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Reactions of reduced cyclophanes: Electrophilic bromination – A double homoconjugate addition

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Abstract: As part of a reawakening of interest in the chemistry of [2.2]paracyclophane derivatives a program to exploit the complexity of partially reduced cyclophanes has begun. This report describes the results of initial experiments into the reactions of tetrahydroparacyclophane with electrophilic reagents. At low temperature tetrahydroparacyclophane undergoes two homoconjugate brominations with a high degree of diastereoselectivity producing a single compound whose structure has been determined by single crystal x-ray diffraction. © 1999 Elsevier Science Ltd. All rights reserved.

The synthesis and reactions of cyclophanes have attracted organic chemists for four decades. Aside from the challenges inherent in the preparation of the members of this group the unique electronic properties brought about by the close proximity of two otherwise isolated pi-electron systems have attracted considerable interest. A number of reports of transannular reactions between aromatic rings have been noted [1]. Partially reduced [2.2]paracyclophane would seem to be an attractive model with which to examine the chemistry of proximate but non-conjugated pi systems. The structure of tetrahydro[2.2]paracyclophane (1) obtained via Birch Reduction of [2.2]paracyclophane is well established [2]. Few studies, however, have been reported concerning subsequent reactions of this material.

Only more highly reduced compounds, a tetraepoxide and a dibromocarbene adduct are to be found in the literature [2d, 3a-d]. Unpublished results have indictated that bromination of **1** at low temperatures produced a tetrabromide with two bridges joining the two "decks" of the tetraene [2c]. For two reasons this result was deemed worthy of reinvestigation. First, the structure of the tetraene assumed in the early bromination study was later shown to be incorrect and second, numerous reports of electrophilic additions to molecules with proximate double bonds indictated that bridging between the decks would be in a "diagonal" rather than the "perpendicular" fashion of Myers [4].

The low temperature bromination of tetrahydro[2.2]paracyclophane was carried out and shown to produce one product. The spectral and analytical data corresponded well with the earlier reported values. An unequivocal assignment was still not possible despite extensive NMR studies. Material upon which the NMR studies were performed crystallized during low temperature storage serendipitously providing a high quality crystal which allowed the X-ray determination of the structure shown in Scheme 1.

The transannular interaction between double bonds within the same cyclohexadiene ring is reasonable when the structure of **1** is examined closely. The double bonds with in each cyclohexadiene ring are predicted by molecular mechanics calculations to be separated by just over 2.0 Å while the

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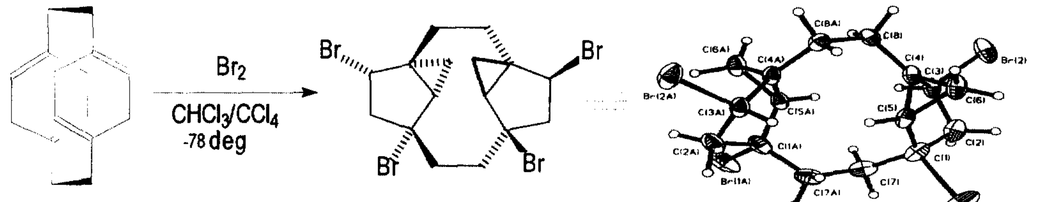
distance between pi bonds in different rings is over 3.0 Å. This type of transannular reaction has not previously appeared in the literature.

Scheme 1



1 2

The symmetry seen in 2 is interesting in that the two bicyclo[3.1.0] subunits are related by a simple rotation about an axis through the bridging groups. The reason for this is not obvious. It is possible that formation of the first cyclopropane ring induces a conformational change which favors the formation of the second three-membered ring in the position shown.

In conclusion the bromination of tetrahydro[2.2]paracyclophane is shown to produce a novel pentacyclic skeleton. The reactions of other electrophilic reagents with this interesting tetraene are being investigated.

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[5] In addition to x-ray data the following analytical data for 2 were obtained. ^{1}H NMR (500 Mhz, CDCl$_3$) δ 0.917 (ddd, 1H, J = 1.0, 7.0, 14 Hz), 1.01-1.10 (m, 2H), 1.814 (dd, 1H, J = 4.5, 9.0 Hz), 1.85-1.95 (m, 1H), 2.06-2.15 (m, 1H), 2.39 (dd, 1H, J = 9.5, 14 Hz), 2.66-2.77 (m, 2H), 4.32-4.37 (ddd, 1H, J = 1.0, 7.5, 13); ^{13}C NMR, DEPT (125 Mhz, CDCl$_3$) δ C: 69.068, 37.195, CH: 55.163, 38.347, CH$_2$: 50.465, 39.000, 25.371, 15.358. Anal. Calculated for $C_{16}H_{20}Br_4$: C, 36.16; H, 3.79; Br, 60.08. Found: C, 36.21; H, 3.84; Br, 60.21.