SYNTHESIS OF CIS AND TRANS DECALINS BY BORON ANNULATION

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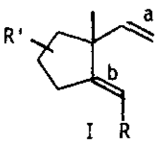
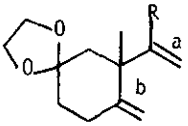
Abstract- Hydroboration and cyanidation of 1,4-diene 1 afforded bicyclic compounds 2 (trans) and 3 (cis). Boron annulation of diene 7 (R=CH_3) yielded cis and trans decalones. Simple and competitive hydroboration of 1,4-dienes 1 and 7(R=CH_3 and Sϕ) were analyzed for regio- and stereoselectivity.

We have begun an investigation to further extend boron annulation as a technique for carbocyclic synthesis[1]. The success of this procedure is dependent upon control of stereo and electronic factors of the participating olefins. Boron annulation with dienes of type I readily form trans-bicyclic ring systems due to (1) the distinct reactivity differences of olefin-a over-b with boron hydrides and (2) the intramolecular addition of boron and hydrogen to olefin b.[2] Recently we have prepared a series of prognosticative dienes (type II), the olefins of which were much closer in reactivity relative to hydroboration than in the type I system. It was hoped that by modifying the annulation diene, cis bicyclic ring systems would become available.



I

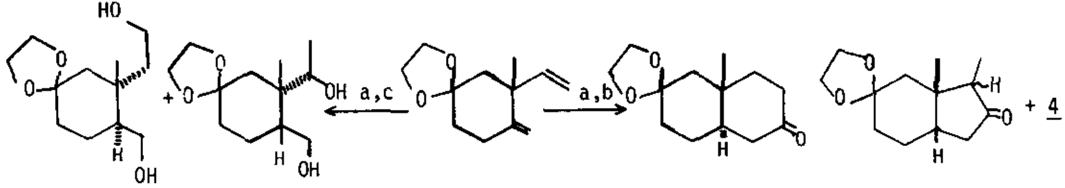
R=alkyl



II

R=H, alkyl, SPh

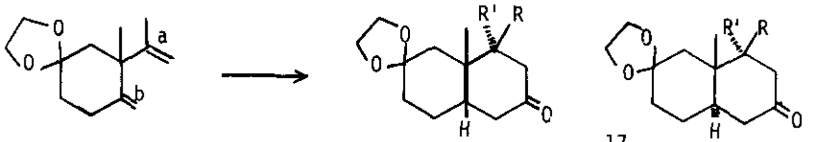
The initial experiments were directed at diene 1 that is readily available from Hagemanns ester as shown in Scheme I. Hydroboration[3] and cyanidation[4] (NaCN, TFAA, H_2O_2-NaOH) of 1 gave two ketonic products (2, 3)in the ratio of 2 to 5 (25% total yield) and a diol which was subsequently identified as 4 (22%). The minor isomer was identified as trans-decalone 2 by spectral means and comparison to an authentic sample.[5] The major isomer was presumed to be the monoketal of cis-hydrindanedione 3 based on ir ($\lambda_{max}^{CHCl_3}$: 1735 cm^{-1}) and pmr (δ_{CDCl}^{TMS} : 1.01-0.77 overlapping singlet and doublets). *Variation of the cyanidation procedures* (NaCN, $Ph\text{-}C\begin{smallmatrix}\nearrow O\\ \searrow Cl\end{smallmatrix}$, 8 hr, $NaOH\text{-}H_2O_2$) improved the yields of the ketonic products (50%) altering the 2 to 5 ratio to 3 / 2. Seemingly the cyanidation procedure leading to 2 is slower than for 3.[6] Supportive of this observation was the *isolation of decreasing amounts of diol 4 and no 5 from these latter cyanidation reactions*. The hydrindane structure (3) was assigned by hydroborating 1[3]. This yielded two isomeric diols 4 and 5 (3 / 1 respectively, 90% total). Diol 5 (and therefore hydrindane 3) could be assigned to the "cis"- series of compounds *due to the pmr differences relative to a comparison sample of* isomeric trans-diol 6 prepared by independent routes.[7]



4   5, β-H   6, α-H   1   2   3

a. $H_2B\text{-}R^3$, THF, $^-80° \rightarrow RT$; b. NaCN, TFAA, $H_2O_2\text{-}NaOH$; c. $H_2O_2/NaOH/H_2O$

The trans system-2 is formed from 1 by two possible reaction paths: (1) Attachment of H_2BR *to olefin-a first then intramolecular delivery of boron* hydride to olefin-b and/or (2) addition to the α-face of olefin-b, followed by addition to olefin-a at its terminus.[8] The cis-system must come from addition to the β face of olefin-b first, then addition to olefin-a to form the "preferred" 5-membered ring.[9]



