TILDEN LECTURE*

Carbon–Carbon Bond Formation Involving Boron Reagents

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1 Introduction

The uses of boron reagents in organic synthesis are so various and the subject so vast that it is impossible to cover all aspects in a single lecture. In Figure 1, are listed some of the topics that are being omitted, each of which is interesting and useful. Some, such as boron reagents as reductants are worthy of many lectures and their omission simply reflects the organic chemist's abiding and necessary interest in the central theme of the efficient welding together of carbon frameworks.

TOPICS OMITTED

1. Boron reagents as reductants.
2. Boron reagents as protecting groups.
3. The preparation of organoboranes.
4. Formation of O—C, N—C, Hal—C, S—C and Metal—C bonds.
5. The photochemistry of organoborates.

Figure 1

The themes that will be discussed are summarized in Figure 2. Although, for convenience, the topics are labelled separately they interact with each other and their use in tandem can lead to unique synthetic routes.

2 Electrocyclic Reactions

The basis of these reactions is summarized in Figure 3, in which X can be CR_2, NR, or O, and the double or triple bond may be C=C, C=O, C=N, C≡C—Z, or C≡N. [In the Figures that follow a 'thick' bond denotes a new

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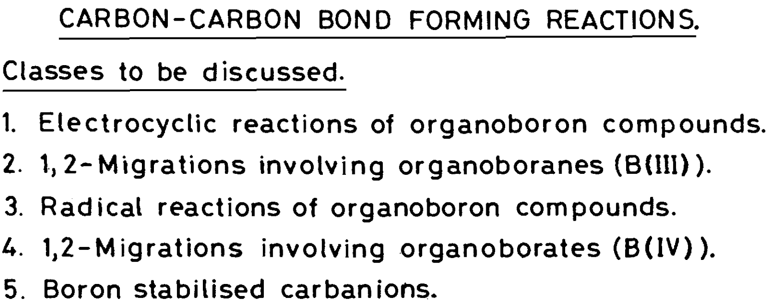
*First presented at a meeting of the Perkin Division of the Royal Society of Chemistry at the Scientific Societies' Lecture Theatre, London, on 15 December 1981.



CARBON-CARBON BOND FORMING REACTIONS.

Classes to be discussed.

1. Electrocyclic reactions of organoboron compounds.
2. 1,2-Migrations involving organoboranes (B(III)).
3. Radical reactions of organoboron compounds.
4. 1,2-Migrations involving organoborates (B(IV)).
5. Boron stabilised carbanions.

Figure 2

carbon–carbon bond made in the reaction. Wedged and dashed bonds retain their usual significance.]

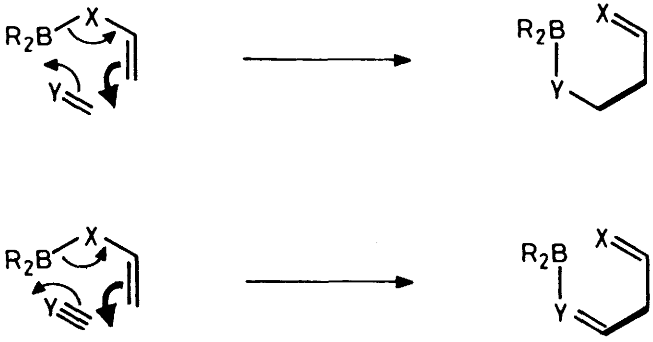


Figure 3

A. Allylboranes.—The usefulness of allylboranes can be diminished by permanent allyl migrations, which can not only lead to mixtures of the type $=B-CR_2CH=CH_2$ and $=B-CH_2CH=CR_2$ but also undermine the configurational identity of a double bond. This can be overcome in three ways: (*a*) by substituting at boron with substituents (NR_2, OR) capable of π back-donation,[1] (Figure 4), (*b*) by complexing with amines,[2] and (*c*) by large steric interactions, as with 9-BBN-allylboranes.[2]

The insertion reactions of allylboranes have been extensively studied.[3,4] Examples from a wealth of chemistry are shown on Figures 5 and 6. In Figure 5

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[1] K. G. Hancock and J. D. Kramer, *J. Organomet. Chem.*, 1974, **64**, C29, *cf. J. Am. Chem. Soc.*, 1973, **95**, 6463.

[2] G. W. Kramer and H. C. Brown, *J. Organomet. Chem.*, 1977, **132**, 9.

[3] B. M. Mikhailov, *Pure Appl. Chem.*, 1974, **39**, 505—523.

[4] B. M. Mikhailov, *Sov. Sci. Rev., Sect, B, Chem. Rev.*, 1980, 283—355.

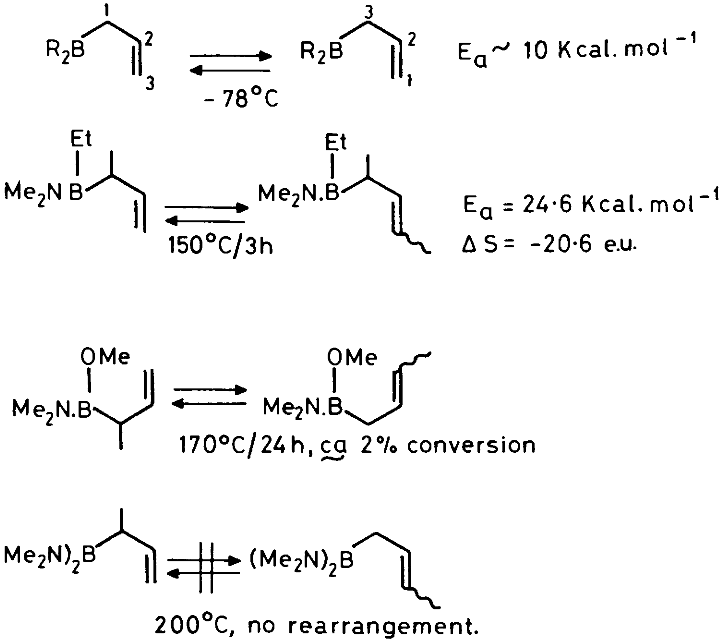

Figure 4

the first intermolecular insertion reaction is followed by a second intramolecular insertion at higher temperature. Finally, at yet higher temperatures, a reorganization ensues, which gives borabicyclic compounds with great ease. The reaction is general, and when X = R, the temperatures required for the second and third rearrangements are lowered.

A similar reaction occurs with allenes, and by suitable manipulation (Figure 6), boradamantane is readily produced from allene and triallylborane. Substituted allenes yield the corresponding boradamantanes. By gentle processes, which will be illustrated later, the boron atom can be replaced by carbon, thus giving rise to unusual but rational syntheses of difficultly available carbocycles.

Benzylboranes behave similarly to allylboranes[5] (Figure 7) with the happy limitation that, due to a ready prototropic shift, the reaction proceeds only to the first stage, giving rise to the equivalent of pure *ortho*-substitution.

This situation can be induced more generally by use of a dialkyl allylborane[6] (Figure 8). Of course there are very many variations on this general theme one such, leading to a 1,3-diketone synthesis is shown in Figure 9.[7]

[5] B. M. Mikhailov, Y. N. Bubnov, S. A. Korobeinikova, and S. I. Frolov, *J. Organomet. Chem.*, 1971, **27**, 165.

[6] B. M. Mikhailov, Y. N. Bubnov, and S. A. Korobeinikova, *Izv.Akad.Nauk. SSSR, Ser Khim.*, 1970, 2631; *J.Prakt.Chem.*, 1970, **312**, 998.

[7] V. A. Dorokhov and B. M. Mikhailov, *Dokl.Akad.Nauk SSSR, Ser Khim.*, 1969, **187**, 1300, *Chem. Abstr.*, 1969, **71**, 124551r.

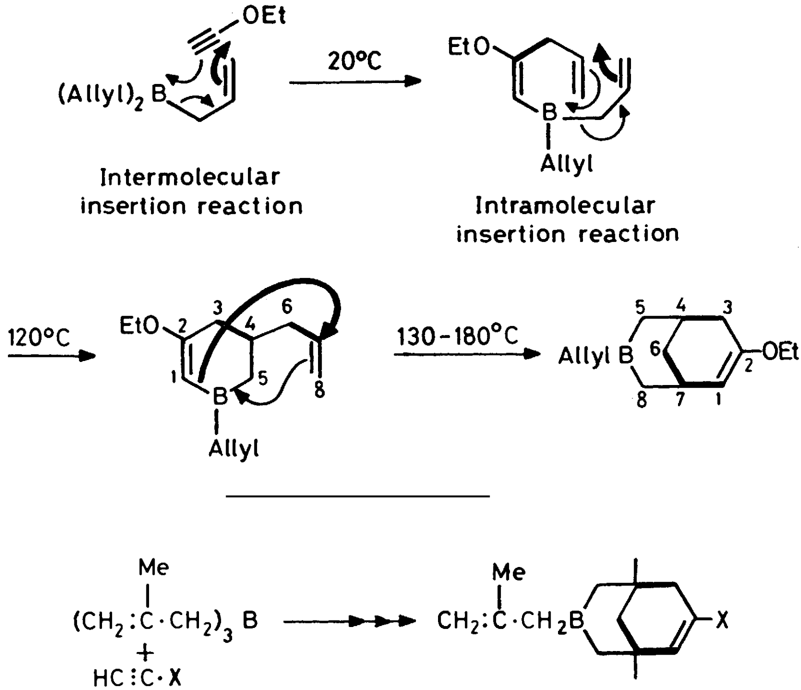

Figure 5

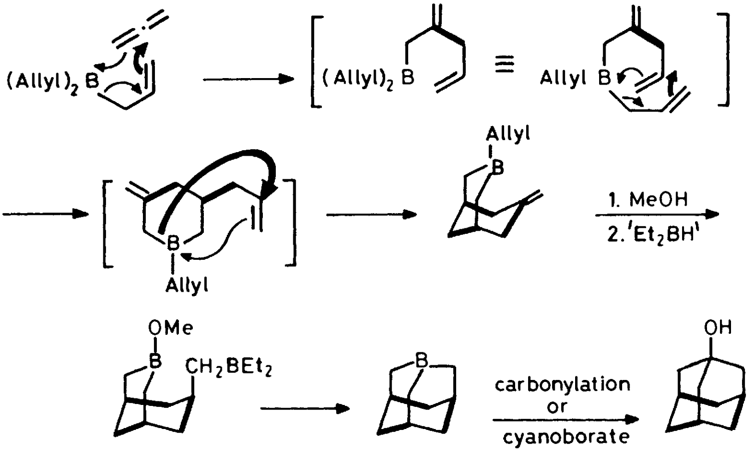

Figure 6

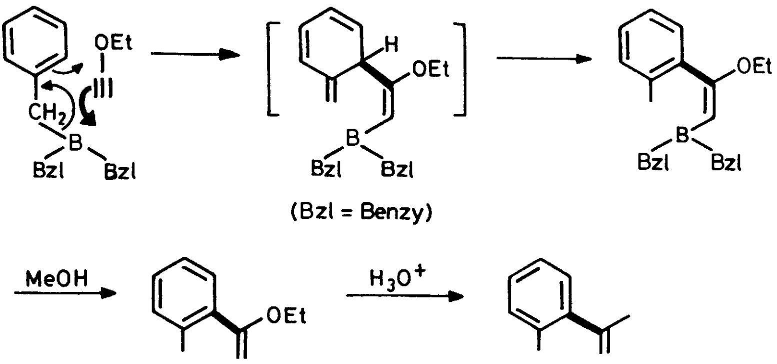

Figure 7

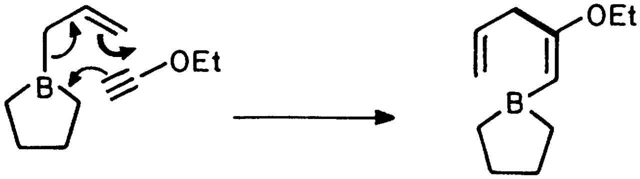

Figure 8

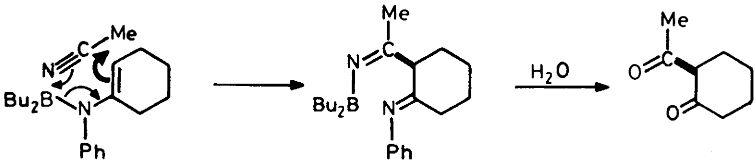

Figure 9

The known cyclic insertion reactions of aldehydes with allylboranes have been combined with knowledge of the configurational stability of dialkoxy- and diamino-allylboranes to produce enantio- and stereo-selective syntheses that proceed in high yield in mild conditions. Figure 10 shows the general process, of which three examples (*a*)[8], (*b*)[9], and (*c*)[10] are given in Figure 11.

Of course ozonolysis of the alkenes produces yields of carbonyl compounds that would otherwise require synthesis by highly selective aldol condensations.

[8] T. Herold, U. Schrott, and R. W. Hoffmann, *Chem. Ber.*, 1981, **114**, 359.

[9] R. W. Hoffmann and W. Ladner, *Tetrahedron Lett.*, 1979, 4653.

[10] R. W. Hoffmann and B. Kemper, *Tetrahedron Lett.*, 1980, 4883.

