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PREPARATION OF 1,3-DIOLS BY METALATION–HYDROBORATION OF ALKYNES

A 1,2-HYDROGEN MIGRATION FROM BORON TO CARBON

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Abstract—Metalation of a series of 1- and 2-alkynes with subsequent treatment with diborane and oxidation gave 1,3-diols exclusively. Deuteroboration of the lithiated acetylenes established the occurrence of a displacement of one of the B atoms by deuterium in *gem*-diboronated compounds. Hydroboration of several acetylenes and acetylides was also studied.

The classical work of Brown on hydroboration has provided the chemist with a versatile tool for transformation of olefins and acetylenes via boranes into alcohols, carbonyl derivatives and a great number of other classes of compounds.[1-3] More recently it was found, that lithium compounds[4-9] could be converted by reaction with diborane into organoboron derivatives and subsequently to alcohols. Other organometals such as arylmercury[10] arylthalium[11] or Grignard[12] compounds gave similar results.[10-13] It was reported that products of dimerization and reduction were formed[9] on treatment of benzylic lithium derivatives with borane, whereas similar compounds have yielded in our hands[5,6] good yields of benzylic alcohols.

Metalation of allylbenzenes with butyllithium, reaction of the metalated product with diborane and subsequent oxidation yielded 1,3-diols.[4] This method, however, was of limited application, since allylic lithiation of monoolefins, not containing an activating group is not always easy. On the other hand, metalation of acetylenes, even without an additional activating group proceeds smoothly at the propargylic position,[14] leading to mono-, di- and tri-lithio derivatives. The hydroboration of these derivatives was therefore studied.

Metalation of 1-phenylpropyne (1) with 2 moles of BuLi in ether gave[15] the dilithio derivative (2). Reaction of this compound with borane and subsequent oxidation yielded 1-phenyl-1,3-propane diol (3). The same product was obtained by hydroboration-oxidation of the trilithio derivative 4, prepared from 1 by the reaction with excess BuLi.[15] Metalation of 1-phenyl-1-butyne (5) yielded in a similar manner the dilithio derivative (6), that led in the reaction with diborane and subsequent oxidation to a 1:2 mixture of the *threo* and *erythro* diols (7). In addition, a small amount of 1-phenyl-1-hydroxybutan-3-one (8) was also obtained. Hydroboration of the monolithio derivative[15] (9) gave also a mixture of the *threo* and *erythro* 7. All these alcohols have been converted into acetates with acetic anhydride.