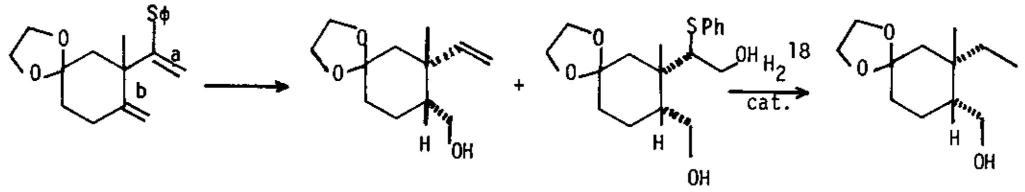
7, R=CH_3

8a, R'=CH_3, R=H(55%)[17]   8b, R'=CH_3, R=H(20%)

8c R'=H,R=CH_3(22%)   8d, R'=H,R=CH_3(3%)

cis/trans= 3/1

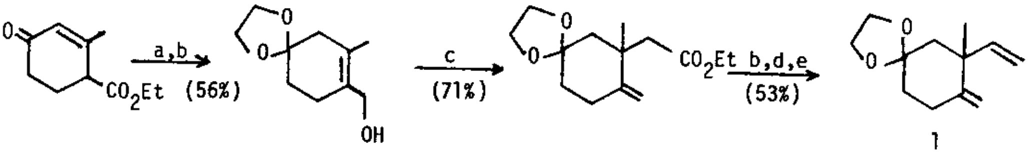
In order to form more cis-bicyclic compounds, *initial addition to olefin* b, *first must be* maximized. Therefore dienes 7 and 9, with varying substitution that would hinder or deactivate olefin a relative to b, was prepared by modifying the diene 1 preparation of Scheme I.[10] Hydroboration and/or boron annulation on *these modified dienes was conducted with reversal* of the cis, trans ratios observed with diene 1. Diene 7 (Scheme II) afforded all four of the expected decalin stereoisomers with the cis series predominating 3 to 1 (80% yield).[11] Diene 9 (R=SPh, Scheme II)[12] was observed to give some β-cleavage of the thiophenyl *group on hydroboration and* cyanidation. Rather than pursuing cyanidation or carbonylation on a mixture of boron containing intermediates, the simple hydroboration of 9 was analyzed. Reduction of all such hydroboration products (10 and 11) formed cis ketal 12.[13]



9 10 (67%) 11 (10%) 12

The relative competitiveness of olefins a and b in 1 and 7 were tested based on reactivity towards 9-BBN. In diene 1, pmr aliquots showed the ratio of addition to olefin-a relative to b of 3 to 1 which is consistent with the products found (vide supra). Where as in 7 the ratio of reaction of a to b was 1 to 3.

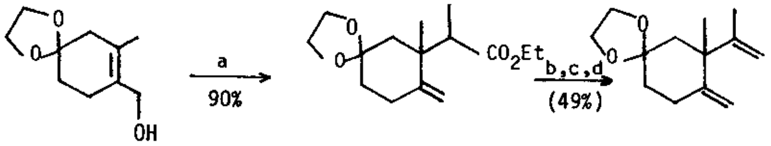
Scheme I



1

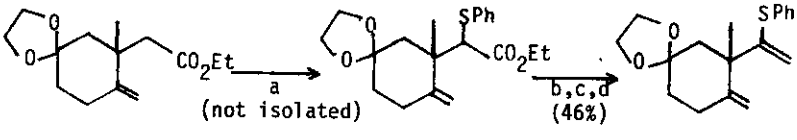
a. TsOH, PhH, $HOCH_2CH_2OH$, Δ; b. LAH, RT, ether; c. $CH_3C(OCH_2CH_3)_3$, Δ; d. NaH, $(CH_3)_2N\overset{S}{C}\text{-Cl}$,THF; e. 300°.

Scheme II



7, R= CH_3

a. $CH_3CH_2C(OCH_2CH_3)_3$, Δ; b. LAH, RT, ether; c. NaH, $(CH_3)_2N\overset{S}{C}\text{-Cl}$, THF; d. 300°.



7, R=Sϕ

a. Lithium isopropylcyclohexylamide, diphenyldisulfide; b. LAH, ether, RT;
c. PPh_3/CCl_4; d. potassium t-butyl alcohol.

The variation of substitution on olefin a in type II dienes predictably alters the regioselectivity of initial hydroboration. Once the initial hydroboration has occurred, the stereochemical outcome of the second hydroboration is determined. Thus *cis* or *trans* bicyclic systems can easily be formed with good stereoselectivity by controlling olefin substituents in cyclic systems. These initial successes have spurred us to attempt additional natural product synthesis by boron annulation.