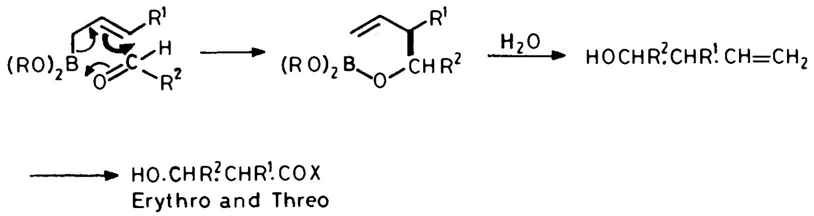

Figure 10

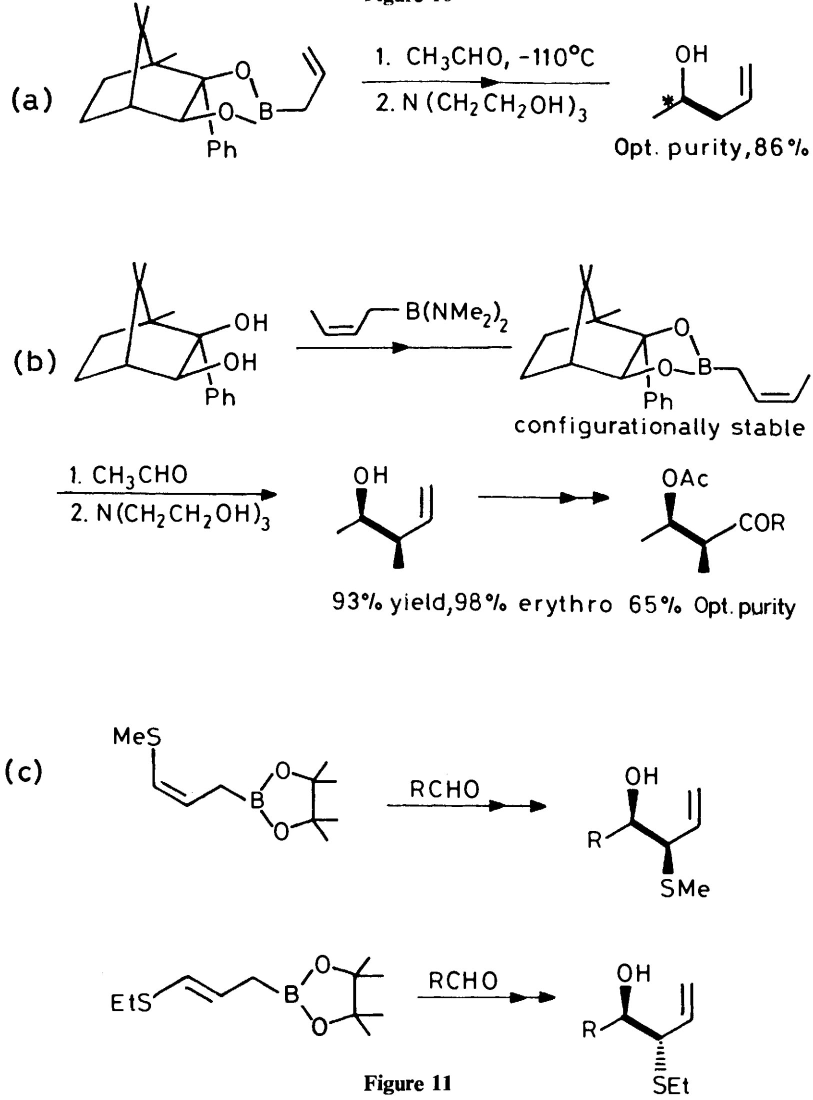

Figure 11

These, and other reactions to be discussed, proceed *via* well defined transition states[11] that are particularly tight due to the short B—O bond (Figure 12).

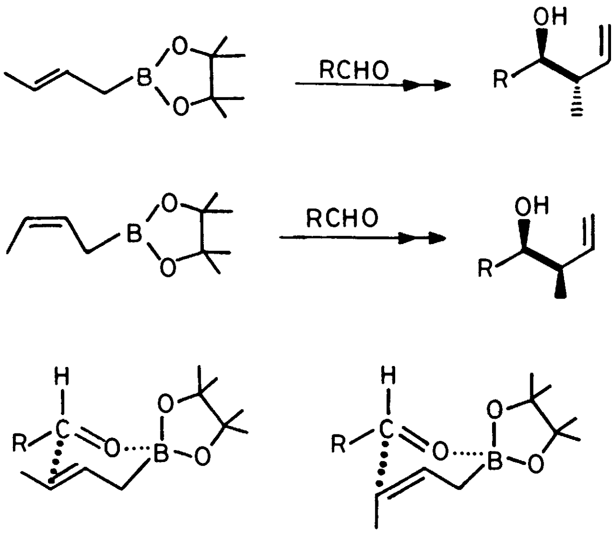

Figure 12

B. Vinyloxyboranes.—These are well defined and readily available compounds[12] that do not suffer from the danger of allylic rearrangement and also undergo electrocyclic reactions. The contrast between the reactions of vinyloxyboranes and vinyloxysilanes is shown in Figure 13.[13] Clearly the borane is not acting as a simple enolate derivative, but instead is undergoing an electrocyclic reaction analogous to those of allylboranes. Once more an electrocyclic reaction involving a rigid transition-state allows control of stereochemistry in the synthesis of aliphatic systems.

The precise organoborane used can be important (Figure 14) as, when the vinyloxyborane is produced by an equilibrium reaction, the bulk of the groups can control the stereochemistry of the double bond and hence the relative stereochemistry of the product.[14]

Ketene acetals and thioacetals[15] (Figure 15) also undergo the same type of reaction leading directly to important intermediates on the route to the

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[11] R. W. Hoffmann and H. J. Zeiss, *J. Org. Chem.*, 1981, **46**, 1309.

[12] R. Köster and W. Fenzl, *Angew. Chem., Int. Ed. Engl.*, 1968, 7, 735.

[13] S. Kuwajima, M. Kato, and A. Mori, *Tetrahedron Lett.*, 1980, 4291.

[14] D. E. van Horn and S. Masamune, *Tetrahedron Lett.*, 1979, 2229.

[15] M. Hirame, D. S. Garvey, L.D.-L. Lu, and S. Masamune, *Tetrahedron Lett.*, 1979, 3937.

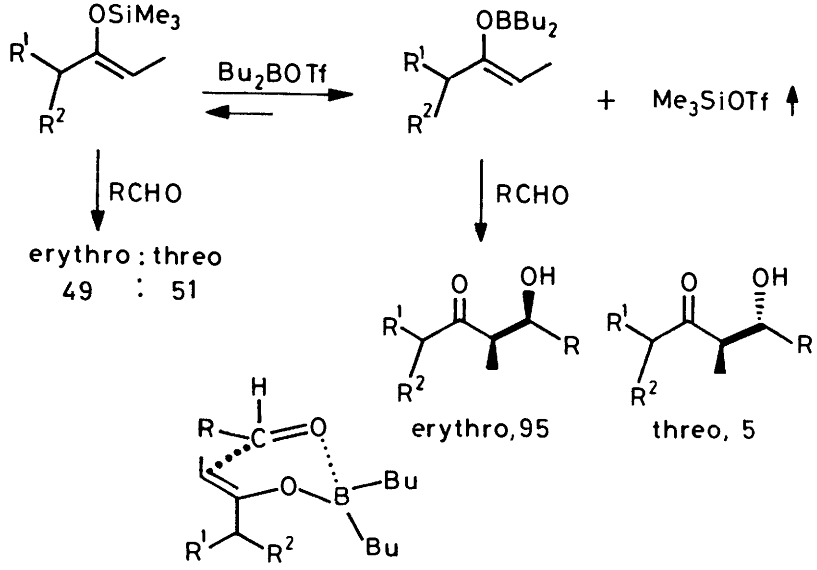


Figure 13

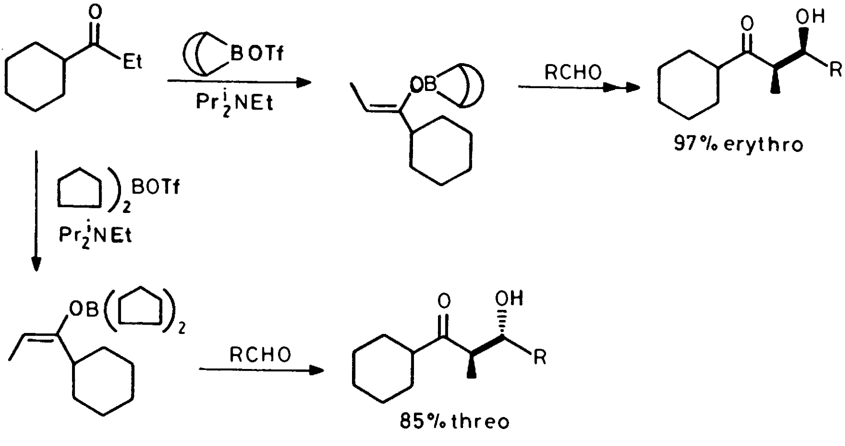
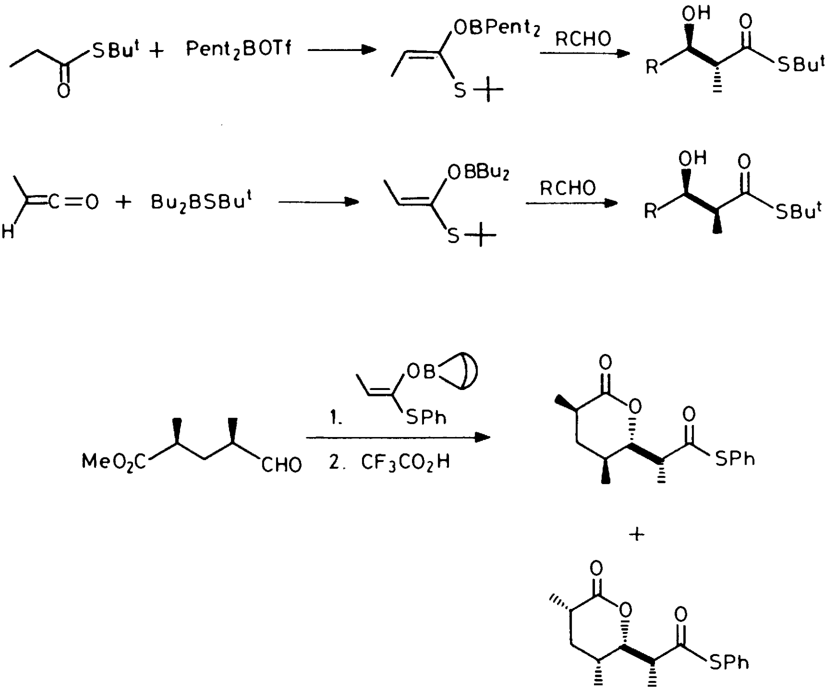


Figure 14

production of macrolide antibiotics, perhaps the most active field of current synthetic effort.

The enantio- and stereo-selectivity of the reactions has recently resulted in a



Two isomers only

Figure 15

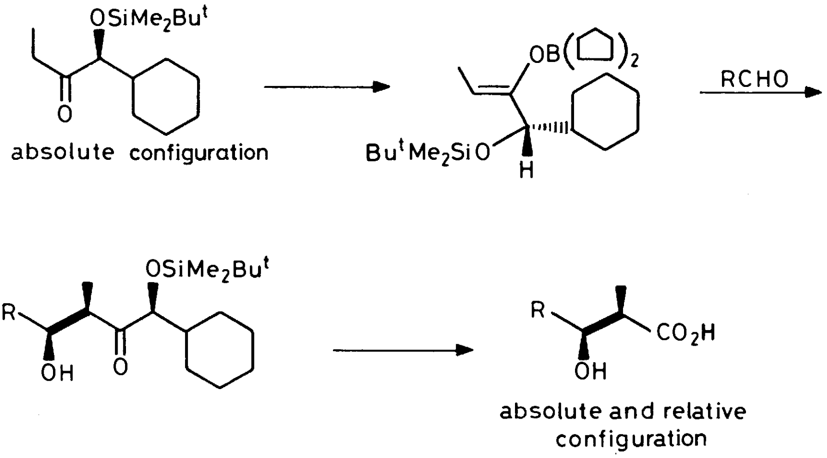


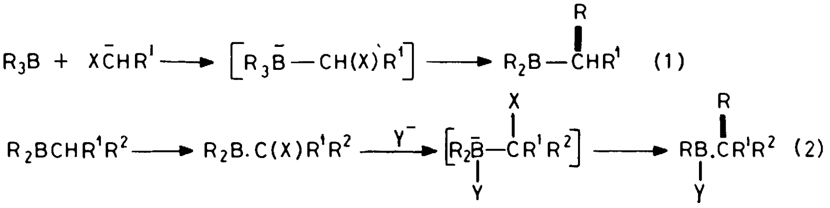
Figure 16

synthesis of 6-deoxyerythronolide;[16] a portion of this synthesis is shown on Figure 16.

The stereochemical control in the build up of highly functionalized aliphatic systems effected by the use of electrocyclic insertion reactions of allyl- and vinyl-oxyboranes is unique and its importance in organic synthesis, large already, is rapidly growing. Vinyloxyboranes can also be advantageously used as simple enolates for halogenation and alkylation (ref. 17, p. 920).

