observations are consistent with the postulate that the reaction rate of acetate with the carbocation is relatively slow in comparison with that by which the initially formed ion isomerizes to the more stable one. Calculations and experimental data on the heats of hydrogenation[13] indicate that cyclic cis olefins with nine or fewer carbons are more stable than the corresponding trans isomer. For cyclodecene and larger cyclic olefins the trans compound is the more stable. Our results on the geometry of the allylic acetate formed in these reactions as a function of ring size parallel the calculated and experimentally observed stabilities of the most stable cyclic olefins.

Conclusion

This study has shown that is is possible to control the stereochemistry of the eight- and nine-membered olefins formed from silver ion promoted solvolyses of the same intermediates by modifying the reaction conditions. Our results suggest that these solvolyses yield the most stable cycloalkenes. Three-bond proton–carbon coupling constants, obtained using the selective proton-flip experiment, have been shown to permit a facile assignment of the geometry of trisubstituted olefins. Since three-bond proton–carbon coupling constants have been shown to be useful for stereochemical assignments increased use of this NMR technique may be anticipated.

Experimental Section

EI–mass spectra were obtained by the NIH microanalytical laboratory. ^{1}H NMR spectra were collected on a Varian H-220 spectrometer, and ^{13}C NMR spectra were measured with a Nicolet 270 spectrometer (67.8 MHz). $CDCl_3$ was used for measuring ^{1}H NMR spectra and acetone-d_6 for ^{13}C NMR spectra.

Dibromocyclopropane derivatives were prepared by the procedure of Skottebol and Solomon.[4] General procedure for silver ion catalyzed solvolysis: An acetonitrile solution (5 ml) of the dibromo compound (5 mmol) was heated in the presence of 1.1 equiv of AgOAc and 1 mL of AcOH on a steam bath for 2 h. The solution was filtered and the precipitate washed with ether. The combined filtrates were washed with aqueous $NaHCO_3$, dried, and concentrated. The crude acetates were purified by column chromatography on silica gel.

(*Z*)-2-Bromo-2-cyclodecen-1-yl Acetate (4a). Cyclononene was prepared from cyclononenone (5 g) by reduction with sodium borohydride in methanol to yield cyclononanol, which was dehydrated at 170 °C, by heating with 85% H_3PO_4 for 1 h. The reaction mixture was cooled, diluted with water, and extracted into hexane. The hexane solution was passed through silica gel to remove polar impurities. The crude olefin (3.17 g) was used to prepare dibromobicyclo[7.1.0]decane (2.48 g, bp 129–134 °C/2.6 torr) by treatment with potassium *tert*-butoxide and bromoform as described by Skottebol and Solomon.[4] Solvolysis of the dibromobicycloalkane with AgOAc, MeCN, and AcOH as described above yielded, after chromatography on silica gel, 731 mg of **4a**: colorless oil; EI–MS, found 195.1384 ($C_{12}H_{19}O_2$, M^+ – Br); ^{1}H NMR 1.06–1.84 (m, 12 H), 2.08 (s, 3 H), 2.06–2.23 (m, 1 H), 2.25–2.45 (m, 1 H), 5.16 (dd, J = 5.2, 9.2 Hz, 1 H), 6.26 (dd, J = 6.4, 8.4 Hz, 1 H).

(*Z*)-2-Bromo-2-cycloundecen-1-yl Acetate (5a). Cyclodecene was prepared by heating cyclodecanol (obtained from sodium borohydride reduction of the ketone) with 85% H_3PO_4 at 170 °C for 1 h. The crude olefin was isolated and reacted with potassium *tert*-butoxide and bromoform as described above. Solvolysis of the crude dibromobicyclo[8.1.0]undecane as described above yielded after chromatography a sample of pure **5a**: colorless oil; EI–MS found 209.1525 ($C_{13}H_{21}O_2$, M^+ – Br); ^{1}H NMR 1.06–1.88 (m, 14 H), 2.09 (s, 3 H), 2.23 (m, 1 H), 2.48 (m, 1 H), 5.17 (dd, J = 8.5, 5.0 Hz, 1 H), 6.19 (dd, J = 9.0, 5.8).