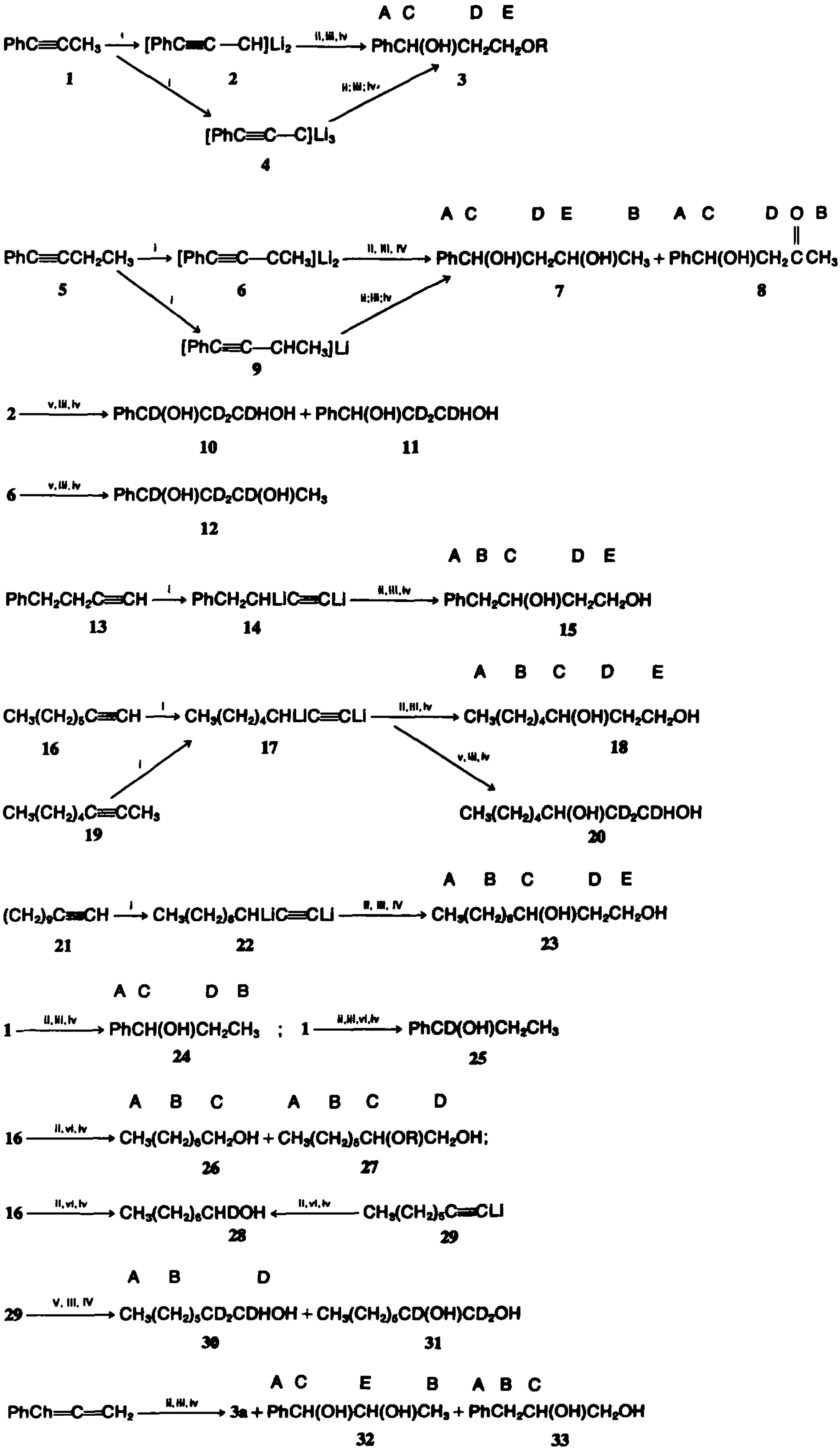
Deuteroboration oxidation of 2 led to a mixture deuterated diols (10 and 11). A similar reaction of 6 gave the tetradeuterated diol (12) containing a small amount of the same diols with hydrogen instead of deuterium at the 1- and 3-positions.

The 1,3-relative disposition of the two B atoms and subsequently the two hydroxyls is not determined by the presence of a phenyl group linked directly to the propargylic system, since hydroboration of the dilithio compound (14) derived from 4-phenylbut-1-yne (13) gave 4-phenylbutane-1,3-diol (15). Similarly aliphatic acetylenes led via their dilithio derivatives[16] to 1,3-diols. Thus, lithiation of 1-octyne (16) and subsequent hydroboration-oxidation of its dilithio derivative (17) gave octane-1,3-diol (18). The same diol was obtained on dilithiation–hydroboration–oxidation of 2-octyne (19), since 17 was formed as an intermediate.[17] Deuteroboration–oxidation of 17 gave 20. Hydroboration– oxidation of the dilithio derivative (22) of 1-dodecyne (21) gave dodecane-1,3-diol (23).

