

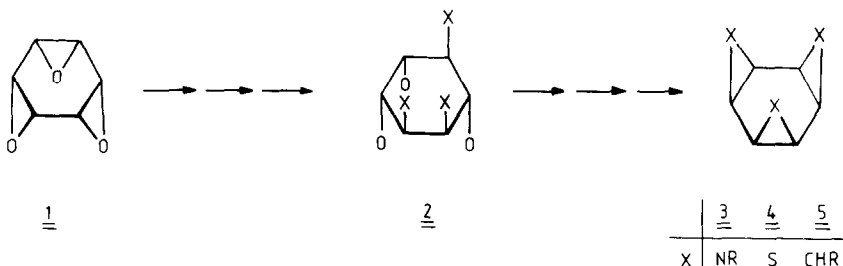
cis-TRIS- $\sigma$ -HOMOBENZENES FROM cis-BENZENETRIOXIDE

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In benzene trioxide regiospecific (scyllo) threefold substitution is achieved with selected carbanions - opening up promising pathways to cis-tris- $\sigma$ -homobenzenes.

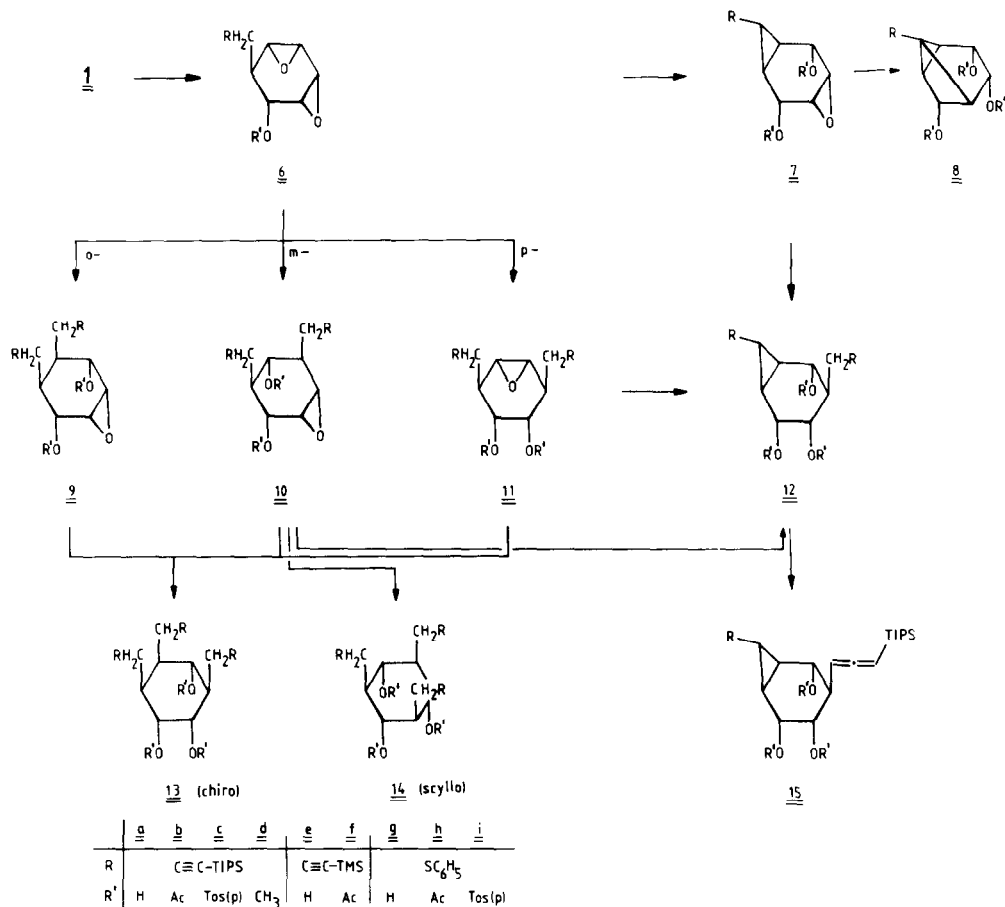
In cis-benzenetrioxide 1 three-fold epoxide opening (2) is achieved cleanly and regioselectively (chiro) with a variety of O-, N- and S-nucleophiles <sup>1)</sup>. Starting from the appropriate polyfunctionalised cyclohexanes 2 cis-benzenetrisimines (3) <sup>2)</sup> and cis-benzenetrisulfide (4) <sup>3)</sup> have been constructed. Efforts to prepare the carbocyclic cis-tris- $\sigma$ -homobenzenes 5 via analogous three-fold epoxide  $\rightarrow$  cyclopropane transformations have thus far failed.



