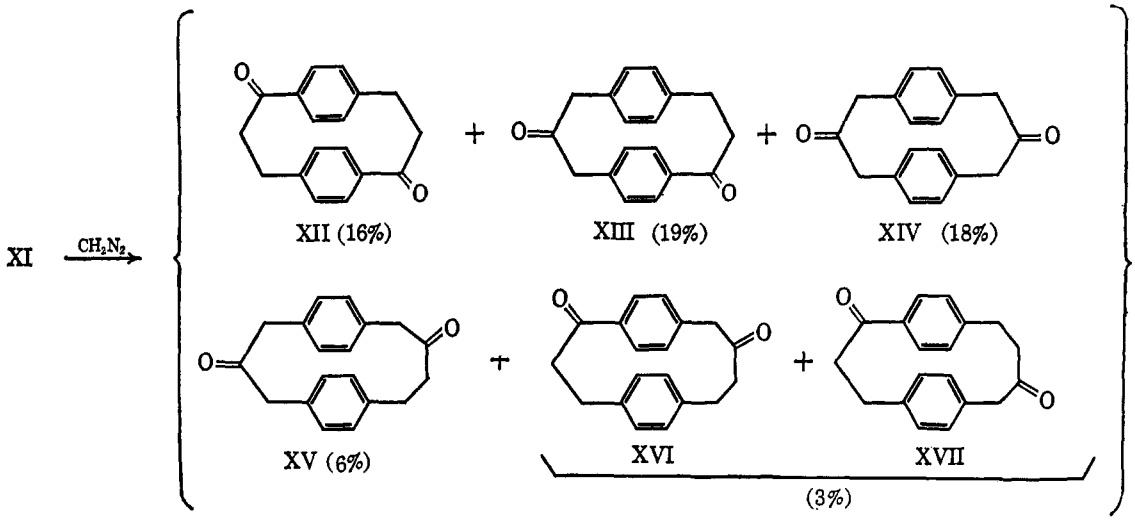
(4) (a) K. C. Dewhirst and D. J. Cram, *J. Am. Chem. Soc.*, **80**, 3115 (1958); (b) D. J. Cram and K. C. Dewhirst, *ibid.*, **81**, 5963 (1959).

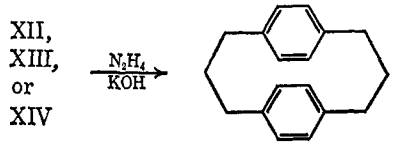
(5) C. D. Gutsche, *Org. Reactions*, **8**, 364 (1954).

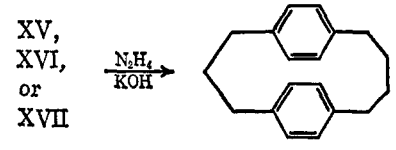
(6) H. O. House, E. J. Grubbs, and W. F. Cannon, *J. Am. Chem. Soc.*, **82**, 4099 (1960).

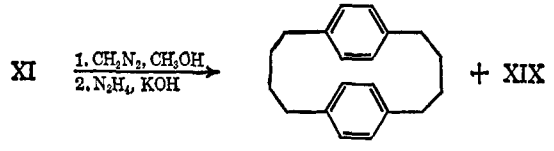
(7) R. H. Boyd, *Tetrahedron*, **22**, 119 (1966).

(8) (a) F. Arndt, J. Amade, and W. Ender, *Monatsh.*, **59**, 202 (1932); (b) E. Mosettig, *Ber.*, **61**, 1391 (1928).









biradical intermediate and is dependent on stabilization of each of the two-carbon radicals by an attached benzene ring.

The fragmentation of the [2.4]paracyclophane diketone produced in the preparation of [3.3]paracyclophane simplified the isolation of the latter compound since *p,p'*-bis(*p*-tolyl)butane is easily separated from the [3.3] cycle, whereas the [2.4] cycle is not.

Spectra

Nuclear Magnetic Resonance Spectra. The ring sizes of the various homologous ketones were determined from their elemental analyses and by their conversion to known hydrocarbons.[2] The isomeric ketones were differentiated and identified by their nmr spectra, each ketone exhibiting unique combinations of bands. Table II records the numbers of protons, the pattern, the chemical shift, and the structural assignments. Ketones XVI and XVII were not separated from one another, but are enough structurally similar to allow the spectra of the mixture to be treated as a single chemical entity. The patterns of structural assignments were based on a simple process of utilizing the smaller and the simpler cyclic ketones as models for the more complex, and successive comparisons of the homologs produced a classical example of structure determination by the use of nmr.

