META-BRIDGED AROMATIC COMPOUNDS

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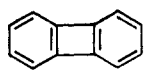
I. INTRODUCTION

The common polynuclear aromatic compounds are fused by *ortho* bridges and the chemistry of these is exceedingly well-known for the simple cases such as naphthalene, phenanthrene and anthracene. Recently some of the more interesting of these *ortho*-bridged molecules have been investigated with renewed interest. Among these are benzocyclobutene (I) (25) and biphenylene (II) (9) which have been studied in connection with some aspects of aromaticity. These *ortho*-

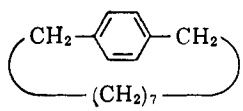
I



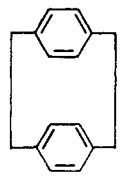
II

bridged polynuclear aromatic hydrocarbons are generally planar or very nearly so.

A second class of bridged aromatic compounds is that known as the *paracyclophanes*, typified by [9]paracyclophane (III) and by [2.2]paracyclophane (IV). Cram and his co-workers (26, 30) have contributed immensely to our knowledge of this class of compounds. In particular, they have been able to show the size limitations of the bridges necessary to form a stable



III



IV

compound; furthermore, they have investigated a number of interesting transannular effects and reactions which occur in this system. The abnormal ultraviolet spectra of these compounds is attributed to two factors: the bent benzene rings and transannular electronic interactions of the two aromatic systems.

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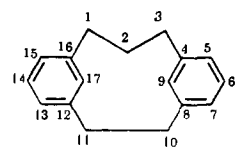
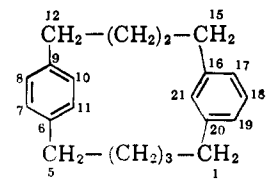
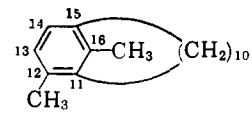
The third class of benzenoid bridged ring compounds is known as the *metacyclophanes*. This review is concerned with aromatic molecules of this class of 1,3-bridged compounds. Several examples are given below with the numbering system and names of these compounds (56).



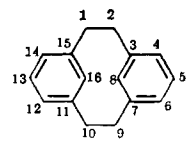
[3.2]Metacyclophane



[5-*p*-4-*m*]Cyclophane

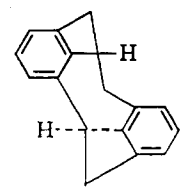


12,16-Dimethyl[10]metacyclophane



[2.2]Metacyclophane

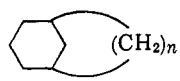
The gross geometry of the [2.2]metacyclophanes containing two aromatic nuclei is an unusual one. The two benzenoid rings lie in parallel planes and each ring is slightly distorted from planarity due to the overcrowding of the carbon atoms at the 8- and 16-positions. Thus the substituents at these positions lie over the benzene ring to which they are not directly attached. A view is shown below. Those molecules containing only



one aromatic ring would also be expected to show some distortion in cases where only a few members comprise the bridge.

This review will be sub-divided on the basis of the number of aromatic rings which are present in the

molecule. In general, compounds such as V will not be included even though they contain 1,3-bridged systems and presumably some could be transformed into aromatic species. The literature available to the author to December, 1961, has been included. A general review of macrocyclic ring compounds and transannular reactions by Prelog (50) has been published; however, besides a seminar abstract (19), no other review has appeared concerning this class of compounds.

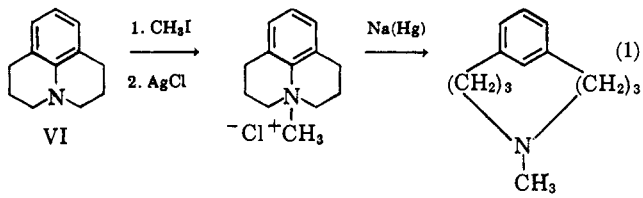


V

II. Compounds Containing One *meta*-Bridged Aromatic Ring

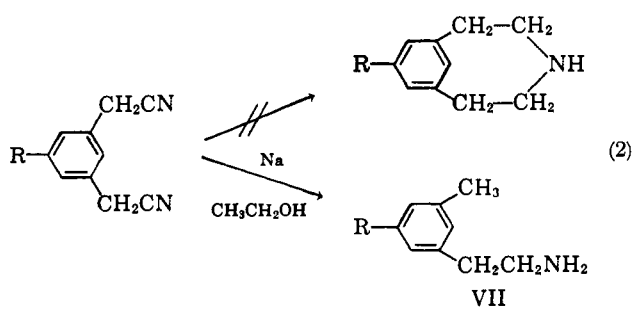
The investigation of the preparation of compounds of this type was prompted by the lack of a suitable answer to the question, "What is the minimum number of atoms necessary to form a bridge between the *meta*-positions of a benzene ring?" At the same time, of course, research was being carried out in order to gain information about *para*-bridges.

One of the first *meta*-bridged compounds containing one aromatic ring was prepared (21, 23) starting from the naturally occurring julolidine (VI) by the sequence outlined in Equation 1.



(1)

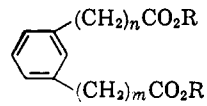
Although these workers (20, 22) also reported the formation of two additional *meta*-bridged compounds by the dinitrile cyclization method employing sodium in alcohol (Equation 2), it remained for Titley (58) to show that the bridged compounds (and further transformation products) were not obtained in either case



(2)

R = —H, —CH_3

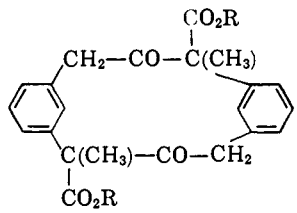
but rather the primary amine (VII) was the product described as the bridged compound. Indeed, even the original workers could not repeat their previous results. In a direct attempt to carry out authentic cyclizations of a similar type, Titley (59) investigated the Dieckmann reaction in the *meta*- and *para*-series using compounds of the type



R = —CH_3 or —CH_2CH_3

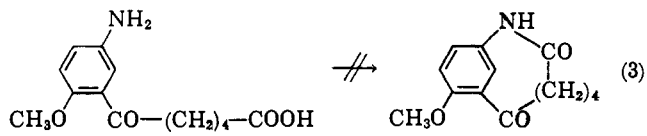
n	*m*
2	2
0	2
1	1
1	0

These were treated with sodium in toluene at 100° and the method of isolation involved treatment of the complex mixture of sodium salts with methyl iodide and subsequent separation of the alkylated product by distillation. Although it was presumed that certain dimeric products were obtained, which had structures typified by VIII, no further evidence was offered for these structures, nor could the simple bridged aromatic compounds be obtained.



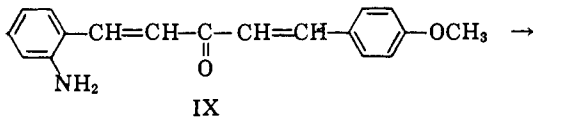
VIII

The failure of the above cyclizations to yield definite *meta*-bridged products is attributed to the short chain length, although an attempt by Plant (48) to form a cyclic amide also failed (Equation 3). Because the facile ring-closure of *o*-aminobenzal-*p*-anisalacetone (IX) and similar compounds affords quinoline derivatives, an attempt was made to carry out the corresponding reaction in the *meta*-series (Equation 5). As would be expected, no conditions could be found to effect the conversion (47).

