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CHELATION-CONTROLLED STEREOSELECTIVITY IN THE ALKYLLITHIUM CLEAVAGE OF AN ALLYLIC ETHER. THE SYNTHESIS OF CIS,ENDO-2,6-BIS(HYDROXYMETHYL)BICYCLO[3.3.0]OCTA-3,7-DIENE.

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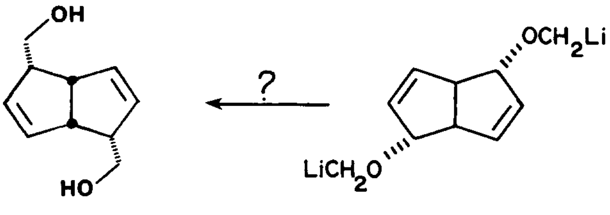
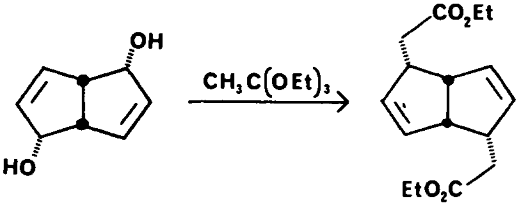
Attempted anionic bis[2,3] sigmatropic rearrangement of i was circumvented by an S_Ni' displacement producing tricyclic ether 6. n-Butyllithium and lithium methanol dianion readily attacked 6 in an S_N2' fashion to afford alcohol 7 and the title compound, respectively.

For a project in this laboratory aimed at the synthesis of dodecahedrane,[1] we needed to prepare cis,endo-2,6-bis(hydroxymethyl)bicyclo[3.3.0]octa-3,7-diene 1. The successful transformation of cis,endo-diol 2 to diester 3 via bis-orthoester Claisen rearrangement[2] led us to consider an approach to diol 1 involving a bis[2,3] sigmatropic rearrangement. The recently described method of Still and Mitra seemed ideally suited for this transformation,[3,4] although no example was cited using cyclopentenol-derived systems.



1



2

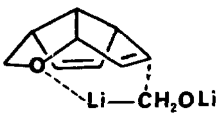
3

The *bis*-tri-*n*-butylstannylmethyl ether **4a**[5] was obtained in 95% yield by alkylation of the *bis*-potassium alkoxide of **2a** (KH, THF, 0°C, 1 h; 22°C, 2 h) with iodomethyltri-*n*-butyltin[6] (36 h, 22°C). Addition of **4a** to 2.0 eq. of *n*-butyllithium (THF, -78°C, 15 min) resulted in complete destannylation, as evidenced by the isolation of dimethyl ether **5** upon quenching at -78°C. However, on warming the solution of the intermediate, dianion *i* did not undergo an anionic bis-[2,3] sigmatropic reaction as expected, but gave instead the tricyclic ether **6a** (-30°C, 36 h) in 70% isolated yield.[7] The formation of **6a** evidently takes place by proton abstraction from the solvent to give *ii* which then undergoes rapid $S_N i'$ displacement of methoxide.

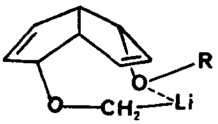
This mechanism is supported by deuterium labeling experiments. Diol **2b** was prepared by sodium borodeuteride/cerous chloride reduction[8] of bicyclo[3.3.0]octa-3,7-diene-2,6-dione[9] (2 h, -15°C; 100% 8:1 *cis*,*endo*:*trans* mixture; 40% *cis*, *endo* isolated). Conversion to **4b** followed by addition of **4b** to 2.0 eq. of *n*-butyllithium (45 min, -78°C; 22 h, -30°C) afforded **6b**, the ^{1}H NMR of which showed the absence of signals at δ 5.75 and δ 4.92 when compared to **6a**. This interpretation is further born out by the expedient preparation of **6a**, in which only 1 eq. of *n*-butyllithium is employed (ether, -78°C, 1 h; 6 h, 0°C; 8 h, 22°C; 75%).[10]

It was found that alcohol **7**, a ubiquitous minor product in reactions of **4** with excess *n*-butyllithium (>2 eq.), could be prepared cleanly from tricyclic ether **6a** with *n*-butyllithium in 80% yield (ether, 0°C, 3 h). The stereochemistry of the butyl substituent in **7** could not be extracted from ^{1}H NMR decoupling experiments. However, when **6a** was reacted with methanol dianion[11,12] ("LiCH$_2$OLi", ether, 2 h 0°C), only one product, diol **1**, was isolated in 47% yield after chromatography to remove tetrabutyltin. Consistent with the symmetrical nature of **1**, only five signals were observed in its ^{13}C NMR spectrum.[7] The diacetate of **1** (acetic anhydride, pyridine, CHCl$_3$, reflux 1 h, 100%) displayed a single peak for the acetate methyl groups in its high resolution ^{1}H NMR spectrum.[7] When the crude reaction mixture is treated with acetic anhydride, diacetate **8** is obtained directly in 49% yield, accompanied by a small amount (<2%) of another unidentified acetate, possibly the isomeric *trans* diacetate.