A number of interesting structural features are visible in the data of Table II. The aromatic protons of the paracyclophanes are moved upfield from those of open-chain models. For example, 1,4-bis(*p*-tolyl)-butane exhibits aromatic proton absorption at τ 2.95, whereas those of the [2.3]-, [2.4]-, [3.3]-, [3.4]-, and [4.4]-paracyclophanes absorb from τ 3.34 to 3.63. This shift is attributed to two effects: transannular interactions between the protons of one ring and the ring current of the second ring; rehybridization of the carbon atoms carrying the protons toward sp^3 due to deformation of the benzene rings from their normal planar configuration (sp^2 hybridization). This shift to higher fields drops off regularly as the rings become farther from one another, as is expected.

Although the spectra of the aromatic protons of [2.3]-, and [3.4]paracyclophanes exhibit the expected A_2B_2 patterns, that of [2.4]paracyclophane contains a singlet for the aromatic protons (τ 3.48). Similarly, the aromatic protons of the benzene ring farthest from the ketone group of 2-keto[2.4]paracyclophane (VII) absorb as a singlet at τ 3.48. Another anomaly is found in the fact that in the ketones (V, XII, XIII, XV, XVI, and XVII) that contain the group, $ArCH_2$-CH_2CO, the protons absorb as a singlet. Apparently, the effects of the aryl and carbonyl groups on the chemical shift of the attached methylene's protons fortuitously are about equal to one another.

Although the crystallographic structure of [3.3]-paracyclophane is highly unsymmetrical,[3a] the aromatic protons occur as a singlet. Apparently, in solution at room temperature the different conformations of the molecule are interconverting rapidly enough to produce an average and therefore effectively equivalent absorption for the aromatic protons. This averaging involves both ring inversion and a scissors movement of the two benzene rings with respect to one another. Ring inversion in [2.3]-, [2.4]-, and [3.4]paracyclophanes are also probably occurring, as well as a scissors movement in the last two hydrocarbons. Low-temperature studies are in progress.

Infrared Spectra. Table III records the infrared carbonyl frequencies of the cyclic ketones along with those of an open-chain model compound. The unconjugated carbonyl frequencies range from 1695 to 1709 cm^{-1}, whereas normally carbonyl groups range

Table II. Nuclear Magnetic Resonance Spectra of Paracyclophanes and Their Derivatives[a]

Compound Name	No.	Aromatic protons No.	Pattern	τ, ppm	No.	Pattern	τ, ppm	Methylene protons No.	Pattern	τ, ppm	No.	Pattern	τ, ppm	No.	Pattern	τ, ppm
1-Keto[2.2]-PC	IV	4	Singlet	3.37[b]	4	Singlet	3.42[c]	4	Singlet	6.93[d]	2	Singlet	6.13[e]	...	...	...
[2.2]PC	II	8	Singlet	3.63[c]	...	...	...	4	Singlet	6.95[d]	...	...	...	...	...	...
1-Keto[2.3]-PC	V	4	A_2B_2	3.15[b]	4	Singlet	3.55[c]	4	Singlet	7.08[d]	...	...	...	4	Singlet	6.93[f]
2-Keto[2.3]-PC	VI	8	A_2B_2	3.40[c]	...	...	...	4	Singlet	7.02[d]	4	Singlet	6.28[e]	...	...	...
[2.3]PC	VIII	8	A_2B_2	3.52[c]	...	...	...	4	Singlet	7.03[d]	4	Triplet	7.29[g]	2	Multiplet	7.90[h]
2-Keto[2.4]-PC	VII	4	Multiplet	3.33[i]	4	Singlet	3.48[c]	4	Singlet	7.00[d]	2	Singlet	6.60[e]	4	Multiplet	7.37[m]
[2.4]PC	IX	8	Singlet	3.48[c]	...	...	...	4	Singlet	7.02[d]	4	Multiplet	7.73[j]	4	Multiplet	8.57[k]
1,10-Diketo-[3.3]PC	XII	8	A_2B_2	3.03[b]	...	...	...	...	...	...	...	...	...	8	Singlet	6.97[f]
1,11-Diketo-[3.3]PC	XIII	4	A_2B_2	2.89[b]	4	Multiplet	3.29[c]	2	Singlet	6.15[l]	2	Singlet	6.26[e]	4	Singlet	7.07[f]
2,11-Diketo-[3.3]PC	XIV	8	Singlet	3.07[c]	...	...	...	...	...	...	8	Singlet	6.25[e]	...	...	...
[3.3]PC	XVIII	8	Singlet	3.40[c]	...	...	...	8	Triplet	7.38[g]	4	Multiplet	8.07[h]	...	...	...
2,12-Diketo-[3.4]PC	XV	8	Multiplet	3.25[c]	...	...	...	4	Singlet	6.26[e]	2	Singlet	6.52[e]	4	Singlet	7.30[m]
2,13-Diketo-[3.4]PC	XVI	4	A_2B_2	2.97[b]	4	Multiplet	3.42[c]	4	Singlet	7.32[m]	2	Singlet	6.43[e]	4	Multiplet	7.01[f]
2,11-Diketo-[3.4]PC	XVII															
[3.4]PC	XIX	8	A_2B_2	3.38[c]	...	...	...	4	Triplet	7.25[g]	6	Multiplet	7.75[h,i]	4	Multiplet	8.40[k]
[4.4]PC	XX	8	Singlet	3.34[c]	...	...	...	...	...	...	8	Multiplet	7.71[j]	8	Multiplet	8.43[k]