(*Z*)-2-Bromo-2-cyclotridecen-1-yl Acetate (6a). Commercial *trans*-cyclododecene was used in the reaction sequence described above to prepare (*E*)-2-bromo-2-cyclotridecen-1-yl acetate (**6a**): colorless oil; EI–MS found 237.1857 ($C_{15}H_{25}O_2$, M^+ – Br); ^{1}H NMR 1.12–1.53 (m, 15 H), 1.57–1.78 (m, 2 H), 1.81–1.99 (m, 1 H), 2.06 (s, 3 H), 2.09–2.25 (m, 1 H), 2.28–2.47 (m, 1 H), 5.25 (dd, J = 4.0, 10.2 Hz, 1 H), 6.10 (dd, J = 9.4, 5.4 Hz, 1 H).

Acknowledgment. We thank Dr. Robert J. Highet for valuable discussions.

Registry No. 1, 14310-05-5; 2, 100206-51-7; 3, 100296-00-2; 4, 100206-52-8; 5, 100206-53-9; 6, 100206-54-0; AgOAc, 563-63-3; 7,7-dibromobicyclo[4.1.0]heptane, 2415-79-4; 8,8-dibromobicyclo[5.1.0]octane, 7124-41-6; 9,9-dibromobicyclo[6.1.0]nonane, 1196-95-8; 10,10-dibromobicyclo[7.1.0]decane, 36262-23-4; 11,11-dibromobicyclo[8.1.0]undecane, 64480-09-7; 13,13-dibromobicyclo[10.1.0]tridecane, 17301-57-4; cyclononenone, 100206-56-2; cyclononanol, 24469-56-5; cyclononene, 3618-11-9; cyclodecenone, 100206-55-1; cyclodecanol, 1724-39-6; cyclodecene, 3618-12-0; *trans*-cyclododecene, 1486-75-5.

(12) Highet, R. J. *J. Org. Magn. Reson.* **1984**, *22*, 136.
(13) (a) Turner, R. B.; Meador, W. R. *J. Am. Chem. Soc.* **1957**, *79*, 4133. (b) Ermer, O.; Lifson, S. *Ibid.* **1973**, *95*, 4121. (c) Allinger, N. L.; Sprague, J. T. *Ibid.* **1972**, *94*, 5734.

Reinterpretation of Two Degradations of (–)-Albene

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The natural product (–)-albene, a tricyclic $C_{12}H_{18}$ olefin first isolated in 1962 from *Petasites albus*,[1] was recognized in 1972 to be one of four stereoisomers of 2,6-dimethyltricyclo[5.2.1.0^{2,6}]dec-3-ene.[2] An attempt to differentiate among these four possibilities through two degradative reaction sequences led to the conclusion that (–)-albene should be represented by structure I.[2]

Direct achiral comparisons by proton NMR and infrared spectroscopy demonstrated that *endo*-camphane (XII) derived from (–)-albene through the reactions outlined in Scheme I was structurally identical with authentic *endo*-camphane prepared from (+)-camphene.[2]

The chiral ketone albanone, formulated as V in Scheme I, was converted in three steps to a ketonitrile (Scheme II). The product was assigned structure IX, for it exhibited an ORD curve with negative Cotton effect at 286 nm, while authentic (1*S*)-(+)-camphenilone derived from (+)-camphene showed a positive and somewhat more intense Cotton effect at 280 nm,[2,3] indicative of a minor image relationship between the norcamphor units in the two compounds. Thus the 1*R* absolute stereochemistry was inferred for IX, and (–)-albene was assigned structure I, with absolute stereochemistry implied.[2]

An initial reservation about the photochemical decarbonylation of Scheme I was allayed through a stereorational synthesis of albanone;[4] it and the two degradations were taken as reliable grounds for assigning both relative and absolute stereochemistry for (–)-albene[5] until 1977 when Kreiser and his collaborators[6–10] demonstrated that albene must have endo methyl groups, a conclusion abundantly supported by others through three stereochemically unambiguous total syntheses of *dl*-albene.[11–13] The degradations of Schemes I and II must then be reconsidered and reformulated for a proper understanding.

