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Oxa-Bowls: Towards Hexaoxa[6]peristylane

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Abstract: An approach to hexaoxa-[6]-peristylane **4a** involving multiple intramolecular acetalizations as the key protocol is reported.
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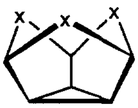
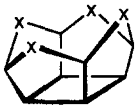
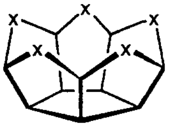
We have conceived novel 'oxa-bowls', the [n]-hetero-[n]-peristylanes **1a-4a**, as a new class of potential ionophores and achieved a short synthesis of pentaoxa-[5]-peristylane **3a**, the first member of this group.[1] Among the carba-analogues **1b-4b** of these hetero-peristylanes, [3]-**1b**, [4]-**2b** and [5]-peristylane **3b** have been synthesized previously.[1,2] However, [6]-peristylane **4b** has proved to be a difficult and as yet unattained proposition, perhaps due to the prohibitive strain that builds-up, as the six-membered 'bottom' of the 'bowl' tends to approach near planarity. Since, the [n]-oxa-[n]-peristylanes, in general, have been found to be more stable than the carba-peristylanes,[1] we reckoned **4a** to be more amenable to synthetic pursuits than **4b** and herein report the progress achieved in that direction.



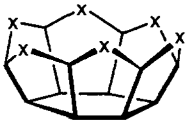
1a. x= O, **b**. x=CH_2



2a,b

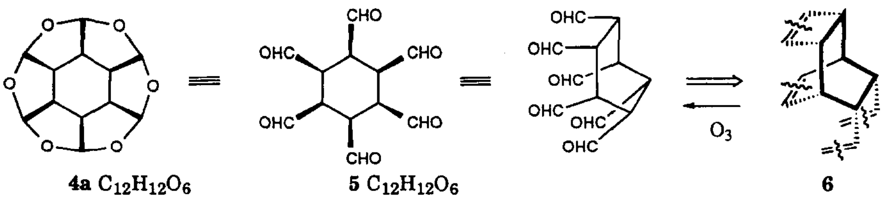


3a,b



4a,b

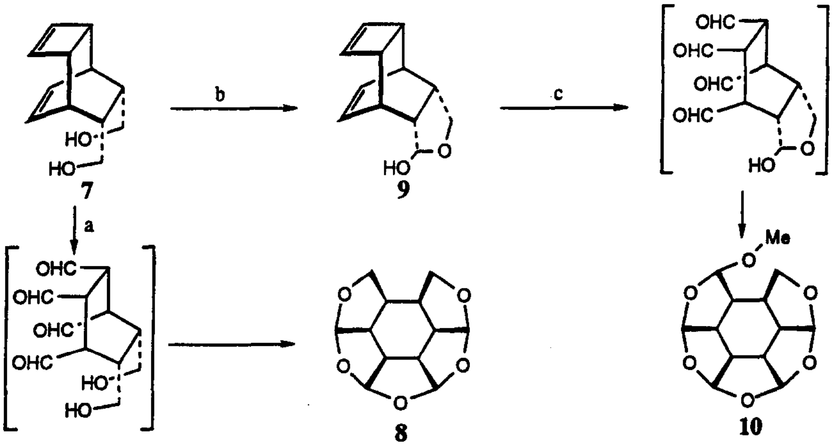
Our synthetic strategy towards **4a** hinged on the recognition that it represents the cyclic acetal form of *all cis* 1,2,3,4,5,6-cyclohexane-hexacarbaldehyde **5**. We envisioned accessing **5** or its equivalent from an *endo,endo*-7,8-disubstituted tricyclo[4.2.2.$0^{2,5}$]deca-3,9-diene **6** through oxidative cleavage, Scheme 1. To test the validity of this approach, we have carried out preliminary studies with the readily available *endo,endo*-tricyclic diene-diol **7**.[3]



Scheme 1

When **7** was subjected to ozonolysis and the reaction product exposed to amberlyst-15, hexacyclic acetal **8**[4] was obtained in 40% yield, through multiple intramolecular acetalizations.

Remarkably, five tetrahydrofuran rings are generated in a 'one-pot' operation, with complete restructuring of the precursor **7**. The structure and C_s-symmetry of **8** followed from its characteristic 6-line ^{13}C NMR spectrum.[4] To further demonstrate the efficacy of our approach, **7** was oxidized with *o*-iodoxybenzoic acid (IBX) to the *endo*-lactol **9**. Ozonolysis and exposure to amberlyst-15 in methanol led to the isolation of hexacyclic methyl ether **10**.[4] Interestingly, in **10** all the six oxygen atoms, required for **4a**, are in position. MMX calculations on **8** and **10** indicate that they possess 'bowl-like' structure with the 'bottom' six-membered ring acquiring a flattened 'boat-like' shape. Efforts are underway to further elaborate **8** and **10** to hexaoxa-[6]-peristylane.



Scheme 2

Reagents & Yields: (a) (i) O_3, CH_2Cl_2, DMS, -78°C; (ii) amberlyst-15, RT, 3h, 40%. (b) IBX, DMSO:acetone, RT, 1h, 85-90%. (c) (i) O_3, CH_2Cl_2, DMS, -78°C; (ii) MeOH, amberlyst-15, RT, 4h, 8%.

Acknowledgement

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References & Notes

1. Mehta, G.; Vidya, R. *preceding communication.*
2. Anand, N.; Bindra, J.S.; Ranganathan, S. *Art in Organic Synthesis*, 2nd Edition, John Wiley & Sons, New York, 1987.
3. Avaram, M.; Sliam E.; Nenitzescu, C.D. *Ann.* **1960**, *184*, 636.
4. All new compounds were duly characterized. Selected spectral data:
   8: ^1H NMR (200 MHz, $CDCl_3$): δ 5.99 (d, J=4Hz, 2H), 5.75 (d, J=4Hz, 2H), 4.43-4.35 (m, 2H), 4.05-3.97 (m, 2H), 2.99-2.53 (series of m, 6H); ^{13}C NMR (50.0 MHz, $CDCl_3$, DEPT): δ 114.59 (CH), 111.80 (CH), 71.71 (CH_2), 40.62 (CH), 39.45 (CH), 35.10 (CH); *m/z* 239 [M^++1].
   10: 5.94 (d, J=4Hz, 2H), 5.45 (d, J=4Hz, 1H), 5.40 (d, J=4Hz, 1H), 4.96 (d, J=2Hz, 1H), 4.21-4.12 (m, 1H), 3.92-3.86 (m, 1H), 3.37 (s, 3H), 2.85-2.54 (series of m, 6H); ^{13}C NMR (50.0 MHz, $CDCl_3$, DEPT): δ 110.98 (CH), 110.78 (CH), 108.05 (CH), 101.54 (CH), 101.46 (CH), 69.57 (CH_2), 54.98 (CH_3), 44.80 (2CH), 43.19 (CH), 42.99 (CH), 42.76 (CH), 33.84 (CH); *m/z* 267[M^+-1], 237[M^+-31].

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