Journal of Organometallic Chemistry, 152 (1978) 265—270

OXIDATIVE REARRANGEMENT OF *B*-METHYLATED 1-ALKENE-1,1-DIBORONIC ESTERS TO METHYL KETONES

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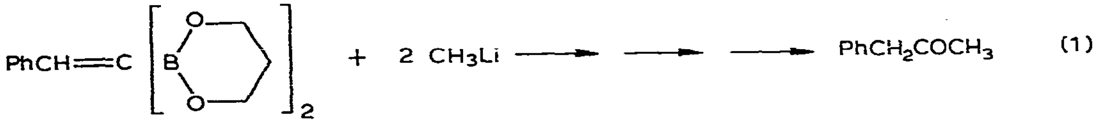
(Received December 12th, 1977)

Summary

Treatment of 1,1-bis(trimethylenedioxyboryl)-2-phenylethene (I) or the analogous 2-cyclohexyl compound (II) with two mol of methyllithium followed by oxidation with alkaline sodium perborate (under air) gives good yields of phenylacetone or cyclohexylacetone, which are the products of methyl migration from boron to carbon. Reactions of I with other organolithiums lead to lower yields of ketones, as do reactions of 2,2-disubstituted alkene-1,1-diboronic esters with methyllithium. Examination of the reaction intermediates by ^{1}H NMR revealed that methyl migration is not brought about by water or acid and does not occur until the oxidation step. These results illustrate that structures of organoborane intermediates which contain reactive neighboring groups cannot be assigned solely on the basis of their peroxide oxidation products.

Introduction

The reaction of 1,1-bis(trimethylenedioxyboryl)-2-phenylethene (I) with 2 mol of methyllithium followed by iodine and sodium hydroxide and then hydrogen peroxide was reported by Matteson and Hagelee to give phenylacetone in 30% yield [1]. We have now found that this transformation (eq. 1) can be carried out in good yield, but the pathway is not at all what it was originally imagined to be.



(1)

(I)

The original model for attempting conversion 1 was the rearrangement of *B*-alkenyl-*B*-alkylboranes discovered by Zweifel and coworkers [2] and utilized successfully in this laboratory [3] and elsewhere [4]. However, attempted duplication of conversion 1 generally gave yields closer to 5% than the 30% reported [1], which may have been an artifact of gas chromatography. When iodine was omitted and methyl iodide used instead, the yield of phenylacetone rose to 73%.

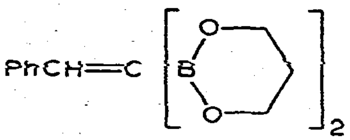
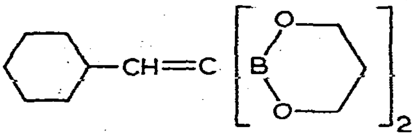
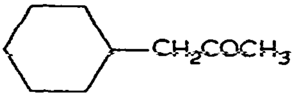
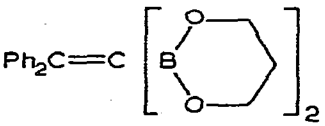
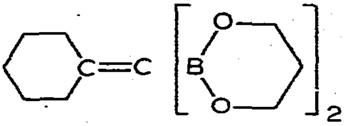
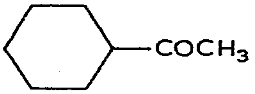
Having found an efficient reaction, we undertook a brief exploration of its synthetic utility and then of its pathway.

Results and discussion

Alkene-1,1-diboronic esters (I—IV) were allowed to react with methyllithium and I with various organolithiums with the results summarized in Table 1. Methyl

TABLE 1

REACTIONS OF 1-ALKENE-1,1-DIBORONIC ESTERS WITH 2 RLi FOLLOWED BY OXIDATION WITH SODIUM PERBORATE

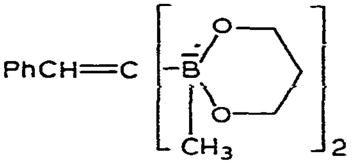
Boronic Ester	RLi	Product	Yield[a] (%)
 (I)	CH_3Li	$PhCH_2COCH_3$	75
 (II)	CH_3Li		76[b]
 (III)	CH_3Li	$Ph_2CHCOCH_3$	1.3[b]
 (IV)	CH_3Li		41
I	C_2H_5Li	$PhCH_2COCH_2CH_3$	38
I	$CH_3(CH_2)_3Li$	$PhCH_2CO(CH_2)_3CH_3$	17[c]
I	PhLi	$PhCH_2COPh$	53
I	$PhCH_2Li$	$PhCH_2COCH_2Ph$	25

