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THE POSSIBILITY OF PREPARATION OF cis-Tris-σ-HOMOBENZENES FROM cis-Bis-σ-HOMOBENZENES

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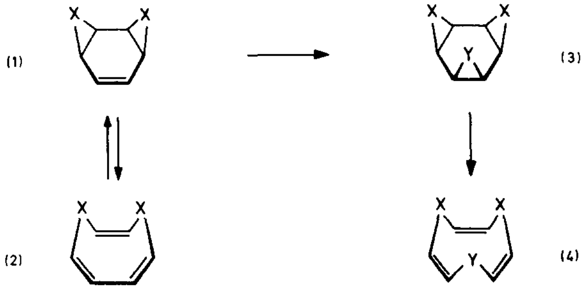
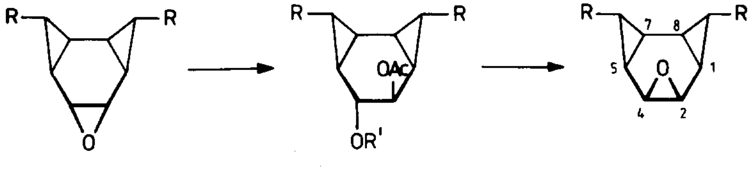
The cis-tris-σ-homobenzenes (3) are valuable synthetic intermediates, e.g. for 1,4,7-cyclononatrienes (4) via [σ2s+σ2s+σ2s]-cycloreversion. Of known approaches to the carbo- and heterocycles (3) 1),the route (1) ⟶ (3) has been restricted so far to the dioxa-(1b) 2) and suitably N-substituted diaza-bis-σ-homobenzenes (1c) 3): in contrast to the carbotricycle (1a) 4) these are kinetically and thermodynamically stable enough to allow transformations such as epoxidation (Y=O) and CH_2N_2-addition (ultimately Y=CH_2), the cis-addition often being favoured. In the cis-bis-σ-homobenzene-diester (1d), recently prepared by Kaupp and Rösch 5), as well as in the dinitrile (1f),obtained from (1d) through (1e),the basic skeleton (1a) is stabilized to such an extent 6) that analogous transformations could be examined.



	a	b	c	d
X	CH_2	O	NR	$CHCO_2CH_3$

	e	f	g
X	$CHCONH_2$	CHCN	CHBr

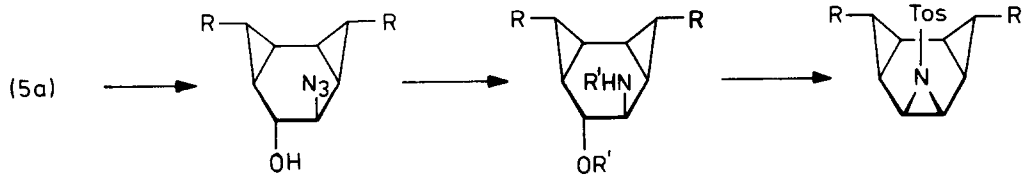
(1d) was oxidized with m-chloroperbenzoic acid to (5a) 5). When this reaction was repeated we found that besides (5a) the cis-isomer (7a) was also formed and that the relative amount of (7a) increases with reaction temperature ((5a):(7a) ca. 17:1 at 0°C, ca. 4:3 at 80°C). The less soluble (5a) is isolated by fractional crystallisation, (7a) by chromatography (SiO_2, benzene, >150°C dec. (isom.); ^{1}H-NMR($CDCl_3$):τ=6.30 (OCH_3), 6.58 (2(4)-H), 8.15(1(5)-,7(8)-H), 8.82(6(9)-H); readily distinguished from (5a) by $J_{1,2}$=3.0 Hz and the anisotropy effect of O upon 6(9)-H 4)). As we are more interested in (7a) we have worked out a conversion of (5a) into (7a) 7). The total yield after selective formation [sodium acetate/acetic acid, 75°C, 5 d; at higher temp. the proportion of diacetate (6a)(R'=Ac), increases; m.p. 98-99°C, $J_{4,5}$=3.2, $J_{5,6}$=8.1, $J_{6,7}$=3.7 Hz] of the monoacetate (6a) (R'=H, $J_{4,5}$=3.2, $J_{5,6}$=8.1, $J_{6,7}$=3.7 Hz), tosylation ((6a), R'=p-tos, m.p. 159-160°C; $J_{4,5}$=4.5, $J_{5,6}$=7.5, $J_{6,7}$=3.5 Hz), saponification of the acetate and ring closure (ammonia, methanol 20°C) is at least 60%. In the case of oxidation of the dinitrile (1f) to give (5b)(m.p. 167-168°C; ^{1}H-NMR(CDCl$_3$):τ=6.67, 7.87, 7.96, 9.91; $J_{1,2} \leq 0.5$ Hz) and (7b) (>150°C dec. (isom.); ^{1}H-NMR(CDCl$_3$):τ=6.47, 8.06 (4H), 9.12; $J_{1,2}$=3.0 Hz) the proportion of the cis-isomer is even greater ((5b):(7b) ca. 3:2 at 25°C, ca. 2:3 at 60°C).



