

BORON ANNULATION: SYNTHESIS OF TRANS-DECALIN  
NATURAL PRODUCT SYNTHONS

Curtis J. Reichel and Thomas A. Bryson

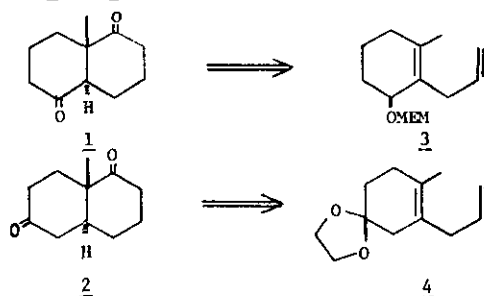
Department of Chemistry

University of South Carolina

Columbia, South Carolina 29208

**Abstract-** Boron annulation of olefins 3, 4 and 14 has afforded decalin synthons 1 and 2 and perhydrophenanthrone 15, respectively. The A, B ring juncture of 15 and the ring systems of 1 and 2 were found to be trans.

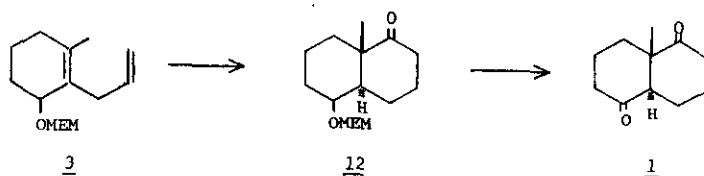
It is strategically attractive to assemble carbocyclic ring systems from olefins via a stereochemically sensitive boron hydride template, then replace the boron center with carbon.<sup>1</sup> In recent papers, we have disclosed the synthesis of steroids<sup>2,3</sup> and terpenoid compounds<sup>4</sup> prepared by application of stitching and riveting. In an effort to extend the precision of stereochemical predictions for this annulation process, we sought to prepare classical decalin synthons employing dienes with one tetrasubstituted olefin. Two such systems, 1<sup>5</sup> and 2<sup>6</sup>, were antithetically viewed as being derived from dienes 3 and 4, respectively.



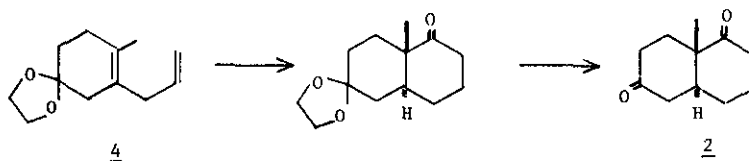
Diene 3 was prepared from 2-allyl-1,3-cyclohexanedione 5<sup>7</sup> (Scheme I). Dienone 7 was synthesized from the vinylogous ester 6<sup>7</sup> by Grignard addition of methyl magnesium iodide followed by acid workup. Reduction of the ketone to produce alcohol 8<sup>8</sup> and protection as the  $\beta$ -methoxyethoxymethyl (MEM) ether<sup>9</sup> afforded diene 3. Diene ketal 4 was prepared from 6-methoxy-1-tetralone 9 as shown on Scheme II. Reduction of the ketone<sup>8</sup> moiety followed by dehydration gave olefin 10. Ozonolysis<sup>10</sup> of the olefin produced a diacid which was reduced<sup>8</sup> stepwise to a diol and then to alcohol 11, (hydrogenolysis).<sup>11</sup> Birch reduction<sup>12</sup> of the aromatic ring,

ketal exchange<sup>13</sup>, and dehydration of the alcohol moiety by the method of Grieco<sup>14</sup> produced diene ketal 4.

