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THE USE OF BENZOCYCLOBUTENES AS INTERMEDIATES IN SYNTHESES OF MULTIBRIDGED CYCLOPHANES

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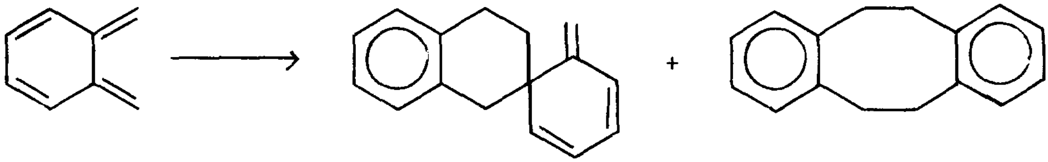
o-Xylylenes (1), generated either by valence tautomerization of benzocyclobutenes or by other means, have proved to be valuable synthetic intermediates. One application of particular interest is their dimerization which, depending on the temperature employed, may yield primarily either a spiro-di-*o*-xylylene (2) or a dibenzocyclooctadiene derivative (3).[1] Since the direct thermal formation of 3 from 1 is forbidden by the rules for conservation of orbital symmetry,[2] the possibility that 3 may be the result of a sigmatrophic rearrangement of 2 cannot be ignored. On the other hand, *o*-xylylenes are not ordinary dienes, and the possibility of either a direct, concerted [4+4] cycloaddition or a non-concerted, radical dimerization remains.



1 2 3

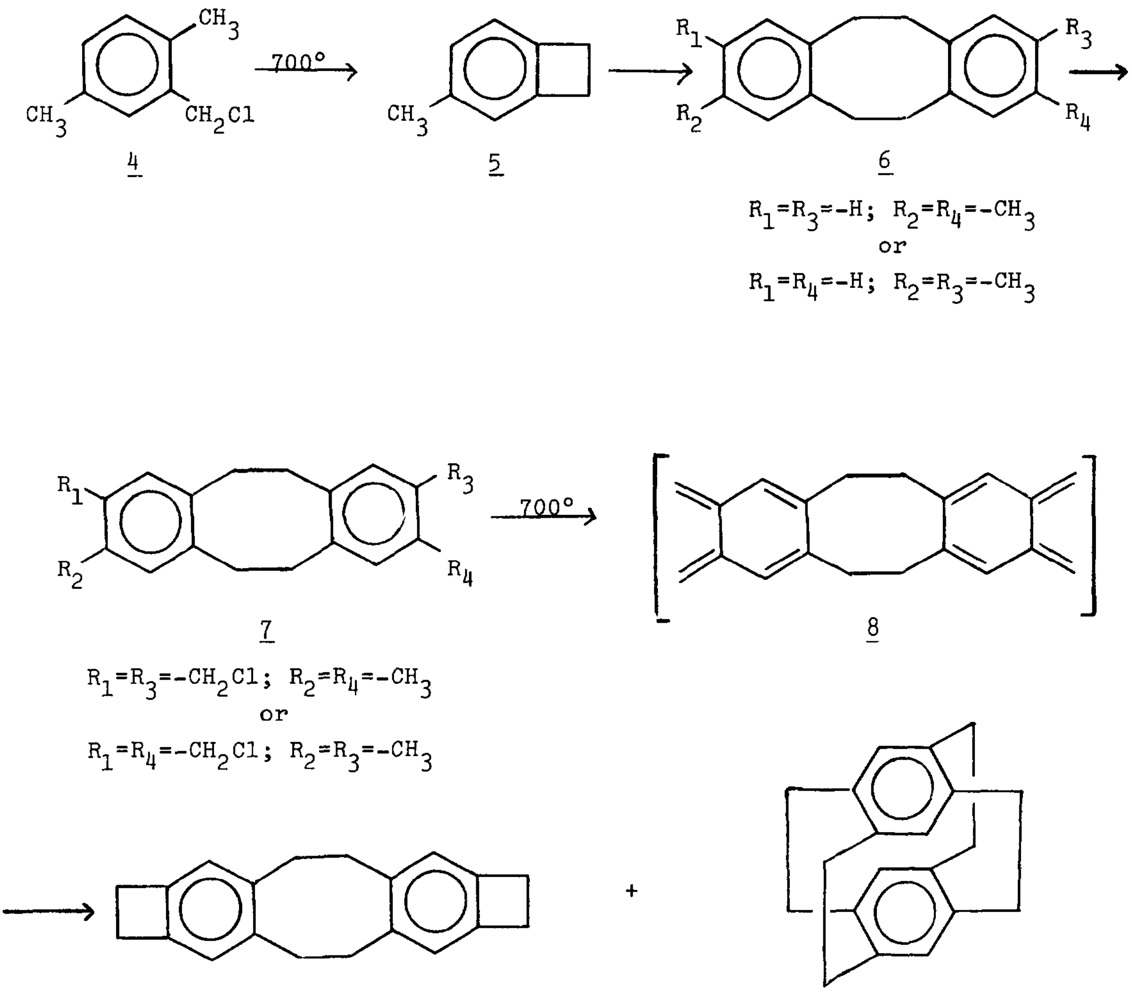
The question of the mechanism of the formation of 3 from 1 is especially pertinent to possible syntheses of multibridged cyclophanes from precursors containing two layered benzocyclobutene moieties. The geometrical constraints of the cyclophanes prohibit the intermediacy of spiro-di-*o*-xylylenes such as 3. Thus, the use of layered benzocyclobutenes to form multibridged cyclophanes is dependent upon the direct coupling of two *o*-xylylenes to give 3 and cannot involve spiro intermediates such as 2. Recently, we examined the pyrolysis of [2.2](3,6)benzo[1,2;4,5]dicyclobutenophane and found that the product, instead of being [2.2.2.2.2.2](1,2,3,4,5,6)cyclophane, was hexaradialene.[3] The fact that in this case the thermal rearrangement followed an alternate path to dimerization raised doubt about whether the direct o-xylylene dimerization is possible in layered cyclophanes.

