isolated (+)-koumidine (**3**).[6] Its ^1H NMR, IR, MS, mp were identical with an authentic sample of (−)-koumidine, but it had an equal and opposite $[\alpha]^{25}_D$ +11.1° (*c* 0.360 in MeOH).

The alkaloids of the koumine-sarpagine group which also includes gelsemine have not yielded to total synthesis. The crucial intramolecular Michael reaction[16] [**12** into **13**/**14**] offers a new way for making quinuclidines that may be valuable in other areas of alkaloid synthesis.[17]

Acknowledgment. The National Institutes of Health are gratefully thanked for their support, and Dr. B. B. Mugrage thanks the NIH for a post doctoral fellowship (GM-12226). Professor M. Hesse and Professor G. Cordell are warmly thanked for authentic samples of (−)-taberpsychine and (−)-koumidine, respectively. Dr. John Huffman, Molecular Structure Center, Indiana University, Bloomington, IN 47405, is thanked for X-ray structural determinations.

(16) Trost, B. M.; Shuey, C. D.; DiNinno, F., Jr. *J. Am. Chem. Soc.* **1979**, *101*, 1284.
(17) All new compounds were characterized by ^1H NMR, ^{13}C NMR, IR, HRMS and/or microanalysis.

Generation of Chiral Organoaluminum Reagent by Discrimination of the Racemates with Chiral Ketone

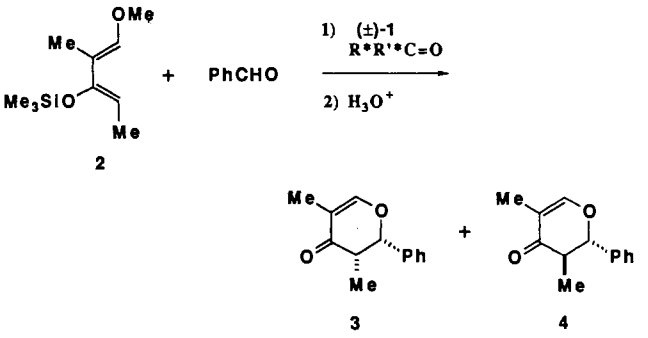
Keiji Maruoka and Hisashi Yamamoto*

Department of Applied Chemistry
Nagoya University
Chikusa, Nagoya 464-01, Japan

Received October 5, 1988

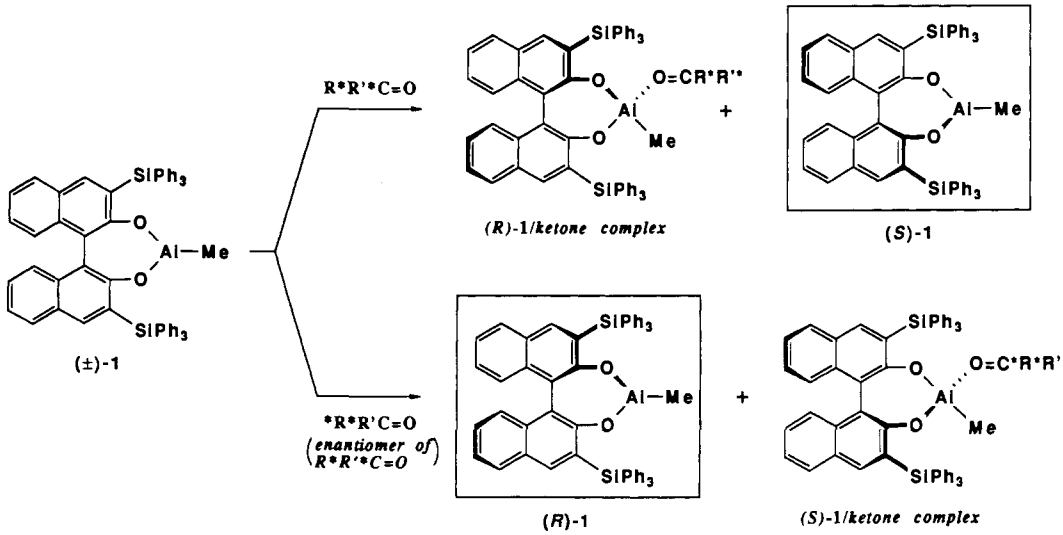
We have recently demonstrated a new, chiral organoaluminum catalyst which is highly effective for the introduction of chirality into cyclic as well as acyclic systems.[1,2] We also reported that bulky organoaluminum reagent MAD is capable of forming a selective 1:1 complex with specific carbonyl substrates.[3] One would therefore expect that certain chiral ketones may discriminate between racemic organoaluminum reagents of type **1** by diastereoselective complexation, and the remaining chiral organoaluminum reagent (*R*)-**1** or (*S*)-**1** would be utilized in situ as a chiral Lewis acid for asymmetric synthesis as illustrated in Scheme I. Here we wish to report our initial results of this study.

