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cis-OXA,AZA-σ-HOMOBENZENES**

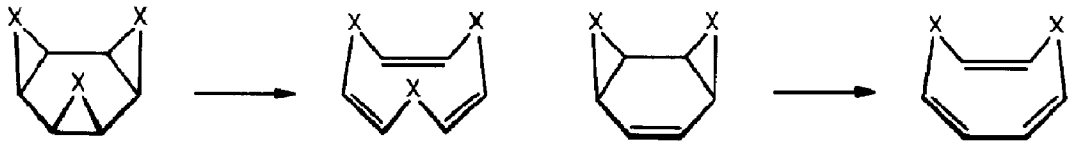
Syntheses,[2+2+2]-Cycloreversion Reactions

Horst Prinzbach*, Klaus-Helmut Müller, Clemens Kaiser and Dieter Hunkler

Chemisches Laboratorium der Universität Freiburg i.Br., BRD

cis-Dioxa,aza-tris-(8) and cis-oxa, aza-bis-σ-homobenzenes (21) have been synthesised. With activation barriers, which clearly support the concerted mechanism, they undergo [2+2+2]-cycloreversion yielding 7H-1,4,7-dioxazonines (9) and 4H-1,4-oxazocines (22), resp.

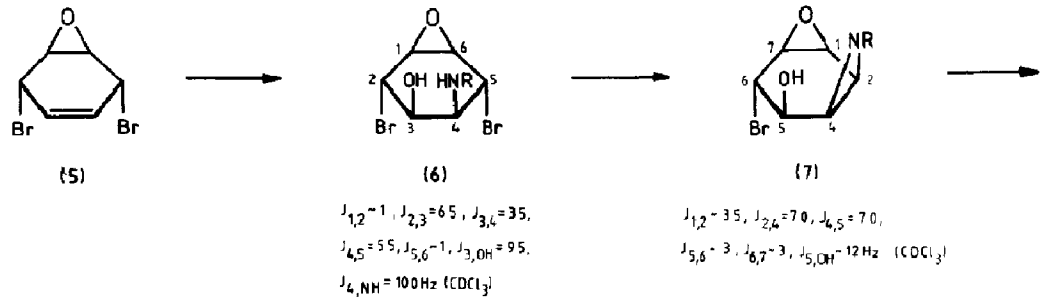
Important aspects in the chemistry of the cis-trihetero-tris-(1) and cis-diheterobis-σ-homobenzenes (3) are their [2+2+2]-cycloreversions ((1) ⟶(2) [1]; (3) ⟶(4) [2]) and the influence of the heteroatoms upon the kinetics and thermodynamics of these processes. For the 1,4-dihydro-1,4-diazocines (4)(X=NR) obtained in this way, the



(1) (2) (3) (4)

interplay between the nature of the N-substituents and the geometry ("aromaticity") has been impressively documented [2b,3]. In this context "mixed" frameworks, like the oxa,aza-systems (8) and (21) presented here, are of particular interest.

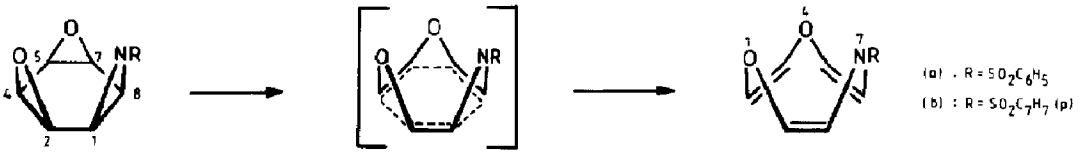
The starting material for (8a,b) is - as in the case of the trioxide (1)(X=O)-



(5) (6) (7)

$J_{1,2}$ ~ 1, $J_{2,3}$ = 6.5, $J_{3,4}$ = 3.5, $J_{4,5}$ = 5.5, $J_{5,6}$ ~ 1, $J_{3,OH}$ = 9.5, $J_{4,NH}$ = 10.0 Hz ($CDCl_3$)

$J_{1,2}$ ~ 3.5, $J_{2,4}$ = 7.0, $J_{4,5}$ = 7.0, $J_{5,6}$ ~ 3, $J_{6,7}$ ~ 3, $J_{5,OH}$ ~ 12 Hz ($CDCl_3$)



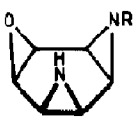
(8) (9)

