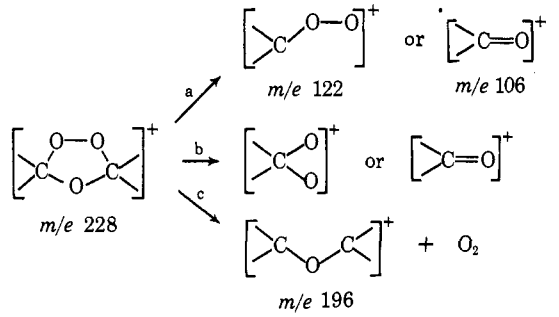


Table I shows the percentage of the molecules which have M + 2 (due to the replacement of ^{16}O by ^{18}O) in the *m/e* 196, 122, and 106 fragments. Whatever the mode of fragmentation[6] (a or b), the sum of the incorporations of ^{18}O in the *m/e* 122 and 106 fragments represents the total labeling of the ozonide ring. This sum can be greater than or equal to the labeling of the ether oxygen. If the total labeling in the *m/e* 122 and 106 fragments exceeds that of *m/e* 196, then ^{18}O incorporation in the peroxidic oxygens takes place, whereas equal labeling in the *m/e* 122 and 106 fragments and in the *m/e* 196 fragment means that all the ^{18}O is found in the ether oxygen.

Table I

Olefin isomer	Temp, ozonolysis, °C	Ozonide mp, °C	% ^{18}O at fragments *m/e* 196	*m/e* 122	*m/e* 106
cis	−78	74	5.0 ± 0.3	4.5 ± 0.1	0.86 ± 0.06
		94	5.9 ± 0.5	4.2 ± 0.1	1.15 ± 0.05
	25	74	7.4 ± 0.3	5.7 ± 0.1	1.85 ± 0.05
trans	25	74	6.6 ± 0.2	5.4 ± 0.1	1.16 ± 0.08
		82	5.0 ± 0.4	4.2 ± 0.1	0.56 ± 0.05
	−20	82	5.1 ± 0.35	4.9 ± 0.1	0.67 ± 0.04

These results show that the total per cent labeling in the *m/e* 122, and 106 fragments does not (within experimental errors) exceed significantly the labeling in the *m/e* 196 fragment. We conclude therefore that the ozonolysis of *cis*- and *trans*-stilbenes under our experimental conditions leads to a major incorporation of ^{18}O in the ether oxygen. Thus the mode of attack given by (2) does not occur except perhaps to a small extent (~10% or less) at the lower temperatures.

Mechanism 3 agrees with the presented results (as does mechanism 1) and may be retained as long as a reaction between molozonide and aldehyde needs to be considered. Mechanisms 2 and 3 differ by the mode of attack, but, since the seven-membered ring intermediate is the same, they are equally flexible in the attempt to explain the facts observed by Murray, *et al.*,[2,3] concerning the *cis*- and *trans*-ozonide distributions.

The mass spectra were recorded using a Hitachi RMU-6D mass spectrometer; the nmr spectra were recorded with a Varian A-60 spectrometer, using tetramethylsilane as internal reference.

Acknowledgment. The authors express their gratitude to Professor Y. Rousseau and to Mr. M. Bertrand for their analysis of the mass spectra. The financial support given by the National Research Council of Canada is gratefully acknowledged.

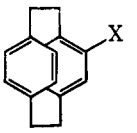
(6) A detailed study on the mass spectrometry of ozonides by Y. Rousseau, M. Bertrand, and S. Fliszár will be published shortly.

S. Fliszár, J. Carles, J. Renard
Department of Chemistry, University of Montreal
Montreal, Quebec, Canada
Received November 27, 1967

Transannular Directive Influences in Electrophilic Substitution of [2.2]Paracyclophane

Sir:

Chemical and spectral evidence indicates the presence of strong transannular electronic interactions in [2.2]paracyclophane and its derivatives.[1] The electronic demands of electrophilic substitution are high and, as applied to monosubstituted [2.2]paracyclophanes (I),



I

should become manifest in transannular directive influences upon introduction of a second group into the system. Table I records the results of an investigation of such directive influences.