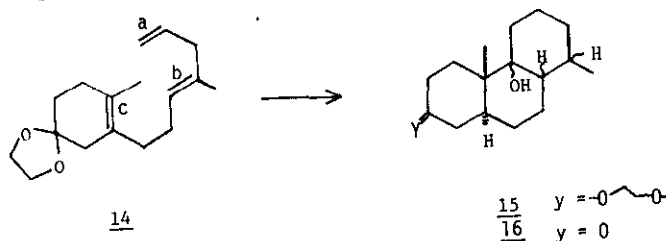
Annulation of diene 3 (hexylborane/ $\alpha,\alpha$ -dichloromethyl methyl ether)<sup>15</sup> yielded a ketone (12) whose nmr spectra was complicated by an epimeric center at C-5. In order to circumvent this problem, the MEM ether was hydrolyzed<sup>9</sup> and the resulting alcohol oxidized<sup>16</sup> (Jones) to trans dione 1 [45% from 3; ir (CHCl<sub>3</sub>): 1720, 1715, cm<sup>-1</sup>;  $\delta_{\text{CDCl}_3}^{\text{TMS}}$  2.3-1.4(m,13H), 1.2 (s,3H); mp 66-67°C] which exhibited physical characteristics identical to literature values.<sup>5</sup> It is possible that the oxidation of 12 epimerized the C-9 hydrogen, but the well known mode of hydroboration and the position of the methyl groups (epimeric mixture,  $\delta_{\text{CDCl}_3}^{\text{TMS}}$  1.2 (s,3H)) would strongly suggest that this annulation process is specific for the trans ring junction.



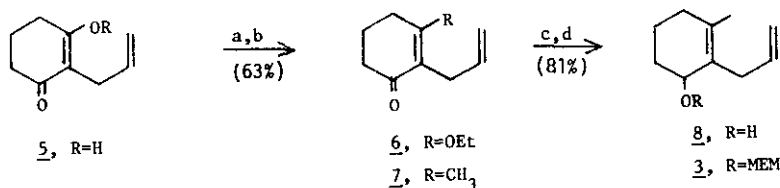
Annulation of diene 4 utilizing the same procedure as above, followed by removal of the ketal<sup>6</sup> produced the trans-dione 2 (50% from 4) which was identical in all respects to literature values<sup>6</sup> and an authentic sample.



For further prognostications relative to boron annulation, 11 was converted to triene 14, as shown on Scheme III. The substitution pattern on olefins a, b and c in 14 were designed to assure controlled inter- and intramolecular addition of BH<sub>3</sub> to olefins a, then b and finally c. Hydroboration (BH<sub>3</sub>-THF, 0°, THF, 3 hr), then riveting with  $\alpha,\alpha$ -dichloromethyl methyl ether (Li<sup>+</sup>OCET<sub>3</sub>, then H<sub>2</sub>O<sub>2</sub>, NaOH) give tricyclic system 15; [ir(film)3500 cm<sup>-1</sup>;  $\delta_{\text{CDCl}_3}^{\text{TMS}}$  0.8(s, 3H,C-10), 0.75 (d, 3H, JHz=4, C-14 methyl)] and 16 on hydrolysis of the ketal [ir(film)1710]. Although stereochemical analysis of this product is currently ongoing, the pmr chemical shift of the C-10 methyl group is indicative of an A-B ring trans juncture. The B-C ring junction and the C-14 methyl group