[a] Varian A-60 analytical nmr spectrophotometer, with 1% tetramethylsilane as internal standard, and deuteriochloroform as solvent except with IX and XX, where carbon tetrachloride was employed. [b] Protons of conjugated benzene ring. [c] Protons of unconjugated benzene ring. [d] Protons of ethylene bridge. [e] Protons α to both aryl and carbonyl groups. [f] Protons of ethylene α to aryl on one side and α to carbonyl on other. [g] Protons α to aryl on trimethylene bridge. [h] Protons β to aryl on trimethylene bridge. [i] Protons on benzene ring which is α to carbonyl group. [j] Protons α to aryl on tetramethylene bridge. [k] Protons β to aryl on tetramethylene bridge. [l] Protons α to both conjugated aryl and carbonyl groups. [m] Protons of ethylene α to aryl on one side and α to carbonyl on other, all part of four-carbon bridge.

Table III. Maxima in the Absorption Spectra in the Infrared[a] and Ultraviolet[b] of Cyclic Ketones and Open-Chain Model Compounds

Compound Name	No.	Infrared peak position, cm^{-1}	Ultraviolet, λ_{max}, mμ (ε)
Methyl *p*-tolyl ketone	...	1680	... ...
1-Keto[2.2]PC	IV	1698	223 (10,790); 334 (240)
1,9-Diketo[2.2]PC	XI	1701	... ...
1,10-Diketo[2.2]PC	X	1702	... ...
1-Keto[2.3]PC	V	1668	229 (10,050); 260 (4600);[c] 295 (280);[c] 330 (400)[c]
2-Keto[2.3]PC	VI	1697	222 (15,300); 275 (380); 307 (197)
2-Keto[2.4]PC	VII	1706	217 (13,100); 285 (709)
1,10-Diketo[3.3]PC	XII	1688	226 (10,350); 270 (10,400); 322 (250)[c]
1,11-Diketo[3.3]PC	XIII	1674, 1701	221 (10,150); 236 (10,300); 285 (3400); 302 (2300)
2,11-Diketo[3.3]PC	XIV	1695	220 (10,900); 240 (2000)[c]; 299 (360); 312 (310)
2,12-Diketo[3.4]PC	XV	1702	219 (12,280); 245 (2600)[c]; 289 (742)
2,13-Diketo[3.4]PC	XVI	1673, 1707	250 (7040); 285 (3700); 320 (500)[c]
1-Keto[4.4]PC[d]	...	1664	263 (9000); 278 (4000)
2-Keto[4.4]PC[d]	...	1709	267 (720); 272 (750); 287 (600)

[a] Perkin-Elmer 421 grating spectrophotometer, 1–2% solutions by weight in chloroform. [b] Cary Model 14 spectrophotometer, 1-cm cell, 95% ethanol. [c] Shoulder. [d] See ref 4b.

from 1706 to 1720 cm^{-1} in unstrained saturated rings.[9] As the paracyclophane ring system becomes more strained, the carbonyl absorption shifts to lower frequencies. Some of this shift is probably associated with the presence of α-aryl groups, particularly in VI and XIV, which contain such substituents. The greater than normal C–C–C bond angles in the smaller paracyclophanes[3] is probably responsible for the rest of the shift to lower frequencies. The same kind of angle strain is also present in cyclodecanone and cyclononanone, which absorb at 1704 and 1703 cm^{-1}.

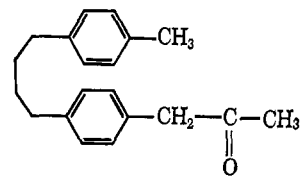
The conjugated ketones absorb at frequencies that range from 1664 to 1702 cm^{-1}, the more strained and smaller ring systems possessing the higher frequencies. Molecular models of the ketones derived from [2.2]paracyclophane indicate that no conjugation should exist between the carbonyl group and the benzene ring, and thus the absorption is toward wavelengths characteristic of unconjugated ketones. The expanded C–C–C bond angle probably is also some-

(9) L. J. Bellamy, "The Infrared Spectra of Complex Molecules," 2nd ed, John Wiley and Sons, Inc., New York, N. Y., 1958, p 137.

what responsible. On the other hand, two of the ketones, 1-keto[2.3]paracyclophane (V) and 1-keto[4.4]-paracyclophane exhibit frequencies well below that of the conjugated model, methyl *p*-tolyl ketone. Molecular models indicate that in the two cyclic ketones, the carbonyl groups can only partially conjugate with the benzene ring, and that conformational mobility is somewhat low. It is not clear why these frequencies should be so low, but a possibility is that the bond angles are expanded enough to more than compensate for the loss in conjugation. Furthermore, in the [2.2] system, the carbonyl group has a frequency lowering α-aryl group as well as a directly attached aryl.

