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Preliminary communication

A FACILE SYNTHESIS OF α-CHLOROBORONIC ESTERS VIA THE BASE INDUCED REACTION OF α,α-DICHLOROMETHYL METHYL ETHER WITH HINDERED BORINIC ESTERS

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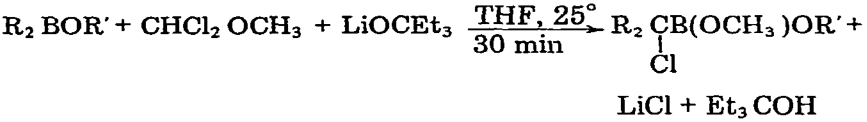
Summary

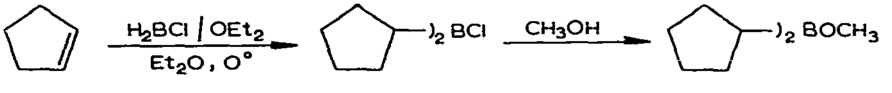
Treatment of hindered borinic esters, R_2BOR', with an equimolar quantity of α,α-dichloromethyl methyl ether and lithium triethylcarboxide yields the α-chloroboronic esters, $R_2CHClB(OCH_3)OR'$, in excellent yields. In cases where the steric requirements of R are not sufficient, the steric requirements of R′ can be increased to achieve the synthesis.

Esters of α-haloboronic acids exhibit remarkable potentiality for synthetic transformations [1]. However, the available synthetic routes for their preparation are relatively few and quite limited in scope [1]. The recently discovered synthesis of ketones via the base induced reaction of α,α-dichloromethyl methyl ether (DCME) with esters of borinic acids [2] led us to explore the possibility that this reaction might serve as a general route to α-chloroborinic acids. Indeed, by proper control of the steric factor it proved possible to develop such a general synthesis (eqn. 1).



$$R_2BOR' + CHCl_2OCH_3 + LiOCEt_3 \xrightarrow[30\ min]{THF,\ 25^\circ} R_2\underset{\displaystyle Cl}{\underset{|}{C}}B(OCH_3)OR' + LiCl + Et_3COH \qquad (1)$$

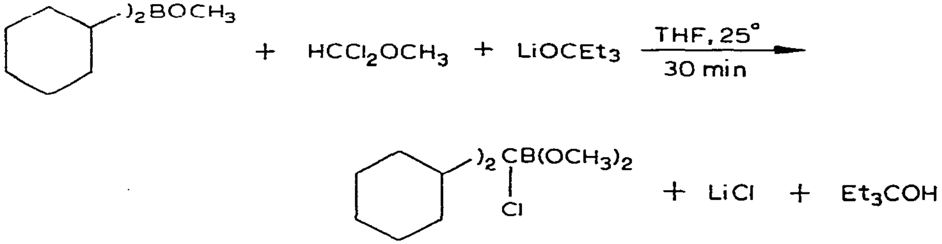
Dialkylborinates are now readily available via the hydroboration of the respective olefins with monochloroborane etherate, followed by alcoholysis of the product [3] (eqn. 2).



(2)

We discovered that treatment of relatively hindered methyl borinates, such as dicyclohexyl or di-*exo*-norbornyl, with one molar equivalent of DCME and

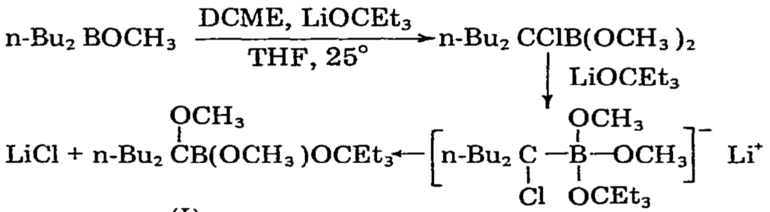
LiOCEt$_3$ proceeds smoothly to yield the desired α-chloro derivative (eqn. 3)



(3)

Unfortunately, the reaction failed with less hindered borinic acid derivatives, such as methyl di-n-butyl- and dicyclopentylborinates.

Investigation revealed that in these less hindered cases the product was largely the α-methoxy derivative. This intermediate presumably arises from a competitive coordination of the base with the boron atom of the initial product, followed by a transfer of the methoxy group [4] (eqn. 4).



$$\text{n-Bu}_2\text{BOCH}_3 \xrightarrow[\text{THF, }25^\circ]{\text{DCME, LiOCEt}_3} \text{n-Bu}_2\text{CClB(OCH}_3)_2 \qquad (4)$$

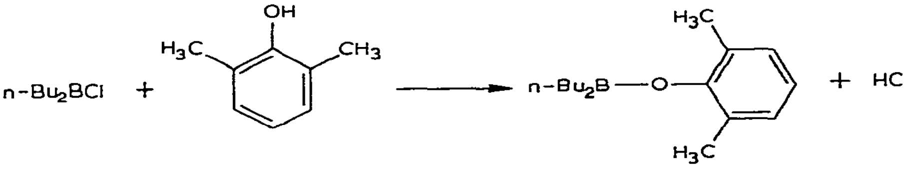
$$\text{n-Bu}_2\text{CClB(OCH}_3)_2 \xrightarrow{\text{LiOCEt}_3} \left[\text{n-Bu}_2\,\underset{\text{Cl}}{\text{C}}-\underset{\text{OCEt}_3}{\overset{\text{OCH}_3}{\text{B}}}-\text{OCH}_3\right]^- \text{Li}^+$$

$$\text{LiCl} + \text{n-Bu}_2\,\overset{\text{OCH}_3}{\text{C}}\text{B(OCH}_3\text{)OCEt}_3 \longleftarrow \left[\text{n-Bu}_2\,\underset{\text{Cl}}{\text{C}}-\underset{\text{OCEt}_3}{\overset{\text{OCH}_3}{\text{B}}}-\text{OCH}_3\right]^- \text{Li}^+$$

(I)

Indeed, I (methyl triethylcarbinyl 5-methoxy-5-nonylboronate) was isolated and fully characterized by NMR, mass and IR spectral data. It was isolated in 65% yield from a reaction mixture in which two molar equivalents of base were used.