(a) : R = $SO_2C_6H_5$
(b) : R = $SO_2C_7H_7$ (p)

the anti-cis-dibromoepoxycyclohexene (5) [1a]. Using the Sharpless procedure [4] (5)

can be cis-hydroxyaminated on the side of the epoxy-oxygen atom yielding the 1α, 2α, 3β, 4β, 5α, 6α-anhydroinositol derivatives (6a,b)(chloramine B,-T,60°C, 25h). Yields (12-15%) are still very moderate, being reduced inter alia, by epimerisation of (5) [5] *). Aziridine formation to (7a,b) is practically quantitative upon treatment with 1 equiv. DBN (THF, 20°C). In aprotic media (7a,b) preferably adopt the hydrogen-bridged, half-chair conformation with the OH/Br-groups quasi-trans-diaxial (e.g. $J_{5,6}$(acetates) = 7.5 Hz). Despite this the conversion of (7a,b) into the dioxa,aza-homobenzenes (8a,b)(m.p. 211°C(dec.), 219-220°C(dec.)) with various bases (DBN, K-t-butylate, sodium glycolate, THF) is not uniform (60-70%). Between 190-210°C (8a,b) are cleanly isomerised to the highly flexible 7H-1,4,7-dioxazonines (9a,b)((8a):$t_{1/2}$ (200°C)=20 min; $\Delta G^{\ddagger}$ = 135.5 kJ·mol^{-1}, E_a = 148±4 kJ·mol^{-1}, A = 8.9·10^{13}, $CDCl_3$). Thus, (8a,b) are more stable than the triimine (1) (X=N-Tos, $\Delta G^{\ddagger}$(149.1°C) = 132 kJ·mol^{-1}, ($CDCl_3$)) [1b] and less stable than the trioxide (1) (X=O, $\Delta G^{\ddagger}$(235°C) = 159 kJ·mol^{-1}, $CDCl_3$) [2b] - the activation parameters being in full agreement with a cooperative mechanism (-[σ2s+σ2s+σ2s]) and implying additive contributions from each of the 3-membered rings to the activation barrier.

Several pathways have been pursued to (21), a versatile precursor e.g. of further "mixed" tris-σ-homobenzenes. The one employed for the preparation of the diimines (3)



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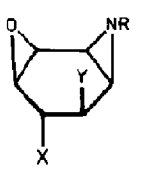

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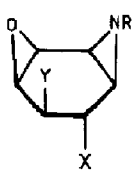

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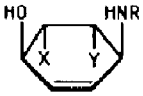

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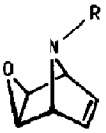
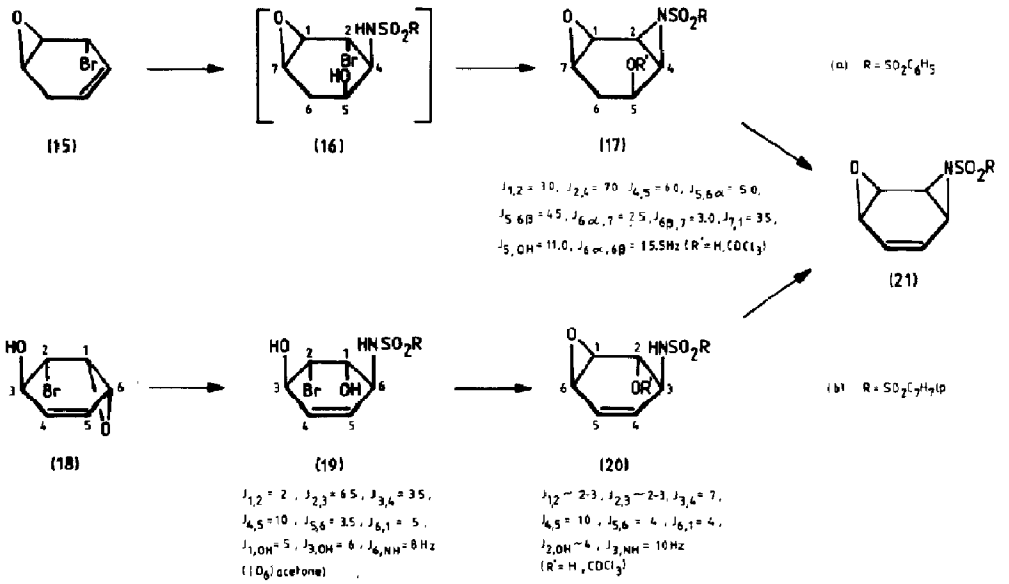


