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SKELETAL EXPANSIONS of (HOMO) DODECAHEDRANES NOVEL HETEROPOLYCYCLIC CAGE STRUCTURES

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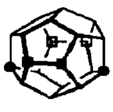
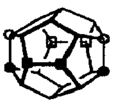
Summary. The carbonyloxide/ketone intermediates resulting from ozonolysis of unsaturated (bishomo)dodecahedranes, sterically inhibited to form secondary ozonides, are (in participating solvents) exploited for the expansion of the molecular peripheries by oxa (dioxa) linkages, thus opening access to a variety of intriguing expanded dodecahedral cage structures. Dehydration of the α,α'-dihydroxyethers provide the corresponding caged di(tetra)ketones with unusually proximate, nearly *syn*-periplanar C=O functions.

Pentagonal dodecahedranes with up to six (A)[1] and eight carbons being pairwise functionalized (**B**)[2] are accessible through the S_N2 and aldol versions of our pagodane → dodecahedrane route.[3] The directly installed functional groups serve as handles for further structural modifications, e.g. annulations and ring expansions (monohomo - tetrahomo dodecahedranes **C-F**)[4]. In this letter we report on our attempts to effect skeletal ring expansions of unsaturated bishomododecahedranes **1-4** through ozonolysis, particularly of type **D** (bishomo) → **E** (trishomo) and **D** (bishomo) → **F** (tetrahomo).[5]


A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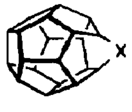

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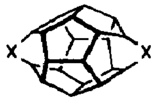

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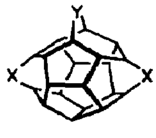

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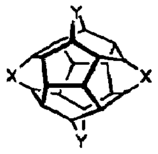
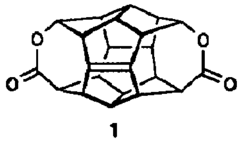
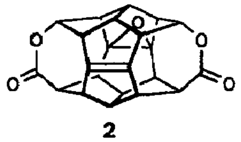


F

The expectation, supported by calculations, was that under the geometrical situation given in the cage skeletons **1-4** intramolecular carbonyl oxide/ketone capture to yield secondary ozonides would be prohibited and that in participating solvents installation of dioxa and oxa bridges into skeletons **C-F** (X,Y = O-O, O) through intramolecular hemi(per)acetalization[6] would become highly efficient. The di- and tetraketones as potential products under reductive work-up conditions are valuable as synthetic intermediates per se;[7] in addition they feature unusually proximate and nearly *syn*-periplanar orientations of the ketone functions[8] which are forced into conformationally unusual cyclooctane-1,5-dione subunits.[9]



1



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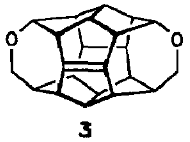
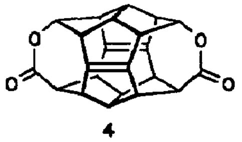


