Reaction of Allylic Boron and Aluminum "Ate" Complexes with Organic Halides and Carbonyl Compounds. Trialkylboranes as Regio-, Stereo-, and Chemoselective Control Elements[1]

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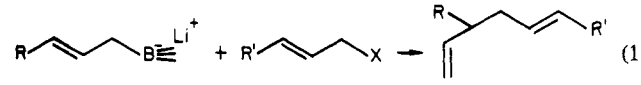
Abstract: Lithium allylic boron ate complexes, prepared by the addition of trialkylboranes to an ether solution of allylic lithium compounds, regioselectively react with allylic halides to produce head-to-tail 1,5-dienes (eq 1). The ate complexes are also prepared from the reaction of allylic boranes with alkyllithium derivatives. Magnesium or copper allylic boron ate complexes are less effective. Lithium crotyl boron ate complexes undergo a rapid reaction with aldehydes with good threoselectivity (eq 2). The selectivity is affected by the steric hindrance of trialkylboranes, as explained by the steric parameters of the 6-membered transition state. The ate complexes react with α,β-unsaturated ketones in a competitive manner of 1,2 and 1,4 addition, while they add to cinnamaldehyde exclusively in a 1,2 manner. The chemoselective aspects are only briefly investigated. ^1H and ^{13}C NMR spectra of lithium allylic boron ate complexes clearly indicate (i) the prevention of allylic rearrangement, (ii) the predominant trans geometry of the crotyl unit in comparison with the corresponding trivalent crotylboron, and (iii) the relative importance of σ–π conjugation between the double bond and the carbon–boron bond (eq 3).

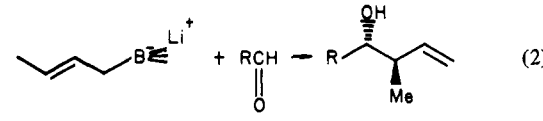
The utility of allylic moieties in the construction of complex molecules and their essential feature as biosynthetic intermediates[2] have been amply demonstrated, and the development of new allylic organometallic reagents possessing high regio-, stereo-, and chemoselectivities has been a long standing problem in organic synthesis.[3] Normally, allylic organometallic reagents (allyl–M) such as M = Li,[4] Na,[4] K,[5] Mg,[4,6] B,[7] Al,[4] Sn,[8] Si,[9] Zn,[4] Cd,[4] Cu,[10,11] Cr,[12] and Ni[11] act as nucleophiles toward organic halides or carbonyl compounds, while an allylic palladium derivative exhibits electrophilic characteristics.[11,13,14] Among the nucleophilic reagents, reagents with M = Li, Na, K, Mg, Al, Zn, Cd, Cu, and Ni react quite smoothly with both halides and carbonyl compounds. Unfortunately, however, the high reactivity frequently causes the loss of regio-, stereo-, and chemoselectivities. For example, (i) the Wurtz-type coupling reaction with allylic halides is lacking in regioselectivity. (ii) The crotyl derivatives react with aldehydes to give a diastereoisomeric mixture of threo and erythro α-methyl alcohols. The stereoselectivity is usually very low. (iii) Discrimination between ketones and aldehydes or between alkyl halides and allylic halides via such reactive organometallic reagents is very difficult.

Allyl silanes and stannanes are less reactive; they react with carbonyl compounds with the aid of Lewis acids.[15,16] Although the reaction of allylic silanes with certain halides also proceeds in the presence of Lewis acids,[17] that of allylic stannanes requires catalytic amounts of palladium salts.[18] Allylic boranes[7] and chromium compounds[12] undergo a facile reaction with carbonyl compounds without any assistance of Lewis acids, and the reaction is believed to proceed through a cyclic transition state where the electrophilic boron[7] or chromium[19] atom coordinates to the carbonyl oxygen. On the other hand, the reaction of allylic boranes with halides does not proceed smoothly under the normal reaction conditions. We have sought a new allylic organometallic compound, whose chemical reactivity lies between that of the reactive former nucleophilic reagents and that of the less reactive latter group.

Previously, we introduced a new class of allylic organometallic compound, allylic boron ate complexes.[1a] We will give a fully detailed report of that work together with brief investigation on allylic aluminum ate complexes. The results reported here indicate (1) that lithium allylic boron ate complexes regioselectively react with allylic halides to produce the head-to-tail 1,5-dienes (eq 1), (2) that lithium crotylboron ate complexes undergo a rapid reaction with aldehydes with good threoselectivity (eq 2), (3) the chemoselectivity of the ate complexes, and (4) the relative importance of σ–π conjugation between the double bond and the carbon–boron bond in the ate complexes (eq 3).



(1)



(2)

(1) For a preliminary report on some aspects of the present study, see (a) Yamamoto, Y.; Maruyama, K. *J. Am. Chem. Soc.* **1978**, *100*, 6282. (b) Yamamoto, Y.; Yatagai, H.; Naruta, Y.; Maruyama, K.; Okamoto, T. *Tetrahedron Lett.* **1980**, 3599.

(2) For example: Poulter, C. D.; Rilling, H. C. *Acc. Chem. Res.* **1978**, *11*, 307.

(3) Magid, R. M. *Tetrahedron* **1980**, *36*, 1901.

(4) Courtois, G.; Miginiac, L. *J. Organomet. Chem.* **1974**, *69*, 1.

(5) (a) Schlosser, M. *Angew. Chem., Int. Ed. Engl.* **1974**, *13*, 701. (b) Schlosser, M.; Hartmann, J. *J. Am. Chem. Soc.* **1976**, *98*, 4674. (c) Yasuda, H.; Ohnuma, Y.; Yamauchi, M.; Tani, H.; Nakamura, A. *Bull. Chem. Soc. Jpn.* **1979**, *52*, 2036.

(6) Benkeser, R. A. *Synthesis* **1971**, 347.

(7) (a) Mikhailov, B. M. *Organomet. Chem. Rev., Sect. A* **1972**, *8*, 1. (b) Kramer, G. W.; Brown, H. C. *J. Organomet. Chem.* **1977**, *132*, 9. (c) Kramer, G. W.; Brown, H. C. *J. Org. Chem.* **1977**, *42*, 2292.

(8) Pereyre, M.; Pommier, J.-C. In "New Application of Organometallic Reagents in Organic Synthesis"; Seyferth, D., Ed.; Elsevier: Amsterdam, 1976; p 161.

(9) Chan, T. H.; Fleming, I. *Synthesis* **1979**, 761.

(10) (a) House, H. O.; Fischer, W. F., Jr. *J. Org. Chem.* **1969**, *34*, 3615. (b) Normant, J. F. *Synthesis* **1972**, 63.

(11) Noyori, R. In "Transition Metal Organometallics in Organic Synthesis"; Alper, H., Ed.; Academic Press: New York, 1976; p 73.

(12) Okude, Y.; Hirano, S.; Hiyama, T.; Nozaki, H. *J. Am. Chem. Soc.* **1977**, *99*, 3179.

(13) Trost, B. M. *Tetrahedron* **1977**, *33*, 2615. Tsuji, J. "Organic Synthesis by Means of Transition Metal Complexes"; Springer Verlag: Berlin, 1975.

(14) The information on M = Hg and Zr is lacking. We are now investigating these allylic organometallic reagents.

(15) For example: Hosomi, A.; Shirahata, A.; Sakurai, H. *Chem. Lett.* **1978**, 901.