3 1,2-Migrations of Organoboranes

If a transiently four-covalent boron atom bearing an organyl group is adjacent to an electron deficient carbon atom or one bearing a leaving group, then 1,2-migration of the organyl group from boron to carbon can occur. The migration most frequently proceeds with retention of configuration of the migrating group and therefore any stereochemistry built in by, say hydroboration, is retained in the product borane. There are several ways of attaining the situation leading to migration, perhaps the most general being shown in equations 1 and 2 of Figure 17. Equation 1 illustrates the reaction of a triorganylborane with a carbenoid *i.e.* an anion bearing an appropriate leaving group, whilst equation 2 shows α-substitution of an organoborane followed by migration induced by nucleophilic attack on boron.[17]



$$R_3B + X\bar{C}HR^1 \longrightarrow \left[R_3\bar{B}-CH(X)R^1\right] \longrightarrow R_2B-\overset{R}{C}HR^1 \quad (1)$$

$$R_2BCHR^1R^2 \longrightarrow R_2B.C(X)R^1R^2 \xrightarrow{Y^-} \left[R_2\underset{Y}{\bar{B}}-\overset{X}{C}R^1R^2\right] \longrightarrow R\underset{Y}{B}.\overset{R}{C}R^1R^2 \quad (2)$$

Figure 17

There are many examples of equation 1, including the use of anions derived from α-halocarbonyl compounds [18a] and α-halonitriles[18b] (Figure 18). It should be noted that the intermediate organylboranes may not have the exact structures shown owing to the possibility of oxyallylborane rearrangement or its equivalent. An example showing a double alkylation of a dihalonitrile[19] is shown and also the direct production of a carboxylic acid in which phenoxide acts as a leaving group.[20] The use of alkyl-9-BBN derivatives is successful in both types

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[16] S. Masamune, W. Choy, F. A. J. Kerdesky, and B. Imperiali, *J. Am. Chem. Soc.*, 1981, **103**, 1566.

[17] A. Pelter and K. Smith, 'Comprehensive Organic Chemistry' Vol. 3, ed. D. N. Jones, Pergamon Press, Oxford, 1979, p. 791—904.

[18] (*a*) H. C. Brown, H. Nambu, and M. M. Rogić, *J. Am. Chem. Soc.*, 1969, **91**, 6852. (*b*) H. C. Brown, H. Nambu, and M. M. Rogić, *ibid.*, 1969, **91**, 6854.

[19] H. Nambu and H. C. Brown, *J. Am. Chem. Soc.*, 1970, **92**, 5790.

[20] S. Hara, K. Kishimura, and A. Suzuki, *Tetrahedron Lett.*, 1978, 2891.

of reaction, so allowing full utilization of the alkyl groups.[21] As compared with alkylations of enolate anions with alkyl halides or their equivalents, reactions using organoboranes have the advantage of allowing arylation, vinylation, and alkylations with groups such as cyclohexyl and 2-norbornyl that are resistant to *S*N2 displacement but migrate readily with retention of configuration.

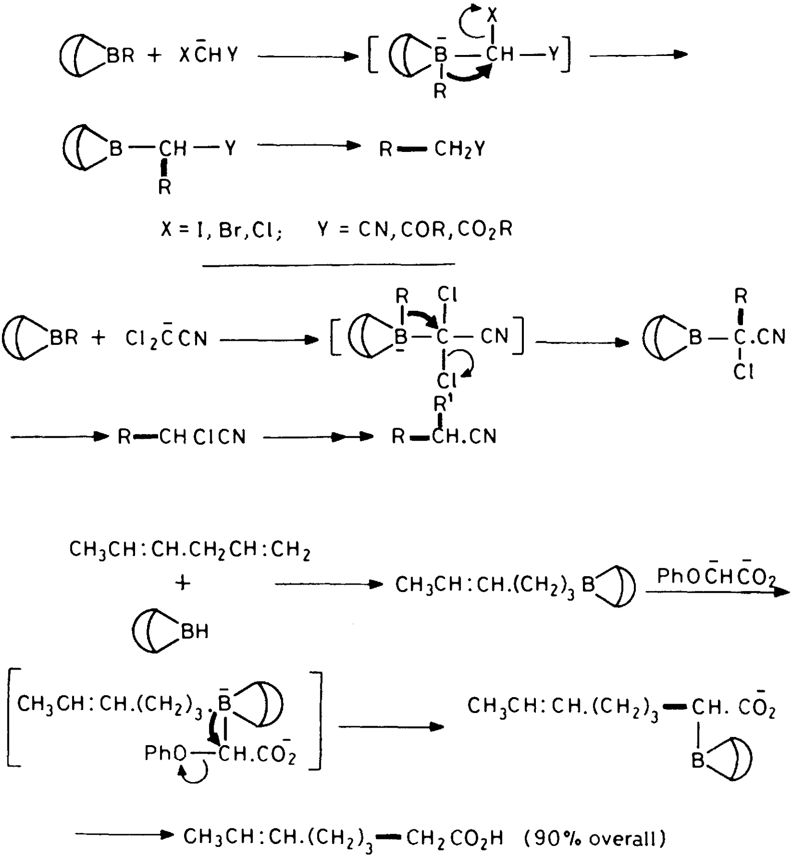

Figure 18

Use of the anion from dichloromethoxymethane (Figure 19) allows three migrations to proceed with even very hindered alkyl groups,[21] whilst use of alkoxydialkylboranes yields ketones.[22]

[21] H. C. Brown and B. A. Carlson, *J. Org. Chem.*, 1973, **38**, 2422.
[22] B. A. Carlson and H. C. Brown, *Synthesis*, 1973, 776.

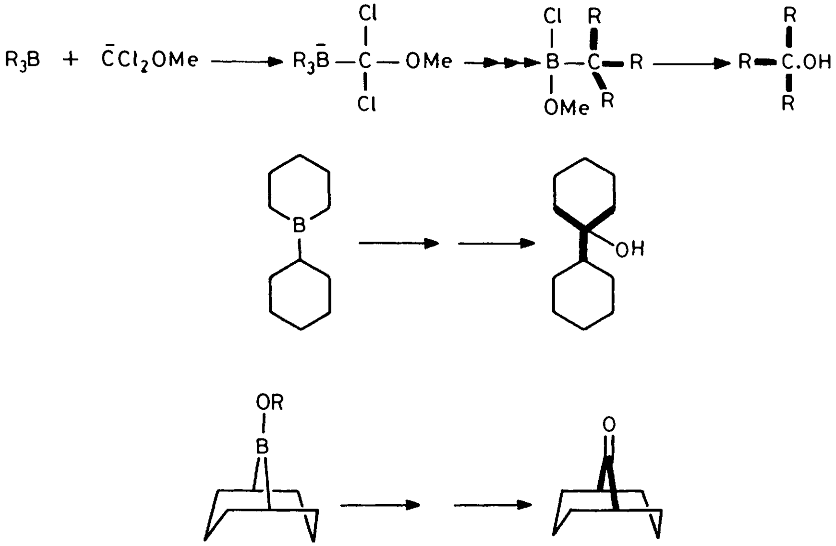

Figure 19

The readily available tris(phenylthio)methane anion similarly can be manipulated to give three migrations from boron to carbon.[23] Two migrations are spontaneous however, and the reaction is readily stopped to give ketones on oxidation (Figure 20). The reaction bears a generic similarity to the use of benzodithiolium carbanions, which can also yield ketones and trialkylcarbinols, but this time with only one and two migrations respectively from boron to carbon (Figure 20).[24] In each case the initial migration produces a nucleophilic species that can co-ordinate to boron and induce a further migration.

The attacking species can be an ylide (equation 1; X positively charged) as in Figure 21, in which the leaving groups attached in the α-position are $^{+}SMe_2$[25] and $^{+}N_2$.[26] The reactions proceed efficiently in mild conditions, utilization of the alkyl or aryl groups being enhanced by use of the readily available chloro- or dichloro-organoboranes.[27]

Into this category comes the carbonylation reactions of organoboranes

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[23] A. Pelter and J. Madhusudhana Rao, *J. Chem. Soc., Chem. Commun.*, 1981, 1149.

[24] S. Ncube, A. Pelter, and K. Smith, *Tetrahedron Lett.*, 1979, 1893; 1895.

[25] J. J. Tuffariello, P. Wojtkowski, and L. T. C. Lee, *Chem. Commun.*, 1967, 505.

[26] J. Hooz *et al.*, *J. Am. Chem. Soc.*, 1968, **90**, 5936; 6891. *Can. J. Chem.*, 1970, **48**, 868; 1971, 49, 2371.

[27] J. Hooz, J. N. Bridson, J. G. Calzada, H. C. Brown, M. M. Midland, and A. B. Levy, *J. Org. Chem.*, 1973, **38**, 2574.

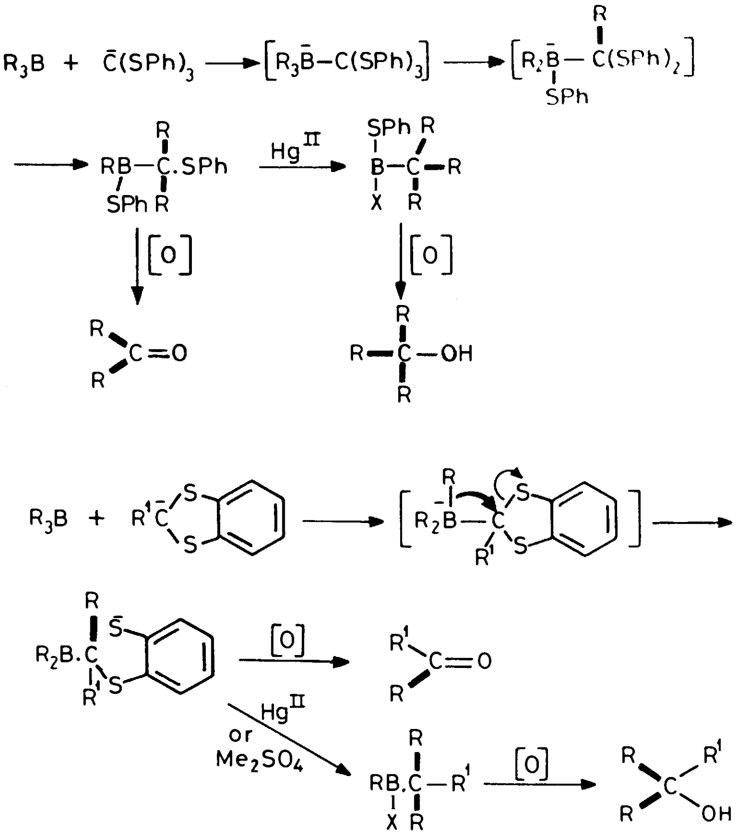

Figure 20

(Figure 22).[28] These, as well as providing facile routes to aldehydes[29] and primary-carbinols[30] of known regio- and stereo-chemistry, yield, by two- and three-bond connection reactions, either ketones[31] or tertiary carbinols[32] respectively. In this way the facility of production of cyclic organoboranes can be transferred to the synthesis of unique functionalized carbocyclic compounds. Examples of these transformations are given in Figure 23. Many substituted boradamantanes (see Section 1) have been transformed to the corresponding adamantanes.[4]

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[28] M. E. Hillman, *J. Am. Chem. Soc.*, 1962, **84**, 4715; 1963, **85**, 982, 1626. H. C. Brown, 'Boranes in Organic Chemistry', Cornell University Press, Ithaca, 1972.

[29] H. C. Brown, M. M. Rogić, M. W. Rathke, and G. W. Kabalka, *J. Am. Chem. Soc.*, 1969, **91**, 2150; H. C. Brown and R. A. Coleman, *ibid.*, 1969, **91**, 4604.

[30] H. C. Brown, T. M. Ford, and J. L. Hubbard, *J. Org. Chem.*, 1980, **45**, 4067.

[31] H. C. Brown and E. Negishi, *Chem. Commun.*, 1968, 594.

[32] H. C. Brown and E. Negishi, *J. Am. Chem. Soc.*, 1967, **89**, 5478; 1969, **91**, 1224.

