cephalosporins the amide group is always located on the β face. The epimerization of the 7α-amide function in **5** was achieved according to the elegant method of Baldwin and co-workers[17] and Koppel and Koehler.[18] They demonstrated that methanol adds to acylimines derived from 7β-amidocephems stereoselectively from the α face, and, consequently, the amide group assumes the biologically active β configuration.

In order to isomerize the α-amide side chain to the β orientation, compound **5** was methoxylated with lithium methoxide and *tert*-butyl hypochlorite in THF at −70 °C for 30 min,[18] and 7β-(phenylacetamido)-7α-methoxy-1-oxacephem ester **6**[19] was obtained as crystals: mp 187–187.5 °C (acetone); 88% yield; NMR (acetone-d_6) δ 1.99 (s, 3, CH_3), 3.46 (s, 3, OCH_3), 3.68 (s, 2, CH_2Ph), 4.34 (br s, 2, C_2H), 5.05 (s, 1, C_6H), 6.91 (s, 1, $CHPh_2$), 7.3 (m, 15, aromatic H); IR ($CHCl_3$) 1780 cm^{-1}; mass spectrum, *m/e* 512.

The ester group in **6** was removed with trifluoroacetic acid in anisole at 0 °C for 10–12 min, and the free acid **7** was isolated in 84% yield: mp 169–170 °C (acetone); NMR δ (acetone-d_6) 2.00 (s, 3, CH_3), 3.43 (s, 3, OCH_3), 4.39 (br s, 2, C_2H), 5.08 (s, 1, C_6H), 7.35 (s, 5, aromatic H); IR (KBr) 1782 cm^{-1}.

The 7β-(phenylacetamido)-7α-methoxy-3-methyl-1-oxacephem acid **7** proved in in vitro tests to be biologically active against gram-negative bacteria.

Registry No. 1, 76172-98-0; 2, 76190-18-6; 3, 76172-99-1; 4a, 76173-00-7; 4b, 76173-01-8; 5, 76231-32-8; 6, 76173-02-9; 7, 76173-03-0; benzhydryl 7α-(phenylacetamido)-3-methyl-3-cephem-4-carboxylate, 76173-04-1; toluenesulfenyl chloride, 933-00-6.

(17) J. E. Baldwin, F. Urban, R. D. G. Cooper, and F. L. Jose, *J. Am. Chem. Soc.*, **95**, 2401 (1973).
(18) G. A. Koppel and R. E. Koehler, *J. Am. Chem. Soc.*, **95**, 2403 (1973).
(19) The β configuration of the amide group in compounds 6 and 7 is also substantiated by antibacterial activity of the acid 7 as discussed below.

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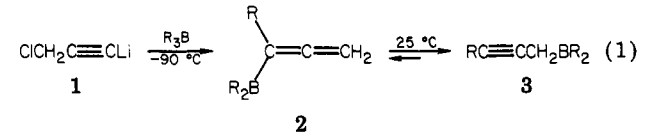
Synthesis of 1,3-Enynols and 1,2,4-Trienols via Allenic and Propargylic Borane Intermediates

Summary: Sequential treatment of lithium chloropropargylide **1** with thexylalkenylchloroboranes and aldehydes affords, depending on the reaction conditions, 1,3-enynols or 1,2,4-trienols.

Sir: Treatment of lithium chloropropargylide **1** with trialkylboranes at low temperature results in the transfer of one alkyl group from boron to the propargylic moiety to furnish allenic boranes **2**.[1] On being warmed to room temperature, these rearrange to the thermodynamically more stable propargylic boranes **3** (eq 1).[2] The organo-

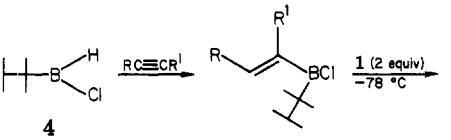


1 **2** **3**

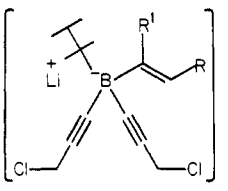
boranes **2** and **3** have proven to be versatile intermediates which react with protic reagents and with aldehydes to afford alkylallenes[1,3] or alkynes[3] and homopropargylic[2] or α-allenic alcohols,[2] respectively.

It is apparent that the synthetic utilities of the allenic and propargylic boranes would be greatly enhanced if the conversion **1** → **2** could be extended to the transfer of alkenyl groups. This would provide access to 1-alkenylallenic boranes **7** and via rearrangement of these to 3-alkenylpropargylic boranes **8**. Thus, we report here that these transformations have now actually been achieved and that the organoboranes **7** and **8** react with aldehydes to produce stereochemically defined 1,3-enynols **9** and 1,2,4-trienols **10** not readily accessible via previously available methodologies.