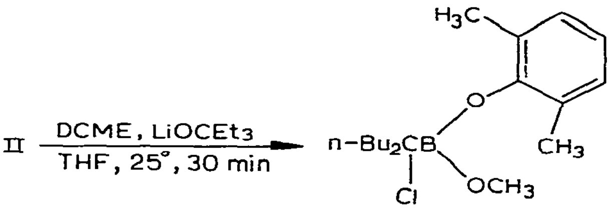
Evidently the good yields realized in the dicyclohexyl and di-*exo*-norbornyl cases must arise from a relatively difficult coordination of the base with the boron atom in the α-chloro product (eqn. 4). Perhaps the presence of an ester grouping with greater steric requirements might circumvent this undesired side-reaction. Indeed, treatment of di-n-butylboron chloride with 2,6-dimethylphenol yielded the corresponding boronic ester, II (eqn. 5).



(II)

(5)

Treatment of II with DCME and base yielded the desired α-chloroborinic ester III in 70% yield (isolated) (eqn.6).



(III)

(6)

This procedure also proved successful with other less hindered derivatives such as the dicyclopentyl- and diphenylborinates. It also accommodated dialkyl borinates with two different alkyl groups.

The experimental results are summarized in Table 1.

TABLE 1

PREPARATION OF α-CHLOROBORONIC ESTERS, $RR''CClB(OCH_3)OR'$, VIA REACTION OF BORINIC ESTERS, $RR''BOR'$, WITH DCME AND LITHIUM TRIETHYLCARBOXIDE

R	R''	R'	Yield (%) (isolated)	Physical properties [a]
n-Butyl	butyl	2,6-dimethylphenyl	70	b.p. 118–120° (0.03 mm/Hg)
Phenyl	phenyl	2,6-dimethylphenyl	80 [e]	m.p. 53–54° [b]
Cyclopentyl	cyclopentyl	2,6-dimethylphenyl	87	m.p. 79–80° [b]
exo-Norbornyl	*exo*-norbornyl	methyl	89	[c]
Cyclohexyl	cyclohexyl	methyl	86	m.p. 50.5–52.5° [b]
2,3-Dimethyl-2-butyl	cyclopentyl	methyl	80 [d]	b.p. 84–88° (0.03 mm/Hg)

[a] All new compounds gave satisfactory NMR and, mass spectra and correct elemental analyses for C, H, B and Cl. [b] Recrystallized from pentane at −78° under nitrogen. [c] All attempts to recrystallize the resulting oil failed, presumably due to existence of a diastereoisomeric mixture. [d] 100% excess DCME and lithium triethylcarboxide were used. [e] The 2,6-dimethylphenyl ester of diphenylborinic acid was prepared by reaction of diphenylboron bromide (Alfa Ventron) with 2,6-dimethylphenol in pentane at room temperature. The resulting oil was recrystallized from pentane at −78° under nitrogen, m.p. 63–64°.

The following procedure for preparation of the dimethyl ester of dicyclohexylchlorocarbinylboronic acid is representative. A dry 200-ml flask, fitted with a septum inlet, magnetic stirrer, and reflux condenser, was flushed with nitrogen and maintained under a static pressure of the gas. In this flask was placed 19.6 ml of a 2.55 *M* solution of borane (50 mmol) in THF and 20.0 ml of THF; 9.6 g (100 mmol) of cyclohexene was added. After 1 h at 0° 1.6 g (50 mmol) of methanol was added to form the ester, methyl dicyclohexylborinate. To the reaction mixture was added at 0° 5.0 ml (6.53 g) (~ 10% excess) of DCME followed by 28.25 ml of a 1.77 *M* solution of lithium triethylcarboxide (50 mmol) in hexane over 5 min. The reaction mixture was allowed to come to room temperature and maintained there for 30 min. A heavy white precipitate, lithium chloride, was observed. The solvents were then evaporated via aspirator (1 h, 25°, 15 mm). The residue was washed with 3 × 25 ml of pentane and filtered under nitrogen. The filtrate was then evaporated at 15 mm at 25° to remove pentane and then at 0.1–0.3 mm at 25° (2–3 h) to remove triethylcarbinol. The resulting oil was taken up in pentane and recrystallized at −78° (under nitrogen). There was obtained 12.23 g (85.5% yield) of material m.p. 50.5—52.5°; NMR (CCl_4, TMS) δ 0.9—2.2 (m, 22H) and 3.76 (s, 6H) ppm.

The following procedure was utilized to convert the dialkylboron chloride derivatives into the 2,6-dimethylphenyl borinates. To a 100-ml flask charged with 6.30 g (39.3 mmol) of di-n-butylboron chloride [3] in 40 ml dry ether was added at 0° under nitrogen a solution of 4.80 g (39.3 mmol) of 2,6-dimethylphenol in 40 ml dry ether. The reaction mixture was stirred 15 min at this temperature and then maintained at room temperature for 15 min. Ether and hydrogen chloride produced in the reaction were removed at 15 mm and 25° over 1 h. The remaining material was used directly for reactions with the base and DCME, as described above.

It is evident that this development provides a simple, general entry into the α-chloroboronates and makes these derivatives readily available for study. Some time ago it was suggested that α-chloroboron derivatives might be a source of carbenes [5]. The ready availability of these derivatives should now permit a detailed examination of this proposal.

Acknowledgements

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