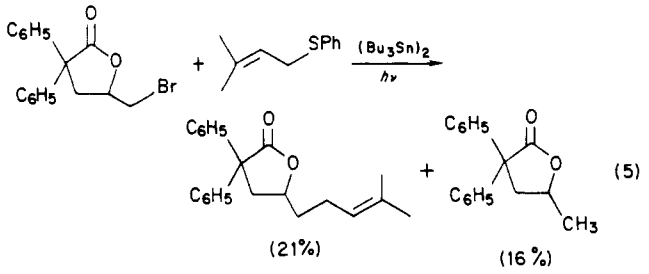
Attempts to extend this process to sulfides bearing alkyl substitution at the allylic terminus have been unsuccessful. For example, if 1-(phenylthio)-3-methyl-2-butene (the allylically transposed isomer of **5**) is reacted with substrate **19**, then no products from direct S_H2' reaction are found: only **17** and the reduction product from **19** are isolable, albeit in poor yield.[15] (Note eq 5).



(5)

Although the yields of this process are not as high as for allylation using allyltri-*n*-butylstannane, the success of this rather complex chain process despite numerous a priori reasonable side reactions is noteworthy, as is the separation of chain-carrying steps[16] in the mechanism. The results described herein demonstrate that the design of complex free radical chains for use in organic synthesis is feasible, and further investigations along such lines are in progress in our laboratories.

Acknowledgment. We thank the National Science Foundation for generous support of this research.

Registry No. **5**, 34043-60-2; **6**, 701-75-7; **7**, 540-51-2; **8**, 42272-94-6; *cis*-**9**, 928-91-6; *trans*-**9**, 928-92-7; **10**, 627-18-9; **11**, 13175-35-4; *cis*-**12**, 50273-95-5; *trans*-**12**, 25143-94-6; **13**, 574-98-1; **14**, 99097-66-2; *cis*-**15**, 99097-67-3; *trans*-15, 99097-68-4; **16**, 53560-49-9; **17**, 99097-69-5; *cis*-**18**, 99097-70-8; *trans*-18, 99097-71-9; **19**, 83160-36-5; **20**, 83160-38-7; **21**, 19914-92-2; **22**, 99097-72-0; **23**, 99097-73-1; **24**, 71404-67-6; hexabutylditin, 813-19-4.

(15) (a) The production of **17** may be rationalized by allylic rearrangement of 1-(phenylthio)-3-methyl-2-butene to give **5**, followed by reaction of **5** with a carbon-centered radical generated from **19**. For leading references on the rearrangement of allylic sulfides, note: Kozikowski, A. P.; Huie, E.; Springer, J. P. *J. Am. Chem. Soc.* **1982**, *104*, 2059 and references therein. (b) Similar results were obtained for reaction of **19** with 1-(phenylthio)-2-butene (the allylically transposed isomer of **6**). In this case, 42% of the reduced product was obtained, along with 7% of **18** and 7% of the product of direct S_H2' substitution.

(16) In free radical allylation using allylstannanes, C–C bond formation and generation of substrate radicals are inevitably linked to one another, since chain-carrying stannyl radicals are generated directly from the C–C bond forming event. In the present process, C–C bond formation and generation of chain-carrying stannyl radicals occur as separate and discrete steps in the chain.