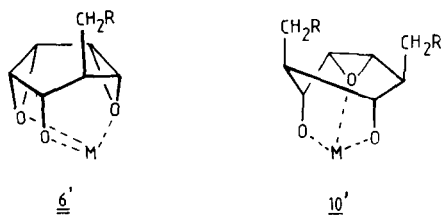
The strongly basic C-nucleophiles either caused eliminations (mainly phenolic products with e.g. NaCN, LiCH<sub>2</sub>CO<sub>2</sub>Li) <sup>4)</sup> or led to intramolecular reactions (i.a. to 7 with NaCH(CN)<sub>2</sub>, NaCH(CO<sub>2</sub>CH<sub>3</sub>)<sub>2</sub> <sup>4)</sup>, to 8 with <sup>t</sup>BuSOCH<sub>2</sub>Li, to 12 with C<sub>6</sub>H<sub>5</sub>SO<sub>2</sub>CH<sub>2</sub>Li, <sup>t</sup>BuSO<sub>2</sub>CH<sub>2</sub>Li). Progress towards the transformation 1  $\rightarrow$  5 is reported in this paper.

It was known that lithio TIPS-propyne (A), as well as lithio TMS-propyne, in contrast to several other organometallic reagents <sup>5)</sup>, selectively effects S<sub>N</sub>2 opening of cyclohexene oxide <sup>6)</sup>. And indeed, with this reagent appreciable amounts of substitution products from 1 were isolated: With 1 eq A (-50°, THF/HMPA, 20 min), 28% m-bisadduct 10a(b) <sup>7)</sup>, 10% mono-6a(b) and 3% isomerised bisadduct 12a(b) (at higher temperature (0°C) in the reaction mixture 6a is converted to 7a/8a, 10a to 12a); with 3 eq A (-78°, THF, 20 min), 58% 10a, 2% each of 11a and 14a and traces (<1%) of 6a and 12a; with 5 eq A (THF, -78° to r.t., 10 h) 23% 12a and 45% 14a along with 10% of the allene 15a. The desired scyllo-triol 14a is obtained in a preparatively useful and reproducible 50-55% yield if A is replaced by the higher order mixed organocuprate (TIPS-C $\equiv$ C-CH<sub>2</sub>)<sub>2</sub>Cu(CN)Li<sub>2</sub> <sup>8)</sup>. No o-bisadduct 9a or chiro-trisadduct 13a was detected. This 1,3-selectivity in the substitution of 6a and 10a is remarkable compared with the previous fin-

dings with O-, N- and S-nucleophiles (in protic media) - and is probably due to complexed all-axial conformations ( $\underline{6'}/\underline{10'}$ ) thought to be important in aprotic media. This view is confirmed



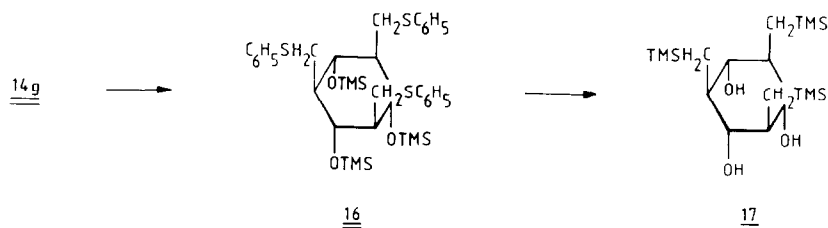
by the finding that the di-methyl ether  $\underline{10d}$  under the same reaction conditions yields a 1:1-mixture of the di-methyl ethers of chiro-/scyllo- $\underline{13a}/\underline{14a}$ . Noticeably lithio TMS-propyne <sup>9)</sup> gi-



