2.39 (s, 3 H), 2.57–3.25 (m, 9 H), 7.27 (d, J = 7.5 Hz, 2 H), 7.93 (d, J = 7.5 Hz, 2 H); ^{13}C NMR ($CDCl_3$) δ 21.41 (q), 34.52 (t), 38.32 (d), 40.81 (d), 44.03 (d), 46.20 (d), 46.54 (d), 47.01 (d), 47.17 (d), 49.42 (d), 50.19 (d), 94.74 (s), 126.67 (d), 127.44 (d), 129.40 (d), 130.12 (d), 134.93 (s), 144.55 (s), 205.93 (s). Compound **10** was used as obtained for the next synthetic step, without further purification.

Hexacyclo[5.4.0.0^{2,6}.0^{3,10}.0^{5,9}.0^{8,11}]undecane-8-carboxylic Acid (Homopentaprismane-8-carboxylic Acid, 11). A mixture of **10** (60 mg, 0.18 mmol) and 20% aqueous potassium hydroxide solution (20 mL, excess) was refluxed for 7 h. The resulting mixture was allowed to cool to room temperature and then was washed with methylene chloride (2 × 10 mL) to remove nonacidic impurities. The aqueous layer was cooled to 0 °C, and the pH of the solution was adjusted to 2.0 by dropwise addition of 50% (w/w) aqueous sulfuric acid solution (ca. 7 mL). The resulting turbid mixture was extracted with methylene chloride (3 × 20 mL). The combined organic extracts were washed successively with water (3 × 20 mL) and with brine (3 × 20 mL). The organic layer was dried (anhydrous sodium sulfate) and filtered, and the filtrate was concentrated in vacuo, thereby affording **11** (31 mg, 94%). Pure **11** was obtained by recrystallization from chloroform–hexane as a colorless microcrystalline solid: mp 133–134 °C; IR (KBr) 3500–2300 (br, s), 1640 (s), 1400 (m), 1300 (m), 1252 (m), 1250 (m), 1230 cm^{-1} (m); ^{1}H NMR ($CDCl_3$) δ 1.71 (s, 2 H), 2.73–3.34 (m, 9 H), 10.38 (br s, 1 H); ^{13}C NMR ($CDCl_3$) δ 39.74 (t), 40.39 (d), 44.94 (d), 46.37 (d), 46.83 (d), 48.45 (d), 49.49 (d), 50.66 (d), 50.79 (d), 51.44 (d), 54.37 (s), 180.98 (s).

Anal. Calcd for $C_{12}H_{12}O_2$: C, 76.57; H, 6.43. Found: C, 76.36; H, 6.33.

Acknowledgment. We thank the Air Force Office of Scientific Research (Grant AFOSR-88-0132), the Robert A. Welch Foundation (Grant B-963), and the University of North Texas Faculty Research Committee for financial support of this study.

Registry No. **2**, 58228-93-6; (*E*)-**3**, 120789-84-6; (*Z*)-**3**, 120828-04-8; **4**, 120789-85-7; **5**, 120789-86-8; **6** (isomer 1), 120789-87-9; **6** (isomer 2), 120851-15-2; **6** methyl ester (isomer 1), 120789-91-5; **6** methyl ester (isomer 2), 120851-16-3; **7** (isomer 1), 120789-92-6; **7** (isomer 2), 120851-17-4; **8** (isomer 1), 120789-93-7; **8** (isomer 2), 120851-18-5; **9**, 120789-88-0; **10**, 120789-89-1; **11**, 120789-90-4; $(EtO)_2P(O)CH_2CO_2Et$, 867-13-0.

Reactions of a Semistabilized Arsonium Ylide with Aldehydes: Counterion Effects on Product Selectivity

Jeffrey D. Hsi and Masato Koreeda*

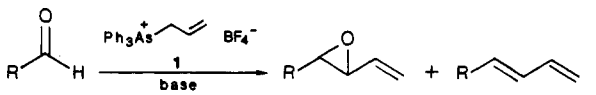
Department of Chemistry, The University of Michigan, Ann Arbor, Michigan 48109

Received December 30, 1988

The reaction of arsonium ylides with carbonyl compounds has been described in the literature over the past 30 years following the initial report by Henry and Wittig.[1] The significant contribution in this field was made by Still in 1981, who demonstrated the synthetic utility of unstabilized arsonium ylides to give *trans*-epoxides exclusively.[2] Various other groups have shown that stabilized arsonium ylides give rise to olefin products only.[3-5] The reaction of semistabilized arsonium ylides with carbonyl compounds results in a mixture of olefin and epoxide products.[6] However, various methods to control the reaction pathway of semistabilized (e.g., benzylic and allylic) arsonium ylides have since appeared in the literature.[7-9]