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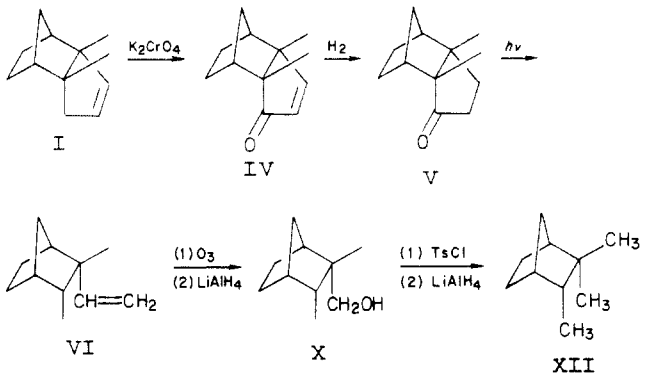
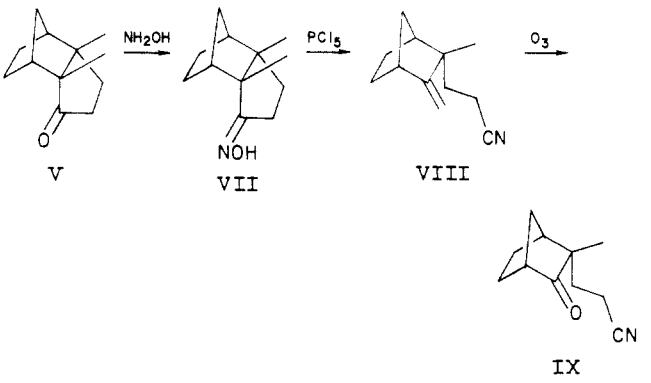
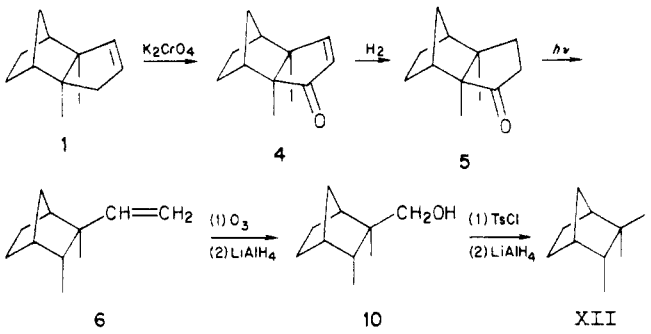
Scheme I. (-)-Albene to *endo*-Camphane[2]



Scheme II. Albanone to 1*R* Keto Nitrile IX[2]

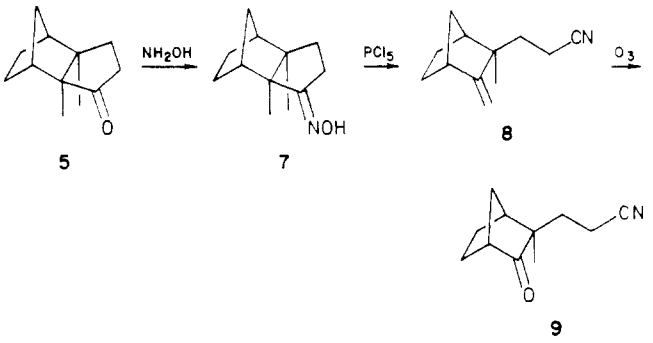


Scheme III. (-)-Albene to *endo*-Camphane



In particular, assignment of absolute configuration to (-)-albene, it was explicitly recognized,[6] would require a new interpretation of the experimental data in the 1972 report. Yet, curiously enough, this requirement has not been satisfied since it became an obvious imperative in 1977, and the assignment of absolute stereochemistry to (-)-albene just after the structural correction was based on evidence derived from a total synthesis,[10] one following the earlier stereorational synthesis of albanone.[4] This assignment has subsequently been reversed,[14,15] and the misinterpreted synthetic work has been explicated and subjected to detailed mechanistic scrutiny.[16]

