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AN ALTERNATE SYNTHESIS OF 2,11-DITHIA[3.3]METACYCLOPHANES[1]

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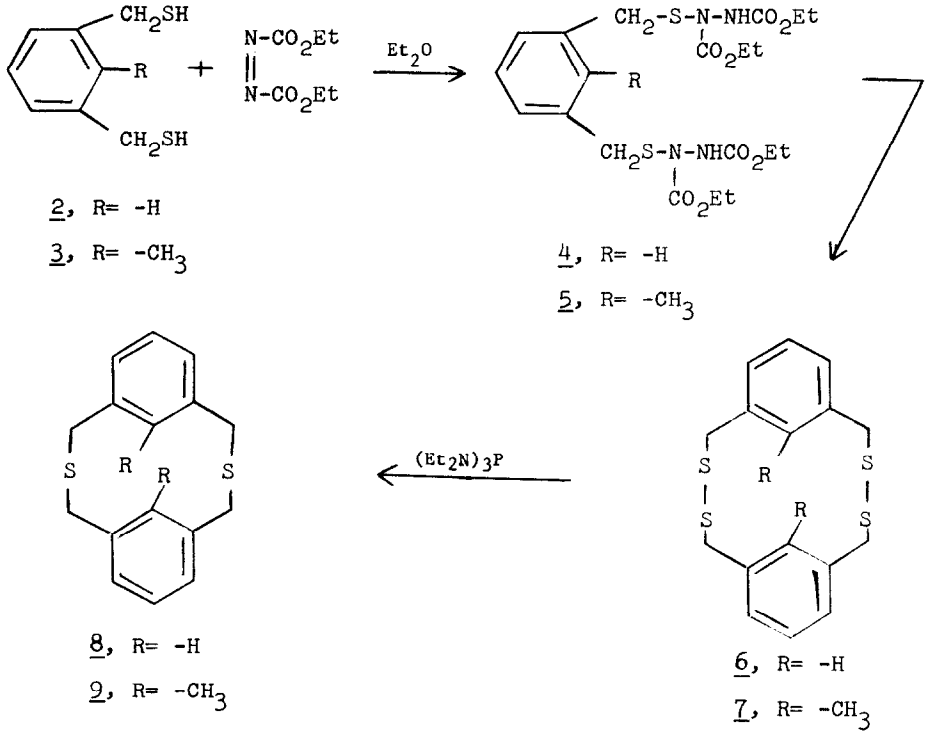
In an accompanying communication[2] we describe a convenient method for the conversion of 2,11-dithia[3.3]metacyclophanes (8) to the corresponding 15,16-dihydropyrenes. Overall this method provides an easy route from the generally available m-xylylene dibromides to the 15,16-dihydropyrenes in which all of the steps are in high yield except the conversion of the m-xylylene dibromides to the 2,11-dithia[3.3]metacyclophanes. Under the usual conditions of treatment with sodium sulfide in boiling ethanol, m-xylylene dibromides are converted to 2,11-dithia[3.3]metacyclophanes in yields ranging from 10 to 25%, depending on the nature of the substituent groups.

Recently Mukaiyama and Takahashi[3] have described a high yield procedure for converting mercaptans to disulfides. As shown, this involves the addition of a mercaptan to diethyl azodicarboxylate followed by reaction with a second mercaptan to give the disulfide 1 and diethyl hydrazodicarboxylate. It seemed possible that this type of reaction might readily be adapted for the

$$RSH + EtO_2C\text{-}N{=}N\text{-}CO_2Et \rightarrow R\text{-}S\text{-}\underset{\displaystyle CO_2Et}{\underset{|}{N}}\text{-}NHCO_2Et \xrightarrow{R'SH} \begin{matrix} R\text{-}S\text{-}S\text{-}R' \\ \underline{1} \\ + \\ EtO_2CNH\text{-}NHCO_2Et \end{matrix}$$

formation of metacyclophanes in as much as the second step could be carried out under high dilution conditions. Also, the method appeared to have merit for preparing metacyclophanes in which the two halves of the metacyclophane molecule were dissimilar.