Ultraviolet Spectra. Table III contains the maxima of the various cyclic ketones of this investigation and two from a previous study.[4b] The normal, high-intensity absorption of aryl ketones in the 250-mμ region[10] is absent in the spectrum of 1-keto[2.2]paracyclophane (IV) but clearly visible in the spectrum of 1-keto[4.4]paracyclophane. This band emerges as the rings enlarge in the formally conjugated ketones, and grows in intensity in the order [2.2] < [2.3] < [3.3] < [3.4] < [4.4] (account is taken of the presence of two chromophores in diketone XII). The ring system of the smaller homologs prevents coplanarity of the carbon atoms of the benzene and carbonyl chromophores. A molecular model of the smallest member of the series (IV) indicates perpendicularity and complete loss of conjugation. The longest wavelength bands of the formally conjugated cycles (320 to 335 mμ) is found at somewhat longer wavelengths than the longest wavelength band in the parent hydrocarbon systems, and could be attributed to either the aromatic system or the carbonyl group. In [2.2]paracyclophane itself, the longest wavelength band is found at 302 mμ, and in [3.4]paracyclophane has decreased to 280 mμ.[11] The spectrum of [4.4]paracyclophane is normal, as is that of 1-keto[4.4]paracyclophane as compared to open-chain models.[4b] The fact that the longest wavelength band of the formally conjugated cyclic ketones does not decrease much in wavelength as the cycles become larger ($\sim$15 mμ) suggests that this long wavelength band is associated with the n to π^* transition of the carbonyl group (normally found at about 285 mμ) subjected to the inductive and field effects of an attached benzene ring that cannot conjugate (fully) with the carbonyl group.

A low-intensity band is also found in the 287- to 307-mμ region in those cyclic ketones that have aryl groups attached to the α carbon (VI, VII, XIV, XV, and 2-keto[4.4]paracyclophane).[12] This band occurs at about 285 mμ (ϵ 200) in open-chain model compound XXI. Inclusion of the α-aryl ketone group in the [4.4] ring system results mainly in an enhancement of intensity (287 mμ (ϵ 600)). As the bridge not carrying the carbonyl group decreases in size to three methylenes to two methylenes, the band moves from 289 mμ (ϵ 742) to 285 mμ (ϵ 709). The symmetrical diketone, 2,11-diketo[3.3]paracyclophane (XIV) has two aryl groups



XXI

α to each carbonyl group, and the band occurs at 312 mμ (ϵ 310). Apparently both the wavelength and intensity of this band are subject to conformational effects of the benzene ring.

Experimental Section

Materials. Recrystallization of commercial grade [2.2]paracyclophane (II) from chloroform gave material, mp 286–287°. Reagent grade chloroform, anhydrous diethyl ether, methanol, glacial acetic acid, diethylene glycol, dichloromethane, and carbon tetrachloride were employed as solvents. Carbon tetrachloride was dried over molecular sieves (Linde Type 4A) before use. Reagent grade N-bromosuccinimide, silver acetate, and Diazald were used without further purification. Melting points were taken on a Fisher-Johns melting block and are uncorrected.

Chromatography. Silica gel layers, 0.25-mm thick on glass plates, were used in the thin layer chromatography (tlc). The plates were developed in an iodine chamber.

Analytical vapor phase chromatography (vpc) was performed on an F and M temperature program Model 720 machine. A 3-ft column packed with 20% silicone gum on 60–80 mesh firebrick, 0.25 in. in diameter, was used in all analytical work. The temperature was isothermal, and a helium pressure of 35 psi was used. The retention times of the hydrocarbons and diketones at 260° in min were as follows: hydrocarbon II, 4.8; hydrocarbon VIII, 5.9; *p,p'*-bis(*p*-tolyl)butane, 6.0; hydrocarbon IX, 7.2; hydrocarbon XVIII, 7.5; hydrocarbon XIX, 9.4; diketone mixture, X and XI, 10.3; hydrocarbon XX, 11.3; diketone XIV, 16.0; diketone XIII, 19.0; diketone XII, 21.0; diketone XV, 23.0; diketone XVI, 25.0. The retention times of the monoketones at 250° in min were as follows: ketone IV, 6.7; ketone VI, 8.0; ketone V, 10.5; ketone VII, 10.8. Preparative vpc was performed on a homemade (thermal conductivity detector) machine with a 6-ft column, 0.75 in. in diameter, with the same packing as the analytical column. The column temperature was 170° for the separation of the hydrocarbons and monoketones, and the temperature was 190° for the diketones. The preheater temperature was 220° and 15 psi of helium pressure was employed.