Scheme IV. Albanone to 1*R* Keto Nitrile 9



Schemes III and IV present our reinterpretation of the two degradations. Only one chemical transformation, the photochemical decarbonylation, do we view as proceeding with different reaction stereochemistry, though every structure of Schemes I and II, save for the *endo*-camphane product which was compared with authentic material, has had to be revised.

Both degradations,[2] one may now observe clearly, obscured exo,endo relationships. In the reactions leading from (-)-albene to *endo*-camphane, the exo,endo distinction was lost as the vinyl group was converted to a methyl substituent; stereochemistry at C(3) of camphane was correctly assigned but wrongly interpreted as resulting from an inversion during a photodecarbonylation.[17] In the second degradation, exo,endo stereochemistry at C(2) of the product was lost and at C(3) the methyl vs. β-cyanoethyl stereochemical dispositions were not detected by the ORD method used to assess the absolute stereochemistry of the norcamphor derivative obtained.

Experimental conformation of the reassignment of stereochemistry for the ketonitrile degradation product from IX to **9** has been obtained through a direct comparison of authentic 3-*exo*-cyanoethyl-3-*endo*-methylbicyclo[2.2.1]heptan-2-one (**9**), prepared through reaction of the enamine derived from 3-methylbicyclo[2.2.1]heptan-2-one and morpholine with acrylonitrile. This keto nitrile **9** and a sample of "keto nitrile IX" prepared in Prague some 15 years ago had identical chromatographic, mass spectrometric, and spectroscopic characteristics.

Although exo,endo structural aspects were misconstrued when the degradations of Schemes I and II were originally interpreted,[2] the reaction sequence leading from albanone to a ketonitrile did furnish valuable information about absolute stereochemistry: the 3,3-disubstituted norcamphor molecule derived from (-)-albene must be 1*R*, and

(1) Hochmannová, J.; Novotný, L.; Herout, V. *Collect. Czech. Chem. Commun.* **1962**, *27*, 2711–2714. See also: Novotný, L.; Herout, V. *Ibid.* **1965**, *30*, 3579–3581.
(2) Vokáč, K.; Samek, Z.; Herout, V.; Šorm, F. *Tetrahedron Lett.* **1972**, 1665–1668.
(3) Coulombeau, C.; Rassat, A. *Bull. Soc. Chim. Fr.* **1966**, 3752–3762.
(4) Lansbury, P. T.; Borden, R. M. *Tetrahedron Lett.* **1973**, 5017–5020. Lansbury and Boden questioned the stereochemistry of this photodecarbonylation and speculated that the camphane degradation product might be the exo isomer. Both endo and exo forms of camphane from reduction of (+)-camphene are levorotatory: Rudakov, G. A.; Vereshchagina, A. A.; Nesterov, G. V. *Gidroliz. Lesokhim. Prom-st.* **1982**, *3*, 9–10.
(5) Klyne, W.; Buckingham, J. "Atlas of Stereochemistry"; 2nd ed.; Oxford University Press: New York, 1978; Vol. 1, p 85.
(6) Kreiser, W.; Janitschke, L.; Sheldrick, W. S. *J. Chem. Soc., Chem. Commun.* **1977**, 269–270.
(7) Kreiser, W.; Janitschke, L.; Ernst, L. *Tetrahedron* **1978**, *34*, 131–134.
(8) Kreiser, W.; Janitschke, L. *Tetrahedron Lett.* **1978**, 601–604.
(9) Kreiser, W.; Janitschke, L.; Voss, W.; Ernst, L.; Sheldrick, W. S. *Chem. Ber.* **1979**, *112*, 397–407.
(10) Kreiser, W.; Janitschke, L. *Chem. Ber.* **1979**, *112*, 408–422.
(11) Baldwin, J. E.; Barden, T. C. *J. Org. Chem.* **1981**, *46*, 2442–2445.
(12) Trost, B. M.; Renaut, P. *J. Am. Chem. Soc.* **1982**, *104*, 6668–6672.
(13) Manzardo, G. G. G.; Karpf, M.; Dreiding, A. S. *Helv. Chim. Acta* **1983**, *66*, 627–632.
(14) Baldwin, J. E.; Barden, T. C. *J. Org. Chem.* **1983**, *48*, 625–626.
(15) Mechanistic concerns led some to question the assigned absolute stereochemistry: Money, T. In "Terpenoids and Steroids"; The Chemical Society: London, 1979; Vol. 9, p 94. Roberts, J. S. "Terpenoids and Steroids"; The Chemical Society: London, 1981; Vol 10, p 20.
(16) Baldwin, J. E.; Barden, T. C. *J. Am. Chem. Soc.* **1983**, *105*, 6656–6662.
(17) Such photodecarbonylations may be well-known [Weiss, D. S. In "Organic Photochemistry"; Padwa, A., Ed.; Dekker: New York, 1981; Vol. 5, Chapter 4], but they have not been well characterized stereochemically as functions of ring size, substituents, and geometric constraints.