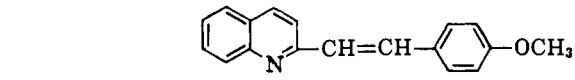


(3)

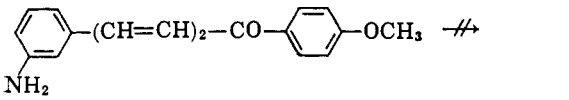
The specific examples and results described above are, for the most part, the few early cases reported in the literature. The first systematic approach to the study of these systems was begun by Ziegler and Lüttringhaus. However, shortly before this, Ruzicka, Buijs, and Stoll (54), who had been studying the formation of large membered rings, reported the successful preparation of ketone XI by carrying out the dry

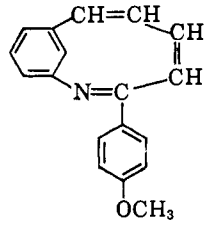


IX



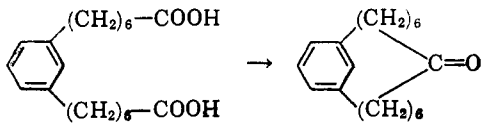
(4)





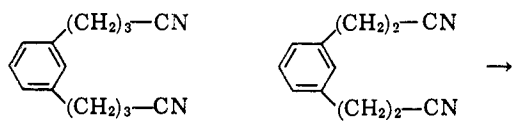
(5)

distillation of the cerium salt of diacid X. The ketone was isolated as the semicarbazone in about 2% yield and the pure compound, a viscous, colorless, high-boiling oil, was obtained by hydrolysis.

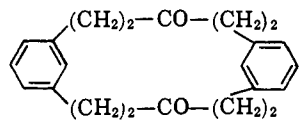


X XI

The fact that many-membered cyclic ketones may be prepared by the cyclization of dinitriles, using a strong base such as sodium ethylanilide, led Ziegler and Lüttringhaus (66) to apply this method to similar compounds in the *meta*-bridged benzene ring series. Although dinitrile XII afforded only a complicated mixture of products which was not further investigated, the lower homolog (XIII) afforded a compound whose structure was believed to be that of diketone XIV.

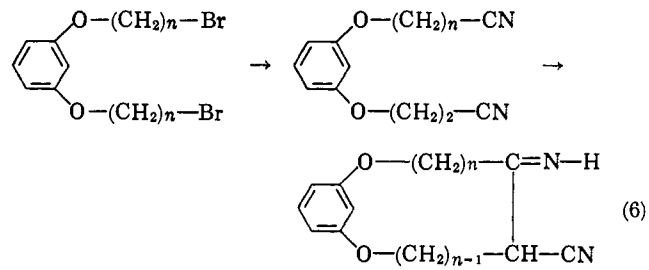


XII XIII



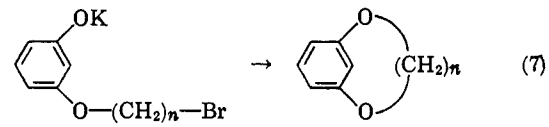
XIV

In neither case was the simple *meta*-bridged compound obtained. Most of the compounds prepared by these workers were cyclic polymethylene resorcinols, hydroquinones, naphthols and similar compounds. This general approach to these syntheses took one of two courses: either the conversion of the corresponding ω,ω'-dibromoalkyl-resorcinol diether to the corresponding dicyano compound and subsequent cyclization (Equation 6) or the high dilution cyclization of the

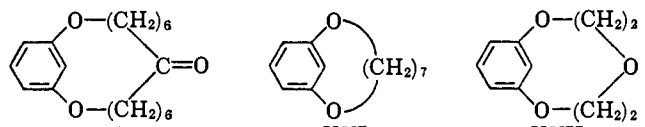


(6)

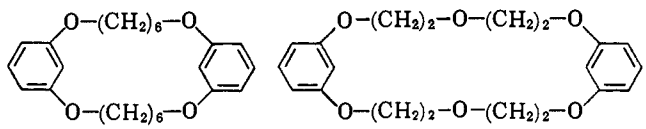
ω-bromo half-ether using potassium hydroxide in anisole or benzene (Equation 7). Examples of compounds prepared by the former method (XV) and by the latter (XVI, XVII, XVIII, XIX) are shown below.



(7)

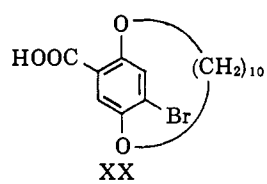


XV XVI XVII



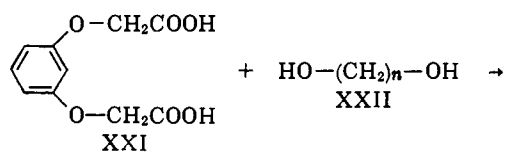
XVIII XIX

The optical activity of suitably substituted compounds in this series was discussed by Ziegler and Lüttringhaus (66) and compound XX in the *para*-bridged series was prepared and resolved by Lüttringhaus and Gralheer (44). No *meta*-bridged structures were studied; however, the same arguments apply to these compounds.

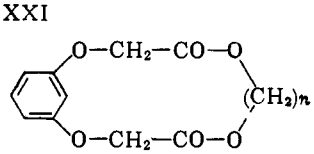


XX

Compounds of the resorcinol ether type were also prepared by Spanagel and Carothers (57). These workers used a depolymerization method whereby acid XXI was esterified with various glycols (XXII) and the resulting polyesters were depolymerized by heating in vacuum. By this procedure *meta*-bridged compounds



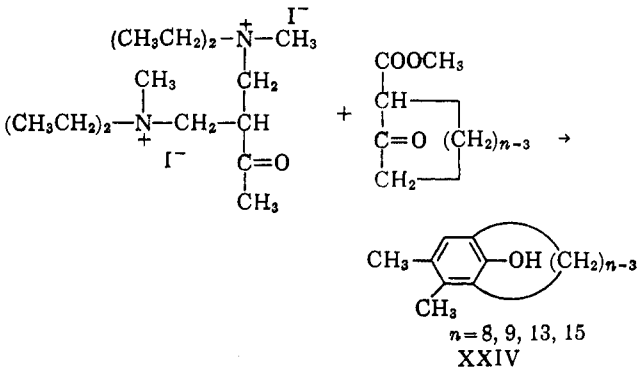
XXI XXII



XXIII

(XXIII, n = 2–4, 6, 9, 10) were obtained in yields of 16–35%. They further point out a very important fact regarding the question of the minimum number of atoms in the *meta*-bridge: changes in chain members (*i.e.*, replacement of —CH_2— by —O— or by —CO—) result in relatively large changes in the stability and steric requirement of the resulting system because of concurrent changes in the valence angles. Thus, the question must be answered individually for each series of compounds under examination. Results obtained in the resorcinol ether series, for example, should not be carried over *a priori* to the carbocyclic one.