In our initial studies, we probed the possibility of selectively transferring the alkenyl groups of dialkylalkenylboranes onto lithium chloropropargylide **1**. Unfortunately, treatment of dicyclohexyl- or disiamyl(*trans*-1-octenyl)borane[4] with **1** in both cases resulted in nearly exclusive migration of the saturated moieties. It occurred to us that the use of thexylalkenylchloroborane **5** might provide a solution to the problem, since the thexyl group exhibits a low migratory tendency in many organoboron-mediated carbon–carbon bond-forming reactions.[5] We have recently shown that thexylchloroborane **4** is readily accessible through the reaction of thexylborane with ethereal hydrogen chloride.[6] The reagent cleanly monohydroborates 1-alkynes and disubstituted alkynes to produce the thexylalkenylchloroboranes **5**.



4 **5**



6

We were gratified to observe that addition of the thexylalkenylchloroboranes **5** to 2 equiv of lithium chloropropargylide **1** at −78 °C furnished, via the intermediacy of the ate complexes **6**, the alkenylallenic boranes **7**. Treatment of the reaction mixture containing **7** with an aldehyde afforded the 1,3-enynol **9**. However, if the initially formed organoborane **7** was brought to room tem-

(1) Leung, T.; Zweifel, G. *J. Am. Chem. Soc.* **1974**, *96*, 5620.
(2) Zweifel, G.; Backlund, S. J.; Leung, T. *J. Am. Chem. Soc.* **1978**, *100*, 5561.
(3) Midland, M. M. *J. Org. Chem.* **1977**, *42*, 2650.
(4) The organobroanes were obtained by hydroboration of 1-octyne with dicyclohexylborane and disiamylborane, respectively.
(5) Brown, H. C. "Boranes in Organic Chemistry"; Cornell University Press: Ithaca, New York, 1972. Pelter, A.; Smith, K. In "Comprehensive Organic Chemistry"; Barton, D. H. R., Ollis, W. D., Eds.; Pergamon Press: Oxford, 1979; Vol. III. Negishi, E.; Brown, H. C. *Synthesis* **1974**, 77.
(6) Zweifel, G.; Pearson, N. R. *J. Am. Chem. Soc.* **1980**, *102*, 5919.

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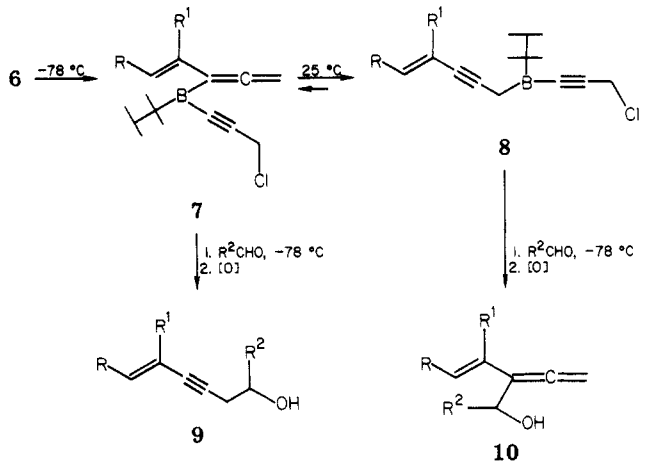
Scheme I



perature, it rearranged to the 3-alkenylpropargylic borane 8. Reaction of this with an aldehyde produced the 1,2,4-trienol 10 (Scheme I).[7]

The formations of the alcohols 9 and 10 imply that the reactions of the allenic carbon–boron and propargylic carbon–boron bonds of 7 and 8, respectively, with the carbonyl group of aldehydes must have both proceeded with bond transpositions.[2] NMR examination of the alcohols obtained in this study revealed that migrations of the alkenyl groups occurred with retention of configuration. The lack of thexyl-migrated products (<4%) indicates that the thexyl moiety provides an effective anchor group for these types of anionotropic rearrangements.