hence (−)-albene must be 1*S*,7*R*! Only two of the four tricyclo[5.2.1.0^{2,6}]dec-3-ene isomers under consideration[2] could have given the results reported, one with exo methyl groups and one with endo methyls. The norcamphor unit in the keto nitrile degradation product which showed the negative Cotton effect limited the absolute stereochemical assignment for (−)-albene to I or 1; as soon as it became known that the methyls in (−)-albene are endo,[5] the absolute stereochemistry of (−)-albene might have been seen to be as shown in 1. If (−)-albene were the mirror image of 1, as proposed by Kreiser and co-workers,[10,18] the keto nitrile from the degradation of albanone would have been *ent*-**9**, which would have shown a positive Cotton effect, and the degradation findings of the Prague group would have been inexplicable. The absolute stereochemistry of (−)-albene one can deduce from the present reinterpretation of the 1972 degradative work[2] agrees with our chemical correlation[14] between a chiral synthetic precursor to both (+)-albene and (−)-β-santalene: (−)-albene is the 1*S*,2*S*,6*S*,7*R* isomer of 2-*endo*,6-*endo*-dimethyltricyclo-[5.2.1.0^{2,6}]dec-3-ene, structure 1.

Experimental Section

Analytical gas chromatographic analyses were done using a 0.2-mm i.d. 12.5-m cross-linked dimethyl silicone fused silica capillary column, a Hewlett-Packard (HP) 5790 instrument, and a HP 3390A reporting integrator; preparative separations were accomplished with a 0.63 cm × 1 m silicone QF-1 on Chromosorb W column and a Varian Aerograph A90-P3 instrument. The GC/MS data were secured with HP 5890, 5970B, and 9836 instruments and computer. Both ^{1}H and ^{13}C NMR spectra were obtained on a General Electric GN 500 MHz for ^{1}H (125.76 MHz for ^{13}C) spectrometer.

3-*exo*-(Cyanoethyl)-3-*endo*-methylbicyclo[2.2.1]heptan-2-one. To a stirred solution of 3-*endo*-methylbicyclo[2.2.1]heptan-2-one[16] (1.69 g, 14 mmol), morpholine (4.73 g, 54 mmol; dried over 4A molecular sieves) and *o*-xylene (50 mL; dried over sodium) at 0 °C was added dropwise over a 20-min period 1.29 g (6.8 mmol) of $TiCl_4$.[19,20] The stirred reaction mixture was allowed to warm to room temperature and, after 36 h, was filtered. Distillation at atmospheric pressure left a residue, which, upon Kugelrohr distillation at 16 torr and a bath temperature of 90–95 °C, gave 1.42 g of a clear yellow oil. This impure enamine, 20 mL of absolute ethanol, and 20 mL of freshly distilled acrylonitrile were combined and heated to reflux for 24 h.[20] The reaction mixture was diluted with 10 mL of water, heated to reflux 1 h, cooled, and extracted with ether. The ethereal extract was washed with 1 N hydrochloric acid, dried over magnesium sulfate, and filtered. Concentration and Kugelrohr distillation at 16 torr and a bath temperature of 140–150 °C gave 3-*exo*-(cyanoethyl)-3-*endo*-methylbicyclo[2.2.1]heptan-2-one (200 mg; 94% purity according to capillary GC analysis).