The remarkable *endo* stereoselectivity may be accounted for by a six-membered transition state *iii* in which the organolithium reagent is chelated to the ether oxygen. Lithium-oxygen chelation may also be responsible for the exceptionally facile $S_N i'$ displacement in *ii*.

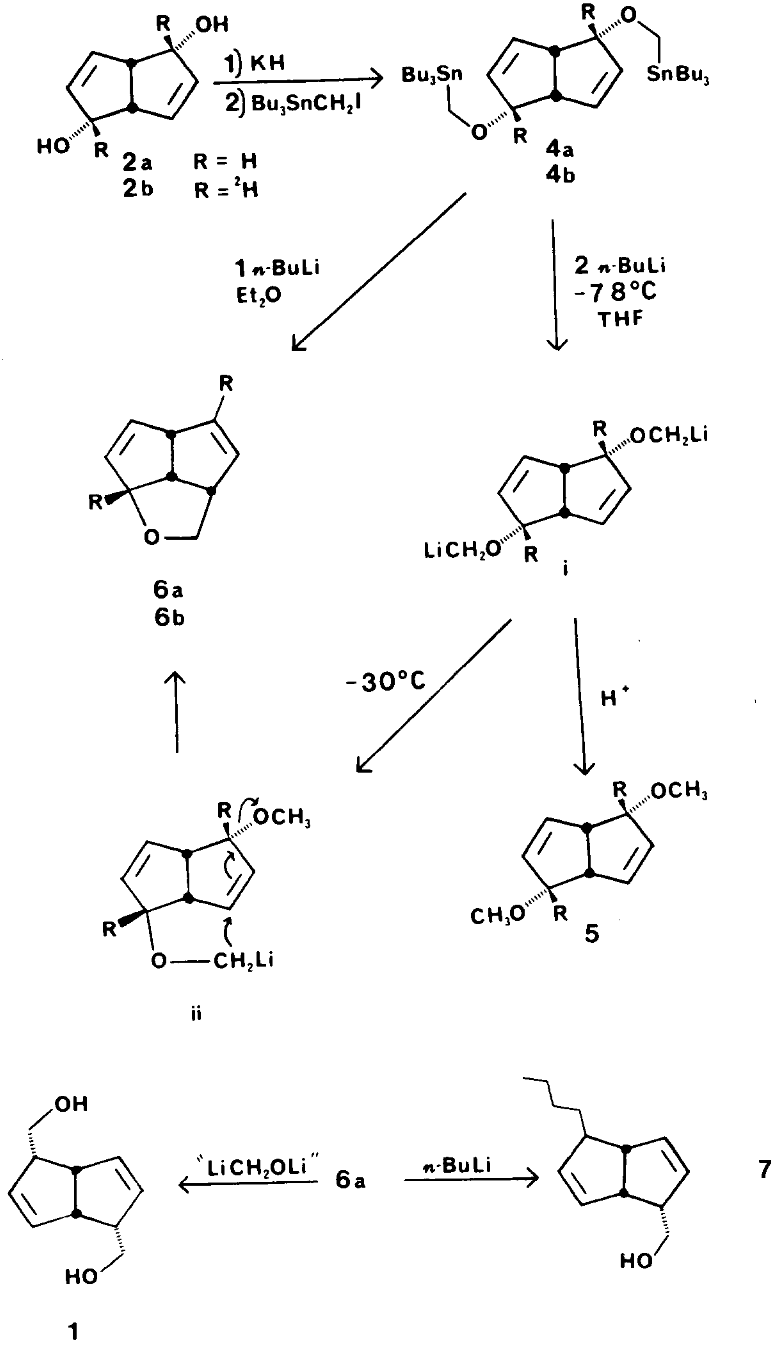


iii



ii

The use of diol **1** in our approach to dodecahedrane is currently being pursued.