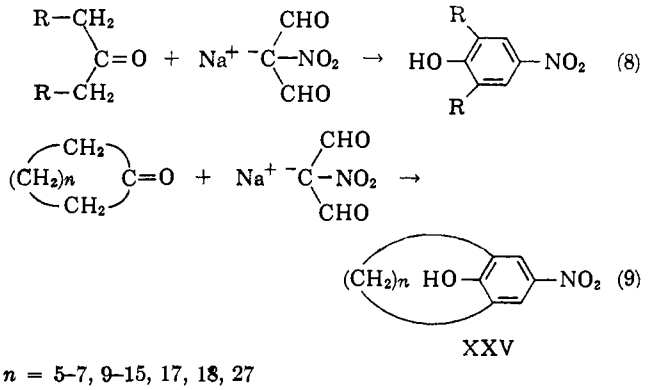
Interesting cases of the preparation of polymethylene *meta*-bridged compounds are those of phenols XXIV, whereby the aromatic system is formed from two non-aromatic constituents. Although the reaction has not been exhaustively examined, it is presumably a general one for systems of this type.



n = 8, 9, 13, 15

XXIV

Perhaps the most comprehensive study of a series of *meta*-bridged compounds has been that carried out by Prelog and Wiesner (51) on bridged *p*-nitrophenols. The general method was first applied to the preparation of 2,6-disubstituted *p*-nitrophenols by Hill (33–35) and later used by Jones and Kenner (38). As shown in Equation (8), condensation of a ketone (containing two α-methylene groups in the cases cited) with the sodium salt of nitromalonaldehyde leads directly to the phenol. The use of cyclic ketones leads to the formation of *meta*-bridged analogs (Equation 9). The yield in most cases is 40–70%.



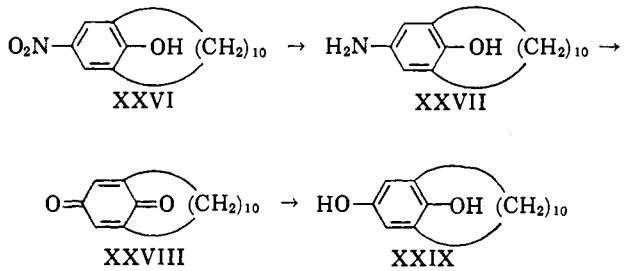
(8)

(9)

XXV

n = 5–7, 9–15, 17, 18, 27

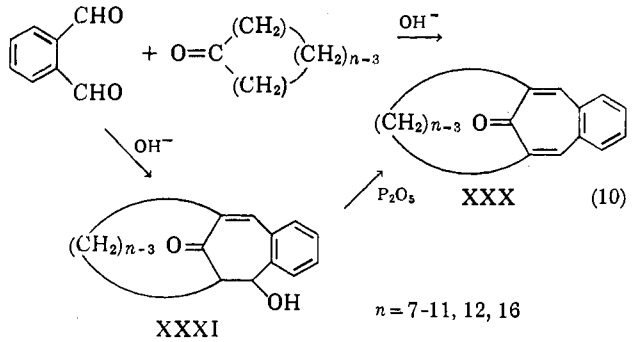
The ultraviolet spectrum of each of these *meta*-bridged phenols is in fair agreement with that of *p*-nitrophenol itself, excluding the lowest member (XXV, n = 5) of the series. Indeed, the spectrum indicates that this molecule exists mainly in the keto tautomeric form. Thus, the minimum number of members needed in the bridge in this series is six (*i.e.*, nine members in the cycle) in order to maintain the aromatic system. Further, one member of this series (XXVI) was reduced with Raney nickel in alcohol and the amino phenol (XXVII) was oxidized to the quinone (XXVIII). Subsequent reduction of the latter led to the *meta*-bridged hydroquinone (XXIX).



XXVI XXVII

XXVIII XXIX

A similar condensation (40) was used to prepare a series of 2,7-polymethylene-4,5-benzotropolones (Equation 10). With some cyclanones, the desired compound (XXX) was obtained directly while in other cases it was necessary to dehydrate the intermediate hydroxy



n = 7-11, 12, 16

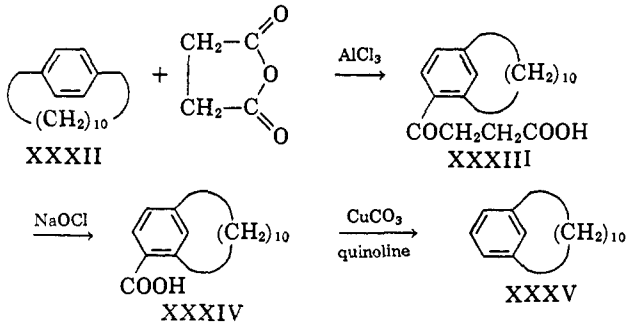
(10)

XXXI

ketone (XXXI) in a separate step. The change in properties with decreasing chain length was ascribed to steric inhibition of resonance of the benzotropylium system. Heat of combustion measurements on several compounds add further support to this argument (55).

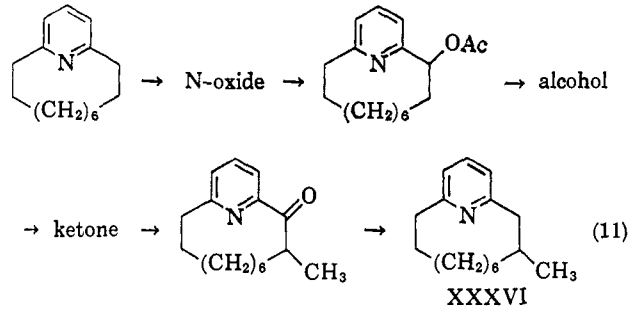
A series of transformations leading from [10]paracyclophane (XXXII) to [10]metacyclophane (XXXV) has been described by Blomquist, Stahl, Meinwald and Smith (14). Succinoylation of [10]paracyclophane (XXXV) using aluminum chloride led to the rearranged 12-(ω-carboxypropionyl)-[10]metacyclophane (XXXIII), which was oxidized to the 12-carboxy[10]-metacyclophane (XXXIV) and subsequently decarboxylated to [10]metacyclophane (XXXV) itself. The initial rearrangement also takes place with [9]paracyclophane under similar conditions. Although this is

the first specific example of the rearrangement of this type (*i.e.*, para- to metacyclophane), the general reaction has been described previously (3, 4, 27, 38).



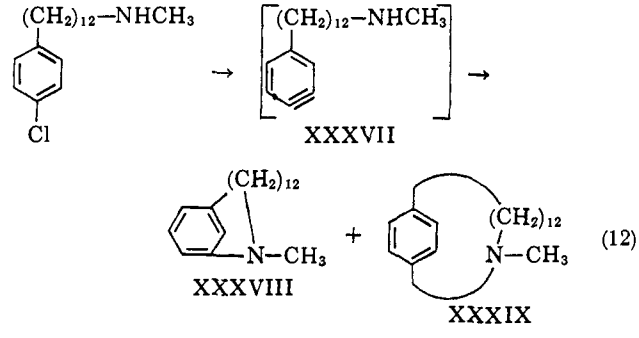
XXXII XXXIII XXXIV XXXV

A natural product, muscopyridine (XXXVI), has been synthesized and shown to be a *meta*-bridged pyridine derivative (11). A portion of the synthesis is shown in Equation 11, starting from the first *meta*-bridged compound obtained in the series.



