Anal. Calcd for $C_{11}H_{13}ClO_3$: C, 57.78; H, 5.73. Found: C, 57.81; H, 5.78.

**4-Carbomethoxy-4-methyl-2,5-cyclohexadien-1-one (7).** 7 was obtained from 3-carbomethoxy-3-methyl-1,4-cyclohexadiene[8] as a colorless oil in 57% yield by the method involving $CrO_3$ described in ref 3. Spectral data are in agreement with those reported in the literature.[5]

**3-Carbomethoxy-4-methylphenol (8b).** 8b was prepared from 7 as colorless crystals [mp 73–74 °C (lit.[9] mp 74–75 °C)] in 75% yield. Spectral data for 8b were not reported:[9] $^1$H NMR ($CDCl_3$) $\delta$ 2.51 (s, 3 H), 3.89 (s, 3 H), 4.81 (s, 1 H), 6.92 (dd, $J$ = 9 Hz, $J$ = 3 Hz, 1 H), 7.12 (d, $J$ = 9 Hz, 1 H), 7.40 (d, $J$ = 3 Hz, 1 H); IR (film) 3315, 1685, 1220 cm$^{-1}$; chemical ionization mass spectrum, $m/z$ (relative intensity) 167 ($M^+$ + 1, 100).

**2-Butyl-3-carbomethoxy-3-(4-chlorobutyl)-1-methoxy-1,4-cyclohexadiene (10).** A solution of 9 (0.94 g, 4.2 mmol; prepared by esterification of 2-butyl-3-methoxybenzoic acid[10]) and *tert*-butyl alcohol (0.31 g, 4.2 mmol) in dry THF (5 mL) was cooled to −78 °C. Liquid ammonia (50 mL) and then potassium (0.44 g, 11.3 mmol) were added to the stirred reaction mixture. After 0.5 h at −78 °C, 1-bromo-4-chlorobutane (0.86 g, 5 mmol) was added. The reaction mixture was stirred at −78 °C for 0.5 h and quenched with excess solid $NH_4Cl$. After evaporation of ammonia, the residue was partitioned between ether (60 mL) and water (10 mL). The two layers were separated, and the organic phase was washed with brine (10 mL) and dried over magnesium sulfate. Concentration under reduced pressure gave a yellow oil that was purified by flash chromatography (silica gel; hexane/ethyl acetate, 2.3:1) to afford a colorless oil (1.1 g, 82%): $^1$H NMR ($CDCl_3$) $\delta$ 0.88 (m, 3 H), 1.18–1.40 (m, 6 H), 1.60–2.05 (m, 6 H), 2.85–2.95 (m, 2 H), 3.52 (t, $J$ = 6.7 Hz, 2 H), 3.58 (s, 3 H), 3.65 (s, 3 H), 5.40–5.52 (m, 1 H), 5.9–6.0 (m, 1 H); IR (film) 1720, 1650 cm$^{-1}$; chemical ionization mass spectrum, $m/z$ 315 ($M^+$ + 1).

**3-Butyl-4-carbomethoxy-4-(4-chlorobutyl)-2-methoxy-2,5-cyclohexadien-1-one (11):** Obtained from 10 as an oil in 34% yield by the method involving $CrO_3$ described in ref 3; $^1$H NMR ($CDCl_3$) $\delta$ 0.91 (m, 3 H), 1.1–1.5 (m, 6 H), 1.65–1.9 (m, 2 H), 2.0–2.3 (m, 4 H), 3.49 (t, $J$ = 6.5 Hz, 2 H), 3.68 (s, 3 H), 3.82 (s, 3 H), 6.40 (s, $J$ = 9.9 Hz, 1 H), 6.65 (d, $J$ = 9.8 Hz, 1 H); IR (film) 1730, 1660, 1640 cm$^{-1}$; chemical ionization mass spectrum, $m/z$ 329 ($M^+$ + 1).

Anal. Calcd for $C_{17}H_{25}ClO_4$: C, 62.09; H, 7.66. Found: C, 61.88; H, 7.55.