[a] By gas chromatography. [b] 2 CH_3I added before oxidation. [c] When 2 CH_3I was added, 14% $PhCH_2CO(CH_2)_3CH_3$ and 13% $PhCH_2COCH_3$ resulted.

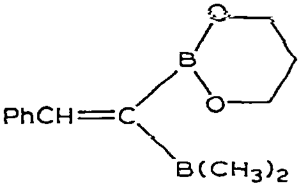
iodide proved irrelevant, as shown by the 75% yield of phenylacetone from I when CH_3I was omitted. Two mol of methyllithium per mol of I were essential for good yields.

The yields with groups other than methyl (Table 1) are disappointing from a synthetic point of view, and anomalous inasmuch as methyl is usually the poorest migrating group [5] instead of the best.

Reaction of I with 2 mol of methyllithium should result in *B*-methylation to form V or perhaps VI or a mixture of the two.



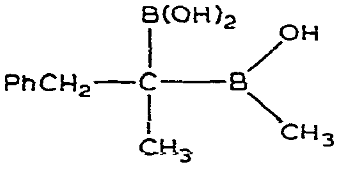
(V)



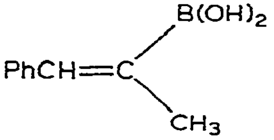
(VI)

Formation of phenylacetone requires transfer of one of the *B*-methyl groups to carbon at some stage of the reaction.

The obvious, but incorrect, interpretation would involve *C*-protonation of V or VI during aqueous work-up, with rearrangement and hydrolysis to VII. Good precedents exist [5,6], although no acid was used in our work-up procedure. An alternative intermediate to be considered is VIII, though a nonoxidative pathway from V or VI to VIII is, by definition, difficult to imagine.



(VII)

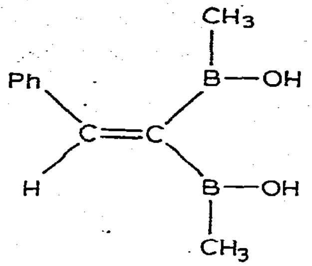


(VIII)

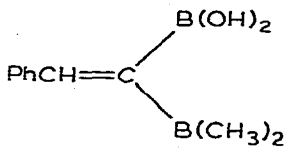
Definitive information was provided by ^1H NMR spectra. Concentration of the tetrahydrofuran (THF) solution of *B*-dimethylated I under vacuum yielded a viscous residue, NMR ($CDCl_3$) δ0.0 (s, 3, B—C$\underline{H}_3$), 0.2 (s, 3, B′—C$\underline{H}_3$), 6.9 (s, 1, C$\underline{H}$=C), and 7.2 ppm (s, 5 $C_6\underline{H}_5$), as well as two large, unresolved peaks at 1.8 and 3.9 (25—30 each, THF + O(C$\underline{H}_2$)$_3$O). The lines were broad, but the result is clearly consistent with structure V or perhaps a mixture of V and VI.

With careful protection from air, an aqueous solution of the crude V was extracted with $CDCl_3$ to remove part of the propanediol and THF, then acidified with 6 *M* hydrochloric acid, which precipitated an oil. The NMR ($CDCl_3$) was well resolved, δ 0.40 (s, 3, B—C$\underline{H}_3$), 0.60 (s, 3, B′—C$\underline{H}_3$), 7.42 ppm (s, ~10, $C_6\underline{H}_5$ + C$\underline{H}$$Cl_3$ from H—D exchange), and 7.67 (s, width at half-height 4 Hz, 1, C$\underline{H}$=C), plus the characteristic THF multiplets at δ 1.80 and 3.77 ppm (~6$\underline{H}$ each) and several small impurity peaks, including some 1,3-propanediol. This result is clearly consistent with structure IX, perhaps mixed with some X or closely related species.