1-Keto[2.2]paracyclophane (IV). To a 500-ml, three-neck, round-bottom flask fitted with a truebore stirrer, condenser with drying tube, and glass stopper was added [2.2]paracyclophane (9.5 g), 13.0 g of N-bromosuccinimide, benzoyl peroxide (100 mg), and 300 ml of dry carbon tetrachloride. The solution was refluxed with ultraviolet irradiation (Hanovia Model 30620 ultraviolet lamp equipped with a Pyrex filter) for 10 hr. The solution was then cooled to room temperature and filtered to remove succinimide. The carbon tetrachloride was evaporated on a steam bath in a rotary evaporator, and the residue was dissolved in benzene (70 ml). The benzene solution was absorbed on a column of 1.5 kg of silica gel made up in pentane. Elution with pentane (5 l.) produced starting material (800 mg, 8%). Elution of the column with 3% ether–pentane produced 4.2 g of a mixture of mono-, di-, and tribromides, identified by comparison of tlc and vpc of authentic materials.[4a] Elution of the column with 5% ether–pentane produced only small amounts of material. Elution of the column with 10% ether–pentane produced 1-keto[2.2]paracyclophane (IV), 2.0 g (20%). Further elution of the column with 20% ether–pentane produced 600 mg (6%) of 1-hydroxy[2.2]paracyclophane. Recrystallization of 100 mg of the alcohol from ethanol gave material, mp 225–227°, which upon admixture with an authentic sample of mp 225° showed no depression.[4a] The nmr, tlc, R_f, and vpc retention times of the alcohol product were identical with those of an authentic sample. Elution of the column with 60% ether–pentane and 80% ether–pentane produced mixtures of compounds which were not identified. A 100-mg sample of ketone IV was recrystallized from ethanol to give material, mp 195–196°. *Anal.* Calcd for $C_{16}H_{14}O$: C, 86.44; H, 6.36. Found: C, 86.46; H, 6.10.

A 40-mg sample of IV was converted to its yellow 2,4-dinitrophenylhydrazone derivative by the usual method, mp 234–236°.

(10) H. H. Jaffé and M. Orchin, "Theory and Application of Ultraviolet Spectroscopy," 2nd ed, John Wiley and Sons, Inc., New York, N. Y., 1962, p 257.

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Wolff–Kishner Reduction of 1-Keto[2.2]paracyclophane (IV). Ketone IV (100 mg) was added to a solution of 0.5 ml of 99% hydrazine hydrate and 0.2 g of potassium hydroxide in 10 ml of diethylene glycol, and the resulting solution was refluxed for 1 hr. At the end of this time, the reflux condenser was removed and was replaced only when the boiling solution reached a temperature of 190°. The solution was then refluxed for an additional 2 hr. The reaction mixture was cooled, diluted with water, and extracted with ether. The ether layer was dried over magnesium sulfate and evaporated to give 80 mg of crude II and *p,p'*-dimethylbibenzyl. Integration of the aromatic peaks in the nmr spectrum of the two compounds indicated 60% of II was present and 40% of the open-chain compound. The hydrocarbons were separated by preparative vpc. The presence of II was confirmed by comparison of its nmr, tlc, R_f, and vpc retention time with authentic [2.2]paracyclophane. Hydrocarbon *p,p'*-dimethylbibenzyl, mp 77–79°, upon admixture with an authentic sample[2a] of mp 79–80° showed no melting point depression. The nmr spectrum and vpc retention time of the material were identical with those of the authentic sample.

Preparation of Tetrabromides of II. A refluxing mixture of [2.2]-paracyclophane (20.0 g), 110 g of N-bromosuccinimide, 300 mg of benzoyl peroxide, and 750 ml of dry carbon tetrachloride was irradiated with ultraviolet light (Hanovia Model 30620 lamp) for 54 hr. The mixture was filtered to remove succinimide, and the carbon tetrachloride was evaporated at 100° under vacuum. The residue was mixed with 200 ml of dichloromethane and the solid was filtered to give 13.8 g of 1,1,9,9-tetrabromo[2.2]paracyclophane.[4a] The filtrate was diluted to 500 ml with dichloromethane and the solution was extracted with water, 5% sodium hydroxide twice, and once again with water. The organic layer was then dried over magnesium sulfate and the solvent was removed on a rotary evaporator to give 37.2 g of compound. The total yield of brominated material was 51.0 g. The theoretical yield of tetrabromide mixture was 50.2 g.