XXXVI

The intramolecular ring closure (Equation 12) of benzyne intermediate XXXVII affords *meta*- and *para*-bridged amines (XXXVIII and XXXIX).



XXXVIII XXXIX

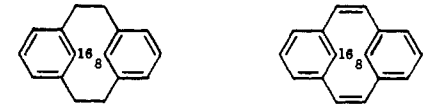
The reaction has been carried out with both phenyllithium and with sodium amide; the yield of the *meta*-isomer is 29–51% and that of the *para*-isomer is 3–6%, depending on the base and reaction conditions employed (37).

In summary, it can be seen that much of the early work concerning the investigation of *meta*-bridged compounds containing one aromatic ring was directed toward the preparation of only the lowest members in the series. Only the later studies of resorcinols and esters and then of the *p*-nitrophenols afforded a continuum of compounds whereby a better understanding of these systems was obtained. These later investigations proved particularly fruitful because of the increased general knowledge concerning the preparation of large cyclic compounds.

III. COMPOUNDS CONTAINING TWO *meta*-BRIDGED AROMATIC RINGS

A. PREPARATION, STRUCTURE, REACTIONS AND DERIVATIVES OF [2.2]METACYCLOPHANE

[2.2]Metacyclophane (XL) was the first authentic *meta*-bridged aromatic compound to be prepared. Although this work was described in a note published by Pellegrin (46) in 1899, it apparently was overlooked until 1950.

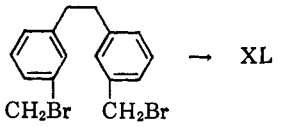


XL XLI

By heating a mixture of two moles of bromobenzene and one mole of α,α'-dibromo-*m*-xylene with sodium in ether, [2.2]metacyclophane was isolated in 0–18% yield. In addition, he isolated biphenyl, the expected product formed by the Wurtz reaction of bromobenzene and sodium, and a hydrocarbon, $C_{16}H_{12}$, to which he assigned the structure of [2.2]metacyclophane-1,9-diene (XLI). Although [2.2]metacyclophane is resistant to oxidation, the ultimate analysis and molecular weight data (cryoscopic determination in benzene) are consistent with the assigned structure.

Using a modification of Pellegrin's synthesis, Baker, McOmie and Norman (7,8) obtained [2.2]metacyclophane in 12% yield. The structure was reconfirmed and the compound was dehydrogenated with palladium-on-charcoal, affording pyrene in 62% yield (20% recovery of [2.2]metacyclophane). They were unable to isolate the diolefin (m.p. 191°). Calculations and models of this compound indicate clearly that the severe nonbonded repulsions which would result from the 8- and 16-interactions of a planar compound would render this molecule one of extremely high energy. Although the ultimate analysis and molecular weight data which Pellegrin reported are consistent with this structure, neither the authentic diolefin nor any other compound with these properties has been prepared since by this method.

In addition to the preparation of [2.2]metacyclophane in 33% yield (16) by the dimerization of α,α'-dibromo-*m*-xylene employing the disodium tetraphenylethane catalyst studied by Müller and Röscheisen (45), the intramolecular ring closure of 3,3′-bis-(bromomethyl)-bibenzyl (XLII) has afforded the hydrocarbon in 77% yield (42).



XLII

Models of [2.2]metacyclophane show that it may exist in three main configurations: (1) A step-like *trans*-form in which the benzene rings are arranged in parallel planes, (2) two identical *cis*-forms with the benzene rings inclined at an angle of about 60° and (3) a twisted form through which the *cis*-form must pass during interconversion (62). The suggestion (7) that its geometry was of the *trans*-, stepped type was confirmed by the X-ray measurements of Brown (24).

Since each molecule of [2.2]metacyclophane has a center of symmetry and consists of two benzene rings joined by two dimethylene linkages in the *meta*-position, this has the effect of producing a ten-membered ring system flanked by two six-membered benzene rings. The stepwise configuration of the benzene rings permits adequate clearance between the central carbon

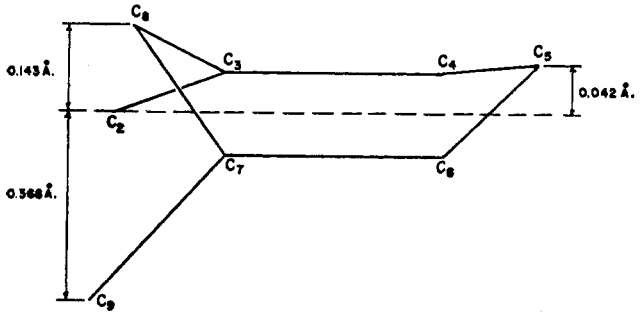


Fig. 1.—Benzene ring distortion in [2.2]metacyclophane, after Brown.[24]

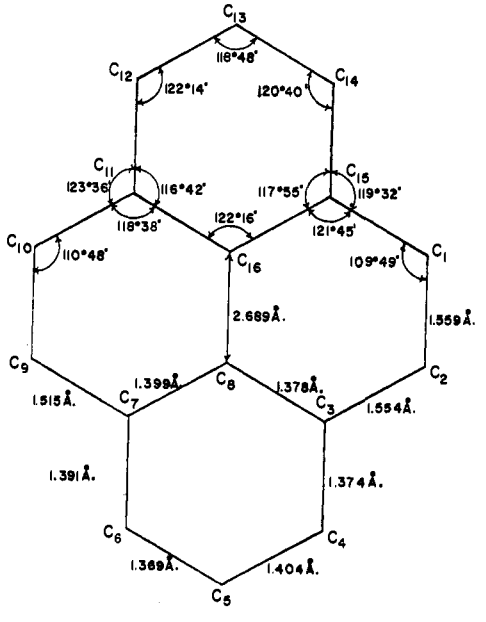
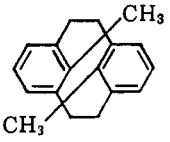


Fig. 2.—Dimensions of [2.2]metacyclophane, after Brown.[24]

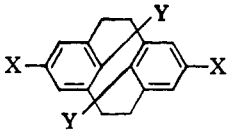
atoms and their attached hydrogen atoms. If the hexagonal rings were planar and undistorted, the C_8–C_{16} distance would be almost the same as the C_1–C_2 distance (1.56 Å.), which is impossibly close for nonbonded atoms. Carbon atom 8 is displaced out of the mean plane of $C_3C_4C_6C_7$ by 0.143 Å., and the methylene carbon atoms (C_1 and C_2) are displaced by about 0.4 Å., so that the substituting bonds make angles of about 15° with the mean plane of the ring (see Figure 1). A secondary effect is that carbon atom 5 at the opposite end of the benzene ring is also displaced out of the plane by 0.042 Å. The result of this distortion is to increase the distance between C_8 and C_{16} to 2.689 Å. (see Figure 2).

