Pergamon

Tetrahedron Letters, Vol. 38, No. 23, pp. 4173-4176, 1997

0040-4039/97 $17.00 + 0.00

PII: S0040-4039(97)00813-7

Oxa-Bowls: The Pentaoxa[5]peristylane

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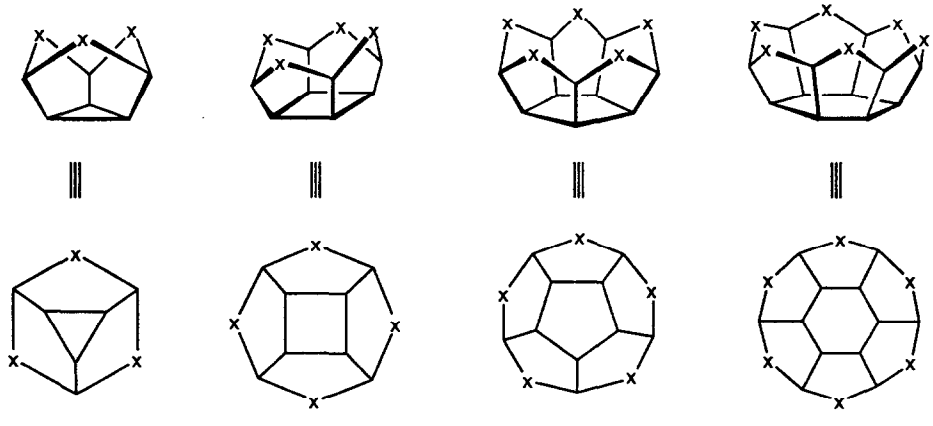
Abstract: The first synthesis of parent pentaoxa-[5]-peristylane, from a readily available and stereochemically well-defined norbornene precursor, employing a cascade of intramolecular acetalizations as the stratagem, is reported.

[n]-Peristylanes **1-4** (n=3-6) are a class of aesthetically pleasing and topologically novel, molecular entities in which the carbon atoms of an inner [n]-membered ring clasp the alternate corners of an outer [2n]-membered ring. Such a fascinating union generates a range of 'bowl'-shaped molecules, with [n+1]-number of rings and potential C_{nv}-symmetry, whose 'walls' are exclusively composed of five-membered rings. With such alluring structural features, [n]-peristylanes have naturally attracted considerable attention and [3]-**1a**,[1] [4]-**2a**[2] and [5]-peristylane **3a**[3] have succumbed to synthesis through imaginative strategies. We have now conceived of a new family of [n]-hetero-[n]-peristylanes **1b-4b** (X=O, N, S, etc.) in which all the methylene groups on the rim of the 'bowl' are replaced by a hetero atom. The resulting 'hetero-bowls' **1b-4b** are not only expected to be more stable[4] than their carba-analogues **1a-4a**, due to the elimination of HC-CH_2 torsional strain, but have the potential to exhibit avidity for metal ions and small molecules. In a sense, **1b-4b** can be regarded as a new class of ionophores that have remained unknown so far. In this communication, we

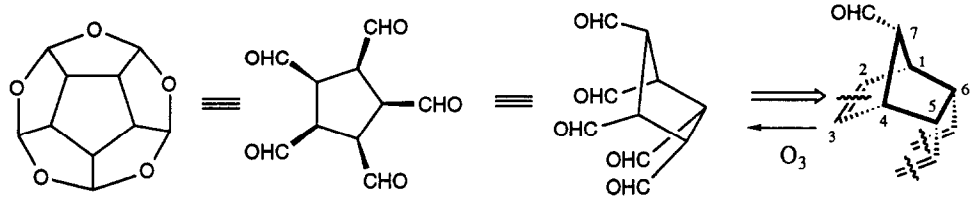


1a. x= CH_2
b. x=O

2a,b **3a,b** **4a,b**

report the synthesis and characterization of pentaoxa-[5]-peristylane **3b** (X=O), the first member of the new family of 'oxa-bowls' and demonstrate the efficacy of a cascade process for rapidly assembling multiple tetrahydrofuran rings through intramolecular acetalization protocols.[5]