When m-xylylene dimercaptan (2) was allowed to stand in ether at room temperature with diethyl azodicarboxylate, the desired adduct 4 formed in essentially quantitative yield as a viscous oil. Separate solutions of 4 and of m-xylylene dimercaptan (2) in benzene were added simultaneously using two Hershberg funnels over a period of 12 hours to a boiling solution of benzene. After concentration of the solution and chromatography of the residue over silica gel using a 1:1 benzene-hexane mixture, there was isolated 6.26 g. (67%) of white crystals. This was rechromatographed to give 4.67 g. (50%) of 6 as pure white crystals, m.p. 171.5-172.5°.[a] Since the yields of metacyclophanes in dimerization reactions are usually in the range of 25%, the high yield obtained in the formation of 6 is somewhat surprising and gratifying.



2, R= -H
3, R= $-CH_3$

4, R= -H
5, R= $-CH_3$

8, R= -H
9, R= $-CH_3$

6, R= -H
7, R= $-CH_3$

[a] For all new compounds being reported satisfactory elemental analyses and mass spectra have been obtained.

Harpp, Gleason, and Snyder have studied the conversion of disulfides to monosulfides using tris(diethylamino)phosphine and have found this to be a smooth reaction proceeding in high yield, presumably by an intramolecular process.[4] Therefore, this seemed to be the method of choice for converting 6 to the desired 2,11-dithia[3.3]metacyclophane (8). A solution of 6 and tris(diethylamino)phosphine in benzene was boiled under reflux for 3 hours. After concentration of the solution followed by chromatography of the residue over silica gel using a 1:1 benzene-hexane mixture, 8 was isolated in 41% yield as white needles, m.p. 120-121°.[b] In the case of 8 there is no appreciable barrier to conformational flipping and so a single pure compound is formed.

In view of these results, it was of interest to repeat the sequence with a methyl group as an internal substituent. Again, the reaction of 2,6-bis-(mercaptomethyl)toluene (3) with diethyl azodicarboxylate proceeded smoothly in essentially quantitative yield to give 5 as a thick viscous oil. However, the high dilution reaction of 5 and 3 in boiling benzene proceeded in only 10% yield to give 7 as white crystals, m.p. 178-180°. It is not clear why the methyl substituent should have such a deleterious effect on the yield in the metacyclophane-forming reaction.

In its nmr spectrum 7 showed an aromatic singlet (6H) at τ 2.89, a methylene singlet (8H) at τ 6.36, and a methyl singlet at τ 7.95. Thus, there is no indication in the nmr at room temperature of an energy barrier to conformational flipping. Apparently, the fourteen membered ring is sufficiently

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[b] Both Vögtle[5] and Sato[6] have previously prepared 8 and Sato describes it as white crystals, m.p. 155.5-156.5°. Since our analytical and mass spectral data fit 8 and our nmr data agrees with that previously reported, we presume that we have isolated a different crystalline modification of 8, particularly since our preparation of 8 by Vögtle's procedure gives crystals, m.p. 120-121°, identical with our preparation described above.

large that the methyl groups can bypass each other with ease. However, as discussed earlier,[2] there is a large barrier to conformational flipping in the corresponding sulfide 9. In the case of 9, the cis and trans conformers are separable and show no tendency for interconversion under normal reaction conditions. Since the cis-conformer of 9 is the precursor to the new and interesting class of cis-[2.2]metacyclophanes, the sulfur extrusion reaction to convert 7 to 9 was of concern as a possible way to increasing the ratio of cis to trans conformers during the formation of 9. In the formation of 9 by the ordinary sodium sulfide dimerization reaction the ratio of cis to trans conformers was only 1:7.[2]

When a mixture of 7 and tris(diethylamino)phosphine in boiling benzene was allowed to react for 3 hours, isolation and purification by chromatography gave in overall yield the cis and trans isomers of 9 in a ratio of 1:4. Their properties were identical to the authentic samples described previously.[2] Thus, this method does lead to an improvement in the cis-trans ratio of the isomers of 9 formed. However, this advantage is probably more than offset by the inconvenience of the additional steps required by this method.

In other examples, particularly for the synthesis of unsymmetrically substituted 2,11-dithia[3.3]metacyclophanes, this route may have real advantages.

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