The Trioxa[5]-peristylane System

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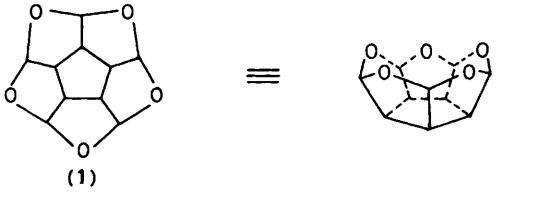
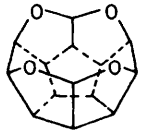
A novel, short approach to the title hexacyclic system *via* an organoselenium reagent based intramolecular trapping of an acetal moiety is described.

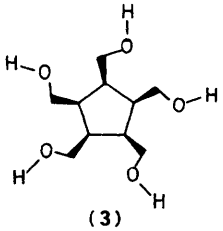
The design of molecular assemblies with chemically distinct surfaces has received a great deal of attention in recent years because of their role in complexation chemistry, ion-transport phenomena, surfactant chemistry, and in enzyme mimicry. Arising from our interest in pentagonal dodecahedrane and its fragments,[1] we became interested in the globular system such as (**1**) (pentaoxa[5]-peristylane) and (**2**) (tetraoxaoctaquinane) having a lipophilic convex surface and polar binding sites interspersed on its 10-membered fluted perimeter. To our knowledge, such systems have not been conceived previously[2] and the closest literature analogy is the recently



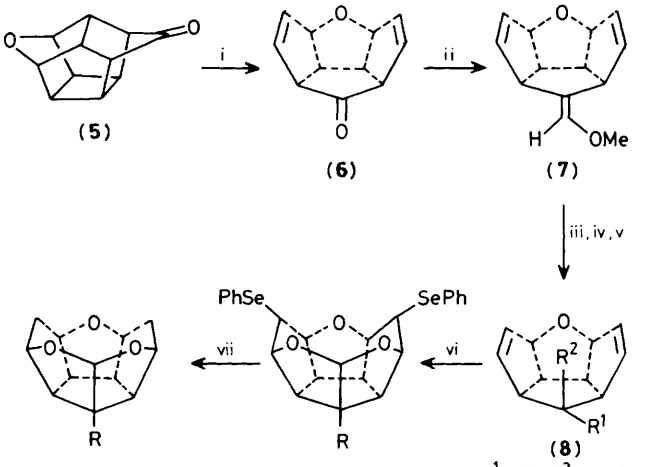
(**1**)



(**2**)



(**3**)



(**5**) (**6**) (**7**) (**8**) (**4**) R = Me (**9**) R = Me

a; R^1 = H, R^2 = CHO
b; R^1 = CHO R^2 = H
c; R^1 = Me R^2 = CHO
d; R^1 = Me, R^2 = OMe, OMe

Scheme 1. i, 625 °C, fvp; ii, $MeOCH_2P^+Ph_3Cl^-$–sodium-t-amyloxide–Et_2O; iii, 35% $HClO_4$, Et_2O–H_2O, heat, 63% from (**6**); iv, NaH–MeI–THF, 50 °C; v, $(MeO)_3CH$–pyridinium toluene-*p*-sulphonate, heat, 30% from (**8b**); vi, PhSeCl–CH_2Cl_2, −78 → 0 °C, 26%; vii, Bu^n_3SnH–toluene–azobisisobutyronitrile, heat, 75%.

reported[3] synthesis of (**3**), a ring opened version of (**1**). Herein we report the first synthesis of a heterocyclic [5]-peristylane (**4**),[4]† a congener of (**1**), by a flexible strategy that involves organoselenium mediated intramolecular trapping of an acetal moiety by two strategically placed double bonds as the key step. The approach also enables easy addition of a hydrophobic moiety or other groups on the molecular posterior through variation of R.

The synthetic sequence leading to trioxa[5]-peristylane (**4**) from the readily available[1c] hexacyclic keto-ether (**5**) is depicted in Scheme 1. Wittig olefination of (**6**), obtainable from (**5**) through flash vacuum pyrolysis (fvp),[5] with methoxymethylenetriphenylphosphorane furnished (**7**). Acid hydrolysis of (**7**) initially gave the *endo*-aldehyde (**8a**) which rapidly isomerised to the thermodynamically more stable *exo*-aldehyde (**8b**)‡ under the reaction conditions. Alkylation of (**8b**) with MeI–KH in tetrahydrofuran (THF) added the methyl group on the convex face and the resultant labile (**8c**)‡ had its aldehyde group projecting firmly into the folded molecular cavity. The *endo*-aldehyde (**8c**) was readily transformed into the crystalline acetal (**8d**)‡ and its exposure to phenylselenyl chloride led to intramolecular etherification at both the available sites and (**9**)‡ was obtained in modest yield. As planned, the electrophilic selenium reagent approached the olefinic bonds from the convex face and the resulting intermediate trapped the strategically placed *endo*-acetal group. The final step of reductive deselenylation was readily achieved with tri-n-butylstannane to deliver (**4**),‡ m.p. 89 °C, exhibiting an eight-line ^{13}C n.m.r. spectrum with diagnostic resonances.

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† Systematic name: 13-methyl-2,4,8-trioxahexacyclo[7.5.1.$0^{3,13}$.$0^{5,12}$.$0^{7,11}$.$0^{10,14}$]pentadecane.

‡ Compound (**8b**): m.p. 77 °C, i.r. (KBr): 2700, 1720, 1620 cm^{-1}; ^1H n.m.r. ($CDCl_3$, 100 MHz): δ 9.65 (1H, s), 5.62 (4H, br. s), 5.24 (2H, br. s), 3.58 (4H, br. s), 2.8 (1H, s); ^{13}C n.m.r. ($CDCl_3$, 25 MHz): δ 180.4, 126.0, 124.1, 87.6, 61.8, 56.5, 54.9; (**8c**): m.p. 88 °C, i.r. (neat): 2715, 1720 cm^{-1}; ^1H n.m.r. ($CDCl_3$, 100 MHz): δ 9.7 (1H, s), 1.22 (3H, s); (**8d**): m.p. 129 °C, i.r. (KBr): 1260, 1060 cm^{-1}; ^1H n.m.r. ($CDCl_3$, 100 MHz): δ 5.6 (4H, ABq, *J* 6 Hz), 5.18 (2H, m), 2.76 (2H, br. s), 1.11 (3H, s); ^{13}C n.m.r. ($CDCl_3$, 25 MHz): δ 139.7, 109.5, 89.4, 69.0, 58.1, 51.5, 27.4; (**9**): m.p. 175—176 °C, ^1H n.m.r. (100 MHz, $CDCl_3$): δ 7.4—7.5 (4H, m), 7.18—7.3 (6H, m), 5.37 (1H, s), 4.88 (2H, d, *J* 8 Hz), 4.48 (2H, d, *J* 6 Hz), 4.3 (2H, s), 3.38—3.58 (2H, m), 3.0—3.2 (2H, m), 1.36 (3H, s); (**4**): m.p. 89 °C, ^1H n.m.r. ($CDCl_3$, 100 MHz): δ 5.38 (1H, s), 4.89 (2H, dd, *J* 5.5 Hz), 4.44 (2H, dd, *J* 4 Hz), 3.3 (2H, m), 3.0 (2H, m), 2.6 (2H, d, *J* 15 Hz), 1.7 (2H, dt, J^1 15, J^2 5.5 Hz), 1.4 (3H, s); ^{13}C n.m.r. ($CDCl_3$, 25 MHz): δ 120.9, 90.4, 88.5, 69.6, 67.5, 60.5, 41.7, 24.5.

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