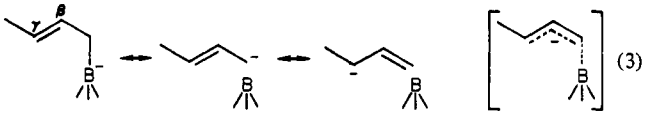
(16) For example: Naruta, Y.; Ushida, S.; Maruyama, K. *Chem. Lett.* **1979**, 917.

(17) Fleming, I.; Paterson, I. *Synthesis* **1979**, 446. Sasaki, T.; Usuki, A.; Ohno, M. *Tetrahedron Lett.* **1978**, 4925. Godschalx, J.; Stille, J. K. *Ibid.* **1980**, 2599.

(18) Kosugi, M.; Kurino, K.; Takayama, K.; Migita, T. *J. Organomet. Chem.* **1973**, *56*, C11. Kosugi, M.; Sasazawa, K.; Shimizu, Y.; Migita, T. *Chem. Lett.* **1977**, 301. Kosugi, M.; Arai, H.; Yoshino, A.; Migita, T. *Ibid.* **1978**, 795.

(19) Heathcock, C. H.; Buse, C. T. *Tetrahedron Lett.* **1978**, 1685.

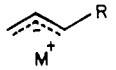
0002-7863/81/1503-1969$01.25/0



(3)

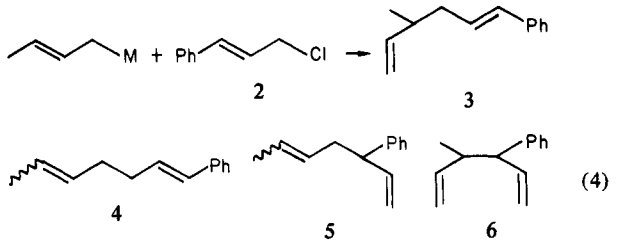
Results and Discussion

Reaction with Allylic Halides. Regiochemical Control. The nucleophilic substitution reaction of allylic substrates (X = halogen, OAc, OTs, ...) with alkyl or aryl organometallic reagents proceeds via α and/or γ attack. Regioselective α attack is ordinarily achieved by using allylic substrates containing oxygen in the leaving group, while regioselective γ attack is realized via a new alkylating reagent $RCu{\cdot}BF_3$.[3,20] On the other hand, the reaction of allylic halides with allylic organometallic reagents is accompanied with an additional regiochemical complication. Especially, the reaction of heteroatom-substituted allylic organometallic reagents (**1**) is highly complicated, and the regio-



1, M = Li, Mg, Cu, Cd, ...;
R = B, Si, N, P, O, S, Se, X, ...

chemistry depends upon too many factors.[3,21,22] The substitutent in this study is limited to an alkyl or aryl to make the discussion clear. As we previously reported,[1a] the reaction of lithium allylic boron ate complexes with allylic halides proceeds via the regiocontrolled head-to-tail coupling mode (γ-α' coupling). Initially, we precisely investigated the optimum condition in the reaction of crotyl organometallic reagents with cinnamyl chloride (eq 4) (Table I).

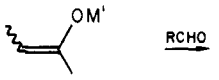


(4)

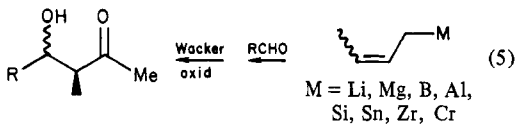
As evident, lithium crotyl borates in ether exhibit high regioselectivity (entries 5 and 7–9) while the corresponding magnesium and copper borates do not give a satisfactory result (entries 13–15). Interestingly, the steric hindrance around the boron atom plays a major role in regioselectivity (entries 7, 9, and 10). The regioselectivity of the $B(s\text{-}Bu)_3$–**7** system is similar to that of **7** by itself (entries 1 and 10), presumably owing to the formation of the loose complex. Although the highest regioselectivity is realized via the *n*-Bu-9-BBN ate complex (BBN, borabicyclo-[3.3.1]nonane) (entries 8 and 9) in which the steric hindrance around boron atom is minimum, the major drawback is the formation of reduced products, β-methylstyrene and allylbenzene.[23] Oxygen should be rigorously excluded from the reaction vessel (entries 11 and 12). Probably, the tight ate complex may be partially decomposed or may undergo isomerizations in the presence of trace amounts of oxygen.[24] The ate complex prepared from crotyl-9-BBN (**11**)[25] and *n*-BuLi exhibits good regioselectivity (entry 16) though it is not so high as that from **7** and *n*-Bu-9-BBN. This result may indicate that both ate complexes do not possess a completely identical reactivity toward the allylic halides.

The reaction of various allylic halides with several allylic boron ate complexes was examined to establish a high generality of control of regiochemistry (Table II). As mentioned later, ^{13}C NMR spectra of lithium crotyl-9-BBN ate complex clearly indicate that 1-methylallyl isomer is not involved (entries 7–11).[26] As a logical extention, we speculated on the straight chain structure for the cinnamyl ate complex (entries 3–5).[27] The high regiocontrolled γ-α' coupling is generally realized for primary allylic halides (entries 1–4, 7–8, and 10), while the regioselecitivty, as well as the reactivity, remarkably decreases for secondary allylic halides (entries 5 and 9). It should be emphasized that the coupling products between the alkyl groups of boron and the allylic moieties of halides are not detected.[28] In conclusion, the problem on the regiochemical control in the Wurtz type coupling reaction is to a certain extent solved through the formation of boron ate complexes.[29] To control stereochemistry is a problem for the future.

Reaction with Aldehydes. Stereochemical Control. Recently, a lot of attention has been focused on diastereoselective synthesis of β-hydroxycarbonyl compounds which may be applicable to the synthesis of polyether,[30] ansamycin,[31] or macrolide antibiotics.[32] The hitherto known solution to this problem is to use the addition reaction of metal enolates[33] or 2-alkenylmetal derivatives[34] to aldehydes (eq 5). For example, erythroselective condensation



M′ = Li, Mg, Zn, B, Al, Si, Sn, Zn



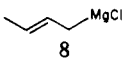
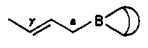
(5)

M = Li, Mg, B, Al, Si, Sn, Zr, Cr

is realized via certain (*Z*)-metal enolates or (*Z*)-2-alkenylmetal derivatives.[35] Unfortunately, however, threoselective coupling via the alkenylmetal route has not been achieved;[36] crotyllithium or -magnesium derivatives exhibit quite low threoselectivity.[37] We

