

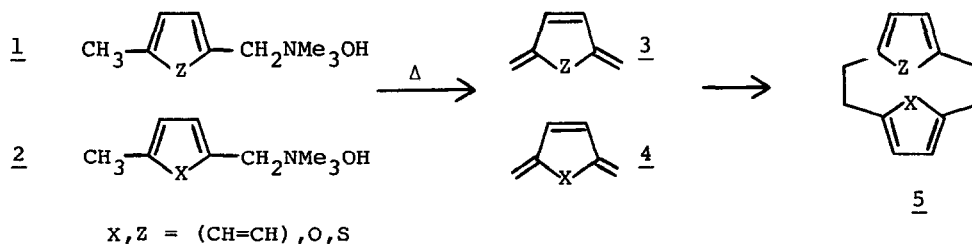
SYNTHESIS OF [4.2]CYCLOPHANES

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Summary. Vinyl *p*-xylylene cross-dimerizes with other xylylene-type intermediates to yield cycloadducts of the [8+6] and [6+6] type. This reaction provides a simple entry to the [4.2]paracyclophane system as well as the analogous [4.2]cyclophanes containing furan and pyrrole moieties.

The synthetic utility of 1,6-Hofmann eliminations for the generation of cyclophanes is well established.¹ Pyrolysis of 1 (or 1 plus 2) affords, via xylylene-type intermediates 3 and 4, the homodimer 5 (X=Z) or the crossed dimer 5. This approach has been the most general one to a wide variety of structures of type 5. The 1,6-Hofmann elimination route necessarily generates xylylene intermediates with two extra-annular carbons and thus provides cyclophanes with solely two-carbon bridges. Cyclophanes with longer bridges have been prepared by methods which are lacking in generality and often tedious.² We report now a direct synthesis of [4.2]paracyclophane as well as a simple entry, for the first time, to double-bond functionalized [2.2] and [4.2]cyclophanes containing heteroaromatic nuclei. The key intermediate is the vinyl *p*-xylylene 7 generated via a 1,8-Hofmann elimination.



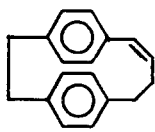
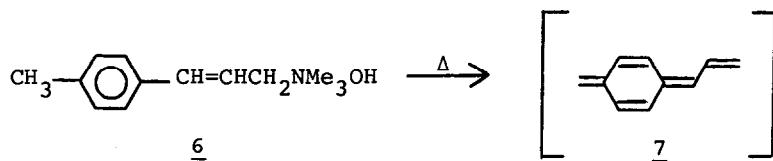
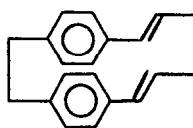
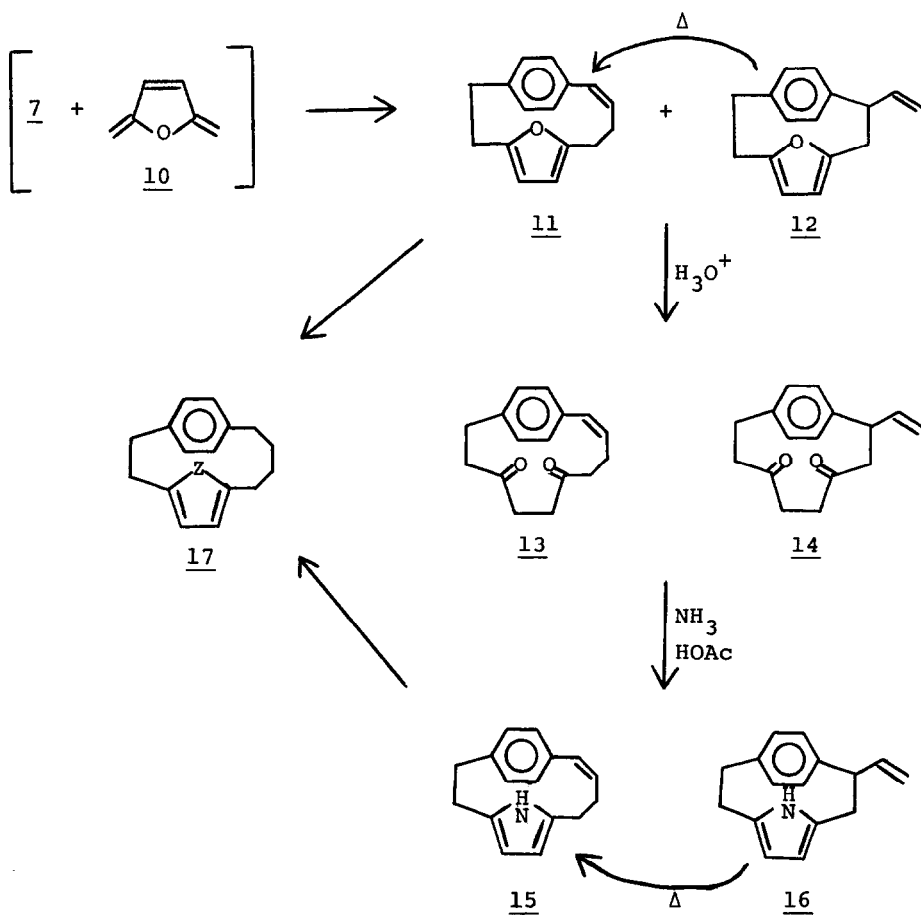
Pyrolysis³ of 1 [$Z=(CH=CH)$] with 6⁴ affords a mixture (37% combined yield) of the cyclized products 8, 9 and [2.2]paracyclophane [5, $X=Z=(CH=CH)$]; nmr analysis of the mixture indicates conversions of 19, 15, and 33%, respectively. Chromatographic separation yields the desired crossed dimer 8^{5(b)} in 12% yield; catalytic hydrogenation gives the saturated [4.2]paracyclophane.⁵

Having established that 7 will undergo a formal [8+6] crossed-cyclization, its reaction with intermediate 10⁶ was examined. In addition to the homo-dimers of 7 and 10, the crossed products 11 and 12 were formed (6 and 18% by nmr analysis; 4 and 12%, respectively, by chromatographic isolation).⁷ Unlike 1-vinyl[2.2]paracyclophane which ring expands^{5(b)} to 8 at temperatures as low as 100°, 12 is quite stable at this temperature. Above about 135°, however, it cleanly rearranges to 11, enhancing the yield of this novel system. Hydrolysis of 11 and 12 provides the unsaturated diketones 13 (52%) and 14 (77%). Paal-Knorr cyclization⁸ generates the pyrrole systems 15 (61%) and 16 (68%), the latter giving the former on heating above 120°. Finally, hydrogenation of 11 and 15 readily provides the parent ring systems [4]paracyclo[2](2,5)furanophane and [4]paracyclo[2](2,5)pyrrolophane (17, $Z=O$ and NH , respectively).

Since the thermal ring expansions of 1-vinyl[2.2]paracyclophane to 8^{5(b)} and 12 to 11 will take place at temperatures under which the Hofmann eliminations occur,³ 8 and 11 may be produced solely by this pathway. A full discussion of this question and related mechanistic considerations will appear in the complete paper.

Recent work⁹ on p-xylylene dimerizations indicates that the adjustment of reaction parameters in the Hofmann elimination can markedly increase product yields. In this regard the conversions reported here have not been optimized. Work in progress is directed toward this end as well as determining the conformational behavior^{8,10} of the novel [4.2]cyclophanes. The wealth of chemistry based on [2.2]cyclophanes^{2,10} may now be conveniently extended to the [4.2] analogs through the use of intermediate 7.

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