The absence of any absorptions between δ 2.0 and 3.6 ppm and between 0.7



(IX)



(X)

and 1.7 ppm definitively rules out the possibility of any significant amount of the rearrangement product VII, which would have to show a CH_2 singlet near δ 2.83 ppm, the position of the CH_2 of $PhCH_2CH(BO_2C_2H_4)_2$ [7], as well as a CH_3 singlet near δ 1.0 ppm, models being provided by $PhC(BO_2C_2H_4)_2CH_3$, δ 1.10 ppm [7], and $CH_3CH[B(OH)_2]_2$, δ 1.0 ppm [8]. The upfield THF multiplet could conceivably conceal up to 10—20 mol percent of the CH_3 singlet of VIII relative to IX, but it is clear that VIII cannot be the major species present at this stage. Phenylacetone is absent.

Since it appeared that we would be unable to isolate the air sensitive and noncrystalline intermediate, some additional evidence was sought by further NMR correlations. The pinacol ester analogue of I, $PhCH{=}C[BO_2C_2(CH_3)_4]_2$ (XI), was synthesized and similarly converted to the hydrolyzed *B*-methyl derivative (IX). The NMR spectrum was the same, except that the amount of residual THF was somewhat greater and the $CHCl_3$ peak fortuitously shifted apart from the C_6H_5, which gave the correct relative integral. The residual pinacol peak at δ 1.25 ppm corresponded to 25—30% of the original pinacol content. There was no B—OH in either this or the previous spectra, but fully characterized boronic acids sometimes fail to show a B—OH peak in $CDCl_3$ [3], perhaps due to boronic anhydride formation. *B*-Methylation of the cyclohexyl compound $C_6H_{11}CH{=}C(BO_2C_3H_6)_2$ (II) yielded a derivative having *B*-methyl singlets at δ 0.47 and 0.57 ppm and the $C\underline{H}{=}C$ doublet at δ 6.74 ppm (*J* 10 Hz, line widths at half-height 4 Hz). *B*-Methylation of the cyclohexylidene compound $(CH_2)_5C{=}C(BO_2C_3H_6)_2$ (IV) led to a single *B*-methyl peak at δ 0.51 ppm, suggesting that the pairs of *B*-methyl peaks seen in the other products are due to nonequivalent boron atoms as in structure IX, not to a mixture of *B*-methylated products. Spectral correlations also permitted assignment of the $C\underline{H}{=}C$ peak of I, not previously recognized [1], at δ 7.65 ppm.

It was verified that the intermediate IX does yield phenylacetone on oxidation with alkaline sodium perborate under the usual conditions, which include stirring without protection from air. It was also found that stirring a basic solution of IX in air without perborate yielded enough phenylacetone to detect by NMR, GLC, and formation of a 2,4-dinitrophenylhydrazone. However, in a single experiment, alkaline sodium perborate in an argon-purged NMR tube failed to oxidize the presumed IX. Poor mixing could have been a factor, but the slow reaction is anomalous.

Clearly migration of the methyl group from boron to carbon occurs during the oxidation step and not before. There is some precedent in the free radical carbon—carbon bond cleavage during the oxidation of *gem*-diboryl compounds found by Pasto and coworkers [9], and we have observed cleavage of $RR'C=CHB(OH)_2$ to $RR'C=O$ as a side reaction in the deboronation with hydrogen peroxide, which was minimized but not fully suppressed by using sodium perborate as the oxidant [10]. Since IX combines both structural features, some anomaly might have been anticipated, but the rearrangement is new.

The question may be raised whether the rearrangement is caused by perborate or free oxygen. However, alkaline hydrogen peroxide solutions liberate oxygen, and autoxidations generate peroxides, and from a practical point of view it would be difficult to have one reagent present without some of the other. Numerous speculative mechanisms, with or without radical chain autoxidation [11] or intramolecular methyl migration, can be imagined.