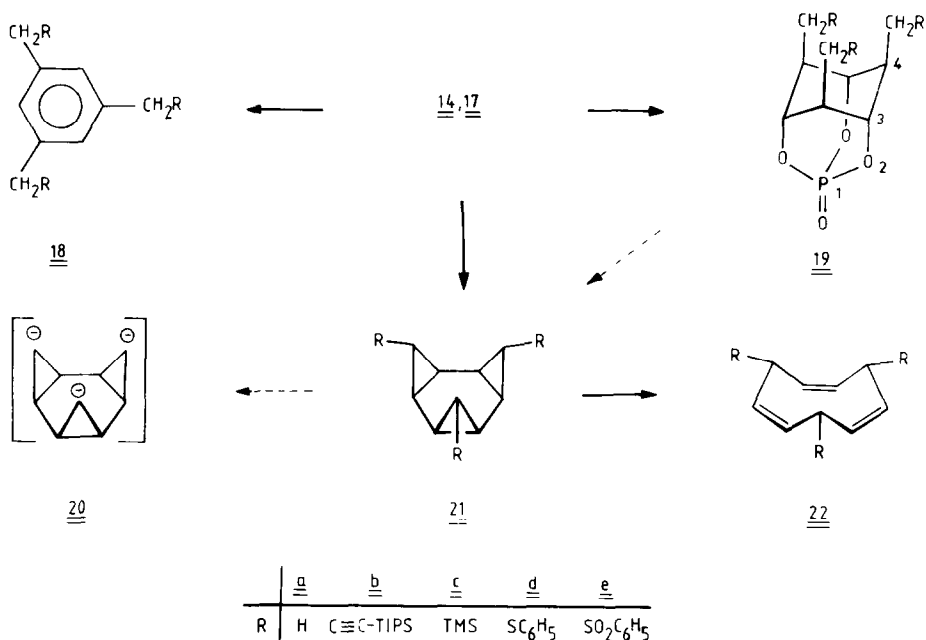
ves differing results: With 3 eq of reagent 43% of the m-bisadduct  $\underline{10e(f)}$  were obtained, which however could not be transformed to  $\underline{13e}/\underline{14e}$  on further treatment; instead cyclisation to  $\underline{12e(f)}$  and cleavage of the TMS groups took place. Phenylthiomethylithium <sup>10)</sup>, however, behaves in a way very similar to the above organocuprate. In

THF (0°C) with a large excess of reagent (10 eq) 45-50% of the scyllo-triol  $\underline{14g(h)}$  (no chiro- $\underline{13g(h)}$ ) are formed along with traces (<2%) of  $\underline{12g(h)}$ ; with a smaller excess of reagent  $\underline{6g(h)}$ ,  $\underline{10g(h)}$  and  $\underline{11g(h)}$  are identified additionally. It is worth while to note that using  $\underline{14g}$  substituents become feasible which are not possible with  $\underline{1}$  directly. Thus by treatment with Li-

di-tert-butylbiphenyl <sup>11)</sup> the tris-trimethylsilyl ether 16 undergoes complete desulphuration and triple Si shift to the scyllo-tris (trimethylsilylmethyl) cyclohexanetriol 17 ( $-78^{\circ}$ , 36%, not optimised) <sup>12)</sup>



With the scyllo-tritosylate 14c as an intermediate, transformation of the type 1  $\rightarrow$  5 was realised for the first time. Using excess (ca. 6 eq) LDA or n-BuLi ( $-30$  to  $-15^{\circ}\text{C}$ ) three cyclopropane rings are formed, if only in modest yield (ca. 5%). The cis-tris- $\sigma$ -homobenzene 21b ( $^1\text{H-NMR}(\text{CDCl}_3)$ :  $\delta$  = 1.49 (d, 6H), 1.01 (m, 63 H), 0.13 (t, 3 H),  $J$  = 3.5 Hz; MS:  $m/e$  = 660 ( $\text{M}^+$ )) is stable at room temperature; at  $100^{\circ}\text{C}$  it cleanly undergoes  $[\sigma 2 + \sigma 2 + \sigma 2]$ -cycloreversion to 22b ( $^1\text{H-NMR}(\text{CDCl}_3)$ :  $\delta$  = 5.27 (m, 6 H), 4.67 (m, 3 H), 1.06 (m, 63 H). In contrast, the tritosylate 14i under the same conditions (or with  $^t\text{BuLi}$ , THF/HMPA at  $-78^{\circ}\text{C}$ ) <sup>15)</sup> is decomposed instantly,



no 21d - an attractive precursor (C-S cleavage (20?) can be brought about at  $-78^{\circ}\text{C}$ ) of the still missing, presumably rather labile, hydrocarbon 21a <sup>2, 16)</sup> - was found. DBN transforms 14c and 14i quantitatively to the 1,3,5-trisubstituted benzenes 18b, d. As expected, the scyllo-cyclohexanes 14/16/17 preferentially adopt all-equatorial conformations ( $J_{1,2} \approx 10$  Hz). Nevertheless, the adamantoid phosphates 19b-e can be obtained from 14a, g/17 (e.g. 19b: POCl<sub>3</sub>, pyridine,  $70^{\circ}\text{C}$ , 50%,  $J_{3,4} \approx 1$  Hz,  $^3J_{\text{H,P}} = 20$  Hz) <sup>17)</sup>. The usefulness of such phosphates as alternative precursors of cis-tris- $\sigma$ -homobenzenes (21) is under investigation.

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