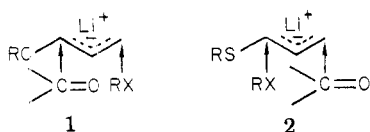## High Control of the Regiochemistry in Reactions of Heterosubstituted Allylic Carbanions via Allylic Aluminum "Ate" Complexes

Summary: The regiochemistry in reactions of heterosubstituted allylic carbanions is highly controlled via allylic aluminum "ate" complexes which direct both carbonyl compounds and reactive halides to the α position with exceptionally high regioselectivity.

Sir: The regiochemistry of reactions of heterosubstituted allylic carbanions depends upon too many factors,[1] and development of a new methodology to control the regiochemistry with a predictable value is highly desirable from both practical and theoretical angles. For example, the alkoxy derivative 1 generally reacts with alkyl halides at the γ position and carbonyl compounds at the α position, while the reaction of the alkylthio derivative 2 takes an entirely opposite direction under the normal conditions.[2]

We report a new and convenient procedure for controlling the regiochemistry via allylic aluminum "ate" complexes 3 which direct both carbonyl compounds and reactive

halides to the α position with exceptionally high regioselectivity regardless of the nature of the substituent (RO or RS) (eq 1). Such an independence from both substrate and reagent electronic factors is totally unprecedented in allyl anion chemistry.

X = RO or RS

E is a carbonyl compound or reactive halide
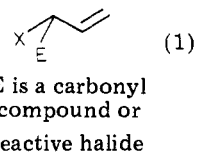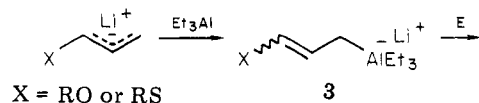
We recently reported that the regiocontrolled coupling between the allyloxy carbanion 1 and prenyl bromide is realized via the allyloxy carbanion–boron "ate" complex.[3] Unfortunately, however, an application of the "ate" complex to carbonyl derivatives gave a poor result and similar application of (alkylthio)allyl carbanion–boron "ate" complexes was limited to only a few reactions.[4] The difficulty appeared largely steric in origin and appeared to lie in the reaction step of the "ate" complex rather than its formation step. Use of allylic aluminum "ate" complexes seemed to provide a solution to this problem, since the longer C–Al bond should exert less steric hindrance and the more ionic

Table I. Reaction of Heterosubstituted Allylic Carbanions with Electrophiles via 3[a]

allylic carbanion	electrophile	additive[b]	α attack,[c] %	γ attack,[c] %	total yield,[d] %
1 (R = *i*-Pr)	benzaldehyde	Et₃Al	>99	<1	81 (95)
		none	28	72	(95)
	cyclohexanone	Et₃Al	~100		74 (92)
		Et₃B			NR[e]
	crotonaldehyde	Et₃Al	~100		71[f]
		none	60	40	74
	prenyl chloride	Et₃Al	80	20	(80)
		Et₃B	61	39	low
2 (R = *i*-Pr)	*n*-butyraldehyde	Et₃Al	95	5	77 (92)
		none	43	57	(80)
	isobutyraldehyde	Et₃Al	99	1	75 (92)
	cyclohexanone	Et₃Al	92	8	77
	2-octanone	Et₃Al	94	6	76
	acetophenone	Et₃Al	95	5	74 (90)
		Et₃B	45	55	(82)
		none	29	71	(85)
	crotonaldehyde	Et₃Al	94	6	77[f]
		none	35	65	75
	crotyl chloride	Et₃Al	99[g]	1	78

[a] All reactions were carried out on a 1-mmol scale with the same procedure as described in the text. The products were identified by NMR, IR, and mass spectroscopy, elemental analysis, or comparison with authentic materials. [b] "None" indicates the normal reaction without the additives. [c] By GLC analysis. [d] Isolated yield. [e] The coupling products were not detected. [f] The 1,4-addition product was not obtained and the geometrical integrity of the crotyl unit was retained. [g] Contaminated with small amounts of the α,α'-coupling product.[4]