Preparative gas chromatography gave a colorless sample of ketone **9** estimated to be 99.8% pure; mass spectrum (70 eV), *m/e* (relative intensity) 177 (M$^+$, 13), 136 (8), 134 (9), 108 (51), 93 (20), 81 (29), 67 (100), 55 (22), 53 (20), 41 (56), 39 (44); ^{13}C NMR ($CDCl_3$) δ 220.17, 119.83, 50.03, 48.86, 43.99, 34.85, 31.09, 24.71, 23.11, 17.94, 12.53; ^{1}H NMR CH_3 singlet at δ 1.024; IR (CCl_4) 2250, 1740 cm^{-1}.

A sample of "keto nitrile IX"[2] sent from Prague, bp 120 °C (12 torr), had an identical vapor-phase chromatographic retention time (11.56 min, column helium flow 1 mL/m, temperature increase 7 °C/m from 80 to 250 °C): mass spectrum, *m/e* 177 (M$^+$, 4), 136 (6), 134 (7), 108 (53), 93 (22), 81 (31), 67 (100), 55 (23), 53 (21), 41 (57), 39 (45); ^{13}C NMR δ 220.19, 119.80, 50.04, 48.85, 44.03, 34.85, 31.09, 24.69, 23.10, 17.95, 12.53; ^{1}H NMR CH_3 singlet at 1.024; IR[2] 2249, 1741 cm^{-1}.

Acknowledgment. We thank Professor V. Herout of the Institute of Organic Chemistry and Biochemistry, Czechoslovak Academy of Science, Prague, for his supportive interest in the present work and for providing us with a sample of "keto nitrile IX".[2] We are indebted to the National Science Foundation for partial support of our work on (−)-albene.

Registry No. 1, 38451-64-8; **9**, 100759-23-7; (1*R*,4*R*)-3-*endo*-methylbicyclo[2.2.1]heptan-2-one, 100759-24-8; (1*R*,4*S*)-2-(*N*-morpholino)-3-methylbicyclo[2.2.1]hept-2-ene, 100606-56-2.

(18) Synthesis is not necessarily a final proof of structure or of absolute stereochemistry, indeed, neither is X-ray crystallography. For recent perspectives on these issues, see: Kelly, T. R.; Saha, J. K.; Whittle, R. R. *J. Org. Chem.* **1985**, *50*, 3679–3685. Corey, E. J.; Desai, M. C.; Engler, T. A. *J. Am. Chem. Soc.* **1985**, *107*, 4339–4341.

(19) White, W. A.; Weingarten, H. *J. Org. Chem.* **1967**, *32*, 213–214.

(20) Cook, A. G.; Meyer, W. C.; Ungrodt, K. E.; Mueller, R. H. *J. Org. Chem.* **1966**, *31*, 14–20.

(21) Compare: Stork, G.; Brizzolara, A.; Landesman, H.; Szmuszkovicz, J.; Terrell, R. *J. Am. Chem. Soc.* **1963**, *85*, 207–222.