(20) Yamamoto, Y.; Yamamoto, S.; Yatagai, H.; Maruyama, K. *J. Am. Chem. Soc.* **1980**, *102*, 2318 and references cited therein.
(21) Yamamoto, Y.; Yatagai, H.; Maruyama, K. *J. Chem. Soc., Chem. Commun.* **1979**, 157.
(22) Yamamoto, Y.; Yatagai, H.; Maruyama, K. *J. Org. Chem.* **1980**, *45*, 195 and references cited therein. We have also studied the regiochemical control of such organometallic reagents via aluminum ate complexes, and the full details will be published in due course.
(23) Yamamoto, Y.; Toi, H.; Murahashi, S.-I.; Moritani, I. *J. Am. Chem. Soc.* **1975**, *97*, 2558.
(24) Stahle, M.; Hartmann, J.; Schlosser, M. *Helv. Chim. Acta* **1977**, *60*, 1730. Oxygen efficiently catalyzes the *Z*/*E* isomerization of (4,4-dimethyl-2-pentenyl)potassium.
(25) Crotyl-9-BBN itself (**11**) did not react with **2** under normal conditions.
(26) The 1-methylallyl isomer is not found for **11** (ref 7b).
(27) Seyferth, D.; Murphy, G. J.; Woodruff, R. A. *J. Organomet. Chem.* **1977**, *141*, 71. The thermodynamically more stable isomer is formed in the reaction of *gem*-dichloroallyllithium with Ph_3B.
(28) The migration aptitude of allylic boron ate complexes toward allylic halides is allyl ≫ methyl > *n*-alkyl. The detailed results will be published in due course.
(29) For a head-to-tail coupling via prenylmagnesium–CuI system, see: D-Boumechal, F.; Lorne, R.; Linstrumelle, G. *Tetrahedron Lett.* **1977**, 1181.
(30) Westley, J. W. *Adv. Appl. Microbiol.* **1977**, *22*, 177. Pressman, B. C. *Annu. Rev. Biochem.* **1976**, *45*, 510.
(31) Wehrli, W. *Top. Curr. Chem.* **1977**, *72*, 21. Rinehart, K. L., Jr.; Shield, L. S. *Fortschr. Chem. Org. Naturst.* **1976**, *33*, 231.
(32) Masamune, S.; Bates, G. S.; Corcorau, J. W. *Angew. Chem., Int. Ed. Engl.* **1977**, *16*, 585.
(33) For a review, Bartlett, P. A. *Tetrahedron* **1980**, *36*, 3. See also: Yatagai, H.; Yamamoto, Y.; Maruyama, K. *J. Am. Chem. Soc.* **1980**, *102*, 4548 and references cited therein.
(34) (a) Reference 33. (b) Hoffmann, R. W.; Ladner, W. *Tetrahedron Lett.* **1979**, 4653. (c) Collum, D. B.; McDonald, J. H., III; Still, W. C. *J. Am. Chem. Soc.* **1980**, *102*, 2118.
(35) Quite recently, erythroselective condensation regardless of the geometry of the starting materials is reported. Yamamoto, Y.; Yatagai, H.; Naruta, Y.; Maruyama, K. *J. Am. Chem. Soc.* **1980**, *102*, 7107.
(36) Threo products are generally favored under thermodynamic control. For example, (*Z*)-bromomagnesium enolate of ethyl *tert*-butyl ketone reacts with benzaldehyde to produce the erythro product kinetically. If the reaction mixture is allowed to stand, the threo isomer is nearly the exclusive product. See: Dubois, J. E.; Fellmann, P. *C. R. Hebd. Seances Acad. Sci., Ser. C.* **1972**, *274*, 1307. However, it takes ordinarily a long time. Fellmann, P.; Dubois, J. E. *Tetrahedron* **1978**, *34*, 1349. There is also such a possibility for the 2-alkenylmetal route, since the reaction of crotyllithium or -magnesium derivatives with certain carbonyl compounds is reversible. Benkeser, R. A.; Siklosi, M. P.; Mozdzen, E. C. *J. Am. Chem. Soc.* **1978**, *100*, 2134. Therefore, the reaction mixture was allowed to stand at room temperature for a prolonged time, but the rate of isomerization was negligible.

Table I. The Reaction of Crotyl Organometallic Reagents with **2**[a]

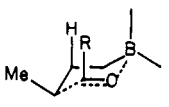
entry	crotylmetal	additive	ratio of coupling products,[b] % 3	4	5	6	total yield,[b] %	reduced product,[b] %
1	 **7**	none	22	71 (59, 41)[c]	3	4	(75)	trace
2	 **8**	none	72	10 (40, 60)[c]	3	15	83	1
3	 **9** (from **7**)	none	59	21 (81, 19)[c]	10	10	29	
4	 **10** (from **8**)	none	53	33 (75, 25)[c]	1	13	51	
5	**7**	n-Bu_3B	87	13 (85, 15)[c]	trace	trace	(78)	3
6	**7**	n-Bu_3B, THF	44	6 (50, 50)[c]	35	15	83	1
7	**7**[d]	n-Bu_3B	91	9 (55, 45)[c]	trace	trace	88	3
8	**7**	n-Bu-9-BBN	97	3			63	15[e]
9	**7**[d]	n-Bu-9-BBN	97	3			78	14[e]
10	**7**[d]	s-Bu_3B	36	64	trace	trace	80	1
11	**7**[d]	n-Bu-9-BBN, air (0.2 mL)[f]	90	10	trace	trace	80	10[e]
12	**7**[d]	n-Bu-9-BBN, air (2 mL)[f]	51	49	trace	trace	38	5
13	**8**[d]	n-Bu-9-BBN	82	18			92	6
14	**8**[d]	n-Bu-9-BBN, THF	70	21	1	8	81	15[e]
15	**10**	n-Bu-9-BBN	64	35		1	78	1
16	 **11**	n-BuLi	87	13	trace	trace	78	18[e]

[a] All reactions were performed with the same procedure as described in the Experimental Section. Normally, a crotyl organometallic compound (1 mmol), **2** (1 mmol), an additive (1 mmol), and ether as a solvent were used except where otherwise indicated. [b] By GLC (isolated yield). [c] The ratio of the stereoisomers (trans-trans, trans-cis). The ratio of stereoisomers is indicated, where the geometry of cinnamyl unit is retained. [d] **2** (0.5 mmol). [e] Combined yield of β-methylstyrene and allylbenzene, where the former is a major product. [f] Air was introduced by a syringe into the solution of ate complex before the addition of the halide.

discovered that the threoselectivity in the reaction of **7** and aldehydes is enhanced via allylic boron ate complexes (eq 2).[38]

The condensation of **7** with benzaldehyde in the presence of BEt_3, $B(n\text{-}Bu)_3$, or n-butylborepane predominantly produces the threo derivatives (80–83% threo), though the selectivity in the aliphatic aldehydes such as acetaldehyde, propionaldehyde, and isobutyraldehyde is not necessarily so high (60–85% threo). Sterically more hindered $B(s\text{-}Bu)_3$ and less hindered n-Bu-9-BBN are not effective, indicating that the steric circumstances between these two extremes are important for the transition state leading to the threo product. Further, the reaction of ate complexes proceeds with greater threoselectivity than that of the corresponding trivalent crotylborane (**11**). These results suggest that the enhancement of the threoselectivity via the tetravalent boron is ascribed to two factors: (i) the geometry of crotyl unit is fixed predominantly to trans through the prevention of the allylic rearrangement;[7] (ii) the transition state (T_1) of the tetravalent boron

T_1



T_2

leading to the erythro product is destabilized relative to that of the trivalent boron (T_2) by the increase of the 1,3-diaxial interaction.[39,40] Actually, the ratio of peak height in the olefinic region of ^{13}C NMR spectra revealed that the trans/cis of lithium crotyl-9-BBN ate complex is 84/16–80/20, while that of **11** is ca. 69/31.[41] Presumably, T_1 of the ate complex of 9-BBN is more stable than that of BEt_3 or $B(n\text{-}Bu)_3$, and the complex of $B(sec\text{-}Bu)_3$–**7** system is very loose as mentioned above. The ineffectiveness of $AlEt_3$ may also be ascribed to the loose complex.[42] Finally, it sould be noted again that the migration of alkyl groups is not observed and the reduced products are accompanied especially in 9-BBN ate complexes.[43]

Reaction with α,β-Unsaturated Carbonyl Compounds. Regiochemistry. Control of 1,4 vs. 1,2 addition of allylic organometallic reagents[44] to α,β-unsaturated carbonyl compounds is rather difficult compared with that of alkyl organometallic derivatives. Allylic silanes[45] and stannanes[46] undergo 1,4 addtion with the aid of Lewis acids. Allyl copper adds in a 1,4 manner to cyclohexanone, while it undergoes 1,2 addition to 3,5,5-trimethylcyclohexanone.[10a] The other allylic organometallic compounds almost always afford 1,2-addition products.[4] We investigated the regiochemistry of allylic boron and aluminum ate complexes. The results are summarized in the Table III. Although the 1,4 addition to α,β-unsaturated ketones increases with the formation of ate complexes, the effect is not so noteworthy. The ate complexes add exclusively in a 1,2 manner to cinnamaldehyde.