Several of the studied acetylenes have been subjected to hydroboration directly for comparison with the results obtained on metalation–hydroboration. Hydroboration-oxidation of 1 gave the alcohol (24) containing a small amount of the corresponding ketone-propiophenone. Treatment of the hydroboration product of 1 with alkaline deuterium oxide instead of water before oxidation gave a mixture of 24 and 25, showing that the alcohol was formed essentially by hydrolysis[18] of the gem-diboronated intermediate. The exclusive formation of 24 without its positional isomer illustrates the advantage in using excess borane, when full exploitation of the electronic effects leading to stereoselectivity is desired. The use of alkylboranes[19] in the hydroboration of 1 led to an increasing extent of the attack of the 2-position with the increase of the bulk of the groups linked to boron. Even a controlled amount of borane that led to trivinylboranes[19] gave a substantial amount of attack at the less hindered 2-position, since steric instead of electronic effects took control of the course of the reaction.

Hydroboration–oxidation of 16 gave 26 accompanied by 27, but treatment of the product of hydroboration before oxidation with alkaline deuterium oxide gave 28. The same product 28 was obtained by a similar treatment of the acetylide (29). Deuteroboration of 29 gave after treatment with water and oxidation the deuterated alcohol (30) accompanied by a small mount of the diol (31).

The formation of 1,3-diols from propargylic lithium compounds could be explained by the hydroboration of intermediate allenes formed from these derivatives. Such 1,3-directive effects in hydroboration of allenes have been observed[20,21] using BBN (9-borabicyclo[3,3,1]nonane). The hydroboration of phenylallene



(i) BuLi; (ii) BH_3; (iii) H_2O, NaOH; (iv) H_2O_2; (v) BD_3; (vi) D_2O, NaOD.

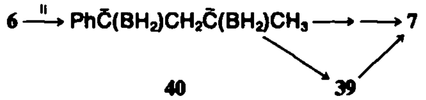
with borane was therefore studied. This reaction and subsequent oxidation yielded a mixture of products composed of 3 (70%), 32 (12.5%) and 33 (17.5%) isolated as their acetates. The large amount of the 1,2-diols (30%) eliminated phenylallene as an intermediate in the hydroboration of propargylic lithium derivatives.

DISCUSSION

The metalation-hydroboration of acetylenes is a very convenient method for the preparation of 1,3-diols. No 1,2-diols have been obtained from the metalated compounds. The directive effect of the boron first introduced in the system is therefore powerful. This high stereoselectivity relative to that observed in the hydroboration of allenes[22,23] and allylboron compounds[24,25] may be due to the larger selectivity of the first step and to the directive effect of the first introduced boron on the position of introduction of the second B atom due to a combined effect of steric and charge interactions. The lithium derivatives are probably attacked first exclusively at one of the propargylic positions whereas allenes might react to a large extent at the central atom.

The hydroboration of the propargylic lithium compounds consists of a complicated sequence of reaction. There are several possible sequences and it is difficult to conclude which of them takes place. The dilithium derivative 6 undergoes four reaction steps with borane (Scheme 1). The first attack might occur at the 1- or 3-position leading to 34 or 35. The following step takes place either at the other propargylic position leading to allenic bis-borates 38 or at the same position yielding the gem-bis-borates 36 and 37. These reactions can also take place concurrently. Moreover, equilibrations between the propargylic boranes and their allenic counterparts can take place. The next two steps involve the hydroboration of the bis-borates yielding (39). Additional reaction sequences could be proposed, e.g. hydroboration of 6 to a bis-borane (40) with charges stabilized at the positions α to the B atoms (Scheme 2). This bis-borane could react with additional borane molecules to give 39 or remain stable in solution until the oxidation step leading to 7. This last eventuality can however be eliminated by the results of deuteroboration of 6 with excess BD_3 where D atoms have been introduced at the 1- and 3-positions. Abstractions of a proton by 40 from borane is not probable since similar compounds[19,37] containing a negative charge or a lithium α to boron do not do this. Our experience with propargyllithium derivatives leads us to prefer the sequence $6 \rightarrow 34 \rightarrow 38 \rightarrow 39 \rightarrow$ or $6 \rightarrow 40 \rightarrow 39$ for the reaction with borane.