From the previous [9,10] and present results, it may be concluded that the carbon skeletons of organoboranes and their peroxide oxidation products sometimes differ. Therefore, proof of structure of organoborane intermediates based solely on peroxide oxidation products cannot be considered valid. Of course, it is well established that ordinary alkylboranes normally give highly specific reactions with alkaline hydrogen peroxide [12], but caution in interpretation seems in order whenever there are neighboring groups, especially if quantitative significance is attached to the product distribution.

Experimental

Gas chromatographic analyses were obtained with a Varian Aerograph Series 1700 instrument equipped with a 3.1 m × 3 mm 10% SE-30 on Chromosorb W(NAW) column, a flame ionization detector, and a Sargent Model SR6 recorder and integrator. Column temperatures were 135—187°C. Authentic samples of the ketones were redistilled and calibrated relative to a suitable reference compound, either undecane, dodecane, or dicyclohexyl. Selected ^1H NMR spectral curves, including all those described in the Results and Discussion, are recorded in R.J. Moody's Ph.D. Thesis, Washington State University, 1977. The methyllithium used was checked periodically by titration with 2-propanol to the phenanthroline endpoint. Other general procedures were the same as described in a preceding article [13].

Alkene-1,1-diboronic esters (I, II, III, IV and XI)

These were prepared as described previously [1] (see also [13]). The pinacol ester $PhCH=C[BO_2C_2(CH_3)_4]_2$ (XI) was prepared in the same manner, except that the starting material was tetrakis(tetramethylethylenedioxyboryl)methane [14]. It is a new compound, recrystallized from ether/pentane, m.p. 70—71°C; ^1H NMR ($CDCl_3$) δ 1.3 (s, 24, $C\underline{H}_3$), 7.5 (m, 5, $C_6\underline{H}_5$), 7.92 ppm (s, 1, $C\underline{H}=C$). Found: C, 67.55; H, 8.57; B, 6.01. $C_{20}H_{30}B_2O_4$ calcd.: C, 67.42; H, 8.43; B, 6.18%. Also new is 1,1-bis(trimethylenedioxyboryl)-2-cyclohexylethene (II), from pentane, m.p. 90—92°C; ^1H NMR ($CDCl_3$) δ 1.2—2.2 (m, 15, $C_6\underline{H}_{11}$ + $CC\underline{H}_2C$), 4.10 (t, 4, $OC\underline{H}_2$), 4.15 (t, 4, $OC\underline{H}_2$), 6.72 (d, 1, J 9 Hz, line widths 4 Hz at half-height, $C\underline{H}=C$). Found: C, 60.44; H, 8.73; B, 8.03. $C_{14}H_{24}B_2O_4$ calcd.: C, 60.43; H, 8.63; B, 7.91%.

B-Methylation of alkene-1,1-diboronic esters and oxidative rearrangement

A solution of 1.84 mmol of the alkene-1,1-diboronic ester in 30 ml of anhydrous THF was cooled with a Dry Ice/acetone bath and stirred under argon during the addition of 2.3 ml (3.6 mmol) of 1.6 *M* methyllithium in ether dropwise from a syringe, then stirred for 2 h at 0°C. (At this point, 3.7 mmol of methyl iodide was added to some of the earlier runs, Table 1.) The solution was concentrated under vacuum, and the residue was treated one of two ways. (1) For the oxidations in Table 1, 20 ml of dichloromethane and 15 ml of water were added, followed by 0.9 g (6 mmol) of sodium perborate tetrahydrate in several portions with stirring (under air). The mixture was stirred 10 min, a measured quantity of the chromatographic reference compound was added from a syringe, 40 ml more dichloromethane was added and the phases separated, and the organic phase was analyzed by gas chromatography. (2) For the NMR spectra, the residue was kept carefully protected from air and 1.5 ml of deuterochloroform was added, enough to dissolve the gummy solid. Either the solution itself was transferred to an argon-purged NMR tube by syringe, or it was stirred for 5 min with 10 ml of water under argon, the deuterochloroform then removed by syringe and discarded, the aqueous phase treated with an additional portion of deuterochloroform and acidified with hydrochloric acid, and the deuterochloroform transferred by syringe, dried over magnesium sulfate, and the NMR spectrum taken, keeping the solution under argon at all times.

Acknowledgment

We thank the National Science Foundation for support, grant no. MPS 75-19557.

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