Chemoselctivity. The chemoselectivity of the ate complexes was only briefly investigated. Lithium, magnesium, and copper crotyltri-n-butylboron ate complexes did not react with n-butyl iodide, crotyl alcohol, crotyl acetate, and cyclohexanone. They undergo

(37) Abenhaim, D.; H-Basch, E.; Freon, P. *Bull. Soc. Chim. Fr.* **1969**, 4038, 4042. Abenhaim, D.; H-Basch, E. *C. R. Hebd. Seances Acad. Sci., Ser. C.* **1968**, *267*, 87.

(38) It is recently reported that certain allylic boranes exhibit high threoselectivity. Yamaguchi, M.; Mukaiyama, T. *Chem. Lett.* **1980**, 993; Yamamoto, Y.; Yatagai, H.; Maruyama, K. *J. Chem. Soc., Chem. Commun.* **1980**, 1072.

(39) Evans, D. A.; Vogel, E.; Nelson, J. V. *J. Am. Chem. Soc.* **1979**, *101*, 6120.

(40) The pentacoordinate transition state of boron (T_1) may be curious. However, we feel that this is not an unreasonable assumption since similar pentacoordinate transition state of carbon is well accepted in a number of reactions. See also ref 20.

(41) Mikhailov reported that the trans/cis ratio of tricrotylborane is 70/30.[7a]

(42) Negishi, E. *J. Organomet. Chem.* **1976**, *108*, 281. See also ref 22.

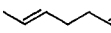
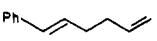
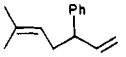
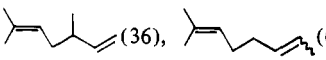
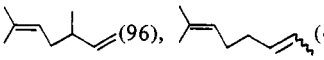
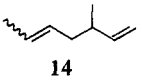
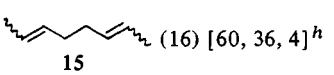
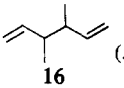
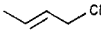
(43) Yamamoto, Y.; Toi, H.; Sonoda, A.; Murahashi, S.-I. *J. Am. Chem. Soc.* **1976**, *98*, 1965.

(44) Normally, the 1,2 addition is favored. Allylic boranes undergo a 1,2 addition, while trialkylboranes add in a 1,4 manner.[7a,c] Allyl Grignard reagents also add in a 1,2 manner.[4,6]

(45) Hosomi, A.; Sakurai, H. *J. Am. Chem. Soc.* **1977**, *99*, 1673.

(46) Hosomi, A.; Iguchi, H.; Endo, M.; Sakurai, H. *Chem. Lett.* **1979**, 977. Naruta, Y. *J. Am. Chem. Soc.* **1980**, *102*, 3774.

Table II. Regiocontrolled Reaction of Allylic Boron Ate Complexes with Allylic Halides[a]

entry	allylic organometal	additive	allylic halide	products (ratio, %)	yield,[b] %
1	 **12**	*n*-Bu_3B		 [c]	72
2	**12**	*n*-Bu_3B			(60)[d]
3	 **13**	*n*-Bu_3B		**5**[c]	(70)[e]
4	**13**	*n*-Bu_3B			(82)
5	**13**	*n*-Bu_3B		**3** (9), **4** (31) [66, 34],[g] **5** (13), **6** (47)	(72)
6	**7**	none		 (36), (64) [56, 44][g]	70
7	**7**	*n*-Bu-9-BBN		 (96), (4)	(53)
8	**7**	*n*-Bu_3B		 (84) [83, 17],[g]  (16) [60, 36, 4][h] **14** **15**	72
9	**7**	*n*-Bu_3B		**14** (53) [81, 19],[g] **15** (47) [58, 37, 5][h]	50
10	**7**	*n*-Bu-9-BBN		**14** (95) [83, 17],[g] **15** (5) [60, 40, ...][h]	45
11	**11**	*n*-BuLi		**14** (76) [79, 21],[g] **15** (24) [56, 42, 2][h]	40
12	**8**	none		**14** (76) [86, 14],[g] **15** (19) [59, 37, 4],[h]  **16** (5) [66, 34][j]	70
13	**8**	none		**14** (20) [86, 14],[g] **15** (74) [57, 36, 7],[h] **16** (6) [50, 50][j]	72
14	**10**	none		**14** (28) [80, 20],[g] **15** (67) [70, 27, 3],[h] **16** (5) [50, 50][j]	72

[a] See footnotes to Table I. [b] GLC yield (isolated yield) of 1,5-dienes. [c] One sharp peak in GLC and strong IR absorption at the region of trans olefin indicated the trans geometry. [d] The reduced products were obtained in ca. 25% yield. [e] Small amounts of isomers were detected. [f] The reaction was quite slow and quenched after 20 h at room temperature. [g] The ratio of stereoisomers [trans, cis]. [h] The ratio of stereoisomers [trans-trans, trans-cis, cis-cis]. [i] Contaminated with 2-bromo-3-butene (15%). [j] The ratio of diastereomers [threo, erythro].

Table III. Reaction of Ate Complexes with α,β-Unsaturated Carbonyl Compounds[a]

allylic organometallic reagent	additive	α,β-unsaturated carbonyl compd	ratio,[b] % 1,2	1,4	yield,[c] %
 **17**	none	$PhCH{=}CHCOCH_3$	100		(81)
17	*n*-Bu-9-BBN	$PhCH{=}CHCOCH_3$	95	5	(70)
12	*n*-Bu-9-BBN	$PhCH{=}CHCOCH_3$	83	17	(72)
12	*n*-Bu-9-BBN	$CH_2{=}CHCOCH_3$	50	50	(30)
 from **12**	*n*-Bu-9-BBN	$PhCH{=}CHCOCH_3$	79	21	80
 from **17**	*n*-Bu-9-BBN	$PhCH{=}CHCOCH_3$	75	25	62
17	Et_3Al	$PhCH{=}CHCOCH_3$	90	10	85
12	*n*-Bu_3B	PhCH=CHCHO	100		(75)
17	*n*-Bu_3B	PhCH=CHCHO	100		92

[a] See footnotes to Table I. [b] The ratio of 1,2 and 1,4 addition, determined by GLC. [c] Combined GLC yield (isolated yield).

a rapid reaction with aldehydes as mentioned above. In comparison with other organometallic reagents, the ate complexes are sensitive to the steric circumstances of carbonyl groups. Consequently, it seems possible to perform a chemospecific reaction via the ate complexes. However, we did not pursue this aspect further.