It remains therefore to explain the introduction of D atoms α- to the OH groups in the diols obtained by deuteroboration of the propargylic lithium derivatives. It seems that the reaction involved is an intramolecular one. This is consistent with the greater propensity of borates to undergo intramolecular than intermolecular reactions.[26] The scrutiny of the results of deuteroboration leads to the following generalizations concerning the introduction of deuterium: (1) At least two geminal B atoms have to be located on the carbon where H (D) is to be introduced, and (2) one of the boron-containing groups is a borate bearing a H (D) and the other is a borane.

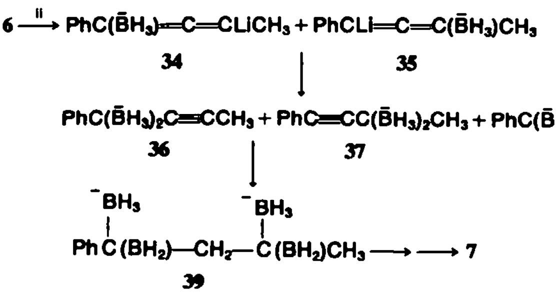


Scheme 2.

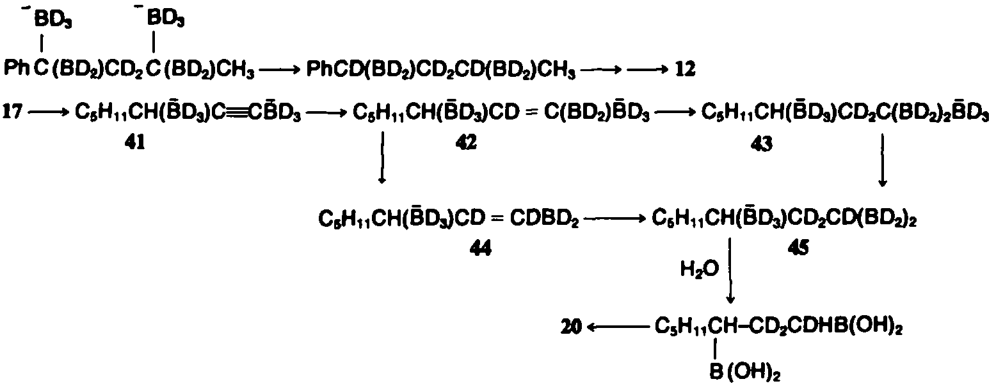
A good illustration for these rules is the product of deuteroboration of 6 (deuterated at carbon 2 and boron) where deuterium is introduced at the positions 1 and 3 and subsequent oxidation leads to 12.

Other examples are the deuteroboration of 17 and 29. Deuteroboration, hydrolysis and oxidation yield from the dianion 17 the diol 20 and from the acetylide 29 the monoalcohol 30, but both products contain two D atoms at C_2, only one at C_1 and none at C_3. The presence of a charge at C_3 in 17 is not enough to introduce a D atom, since only one B atom has been there. Three B atoms have been introduced in 43 at C_1, but only one is displaced by D, since only one of the B atoms was bearing a charge. The second one is replaced by a proton on hydrolysis[18,27] and the third produces on oxidation the OH groups (Scheme 3). This course of the reaction is supported by the formation of 28 on hydroboration of 29 with subsequent deuterolysis and oxidation, when again one boron on the terminal carbon was exchanged by hydrogen, the other by deuterium and the third by a OH group. It seems that hydride transfer is slow in these compounds. The borate group is probably associated by a one-hydrogen bridge with one of the borane molecules in excess in solution. The strength of such H-bonds has been estimated[28] to be higher than $30\ \text{kcal/mole}^{-1}$.