Lanthanides in Organic Synthesis. 2. Reduction of α-Heterosubstituted Ketones

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Reduction of α-heterosubstituted ketones has long been recognized as a useful synthetic transformation. Several distinct classes of heterosubstituted ketones have been used in such transformations in organic synthesis, and many different reducing agents have been utilized to accomplish the desired reductions. For example, a number of reagents have been developed for reduction of α-halo ketones to the corresponding unsubstituted ketones.[1] Keto sulfides, sulfoxides, and sulfones have found considerable utility in organic synthesis, particularly in regioselective ketone alkylation reactions. Generally, these processes necessitate removal of the sulfur-containing functional groups subsequent to alkylation. Several methods have therefore been devised for this purpose.[2] Reduction of α-oxygenated ketones has also seen substantial use as a routine synthetic transformation.[3]

Current methods that achieve these reductions often require rather harsh reaction conditions. Among the more widely utilized methods are zinc metal[1h,i,3a,c,e] and chromous ion induced[1b,3f] reductions. Both of these methods involve

(1) (a) Noyori, R.; Hayakawa, Y. *Org. React. (N. Y.)* **1983**, *29*, 163. (b) Hanson, J. R. *Synthesis* **1974**, 1. (c) Mc Murry, J. E. *Acc. Chem. Res.* **1974**, *7*, 281. (d) Oriyama, T.; Mukaiyama, T. *Chem. Lett.* **1984**, 2069. (e) Ho, T.-L.; Olah, G. A. *Synthesis* **1976**, 807. (f) Ho, T.-L. *Synth. Commun.* **1979**, *9*, 241. (g) Kuivila, H. G.; Menapace, L. W. *J. Org. Chem.* **1963**, *28*, 2165. (h) Corey, E. J.; Gregoriou, G. A. *J. Am. Chem. Soc.* **1959**, *81*, 3127. (i) Zimmerman, H. E.; Mais, A. *J. Am. Chem. Soc.* **1959**, *81*, 3644.

(2) Sulfide reduction: (a) Oki, M.; Funakoshi, W.; Nakamura, A. *Bull. Chem. Soc. Jpn.* **1971**, *44*, 828. (b) Kamata, S.; Uyeo, S.; Haga, N.; Nagata, W. *Synth. Commun.* **1973**, *3*, 265. (c) Coates, R. M.; Pigott, H. D.; Ollinger, J. *Tetrahedron Lett.* **1974**, 3955. (d) Kurozumi, S.; Toru, T. *Synth. Commun.* **1977**, *7*, 427. (e) Vedejs, E.; Arnost, M. J.; Eustache, J. M.; Krafft, G. A. *J. Org. Chem.* **1982**, *47*, 4384. (f) Posner, G. H.; Asirvatham, E. *J. Org. Chem.* **1985**, *50*, 2589. (g) Uenishi, J.; Tomozane, H.; Yamato, M. *J. Chem. Soc., Chem. Commun.* **1985**, 717. Sulfoxide reduction: (h) Posner, G. H. in "Asymmetric Synthesis"; Morrison, J. D., Ed.; Academic Press: New York, 1983; Vol. 2, Chapter 8. Sulfone reduction: (i) Trost, B. M.; Arndt, H. C.; Strege, P. E.; Verhoeven, T. R. *Tetrahedron Lett.* **1976**, 3477. (j) Cavicchioli, S.; Savoia, D.; Trombini, C.; Umani-Ronchi, A. *J. Org. Chem.* **1984**, *49*, 1246.

(3) (a) Rosenfeld, R. S.; Gallagher, T. F. *J. Am. Chem. Soc.* **1955**, *77*, 4367. (b) Chapman, J. H.; Elks, J.; Phillips, G. H.; Wyman, L. J. *J. Chem. Soc.* **1956**, 4344. (c) Rosenfeld, R. S. *J. Am. Chem. Soc.* **1957**, *79*, 5540. (d) Nelson, S. J.; Detre, G.; Tanabe, M. *Tetrahedron Lett.* **1973**, 447. (e) Paquette, L. A.; Ward, J. S.; Boggs, R. A.; Farnham, W. B. *J. Am. Chem. Soc.* **1975**, *97*, 1101. (f) Trost, B. M.; Godleski, S. A.; Ippen, J. *J. Org. Chem.* **1978**, *43*, 4559.

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