Table I. Pattern of Electrophilic Substitution of Monosubstituted [2.2]Paracyclophanes (I)[a]

Run no.	X	Reagent[b]	% *para*	% pseudo-*ortho*[c]	% pseudo-*para*[c]	% pseudo-*meta*[c]	% pseudo-*gem*[c]
1	CO_2CH_3	Br_2, Fe					89[d]
2	$COCH_3$	Br_2, Fe					56[e]
3	CO_2H	Br_2, Fe					63
4	NO_2	Br_2, Fe		2	6	8	70
5	CN	Br_2, Fe		16	25	26	
6	Br	Br_2, Fe	5[f]	16	26	6	
7	Br	CH_3COCl, $AlCl_3$	17[g]	5.6	41		

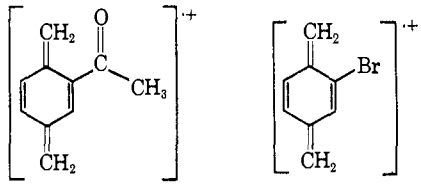
[a] The disubstituted compounds were separated by column chromatography and fractional crystallization unless indicated otherwise. Each compound gave a carbon and hydrogen analysis that deviated less than 0.3% from theory. No value listed indicates that none of that isomer could be detected. [b] Solvent was carbon tetrachloride, dichloromethane, or a mixture of the two. [c] The colloquial nomenclature is self-explanatory: pseudo-*gem* denotes the position directly below the substituent; pseudo-*ortho*, -*para*, and -*meta* denote the positions below the corresponding positions of the substituted ring. [d] Analysis by vpc indicated the product was approximately 98% pseudo-*gem*. [e] Analysis by nmr and vpc indicated that >99% of disubstituted product produced was pseudo-*gem*. [f] Determined by infrared analysis of a mixture with pseudo-*p*-dibromide. [g] Determined by nmr integration of a mixture with pseudo-*p*-bromoacetyl.

Structural assignments were made primarily on the basis of nmr spectra. As previously reported,[1b] a carbomethoxy, acetyl, or nitro group results in a substantial downfield shift of the *ortho* proton (0.6, 0.4, and 0.7 ppm, respectively, from the bulk of the aromatic protons). Similarly, 4-bromo[2.2]paracyclophane has one proton 0.7 ppm downfield, but the signal has a splitting pattern characteristic of a proton split by

(1) (a) D. J. Cram, *Record Chem. Progr.*, 20, 71 (1959); (b) L. A. Singer and D. J. Cram, *J. Am. Chem. Soc.*, 85, 1080 (1963).

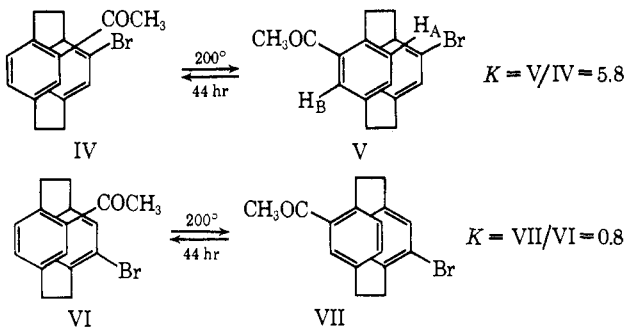
hydrogens *ortho*, *meta*, and *para* to it. Accordingly, this signal has been assigned to the proton directly transannular (pseudo-*gem*, see footnote *c*, Table I) to the bromine.[2] These features of the nmr spectra coupled with elemental analysis, functional group interconversions, degradation to benzene derivatives, and mass and infrared spectra provide unambiguous structural assignments for a large number of disubstituted [2.2]paracyclophanes.