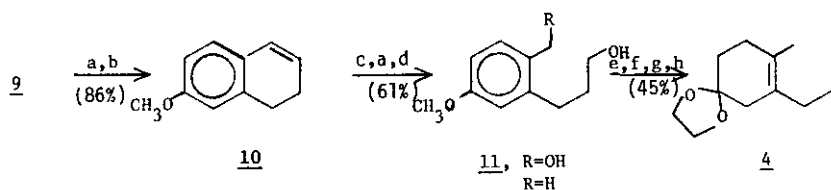


## SCHEME I



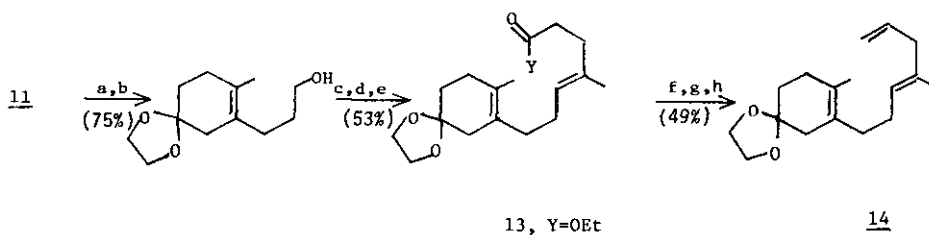
a. EtOH/TsOH/PhH; b.  $CH_3MgI$ , THF,  $0^\circ$ , then 20% HCl; c. LAH, THF,  $0^\circ$ ; d. MEMCl DMAP, Pyridine.

## SCHEME II



a. LAH, THF,  $0^\circ$ ; b. 1N HCl; c.  $O_3/H_2O_2-H_2O$ ; d.  $H_2, Pd/C$ , HCl ethanol; e.  $Na/NH_3/THF/ethanol$ ,  
 f.  $HOCH_2CH_2OH$ ,  $(HO_2C)_2$ ,  $PhCH_3$ ; g.  $o-NO_2PhSeCN$ ; h.  $\Delta$

## SCHEME III



a.  $Na/NH_3/THF/ethanol$ ; b.  $HOCH_2CH_2OH$ ,  $(HO_2C)_2$ ,  $PhCH_3$ ; c. PCC; d. 2-propenyl magnesium bromide,  
 ether,  $0^\circ$ , then  $NH_4Cl$ ; e. triethyl orthoacetate,  $\Delta$ ; f. LAH, ether,  $0^\circ$ ; g.  $o-NO_2PhSeCN$ ,  $PBu_3$ ,  
 THF, then  $H_2O_2$ , h.  $\Delta$ .

relative stereochemistry is presently undefined and is the object of current studies. The ease of formation of compounds 1, 2, and 14 with trans ring junctions has encouraged us to apply boron annulation to more challenging carbocyclic natural products.

Acknowledgement: This work was supported by the Public Health Service, GM-26820.

#### References

1. H. C. Brown, Organic Synthesis Via Boranes, Wiley-Interscience, 1975.
2. T. A. Bryson and W. E. Pye, J. Org. Chem., 1977, 42, 3214.
3. T. A. Bryson and C. J. Reichel, Tetrahedron Lett., 1980, 21, 2381.
4. C. F. Reichert, W. E. Pye, and T. A. Bryson, Tetrahedron, 1981, 37, 2441.
5. V. Prelog, W. Acklin, F. Schenker, B. Serdarevic, and P. Water, Helv. Chem. Acta, 1965, 48, 1725.
6. G. Bauduin and Y. Pietrasanta, Tetrahedron, 1973, 29, 4225.
7. R. B. Gammill, Ph.D. Dissertation, 1976, p. 104.
8. V. M. Micovic and M. L. J. Mihailovic, J. Org. Chem., 1953, 18, 1190.
9. E. J. Corey, R. L. Danheiser, S. Chandrasekaran, P. Siret, G. E. Keck, and J. Gras, J. Amer. Chem. Soc., 1978, 100, 8031.
10. M. I. Fremery and E. K. Fields, J. Org. Chem., 1963, 28, 2537.
11. R. E. Bowman, J. Chem. Soc., 1950, 325.
12. S. Danishefsky and P. Cain, J. Amer. Chem. Soc., 1975, 97, 5282.
13. L. F. Fieser and M. Fieser, "Reagents for Organic Synthesis", Vol 1, Wiley and Sons, N.Y., 1967, p. 191.
14. P. A. Grieco, M. Nishizawa, T. Oguri, S. D. Burke, and N. Marinovic, J. Amer. Chem. Soc., 1977, 99, 5773.
15. B. A. Carlson and H. C. Brown, Synthesis, 1973, 776.
16. D. J. Pasto and C. R. Johnson, "Organic Structure Determination", Prentice Hall, Englewood, California, 1969, p. 362.

Received, 10th September, 1981