Preparation of Diketones X and XI. The crude tetrabromides (51.0 g), silver acetate (60.0 g), and 800 ml of acetic acid were refluxed for 4 hr. To the solution was then added 50 ml of water and the hot mixture was refluxed for an additional 2 hr. The hot solution was filtered and the solvent was removed on a hot water bath under aspirator vacuum. The residue was dissolved in chloroform (600 ml) and the resulting solution was washed with water and sodium bicarbonate solution. The organic layer was dried and the solvent was removed on a rotary evaporator at 60°. The yield of crude diketone was 22.0 g. The theoretical yield of diketone based on [2.2]paracyclophane as starting material was 22.4 g.

A similar hydrolysis of 10.0 g of crude 1,1,9,9-tetrabromo[2.2]-paracyclophane produced, after crystallization from chloroform and chloroform–ether, 3.6 g of diketone XI (74%). The nmr and vpc retention time of the product were identical with those of an authentic sample.[4a]

Preparation of Diazomethane. Ethereal solutions of diazomethane were prepared by adding a solution of N-methyl-N-nitroso-*p*-toluenesulfonamide (Diazald, Aldrich Chemical Co.) in ether or a mixture of water, ethanol, and potassium hydroxide heated to 65°. The liberated diazomethane was carefully distilled directly into the reaction mixture, which was kept at 0° in an ice bath.

Reaction of Diazomethane and 1-Keto[2.2]paracyclophane (IV). In each experiment, diazomethane (7 mmoles) prepared from 2.2 g of Diazald was distilled into a solution of 150 mg (0.7 mmole) of IV in 75 ml of solvent. The methanol-catalyzed reactions were run with 25 ml of methanol and 50 ml of chloroform. The reaction mixture was kept in an ice bath for the duration of the reaction. At the completion of the reaction, the excess diazomethane was destroyed by careful addition of glacial acetic acid. The solution then was washed with water and sodium bicarbonate solution and dried. The solution was concentrated, and the relative amounts of each component present were determined by integration of their relative peak areas on a F and M Model 720 analytical vpc machine. Since ketones V and VII had similar retention times on vpc, their relative amounts were determined by isolating the mixture by preparative vpc and analyzing the compounds by nmr. Integration of the singlet absorption at τ 6.60 of VII relative to the singlet peak at 7.08 of V gave values accurate to about ±3%. The lower limit for detection of compound IV by vpc is 1%, whereas the lower limit for the presence of V and VI is about 2%. The relative and actual yields of ketones are recorded in Table I.

1-Keto[2.3]paracyclophane (V). A 75-mg sample of V from preparative vpc was recrystallized from ethanol, mp 142–143°. *Anal.* Calcd for $C_{17}H_{16}O$: C, 86.41; H, 6.82. Found: C, 86.43; H, 6.78.

A Wolff–Kishner reduction of 50 mg of V was performed using the conditions described for the reduction of IV. The product was isolated by preparative vpc to give 30 mg (64%). The hydrocarbon was purified by sublimation at 100° (0.05 mm), mp 147–148°. The product possessed an nmr spectrum and vpc retention time identical with that of an authentic sample of [2.3]paracyclophane (VIII).[2a] The sublimed material, upon admixture with an authentic sample,[2a] mp 146–148°, melted at 146–148°.

2-Keto[2.3]paracyclophane (VI). A 100-mg sample of VI obtained from preparative vpc was recrystallized from ether–pentane, mp 96.1–96.6°. *Anal.* Calcd for $C_{17}H_{16}O$: C, 86.41; H, 6.82. Found: C, 86.35; H, 6.80.

The reduction of VI (50 mg) to [2.3]paracyclophane was performed under the previously described conditions to give 35 mg (75%) of VIII, mp 146–147°. An admixture of product with authentic material,[2a] mp 146–148°, melted at 146–148°. The nmr spectrum and vpc retention time of the product were identical with those of the authentic material.[2a]

2-Keto[2.4]paracyclophane (VII). A 100-mg sample of VII obtained from preparative vpc was sublimed at 70° (0.05 mm), mp 81–82°. *Anal.* Calcd for $C_{18}H_{18}O$: C, 86.36; H, 7.25. Found: C, 86.36; H, 7.36.

A Wolff–Kishner reduction using the previously described conditions resulted in the recovery of starting material. The reduction was repeated using 100 mg of VII, 1 ml of 99% hydrazine hydrate, and 0.5 g of potassium hydroxide in 10 ml of diethylene glycol. The mixture was refluxed for 2 hr. At the end of this time, the temperature was raised to 195° and the condenser was replaced. The solution was refluxed at 195° for 4 hr, cooled, and diluted with water. The water layer was extracted twice with ether and the organic layer was dried. The ether was evaporated and the product (88 mg) was purified by preparative vpc to give 65 mg (70%) of material, mp 73–76°. The product had an nmr spectrum and vpc retention time identical with authentic IX.[2a] A sample of product, upon admixture with an authentic sample of IX,[2a] mp 74.4–75°, melted at 73–75°.