(5) (6) (7)

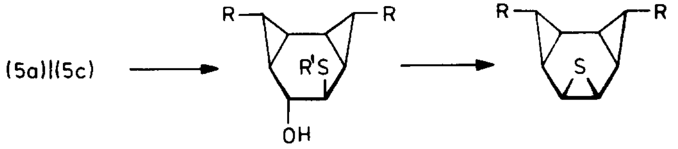
	R
a	CO_2CH_3
b	CN
c	Br

Similarly [7], the cis-aza-tris-σ-homobenzene (10) is synthesized from (5a). The oxirane ring is opened with sodium azide (Mg^{2+}buff. methanol, 64°C, 6 d), to give (8) (oil, 70-80%; $J_{4,5}$=3.0, $J_{5,6}$=9.2, $J_{6,7}$=3.3 Hz). The azide is reduced (Pt/H_2, methanol) to the amine (9) (R'=H), the latter is tosylated (9) (R'=p-tos, m.p. 149-150°C, $J_{5,6}$ = 9.5, $J_{6,7}$=4.2 Hz) and then cyclised with K-t-butoxide (tetrahydrofuran, 20°C)to give (10) (85-90%; >140°C dec. (isom.); ^{1}H-NMR(CDCl$_3$):τ=6.41(OCH$_3$), 6.82, 8.27 (4H), 8.94).



(8) (9) (10)

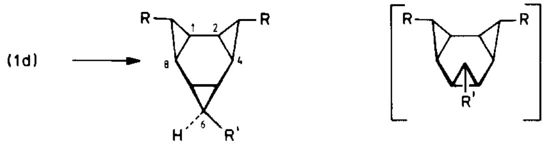
For the cis-thia-tris-σ-homobenzenes (12a)/(12c) proven procedures [8] could also be applied. After reaction of (5a) or (5c) with thiourea (20°C, methanol, sulphuric acid) oily isothiouronium salts (11a)/(11c) were isolated and without characterisation converted into (12a) (90%, m.p. 103-104°C (dec.), ^{1}H-NMR(CDCl$_3$):τ=6.30(OCH$_3$), 6.58, 7.98(4H), 8.94) or (12c) (70%, m.p. 114-114.5°C (dec.), ^{1}H-NMR(CDCl$_3$):τ=6.60, 7.72, 8.15(4H)) resp. by treatment with aqueous sodium carbonate.



(11) (12)

	R
a	CO_2CH_3
c	Br

Though the chances for cis-addition of diazoalkanes or carbenes to (1d) were thought to be slight [9], the reactivity of (1d) in these types of thermal and photochemical processes was examined under different conditions. In contrast to (1b) and (1c), (1d) gives no detectable reaction with diazomethane even after long reaction times and the use of a constant excess of CH_2N_2; with Cu^{1+}-catalysis (tetrahydrofuran, 0^oC)[10] an adduct could be isolated in ca. 50% yield and from the ^1H-NMR-spectrum (180 MHz($CDCl_3$):τ=6.35 (OCH_3), 8.18(1(2)-H), 8.50 (4 (8)-H), 8.72(3(9)-H), 9.02(5(7)-H), 9.28(6'-H), 9.80 (6-H); $J_{3,4}$=4.3, $J_{4,5}$=0, $J_{5,6}$=5.2, $J_{5,6'}$=8.0, $J_{6,6'}$=4.4 Hz)[11] is the trans-species (13a) (m.p. 100-101°C); (14a), for which a higher activation energy for the [σ2s+σ2s+σ2s]-cycloreversion compared with (3a) (E_a ca. 24-28 kcal/mole)[4,12] is expected, would have undoubtably survived under the given conditions . Indeed, from the GC/MS-analysis of the crude reaction mixture indirect evidence is obtained, that (14a) is present in up to 1% yield.