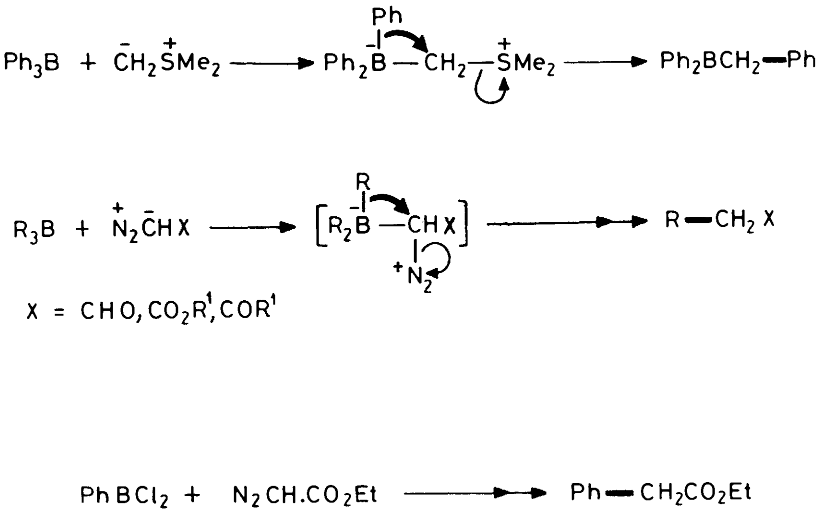

Figure 21

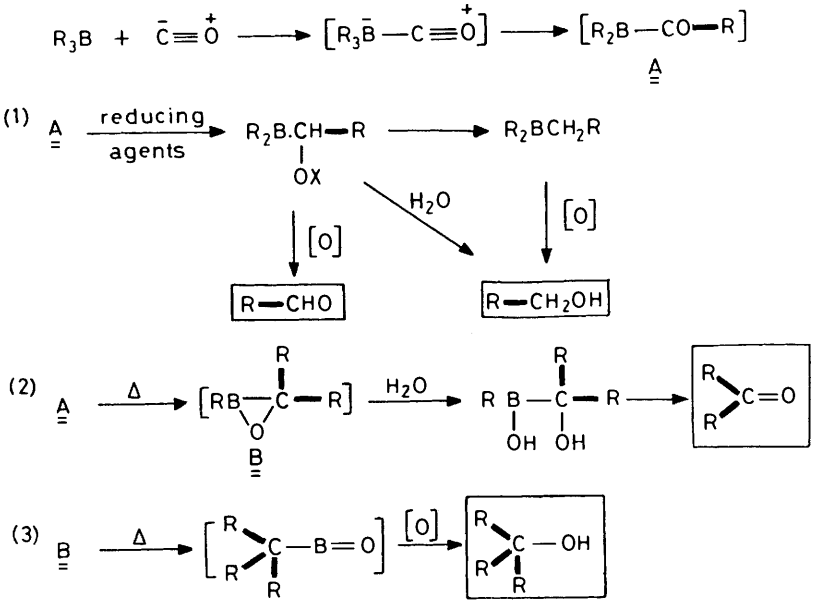

Figure 22

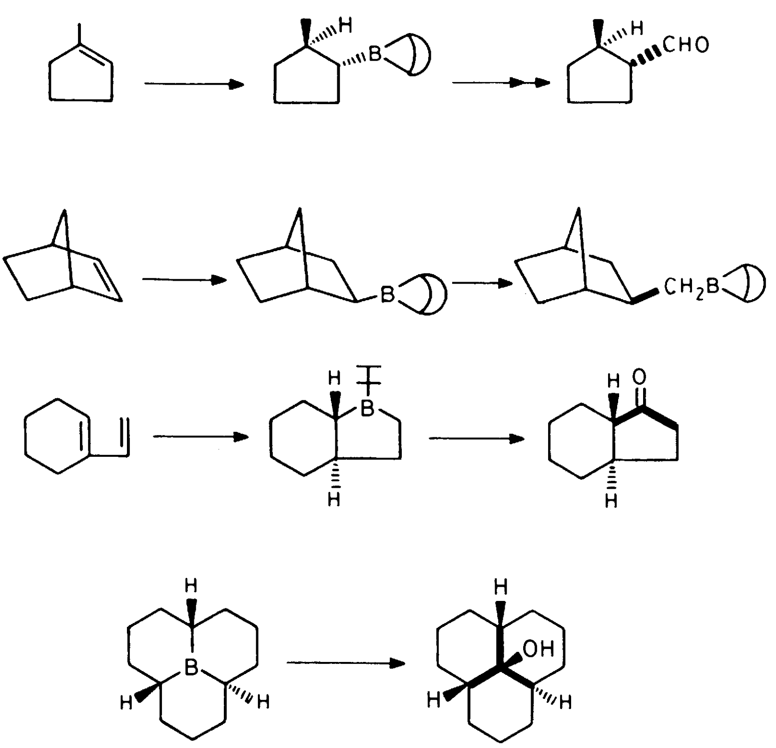

Figure 23

Equation 2 (Figure 17) is exemplified by the facile photochemical α-bromination of organylboranes in the presence of water. The bromination proceeds without cleavage of the B—C bond and if water is present migration is immediate. The process may be repeated to build up highly hindered carbinols with great ease.[33] If it is desired to stop the reaction at one migration only, then full utilization of the alkyl groups can be achieved by use of dialkylhydroxyboranes[34a] or thexylboranes.[34b] Ring structures may also be produced by this reaction[35] (Figure 24).

A further method for the production of α-haloboranes is the hydroboration of vinyl halides. The results shown in Figure 25 indicate that the migration may be controlled so that clean inversion occurs at the migration terminus. This

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[33] C. F. Lane and H. C. Brown, *J. Am. Chem. Soc.*, 1971, **93**, 1025.

[34] (*a*) H. C. Brown, Y. Yamamoto, and C. F. Lane, *Synthesis*, 1972, 303.
(*b*) H. C. Brown, Y. Yamamoto, and C. F. Lane, *ibid.*, 1972, 304.

[35] Y. Yamamoto and H. C. Brown, *J. Org. Chem.*, 1974, **39**, 861.

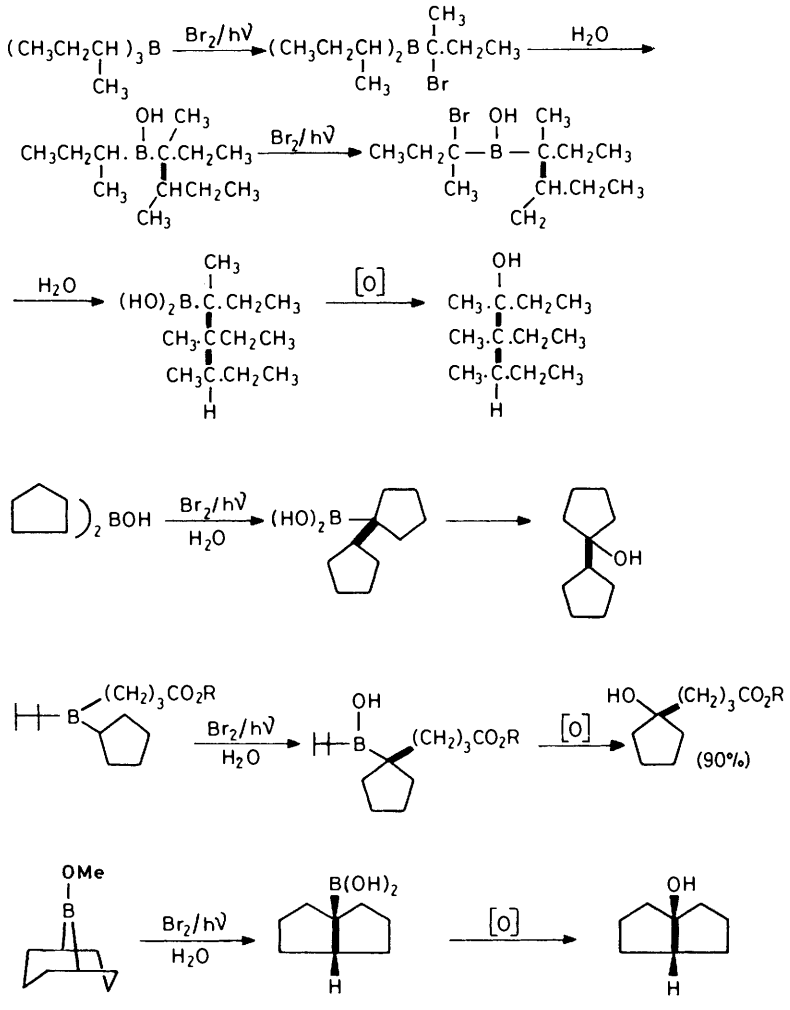

Figure 24

result is sensitive to the complexing agents present, however, and in the presence of THF or Me_2S almost complete stereochemical scrambling occurs.[36]

It is important to note that nucleophilic attack on an α-haloalkenylborane also readily induces migration in which the migrating group retains its configuration and there is clean inversion at the migration terminus (Figure 26).

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[36] M. M. Midland, A. R. Zolopa, and R. L. Halterman, *J. Am. Chem. Soc.*, 1979, **101**, 248.

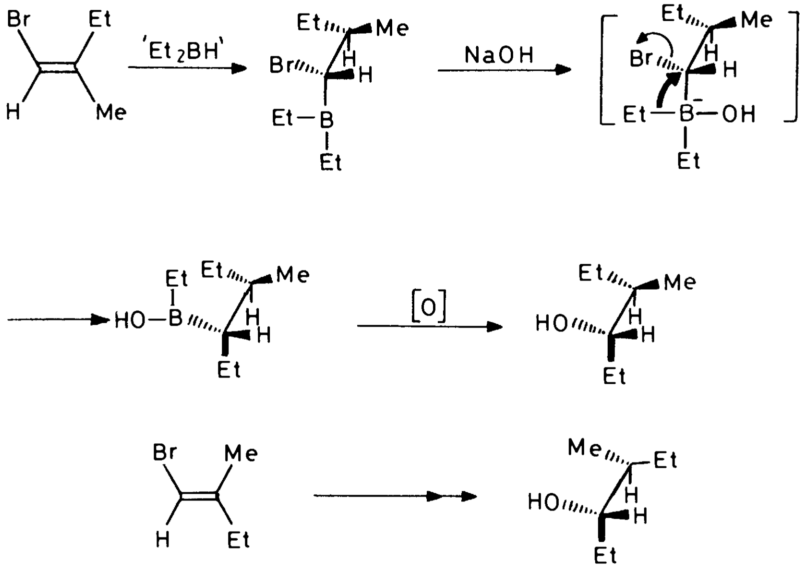

Figure 25

Such processes are of great interest in forming alkenes[37] and dienes[38] of known stereochemistry in mild conditions.

4 C—C Bond Formation by Radical Reactions of Organoboranes

A.—Alkyl Coupling Reactions.—Both trialkylboranes and alkyldihydroxyboranes react with alkaline silver nitrate to give coupled alkanes[39,40] (Figure 27). The reaction appears to proceed through silver alkyls and all alkyl groups are utilized. Mixtures of boranes or mixed trialkylboranes give statistical mixtures of coupled products showing the intermolecular nature of the coupling. Of course, use of excess of any trialkylborane can cause a corresponding increase in the percentage of mixed coupled product when this is required.

The process has been used with readily available borocyclanes to produce cycloalkanes (Figure 27), this mild coupling method having potential in the synthesis of complex carbocyclic compounds.[41]

[37] E. Negishi, J.-J. Katz, and H. C. Brown, *Synthesis*, 1972, 555; E. J. Corey and J. Ravindranathan. *J. Am. Chem. Soc.*, 1972, **94**, 4013.

[38] E. Negishi and T. Yoshida, *J. Chem. Soc., Chem. Commun.*, 1973, 606

[39] H. R. Synder, J. A. Kuck, and J. R. Johnson, *J. Am. Chem. Soc.*, 1938, **60**, 105; 111.

[40] H. C. Brown, C. Verbrugge, and C. H. Snyder, *J. Am. Chem. Soc.*, 1961,**83**, 1001; H. C. Brown and C. H. Snyder, *ibid.*, 1961, **83**, 1002.

[41] R. Murphy and R. H. Prager, *Tetrahedron Lett.*, 1976, 463.