We decided, therefore, to test the question of the direct thermal dimerization of two o-xylylenes in a molecule where alternate pathways for reaction seemed unlikely. The molecule chosen for study was 8, whose preparation was accomplished simply and directly by methods previously reported.[4]

Pyrolysis[4] of 50.0 g of commercially-available 2,5-dimethylbenzyl chloride (4) at 700° gave 24.8 g (65%) of 5 as a colorless oil[5] (^{1}HNMR ($CDCl_3$), δ2.31 (3H, s, $-CH_3$), 3.11 (4H, s, $-CH_2-$), and 6.8-7.1 (3H, m, ArH); mass spectrum (70eV), m/e 118). The dimerization of 5 was accomplished by heating it in diethyl phthalate at 300° for 1 h.,[6] yielding 6 in 48% yield, after sublimation, as a mixture of isomers; white crystals, mp 102.5-106.5°C; ^{1}HNMR ($CDCl_3$), δ2.22 (6H, s, $-CH_3$), 2.99 (8H, s, $-CH_2-$), and 6.78-6.88 (6H, m, ArH). Chloromethylation of 6 was carried out using paraformaldehyde in a mixture of acetic and phosphoric acids to give 7 in 73% yield, after sublimation, as a mixture of isomers; white crystals, mp 197-201°C; ^{1}HNMR ($CDCl_3$), δ2.30 (6H, s, $-CH_3$), 3.00 (8H, s, $-CH_2-$), 4.52 (4H, s, $-CH_2Cl$), and 6.8-7.0 (4H, m, ArH). Gas phase pyrolysis[4] of 7 at 700° gave mainly two products which could be separated and purified by sublimation followed by chromatography over alumina. The first of these products, formed in 26% yield, has been assigned the bis(cyclobuteno)dibenzocyclooctadiene structure 9 based on its properties (^{1}H-NMR ($CDCl_3$), δ2.98 (8H, s), 3.04 (8H, s), and 6.69 (4H, s); and mass spectrum (70eV), m/e 260); whereas the second product, obtained in 17% yield after recrystallization from ethyl acetate, is identical in all respects to an authentic sample of [2.2.2.2](1,2,4,5)cyclophane (10).[7]

When a pure sample of 9 was similarly subjected to gas phase pyrolysis at 700°C, it gave a mixture of 9 and 10 in the ratio of 8:1. On the other hand, gas phase pyrolysis of a pure sample of 10 likewise gave a mixture of 9 and 10 but in the reverse ratio of 1:8. Apparently, at 700°C both 9 and 10 undergo ring opening to give 8. Quite probably, the reaction conditions for the pyrolysis of 7 can be changed to improve the yield of either 9 or 10.

In any case, it is obvious that the direct dimerization of o-xylylenes such as 8 does occur to give multibridged cyclophanes and this promises to be a fruitful synthetic method. It should be noted that the pyrolysis of o-methylbenzyl chlorides to give benzocyclobutenes, i.e. 4→5, is a clean, convenient reaction that is easily adapted to large scale runs. Also, since bis(cyclobuteno)dibenzocyclooctadienes, such as 9, can undergo Diels Alder reactions, these are useful intermediates for a variety of syntheses in addition to multibridged cyclophanes.



4 5 6

$R_1=R_3=-H$; $R_2=R_4=-CH_3$
or
$R_1=R_4=-H$; $R_2=R_3=-CH_3$

7

$R_1=R_3=-CH_2Cl$; $R_2=R_4=-CH_3$
or
$R_1=R_4=-CH_2Cl$; $R_2=R_3=-CH_3$

8

9 (26%)

10 (17%)

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