Table IV. ^1H NMR Spectra of Crotyl Ate Complexes[a]

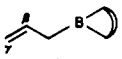
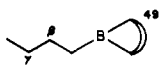
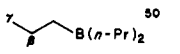
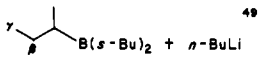
crotylmetal	additive	olefinic region, δ
7	none	1.2 (α-H), 6.0 (β-H), 2.9 (γ-H)[47,48]
7	Et_3B	6.04–5.68, 5.44–5.08
7	Et_3Al	6.18–5.80, 5.00–4.64
11	none	5.75–5.30 (centered at 5.50)
11	*n*-BuLi	6.00–5.60, 5.30–4.90
11	*n*-BuMgCl	5.80–5.40, 4.80–4.40

[a] Chemical shift (δ) from Me_4Si, using ether as a solvent. The area ratio of two kinds of multiplet in the olefinic region is ca. 1:1.

^1H and ^{13}C NMR Spectra. Initially we failed in observing the ^1H NMR spectra of ate complexes.[1a] It was later revealed that two kinds of complex multiplet appeared in the olefinic region of ate complexes (Table IV). The data clearly indicate the stop of the allylic rearrangement. The spectra of olefinic region do not change at room temperature for 12 h under Ar but disappear after 2 days presumably owing to the decomposition of ate complexes. It is notable that the chemical shifts of **7** + BEt_3 are very close to those of **11** + *n*-BuLi. Unfortunately, the assignment of these two peaks by the irradiation of the methylene protons was not successful.

^{13}C NMR spectra solved this problem. The results are summarized in Table V. The C_β and C_γ of **18** and its ate complex are clearly assigned by single-frequency off-resonance decoupled spectra. This method is not applicable to **11** and its ate complex since both carbons exhibit doublet signals, but the assignment is deducible from the results of **18** and its ate complex. On the other hand, the result of the off resonance clearly indicates the absence

Table V. ^{13}C Chemical Shifts and Substituent Effects of Tri- and Tetravalent Boron Atoms[a]

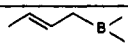
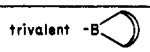
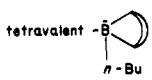
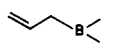
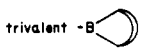
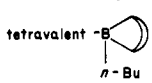
compd	chem shift $\delta(C_\beta)$	chem shift $\delta(C_\gamma)$	substituent effect[b] $\Delta\delta(C_\beta)$	substituent effect[b] $\Delta\delta(C_\gamma)$
11	138.3	*d*	12.5	*d*
	[136.6][c]		[12.3][c]	
11 + *n*-BuLi	140.5	122.6	14.7	−3.2
	[139.1][c]	[122.3][c]	[14.8][c]	[−2.0][c]
 **18**	136.6	(114.0)[e]	3.5	(−1.0)[e]
18 + *n*-BuLi	149.3	109.5	16.2	−5.5
	28.2	27.5	3.2	2.5
n-Bu-9-BBN + *n*-BuLi[49]	29.9	28.9	4.9	3.9
	18.1	17.6	2.0	2.0
	27.1	15.2	2.1	2.0
	125.8	125.8		
	(124.3)[c]	(124.3)[c]		
	133.1	115.0		
	25.0	25.0		
	25.0	13.2		
	16.1	15.6		

[a] In parts per million (±1)(downfield positive) from Me_4Si, converted by using $\delta(C_6D_6)$ 128.7. [b] Higher values correspond to lower shielding. [c] Cis isomer. [d] Not obvious owing to the rapid allylic rearrangement. [e] Estimated from a broad peak.

of 1-methylallyl isomer (Table I, entries 7–11). Chemical shifts of other carbons, not important in the present discussion, are omitted. Chemical shifts of C_β and C_γ of reference compounds such as 2-butene, propene, butane, and propane are also listed in Table V.

The substituent effects of tri- and tetravalent boron atoms are obtained as previously described.[52] For example, $\Delta\delta(C_\beta)$ of **11** (12.5) = $\delta(C_\beta)$ of **11** (138.3) − $\delta(C_\beta)$ of 2-butene (125.8). Two major assumptions are made to calculate the substitutent effect owing to the lack of an appropriate reference compound: (i) $(n\text{-Pr})_2$ and $(s\text{-Bu})_2$ are equivalent to the 9-BBN ring; (ii) $CH_3CH_2CH(CH_3)$ is equivalent to $CH_3CH_2CH_2$. The difference in the substituent effect between tri- and tetravalent boron atoms is summarized in Table VI, again made on the assumption that $(n\text{-Pr})_2$ and $(s\text{-Bu})_2$ are equivalent to the 9-BBN ring. For example, $\Delta\Delta\delta(C_\beta)$ of **11** (9.3) = $\Delta\delta(C_\beta)$ of **11** (12.5) − $\Delta\delta(C_\beta)$ of *n*-Bu-9-BBN (3.2). Comparison of the data in Table VI leads to the following conclusions: (i) the γ-carbons are shielded while the β-carbons are deshielded by both tri- and tetravalent boron atoms; (ii) the extent of the shielding and deshielding is greater in the tetravalent borons (ate complexes) than in the trivalent

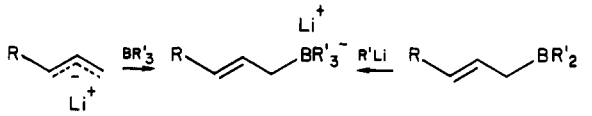
Table VI. Difference in Substituent Effect between Tri- and Tetravalent Boron Atoms

compd	substituent	$\Delta\Delta\delta(C_\beta)$	$\Delta\Delta\delta(C_\gamma)$
	trivalent 	9.3 [9.1][a]	
	tetravalent 	9.8 [9.9][a]	−7.1 [−5.9][a]
	trivalent 	1.5	(−3.0)[b]
	tetravalent 	14.1	−7.5

[a] [cis isomer]. [b] Estimated value.

borons. Consequently, it is now clear that the C_γ of the ate complexes bears a considerable negative charge as shown by a pair of resoance structure (eq 3).[53] This seems to be the reason why allylic boron ate complexes undergo the regioselective coupling at the γ-position with allylic halides. However, the discussion on the precise mechanism of selective γ–α' coupling is premature at this time.

In conclusion, the present development indicates that trialkylboranes may be useful for the regio-, stereo-, and chemoselective control elements of allylic carbanions which possess two potential attacking positions and ambident characteristics. In other words, the selectivity of **7** is enhanced by the control of high reactivity of **7** via the ate complexes. On the other hand, the reactivity of **11** is enhanced through the ate complexes.



Experimental Section

^1H NMR spectra were recorded on a JEOL JNM-MH-100 instrument; chemical shifts (δ) are expressed in parts per million relative to Me_4Si. IR spectra were recorded on a JASCO IRA-1 spectrophotometer. Mass spectra were recorded on a Hitachi GC-M-52 instrument (22 eV). Elemental analyses were performed by the Kyoto University Microanalytical Laboratories, and the results are within the accepted limits (±0.3%). ^{13}C NMR spectra were measured on a JEOL FX-100 spectrometer. The spectra were taken in benzene-d_6 (ca. 50% concentration) and were calibrated by using the solvent resonances as secondary standards. All temperatures were uncorrected.