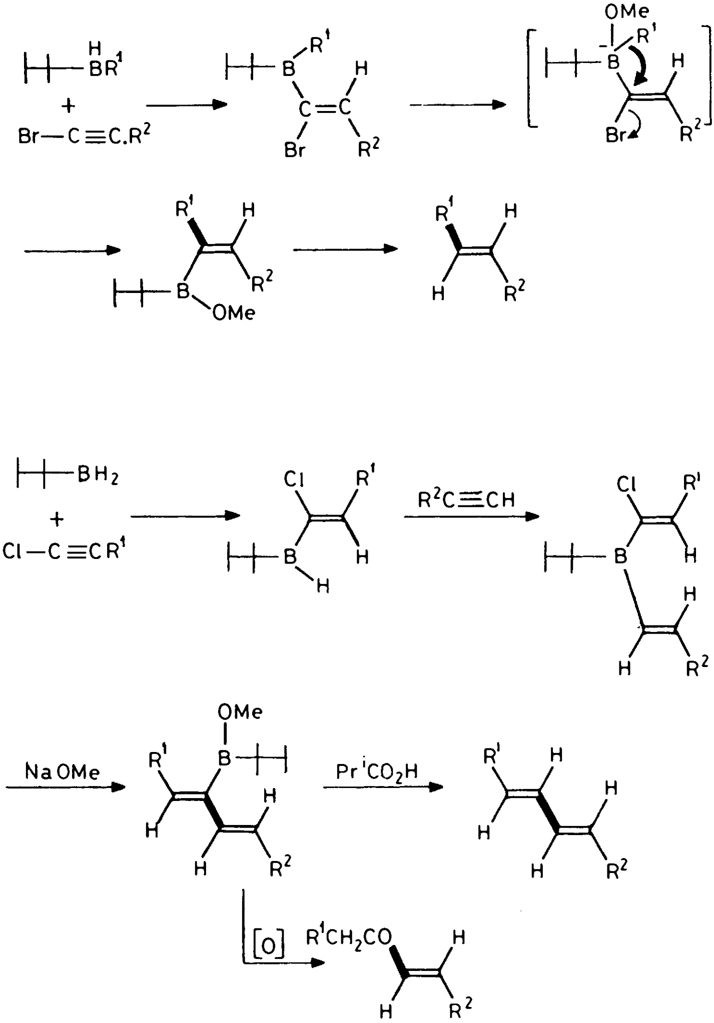

Figure 26

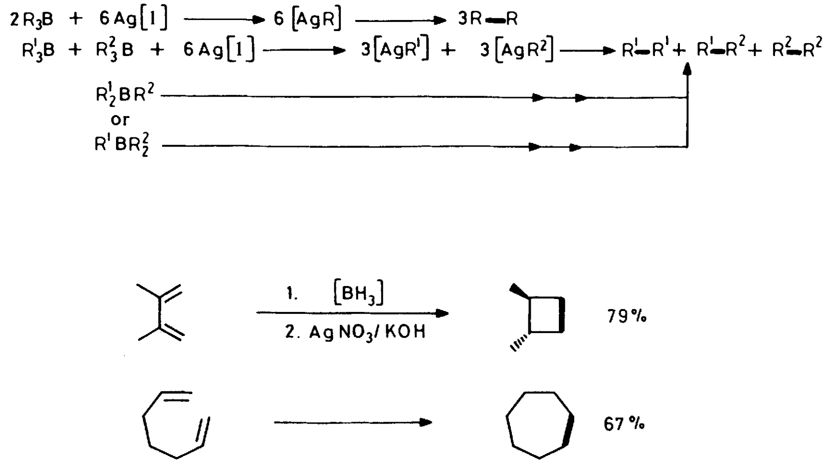

Figure 27

B. Conjugate Addition Reactions of Organoboranes.—Many $\alpha\beta$-unsaturated carbonyl compounds undergo ready 1,4-addition of organoboranes, the reaction proceeding, in general, through a free-radical chain mechanism (Figure 28)[42] though *B*-alkenyl-9-BBN derivatives seem to react by a concerted mechanism involving a six-membered cyclic transition-state.[43] The radical reactions proceed well even with β-unsubstituted enones, which give poor results using copper reagents, and with methyl vinyl ketone and various α-substituted acroleins the reactions are spontaneous. Radical initiation, however, is required for reaction with β-substituted enones.

Related reactions proceed well with ynones and $\alpha\beta$-unsaturated imines as well as $\alpha\beta$-alkenyl- and alkynyl-epoxides.[44] However, electrolytic conditions are required to induce reaction of $\alpha\beta$-unsaturated esters.[45] *para*-Quinones react readily in the presence of oxygen.[46,47]

5 1,2-Migrations Involving Organoborates ($\mathrm{B^{IV}}$)

Organoboranes may be attacked by simple carbanions to yield co-ordinatively saturated organoborates, which show no tendency to undergo migration. However, electrophilic attack β to boron creates a dipole so that migration can

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[42] H. C. Brown *et al.*, *J. Am. Chem. Soc.*, 1970, **92**, 710; 712; 714.

[43] P. Jacob and H. C. Brown, *J. Am. Chem. Soc.*, 1976, **98**, 7832.

[44] A. Suzuki, N. Miyaura, M. Itoh, H. C. Brown, G. W. Holland, and E. Negishi, *J. Am. Chem. Soc.*, 1971, **93**, 2792, *cf. Synthesis*, 1973, 305.

[45] T. Takahashi, K. Yuasa, M. Takuda, M. Itoh, and A. Suzuki, *Bull. Chem. Soc. Jpn.*, 1978, **51**, 339.

[46] M. F. Hawthorne and M. Reintjes, *J. Am. Chem. Soc.*, 1964, **86**, 951; 1965, **87**, 4585.

[47] G. W. Kabalka, *J. Organomet. Chem.*, 1971, **33**, C 25; *Tetrahedron*, 1973, **29**, 1159.

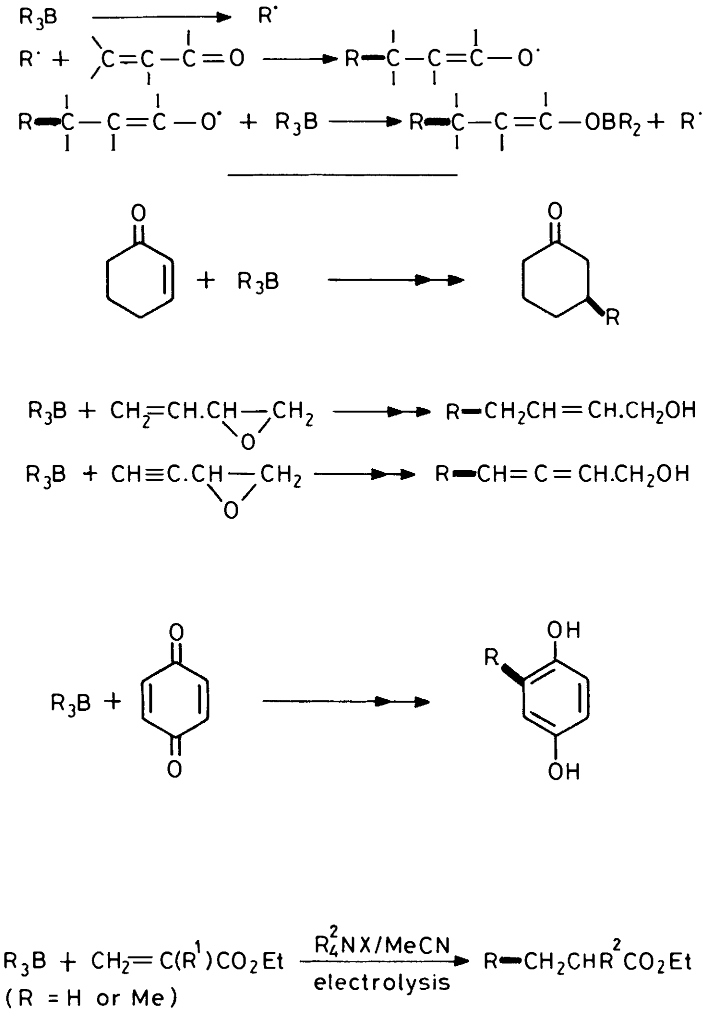
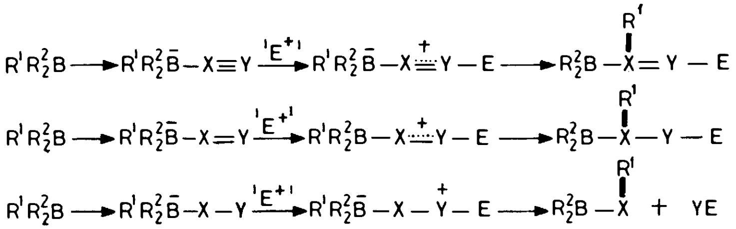


Figure 28

occur (Figure 29). The situation differs from that involving organoboranes inasmuch as the organoborates are stable intermediates and migration is induced by electrophilic rather than nucleophilic attack. Moreover, the nature of the electrophile may be controlled so as to potentiate further reaction after the initial migration. General equations (3)—(5) (Figure 29) were set up[48] and from them a large number of synthetically useful reactions have resulted.[49–51]



$$R^1R^2_2B \longrightarrow R^1R^2_2\bar{B}-X\equiv Y \xrightarrow{E^+} R^1R^2_2\bar{B}-X\overset{+}{\equiv}Y-E \longrightarrow R^2_2B-\overset{R^1}{X}=Y-E \qquad (3)$$

$$R^1R^2_2B \longrightarrow R^1R^2_2\bar{B}-X=Y \xrightarrow{E^+} R^1R^2_2B-X\overset{+}{=}Y-E \longrightarrow R^2_2B-\overset{R^1}{X}-Y-E \qquad (4)$$

$$R^1R^2_2B \longrightarrow R^1R^2_2\bar{B}-X-Y \xrightarrow{E^+} R^1R^2_2\bar{B}-X-\overset{+}{Y}-E \longrightarrow R^2_2B-\overset{R^1}{X} + YE \qquad (5)$$

For carbon - carbon bond formation, X = C in all cases.

Figure 29

The migrating group R^1 can be aryl, alkenyl, or alkynyl as well as alkyl, and R^2 need not be organyl groups but may be OR, NR_2, halogeno, or SR provided these groups do not migrate or interfere with the required reactions. In this way valuable alkyl groups may be conserved. Further variations arise when $R^1R^2R^3B$ is used rather than $R^2_2R^1B$ or R_3B.

A. The Cyanoborate (Cyanidation) Process.—Cyanoborates are readily available, stable salts that are soluble in most organic solvents. Protonation leads to two migrations and oxidation of the product yields ketones.[50] Yields, however, are only *ca.* 50% as a result of abstraction of HCN from $R_3\bar{B}-\overset{+}{C}\equiv NH$ by the basic dimer resulting from two migrations (Figure 30).

Replacement of the proton by acylating agents such as trifluoroacetic anhydride (TFAA), trichloroacetyl chloride, or benzoyl chloride as electrophiles leads to the high yielding two-[48] and three-[49]migration cyanoborate processes (Figure 31).

Many types of structure can readily be produced in mild conditions in good yields. These include fused,[48,52,53] bridged,[48,54] and medium ring ketones[55] often with striking stereospecificity (Figure 32).

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[48] A. Pelter, K. Smith, M. G. Hutchings, and K. Rowe, *J. Chem. Soc., Perkin Trans. 1*, 1975, 129.

[49] A. Pelter, K. Smith, M. G. Hutchings, and K. Rowe, *J. Chem. Soc., Perkin Trans. 1*, 1975, 138.

[50] A. Pelter, M. G. Hutchings, and K. Smith, *J. Chem. Soc., Perkin Trans. 1*, 1975, 142.

[51] A. Pelter, M. G. Hutchings, K. Smith, and D. J. Williams, *J. Chem. Soc., Perkin Trans., 1*, 1975, 145.

[52] G. W. Kabalka, *Synth. Commun.*, 1979, 607.

[53] T. A. Bryson and C. J. Reichel, *Tetrahedron Lett.*, 1980, 2381.

[54] H. C. Brown, J. A. Sikorski, S. U. Kulkarni, and H. D. Lee, *J. Org. Chem.*, 1980, **45**, 4542.

[55] M. E. Garst and J. N. Bonfiglio, *Tetrahedron Lett.*, 1981, **22**, 2075.

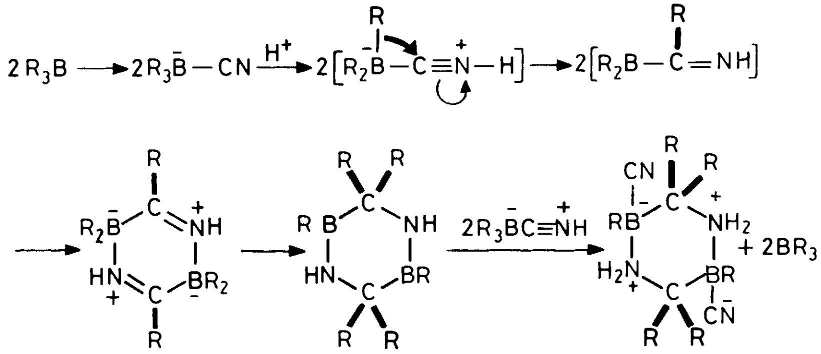

Figure 30

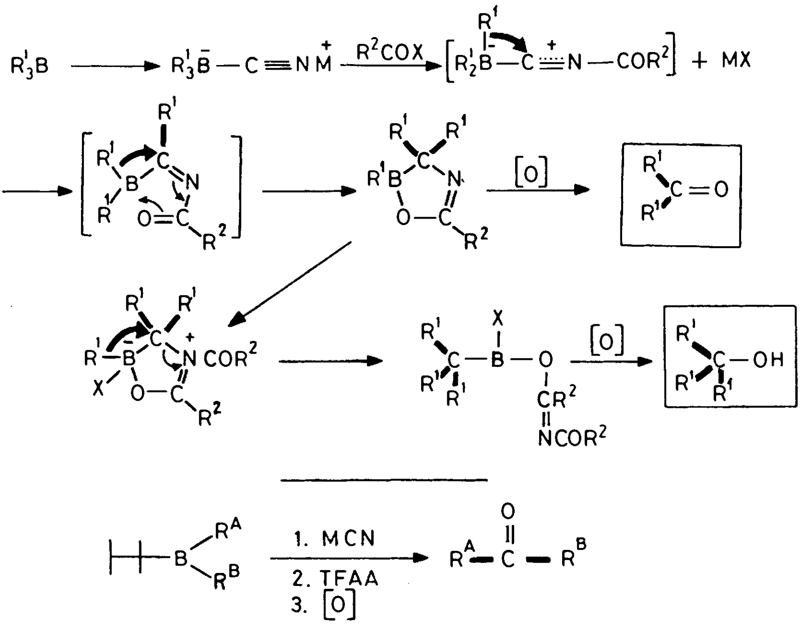

Figure 31

An interesting conjunction of the two migration cyanoborate process with transition-metal stabilized cation chemistry results in the ready construction of a tetracyclic system (Figure 33).[56] It is noteworthy that tris(4-bromobutyl)