Our expectation has been realized by applying the in situ generated catalyst to the asymmetric hetero-Diels–Alder reaction as indicated in Table I. The racemic organoaluminum reagent (±)-**1** was prepared in CH_2Cl_2 as reported previously.[1] Sequential treatment of (±)-**1** with chiral ketone, the diene **2**, and benzaldehyde at −78 °C and stirring of the mixture at this temperature for 3 h afforded hetero-Diels–Alder adducts **3** and **4** after acidic workup. The optical yield of the major cis adduct **3** was determined by HPLC analysis after conversion to the (*R*)-MTPA ester. Note that with the enantiomerically pure organoaluminum reagent (*S*)-**1** the cis adduct **3** was obtained in 95% ee.[1]



Several characteristic features have been noted. (1) Among several terpene-derived chiral ketones examined, *d*-3-bromocamphor was found to be most satisfactory.[4-7] (2) Combination of (±)-**1** and chiral ketone in a 1:1 ratio gave a better result than that in a 2:1 ratio. This suggests that decomplexation of one enantiomeric organoaluminum reagent and the chiral ketone is more readily facilitated than that of the other diastereomeric complex by the addition of aldehyde, thereby allowing the enantioselective activation of the aldehyde for the asymmetric hetero-Diels–Alder reaction. Noteworthy is the fact that the catalytic use of the reagent exhibited higher enantioselection than the stoichiometric use. Although the extent of asymmetric induction in the hetero-Diels–Alder reaction is not yet as satisfactory as that with the optically pure **1**, one recrystallization of the cis adduct **3** of 82% ee (entry 8) from hexane gave the essentially pure **3** (>98% ee with ~60% recovery),[8] thereby enhancing the practicability of this method. (3) Since both *d*-3- and *l*-3-bromocamphor are commercially available, this method allows the synthesis of both enantiomers of hetero-Diels–Alder adducts in a predictable manner (entry 8 vs 9). *d*-3-Bromocamphor is responsible for the generation of (*S*)-**1**. (4) Use of toluene as solvent gave higher cis selectivity at the expense of enantiofacial selectivity (entry 6).

Scheme I



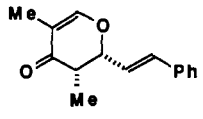
0002-7863/89/1511-0789$01.50/0

Table I. Asymmetric Hetero-Diels-Alder Reaction of the Diene 2 and Benzaldehyde[a]

entry	chiral ketone[b] (equiv)	(±)-1 (equiv)	% yield[c]	% ee[d,e] (confign)
1	*d*-camphor (0.15)	0.3	80 (17)	22 (2*S*,3*S*)
2	*d*-3-bromocamphor (0.15)	0.3	66 (32)	70 (2*S*,3*S*)
3	(2)	2	62 (19)	61 (2*S*,3*S*)
4	(0.3)	0.3	72 (24)	80 (2*S*,3*S*)
5	(0.6)	0.3	60 (31)	75 (2*S*,3*S*)
6	(0.3)	0.3	84 (12)[f]	68 (2*S*,3*S*)
7	(0.2)	0.2	78 (20)	79 (2*S*,3*S*)
8	(0.1)	0.1	78 (19)	82 (>98)[h] (2*S*,3*S*)
9	*l*-3-bromocamphor (0.1)	0.1	75 (18)[g]	82 (2*R*,3*R*)
10	*d*-3-iodocamphor (0.15)	0.3	70 (28)	13 (2*S*,3*S*)
11	*d*-camphorquinone (0.15)	0.3	75 (21)	22 (2*S*,3*S*)
12	*d*-fenchone (0.15)	0.3	62 (28)	2 (2*S*,3*S*)
13	(-)-pinocamphone (0.15)	0.3	67 (25)	2 (2*S*,3*S*)
14	*l*-menthone (0.15)	0.3	70 (27)[g]	5 (2*R*,3*R*)
15	*l*-*cis*-carvone tribromide (0.15)	0.3	53 (45)	19 (2*S*,3*S*)