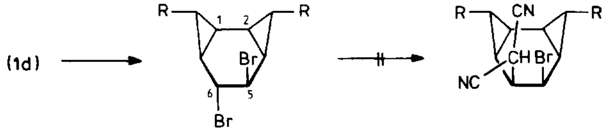


(13) (14)

R = CO_2CH_3

	R'
a	H
b	CO_2CH_3

Upon use of diazoacetic ester the known compound (13b)[13] was not formed either thermally (catalytically) (the reaction temp. was limited because of the equilibrium (1d)⇌(2d) and subsequent side reactions) or by direct or indirect light excitation. Attempts to obtain substitution of the dibromide (15) (m.p. 110-111°C, $J_{4,5}$=$J_{5,6}$=6,

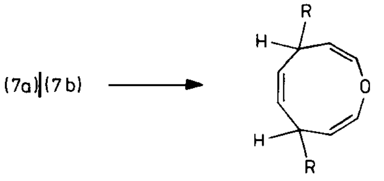


R = CO_2CH_3

(15) (16)

$J_{6,7}$=7 Hz) (which can be quantitatively prepared from (1d)) with carbanions as e.g. the sterically not-too-demanding dicyanomethylanion (to give (16)) were unsuccessful. Obviously the prospects of being able to prepare carbocyclic cis-tris-σ-homobenzenes from cis-bis-σ-homobenzenes are indeed very slight.

The thermolysis of (7a) (benzene, $\Delta G^{\ddagger}_{140^oC}$=32.1 kcal/mole), of (7b) (benzene, $\Delta G^{\ddagger}_{140^oC}$=32.4 kcal/mole) and of (10) (abs. acetone, $\Delta G^{\ddagger}_{140^oC}$=29.6 kcal/mole) proceeds in each case exclusively to the 4,7-dihydrooxonines[14] (17a) (m.p. 37-38°C, ^1H-NMR ($CDCl_3$, 35°C) : τ=3.90 (2(9)-H), 4.37 (5(6)-H), 4.62(3(8)-H), 4.90(4(7)-H), 6.28



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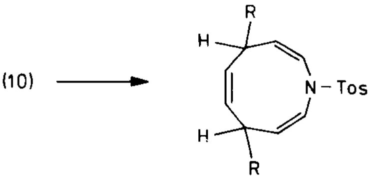

(18)

(OCH_3); $J_{2,3}$=5.0, $J_{2,4}$=1.2, $J_{3,4}$=7.5, $J_{4,5}$=6.2, $J_{4,6}$=2.0 Hz), (17b) (m.p. 110-112°C, ^1H-NMR ($CDCl_3$, 35°C):τ=3.83, 4.35, 4.64, 4.84; $J_{2,3}$=5.0, $J_{2,4}$=1.3, $J_{3,4}$=7.5, $J_{4,5}$=6.6,

$J_{4,6}$=2.0 Hz) or to the 4,7-dihydroazonine 4) (<u>18</u>) (m.p. 161-162°C, ^1H-NMR ($CDCl_3$, -20°C) : τ=4.13, 4.43, 4.50, 4.85, 6.24; $J_{2,3}$=6.9, $J_{2,4}$=0.8, $J_{3,4}$=9.5, $J_{4,5}$=7.1, $J_{4,6}$=1.8 Hz), resp.

The thia-analogs (12a)/(12c) on the contrary undergo loss of sulphur on heating to give (2d)/(2g). By using trimethylphosphite (min. reaction temp. ca. 20°C) to eliminate the sulphur from (12c), the minimum reaction temperature is still too high for isolation of (1g), which could have provided access to the still unknown (1a).

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