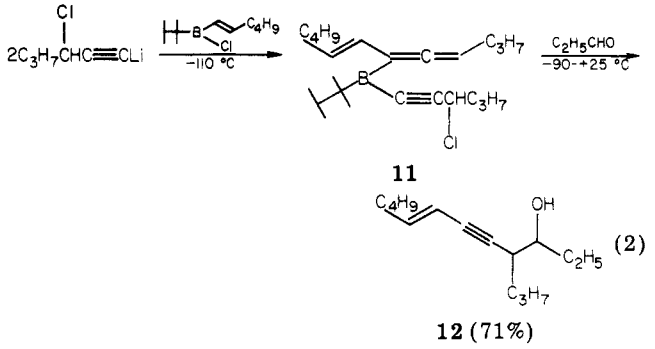
A typical procedure for the preparation of 9 (R = n-C_4H_9, R^1 = H, R^2 = C_2H_5) is as follows. To a cold solution of thexylchloroborane[6] in THF (ice bath) was added 1-hexyne (1.64 g, 20.0 mmol) while the temperature was maintained below 10 °C during the addition. The solution was stirred for 10 min at 0–5 °C and then for 1 h at room temperature. The resultant organoborane 5 was transferred via a double-ended needle into the addition funnel of a flask containing lithium chloropropargylide 1[2] (40.1 mmol) at −78 °C and added to 1 over a 20-min period while the temperature was kept below −67 °C. The mixture was stirred for 30 min at −78 °C (dry ice/acetone bath) and then treated with propanal (1.16 g, 20.0 mmol). After the mixture was stirred for 15 min at −78 °C, it was brought to room temperature (30 min), treated with methanol (10 mL), made basic with 6 N NaOH, and oxidized at 30–50 °C with 30% H_2O_2 (4 mL). The aqueous phase was saturated with solid $K_2CO_3 \cdot 1.5H_2O$ and extracted with ether, and the combined organic phases were washed with saturated aqueous NaCl. Drying ($MgSO_4$) and distillation from a small amount of solid $CaCO_3$ yielded 2.64 g (74%) of 9: bp 68–70 °C (0.05 torr); n^{24}_D 1.4859. Anal. Calcd for $C_{12}H_{20}O$: C, 79.94; H, 11.18. Found: C, 79.77; H, 10.99.[8] It should be noted that whereas the 1,3-enynols are amenable to distillation, the 1,2,4-trienols tend to decompose on being heated.

The above alcohol syntheses are of considerable value in that they allow for great flexibility in the choice of the alkenyl, aldehyde, and propargylic chloride components. As shown in Table I, the structural features of either mono- or disubstituted alkynes and saturated or α,β-unsaturated aldehydes may be incorporated into the alcohols 9 and 10. Also, utilization of substituted propargyl chloride as the alkenyl group acceptor does not adversely affect the yields of enynols. This is exemplified by the conversion shown in eq 2.[9,10] Although only one of the two available 3-chloro-1-alkynyl groups is consumed, the reaction provides access to highly substituted 1,3-enynols.

Table I. Yields of 1,3-Enynols 9 and 1,2,4-Trienols 10

organoborane 5			yield, %[a-c]	
R	R^1	R^2 in R^2CHO	9	10
n-C_4H_9	H	C_2H_5	74	60
		i-C_3H_7	76	
		t-C_4H_9	(88)	(70)
		$H_2C{=}CH$	71	(72)
c-C_6H_{11}	H	C_2H_5	80	
t-C_4H_9		C_2H_5	(88)	
C_6H_5		C_2H_5	65	
C_2H_5	C_2H_5	C_2H_5	61	

[a] The numbers in parentheses are GLC yields. [b] The IR, ^1H NMR, and mass spectral data of the alcohols obtained were consistent with the assigned structures. [c] The alcohols contained less than 1% of the corresponding 1,2,4-trienols and 1,3-enynols, respectively.



12 (71%)

In conclusion, sequential treatment of lithium chloropropargylide 1 with thexylalkenylchloroboranes and aldehydes provides for unique 1,3- and 1,1-alkenylation–alkylations of propargyl chloride. The resultant conjugated 1,3-enynols and 1,2,4-trienols possess functionalities for interconversion into a host of derivatives of potential use in the synthesis of complex molecules. Also, it is conceivable that the 1,2,4-trienols might exhibit physiological activities similar to those found in α-allenic alcohols.[11]

Acknowledgment. We are grateful to the National Science Foundation for support of this work.

(7) We are currently investigating the reaction of allenic (7) and propargylic boranes (8) with ketones.

(8) Spectroscopic data for 9: IR (neat) 3400, 3030, 2229, 1626, 970 cm^{-1}; NMR (CCl_4) δ 6.02 (dt, J = 16, 7 Hz, 1 H), 5.38 (dm, J = 16 Hz, 1 H), 3.58 (p, J = 5 Hz, 1 H), 2.61 (s, 1 H), 2.40 (dd, J = 6, 2 Hz, 2 H), 2.05 (t, J = 7 Hz, 2 H), 1.7–1.1 (m, 6 H), 1.1–0.8 (m, 6 H); exact mass, m/e 180.1504 (calcd for $C_{12}H_{20}O$ m/e 180.1514).

(9) It is noteworthy that warming the allenic borane 11 to room temperature prior to the addition of the aldehyde at −78 °C also affords the alcohol 10. This implies that the organoborane 11 does not rearrange to the propargylic borane on warming. A similar reluctance of disubstituted allenic boranes to rearrange has been previously observed.[3]

(10) The metalation of 3-chloro-1-hexyne with n-butyllithium was carried out at −110 °C.

(11) Galantay, E.; Bacso, I.; Coombs, R. V. *Synthesis* **1974**, 344 and references therein.

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