[a] Unless otherwise specified, the reaction was carried out in degassed CH_2Cl_2 using 1.05 equiv of the diene 2 per benzaldehyde at -78 °C for 3 h. [b] For the preparation of *d*-3-iodocamphor, *d*-camphorquinone, (-)-pinocamphone, and *l*-*cis*-carvone tribromide, see ref 4-7. Other chiral ketones are commercially available. [c] Isolated yield of the cis adduct 3. The values in parentheses refer to the yields of the trans isomer 4. [d] Optical yield of the major cis isomer 3. [e] Determined by HPLC analysis of the (*R*)-(+)-MTPA ester of the alcohol, which was derived from the cis adduct 3 by 1,4-reduction with L-Selectride followed by reduction of the resulting saturated ketone with $NaBH_4$. [f] Use of toluene as solvent. [g] The enantiomers of 3 and 4 were produced. [h] Optical purity was upgraded by recrystallization from hexane.

Similarly, the hetero-Diels-Alder reaction of *trans*-cinnamaldehyde and the diene 2 with 0.2 equiv each of (±)-1 and *d*-3-bromocamphor in CH_2Cl_2 at -78 °C gave rise to the cis adduct 5 in 72% yield (74% ee; 92% ee after one recrystallization from hexane with 30-40% recovery).[9,10]



5

The present approach represents the uniqueness and synthetic utility of the highly oxygenophilic organoaluminum reagents in asymmetric reactions. Here a chiral ketone plays the role of chemical antagonist toward one enantiomer of racemic organoaluminums. Finally, the concept and execution of the work described herein demonstrates a potential for broader applicability of the in situ generated catalyst via diastereoselective complexation in asymmetric synthesis.

(1) Maruoka, K.; Itoh, T.; Shirasaka, T.; Yamamoto, H. *J. Am. Chem. Soc.* **1988**, *110*, 310.
(2) Maruoka, K.; Hoshino, Y.; Shirasaka, T.; Yamamoto, H. *Tetrahedron Lett.* **1988**, *29*, 3967.
(3) Maruoka, K.; Araki, Y.; Yamamoto, H. *J. Am. Chem. Soc.* **1988**, *110*, 2650.
(4) *d*-3-Iodocamphor: Bruhl, J. W. *Ber.* **1904**, *37*, 2163.
(5) *d*-Camphorquinone: Riley, H. A.; Gray, A. R. *Organic Synthesis*; Wiley: New York, 1943; Collect. Vol. II, p 509.
(6) *l*-*cis*-Carvone tribromide: Wolinsky, J.; Hamsher, J. J.; Hutchins, R. O. *J. Org. Chem.* **1970**, *35*, 207.
(7) (-)-Pinocamphone: Brown, H. C.; Garg, C. P. *J. Am. Chem. Soc.* **1961**, *83*, 2952.
(8) In the recrystallization from hexane, the racemic 3 separated out first as colorless crystals, and concentration of the remaining mother liquor yielded the essentially pure 3 (>98% ee) as colorless solids.
(9) With the optically pure 1 the cis adduct 5 was produced in 90% ee.
(10) The trans isomer of 5 was obtained in 22% yield.

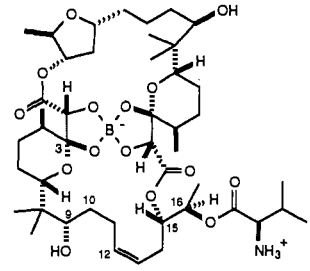
Total Synthesis of Boromycin

James D. White,*[1] Mitchell A. Avery, Satish C. Choudhry, Om Prakash Dhingra, Brian D. Gray, Myung-chol Kang, Shen-chun Kuo, and Alan J. Whittle

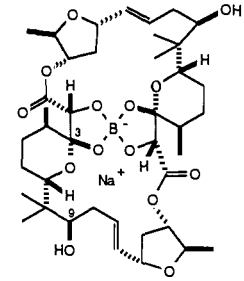
Department of Chemistry, Oregon State University Corvallis, Oregon 97331-4003