Displacement of good leaving groups from carbon by a group migrating from a boron neighboring this carbon is known to occur on saturated[29,30] and olefinic[31,32] carbons. This displacement is particularly easy, when boron is tetracoordinated and bearing a negative charge.[26,30-32] However, the displacement of an electro-positive boron, observed in this work, was unexpected. Although the formation of a boride ion in the intramolecular displacement by a hydride is not impossible (Scheme 4) (transition state 46) since dialkylborides are known,[33] it is more reasonable to assume a derivative of the stable lithium octahydrotriborate as the leaving group. Sodium



Scheme 1.



Scheme 3.

Table 1.

Acetate of Compound	Chemical Shifts (δ) of the protons					
	A	B	C	D	E	$OCOCH_3$
3	7.33(s)	-	6.0(t)	a	4.03(m)	2.0(s),1.96(s)
7x [b]	7.26(s)	1.2(d)	5.7-5.93(t)	a	4.83-5.18(q)	1,93(s),1.96(s)
7y [b]	7.26(s)	1.2(d)	5.63-5.9(t)	a	4.6-4.93(q)	1.96(s),2.0(s)
8	7.32(s)	2.0(s)	5.92-6.04(q)	4.26(m)	-	2.0(s)
15	7.53(s)	3.0(d)	5.35(qui)	1.96(qui)	4.23(t)	2.03(s)
18	1.0(m)	1.43(m)	5.16(qui)	1.96(qui)	4.23(t)	2.06(s)
23	0.96(m)	1.33(m)	5.13(qui)	1.96(qui)	4.23(t)	2.06(s)
24 [d]	7.2(s)	0.83(t)	4.43(t)	1.63(qui)	-	2.21(br.s) (-OH)
26	0.96(m)	1.4(m)	4.23(t)	-	-	2.06(s)
27	0.96(m)	1.4(m)	5.03-5.36(m)	4.16-4.7(m)	-	2.1(s)
32	7.2(m)	1.05(d)	5.63(d)	-	5.15(qui)	1.93(s),1.99(s)
33	7. 15(s)	2.86(d)	5.23-5.03(m)	-	c	1.97(s)

a) hidden partly by the acetates.

b) 7x and 7y are the erythro and threo isomers.

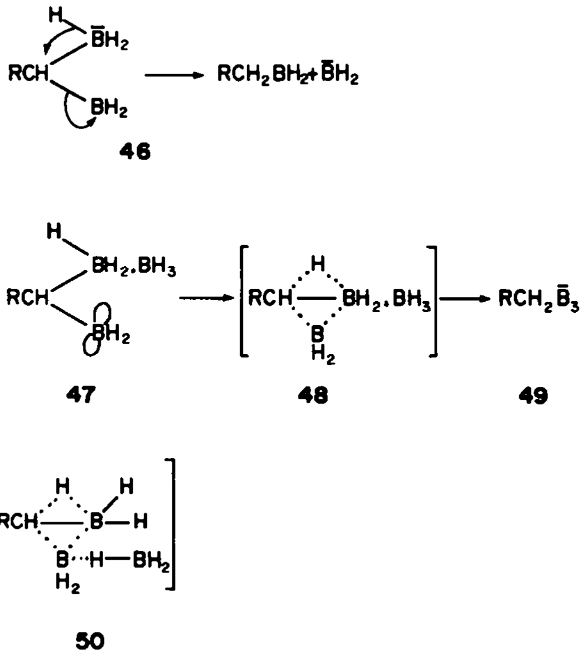
c) overlapped with protons E of 3.

d) the alcohol.

e) (s) = singlet; (d) = doublet; (t) = triplet; (q) = quartet; (qui) = quintet; (m) = multiplet.

Table 2.

Analyses of the acetates of	Calcd. %		Found %		IR spectra, cm^{-1}
	C	H	C	H	
3	66.1	6.77	65.82	6.82	700, 1050, 1235, 1500, 16000, 1750.
7	67.2	7.2	67.12	7.12	700, 760, 1025, 1240, 1450, 1500, 1750.
15	67.2	7.2	67.02	7.30	1250, 1600, 1740.
18	62.6	9.56	62.66	9.80	1250, 1740.
23	67.1	10.4	66.99	10.32	1250, 1740.