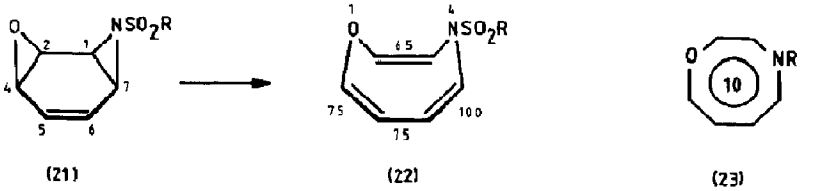
(14)

(X=NR) via N_2O elimination [2b] from suitably substituted oxadiaza-tris-σ-homobenzenes (10) was dismissed, since the latter were accessible only with extreme difficulty [1b]. Similarly, our efforts to photochemically induce a 1,3-nitrogen migration in the recently described system (14) [6] were not successful. The two following approaches - using precursors of the type (11) and (13) - led to our goal: In the reaction sequence (15) ⟶ (16) ⟶ (17) ⟶ (21a)- analogous to (5) ⟶ (8)-the hydroxyamination product (16) is cyclised to (17) (R'=H, m.p. = 145°C) under the weakly basic conditions of the work up [4]. The low yield (12-15%, not optimised) reflects the lack of selectivity in the first step, but this is compensated by the ready availability of (15) [5]. Inspite of the preferred quasi-equatorial position of the OR'-group, in the tosylate (17)(R' = p-tos; m.p. 179°C, $J_{4,5}$ = 2.5, $J_{5,6\alpha}$=6.0, $J_{5,6\beta}$= 11.5, $J_{6\alpha,7}$ = 7.0 Hz, $CDCl_3$) 1,2-elimination to (21a) is achieved at 20°C (THF, K-t-butylate, 75-80%) [7]. In the alternative synthesis selective substitution at C-6 in (18) [8] occurs with chloramine T (as well as with other N-nucleophiles, e.g. $N_3^{\ominus}$) in boiling, buffered methanol. In flexible (19) (>90%, m.p. 204°C, where the half-chair conformation with OH/$NHSO_2$R-groups quasi trans diaxial is favoured ($CDCl_3$)), epoxycyclisation, though effected at 20°C (2.5 equiv. DBN, THF), is marred by unknown side reactions

(60% (20)(R'=H, m.p. 103°C). In accordance with the ready availability of stereoelectronically favourable conformations in (20)(R'=H) and its tosylate (R'=p-tos; m.p. 190°C (dec.), $J_{1,2}$=2,$J_{2,3}$=2,$J_{3,4}$=6.5,$J_{3,NH}$=10.5 Hz) aziridine formation to (21b) using various bases (1.1 equiv. DBN, K-t-butylate, THF) at 20°C is highly selective (>90%).



(21a,b) (e.g. (21b): m.p. 117°C(isom.), $t_{1/2}$(60°C) = 33 min; $\Delta G^{\ddagger}$ =104 kJ·mol^{-1}, $CDCl_3$) readily and quantitatively undergo cycloreversion to the 4H-1,4-oxazocines (22a,b). As expected the oxa,aza-bis-σ-homo-systems (21) are kinetically more stable than the ditosyl-diimine (3)(X=N-p-tos) [9]. Between -60° and +30°C the ^{1}H-NMR spectra ($CDCl_3$) of (22a,b) are only insignificantly temperature dependant. As judged by the vicinal H,H-coupling constants, as well as by the ^{13}C-chemical shifts (e.g. (22a): δ= 140.5(C-8), 130.1(C-2), 122.0(C-5), 111.0(C-6), 106.3(C-7), 106.0 ppm (C-3), $CDCl_3$), (22a,b) prefer a half-chair-like conformation with π-electron delocalisation mainly into the conjugated butadiene-segment. In this respect they resemble



the 1,4-dioxocin ((4),X=O) [2a] more than the (twisted) ditosyl-1,4-dihydro-1,4-diazocine ((4), X=N-p-tos) [2b]. However, as in the latter case, upon heating (22a,b) up to 100°C the equilibrium concentration of the tricyclic educts (21a,b) is not measurable (< 1%). It is being investigated, whether or not a more favourable N-substitution -as known for the 1,4-dihydro-1,4-diazocines [3] - can enforce a more planar ("aromatic") geometry ((23)) upon this mixed 1,4-diheterocin ring system [10].