It is interesting to note that the X-ray crystallographic studies of 8,16-dimethyl-[2.2]metacyclophane (XLIII) show that the central methyl groups either must be very highly hindered or completely blocked in the solid state so that there is no free rotation (15).



XLIII

A study of the nuclear magnetic resonance spectra of [2.2]metacyclophane and several of its derivatives are consistent with this structure (61). In the table below are shown the various compounds which have been examined and the tau values of the central substituents. The position of the central substituent protons is explained qualitatively by the ring current theory (10, 49). It is of interest to note that the methyl groups of hydrocarbon XLIII appear to be restricted in the crystalline state (X-ray) but freely rotating in solution (n.m.r.) even down to −20°. That the two alpha-methylene hydrogens on a given carbon atom are not equivalent is shown clearly by the splitting in the spectrum of the [2.2]metacyclophanes.



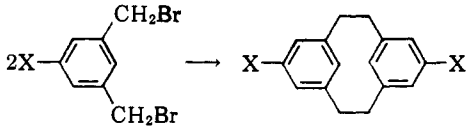
Selected Tau Values for Some [2.2]Metacyclophanes

X	Y	τ_Y-Sharp singlet
—H	—CH_3	9.44[a]
—H	—H	5.83[b]
—CH_3	—H	5.94
—OCH_3	—H	5.99

[a] Toluene (—CH_3) 7.6–7.8τ. [b] Benzene *ca.* 3τ.

The infrared spectrum of these compounds is unexceptional and the ultraviolet absorption maxima of [2.2]metacyclophane occur at 212 mμ (log ϵ 4.56) and 271 mμ (log ϵ 2.65).

Several 5, 13-disubstituted-[2.2]metacyclophanes have been prepared by the modified Wurtz dimerization of the corresponding 3,5-bis-(bromomethyl)-substituted benzenes (Equation 13). An attempt to show that these results constitute a relationship between the per cent. yield and the electron donating power of the sub-

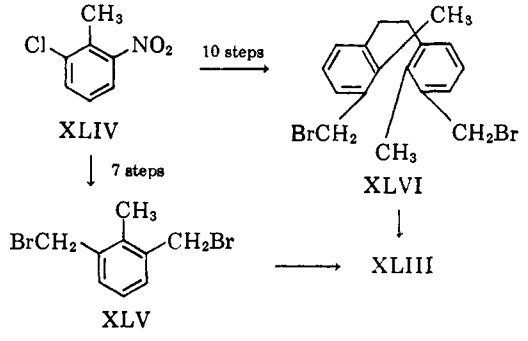


(13)

X = —H, 33% yield
= —CH_3, 7% yield
= —OCH_3, 2.5% yield

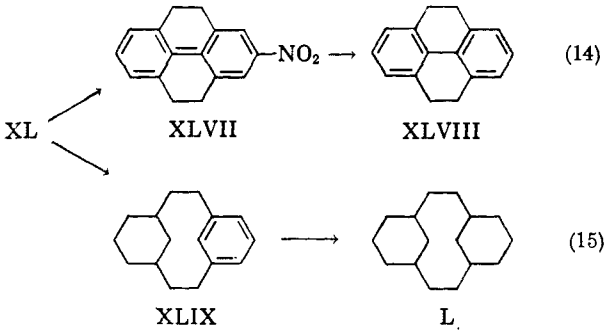
stituent was unsuccessful. Using the fluoro-compound, only small portions of impure [2.2]metacyclophane were obtained. When the nitro-substituent was present, a polymer was obtained which, on reduction with tin and hydrochloric acid, afforded a small amount of solid believed to be the 5,13-diamino[2.2]metacyclophane (16).

The 8,16-dimethyl[2.2]metacyclophane (XLIII) has been prepared by two independent routes starting with 2-chloro-6-nitro-toluene (XLIV). In the first, 2,6-bis-(bromomethyl)-toluene (XLV) was dimerized in 4% yield by the modified Wurtz reaction and in the second, 2,2′-dimethyl-3,3′-bis-(bromomethyl)-bibenzyl (XLVI) underwent a similar intramolecular ring closure in 44% yield (42).



It has been of interest to repeat the work of Pellegrin in order to identify the compound to which he assigned the structure of [2.2]metacyclophane-1,9-diene. To this end, a great many reactions have been carried out in order to introduce functionality into the side chain of the parent hydrocarbon and subsequently introduce a double bond. The chemical reactions presently known are largely of a negative sort. [2.2]Metacyclophane has been treated with *n*-butyllithium, *n*-amylsodium (then carbonation), bromine (18), lead tetraacetate, cumene hydroperoxide–cuprous chloride, chromium trioxide (17), N-bromosuccinimide, bromine under irradiation, *t*-butyl hypochlorite, vanadium pentoxide–hydrogen peroxide, manganese acetate–air, and selenium dioxide (16). All of these reagents might have been expected to introduce functionality into a normal benzylic position; however, in most cases [2.2]metacyclophane was unaffected. In those cases where the recovery of the starting material was not high, only small amounts of decomposition products were obtained. The fact that the nuclear magnetic resonance spectrum shows that the two hydrogen atoms on a given *alpha*-carbon are not equivalent and the fact that this *alpha*-carbon deviates from the plane of the aromatic ring suggest that the usual charge stabilization associated with a benzylic cation, anion or radical cannot be attained readily in this case. The required change in the hybridization of this carbon atom from sp^3 (tetrahedral) to sp^2 (trigonal) is somewhat restricted by the steric requirement of the system.

An interesting reaction of [2.2]metacyclophane has been reported recently (1). Treatment of the hydrocarbon with dilute nitric acid for a short period affords the product of a transannular electrophilic aromatic substitution (XLVII). The gross structure was demon-

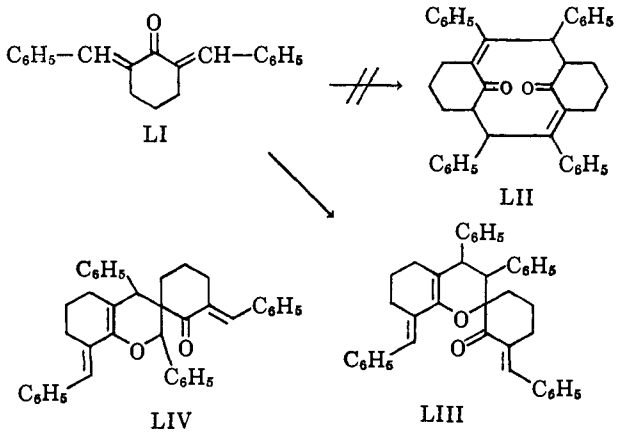


(14)

(15)

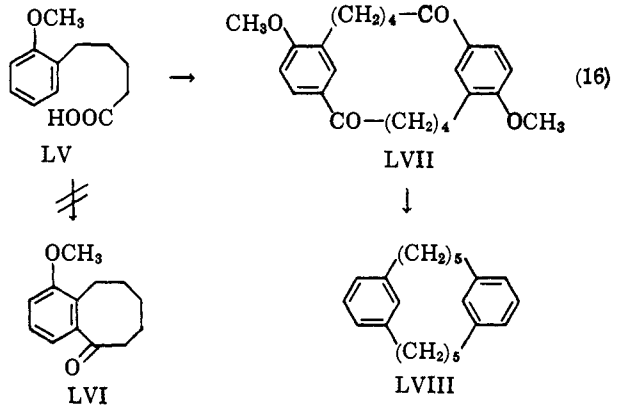
strated by reduction to the known corresponding hydrocarbon (XLVIII). In addition, hexahydro- and perhydro[2.2]metacyclophane (XLIX and L) were prepared by reduction of the parent hydrocarbon (XL).