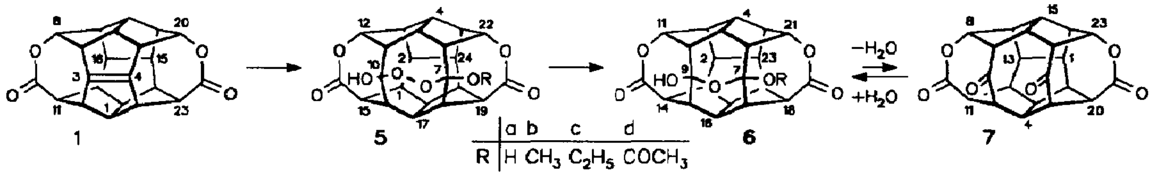
3



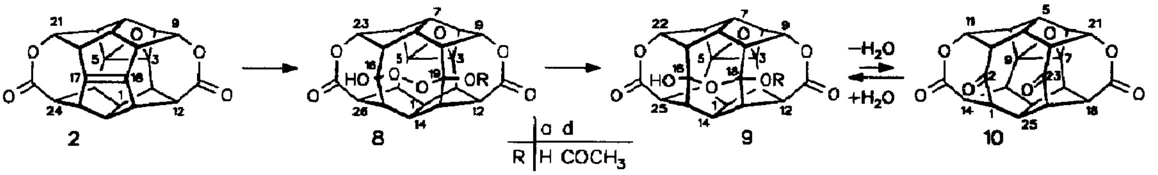
4

Bishomododecahedrenes **1-3** are prepared from diene **4**, which itself is available as an intermediate in the S_N2-version.[1] With their olefinic carbons being only slightly pyramidalized,[10] the four olefins **1-4** were calculated to be hyperstable and **1-3** indeed turned out to be resistant to catalytic hydrogenation; all four were found to be highly unreactive toward dienes and 1,3-dipols (e.g. CH_2N_2).[1,2] Much alike the geometrically similar bissecododecahedradienes,[9] 4 with its very short transannular π,π-distance (2.81 Å, X-ray[11]) is extremely prone to undergo homoconjugate addition reactions.[1,2,12]

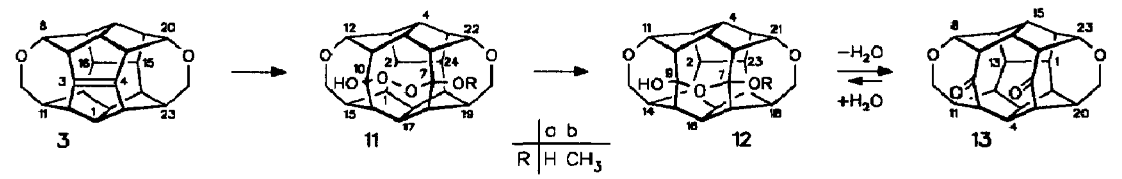
Ene-bislactone **1**, dissolved in acetone/water (10:1), rapidly reacts with ozone (oxygen as carrier) at -78°C. From an experiment taken to complete conversion at room temperature, the solid residue isolated after concentration in vacuo exclusively consisted of the α,α'-dihydroxyperoxide **5a** (dec. 190°C, crystallization from acetone). From reactions carried out in methanol, ethanol or acetic acid/trifluoroacetic anhydride, the semiperoxyacetals **5b-d** were obtained in practically quantitative yields;[13] the portion of the isomeric α-hydroxy (alkoxy) hydroperoxides was found to depend on the substituent R and the solvents used for analysis. In contact with reducing agents, **5a-d** rapidly lose oxygen to give quantitatively the less strained acetals **6a-d**, for which no ketonic equilibrium participants are revealed by NMR- and IR-analysis ($CDCl_3$, CD_3CN, CD_3OD, $[D_6]DMSO$). **6a-d** are also formed exclusively after ozonation followed by reductive workup (e.g. trimethylphosphite, dimethyl sulfoxide. **6a**: from methanol/ether colorless crystals, m.p. > 330°C). Dehydration of **6a** to provide the diketone **7** is complete after heating a DMSO solution in the presence of P_4O_{10} (NMR); addition of water/$NaHCO_3$ totally reforms **6a**, a behaviour typical for the given cyclooctane-1,5-dione entity in **7** (transannular C_6-C_{18} distance: 2.73 Å, O-O distance: 2.84 Å, MM2). So far, however, **7** could not be secured without partial rehydration.



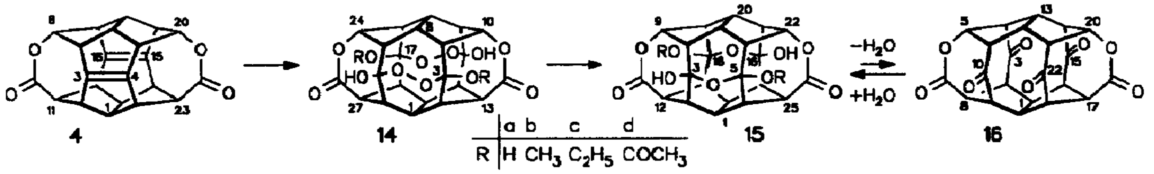
From the analogous ozonation of ene-epoxy-bislactone **2**, the peroxidic products **8a,b** are formed in practically quantitative yield, partly accompanied by their ketonic equilibrium compounds ($CDCl_3$/CD_3OD). After mild reduction of **8a**, acetal **9a** (m.p. > 330°C) was obtained as the single product. Treatment of a DMSO solution of **9a** with P_4O_{10} effects total dehydration to give diketone **10**, which is rehydrated in the presence of water.