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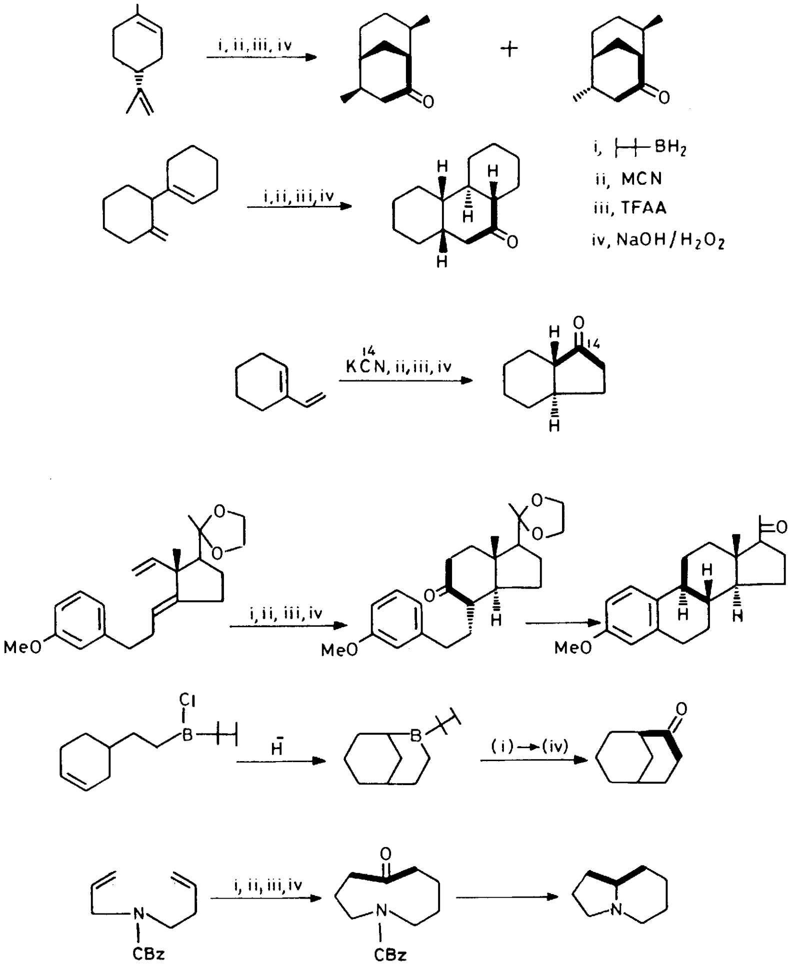
[56] E. Mincione, A. J. Pearson, P. Bovicelli, M. Chandler, and G. C. Heywood, *Tetrahedron Lett.*, 1981, **22**, 2929.



(CBz = carbobenzyloxy)

Figure 32

methanol, though easily produced in the mild conditions of the cyanoborate process, could not be made at all by the carbon monoxide protocol[57] (Figure 33).

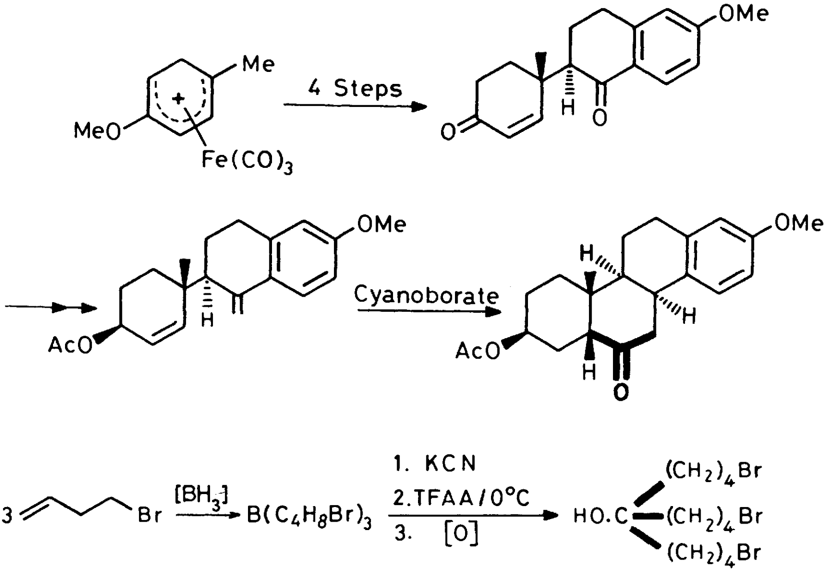


Figure 33

B. Alkynylborates.—Electrophilic attack on alkynylborates may lead to migration and to products in which the entire alkyne unit and the electrophile are incorporated.

Protonation[58] or alkylation[59] give rise to valuable syntheses of ketones (Figure 34) in which the organyl groups have separate origins and in which the regiospecificity of the alkyl groups in $R^1COCHR^2R^3$ is completely assured. Neither protonation nor alkylation with simple alkylating reagents is stereospecific, however, and protonation of the borane intermediates yields mixtures of trisubstituted alkenes.

However, when propargyl bromide, iodoacetonitrile, and α-bromocarbonyl compounds are used as alkyating agents[60] the reactions are completely stereo-

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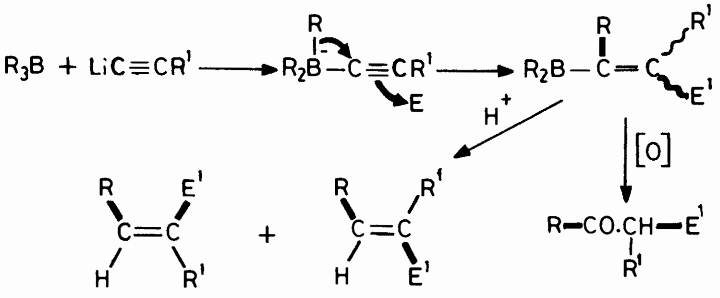
[57] J. E. Hallgren and G. M. Lucas, *Tetrahedron Lett.*, 1980, 3951.

[58] A. Pelter, C. R. Harrison, C. Subrahmanyam, and D. Kirkpatrick, *J. Chem. Soc., Perkin Trans., 1*, 1976, 2435.

[59] A. Pelter, T. W. Bentley, C. R. Harrison, C. Subrahmanyam, and R. J. Laub, *J. Chem. Soc., Perkin Trans. 1*, 1976, 2419.

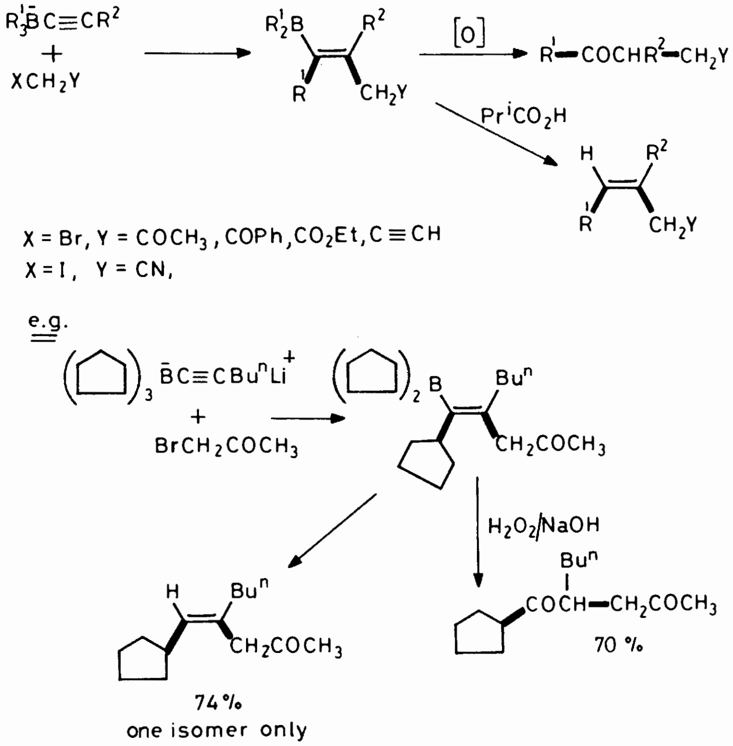
[60] A. Pelter, K. J. Gould, and C. R. Harrison, *J. Chem. Soc., Perkin Trans. 1*, 1976, 2428.



E = HX or R^2X : E^1 = H, R^2

Figure 34

specific (Figure 35) giving direct syntheses of functionalized trisubstituted alkenes as well as γ-keto-esters, nitriles, and alkynes and 1,4-diketones, all useful synthetic intermediates.



X = Br, Y = $COCH_3$, COPh, CO_2Et, C≡CH
X = I, Y = CN,

Figure 35

Alkynylborates are readily manipulated. Some examples of their uses are shown on Figures 36 and 37. The first example is of interest in that, by the use of a dihalide, two migrations are induced in an alkynylborate with the formation of three C—C bonds in all. A first allylic rearrangement is followed by another on hydrolysis.[61]

Alkynylborates will attack electron-deficient rings in a regiospecific fashion as shown by interactions with pyridinium[62] and metal-stabilized cyclohexadienyl cation ring-systems.[63] The latter is of particular interest as the boron may be removed at different stages of manipulation by either hydrolysis or mild oxidation giving rise to a wide variety of products.

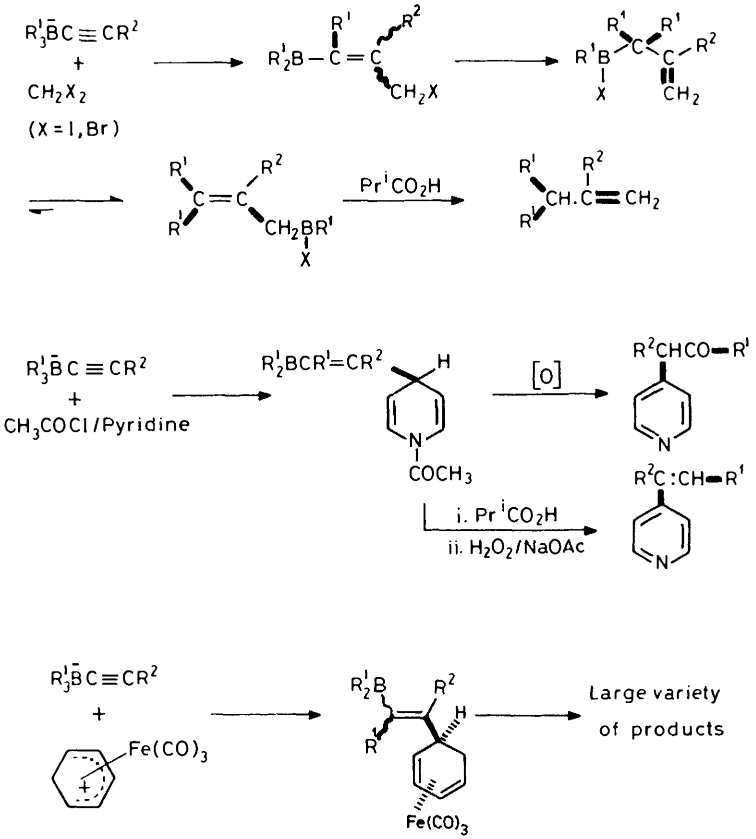


Figure 36

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[61] A Pelter and C. R. Harrison, *J. Chem. Soc., Chem. Commun.*, 1975, 828.

[62] A. Pelter and K. S. Gould, *J. Chem. Soc., Chem. Commun.*, 1974, 347.

[63] A Pelter, K. J. Gould, and L. A. P. Kane-Maguire, *J. Chem. Soc., Chem. Commun.*, 1974, 1029.

An alkynylborate is readily attacked by organometal halides, often with complete regio- and stereo-specificity to yield 1,2-dimetallovinylboranes (Figure 37) from which, for example, the boron may be readily removed to give stereochemically defined vinyl-metal derivatives.[17,64,65]

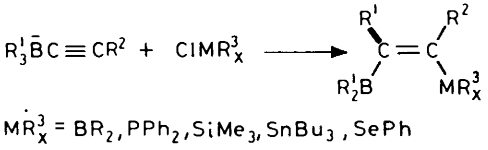

Figure 37

Ethynylborates themselves may be protonated (Figure 38) to yield the vinylboranes that would be obtained if it were possible to carry out Markovnikov hydroboration of a terminal alkyne by a dialkylborane. These intermediates may be manipulated in the usual ways.[66,67] Reaction with butyl-lithium yields a dianion which may be alkylated, this being a general route to alkynylborates.[68,69]

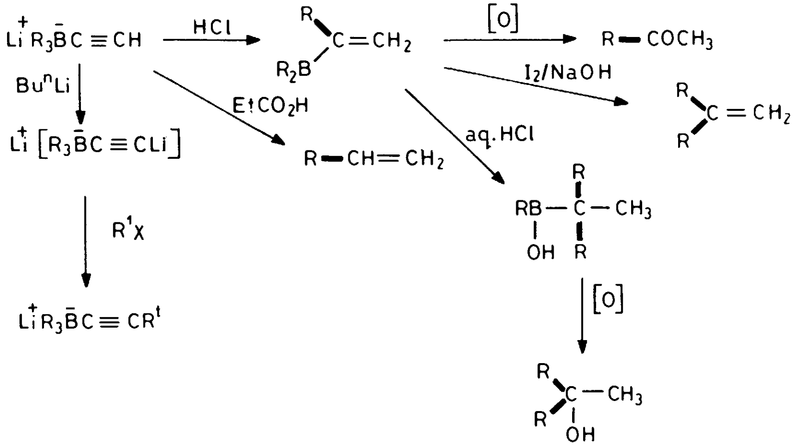

Figure 38

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[64] P. Binger and R. Köster, *Tetrahedron Lett.*, 1965, 1901; *J. Organomet. Chem.*, 1974, **73**, 205; *Synthesis*, 1973, 309.