**Methyl 3-butyl-2-(4-chlorobutyl)-5-hydroxy-4-methoxybenzoate (12):** obtained from 11 as a colorless oil in 60% yield; $^1$H NMR ($CDCl_3$) $\delta$ 0.96 (t, $J$ = 6.7 Hz, 3 H), 1.4–2.0 (m, 8 H), 2.65 (t, $J$ = 6.7 Hz, 2 H), 2.85 (t, $J$ = 6.7 Hz, 2 H), 3.59 (t, $J$ = 6.6 Hz, 2 H), 3.82 (s, 3 H), 3.86 (s, 3 H), 5.68 (s, 1 H), 7.33 (s, 1 H); IR (film) 3420, 1720 cm$^{-1}$; chemical ionization mass spectrum, $m/z$ 329 ($M^+$ + 1).

Anal. Calcd for $C_{17}H_{25}ClO_4$: C, 62.09; H, 7.66. Found: C, 61.89; H, 7.73.

**Acknowledgment.** This research was supported in part by the National Institute of General Medical Science (GM 26568). We thank the Sterling-Winthrop Research Institute for graduate research fellowship support for A.G.T.

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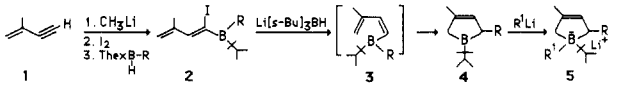
# *Communications*

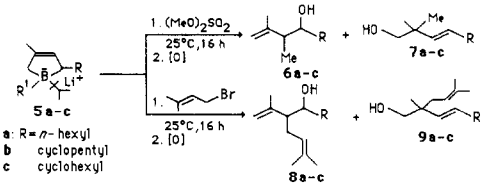
## 3-Borolenes. Their Regio- and Diastereoselective Conversion into Substituted Homoallylic Alcohols

*Summary:* The 3-borolene *ate* complexes derived from isopropenylacetylene react with dimethyl sulfate or with prenyl bromide in a regio- and diastereoselective manner to furnish substituted homoallylic alcohols. The overall reaction represents a dialkylation hydroxylation of the isopropenylacetylene precursor.

*Sir:* Allylic boron compounds have played an important role in the development of new methods for acyclic stereocontrol.[1] The ready accessibility of 3-borolenes (boracyclopent-3-enes) 4 from *cis*-dienylboranes 3 via reductive isomerization of alkylthexyl(1-iodo-1,3-alkadienyl)boranes 2[2] led us to explore their utility as reagents for the stereoselective preparation of substituted homoallylic alcohols. We now report that the *ate* complexes 5 derived from 3-borolenes 4 react with carbon electrophiles such as dimethyl sulfate or prenyl bromide (1-bromo-3-methyl-2-butene) in a regio- and diastereoselective manner to furnish the corresponding substituted homoallylic alcohols. Specifically, we describe our studies of borolenes derived from isopropenylacetylene (2-methyl-1-buten-3-yne, (1) whose use allows for extension of a carbon chain by one isoprene unit.




Preliminary investigations revealed that the borolenes 4[3] (R, = *n*-hexyl, cyclopentyl, cyclohexyl) did not react with dimethyl sulfate. However, their conversion into the corresponding ate complexes 5 with methyllithium enhanced their reactivities toward the alkylating agent to furnish, after oxidative workup, the methylated homoallylic alcohols 6 in 94–98% regioisomeric purities (Table I).[4] The reaction of 5 with methyl iodide was very sluggish. It

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0022-3263/87/1952-5484$01.50/0 

**Table I. Yields of Homoallylic Alcohols Derived from 3-Borolene Ate Complexes and Dimethyl Sulfate or 1-Bromo-3-methyl-2-butene**