Although reports (63, 64) claimed the preparation of a reduced substituted [2.2]metacyclophane (LII) by the dimerization of 1,3-dibenzal-cyclohexanone (LI), it has been shown recently (36) that the dimer is actually compound LIII. Compound LIV was also considered, but ruled out on the basis of the n.m.r. spectrum.

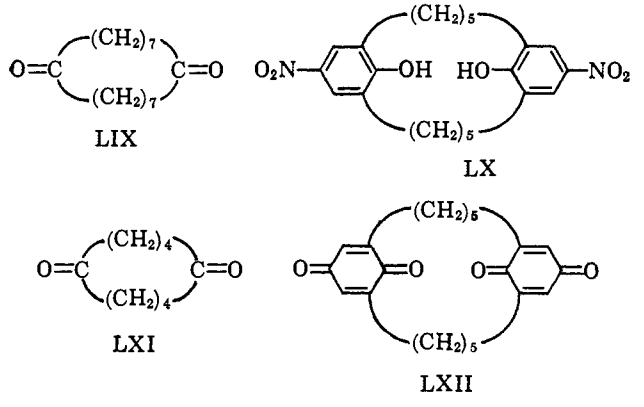


B. OTHER CARBOCYCLES

[5.5]Metacyclophane (LVIII) has been obtained by Bien (12, 13) through the sequence shown in Equation 16, although the initial cyclization with polyphosphoric acid was carried out in the hope of obtaining the methoxysuberone (LVI).



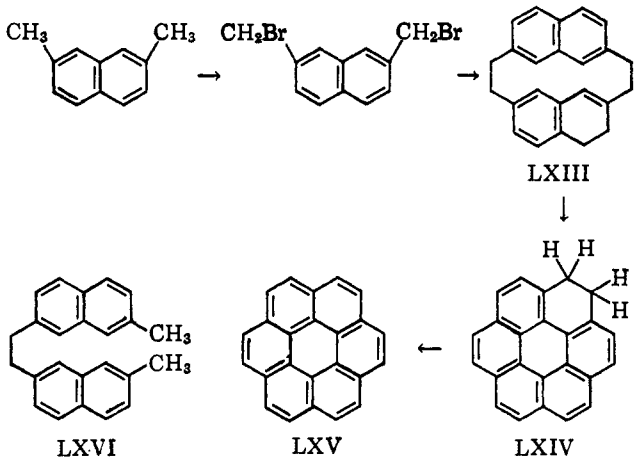
A substituted [5.5]metacyclophane derivative has been prepared (52) using the nitromalonaldehyde procedure described in the previous section. The use of diketone LIX led to the formation of cyclophane LX which was converted (without isolation of the intermediate diamino compound) to the corresponding diquinone LXII. However, similar treatment of diketone LXI gave no definite products.



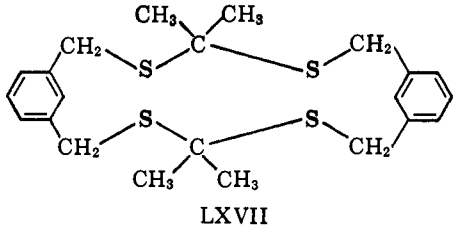
The next higher aromatic homolog, the naphthalene derivative (LXIII), has been prepared in a two-step synthesis (6). The facile conversion of this compound first to 1,2-dihydrocoronene (LXIV) and subsequently to coronene (LXV) itself affords a convenient synthesis of the latter hydrocarbon. In the coupling reaction an appreciable amount of the half-coupled, half-reduced compound (LXVI) was obtained, as is common in these dimerizations.

C. HETEROCYCLES

One of the earliest examples of a heterocyclic *meta*-bridged compound is that reported by Autenrieth and

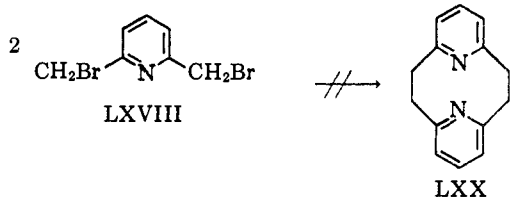


Beuttel (2). The reaction of α,α'-dimercapto-*m*-xylene with acetone gives rise to disulfide LXVII. This work, as does much of the earliest work in this field, bears

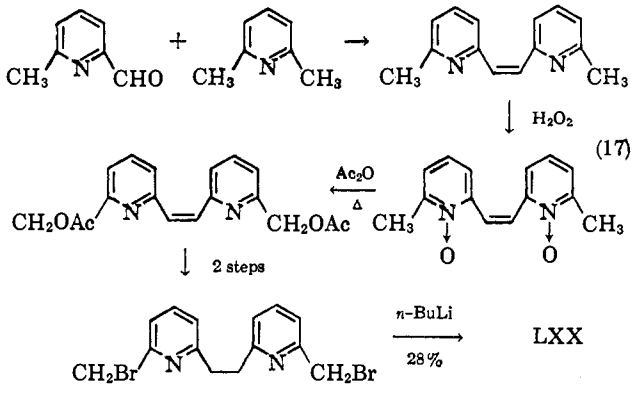


reexamination in light of newer techniques of modern organic chemistry.

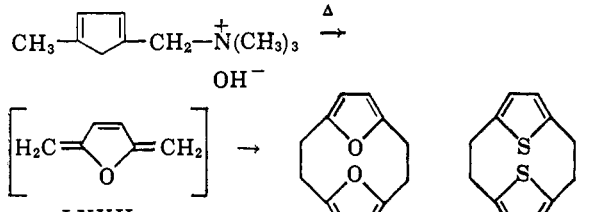
In order to investigate the properties of new aromatic systems, the preparation of the pyridine analog (LXIX) of [2.2]metacyclophane was carried out (5). The attempt to effect a direct coupling of 1,3-bis-(bromomethyl)-pyridine (LXVIII) using sodium failed; however,



the synthesis was accomplished by a longer route employing an N-oxide rearrangement (Equation 17).