Contrasting to **7** and **10**, diketone **13**, obtained analogously from ene-bisether **3** via **11** and **12**, proved less prone to hydration and could be isolated in pure crystalline form without special precautions ($\nu_{C=O}$ = 1672 cm^{-1}, dec. 190°C, transannular C_6-C_{18} distance: 2.71 Å, O-O distance: 2.82 Å, MM2).



Diene bislactone **4** reacts with ozone in the temperature range of -78°C to +25°C without any sign for transannular bond formation, what makes the intervention of any type of ionic intermediate highly improbable.[7] The solid resulting from the reaction in acetone/water (room temp.; 98%), soluble in pyridine, is identified as the tetrahomododecahedranoid bisperoxide **14a**. In the case of **14b-d**, formed analogously and quantitatively by ozonolysis in methanol, ethanol or acetic acid/trifluoro acetic anhydride (of the two isomers formed in roughly equal amounts only one is shown), the tetrahomo bisperoxides are accompanied by varying amounts of deca- and nonacyclic ketonic equilibrium components. Reduction of **14a-d** or ozonolysis of **4** in the solvents used with **1**, followed by reductive workup delivered quantitatively the bisacetals **15a-d**. The water soluble bis(α,α'-dihydroxyether) **15a** (m.p. > 330°C) is dehydrated to tetraketone **16** by heating in DMSO/P_4O_{10}. Like **7** and **10**, tetraketone **16** could so far not be isolated without partial hydration.



The structures of the trishomo (**5**, **6**, **8**, **9**, **11**, **12**) and tetrahomo dodecahedranes (**14**, **15**) are corroborated by their spectral data even though in the MS spectra of the peroxides the molecular ion peak was not generally revealed. Except for the peroxidic products, the $^1H(^{13}C)$-NMR signals could be assigned individually, partly by H,C-COSY experiments.

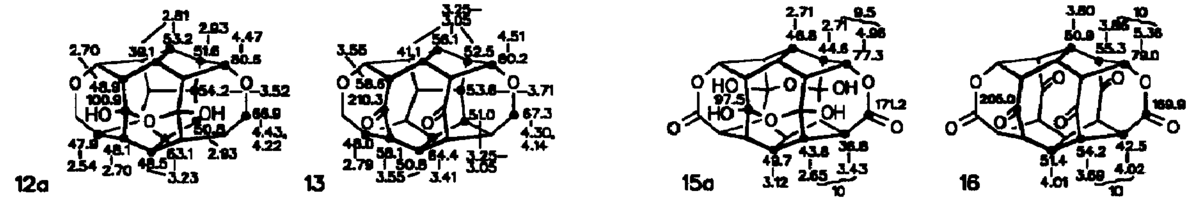
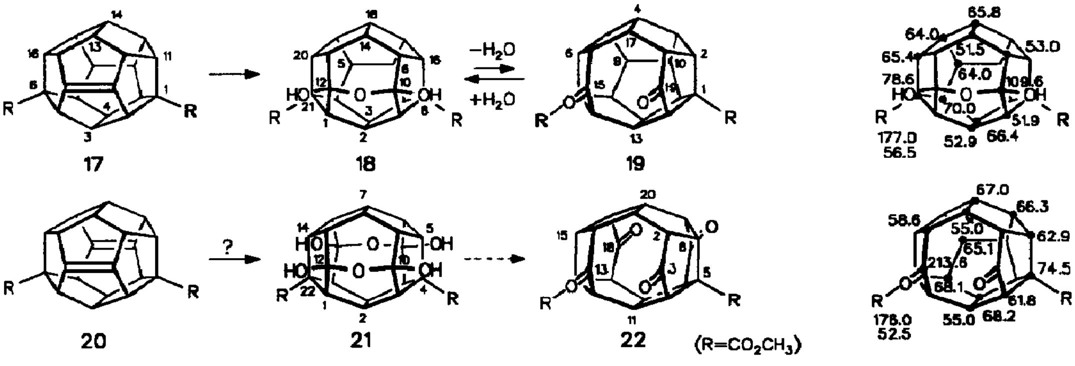


