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A First Selective Synthesis of Cyclopentaveratrylene

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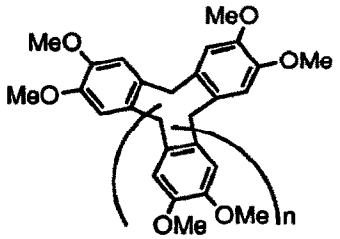
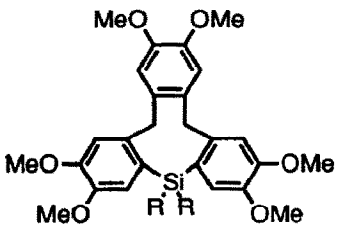
Summary : A selective synthesis of cyclopentaveratrylene (2) starting from 3,4-bis(6-bromoveratryl)veratrole (6) or 3,4-diveratrylveratrole (7) is achieved.

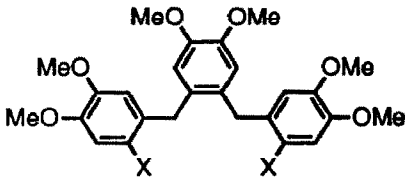
A various type of Host compounds in Host-Guest chemistry, which develops extensively as a mimic model for enzymatic reactions,[1] have been synthesized. Among them, synthesis and characterization of calixarenes, one of cyclophanes, have been performed for investigation on the molecular recognition for the last decade,[2] whereas those of orthocyclophanes have not been done except for cyclotriveratrylene (1) derivatives.[3] Recently, cyclopenta (2)- and cyclohexaveratrylenes (3) are formed as by-products[4] along with 1 and cyclotetraveratrylene (4) in the reaction of veratryl alcohol with acid. However, a selective synthesis of 2 or 3 has been unsuccessful.[5] In this report, we wish to describe a first selective synthesis of cyclopentaveratrylene (2).



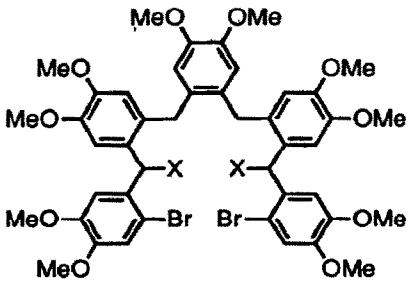
1 : n = 1
2 : n = 3
3 : n = 4
4 : n = 2



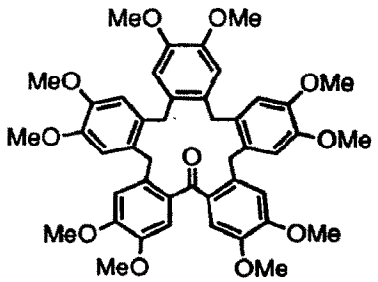
5
R = Me, Ph etc



6 : X = Br
7 : X = H
8 : X = Li



9 : X = OH
10 : X = H



11

We have recently[8] reported that 5-silacyclotriveratrylenes (5) are synthesized from 3,4-bis(6-bromoveratryl)veratrole (6).[8,9] The findings suggested that 6 or its reduced compound (7)[9] might be a suitable starting material for a synthesis of 2. Thus, the dilithio compound (8),[8] generated from 6, was allowed to react with 6-bromoveratraldehyde in THF at -50° C to give dibromo-dihydroxy linear pentamers (9)[10] (amorphous mass; 59%) as a diastereomeric mixture. Deoxygenation (I_2, PPh_3,[11] PhH, reflux) of 9 gave the dibromo-pentamer (10)[10] (amorphous mass; 56%), which was also synthesized by acid treatment (trifluoroacetic acid, CH_2Cl_2, reflux) of 7 with 6-bromoveratryl alcohol (2 equiv.).

Cyclization[12] [*n* BuLi (2.5 eq.), THF, -50 °C; $(EtO)_2CO$ (excess)] of 10 furnished 5-oxocyclopentaveratrylene (11),[10] mp 234-235 °C in 21% yield. Reduction ($NaBH_4$-$AlCl_3$,[14] THF, reflux) of 11 produced cyclopentaveratrylene (2), mp 268-271 °C (lit.[4] 268-270 °C), in 70% yield, ^{1}H-NMR spectral data of which were coincident with those reported in a literature.[4]

Thus, a first selective synthesis of cyclopentaveratrylene (2) was accomplished and application of this methodology to a selective synthesis of larger orthocyclophanes is in progress.

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References and Notes

1. Seel, C.; Vögtle, F. *Angew. Chem. Int. Ed. Engl.* **1992**, *31*, 528 and references cited therein.
2. Gutsche, C. D. *Acc. Chem. Res.* **1983**, *16*, 161; Shinkai, S. *Tetrahedron* **1993**, *49*, 8933 and references cited therein.
3. Collet, A. *Tetrahedron* **1987**, *43*, 5725 and references cited therein.
4. Al-Farhan, E.; Keehn, P. M.; Stevenson, R. *Tetrahedron Lett.* **1992**, *33*, 3591.
5. A selective synthesis of cyclotetra-,[6] cyclopenta-,[6] and cycloheptabenzylenes[7] has been reported.
6. Lee, W. Y.; Park, C. H.; Kim, Y. D. *J. Org. Chem.* **1992**, *57*, 4074.
7. Lee, W. Y.; Park, C. H.; Kim, H.-J.; Kim, S. J. *J. Org. Chem.* **1994**, *59*, 878.
8. Hara, H.; Satoh, H.; Hoshino, O. *Heterocycles*, **1992**, *33*, 43.
9. Umezawa, B.; Hoshino, O.; Hara, H.; Mitsubayashi, S. *J. Chem. Soc. C*, **1970**, 465.
10. All new compounds were fully characterized by ^{1}H-NMR and HRMS.
11. Bohlmann, F.; Staffeldt, J.; Skuballa, W. *Chem. Ber.* **1976**, *109*, 1586.
12. Analogous reaction [$ClCO_2Et$ or $(EtO)_2CO$] of 8 led to 5-oxocyclotriveratrylene[13] (39 or 57%), reduction ($NaBH_4$-$AlCl_3$,[14] THF, reflux) of which gave 1[15] (62%).
13. Cookson, R. C.; Halton, B.; Stevens, I. D. R. *J. Chem. Soc. B*, **1968**, 757.
14. Ono, A.; Suzuki, N.; Kamimura, J. *Synthesis*, **1987**, 736.
15. Umezawa, B.; Hoshino, O.; Hara, H.; Ohyama, K.; Mitsubayashi, S.; Sakakibara, J. *Chem. Pharm. Bull.* **1969**, *17*, 2240.

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