[65] J. Hooz and R. Mortimer, *Tetrahedron Lett.*, 1976, 805.

[66] H. C. Brown, A. B. Levy, and M. Mark Midland, *J. Am. Chem. Soc.*, 1975, **97**, 5017.

[67] H. C. Brown and M. Mark Midland, *J. Org. Chem.*, 1975, **40**, 2845.

[68] K. Utimoto, M. Kitai, M. Naruse, and H. Nozaki, *Tetrahedron Lett.*, 1975, 4233.

[69] K. Utimoto, Y. Yabuki, K. Okada, and H. Nozaki, *Tetrahedron Lett.*, 1976, 3969.

Alkynylborates react with iodine with migration followed by elimination of R_2BI, to give the alkylated alkyne in excellent yield[70] (Figure 39). This has been extended to the coupling of alkynes by use of a dialkynylborate.[71] It is noteworthy that unsymmetrical diynes with long alkyl side-chains can be readily produced by this route, these being available only in low yields by the more

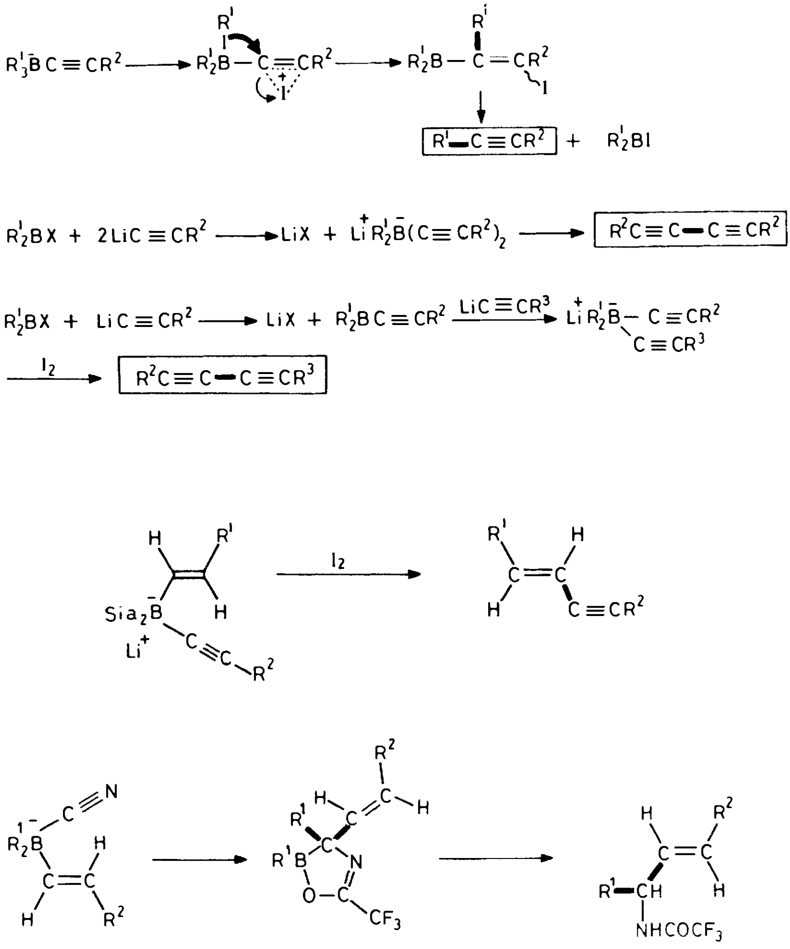


Figure 39

[70] A. Suzuki, N. Miyaura, S. Abiko, M. Itoh, H. C. Brown, J. A. Sinclair, and M. Mark Midland, *J. Am. Chem. Soc.*, 1973, **95**, 3080.

[71] A. Pelter, K. Smith, and M. Tabata, *J. Chem. Soc., Chem. Commun.*, 1975, 857.

usual methods.[72,73] Other reactions of alkynylborates bearing functional groups are shown in Figure 39[74,75] it being of interest that an alkenyl group migrates in preference to a cyano-group under the influence of TFAA.[75]

In order to test whether the ionic chemistry of organoborates was wholly contained in the general equations (3), (4), and (5), unique Michael reactions involving migration from boron to carbon were successfully carried out, showing that neutralization of charge in a dipolar intermediate is *not* necessary but that stabilization of the charge is sufficient for 1,2-migration (Figure 40).[76,77] These

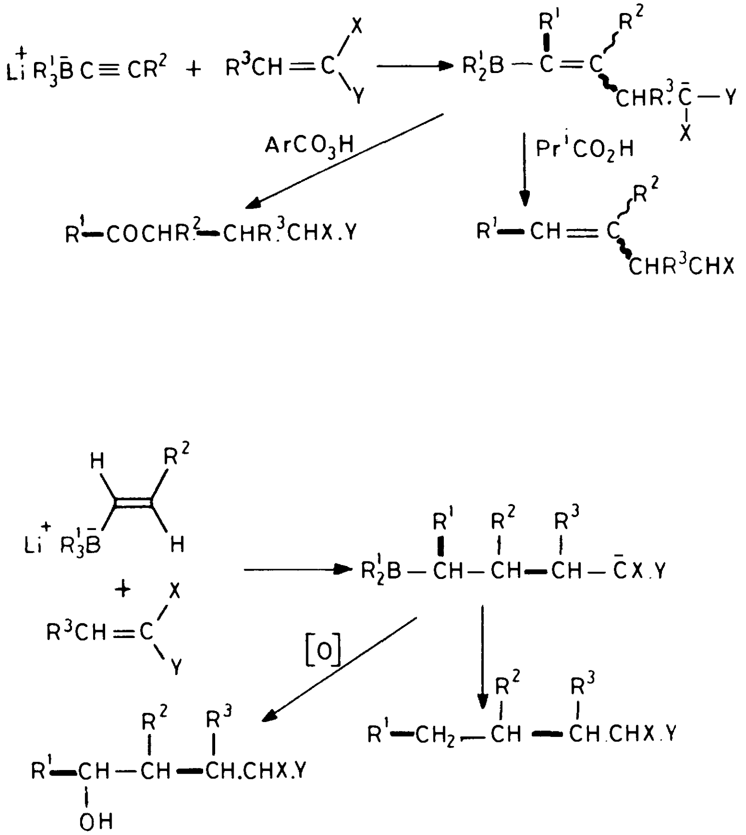
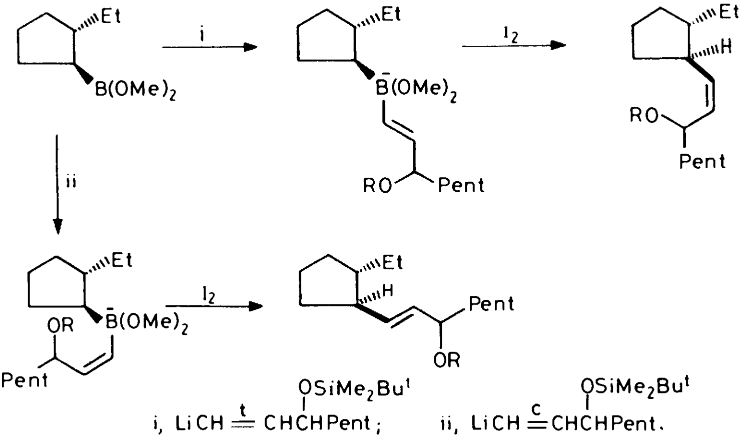


Figure 40

[72] J. A. Sinclair and H. C. Brown, *J. Org. Chem.*, 1976, **41**, 1078.
[73] A. Pelter, R. Hughes, K. Smith, and M. Tabata, *Tetrahedron Lett.*, 1976, 4385.
[74] E. Negishi, G. Lew, and T. Yoshida, *J. Chem. Soc., Chem. Commun.*, 1974, 1411.
[75] A. Pelter, A. Arase, and M. G. Hutchings, *J. Chem. Soc., Chem. Commun.*, 1974, 346.
[76] A. Pelter and L. Hughes, *J. Chem. Soc., Chem Commun.*, 1977, 913.
[77] A. Pelter and J. Madhusudhana Rao, *Tetrahedron Lett.*, 1981, **22**, 797.

reactions have opened up a wholly new field for exploration and, for example, have recently been shown to be applicable to alkenylborates.[78] The successful Michael acceptors, RCH=CXY in general are those in which the pK_a of CH_2XY is not higher than *ca.* 9—11.

C. Alkenylborates.—The reaction of iodine on triorganylethenylborates leads to alkenes.[79] Both secondary alkyl and aryl groups migrate, and by the use of 9-BBN derivatives organyl groups may be fully utilized. If the boron atom is substituted by alkoxy-groups these do not interfere with the reaction and allow full utilization of the alkoxy groups (Figure 41).[80] Migration proceeds with retention of configuration of the migrating group and inversion at the migration terminus.



$\text{i, LiCH} \overset{t}{=} \text{CH}\underset{}{\overset{\text{OSiMe}_2\text{Bu}^t}{\text{CH}}}\text{Pent};\quad \text{ii, LiCH} \overset{c}{=} \text{CH}\overset{\text{OSiMe}_2\text{Bu}^t}{\text{CH}}\text{Pent.}$

Figure 41

Protonation of dialkylalkenylborates with dry hydrogen chloride in either gives the expected one-migration product.[66,67,81] The reactions of alkenylborates with epoxides and aldehydes yield products that on oxidation yield 1,4- and 1,3-diols respectively[82] (Figure 42).

Aromatic borates behave to some extent like alkenylborates, this making possible some very specific substitution and coupling reactions, examples of which are shown in Figure 43.[83,84] The variety of substitution reactions on the

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[78] A. Pelter and F. Gibbs. Unpublished results.

[79] G. Zweifel *et al.*, *J. Am. Chem. Soc.*, 1967, **89**, 3652; 1968, **90**, 6243; 1971, **93**, 6309; 1972, **94**, 6560.

[80] D. A. Evans, F. C. Crawford, R. C. Thomas, and J. A. Walker, *J. Org. Chem.*, 1976, **41**, 3974. *cf. Tetrahedron Lett.*, 1976, 1427 and also A. G. Abatjoglou and P. S. Portoghese, *ibid.*, 1976, 1427.

[81] G. Zweifel and R. P. Fisher, *Synthesis*, 1974, 339.

[82] K. Utimoto, K. Uchida, and H. Nozaki, *Tetrahedron Lett.*, 1973, 4527.

[83] E. R. Martinelli and A. B. Levy, *Tetrahedron Lett.*, 1979, 2313.

[84] I. Akimoto and A. Suzuki, *Synthesis*, 1979, 146.

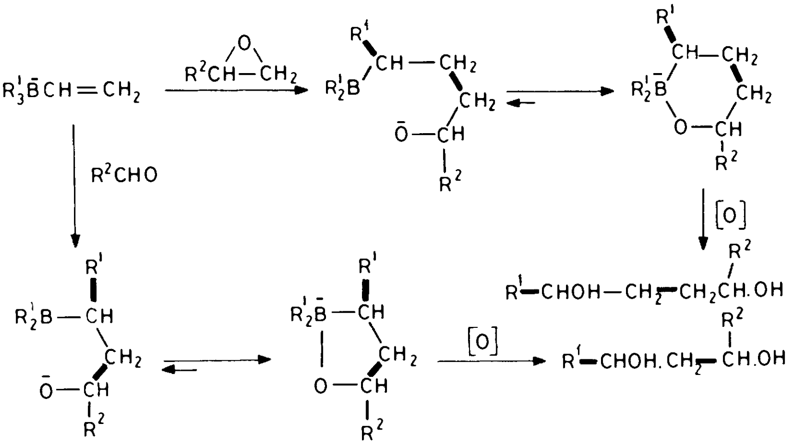


Figure 42

indole moiety is particularly noteworthy.[85] Aromatic groups can be coupled with conservation of the organo-groups by use of readily available crystalline ethanolamine complexes derived from diarylalkoxyboranes.[86,87] The mixed diaryl compounds are available by stepwise displacement of alkoxy-groups from trialkoxyboranes.

2-Bromo-6-lithiopyridine reacts with trialkylboranes to yield borates that undergo extremely facile ring-cleavage, (Figure 44),[88] a reaction similar to those of alkenylborates bearing a leaving group in the α-position.[89] Somewhat surprisingly, α-lithiofuran can behave similarly.[90]

D. α-Thio-organoborates.—It is possible to produce a stable organoborate that contains a functional group capable of being transformed into a good leaving group, so inducing migration. This very general principle is exemplified in a new homologation procedure[91] (Figure 45), which uses thiomethoxymethyl-lithium to form a stable organoborate. Methylation of the sulphur in mild conditions produces an ylide that undergoes migration to give a homologous organoborane, which can be manipulated as required. Use of disiamyl- and 9-BBN groups was successful in conserving groups and novel homologations of aryl and alkenyl (retention of configuration) groups may be carried out in good yields.