**) *Dedicated to Prof. Dr. R. H u i s g e n on the occasion of his 60th birthday - as an expression of our good wishes and a mark of our esteem.*

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*) The new compounds have been fully characterised (elemental analyses, ^{1}H-, ^{13}C-NMR, MS). Some typical ^{1}H-NMR-data ($CDCl_3$, ppm) are given: (8a): δ = 3.33(m, 1(8)-H), 3.45 (m, 2(7)-H), 3.48(m, 4(5)-H); (9a): δ = 5.77(2(3)-H , 6(8)-H), 5.94(5(9)-H); $J_{5,6} = J_{8,9} = 4.5$ Hz; (21b): δ = 6.35(5-H), 6.22(6-H), 3.53(2-H), 3.42(1-H), 3.26 (7-H), 3.20(4-H); $J_{1,2} = 3.5$, $J_{2,4} = 4$, $J_{4,5} = 3.5$, $J_{5,6} = 10.5$, $J_{6,7} = 4$, $J_{1,7} = 6.5$, $J_{4,6} \sim 1$, $J_{2,7} \sim 1$Hz; (22b): δ = 6.65(5-H), 6.30(8-H), 6.14(3-H), 6.12(2-H), 5.44(6-H), 5.12(7-H).

1a) (Trioxide): R. Schwesinger, H. Prinzbach, Angew. Chem. Int. Ed. 11, 942 (1972); E. Vogel, H.-J. Altenbach, C.-D. Sommerfeld, ibid. 11, 939 (1972); R. Schwesinger, H. Fritz, H. Prinzbach, Chem. Ber. 112, 3318 (1979);

1b) (Triimine): H. Prinzbach, R. Schwesinger, M. Breuninger, B. Gallenkamp, D. Hunkler, Angew. Chem. Int. Ed. 14, 347 (1975); R. Schwesinger, M. Breuninger, B. Gallenkamp, K.-H. Müller, D. Hunkler, H. Prinzbach, Chem. Ber., in press.

2a) (Dioxide): H.-J. Altenbach, E. Vogel, Angew. Chem. Int. Ed. 11, 937 (1972);

2b) (Diimine): H. Prinzbach, M. Breuninger, B. Gallenkamp, R. Schwesinger, D. Hunkler, Angew. Chem. Int. Ed. 14, 348 (1975); M. Breuninger, R. Schwesinger, B. Gallenkamp, K.-H. Müller, H. Fritz, D. Hunkler, H. Prinzbach, Chem. Ber., in press.

3) M. Breuninger, B. Gallenkamp, K.-H. Müller, H. Fritz, H. Prinzbach, J.J. Daly, P. Schönholzer, Angew. Chem. Int. Ed. 18, 964 (1979); H.-J. Altenbach, H. Stegelmeier, M. Wilhelm, B. Voss, J. Lex, E. Vogel, ibid. 18, 962 (1979).

4) E. Herranz, K.B. Sharpless, J.Org.Chem. 43, 2544 (1978); cit. lit.

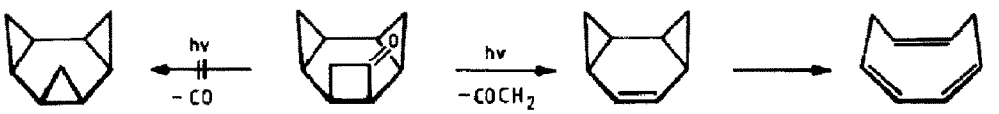
5) H. Prinzbach, R. Keller, R. Schwesinger, Angew. Chem. Int. Ed. 14, 632 (1975).

6) H. Prinzbach, H. Babsch, Heterocycles 11, 113 (1978).

7) H. Prinzbach, H.-W. Schneider, Tetrahedron Lett. 1975, 3073.

8) H.-J. Altenbach, H. Stegelmeier, E. Vogel, Tetrahedron Lett. 1978, 3333.

9) Of the still unknown parent C-homobenzenes (1) and (3) ($X=CH_2$) the latter could be shown to be the product of low temperature photolysis of the [2.1.1]-ketone (24).



(24)

The ease of the cycloreversion ($<0^{\circ}C$) is in agreement with the expectations (H. Prinzbach, H.-P. Schal, D. Hunkler, H. Fritz, Angew. Chem., in press).

10) A.G. Anastassiou, H.S. Kasmai, Adv. Heterocycl. Chem. 23, 55 (1978).

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