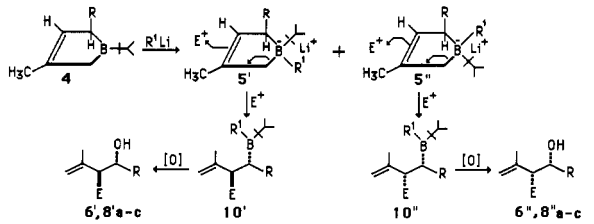
| R = | $R^1$ = | electrophile[a] | E | | yield, %[b-d] | ratio of 6′ and 6″ or 8′ and 8″[e] |
|---|---|---|---|---|---|---|
| $n$-$C_6H_{13}$ | $CH_3$ | A | $CH_3$ | **6a** | 77 (98) | 63:37 |
| | $n$-$C_4H_9$ | A | $CH_3$ | **6a** | 78 (97) | 88:12 |
| | $CH_3$ | B | $Me_2C{=}CHCH_2$ | **8a** | 73 (94) | 88:12 |
| | $n$-$C_4H_9$ | B | $Me_2C{=}CHCH_2$ | **8a** | 84 (90) | 98:2 |
| c-$C_5H_9$ | $CH_3$ | A | $CH_3$ | **6b** | 77 (96) | 83:17 |
| | $CH_3$ | B | $Me_2C{=}CHCH_2$ | **8b** | 83 (91) | 94:6 |
| c-$C_6H_{11}$ | $CH_3$ | A | $CH_3$ | **6c** | 73 (98) | 96:4 |
| | $CH_3$ | B | $Me_2C{=}CHCH_2$ | **8c** | 78 (85) | 99:1 |

[a] A = $(MeO)_2SO_2$; B = $Me_2C{=}CHCH_2Br$. [b] Isolated yields. [c] In parentheses are the regioisomeric purities. [d] The spectral data of the reported compounds were consistent with the assigned structures. [e] The anti–syn ratios of the diastereomeric alcohols were determined by GLC analysis on a 30-m J&W SE-54 column.

should be noted that the borolene ate complexes **5** possess four potential nucleophilic sites ($\alpha$, $\alpha'$, $\beta$, $\beta'$) for reaction with electrophiles. For steric reasons, attack of the electrophile at the sterically less hindered $\beta$-positions of **5** is anticipated and is in fact observed. Addition of the electrophile at the methyl-substituted carbon of **5** accounts for the presence of the minor regioisomeric alcohol **7**.[5] Treatment of **5** with prenyl bromide instead of dimethyl sulfate also resulted in the preferential alkylation at the $\beta$ position to afford the corresponding alcohols **8** (Table I). However, prenylation was slightly less regioselective than methylation. It is important to note that the structures of the unsaturated alcohols **8** obtained from **5** and prenyl bromide are consistent with a direct $S_N2$ attack upon the electrophile by the organoboron ate complex.

It was gratifying to note that the alkylation reactions were not only regioselective but also diastereoselective. For example, the reaction of **5c** with dimethyl sulfate followed by oxidative workup produced a 96 to 4 mixture of the diastereomeric alcohols **6′c** and **6″c**. As shown in Table I the diastereoselectivity is markedly affected by the size of the substituent at the C-2 position of the borolene as well as by the nature of the alkylating agent employed. Thus, replacing the cyclohexyl group in **5** ($R^1 = CH_3$) by a $n$-hexyl group decreased the amount of the major diastereomer from 96% to 63%. Interestingly, the borolenes **5** ($R^1 = CH_3$) exhibited higher diastereoselectivities toward prenyl bromide as compared to dimethyl sulfate. Finally, using $n$-butyllithium instead of methyllithium for the preparation of the ate complex **5** ($R^1 = n$-$C_4H_9$) resulted in a marked improvement in diastereoselectivity with both alkylating agents.[6,8]

The diastereofacial selectivities observed in the above carbon–carbon bond formation reactions may be rationalized as follows. Complexation of the borolenes **4** with the alkyllithiums from the less hindered side gives through kinetic control preferentially the ate complexes **5′**. To avoid steric interaction with the R group and the bulky thexyl group, the entering alkylating agent attacks the *Re* face of the double bond of **5′**.[10] Concomitant bond transposition leads to the organoborane **10′**, which on oxidation yields the alcohols **6′** and **8′** having the anti configuration.[11] The formation of the minor diastereomeric alcohols **6″** and **8″** may result form capture of the electrophile from the *Si* face of the ate complexes **5″** which is formed in competition with **5′** during the ate complex formation.