Figure 1: NMR data (400/100.6 MHz) of **12a**, **13** ($CDCl_3$), **15a** and **16** ([D_6]DMSO)

In contrast to **1-4**, the unsaturated pentagonal dodecahedranes like **17** and **20** are highly pyramidalized, not hyperstable, rather reactive in [4+2] cycloadditions and extremely sensitive toward oxygen[1]. For this latter reason, complications had to be suspected for their ring expansions through ozonization. After defined exposure of **17** to ozone (a saturated solution of ozone in CH_2Cl_2/acetic acid 10:1 was added at -78°C to a solution of **17**), oxahomododecahedrane **18** (m.p. > 330°C) could be secured in only moderate yields (up to 20%), the (known) epoxide of **17** being no component of the crude, partly polymeric residue. In DMSO, **18** was dehydrated to the secododecahedrane-15,19-dione **19** (transannular C_{15}-C_{19}-distance: 2.63 Å, O-O-distance 2.76 Å, MM2),[14] which again could not be isolated without partial rehydration.



After analogous exposure of diene-diester **20** to ozone, the bishomo dioxa-cage **21** could not be identified by ^1H-/ ^{13}C-NMR and MS data, which indicate a complex mixture of products including higher oxygenated ones.

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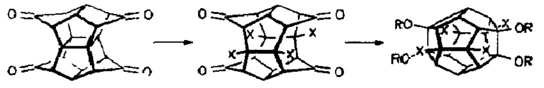
REFERENCES AND NOTES

1) R. Pinkos, J.-P. Melder, K. Weber, D. Hunkler, H. Prinzbach, *J. Am. Chem. Soc.* **1993**, *115*, 7173 and cit. lit.
2) J.-P. Melder, R. Pinkos, H. Fritz, J. Wörth, H. Prinzbach, *J. Am. Chem. Soc.* **1992**, *114*, 10213 and cit. lit.
3) H. Prinzbach, W.-D. Fessner, *Novel Organic Polycycles - an Adventure in Molecular Architecture* in *Organic Synthesis: Modern Trends* (O. Chizhov, Ed.) p. 23, Blackwell, Oxford **1987**; W.-D. Fessner, H. Prinzbach, *The Pagodane Route to Dodecahedrane* in *Cage Hydrocarbons* (G.A. Olah, Ed.), Wiley, New York **1990**, p. 353.
4) For mono-homo structures s. L.A. Paquette The [*n*]Peristylane-Polyhedrane connection in *Cage Hydrocarbons* (G.A. Olah, Ed.), Wiley, New York **1990**, p. 313.
5) T. Voss, *Diplomarbeit*, University of Freiburg **1991**, T. Voss, *Part of Dissertation*, University of Freiburg.
6) P.S. Bailey, *Ozonation in Organic Chemistry*, Academic Press, New York **1978**, 1, **1982**, 2; G. Zvilichovsky, B. Zvilichovsky in *The Chemistry of Hydroxyl, Ether and Peroxide Groups* (S. Patai, Ed.) Wiley, New York **1993**; H. Stetter, P. Tacke, J. Gärtner, *Chem Ber.* **1964**, *97*, 3480; B. Föhlisch, U. Dukek, I. Graeßle, B. Novotny, E. Schupp, G. Schwaiger, E. Widmann, *Liebigs Ann. Chem.* **1973**, 1839; K. Griesbaum, W. Volpp, R. Greinert, H.-J Greunig, J. Schmid, H. Henke, *J. Org. Chem.* **1989**, *54*, 383.
7) J.-P Melder, H. Prinzbach, *Chem. Ber.* **1991**, *124*, 1271. In our tactical scheme for the preparation of highly functionalized dodecahedranes from appropiately activated bisseco precursors, reductive C-C bond formation between opposite carbonyl groups (**24** → **25**) was one of the alternatives considered.[3] Unfortunately, the prototypical pagodane-4,9,14,19-tetrone **23**, (C-CO-C = 100°) could not be isolated because of its extreme propensity for hydrate (acetal) formation.