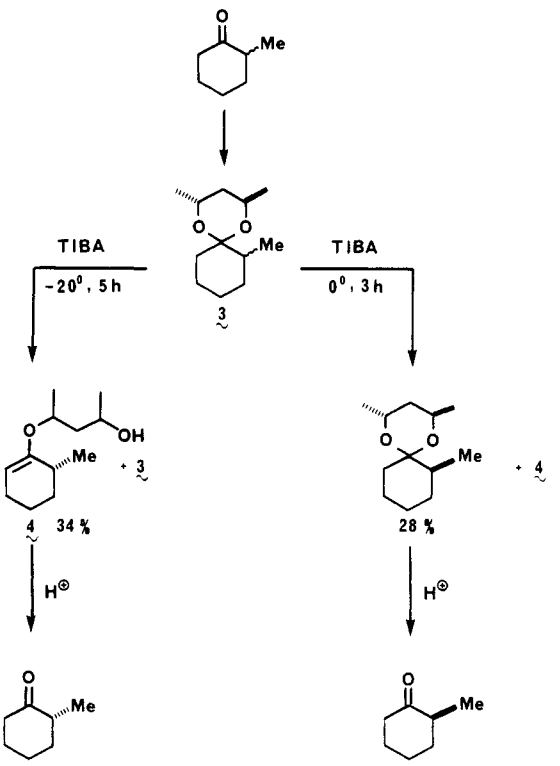
Gary E. Keck,* Jeffrey H. Byers
Department of Chemistry
University of Utah
Salt Lake City, Utah 84112
Received June 10, 1985

Resolution of Ketones via Chiral Acetals. Kinetic Approach

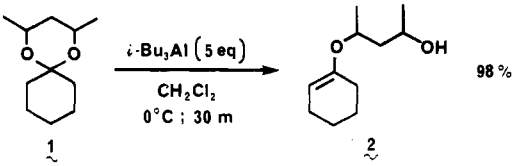
Summary: When a chiral acetal is treated with triisobutylaluminum at low temperature, one diastereoisomer reacts much faster than the other and the resulting enol ether is transformed to optically pure ketone.

Sir: In contrast to the generation of optically active carbonyl compounds by asymmetric alkylation, which is now used with great frequency in synthesis and for which many selective reagents are known,[1] methods for the efficient resolution of carbonyl compounds are still quite limited. Classical approaches to the optical activation of ketones are not always reliable.[2,3] This communication reports the successful development of a new type of resolution for ketones based on a kinetic approach.

Scheme I



We have recently described the nucleophilic cleavage of chiral acetals derived from (–)-(2*R*,4*R*)-2,4-pentanediol using organometallic reagents.[4] By studying this reaction in detail, it was discovered that an enol ether was formed under certain reaction conditions. Thus, treatment of acetal **1** with triisobutylaluminum (TIBA) in dichloromethane at 0 °C for 30 min produced the enol ether **2** in



(1) For reviews, see: "Asymmetric Synthesis", Vol. 2 and 3, Morrison, J. D., Ed.; Academic Press: New York, 1983 and 1984.

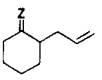
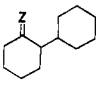
(2) For reviews, see: Wilen, S. H. In "Topics in Stereochemistry"; Eliel, E. L., Allinger, N. L., Eds.; Wiley-Interscience: New York, 1971; Vol 6, p 107. See also: Newman, P. "Optical Resolution Procedures for Chemical Compounds"; Optical Resolution Information Center: Manhattan College, New York, 1984; Vol 3, p 479.

(3) Recently Johnson reported an elegant resolution technique of ketone based on the addition of an optically pure sulfoximine: Johnson, C. R.; Zeller, J. R. *J. Am. Chem. Soc.* **1982**, *104*, 4021; *Tetrahedron* **1984**, *40*, 1225.