Received October 3, 1988

The molecular architecture of boromycin (**1**),[2] with its borate core embedded in a densely functionalized superstructure of oxygen substituents, presents a synthetic challenge that demands careful strategic analysis. Exquisitely designed for its role of encapsulation and transport of alkali metal cations, the structure of **1** differs from that of the symmetrical diolide aplasmomycin (**2**)[3] in two important respects. These are (a) reversal of hydroxyl configuration at C(9) and (b) an open quadrant in the lower right segment [C(12)-C(16)] of **1** that provides a locus for attachment of a D-valinyl ester whose protonated amino group occupies the orifice of the natural cryptand. A progression of synthetic and related studies has laid valuable groundwork for our approach to **1**[4-10]



1



2

and has also culminated in a recent total synthesis of **2**,[11] but significant revision of earlier plans has been necessary to conclude these efforts. We now report the first total synthesis of **1** employing a strategy that elaborates and couples in head-to-tail fashion protected versions of the upper and lower half structures to produce a 34-membered macrocycle. The finale to this sequence is a ring contraction ("double Chan" reaction) based on the rearrangement of an α-acyloxyacetate to an α,β-enediolate[12] and previously exemplified in our synthesis of **2**.[11]

Ortholactone **3**, available from (*R*)-(+)-pulegone,[9] provided the C(3)-C(10) segment common to the two halves of **1** and was

(1) Fellow of the John Simon Guggenheim Memorial Foundation, 1988-1989.
(2) (a) Hütter, R.; Keller-Schierlein, W.; Knusel, F.; Prelog, V.; Rodgers, G. C., Jr.; Suter, P.; Vogel, G.; Voser, W.; Zahner, H. *Helv. Chim. Acta* **1967**, *50*, 1533. (b) Dunitz, J. D.; Hawley, D. M.; Miklos, D.; White, D. N. J.; Berlin, Y.; Marušič, R.; Prelog, V. *Helv. Chim. Acta* **1971**, *54*, 1709. (c) Marsh, W.; Dunitz, J. D.; White, D. N. J. *Helv. Chim. Acta* **1974**, *57*, 10.
(3) (a) Okazaki, T.; Kitahara, T.; Okami, Y. *J. Antibiot.* **1975**, *28*, 176. (b) Okami, Y.; Okazaki, T.; Kitahara, T.; Umezawa, H. *J. Antibiot.* **1976**, *29*, 1019. (c) Nakamura, H.; Iitaka, Y.; Kitahara, T.; Okazaki, T.; Okami, Y. *J. Antibiot.* **1977**, *30*, 714. (d) Sato, K.; Okazaki, T.; Maeda, K.; Okami, Y. *J. Antibiot.* **1978**, *31*, 632.
(4) Avery, M. A.; White, J. D.; Arison, B. H. *Tetrahedron Lett.* **1981**, *22*, 3123.
(5) White, J. D.; Avery, M. A.; Choudhry, S. C.; Dhingra, O. P.; Kang, M.-c.; Whittle, A. J. *J. Am. Chem. Soc.* **1983**, *105*, 6517.
(6) White, J. D.; Kang, M.-c.; Sheldon, B. G. *Tetrahedron Lett.* **1983**, *24*, 4539.
(7) White, J. D.; Choudhry, S. C.; Kang, M.-c. *Tetrahedron Lett.* **1984**, *25*, 3671.
(8) Somers, T. C.; White, J. D.; Lee, J. J.; Keller, P. J.; Chang, C.-j.; Floss, H. G. *J. Org. Chem.* **1986**, *51*, 464.
(9) White, J. D.; Kuo, S.-c.; Vedananda, T. R. *Tetrahedron Lett.* **1987**, *28*, 3061.
(10) For an approach to **1** based on a different strategy, see: (a) Hanessian, S.; Delorme, D.; Tyler, P. C.; Demailly, G.; Chapleur, Y. In *Current Trends in Organic Synthesis*; Nozaki, H., Ed.; Pergamon: New York, 1983; p 205 and references cited therein. (b) Hanessian, S.; Delorme, D.; Tyler, P. C.; Demailly, G.; Chapleur, Y. *Can. J. Chem.* **1983**, *61*, 634.

0002-7863/89/1511-0790$01.50/0