In conclusion, the 3-borolene ate complexes **5** possess considerable potential for use as templates for the diastereoselective methylation and prenylation of isopropenylacetylene. Moreover, the reaction provides for the introduction of two alkyl groups as well as for a hydroxyl group onto the isopropenylacetylene precursor in a one-pot reaction. It should be noted that the homoallylic alcohols **6** obtained from treatment of **5** with methyl sulfate embody the botryococcene part structure,[12] a terpenoid that does not obey the isoprene rule. Also, the alcohols **8** derived from **5** and prenyl bromide contain the lavandulyl monoterpenoid skeletons.[13]

**Acknowledgment.** We thank the National Science Foundation for financial support of this work.

**Supplementary Material Available:** Experimental details for the synthesis of the compounds **6a–c** and **8a–c** (6 pages).

(5) The structures proposed for the minor regioisomers were consistent with the $^1H$ NMR data obtained.

(6) To insure that the diastereomeric alcohols were indeed separable by gas chromatography, the alcohols were oxidized to the ketone with pyridinium chlorochromate.[7] Reduction of the carbonyl group with $LiAlH_4$ afforded mixtures of the diastereomeric alcohols which could indeed be separated by GLC.

(7) Corey, E. J.; Suggs, J. W. *Tetrahedron Lett.* **1975**, *31*, 2647.

(8) The assignment of the anti and syn configuration to the **6′** and **6″** (R = $n$-hexyl) are based on the $^1H$ NMR (360 MHz) coupling constants of the protons at the stereogenic centers of the $\beta$-hydroxy ketones derived by ozonolysis of the diastereomeric mixture of alcohols. The major diastereomer had a $J$ value of 6.9 Hz, whereas the minor isomer had a $J$ value of 3.3 Hz. For assignments of $\beta$-hydroxy ketones based on $J$ values, see ref 9.

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(10) The argument only holds if the ate complexes **5** initially formed do not equilibrate prior to their reaction with the electrophile. Unfortunately, $^1H$ NMR examination of the reaction mixture did not provide evidence that the ate complex **5′** is in fact the major species present or that we are dealing with an equilibrium mixture.

(11) Only one enantiomer is shown. The stereochemical assignments of the alcohols obtained in this study have been done by using the anti–syn terminology. For a recent discussion of other terminologies, see: Brewster, J. H. *J. Org. Chem.* **1986**, *51*, 4751. Brook, M. A. *J. Chem. Educ.* **1987**, *64*, 218. Seebach, D.; Prelog, V. *Angew. Chem., Int. Ed. Engl.* **1982**, *21*, 654.

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## Exceptionally Facile Reduction of Carboxylic Esters to Aldehydes by Lithium Aluminum Hydride in the Presence of Diethylamine[1]

*Summary:* Both aliphatic and aromatic carboxylic esters are readily reduced to the corresponding aldehydes by lithium aluminum hydride in the presence of excess diethylamine in pentane in excellent yields at room temperature.

*Sir:* The development of a simple synthetic route to aldehydes from readily available carboxylic acid derivatives is an important goal in organic chemistry. Many useful reducing agents have been reported, especially for the transformation of carboxylic esters to the corresponding aldehydes, e.g., lithium tri-*tert*-butoxyaluminum hydride,[2] diisobutylaluminum hydride,[3] sodium aluminum hydride,[4] and bis(4-methyl-1-piperazinyl)aluminum hydride.[5] However, these reagents cannot achieve a very general reduction of both aliphatic and aromatic carboxylic esters.

In the course of exploring a practical method for reduction of such derivatives to aldehydes by using lithium aluminum hydride (LAH) itself, we have found that this reagent in the presence of excess diethylamine effects the desired transformation in high yields.

LAH possesses 4 equiv of hydride, and all are strong enough to reduce carboxylic esters to their final alcohol stages. However, in the presence of excess diethylamine (DEA), only one hydride equivalent is available for reduction, while the other hydrides ($AlH_3$) are held in the stable alane–amine complex, which precipitates from pentane solution.

This system reduces aliphatic carboxylic esters examined to aldehydes in yields of 90–96%, regardless of structural type. Even aliphatic diesters such as diethyl sebacate (**1**) and diethyl adipate (**2**) are converted into the dialdehydes with 2 equiv of LAH in yields of 94–97%. $\alpha,\beta$-Unsaturated esters such as ethyl acrylate (**3**), ethyl crotonate (**4**), and ethyl cinnamate (**5**) are readily converted into the corresponding olefinic aldehydes in yields of 93–94%.

The reduction of aromatic esters **6** by this system works equally well, giving yields of 92–94% within 0.5 h at room temperature (Chart I).