(4) (a) Mori, A.; Fujiwara, J.; Maruoka, K.; Yamamoto, H. *J. Organomet. Chem.* **1985**, *285*, 83. Mori, A.; Fujiwara, J.; Maruoka, K.; Yamamoto, H. *Tetrahedron Lett.* **1983**, *24*, 4581. Mori, A.; Maruoka, K.; Yamamoto, H. *Ibid.* **1984**, *25*, 4421. See also: (b) Bartlett, P. A.; Johnson, W. S.; Elliott, J. D. *J. Am. Chem. Soc.* **1983**, *105*, 2088. (c) Johnson, W. S.; Elliott, R.; Elliott, J. D. *Ibid.* **1983**, *105*, 2904. (d) Elliott, J. D.; Choi, V. M. F.; Johnson, W. S. *J. Org. Chem.* **1983**, *48*, 2294. (e) Choi, V. M. F.; Elliott, J. D.; Johnson, W. S. *Tetrahedron Lett.* **1984**, *25*, 591. (f) Ghribi, A.; Alexakis, A.; Normant, J. F. *Ibid.* **1984**, *25*, 3083. (g) Lindell, S. D.; Elliott, J. D.; Johnson, W. S. *Ibid.* **1984**, *25*, 3947. (h) Johnson, W. S.; Crackett, P. H.; Elliott, J. D.; Jagodzinski, J. J.; Lindell, S. D.; Natarajan, S. *Ibid.* **1984**, *25*, 3951. (i) Johnson, W. S.; Edington, C.; Elliott, J. D.; Silverman, I. R. *J. Am. Chem. Soc.* **1984**, *106*, 7588.

0022-3263/85/1950-5444$01.50/0

Table I. Resolution of Ketones Using Chiral Acetals[a]

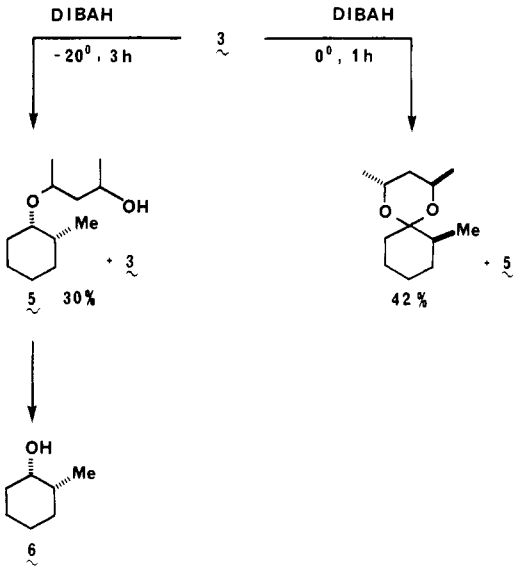
entry	acetal[b]	aluminum reagent (equiv)	reactn condn °C, h	enol ether yield (%)[c] (ratio)[d]	recovered acetal yield (%)[c] (ratio)[e]
1		TIBA (2)	0, 3		28 (<1:99)
2		TIBA (2)	−20, 5	34 (>99:1)	
3		DIBAH (2)	−20, 3		42 (<1:99)
4		TIBA (4)	−20, 2		35 (1:99)[f]
5		TIBA (2)	−20, 1	33 (97:3)[f]	
6		TIBA (4)	−20, 3		25 (<1:99)
7		TIBA (4)	−20, 1		49 (36:64)
8		TIBA (6)	−20, 1		20 (26:74)
9		TIBA (4)	−20, 0.5		36 (12:88)
10		TIBA (4)	−20, 3		18 (1:99)
11		DIBAH (4)	−20, 0.5		27 (2:98)
12		DIBAH (1.5)	0, 0.5		37 (2:98)
13		DIBAH (4)	−20, 1.5		18 (<1:99)

[a] All the reactions were performed as described in the text. [b]  . [c] Isolated pure product. All products were characterized by analytical and spectral data. [d] GC analyses were carried out after the transformation to the corresponding acetal by treatment with a catalytic amount of pyridinium tosylate in anhydrous benzene. [e] The diastereoselectivity was determined by GC analyses of the product. [f] The ratio was determined after hydrogenation of the olefin.

98% yield.[5] The availability of enol ethers from acetals under mild conditions attracted our attention as a potential means of ketone resolution. This communication describes the realization of such a process and is illustrated in Scheme I.