R
OH
HO
R
2a R = H
2b R = ²H
1) KH
2) Bu₃SnCH₂I
Bu₃Sn
O
R
O
SnBu₃
4a
4b
1 n-BuLi
Et₂O
2 n-BuLi
-78°C
THF
R
R
O
6a
6b
R
OCH₂Li
LiCH₂O
R
i
-30°C
H⁺
R
OCH₃
R
O
CH₂Li
ii
R
OCH₃
CH₃O
R
5
OH
HO
1
"LiCH₂OLi"
6a
n-BuLi
HO
7

References and Notes

1. Taken from the Ph.D. Thesis of T. A. Monego, Michigan State University, September, 1982.
2. Farnum, D. G.; Hagadorn, A. A. III *Tetrahedron Lett*. **1975**, 3987.
3. Still, W. C.; Mitra, A. *J. Am. Chem. Soc*. **1978**, *100*, 1927.
4. Still, W. C.; McDonald, J. H. III; Collum, D. B.; Mitra, A. *Tetrahedron Lett*. **1979**, 593.
5. All new compounds exhibited satisfactory ^{1}H NMR, IR and MS data.
6. Still, W. C. *J. Am. Chem. Soc*. **1979**, *100*, 2226.
7. **6a**: ^{1}H NMR (CDCl$_3$, 250 MHz) δ 5.98 (1H, dd, J = 6, 2 Hz), 5.75 (1H, dt, J = 6, 2 Hz), 5.68 (1H, dt, J = 6, 2H Hz), 5.50 (1H, dt, J = 6, 2 Hz), 4.92 (1H, dd, J = 8, 2 Hz), 3.93 (1H, dd, J = 9, 7 Hz), 3.68 (1H, dd, J = 9, 4 Hz), 3.64 (1H, m), 3.49 (1H, q, J = 8 Hz), 3.26 (1H, m); ^{13}C NMR (CDCl$_3$, 62.8 MHz) 138.76, 134.41, 131.29, 129.59, 87.95, 74.95, 57.01, 50.75, 50.63, ppm. **6b**: ^{1}H NMR (CDCl$_3$, 250 MHz) δ 5.96 (1H, dd, J = 6, 2 Hz), 5.67 (1H, dd, J = 6, 2 Hz), 5.49 (1H, br s), 3.93 (1H, dd, J = 9, 7 Hz), 3.67 (1H, dd, J = 9, 4 Hz), 3.63 (1H, m), 3.49 (1H, t, J = 8 Hz), 3.24 (1H, m). **7**: ^{1}H NMR (CDCl$_3$, 250 MHz) δ 5.71 (1H, m), 5.62 (2H, AB q, J = 6 Hz, Δν = 11 Hz), 3.72 (1H, dd, J = 10, 6 Hz), 3.68 (1H, dd, J = 10, 7 Hz), 3.45 (2H, m), 3.01 (1H, m), 2.74 (1H, m), 1.35 (7H, m, includes OH), 0.89 (3H, br t). **1**: ^{1}H NMR (CDCl$_3$, 250 MHz) δ 5.82 (2H, dt, J = 6, 2 Hz), 5.61 (2H, dt, J = 6, 2 Hz), 3.74 (2H, dd, J = 11, 7 Hz), 3.68 (2H, dd, J = 11, 8 Hz), 3.58 (2H, m), 3.04 (2H, m), 1.50 (2H, br s, OH); ^{13}C NMR (CDCl$_3$, 62.8 MHz), 131.67, 131.35, 63.72, 51.22, 50.48 ppm. **8**: ^{1}H NMR (CDCl$_3$, 250 MHz) δ 5.69 (2H, dt, J = 6, 2 Hz), 5.55 (2H, dt, J = 6, 2 Hz), 4.10 (2H, dd, J = 11, 7 Hz), 3.99 (2H, dd, J = 11, 9 Hz), 3.56 (2H, m), 3.13 (2H, m), 2.08 (6H, s); ^{13}C NMR (CDCl$_3$, 62.8 MHz) 170.99, 131.47, 130.82, 65.34, 50.52, 47.48, 20.99 ppm.
8. Luche, J. L. *J. Am. Chem. Soc.* **1978**, *100*, 2226.
9. Hagadorn, A. A. III; Farnum, D. G. *J. Org. Chem*. **1976**, *42*, 3765.
10. *n*-Butyllithium has been observed to cleave *n*-alkyl allyl ethers in refluxing hexane: Broaddus, C. D. *J. Org. Chem*. **1965**, *30*, 4431.
11. Seebach, D.; Meyer, N. *Angew. Chem*. Int. Eng. Ed. **1976**, *15*, 438.
12. Prepared by the reaction of *n*-butyllithium with Bu$_3$SnCH$_2$OH (see Ref. 8).
13. We thank the Research Corporation for a special grant and Michigan State University for an All-University Research Initiation grant in partial support of this work.

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