(1) Seebach, D.; Geiss, K. H. "New Application of Organometallic Reagents in Organic Synthesis"; Seyferth, D., Ed., Elsevier: Amsterdam, 1976; p 1.
(2) For allyloxy carbanions: (a) Evans, D. A.; Andrews, G. C.; Buckwalter, B. *J. Am. Chem. Soc.* 1974, *96*, 5560. (b) Still, W. C.; Macdonald, T. L. *Ibid.* 1974, *96*, 5561. (c) Still, W. C. *Tetrahedron Lett.* 1976, 2115. (d) Still, W. C.; Macdonald, T. L. *J. Org. Chem.* 1976, *41*, 3620. (e) Hartmann, J.; Muthukrishnan, R.; Schlosser, M. *Helv. Chim. Acta* 1974, *57*, 2261. (f) Trost, B. M.; Latimer, L. H. *J. Org. Chem.* 1977, *42*, 3212. (g) Kozikowski, A. P.; Isobe, Biellmann, *Tetrahedron Lett.* 1979, 833. For (alkylthio)allyl carbanions: (h) Biellman, J. F.; Ducep, J. B. *Ibid.* 1968, 5629. (i) Oshima, H.; Yamamoto, H.; Nozaki, H. *J. Am. Chem. Soc.* 1973, *95*, 7926. (j) Atlani, P. M.; Biellmann, J. F.; Dube, S.; Vicens, J. J. *Tetrahedron Lett.* 1974, 2665. (k) Torii, S.; Tanaka, H.; Tomotaki, Y. *Chem. Lett.* 1974, 1541. (l) Geiss, K.; Seuring, B.; Pieter, R.; Seebach, D. *Angew. Chem., Int. Ed. Engl.* 1974, *13*, 479. (m) Evans, D. A.; Andrews, G. C. *Acc. Chem. Res.* 1974, *7*, 147. (n) Taguchi, T.; Okamura, H.; Takei, H. *Chem. Lett.* 1975, 853. (o) Cohen, T.; Bennett, D. A.; Mura, A. J. *J. Org. Chem.* 1976, *41*, 2506. (p) Seebach, D.; Geiss, K. H.; Pohmakoti, M. *Angew. Chem., Int. Ed. Engl.* 1976, *15*, 437.

nature of the C–Al bond should facilitate the coupling reactions.[5] Indeed, this proved to be practical, and the predominant to exclusive attack at the α position was realized irrespective of the substrates and reagents (eq 1) (Table I).

It is clear from Table I that the allylic aluminum "ate" complexes 3 possess a wide applicability for control of the regiochemistry. Unfortunately, *n*-butyl iodide does not react with 3; the halide is limited to allylic or benzylic types. The high regioselectivity and convenient workup process[6] enhance the usefulness of this procedure. Use of

(3) Yamamoto, Y.; Maruyama, K. *J. Am. Chem. Soc.* 1978, *100*, 6282.
(4) Yamamoto, Y.; Yatagai, H.; Maruyama, K. *J. Chem. Soc., Chem. Commun.* 1979, 157.
(5) Negishi, E. *J. Organomet. Chem.* 1976, *108*, 281.

decreased amounts of Et₃Al ($^1/_2$ or $^2/_3$ equiv) caused a marked decrease of the regioselectivity, and use of excess amounts of the additive did not exert any significant influence upon the reaction course.[7] Furthermore, the products arising from the transfer of the ethyl group were not detected. Although we do not have as yet definite evidence for the structure of 3 and a clear understanding of the mechanism, the present development undoubtedly provides a new methodology in the field of allyl carbanion chemistry and it has predictive value. We are currently extending this method to other heterosubstituted allyl carbanions.

The preparation of 3-(isopropylthio)-4-hydroxy-1,5-heptadiene is representative. To a solution of allyl isopropyl sulfide (1 mmol, 0.13 mL) in dry ether (3 mL) was added sec-butyllithium in pentane (1.04 M, 1 mmol) at –78 °C under N₂. After 30 min at –35 to –40 °C, the solution was again cooled to –78 °C. Addition of Et₃Al (15% in hexane, 1 mmol) caused the formation of a white precipitate. After a few minutes, crotonaldehyde (~1 mmol, 90 μL) was slowly added, and the mixture (pale yellow) was allowed to warm slowly to room temperature (2 h). The reaction mixture was cooled by an ice bath and a mixture of MeOH–H₂O was slowly added to destroy Et₃Al. The organic layer was separated, dried, and condensed. Distillation through a Kugelrohr apparatus gave the desired product: 0.143 g, 77%; bp 110–114 °C (2 mmHg).[8]

---

(6) The oxidation by H₂O₂–NaOH in the reaction of boron "ate" complexes frequently produces undesirable byproducts.

(7) The chemistry of organoaluminum "ate" complexes has not yet been studied as extensively as that of boron "ate" complexes; Tochtermann, W. Angew. Chem., Int. Ed. Engl. 1966, 5, 351.

(8) GLC analysis of the reaction mixture before distillation revealed an α:γ ratio of 94:6.

Yoshinori Yamamoto,* **Hidetaka Yatagai**
Kazuhiro Maruyama

Department of Chemistry
Faculty of Science
Kyoto University
Kyoto 606, Japan

Received September 17, 1979