As an example of structure determination, the exclusive product of nuclear bromination of 4-acetyl[2.2]-paracyclophane exhibited a mass spectrum (12 ev) with predominant peaks at *m/e* 146, 182 (184), and 328 (330), which correspond to ion radicals II and III and the parent molecular ion, respectively. The aromatic region of the nmr spectrum possesses a doublet at τ 2.87 (1 H, J = 2 cps) and a multiplet at τ 3.3–3.5

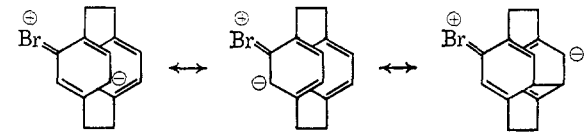


II III

(5 H). Of the four isomers consistent with the mass spectral data, only IV and VI are expected to possess one downfield aromatic proton. Thermal isomerization of the bromination product gave as the major component the isomer whose nmr spectrum includes two doublets at τ 2.78 (H_A, J = 7.8 cps) and 3.02 (H_B, J = 2 cps) in the region downfield from the bulk of the aromatics. This spectrum is consistent only with compound V (pseudo-*m*-bromoacetyl isomer). Similar reasoning was applied to isomers VI and VII, which were also found to thermally isomerize to give an equilibrium mixture. The fact that the equilibria IV $\rightleftarrows$ V and VI $\rightleftarrows$ VII did not leak into one another confirms the conclusion derived earlier that xylylenes are not intermediates in these reactions.[3] Isomerizations such as these brought to hand some of the less available isomers and added to the fabric of internal consistency in structural assignments of the disubstituted [2.2]paracyclophanes.

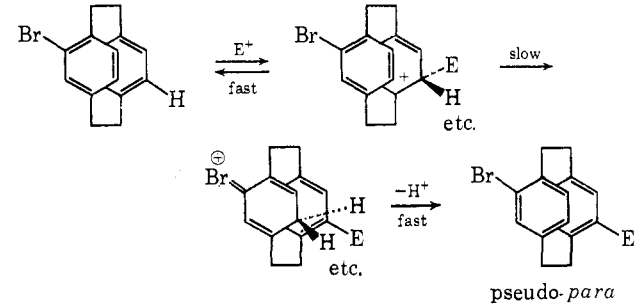


The data of Table I indicate that in no case is the major product predicted by the charge distribution shown in resonance structure VIIIc.[4] Rather, in all runs except bromination of 4-cyano[2.2]paracyclophane, the major product reflects attack pseudo-*gem* to the most *basic position* or *substituent* of the substituted ring. For example, bromination of 4-bromo[2.2]-paracyclophane (run 6) gives seven times more pseudo-*ortho* and pseudo-*para* than pseudo-*meta*, and the *ortho* and *para* positions of the starting material carry more negative charge than the *meta* position (see structures VIIIa and VIIIb).



VIIIa VIIIb VIIIc

This correlation suggests that the product-determining step is proton transfer to an acceptor site on the originally substituted ring. The geometry of [2.2]paracyclophane is ideally suited for such proton transfer,[5] and the aromatic nuclei are expected to be of at least comparable base strength to the solvent, bromide ion, or aluminum tetrachloride ion. The proximity of the rings hinders approach by these external bases and should favor intramolecular processes. For the acetyl, carbomethoxy, carboxy, and nitro derivatives of [2.2]-paracyclophane, bromination (runs 1–4) occurs exclusively or predominantly in the position pseudo-*gem* to these groups to give the thermodynamically least stable isomer. The oxygens of these groups are ideally positioned to accept a proton from the pseudo-*gem* position. The lower specificity of the nitro compound probably reflects its lower basicity.[6] The cyano group apparently cannot function as an internal base because of its linear structure, and no pseudo-*gem* product was observed in run 5. The random product pattern observed in run 5 rules out specific conjugative or inductive effects on positions of substitution. The mechanism favored by the data is illustrated with 4-bromo[2.2]paracyclophane as substrate (runs 6 and 7). In the over-all scheme, the electrophile attacks the face of the unsubstituted ring, a proton is transferred from ring to ring, and the proton departs from the face of the originally substituted ring. Thus, electrophiles enter and depart from the system by the least hindered paths.