Reaction of 1,9-Diketo[2.2]paracyclophane (XI) and Diazomethane. An ethereal solution of diazomethane (approximately 70 mmoles) was distilled into a solution of 1.95 g of XI (8 mmoles) in 300 ml of chloroform. The reaction mixture was kept in an ice bath for 26 hr. After the excess diazomethane was decomposed with glacial acetic acid, the solution was washed with water and sodium bicarbonate solution, and the organic layer was separated and dried. The solution was then concentrated to about 30 ml on a steam bath and adsorbed on a column of 250 g of silica gel (unactivated) made up in pentane. Elution of the column with pure pentane, 15% ether–pentane, and 10% ether–pentane produced only small amounts of oils and semicrystalline material. Elution with 20% ether–pentane produced 840 mg of material which was mainly 2,11-diketo[3.3]paracyclophane (XIV) and 2,12-diketo[3.4]-paracyclophane (XV). Integration of the peak areas on an analytical vpc indicated about 410 mg of XIV (18%) and 140 mg of XV (6%). Elution of the column with 25% ether–pentane produced 80 g (3%) of a mixture of [3.4]paracyclophane diketones, XVI and XVII, which contained a small amount of XIII. Diketone XIII, 425 mg (19%), was eluted with 30% ether–pentane. Elution with 40% ether–pentane produced 360 mg (16%) of 1,10-diketo-[3.3]paracyclophane (XII). Further elution of the column with up to 80% ether–pentane produced only traces of material. The yields reported in this section are absolute and are based on diketone XI as starting material.

2,11-Diketo[3.3]paracyclophane (XIV). A pure sample of XIV was isolated by preparative vpc. Recrystallization of 100 mg of the compound from ethanol gave material, mp 268–269°. *Anal.* Calcd for $C_{18}H_{16}O_2$: C, 81.79; H, 6.10. Found: C, 81.88; H, 6.25.

A Wolff–Kishner reduction was performed on the chromatographic fraction containing XIV and [3.4]paracyclophane diketone XV. A mixture of 840 mg of diketones, 2 ml of 99% hydrazine hydrate, and 1.0 g of potassium hydroxide in 20 ml of diethylene glycol was refluxed for 1 hr. The condenser was then removed and the solution was heated to 190°. The condenser was then replaced, and the solution was refluxed for 2 hr. The usual work-up procedure was followed, and the hydrocarbons were then separated on preparative vpc. The major product of the reduction, [3.3]paracyclophane (290 mg of XVIII, 80% based on XIV) corresponds to the reduction product from XIV. Hydrocarbon XVIII was identified by its nmr spectrum and mp 104–105°. The other major product from the reduction, [3.4]paracyclophane (110 mg of XIX, 87% based on XV) corresponds to the reduction product of [3.4]-

paracyclophane diketone XV. Hydrocarbon XIX, mp 115–117°, upon admixture with an authentic sample, mp 116–118°, melted at 115–118°. The nmr spectrum and vpc retention time of XIX was identical with that of authentic material.[13]

1,11-Diketo[3.3]paracyclophane (XIII). A 100-mg sample of XIII, obtained from column chromatography, was recrystallized from ethanol, mp 146.5–147.5°. *Anal.* Calcd for $C_{18}H_{16}O_2$: C, 81.79; H, 6.10. Found: C, 81.88; H, 6.13.

A Wolff–Kishner reduction of 358 mg of XIII as previously described produced 254 mg (80% based on XIII) of [3.3]paracyclophane (XVIII), mp 104–105°. The product formed a characteristic blue-black complex with tetracyanoethylene, and its nmr spectrum was identical with the spectrum of the reduction product of XIV.

1,10-Diketo[3.3]paracyclophane (XII). A 100-mg sample of XII, obtained from column chromatography, was recrystallized from ethanol, mp 272–273°. *Anal.* Calcd for $C_{18}H_{16}O_2$: C, 81.79; H, 6.10. Found: C, 81.89; H, 6.11.

A Wolff–Kishner reduction of 200 mg of XII, obtained from column chromatography, produced 155 mg (89% based on XII) of XVIII, mp 104–105°. The product formed a blue-black complex with tetracyanoethylene, and its nmr spectrum was identical with the spectrum obtained from the reduction product of XIII and XIV. Mixture melting points of the reduction products of XII, XIII, and XIV upon admixture melted at 103–105°, indicating no depression.

2,12-Diketo[3.4]paracyclophane (XV). A 90-mg sample of XV was obtained from preparative vpc. Recrystallization of the material from ether–pentane produced a crystalline compound, mp 170.5–172°. *Anal.* Calcd for $C_{19}H_{18}O_2$: C, 81.98; H, 6.52. Found: C, 81.96; H, 6.43.

A Wolff–Kishner reduction of a mixture of XIV and VI has been described above in the section on compound XIV.