Reagents. Reagent grade solvents were purified by standard techniques and kept over a drying agent. *n*-BuMgCl,[54a] PhLi,[54b] **8**,[55] and **17**[55] in ether were prepared by standard procedure, and *n*-butyllithium was a commercial product. **7**,[56] **12**,[56] and **13**[57] were prepared from the corresponding triphenyl- or tri-*n*-butyltin derivatives by the reported procedure. The titrations were performed by Gilman's[58] and Eastham's[59] methods. Cuprous iodide was purchased and purified.[60] Organoboranes such as $B(n\text{-Bu})_3$,[61] $B(s\text{-Bu})_3$,[61] *n*-Bu-9-BBN,[61] *n*-butylborepane,[61] **11**,[7b] and **18**[7b] were prepared by the reported procedure. Et_3B, Et_3Al, and other simple chemicals were purchased and used as such.

(47) Bates, R. B.; Beavers, W. A. *J. Am. Chem. Soc.* **1974**, *96*, 5001. The formation of the ate complex from crotyllithium via the metalation of 2-butene in TMEDA failed, presumably owing to the presence of the amine.
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(49) Yamamoto, Y.; Toi, H.; Sonoda, A.; Murahashi, S.-I. *Chem. Lett.* **1975**, 1199.
(50) Hart, D. J.; Ford, W. T. *J. Org. Chem.* **1974**, *39*, 363.
(51) Stothers, J. B. "Carbon-13 NMR Spectroscopy"; Academic Press: New York, 1972.
(52) Yamamoto, Y.; Moritani, I. *J. Org. Chem.* **1975**, *40*, 3434.
(53) For references on σ–π conjugation on allylic organometallic compounds and related derivatives, see: Hartman, G.; Traylor, T. G. *Tetrahedron Lett.* **1975**, 939. Hosomi, A.; Traylor, T. G. *J. Am. Chem. Soc.* **1975**, *97*, 3682.
(54) (a) "Organic Syntheses"; Wiley: New York, 1973; Collect. Vol. V, p 762. (b) Gilman, H.; Morton J. W., Jr. *Org. React. (N.Y.)* **1954**, *8*, 258.
(55) O'Brien, S.; Fishwick, M.; McDermott, B.; Wallbridge, M. G. H.; Wright, G. A. *Inorg. Synth.* **1971**, *13*, 73.
(56) Seyferth, D.; Jula, T. F. *J. Organomet. Chem.* **1971**, *28*, 73.
(57) Tanigawa, Y.; Moritani, I.; Nishida, S. *J. Organomet. Chem.* **1971**, *28*, 73.
(58) Gilman, H.; Hauben, A. H. *J. Am. Chem. Soc.* **1944**, *66*, 1515.
(59) Watson, S. C.; Eastham, J. F. *J. Organomet. Chem.* **1967**, *9*, 165.
(60) Posner, G. H.; Whitten, C. E.; Sterling, J. J. *J. Am. Chem. Soc.* **1973**, *95*, 7788.
(61) Brown, H. C. "Organic Syntheses via Boranes"; Wiley-Interscience: New York, 1975.

Reaction with Allylic Halides. The following procedure for the reaction of **13** with prenyl bromide in the presence of $B(n\text{-}Bu)_3$ is representative. In a 100-mL flask, equipped with a magnetic stirrer and maintained under N_2, were placed 4.07 g (10 mmol) of cinnamyltri-*n*-butyltin[57] and 20 mL of dry ether. An ether solution of phenyllithium (1.1 M, 10 mmol) was slowly added at room temperature under N_2. After being stirred for a few minutes, the mixture was cooled to −78 °C. Tri-*n*-butylborane (10 mmol, 2.4 mL) was added by a syringe, and stirring was continued for a while at −78 °C. Prenyl bromide (10 mmol, 1.2 mL) was slowly added by a syringe, and the resulting mixture was allowed to warm to room temperature by stirring. The mixture was directly analyzed by GLC or was filtered through the column of alumina by using petroleum ether as an eluant after evaporation of the solvent. Undesired byproducts such as tri-*n*-butylborane or the halide were left in the column, and the desired 1,5-diene was obtained along with phenyltri-*n*-butyltin. Distillation gave the desired diene, 6-methyl-3-phenyl-1,5-heptadiene, 1.52 g, 82%. In the large scale experiment, it is recommended to oxidize trialkylboranes with $NaOH\text{–}H_2O_2$ before filtration. A white crystalline tetraphenyltin, obtained as a byproduct in the reation of **7**, **9**, and **12**, was easily separated. The reaction of **8** in the presence of *n*-Bu-9-BBN was carried out similarly; **8** was used instead of **7**. The direct reaction of **7** or **8** with allylic halides was performed in a similar fashion; to an ether solution of **7** or **8** was added the halide by a syringe at −78 °C under N_2, and the reaction was allowed to warm to room temperature. The copper derivatives, **9** and **10**, were prepared by the simple addition of an equivalent amount of CuI to an ether solution of **7** and **8**, respectively, at −30 to −40 °C under N_2. After being stirred for a while at this temperature, the copper reagents were cooled to −78 °C and then the subsequent operations were carried out as described above. An equivalent amount of *n*-BuLi in hexane was added to an ether solution of **11** at −78 °C under N_2, and the electrophiles such as **2** and crotyl chloride were added at this temperature. The subsequent operations were carried out as described above. In Table I, **3** and **4** were isolated either as described above or by a preparative GLC, while **5** and **6** were isolated from the reaction of entries 3 and 5 of Table II. Irradiation of an appropriate proton was quite helpful for the structure determination by ^1H NMR spectra.

4-Methyl-1-phenyl-1,5-hexadiene (**3**):[62] bp 76–77 °C (1mmHg); IR (cm^{-1}, CCl_4) 1640, 1600, 992, 960, 908; ^1H NMR (CCl_4) δ 1.04 (3 H, d, J = 7 Hz), 1.16–1.32 (3 H, m), 4.88–5.08 and 5.60–6.00 (2 H and 1 H, allyl H), 6.02 (1 H, td, J = 6 and 16 Hz), 6.32 (1 H, d, J = 16 Hz, *E* geometry), 7.16 (5 H, b s); m/e (M^+) 172. Anal. ($C_{13}H_{16}$) C, H.

1-Phenyl-1,5-heptadiene (**4**):[62] bp 76–77 °C (1mmHg); IR (cm^{-1}, CCl_4) 1640, 1600, 962; ^1H NMR (CCl_4) δ 1.62 (3 H, b t, J was not obvious), 2.18 (4 H, b s), 5.30 (2 H, m), 6.00 (1 H, td, J = 6 and 16 Hz), 6.26 (1 H, d, J = 16 Hz, *E* geometry), 7.12 (5 H, b s); m/e (M^+) 172. Anal. ($C_{13}H_{16}$) C, H. Two singlet peaks appeared at the Me region (δ 1.58 and 1.62) by the irradiation of δ 5.30 (MeCH=CH); the latter peak was assigned as the *E* isomer, since it was a major isomer except for entry 2 and strong IR absorption was observed at 962 cm^{-1}. Two peaks were also observed in GLC (DC 550, 2 m), the ratio of which was very close to that of the ^1H NMR spectra.