Our synthetic strategy towards pentaoxa-[5]-peristylane **3b** evolved through the recognition that its structure can be regarded as the cyclic acetal form of, *all cis* 1,2,3,4,5-cyclopentane-pentacarbaaldehyde **5**. To access **5**, we sought to exploit the rigid, stereochemically well-defined norbornene framework through strategic positioning of appropriate substituents that could serve as surrogates for the aldehyde functionality. Thus, we identified *endo,endo*-5,6-divinyl-*anti*-7-formyl-bicyclo[2.2.1]heptene **6** as the equivalent of **5**, in which the C_1—C_2 and C_3—C_4 bonds and the C_5, C_6, C_7 substituents are *all cis* to each other (see dotted lines) on a five-membered ring (C_1 C_7 C_4 C_5 C_6; heavy line) embedded within the norbornyl framework. Controlled oxidation, *e.g.* ozonolysis, of **6** was envisaged to unravel the five-membered ring as well as the requisite aldehyde functionalities to furnish **5** or equivalent which on nucleophile triggered intramolecular cascade cyclization was expected to deliver **3b**, Scheme 1. Successful execution of this strategy from the readily available, *endo,endo*-norbornene derivative **7**[6] is outlined below.

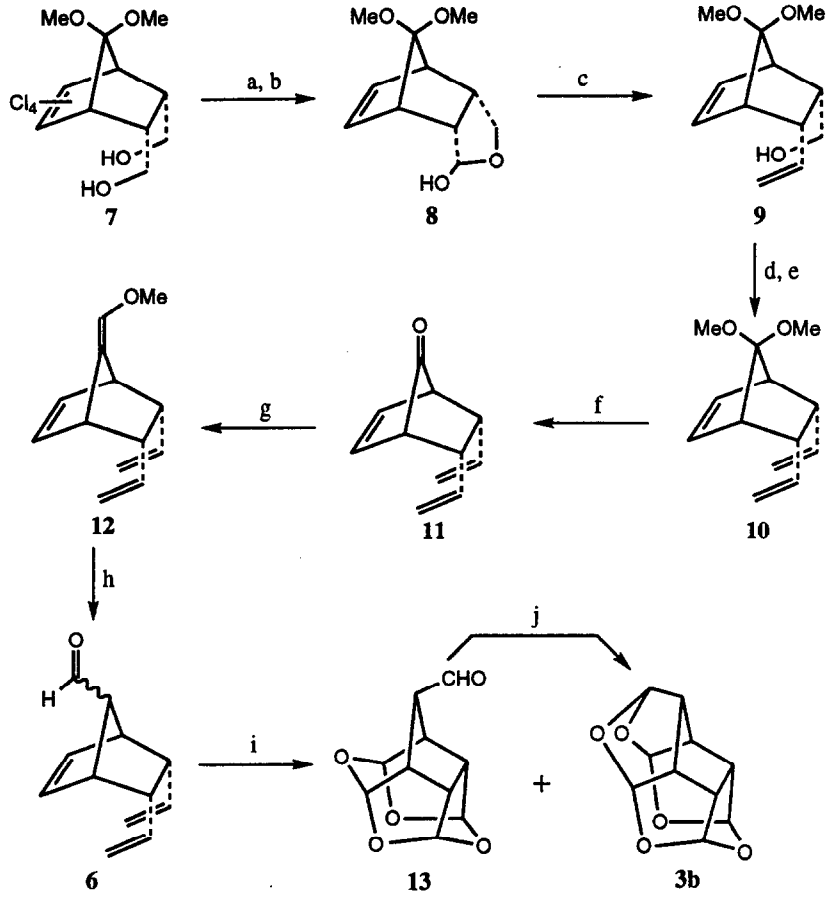


3b $C_{10}H_{10}O_5$ **5** $C_{10}H_{10}O_5$ **6**

Scheme 1

Reductive dechlorination of **7** and oxidation with *o*-iodoxybenzoic acid (IBX) furnished the *endo*-lactol **8**.[7] Wittig olefination of **8** with the ylide derived from triphenylmethylphosphonium bromide proceeded stereoselectively and the *endo,endo*-vinyl carbinol **9**[7] was obtained as the major product (*endo*:*exo*-vinyl 90:10). The *endo*-carbinol **9** was subjected to Swern oxidation and the resulting aldehyde on Wittig olefination furnished the *endo,endo*-5,6-disubstituted derivative **10**[7] as the major product (*endo,endo*:*endo,exo*=85:15), Scheme 2. The *endo,endo*-divinyl acetal **10** was carefully hydrolyzed to the bicyclic trienone **11**[7] and further subjected to Wittig olefination with methoxymethyl phosphorane to furnish the methyl enol-ether **12**.[7] On controlled acid hydrolysis of **12**, aldehyde **6** (*syn*:*anti*=3:1) was obtained, in quantitative yield, as a mixture of diastereomers. On ozonolysis, followed by dimethylsulfide work-up, the aldehyde **6** furnished a mixture (32:68) of pentaoxa-[5]-peristylane **3b** and tetraoxa-aldehyde **13**[7] in 39% yield. The tetraoxa-aldehyde on exposure to amberlyst-15 catalyst could be further transformed into **3b**. Delightfully, the intermediate **5** or equivalent generated during the ozonolysis of **6**, undergoes facile cascade cyclizations as contemplated in Scheme 1, to eventuate in pentaoxa-[5]-peristylanes. The structure of **3b**, mp >230°C (decomp.), followed from its MS (*m*/*z* 211, M^++1), 2 line ^1H NMR spectrum (δ 5.93 & 3.66) and two line ^{13}C NMR