2,11-Diketo[3.4]paracyclophane (XVII). A 60-mg sample of XVII was obtained from preparative vpc. Crystallization of the compound from ether–pentane gave material, mp 126–130°. The broad melting point of the compound and the observation that it does not form well-defined crystals indicate that it may be a mixture of the isomeric conjugated diketones XVI and XVII. The material gave one peak on vpc, and the nmr spectrum indicates unique proton absorption. The nmr, vpc, and ultraviolet spectra of XVI and XVII are expected to be nearly identical. *Anal.* Calcd for $C_{19}H_{18}O_2$: C, 81.98; H, 4.52. Found: C, 81.81; H, 4.38.

Methanol-Catalyzed Reaction of Diazomethane and 1,9-Diketo[2.2]paracyclophane (XI). Method A. An ethereal solution of diazomethane (70 mmoles) was distilled into a solution of 1.0 g of XI dissolved in 300 ml of 5:1 chloroform–methanol. The resulting solution was kept at 0° for 16 hr. The solution was then worked up in the usual way to give 1.1 g of crude product. A Wolff–Kishner reduction was performed on the crude diketone with 4 ml of hydrazine hydrate and 2 g of potassium hydroxide in 25 ml of diethylene glycol. The solution was refluxed for 1 hr in the presence of hydrazine and for 2 hr at 190° after the hydrazine had been removed by distillation. The reaction was worked up in the usual way and the product was purified by passage through a column of 50 g of neutral alumina (Woelm, activity 1). The main product of the reduction, 1,4-bis(*p*-tolyl)butane, mp 73–74°, was isolated by preparative vpc. The hydrocarbon (235 mg) was obtained in 23% yield and a mixture melting point with authentic material,[2a] mp 74–75°, melted at 73–75°. The nmr and vpc retention time of the product were identical with those of the authentic sample. The yield of each of the other hydrocarbons in the mixture was 10% or less by analytical vpc.

Method B. The reaction sequence reported in method A was repeated except that the reaction of XI and diazomethane, was extended in time from 16 to 42 hr. The yield of [4.4]paracyclophane (XX) after vpc was 280 mg (25%) and the yield of [3.4]paracyclophane (XIX) was 125 mg (12%). Compound XX, mp 145–146°, melted at 145–147° as an admixture with authentic [4.4]paracyclophane,[4a] mp 145.5–146.5°. The melting point of the [3.4]paracyclophane (XIX), 117–119°, was also undepressed by admixture with an authentic sample, mp 114–118°.[13] The nmr spectra and vpc retention times of the products were also identical with those of authentic samples.

Direct Preparation of [3.3]Paracyclophane (XVIII). An ethereal solution of diazomethane (15 g, 0.36 mole) was distilled into a solution of 22.0 g of crude diketones X and XI (prepared from 20.0 g of II) in 600 ml of chloroform. The resulting solution (1200 ml) was kept at 0° for 27 hr. After decomposition of the excess diazomethane and the usual isolation procedure, the crude diketones (24 g) were subjected to a Wolff–Kishner reduction. The crude diketone, 40 ml of 99% hydrazine hydrate, and 50.0 g of potassium hydroxide in 250 ml of diethylene glycol were refluxed for 2 hr. The condenser was removed and the hydrazine and water were distilled into a receiver until the temperature reached 190°. The condenser was then replaced and the solution was refluxed for an additional 4 hr. The hydrocarbons were isolated by the usual extraction procedures. The hydrocarbons were separated from polymer and more polar compounds by passage through an alumina column with 5% ether–pentane as eluent. The hydrocarbons (9.23 g) were analyzed on an analytical vpc and were found to contain 55% of XVIII, and 16% of XIX. The vpc yields of [3.3]- and [3.4]paracyclophane, based on [2.2]paracyclophane as starting material, correspond to 23 and 5%, respectively. After separation by preparative vpc, the yield of XVIII was 6.3 g (19%) and the yield of XIX was 1.0 g (4%).

A 100-mg sample of XVIII was crystallized from acetone–methanol, mp 105–105.5°. The reported melting point is 104.3–105.3°.[2d] The compound formed a deep blue complex when added to a solution of tetracyanoethylene in dichloromethane. The ultraviolet spectrum possessed maxima identical with the reported values.[2d] The nmr spectrum of the compound clearly requires the assigned structure. *Anal.* Calcd for $C_{18}H_{20}$: C, 91.47; H, 8.53. Found: C, 91.43; H, 8.50.

The structure of XXII, mp 115–117°, was confirmed by mixture melting point with an authentic sample (mp 116–118°) which melted at 115–118°.[13] The nmr spectrum and vpc retention of the product were identical with those of the authentic sample.

(13) D. J. Cram, R. J. Wechter, and R. W. Kierstead, *J. Am. Chem. Soc.*, **80**, 3126 (1958).