3-Phenyl-1,5-heptadiene (**5**):[62] bp 76–78 °C (1mmHg); IR (cm^{-1}, CCl_4) 1640, 1600, 990, 965, 910; ^1H NMR (CCl_4) δ 1.60 (3 H, d, J = 4 Hz), 2.40 (2 H, dd, J = 6 and 6 Hz), 3.12–3.36 (1 H, m), 4..84–5.04 and 5.74–6.08 (2 H and 1 H, allyl H), 5.24–5.36 (2 H, m), 7.12 (5 H, b s); m/e (M^+) 172. Anal. ($C_{13}H_{16}$) C, H. Irradiation at δ 5.24–5.36 (MeCH=CH) led to a sharp singlet of Me. A sharp peak of GLC (DC 550, 2 m), strong IR band at 965 cm^{-1}, and the result of the irradiation strongly suggested the absence of the *Z* isomer. However, a possibility that small amounts of *Z* isomer may be involved is not completely eliminated.

3-Methyl-4-phenyl-1,5-hexadiene (**6**):[62] bp 76 °C (1mmHg); IR (cm^1, CCl_4) 1640, 1600, 990, 910; ^1H NMR (CCl_4) δ 0.86 and 1.04 (3 H, d, J = 7 Hz), 2.40–2.62 (1 H, m), 2.96–3.20 (1 H, m), 4.76–5.10 and 5.40–6.30 (4 H and 2 H, allyl H), 7.12 (5 H, b s); m/e (M^+) 172. Anal. ($C_{13}H_{16}$) C, H. Two doublets at δ 0.86 and 1.04 were ascribed to the diastereomers, threo and erythro, and actually two peaks appeared in GLC. However, the precise assignment was not performed.

1,5-Heptadiene:[62] bp 95 °C; IR (cm^{-1}, CCl_4) 1640, 990, 965, 910; ^1H NMR (CCl_4) δ 1.68 (3 H, d, J = 4 Hz), 2.10 (4 H, b s), 4.86–5.08 and 5.60–5.90 (2 H and 1 H, allyl H), 5.40 (2 H, b s); m/e (M^+) 96.

1-Phenyl-1,5-hexadiene:[62] bp 68–70 °C (1mmHg); IR (cm^{-1}, CCl_4) 1640, 1600, 990, 965, 910; ^1H NMR (CCl_4) δ 2.26 (4 H, b s), 4.92–5.12 and 5.64–6.02 (2 H and 1 H, allyl H) 6.10 (1 H, td, J = 6 and 16 Hz), 6.36 (1 H, d, J = 16 Hz, *E* geometry), 7.20 (5 H, b s); m/e (M^+) 158.

6-Methyl-3-phenyl-1,5-heptadiene: bp 70–71 °C (1mmHg); IR (cm^{-1}, CCl_4) 1640, 1600, 990, 910; ^1H NMR (CCl_4) δ 1.53 (3 H, s), 1.64 (3 H, s), 2.36 (2 H, dd, J = 7 and 7 Hz), 3.24 (1 H, td, J = 7 and 7 Hz), 4.88–5.10 and 5.76–6.10 (2 H and 1 H, allyl H), 5.04 (1 H, s), 7.12 (5 H, b s); m/e (M^+) 186. Anal. ($C_{14}H_{18}$) C, H.

3,6-Dimethyl-1,5-heptadiene:[63] bp 50 °C (15mmHg); IR (cm^{-1}, CCl_4) 1640, 990, 910; ^1H NMR (CCl_4) δ 0.97 (3 H, d, J = 7 Hz), 1.58 (3 H, s), 1.68 (3 H, s), 1.90–2.10 (3 H, m), 4.76–5.10 and 5.44–5.80 (2 H and 1 H, allyl H), 4.92 (1 H, s); m/e (M^+) 124. Anal. (C_9H_{16}) C, H.

2-Methyl-2,6-octadiene:[64] bp 50 °C (15mmHg); IR (cm^{-1}, CCl_4) 1640, 990, 965, 910; ^1H NMR (CCl_4) δ 1.57 (3 H, s), 1.62 (3 H, b t, J was not obvious), 1.68 (3 H, s), 1.88–2.15 (4 H, m), 5.40 (2 H, b s), 4.95 (1 H, s); m/e (M^+) 124. Anal. (C_9H_{16}) C, H.

Authentic samples were prepared by the reported procedures,[62–64] and compared with the isolated products. 3-Methyl-1,5-heptadiene (**14**), (*E*)- and (*Z*)-2,6-octadiene (**15**), and meso and racemic 3,4-dimethyl-1,5-hexadiene (**16**) were independently prepared by the reported procedure.[65] The reaction mixture was directly analyzed by GC–Mass, and the mass spectra of **14**–**16** were completely identical with those of authentic materials.

Reaction with Aldehydes. The reaction was carried out on a 1-mmol scale, and the same procedure as above was employed. Aldehydes were added by a syringe instead of the halides, and the reaction was quenched at −70 °C with H_2O–MeOH. The reaction mixture containing organoboranes was oxidized with H_2O_2–NaOH at 0 °C, and Et_3Al was decomposed by slow addition of H_2O–MeOH. The organic layer was separated, dried with anhydrous Na_2SO_4, and condensed. The product was directly analyzed by ^1H NMR or by GLC. Filtration through the column of silica gel using petroleum ether–ether (10:1) as an eluant gave the desired product. The ratio of threo and erythro isomer[66] of 2-methyl-1-phenylbut-3-en-1-ol (entries 1–17) was easily determined by the ^1H NMR spectra: erythro (CCl_4) δ 0.93 (3 H, d, J = 7 Hz), 2.00 (1 H, b s, OH), 2.44 (1 H, m), 4.40 (1 H, d, J = 6 Hz), 4.80–5.10 and 5.48–5.82 (2 H and 1 H, allyl H), 7.14 (5 H, b s); threo (CCl_4) δ 0.84 (3 H, d, J = 7 Hz), 2.36 (1 H, m), 2.84 (1 H, b s, OH), 4.24 (1 H, d, J = 8 Hz), 4.84–5.12 and 5.56–5.92 (2 H and 1 H, allyl H), 7.16 (5 H, s). The ratio was based on the integral area ratio of CHO (δ 4.40 and 4.24). These spectroscopic characteristics, as well as IR and mass spectra, were completely identical with those of authentic materials.[34,35] 3-Methyl-4-penten-2-ol (from acetaldehyde), 4-methyl-5-hexen-3-ol (from propionaldehyde), and 2,4-dimethyl-5-hexen-3-ol (from isobutyraldehyde) were identical with authentic samples.[67] The ratio of threo/erythro was determined by using GLC (CW 6000, 2m).[67] Authentic 1-phenyl-3-penten-1-ol, the coupling product at the α-position of **7**, was independently prepared from the reaction of (1-methylallyl)tri-*n*-butyltin with benzaldehyde in the presence of BF_3·OEt_2.[35]