Rate-determining proton transfers in aromatic brominations[7a] and acetylations[7b] are known and were de-

(2) Downfield shifts of the pseudo-*gem* proton are observed with a number of other functional groups including cyano, which also exhibits a small *ortho* shift. Similar shifts of *peri* hydrogens in 1-substituted naphthalene are recorded [G. O. Dudek, *Spectrochim. Acta*, **19**, 691 (1963); P. R. Wells and P. G. E. Alcorn, *Australian J. Chem.*, **16**, 1108 (1963)].

(3) H. J. Reich and D. J. Cram, *J. Am. Chem. Soc.*, **89**, 3078 (1967).

(4) D. J. Cram, W. J. Wechter, and R. W. Kierstead, *ibid.*, **80**, 3126 (1958).

(5) P. K. Gantzel and K. N. Trueblood, *Acta Cryst.*, **18**, 958 (1965).

(6) The approximate pK_a's of the conjugate acids of acetophenone, methyl benzoate, nitrobenzene, and benzonitrile are −6.2, −7.8, −11, and −10.5, respectively [E. M. Arnett, *Progr. Phys. Org. Chem.*, **1**, 223 (1963)].

(7) (a) E. Baciocchi, G. Illuminati, G. Sleiter, and F. Stegel, *J. Am. Chem. Soc.*, **89**, 125 (1967); (b) F. R. Jensen and G. Goldman in "Friedel–Crafts and Related Reactions," Vol. III, Interscience Publishers, Inc., New York, N. Y., 1964, p 1017.

tected by the isotope effect technique. Preliminary results demonstrate substantial deuterium isotope effects in the bromination of 4-methyl[2.2]paracyclophane.[8]

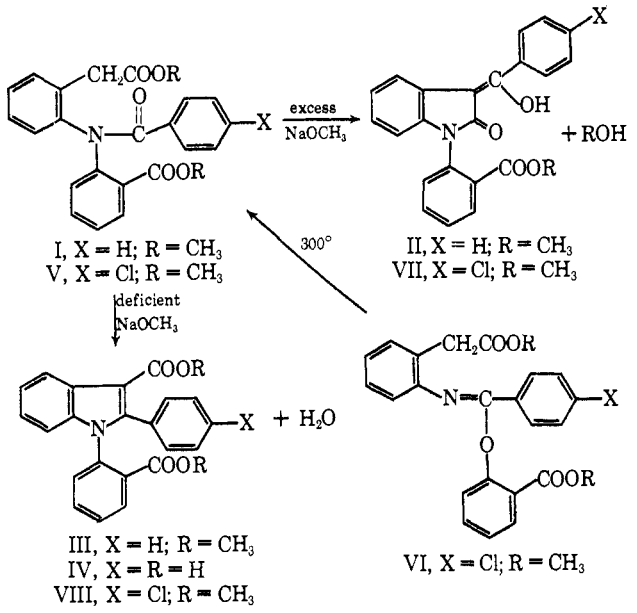
(8) The authors wish to thank the National Science Foundation for a grant used in support of this research. H. J. R. also wishes to acknowledge a U. S. Rubber Co. tuition grant for 1967.

Hans J. Reich, Donald J. Cram
Contribution No. 2173, Department of Chemistry
University of California at Los Angeles
Los Angeles, California 90024
Received October 19, 1967

Isolation of Crystalline Keto–Enol Tautomers. Conversion into Indoles and Oxindoles

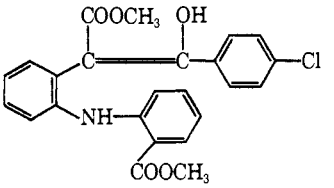
Sir:

Several years ago we reported that treating the N-benzoyldiphenylamine diester I with excess sodium methoxide in benzene failed to give the expected Dieckmann product but instead furnished the oxindole II.[1] It has now been found that use of slightly less than 1 equiv of the same base, followed by acidification with hydrochloric acid, afforded little or no II but gave instead the indole diester III in 63% yield.[2]