[85] A. B. Levy, *Tetrahedron Lett.*, 1979, 4021.

[86] G. M. Davies, P. S. Davies, W. E. Paget, and H. M. Wardleworth, *Tetrahedron Lett.*, 1976, 795.

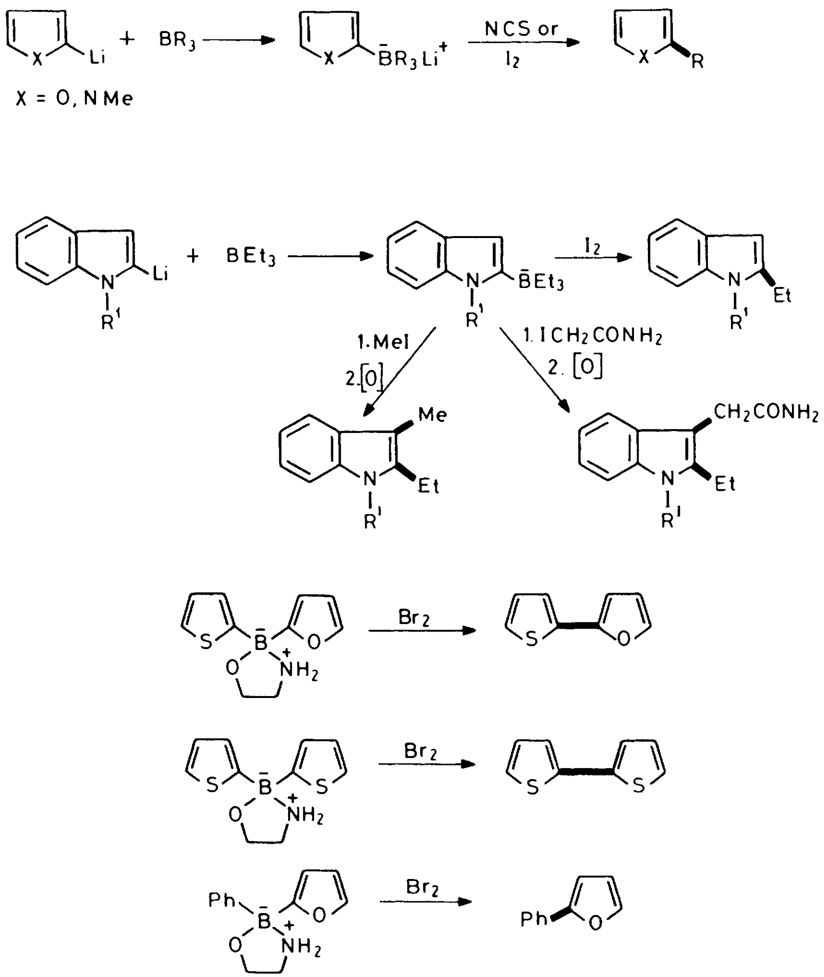
[87] A. Pelter, G. M. Davies, and H. Williamson, Unpublished experiments.

[88] K. Utimoto, N. Sakai, M. Obayashi, and H. Nozaki, *Tetrahedron*, 1976, **32**, 769.

[89] G. Zweifel and H. Arzoumanian, *J. Am. Chem. Soc.*, 1967, **89**, 5086.

[90] A. Suzuki, N. Miyaura, and M. Itoh, *Tetrahedron*, 1971, **27**, 2775.

[91] E. Negishi, T. Yoshida, A. Silveira, Jr., and B. L. Chiou, *J. Org. Chem.*, 1975, **40**, 814.



Li
BR3
X = O, NMe
B̄R3Li+
NCS or
I2
R
BEt3
R1
B̄Et3
Et
1. MeI
2. [O]
Me
1. ICH2CONH2
2. [O]
CH2CONH2
Br2
NH2
Ph
S
O
N

Figure 43

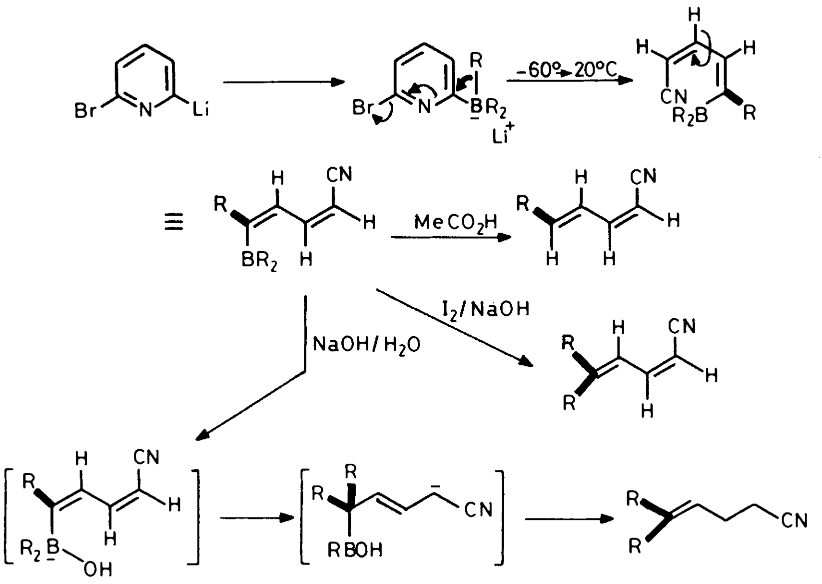


Figure 44

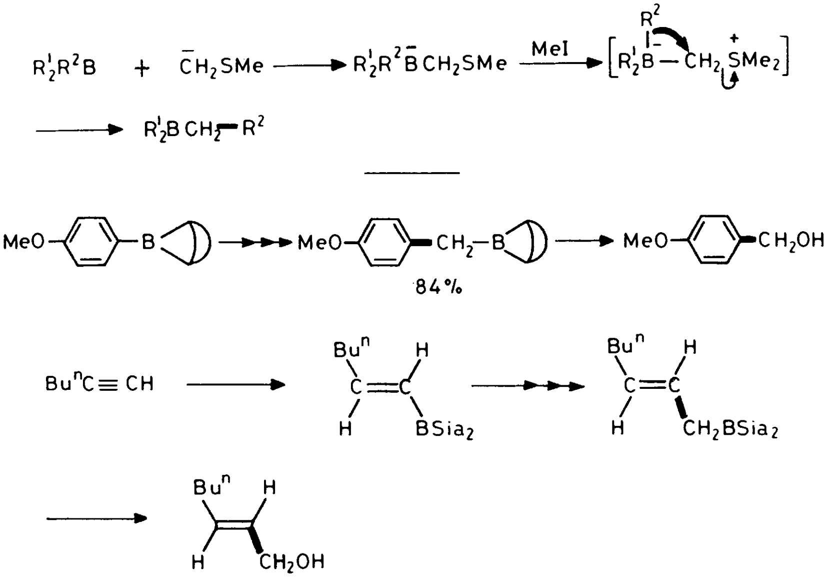


Figure 45

6 Reactions of Boron Stabilized Carbanions

Overlap between the empty orbital on boron and an adjacent non-bonding filled orbital should stabilize a carbanionic centre α to boron.[92] In practice it is difficult to produce such carbanions as the base used for deprotonation will normally complex directly with the boron to yield an organoborate (Figure 46).

To overcome this problem a very general approach is to use a heavily hindered non-nucleophilic base and in this way *B*-methyl-9BBN has been introduced as a methylenation reagent in the boron equivalent to the Wittig reaction, (Figure 46)

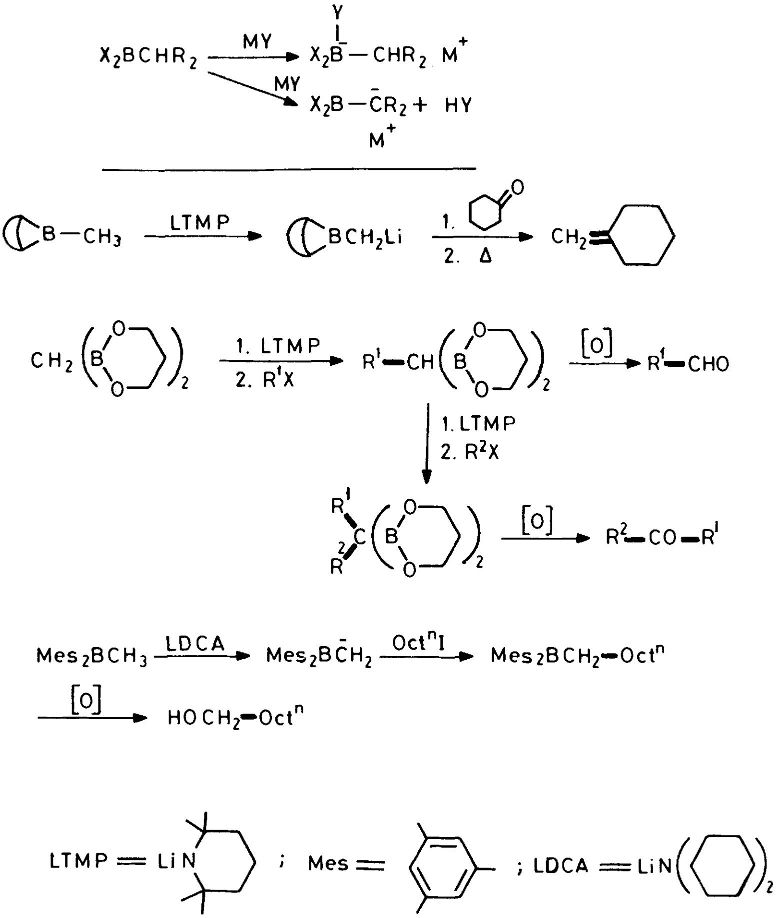


Figure 46

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[92] A. Pross, D. J. DeFrees, B. A. Levi, S. K. Pollack, L. Radom, and W. J. Hehre, *J. Org. Chem.*, 1981, **46**, 1693.

using *N*-lithio-2,2,6,6-tetramethylpiperidine (LTMP) as base.[93] Similarly, a methylene group bearing two dioxaboryl groups, which do not readily complex with bases, yields a stabilized carbanion.[94] An alternative, and equally general approach is to use a very hindered borane so that a simple base may be used. Alkyldimesitylboranes may be handled with great ease as, owing to the extreme hindrance of the environment around boron, it is difficult for complexes to be formed. In this case carbanions α to boron are readily produced at room temperature and behave as expected. Thus *B*-methyldimesitylborane is an excellent homologating reagent whose other reactions are actively under investigation in our laboratories.[95]

A quite different method for the production of carbanions α to boron is the cleavage of 1,1-di[96,97] or 1,1,1-tri-boryl[97] compounds with base (Figure 47). The metal exchange reaction occurs with great ease and the carbanions may be used in the usual ways. One notable reaction[97] sequence uses trisethylenedioxyborylmethane to accomplish the homologation of ketones R^1COR^2 to the aldehydes $R^1R^2CH.CHO$.

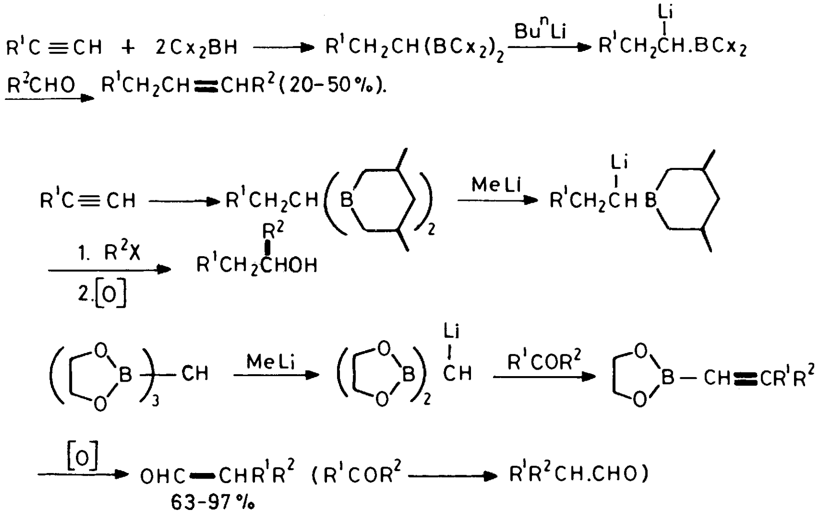

Figure 47

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[93] M. Rathke and R. Kow, *J. Am. Chem. Soc.*, 1972, **94**, 6854.

[94] D. S. Matteson and R. J. Moody, *J. Am. Chem. Soc.*, 1977, **99**, 3196.

[95] J. Wilson, *J. Organomet. Chem.*, 1980, **186**, 297; A. Pelter, L. Williams, and J. Wilson, Unpublished experiments.

[96] G. Cainelli, G. Dal Bello, and G. Zubiani, *Tetrahedron Lett.*, 1965, 3429; 1966, 4315. G. Zweifel *et al.*, *J. Am. Chem. Soc.*, 1967, **89**, 291. *Synthesis*, 1973, 37.

[97] D. S. Matteson *et al.*, *J. Am. Chem. Soc.*, 1975, **97**, 5608; *J. Organomet. Chem.*, 1975, **93**, 21; *Synthesis*, 1975, 147.