Reaction with α,β-Unsaturated Carbonyl Compounds. The reaction was carried out on a 2-mmol scale, and the essentially same procedure as above was employed. The reaction mixture was directly analyzed by GLC (DC 550, 1 m). Authentic samples were prepared according to the reported procedures.[68–72] 4-Phenyl-hept-6-en-2-one:[68] bp 70–72 °C (1mmHg); IR (cm^{-1}, CCl_4) 1722, 1640, 1600, 995, 915; ^1H NMR (CCl_4) δ 1.96 (3 H, s), 2.32 (2 H, t, J = 7 Hz), 2.64 (2 H, d, J = 7 Hz), 3.00–3.30 (1 H, m), 4.85–5.16 and 5.40–5.80 (2 H and 1 H, allyl H), 7.16 (5 H, b s); m/e (M^+) 188. 3-Methyl-1-phenyl-1,5-hexadien-3-ol:[69] bp 70 °C (1mmHg); IR (cm^{-1}, CCl_4) 3300, 1640, 1600, 995, 960, 915; ^1H NMR (CCl_4) δ 1.32 (3 H, s), 2.30 (1 H, b s, OH), 2.33 (2 H, d, J = 7 Hz), 4.93–5.15 and 5.60–6.00 (2 H and 1 H, allyl H), 6.19 (1 H, d, J = 16 Hz), 6.35 (1 H, d, J = 16 Hz), 7.10–7.35 (5 H, m); m/e (M^+) 188. An authentic sample was prepared from the reaction of **18** with benzalactone.[7c,69] Hept-6-en-2-one:[70] bp 56–57 °C (50mmHg); IR (cm^{-1}, CCl_4) 1725, 1640, 990, 910; ^1H NMR (CCl_4) δ 1.22–1.44 (2 H, m), 2.04 (3 H, s), 2.24 (2 H, m), 2.56 (2 H, t, J = 7 Hz), 4.90–5.16 and 5.56–6.00 (2 H and 1 H, allyl H); m/e (M^+) 112. 3-Methyl-1,5-hexadien-3-ol:[71] bp 57–59 °C (45mmHg); IR (cm^{-1}, CCl_4) 3300, 1640, 990,

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910; ^{1}H NMR (CCl_4) δ 1.40 (3 H, s), 2.30 (2 H, d, J = 7 Hz), 4.80–5.20 and 5.56–6.04 (4 H and 2 H, allyl H); m/e (M^+) 112. 1-Phenyl-1,5-hexadien-3-ol:[72] bp 70 °C (1mmHg); IR (cm^{-1}, CCl_4) 3300, 1640, 1600, 995, 960, 910; ^{1}H NMR (CCl_4) δ 2.35 (2 H, t, J = 7 Hz), 2.40 (1 H, b s, OH), 4.95–5.20 and 5.60–6.00 (2 H and 1 H, allyl H), 6.20 (1 H, dd, J = 7 and 16 Hz), 6.35 (1 H, d, J = 16 Hz), 4.25–4.50 (1 H, m), 7.10–7.40 (5 H, m); m/e (M^+) 174. An authentic sample was prepared from the reaction of **18** with cinnamaldehyde.[7c,72]

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Intramolecular Lactonization at a Metal Center. The Rapid Reactions of Coordinated H_2O and OH^- with an Adjacent Carboxylic Acid Residue

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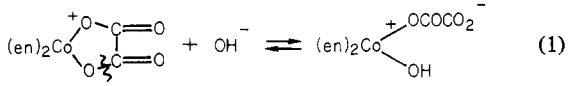
Abstract: ^{18}O-tracer studies show that cyclization of *cis*-$[Co(en)_2(OH_2)(glyOH)]^{3+}$ and *cis*-$[Co(en)_2(OH_2)(glyO)]^{2+}$ (glyOH = N-bound glycine; glyO = N-bound glycinate) to give $[Co(en)_2(glyO)]^{2+}$ containing chelated glycinate occur intramolecularly without displacement of coordinated water. The rates of these reactions are relatively fast with $t_{1/2} \simeq 40$ s at pH 0–1 and $t_{1/2} \simeq 400$ s at pH 4; the overall rate law takes the form $k_{obsd} = (k_H[H^+]^2 + k_H'K_1[H^+] + k_{OH}K_1K_2)/(K_1K_2 + k_1[H^+] + [H^+]^2)$ with $k_H = 1.9 \times 10^{-2}$ s^{-1}, $k_H' = 1.05 \times 10^{-3}$ s^{-1}, $k_{OH} = 1.74 \times 10^{-5}$ s^{-1}, pK_1 = 2.3, pK_2 = 6.3 at 25.0 °C, and μ = 1.0 ($NaClO_4$). The reaction of the *cis*-$[Co(en)_2(OH_2)(glyO)]^{2+}$ ion is catalyzed by general acids (including H_3O^+), and this is interpreted in terms of rate-determining protonation of an intermediate cyclic species. Cyclization in the *cis*-$[Co(en)_2(OH)(glyO)]^+$ ion is considerably slower ($t_{1/2} \simeq 10$ h) and is not catalyzed by monofunctional buffers. Comparisons with O exchange in glycine show large accelerations for the metal-based system (10^7–10^{12} M), and the rates compare favorably with those found for intramolecular lactone formation in purely organic molecules.

Esterification of carboxylic acids R–COO(H) by alcoholic species R′–OH is normally slow in the absence of additional activation or specific coupling reagents.[1] However, by employing the entropic advantages of the intramolecular situation[2] and by using substituents which produce ground state strain,[3,4] ester formation (or lactone formation in the intramolecular case) can be enhanced by factors of up to 10^{15}.[5]

When the alcoholic function involves a metal hydroxide M–OH, the simple bimolecular esterification of carboxylic acids is unknown. Metal hydroxides only add to activated carbonyl functions (e.g., CO_2[6]) or displace "good" leaving groups such as in their reactions with anhydrides,[7] acetylacetone,[8] and the reactive esters 2,4-DNPA and 4-NPA.[9] However, when the process is made intramolecular by incorporating the metal hydroxide and substrate in the same molecule, large increases in rate are again realized. Normal alkyl esters, nitriles, amides, and even peptide fragments can now be readily hydrolyzed.[9]

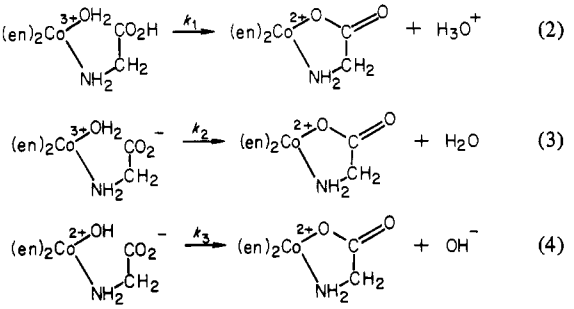
This leads to the possibility of metal esterification of carboxylic acids via the intramolecular process. Although unknown, there are good precedents for this; the reverse of the base-catalyzed ring opening of oxalate in $[Co(en)_2C_2O_4]^+$[10] is a required example (eq 1) and other likely candidates include cyclization in [Co-



(1)

$(EDTA)(OH/H_2O)]^{2-}$[1-11,12] and $[Co(en)_2(OH_2)(C_2O_4)]^{1+}$[13] without cleavage of the metal–oxygen bond.

In this paper we describe the first clear examples of this type of process; the cyclization of N-bound glycine in the *cis*-$[Co(en)_2(OH_2/OH)(glyO/H)]^{3+/2+/1+}$ species. Depending on pH this occurs via the addition of coordinated water or coordinated hydroxide to the carboxylic acid function (reactions 2–4) with the



(2)

(3)

(4)

coordination sphere about the metal remaining intact. These processes can be considered as adjuncts to the H^+- and OH^--catalyzed exchange of oxygen atoms in the $[Co(en)_2(glyO)]^{2+}$

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