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1. T. A. Bryson and C. J. Reichel *Tetrahedron Lett.*, 1980, **21**, 2381, T. A. Bryson, and W. E. Pye, *J. Org. Chem.*, 1977, **42**, 3214, C. F. Reichert, W. E. Pye, and T. A. Bryson, *Tetrahedron*, 1981, **37**, 2441; General reference, H. C. Brown, Organic Synthesis Via Boranes, Wiley-Interscience (1975).
2. Borane addition to olefin-a followed by intramolecular addition to olefin-b forces formation of the *trans*-ring junction in type I dienes.
3. Thexylborane dimethylsulfide complex, H. C. Brown, A. K. Mandal, and S. U. Kulkarni, *J. Org. Chem*, 1977, **42**, 1392.
4. Cyanidation, *A. Pelter, K. Smith, M. G. Hutchings, and K. Rowe*, *J. Chem. Soc., Perkin I*, 1975, 129.
5. A comparison sample of *trans*-monoketal-2 was prepared from the monoketal of 2-methyl-1,4 cyclohexandione[14] following the procedure of R. K. Mathur and A. S. Rao, *Tetrahedron*, 1967, **23**, 1259. For a new preparation of the monoketal of 2-methyl-1,4-cyclohexanedione see reference 15 below.
6. Separation was achieved by chromatography on silica gel, hexane-ether elution.
7. *Trans*-diol 4 is available from hydroboration[3] and peroxide oxidation of 1-ethenyl-5,5-(ethylenedioxy)-2-(hydroxymethyl)-1-methylcyclohexane, see: T. Kametani, M. Tsubuki, and H. Nemoto, *J. Org. Chem.*, 1980, **45**, 4391. *Trans*-diol 6 was prepared from the acetate derivative of the above compound via oxymercuration using the method of H. C. Brown, and W. J. Hammer, *J. Amer. Chem. Soc.*, 1967, **89**, 1522.
8. As in type I dienes, if initial hydroboration occurs on olefin-a or the α face of olefin-b in 1 then ring strain of the intramolecular addition to the other olefin requires formation of a *trans*-boradecalin.
9. Hydroboration of the β-face of olefin-b in 1, provides enough degrees of freedom so that olefin-a can add boron through a preferred 5-membered ring, yielding *cis*-borahydrindanes.
10. Diene-7 was prepared analogous to diene 1, Scheme I, using triethyl orthoproprionate in place

of triethyl orthoacetate. Diene 9 was prepared by sulfenylating the ketal ester of Scheme I according to the method of Trost[16] followed by reduction (LAH) and elimination; see Scheme II.

11. Comparison samples of trans-decalins 8b and 8c were prepared from the 1,α-methyl-$\Delta^{4,5}$-8,8-(ethylenedioxy)-3-octalone and 1,β-methyl-$\Delta^{4,5}$-8,8-(ethylenedioxy)-3-octalone, respectively, using the methods of R. M. Coates and J. E. Shaw, *J. Amer. Chem. Soc.*, 1970, **92**, 5657 and C. J. V. Scanio and R. M. Starrett, *J. Amer. Chem. Soc.*, 1971, **93**, 1539. Cis-octalone 8a was prepared from 1,α-methyl-$\Delta^{4,5}$-8,8-(ethylenedioxy)-3-octalone[16] by hydrogenation (Pd/C).

12. Removal of aliquot after hydroboration showed no vinyl protons. Addition of sodium hydroxide and hydrogen peroxide caused elimination of the thiophenyl group forming the monosubstituted olefin 10.

13. The major product of hydroboration is olefinic alcohol 10 which is isomeric to the trans structure prepared by T. Kametani, et. al., reference 7. Raney Nickel reduction of 11 gave the same product as catalytic hydrogenation of 10.

14. S. A. Navang and P. C. Dutta, *J. Chem. Soc.*, 1960, 2842; D. J. Goldsmith and I. Sakano, *J. Org. Chem.*, 1976, **41**, 2095.

15. The monoketal of 2-methyl-1,4-cyclohexanedione was prepared from 1-methoxy-5-methyl-1,4-cyclohexadiene by ketalization (benzene, HO_2CCO_2H, ethylene glycol), hydroboration (BH_3, THF, H_2O_2-NaOH)[1], and then PCC oxidation.

16. B. M. Trost, T. N. Salzmann, and K. Hiroi, *J. Amer. Chem. Soc.*, 1976, **98**, 4887; B. M. Trost, K. Hiroi, and S. Kurozumi, *ibid.*, 1975, **97**, 438.

17. Ratio of products, total yield was 80%.

18. Compounds 10 and 11 were separated and converted to 12, 10 with H_2-Pd/C and 11 with H_2-Raney Nickel.

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