The reaction also provides a simple procedure for the isolation of the aldehydes products. Thus, the filtration of the alane–amine complex that precipitates at 0 °C, followed by hydrolysis, affords a very good yield of aldehydes.

The following procedure for the reduction of ethyl caproate is illustrative. An oven-dried 25-mL flask, fitted with a side arm and a bent adaptor connected to a mercury bubbler, was charged with 5 mL of 1 M LAH solution in THF (5 mmol).[6] THF was pumped off, and then 5 mL of pentane and 0.73 g of diethylamine (10 mmol, 100% excess) were injected. To this slurry was added 0.72 g (5 mmol) of neat ethyl caproate, and the reaction mixture was stirred for 1 h at room temperature. Analysis with 2,4-dinitrophenylhydrazine indicated a yield of 96%.

The following procedure was used for a larger scale reaction. In the assembly previously described, 50 mL of 1 M LAH solution in THF (50 mmol) was charged. The THF solvent was pumped off, and then 7.3 g of diethylamine in 50 mL of pentane was added. To this slurry was injected ethyl caproate (7.21 g, 50 mmol), and the slurry was stirred vigorously for 1 h at room temperature. The reaction mixture was then cooled to 0 °C, and the pre-

**Chart I**

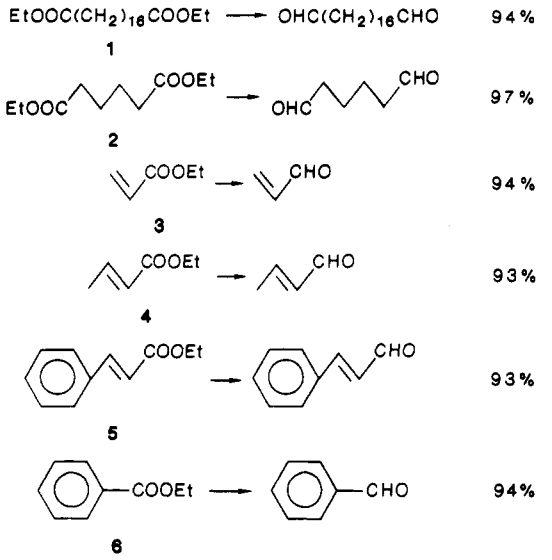


**Table I. Yields of Aldehydes in the Reduction of Representative Carboxylic Esters with Lithium Aluminum Hydride in the Presence of Excess Diethylamine[a] in Pentane at Room Temperature[b]**

| ester | reaction time (h) | yield of aldehyde (%)[c] |
|---|---|---|
| phenyl acetate | 3 | 90 |
| isopropyl acetate | 1 | 93 |
| ethyl butyrate | 0.5 | 95 |
| ethyl isobutyrate | 0.5 | 93 |
| ethyl isovalerate | 2 | 93 |
| ethyl caproate | 1 | 96 (84)[d] |
| ethyl caprylate | 2 | 94 |
| ethyl caprate | 3 | 93 |
| methyl laurate | 6 | 93 (85)[d] |
| ethyl stearate | 6 | 91 |
| diethyl adipate | 1 | 97 |
| diethyl sebacate | 3 | 94 |
| ethyl acrylate | 2 | 94 |
| ethyl crotonate | 3 | 93 |
| ethyl cinnamate | 6 | 93 (79)[d,e] |
| methyl benzoate | 0.5 | 92 |
| ethyl benzoate | 0.5 | 94 (84)[d] |

[a] 100% excess amine used. [b] Treated with 1 equiv of reagent for monocarboxylic and 2 equiv for dicarboxylic esters. [c] Analysis with 2,4-dinitrophenylhydrazine. [d] Isolated yield. [e] No saturated products on the double bond were detected.

(1) Presented at the Asian Chemical Conference at Seoul, Korea, June 29–July 3, 1987.
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(3) Zakharkin, L. I.; Khorlina, I. M. *Tetrahedron Lett.* **1962**, 619.
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(6) The concentration of LAH solution in THF was measured gasometrically by hydrolysis of an aliquot of the solution with a hydrolyzing mixture of THF–2 N HCl (1:1).

0022-3263/87/1952-5486$01.50/0 