The chiral acetal **3** was prepared in >95% yield from the reaction of racemic 2-methylcyclohexanone and (−)-(2*R*,4*R*)-2,4-pentanediol[6] in the presence of a catalytic amount of pyridinium tosylate. Treatment of the diastereomers **3** with 2 equiv of TIBA at −20 °C for 5 h furnished enol ether **4** (34%) along with recovered acetal (62%).[7] Simple chromatographic separation of the enol ether **4** followed by mild acid treatment in benzene regenerated the diastereomerically pure acetal (2*R*,4*R*,7*R*)-**3** (>99% diastereochemically pure by GC analysis). Mild hydrolysis of **4** (0.1 N HCl–acetone, 0 °C, 1.5 h) produced (*R*)-2-methylcyclohexanone $[\alpha]^{24}_{D}$ −15.9° (neat),[8] with an enantiomeric excess of >95%.[9] When the reaction was carried out to about 70% completion (0 °C, 3 h), the recovered acetal was separated chromatographically and shown to be >99% pure by GC analysis. From this acetal (*S*)-2-methylcyclohexanone was prepared in 78% yield: $[\alpha]^{24}_{D}$ +14.9° (neat).[8,10]

Scheme II



The stereochemical outcome of the reaction of diisobutylaluminum hydride (DIBAH) with diastereomers **3** is illustrated in Scheme II. Here, the recovered acetal **3** (42%) was diastereomerically pure (>99%) and the re-

(5) It should be noted that the effective elimination of the acetal was only observed with the acetal from 2,4-pentanediol. Thus, treatment of the ethylene acetal of cyclohexanone with excess TIBA at 25 °C for 24 h gave the reduced cleavage product $(CH_2)_5CHO(CH_2)_2OH$ in 38% yield.

(6) (−)-(2*R*,4*R*)-2,4-Pentanediol was purchased from Wako Pure Chemical Industries Ltd. and recrystallized from ether: Ito, K.; Harada, T.; Tai, A. *Bull. Chem. Soc. Jpn.* **1980**, *53*, 3367.

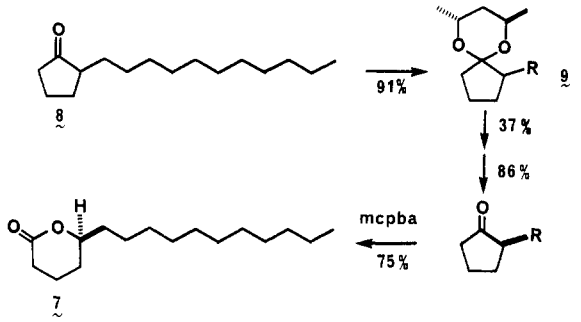
(7) GC analysis (25-m PEG-HT capillary column) of this product revealed a mixture of two diastereoisomers of the ratio of ca. 3:7.

(8) Lit. $[\alpha]^{20}_{D}$ −16.6° (neat): Enders, D. *Chemtech* **1981**, 504. Enders, D.; Eichenauer, H. *Chem. Ber.* **1979**, *112*, 2933.

(9) Optical purity was determined by conversion to *cis*-2-methylcyclohexanol (L-Selectride (Aldrich) at −78 °C) and GC analysis of its (+)-methoxy-α-(trifluoromethyl)phenylacetic acid (MTPA) ester.

(10) Optical purity was >95%ee by the method of ref 9.

Scheme III



duced ether **5** (49%) was obtained in 90% diastereomeric purity by GC analysis.[11,12] Furthermore, pure **5** was readily prepared by terminating the reaction at 30% completion (−20 °C, 3 h). Oxidation followed by basic treatment[4] of **5** gave (+)-(1*S*,2*R*)-2-methylcyclohexanol (**6**),[13] $[\alpha]^{24}_D$ +20.3° (*c* 3.21, ethanol),[14] in 74% yield with >99% de and 98% ee.[15]

The generality of the reaction is apparent from the results summarized in Table I.