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8) R. Bishop, G.-H. Lee, *Aust. J. Chem.* **1987**, *40*, 249; T. J. Chow, T.-K. Wu, *Tetrahedron Lett.* **1989**, *30*, 1279; B. Albert, D. Elsässer, D. Heckel, S. Kopmeier, H.-D. Martin, B. Mayer, T. J. Chow, T.-K. Wu, S.-K. Yeh, *Chem. Ber.* **1991**, *124*, 803; T.S. Chow, T.-K. Wu, J. Org. Chem. **1988**, *53*, 1102.
9) F.A.L. Anet, M.S. Jaques, P.M. Henrichs, A.K. Cheng, J. Krane, L. Wong, *Tetrahedron* **1974**, *30*, 1629; M. Umehara, S. Hishida, M. Okuda, S. Ohba, M. Ito, Y. Saito, S. Zen, *Bull. Chem. Soc. Jpn.* **1990**, *63*, 2002.
10) D. Elsässer, K. Hassenrück, H.-D. Martin, B. Mayer, G. Lutz, H. Prinzbach, *Chem. Ber.* **1991**,*124*, 2863.
11) M. Keller, K. Scheumann, K. Weber, T. Voss, H. Prinzbach, H. Irngartinger, U. Reifenstahl, *Preceding letter.*
12) B.A.R.C. Murty, R. Pinkos, P.R. Spurr, W.-D. Fessner, G. Lutz, H. Fritz, D. Hunkler, H. Prinzbach, *Chem. Ber.* **1992**, *125*, 1719.
13) Nomenclature and numbering are secured from the POLCYC program by G. Rücker, C. Rücker, *Chimia* **1990**, *44*, 116; e.g: **6a**: 7,9-dihydroxy-8,12,20-trioxaundecacyclo$[12.11.0.0^{2,23}.0^{3,11}.0^{4,22}.0^{5,10}.0^{6,21}.0^{7,17}.0^{9,15}.0^{16,25}.0^{18,24}]$pentacosane-13,19-dione; **7**: 9,22-dioxadecacyclo$[11.11.0.0^{2,20}.0^{3,12}.0^{4,19}.0^{5,11}.0^{7,12}.0^{8,14}.0^{15,24}.0^{17,23}]$tetracosane-6,10,18,21-tetrone; **14a**: 3,6,17,20-tetrahydroxy-4,5,11,18,19,25-hexaoxaundecacyclo$[13.13.0.0^{2,13}.0^{3,19}.0^{6,28}.0^{7,24}.0^{8,22}.0^{10,21}.0^{14,20}.0^{16,27}.0^{17,23}]$octacosane-12,26-dione; **15a**: 3,5,16,18-tetrahydroxy-4,10,17,23-tetraoxaundecacyclo$[12.12.0.0^{2,12}.0^{3,8}.0^{5,26}.0^{6,22}.0^{7,20}.0^{9,19}.0^{13,18}.0^{15,25}.0^{16,21}]$hexacosane-11,24-dione; **16**: 4,19-dioxanonacyclo$[14.8.0.0^{2,8}.0^{4,13}.0^{5,11}.0^{9,24}.0^{12,21}.0^{14,20}.0^{17,23}]$tetracosane-3,7,10,15,17,22-hexone; **18**: dimethyl 10,12-dihydroxy-11-oxa-undecacyclo$[10.9.0.0^{2,9}.0^{3,7}.0^{4,21}.0^{5,19}.0^{6,17}.0^{8,16}.0^{10,15}.0^{13,20}.0^{14,18}]$henicosane-8,21-dicarboxylate; **19**: dimethyl decacyclo$[9.9.0.0^{2,8}.0^{3,10}.0^{4,17}.0^{5,9}.0^{6,16}.0^{7,14}.0^{8,16}.0^{13,20}]$icosane-15,19-dione-1,7-dicarboxylate.
14) G.G. Christoph, P. Engel, R. Usha, D.W. Balogh, L.A. Paquette, *J. Am. Chem. Soc.* **1982**, *104*, 784.

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