Scheme 4.

octahydrotriborate is formed easily from sodium tetrahydroborate and diborane.[34] The presence of excess borane permits its assistance in this rearrangement. An assistance by borane was found kinetically in chlorine displacement.[35] The exact nature of the transition state is not known but possible formulations are **47** or **48** (Scheme 4).

The 1,2-hydrogen migration involves either an extrusion **46** of one boron from the molecule or a dyotropic reaction,[36] consisting of a migration of hydrogen from a negatively charged boron to a neighboring carbon simultaneously with the migration of the BH_2 group from this carbon to the neighboring boron: **47**→**48**→**49** (A more involved transition state is **50**). This reaction was not observed in negatively charged gem-diboronated compounds when allyl groups and no hydrogen were present on the B atoms.[32,37,38] An equilibrium between the gem borane-borate and an α-lithioborane obtained by dissociation of a trialkylborane from the molecule was reported.[37,38] The participation of the empty orbital on the borane makes the rearrangement an allowed reaction since it can be considered to proceed with "inversion" on boron, similarly to the suprafacial hydroboration reaction.

EXPERIMENTAL

NMR spectra were recorded on a Varian T60 apparatus or on a Varian HA-100 using TMS as an internal standard in CCl_4. Gas chromatographic separations were performed on a Varian Aerograph A-90-P-3. IR spectra were recorded on a Perkin–Elmer 337 spectrometer. Analysis were performed by Mrs. Goldstein of the Microanalytical Laboratory of the Hebrew University. 1-Phenylpropyne, 1-phenylbutyne, 1-octyne and 2-octyne were commercial samples (Farchan Res. Lab.).

4-Phenylbut-1-yne **13**. An ether soln of 28 g of benzyl bromide was added dropwise in the presence of a catalytic amount of CuCl to an ether soln of propargyl-magnesium bromide prepared from 13.2 g of Mg and 59.6 g of propargyl bromide. Stirring was continued overnight. The mixture was poured then on ice water, acidified with dil. H_2SO_4, the organic layer separated and the solvent evaporated. The residue was distilled at 90–100° (25 mm) (17 g; 79%).

3-Phenyl-prop-1-yne. Hexane was evaporated *in vacuo* from 143 ml of a soln of BuLi 1.6F in hexane. The residue was cooled in an acetone-dry-ice bath, argon was admitted and 100 ml of dry ether were added, followed by 5.0 g of **1**. The mixture was brought gradually to room temp. and left for 8 h. It was poured then on ice-water. The product was distilled after the usual work-up at 80–85° (25 mm) (3 g; 60%).

Phenylallene. 0.15 ml of a soln of methylsulphinylcarbanion[39] 2F in DMSO were added at 10° to a soln of 3 g of 3-phenyl-prop-1-yne in DMSO. The reaction was followed by NMR and when the acetylenic proton disappeared the mixture was poured on ice-water and the product extracted with ether. The ether soln was washed several times with water. The residue was distilled after evaporation at 80–85° (25 mm) (2 g).