The efficiency of our new method is highlighted by a rapid and convenient synthesis of (−)-(*S*)-5-hexadecanolide (**7**), pheromone of *Vespa orientalis*.[16] The sequence of the reactions utilized is outlined in Scheme III. Acetalization of the readily available ketone **8**[17] with (−)-(2*R*,4*R*)-2,4-pentanediol gave diastereomers **9**. Treatment of **9** with 1.5 equiv of DIBAH at 0 °C for 30 min gave, after chromatographic purification, optically pure acetal (2*R*,4*R*,7*S*)-**9** in 37% yield with 97% de. Mild hydrolysis in 0.1 N HCl–acetone furnished pure (*S*)-**8** in 86% yield: $[\alpha]^{24}_D$ +81.0° (*c* 1.04, ether). Baeyer–Villiger oxidation of (*S*)-**8** with *m*-chloroperbenzoic acid in chloroform at 25 °C for 24 h yielded the lactone **7**[18] in 75% yield: $[\alpha]^{24}_D$ −38.3° (*c* 1.17, THF).[16e]

As implied above, the process is remarkably general and should in many cases provide a practical, if not unique, route to optically pure ketones. Another noteworthy aspect of this approach to chiral material is that the enol ether itself may provide a point of departure for further transformations.

Registry No. **1**, 5422-00-4; **2**, 99299-19-1; **3** (isomer 1), 99299-20-4; **3** (isomer 2), 99341-26-1; **4**, 99299-21-5; **5** (isomer 1), 99299-22-6; **5** (isomer 2), 99341-27-2; **5** (isomer 3), 99341-28-3; **6**, 15963-35-6; **7**, 59812-97-4; **8**, 99299-27-1; (*S*)-**8**, 99341-36-3; **9** (isomer 1), 99299-28-2; **9** (isomer 2), 99341-35-2; $(CH_2)_5CHO(CH_2)_2OH$, 1817-88-5; (±)-2-methylcyclohexanone, 24965-84-2; (−)-(2*R*,4*R*)-2,4-pentanediol, 42075-32-1; 2-allylcyclohexanone acetal (isomer 1), 99299-23-7; 2-allylcyclohexanone acetal (isomer 2), 99341-29-4; 2-allylcyclohexanone enol ether, 99299-24-8; 2-cyclohexylcyclohexanone acetal (isomer 1), 99299-25-9; 2-cyclohexylcyclohexanone acetal (isomer 2), 99341-30-7; 3-methylcyclohexanone acetal (isomer 1), 96249-24-0; 3-methylcyclohexanone acetal (isomer 2), 99341-31-8; 3,3,5-trimethylcyclohexanone acetal (isomer 1), 99341-32-9; 3,3,5-trimethylcyclohexanone acetal (isomer 2), 99341-33-0; 2-methylcycloheptanone acetal (isomer 1), 99299-26-0; 2-methylcycloheptanone acetal (isomer 2), 99341-34-1; 2-propylcyclohexanone acetal (isomer 1), 99299-29-3; bicyclo[3.3.0]octan-2-one acetal (isomer 1), 99299-30-6; bicyclo[3.3.0]octan-2-one acetal (isomer 2), 99341-37-4; cyclohexanone ethylene acetal, 177-10-6; (*R*)-2-methylcyclohexanone, 22554-29-6; (*S*)-2-methylcyclohexanone, 22554-27-4; cyclohexanone, 108-94-1; 2-allylcyclohexanone, 94-66-6; 2-cyclohexylcyclohexanone, 90-42-6; 3-methylcyclohexanone, 591-24-2; 3,3,5-trimethylcyclohexanone, 873-94-9; 2-methylcycloheptanone, 932-56-9; *cis*-bicyclo[3.3.0]octan-2-one, 32405-37-1.

Supplementary Material Available: Experimental Section (7 pages). Ordering information is given on any current masthead page.