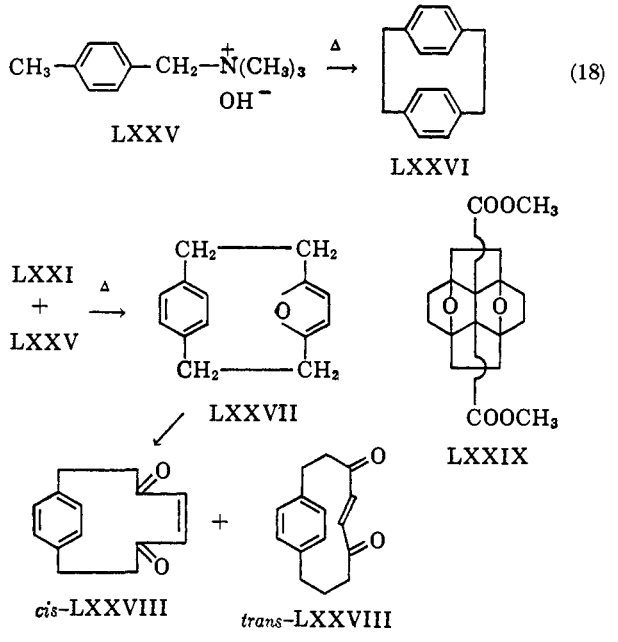


Some interesting heterocyclic *meta*-bridged compounds have been reported recently by the du Pont laboratories (62). These compounds have been prepared by carrying out a 1,6-Hofmann elimination using a diquaternary salt (LXXI). The bis-exocyclic methylene intermediate (LXXII) subsequently undergoes dimerization to give the heterocyclophanes.



LXXII LXXIII LXXIV

Both the furan (LXXIII) and thiophene (LXXIV) analogs have been prepared by this method, which also has been employed for the preparation of [2.2]paracyclophane (LXXVI) (Equation 18). In fact, a "cross-breeding" reaction has been reported recently (29) between the two diquaternary salts (LXXI and LXXV) affording the mixed cyclophane (LXXVII) in 30% yield.



LXXV LXXVI (18)

LXXI + LXXV LXXVII LXXIX

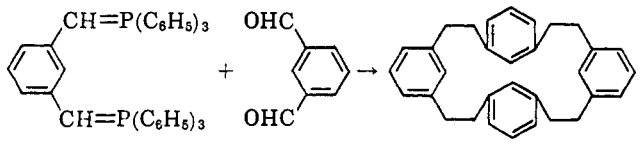
cis-LXXVIII *trans*-LXXVIII

This compound (LXXVII) affords both the *cis*- (LXXVIII) and *trans*- (LXXVIII) isomers on treatment with bromine and methanol at low temperatures. A further transformation of the furan compound (LIII) is the Diels–Alder reaction with dimethyl acetylenedicarboxylate; the adduct (LXXIX) may exist in two forms.

IV. Compounds Containing Three or More *meta*-Bridged Aromatic Ring Systems

The largest class of compounds in this group is that of the pyrrole derivatives (*e.g.*, porphyrins, chlorins, *etc.*) which have been adequately discussed elsewhere (41, 60, 65). However, other than the porphyrins, most of the compounds in this class are macrocyclic polymers which have been isolated.

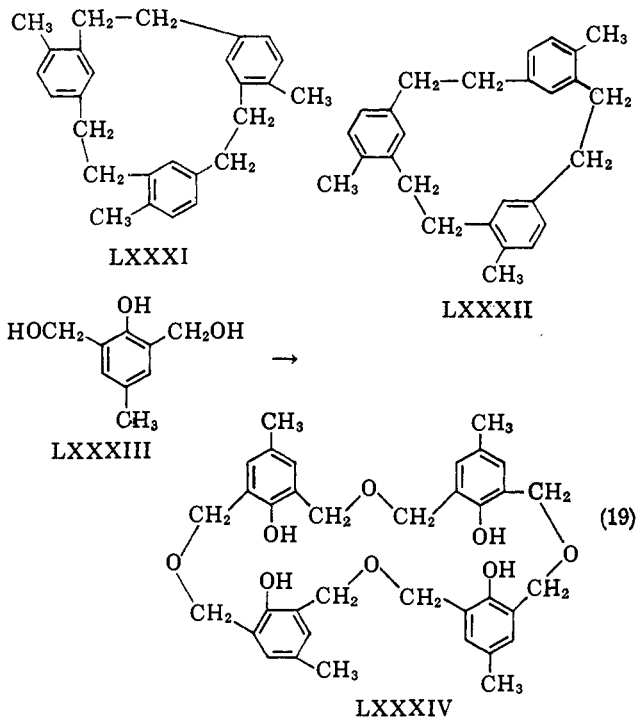
An attempt to prepare the diolefin (XLI) described by Pellegrin using the Wittig reaction afforded a compound to which structure LXXX was assigned. In addition, another unidentified hydrocarbon fraction was obtained (17).



XLXX

A further compound of this type has been obtained by the attempted dimerization of 2′,4′-dibromo-1,2,4-trimethylbenzene using the disodium tetraphenylethane catalyst (32). The compound obtained is believed to be a trimer (LXXXI or LXXXII) or a tetramer.

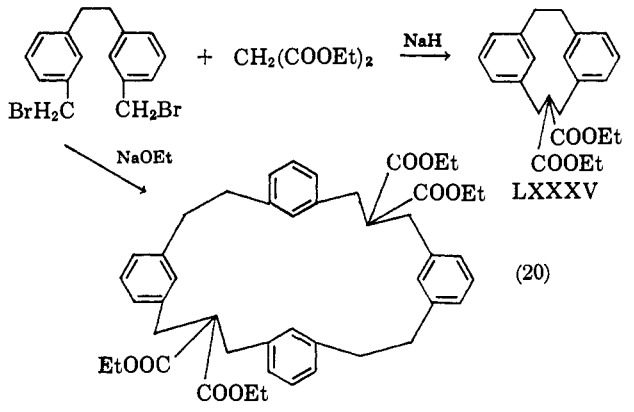
A recent paper (39) describes the tetramerization of phenol LXXXIII (Equation 19).



LXXXI LXXXII

LXXXIII LXXXIV (19)

The attempted preparation of a substituted [3.2]-metacyclophane using the malonic ester synthesis (Equation 20) resulted in the formation of dimer LXXXVI (31). The hydrogen atoms in the methylene bridges of this compound have nearly identical chemical shifts in the n.m.r. spectrum, indicating the expected relatively unrestricted motion of the molecule at room temperature. However, when the reaction was carried out under different conditions, the desired compound (LXXXV) was obtained and its n.m.r. spectrum showed



LXXXVI

clearly the characteristic high field aromatic protons.