1-Dodecyne **43** was prepared by a two-step reaction[40]: KOH (0.2 mole) in water (10 ml) was added to a soln of 1,2-dibromododecane (0.15 mole) in EtOH (100 ml). The soln was refluxed for 2 hr, then concentrated *in vacuo*, poured into water extracted with ether and distilled at 100–105° (1 mm). A mixture of 1- and 2-bromododec-1-enes was obtained. In a separate flask, 100 ml of DMSO were added to 12 g NaH (washed three times with hexane) in N_2 atmosphere. The soln was heated to 65–70° for 1 hr, cooled to 10° and 4.8 g (0.1 mole) of the mixture of bromododecenes was added dropwise. Stirring was continued for 1–2 hr. The soln was then poured into ice-water, the product extracted with ether and the ether soln washed with 5 consecutive portions of water. Separation of the layers and distillation at 95° (1.5 mm) gave 12 g of 1-dodcyne (42%). (Found: C, 86.69; H, 13.5. Calc. for $C_{12}H_{22}$: C, 86.7; H, 13.2) IR: $\bar{\nu}$ (C≡C) 2120 cm^{-1}; NMR, ppm: 1.7 (t)≡CH, 2.0–2.2 (m)–$CH_2C≡C$–, 0.9 (t) CH_3–C–.

Metalation and subsequent hydroboration was carried out by a standard procedure which will be described for **16**. To 48 ml of BuLi in ether (0.072 mole) (obtained as described above from a solution of BuLi in hexane) cooled to −20° were added dropwise 2 g of **16**. The mixture was brought gradually to room temp. and left for 30 hr. It was then added dropwise with a 50 ml syringe to 68.5 ml of a cooled soln (ice) of 2.1M borane in THF (0.144 mole). The soln was stirred for 5 hr, excess borane decomposed slowly with 50 ml of water and the product was oxidized by 50 ml of NaOH (3N), and dropwise addition of 70 ml of H_2O_2 30%. Extraction of the product from the mixture (saturated with K_2CO_3) with three portions of 40 ml of ether and acetylation overnight with 16 ml of Ac_2O–pyridine (1:1) gave 2.4 g (60%) of **18**, b.p. 165–170° (25 mm). The absence of other isomeric diacetates was verified by glc analysis on a 3mx 1/4 column of DEGS 20% on Chromosorb W, mesh size 60/80.

Hydroboration of phenylallene. 1 g of phenylallene was added dropwise to 17 ml of a cooled soln (ice) of 2M borane in THF. Stirring was continued for 3 hr. Excess borane was decomposed slowly with 30 ml of water, and the product oxidised by 30 ml of NaOH (3N), and dropwise addition of 30 ml of H_2O_2 30%. After the usual work up the product was distilled at 100–110° (1 mm) (1.4 g; 70%). Acetylation of the crude product gave a mixture of isomeric diacetates that was only partly separated by glc on a 3m × 1/4 in. column of DEGS 15% at 150°. 33 was not separated well from 3. Both isomers were therefore collected together and the NMR was recorded on their mixture. The signals of 3 could be identified by comparison with the signals of a spectrum of pure 3 produced from hydroboration of 2.

Hydroboration of 1-octyne. 1 g of 16 was added dropwise to 18 ml of a cooled soln (ice) of 2M borane in THF. Stirring was continued for 4 hr. Excess borane was decomposed slowly with 35 ml of water, followed by 35 ml of NaOH 3N. Stirring was continued for 2 hr and the product oxidised by dropwise addition of 35 ml of H_2O_2 30%. After the usual workup the products were analysed by glc at 170° on a 3m × 1/4 in. column of DEGS 20% on Chromosorb W.

BD_3 was prepared according to the procedure recommended by Zweifel[27] from lithium deuteride and boron trifluoride etherate.

Deuteroboration was performed by the same procedure as the hydroboration. Products were separated by glc and identified by their NMR spectrum.

Compound 30: NMR ppm: 0.96 (m, 3H), 1.36 (m, 10H), 4.13 (m, 1H), 2.06 (m, 1H).

Compound 31: Traces of hydrogen at the 1 position but no hydrogen at the 2 position was detected by NMR.

Compound 20. One proton only at the 1 position but no proton at the 2 position was detected by NMR.

Compounds 10 and 11: The NMR spectrum revealed the presence of one proton at position 3, no proton at position 2 and half a proton at position α to the phenyl.

Compound 12: The NMR spectrum revealed traces of hydrogen at positions 1 and 3 and no hydrogen at position 2.

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