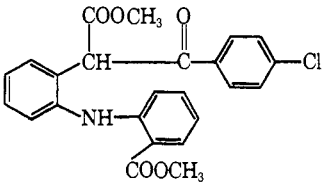


The structure of III, mp 140–144°, was determined by elemental analyses[3] and spectra;[4] the ultraviolet spectrum (λ_{max} 235 mμ (ε 36,200) and 294 (19,600)) was indicative of the indole nucleus while infrared bands at 5.79 and 5.87 μ and nmr peaks at δ 3.75 and 3.43 showed the presence of two carbomethoxy groups.[5] Hydrolysis of III with excess potassium hydroxide in aqueous methanol gave the dibasic acid IV, 85%, mp 215–218° dec, while treatment with 1 equiv of sodium methoxide gave 23% of half-ester acid, mp 259–266°, identical with material previously obtained as a by-product in the synthesis of II.[1]

The *p*-chloro analog V, mp 109–111°, was prepared in 85% yield by Chapman rearrangement[1,6] of the imidate VI, mp 96.5–99°. Reaction of V with excess sodium methoxide in benzene gave the yellow oxindole VII, 71%, mp 179–183°, positive $FeCl_3$ reaction, δ 12.4 (enolic proton) and 3.63 (OCH_3). On the other hand, when the reaction was carried out with a slight deficiency of base,[2] the major product (54%) was neither the oxindole VII nor the indole VIII, but instead an isomer of V shown to be the enol IX, white prisms, mp 110–122° (variable), positive $FeCl_3$ reaction, δ 13.5 (enol OH), 9.33 (NH), and 3.80 and 3.70 (sharp singlets for the two carbomethoxy groups).



IX



X

Recrystallization of the enol from methanol gave two types of prisms which were hand picked. The minor fraction was then used to seed a solution obtained by refluxing the enol in methanol for 1 hr. Slow crystallization resulted, furnishing the keto compound X as pale yellow prisms, mp 93–99°, 68%, negative $FeCl_3$ reaction, δ 9.38 (NH), 5.75 (singlet, CHC=O), and 3.88 and 3.72 (OCH_3). Treatment of either enol IX or keto X with excess sodium methoxide in benzene afforded oxindole VII while the reaction of either isomer with trifluoroacetic acid in chloroform furnished the white indole VIII, mp 194–197.5°, negative $FeCl_3$ reaction, δ 3.78 and 3.45. Both IX and X reacted at once with bromine in carbon tetrachloride, but in each case the isolated product was the indole VIII.

The marked differences in the nmr spectra of IX and X, both with respect to the enolic H and one of the OCH_3 groups, facilitated the analysis of mixtures.[5] Solutions of either compound in deuteriochloroform were essentially unchanged after 24 hr at room temperature, but addition of one drop of triethylamine to either solution furnished the equilibrium mixture containing 30% enol. Refluxing methanol solutions of IX or X for 4 hr led to the same 3:7 ratio, but in boiling hexane (24 hr) the keto form (55%) predominated. When IX or X was heated without solvent, the mixture contained ~25% enol, but equilibration was still incomplete after 3 hr at 100°. At 125° a complex mixture of VII, VIII, IX, and X resulted.

The reaction of the parent compound I with a deficient amount of base was then explored further. *Careful* acidification of the reaction mixture led to a gum which was shown by nmr (δ 13.5 and 5.78) to contain both the enol and keto compounds corre-

(1) J. W. Schulenberg and S. Archer, *J. Am. Chem. Soc.*, **83**, 3091 (1961).

(2) Use of an old bottle of commercial sodium methoxide, which was later found to have a base content of only 80%, led to the serendipitous result.

(3) Satisfactory analyses were obtained for new compounds.

(4) Ultraviolet spectra were run in 95% ethanol, infrared spectra in potassium bromide, and nmr spectra in deuteriochloroform (internal TMS).

(5) I wish to thank Dr. R. K. Kullnig and Miss C. M. Martini for spectral interpretations which were instrumental in establishing the structures of new compounds and the composition of mixtures.

(6) J. W. Schulenberg and S. Archer, *Org. Reactions*, **14**, 1 (1965).