Atsunori Mori, Hisashi Yamamoto*
Department of Applied Chemistry
Nagoya University, Chikusa
Nagoya 464, Japan
Received August 6, 1985

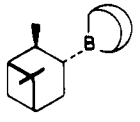
(11) 1*R*,2*R*:1*R*,2*S*:1*S*,2*R*:1*S*,2*S* = 0.7:3.0:89.6:6.7 by GC analysis.
(12) The recovered acetal was further reduced with excess DIBAH (5 equiv) at 25 °C for 6 h to give the cleavage product in 83% yield with low diastereoselectivity: 1*R*,2*R*:1*R*,2*S*:1*S*,2*R*:1*S*,2*S* = 0:64:0:36.
(13) The cis:trans ratio was >99:1 by GC analysis.
(14) Lit. $[\alpha]^{25}_D$ +15.7° (*c* 3.4, EtOH): Jones, J. R.; Takemura, T. *Can. J. Chem.* **1982**, *60*, 2950.
(15) Optical purity was determined by GC analysis of the (+)-MTPA ester.
(16) (a) Ikan, R.; Gottlieb, R.; Bergmann, E. D; Ishay, J. *J. Insect Physiol.* **1969**, *15*, 1709. For the synthesis of **7**: (b) Coke, J. L.; Richon, A. B. *J. Org. Chem.* **1976**, *41*, 3516. (c) Pirkle, W. H.; Adams, P. E. *Ibid.* **1979**, *44*, 2169. Solladié, G.; Moghadam, F. M. *Ibid.* **1982**, *47*, 91. (e) Servi, S. *Tetrahedron Lett.* **1983**, *24*, 2023. (f) Fujisawa, T.; Itoh, T. Nakai, M.; Sato, T. *Ibid.* **1985**, *26*, 771.
(17) Hájek, M.; Málek, J. *Collect. Czech. Chem. Commun.* **1976**, *41*, 746.
(18) Identical in all respects with the reported data.[16]

Diisopinocampheylchloroborane, a Remarkably Efficient Chiral Reducing Agent for Aromatic Prochiral Ketones

Summary: Diisopinocampheylchloroborane, readily prepared in high chemical and optical purities (99% ee) from (+)-α-pinene (92% ee) via hydroboration, followed by treatment with dry hydrogen chloride in ether, reduces ketones at convenient rates at −25 °C. The chiral induction is excellent for the reduction of aromatic prochiral ketones.

Sir: Optically active secondary alcohols are important starting materials for chiral syntheses.[1] Their synthesis by the reduction of prochiral ketones with chiral reducing agents has been actively pursued in recent years by organic chemists. Many interesting reagents have been developed, some of them achieving remarkable success.[2] For example, Noyori's Binal-H reduces several classes of prochiral ketones with high chiral induction.[3]

Trialkylboranes and borohydrides have also been applied as chiral reducing agents.[4] Of these, the Midland reagent, *B*-3-pinanyl-9-borabicyclo[3.3.1]nonane (**1**) (Aldrich, *R*-Alpine-Borane) prepared from (+)-α-pinene has



1

emerged as a very useful chiral reducing agent.[5] Midland and his co-workers initially reported that **1** reduces 1-deuterioaldehydes and α,β-acetylinic ketones in tetrahydrofuran (THF) at room temperature with excellent

(1) For a recent application, see: Rosen, T.; Heathcock, C. H. *J. Am. Chem. Soc.* **1985**, *107*, 3731.
(2) "Asymmetric Synthesis", Vol. 2; Morrison, J. D., Ed., Academic Press: New York, 1983; Chapters 2, 3, and 4.
(3) Noyori, R.; Tomino, I.; Tanimoto, Y.; Nishizawa, M. *J. Am. Chem. Soc.* **1984**, *106*, 6709, 6717.
(4) Reference 3, Chapter 2.
(5) (a) Midland, M. M.; Tramontano, A.; Zderic, S. A. *J. Organomet. Chem.* **1978**, *156*, 203. (b) The other isomer, *S*-Alpine-Borane, is obtained from (−)-α-pinene.

0022-3263/85/1950-5446$01.50/0