spectrum [δ (DEPT) 113.60 (CH) & 58.20 (CH)] and was fully secured through its X-ray crystal structure determination.



Scheme 2

Reagents & Yields: (a) Na-liq.NH_3, THF, EtOH, 50%; (b) IBX, DMSO-acetone, RT, 1h, 100%; (c) $CH_3{}^+PPh_3Br^-$, $Na^+{}^-O^tAm$, THF, RT, 1h, 61%; (d) $(COCl)_2$, DMSO, Et_3N, CH_2Cl_2, -60°C, 30 min, 90%; (e) (c), 70%; (f) Amberlyst-15, acetone, reflux, 2h, 90%; (g) $CH_3OCH_2{}^+PPh_3Cl^-$, $Na^+{}^-O^tAm$, THF, RT, 1h, 50%; (h) 35% $HClO_4$, CH_2Cl_2, RT, 6-8hr, quantitative; (i) O_3, CH_2Cl_2, DMS, -78°C, 2h, 39%; (j) Amberlyst-15, CH_2Cl_2, RT, 4h, 70-75%.

In summary, we have delineated a new strategy towards pentaoxa-[5]-peristylane **3b**, which through tactical modifications, can be readily adapted for the synthesis of other [n]-oxa-[n]-peristylanes.[8]

Acknowledgements

RV thanks CSIR for financial support. GM is a recipient of the S. Ramanujan Research Professorship of the Indian National Science Academy (INSA).

References & Notes

1. (a) Garratt, P.J.; White, J.F. *J. Org. Chem.* **1977**, *42*, 1733. (b) Majerski, Z.; Hamersak, Z.; Minaric-Majerski, K. *J. Chem. Soc. Chem. Commun.* **1985**, 1830. (c) Garratt, P.J.; Doecke, C.W.; Weber, J.C.; Paquette, L.A. *J. Org. Chem.* **1986**, *51*, 449.
2. Paquette, L.A.; Browne, A.R.; Doecke, C.W.; Williams, R.V. *J. Am. Chem. Soc.* **1983**, *105*, 4113; Paquette, L.A.; Fischer, J.W.; Browne, A.R.; Doecke, C.W. *J. Am. Chem. Soc.* **1986**, *107*, 686.
3. Eaton, P.E.; Mueller, R.H. *J. Am. Chem. Soc.* **1972**, *94*, 1014; Eaton, P.E.; Mueller, R.H.; Carlson, G.R.; Cullison, D.A.; Copper, G.F.; Chou, T.C.; Krebs, E.P. *J. Am. Chem. Soc.* **1977**, *99*, 2751.
4. Deduced from detailed Molecular Mechanics, semi-empirical and *ab initio* level calculations on **1a,b-4a,b** carried out in collaboration with Prof. Jemmis; details will be published elsewhere.
5. (a) For earlier efforts towards **3b** from this laboratory, see: Mehta, G.; Rao, H.S.P. *J. Chem. Soc. Chem. Commun.* **1986**, 472. (b) Some derivatives of pentaoxa-[5]-peristylane has been independently synthesized by Prof. H-J. Wu *et al., Tetrahedron Lett.*in press (private communication) .
6. Feichtinger, H.; Linden, H-W. *Chem. Ber.* **1964**, *97*, 2704; Mehta, G.; Khan, F.A. *J. Am. Chem. Soc.* **1990**, *112*, 6140.
7. All new compounds were duly characterized on the basis of their spectral (IR, ^{1}H and ^{13}C NMR) data and ms/elemental analyses. Selected spectral data:

   8: ^{1}H NMR (200 MHz, $CDCl_3$): δ 6.21-6.10 (m, 2H), 5.01 (s, 1H), 4.04-3.96 (m, 1H), 3.50-3.45 (m, 1H), 3.19 (s, 3H), 3.11 (s, 3H), 2.99-2.95 (m, 1H), 2.92-2.90 (m, 1H); ^{13}C NMR (50.0 MHz, $CDCl_3$): δ 132.21, 131.57, 121.73, 99.94, 68.62, 53.03, 52.05, 49.73, 48.42, 47.26, 43.48; *m/z* 212 [M$^+$].

   9: ^{1}H NMR (200 MHz, $CDCl_3$): δ 6.18-6.16 (m, 2H), 5.50-5.28 (m, 1H), 5.18-4.88 (m, 2H), 3.38-3.17 (m, 2H), 3.20 (s, 3H), 3.10 (s, 3H), 2.99-2.91 (br s, 1H), 2.85-2.78 (br s, 1H), 2.70-2.52 (m, 1H), 2.20-2.08 (br s, 2H); ^{13}C NMR (50.0 MHz, $CDCl_3$): δ 138.32, 132.91, 132.85, 118.45, 117.00, 62.52, 51.80, 51.01, 49.79, 47.54, 44.48; *m/z* 210 [M$^+$].

   10: ^{1}H NMR (200 MHz, $CDCl_3$): δ 6.22-6.20 (m, 2H), 5.5-5.3 (m, 2H), 5.07-4.90 (m, 4H), 3.24 (s, 3H), 3.14 (s, 3H), 3.14-3.09 (m, 2H), 2.87 (br s, 2H); ^{13}C NMR (50.0 MHz, $CDCl_3$): δ 139.20, 133.03, 118.21, 115.53, 51.81, 50.74, 49.79, 46.90.

   11: ^{1}H NMR (200 MHz, $CDCl_3$): δ 6.59-6.57 (m, 2H), 5.50-5.30 (m, 2H), 5.14-5.01 (m, 4H), 3.10-2.99 (m, 4H); ^{13}C NMR (50.0 MHz, $CDCl_3$): δ 203.31, 136.79, 131.91, 117.03, 53.02, 44.77.

   12: ^{1}H NMR (200 MHz, $CDCl_3$): δ 6.34 (br s, 2H), 5.47 (s, 1H), 5.50-5.30 (m, 2H), 5.10-4.90 (m, 4H), 3.52 (s, 3H), 3.10-2.97 (m, 4H); ^{13}C NMR (50.0 MHz, $CDCl_3$): δ 139.72, 139.51, 135.90, 135.36, 134.32, 127.21, 115.62, 115.50, 59.49, 50.51, 49.22, 49.13, 46.73.

   13: ^{1}H NMR (200 MHz, $CDCl_3$): δ 9.77 (s, 1H), 5.88 (d, J=4.6Hz, 2H), 5.62 (d, J=6Hz, 2H), 3.46-3.42 (m, 2H), 3.24 (s, 1H), 3.18-3.15 (m, 2H); ^{13}C NMR (50.0 MHz, $CDCl_3$): δ 199.02, 109.84, 102.99, 55.69, 51.92, 45.56; *m/z* 210 [M$^+$].
8. Mehta, G.; Vidya, R. *accompanying communication*

(*Received in UK* 2 *April* 1997; *accepted* 25 *April* 1997)