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V. REFERENCES

(1) Allinger, N. L., DaRooge, M. A., and Hermann, R. B., *J. Am. Chem. Soc.*, **83**, 1974 (1961).
(2) Autenrieth, W., and Buettel, F., *Ber.*, **42**, 4357 (1909).
(3) Baddeley, G., *Quart. Rev.*, **8**, 355 (1954).
(4) Baddeley, G., Holt, G., and Pickles, W., *J. Chem. Soc.*, 4162 (1952).
(5) Baker, W., Buggle, K. M., McOmie, J. F. W., and Watkins, D. A. M., *J. Chem. Soc.*, 3594 (1958).
(6) Baker, W., Glockling, F., and McOmie, J. F. W., *J. Chem. Soc.*, 1118 (1951).
(7) Baker, W., McOmie, J. F. W., and Norman J. M., *Chem. and Ind.*, **77**, (1950).
(8) Baker, W., McOmie, J. F. W., and Norman, J. M., *J. Chem. Soc.*, 1114 (1951).
(9) Baker, W., McOmie, J. F. W., Preston, D. R., and Rogers, V., *J. Chem. Soc.*, 414 (1960), and previous papers in this series.
(10) Becker, E. D., and Bradley, R. B., *J. Chem. Phys.*, **31**, 1413 (1959).
(11) Biemann, K., Büchi, G., and Walker, B. H., *J. Am. Chem. Soc.*, **79**, 5558 (1957).
(12) Bien, S., *Bull. Research Council Israel*, 9A, 82 (1960).
(13) Bien, S., *J. Chem. Soc.*, 4015 (1960).
(14) Blomquist, A. T., Stahl, R. E., Meinwald, Y. C., and Smith, B. H., *J. Org. Chem.*, **26**, 1687 (1961).
(15) Boekelheide, V., private communication.
(16) Boekelheide, V., and Griffin, R. W., Jr., unpublished results.
(17) Boekelheide, V., and Humber, L. G., unpublished results.
(18) Boekelheide, V., and Lindsay, W. S., unpublished results.
(19) Bolhofer, W. A., M.I.T. Organic Chemistry Seminar Abstracts, p. 273 (April 26, 1948).
(20) von Braun, J., and Engel, O., *Ber.*, **58**, 281 (1925).
(21) von Braun, J., Heider, K., and Wyczatkowska, W., *Ber.*, **51**, 1215 (1918).
(22) von Braun, J., Karpf, L., and von Garn, W., *Ber.*, **53**, 98 (1920).
(23) von Braun, J., and Neumann, L., *Ber.*, **53**, 2015 (1919).
(24) Brown, C. J., *J. Chem. Soc.*, 3278 (1953).
(25) Cava, M. P., and Shirley, R. L., *J. Org. Chem.*, **26**, 2212 (1961), and previous papers in this series.
(26) Cram, D. J., *Record Chem. Progr.*, **20**, 71 (1959).
(27) Cram, D. J., and Abell, J., *J. Am. Chem. Soc.*, **77**, 1179 (1955).
(28) Cram, D. J., and Kierstead, R. W., *J. Am. Chem. Soc.*, **77**, 1186 (1955).
(29) Cram, D. J., and Knox, G. R., *J. Am. Chem. Soc.*, **83**, 2204 (1961).
(30) Cram, D. J., and Wilkinson, D. I., *J. Am. Chem. Soc.*, **82**, 5721 (1960), and previous papers in this series.
(31) Griffin, R. W., Jr., and Coburn, R. A., unpublished results.
(32) Griffin, R. W., Jr., and Slater, C. R., unpublished results.
(33) Hill, H. B., *Am. Chem. J.*, **24**, 1 (1900).
(34) Hill, H. B., and Hale, W. J., *Am. Chem. J.*, **33**, 1 (1905).
(35) Hill, H. B., and Torrey, J., *Am. Chem. J.*, **22**, 89 (1899).
(36) House, H. O., and Hortmann, A. G., *J. Org. Chem.*, **26**, 2190 (1961).
(37) Huisgen, R., König, H., and Lepley, A. R., *Ber.*, **93**, 1496 (1960).
(38) Jones, E. C. S., and Kenner, J., *J. Chem. Soc.*, 1842 (1931).
(39) Kämmerer, H., Grossman, M., and Umsonst, G., *Makromol. Chem.*, **39**, 39 (1960).
(40) Kloster-Jensen, E., Tarköy, N., Eschenmoser, A., and Heilbronner, E., *Helv. Chim. Acta*, **39**, 786 (1956).
(41) Lemberg, R., in "Progress in the Chemistry of Organic Natural Products," edited by L. Zechmeister, Vol. 11, p. 299, Springer-Verlag, Wien, 1954.
(42) Lindsay, W. S., Stokes, P., Humber, L. G., and Boekelheide, V., *J. Am. Chem. Soc.*, **83**, 943 (1961).
(43) Lüttringhaus, A., *Ann.*, **528**, 181 (1937).
(44) Lüttringhaus, A., and Gralheer, H., *Ann.*, **550**, 67 (1942).
(45) Müller, E., and Röscheisen, G., *Ber.*, **90**, 543 (1957).
(46) Pellegrin, M. M., *Rec. trav. chim.*, **18**, 457 (1899).
(47) Pfeiffer, P., *J. prakt. Chem.*, **109**, 41 (1925).
(48) Plant, S. G. P., *J. Chem. Soc.*, 1586 (1933).
(49) Pople, J. A., Schneider, W. G., and Bernstein, H. J., "High Resolution Nuclear Magnetic Resonance," McGraw-Hill Book Co., Inc., New York, N. Y., 1959, p. 180.
(50) Prelog, V., in "Perspectives in Organic Chemistry," edited by Sir A. Todd, Interscience Publishers, New York, N. Y., 1956, p. 96.
(51) Prelog, V., and Wiesner, K., *Helv. Chim. Acta*, **30**, 1465 (1947).
(52) Prelog, V., Wiesner, K., and Häfliger, O., *Collection Czech. Chem. Commun.*, **15**, 900 (1950).
(53) Prelog, V., Wirth, M. M., and Ruzicka, L., *Helv. Chim. Acta*, **29**, 1425 (1946).
(54) Ruzicka, L., Buijs, J. B., and Stoll, M., *Helv. Chim. Acta*, **15**, 1220 (1932).
(55) Schmid, R. W., Kloster-Jensen, E., Kovats, E., and Heilbronner, E., *Helv. Chim. Acta.*, **39**, 806 (1956).
(56) Schubert, W. M., Sweeney, W. A., and Latourette, H. K., *J. Am. Chem. Soc.*, **76**, 5462 (1954).
(57) Spanagel, E. W., and Carothers, W. H., *J. Am. Chem. Soc.*, **57**, 935 (1935).
(58) Titley, A. F., *J. Chem. Soc.*, 508 (1926).
(59) Titley, A. F., *J. Chem. Soc.*, 2571 (1928).
(60) Williams, R. J. P., *Chem. Revs.*, **56**, 299 (1956).
(61) Wilson, D. J., Boekelheide, V., and Griffin, R. W., Jr., *J. Am. Chem. Soc.*, **82**, 6302 (1960).
(62) Winberg, H. E., Fawcett, F. S., Mochel, W. E., and Theobald, C. W., *J. Am. Chem. Soc.*, **82**, 1428 (1960).
(63) Yeh, P. Y., *J. Taiwan Pharm. Assoc.*, **5**, 2 (1953).
(64) Yeh, P. Y., Chen, C. T., Ro, S. Y., and Wang, C. H., *J. Am. Chem. Soc.*, **77**, 3415 (1955).
(65) Zeile, K., *Angew. Chem.*, **68**, 193 (1956).
(66) Ziegler, K., and Lüttringhaus, A., *Ann.*, **511**, 1 (1934).