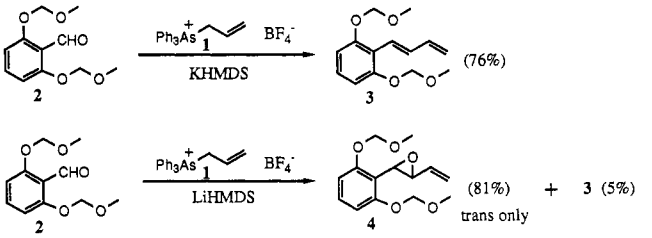
In connection with our synthetic efforts in the aflatoxin area, the reactivity of the ylide generated from allyltriphenylarsonium tetrafluoroborate (**1**) was investigated. We report herein that the selectivity for the formation of either epoxides or olefins is dependent upon the choice of base used for generation of the arsonium ylide. The reaction of arsonium allylides with carbonyl compounds to give epoxides has been reported,[8a] and the counterion dependence of arsonium benzylides on product formation has been discussed;[9] however, this appears to be the first example of counterion-dependent product formation with regard to arsonium allylides.

Table I. Reaction of Allyltriphenylarsonium Ylides with Aldehydes[g]



	R	base	epoxide (%)[a] (trans:cis)[b]	*trans*-diene (%)
1		LiHMDS	**5**[c] (70) (2:1)	**8** (0)
2		LiHMDS	**6**[d] (55) (2:1)	**9** (0)
3	$CH_3(CH_2)_6$	LiHMDS	**7**[c] (71) (2:1)	**10** (0)
4		KHMDS	**5** (0)	**8**[c] (59)
5		KHMDS	**6** (0)	**9**[e] (61)
6	$CH_3(CH_2)_6$	KHMDS	**7** (3) (2:1)	**10**[f] (54)

[a] Isolated yields. [b] As determined by ^{1}H NMR. [c] Reference 16. [d] Reference 17. [e] Reference 18. [f] Reference 19. [g] All compounds gave spectral characteristics consistent with those previously reported.

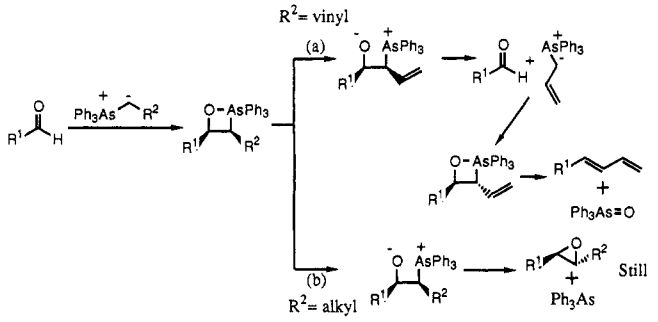


Deprotonation of allyltriphenylarsonium tetrafluoroborate (**1**)[10] with 1.1 equiv of potassium hexamethyldisilazide (KHMDS) in THF at −65 °C and treatment of the resulting ylide with aldehyde **2** gave diene **3** exclusively

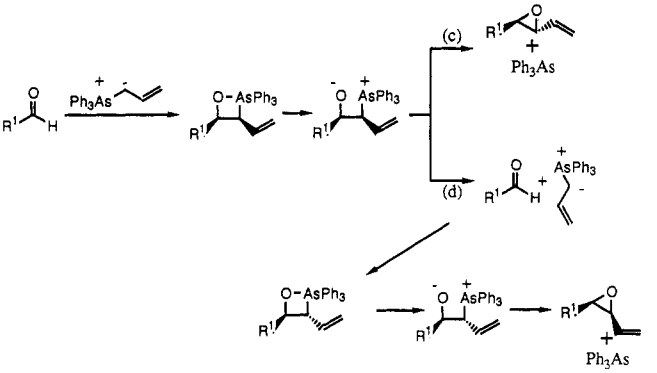
(1) Henry, M. C., Wittig, G. *J. Am. Chem. Soc.* **1960**, *82*, 563. See also references cited in footnote 2 in ref 2.
(2) Still, W. C.; Novack, V. J. *J. Am. Chem. Soc.* **1981**, *103*, 1283.
(3) Trippett, S.; Walker, M. A. *J. Chem. Soc. C.* **1971**, 1114.
(4) (a) Tewari, R. S.; Kendurkar, P. S. *J. Organomet. Chem.* **1973**, *60*, 247. (b) Tewari, R. S.; Kendurkar, P. S. *J. Organomet. Chem.* **1976**, *108*, 175.
(5) Johnson, A. W. *J. Org. Chem.* **1960**, *25*, 183.
(6) Johnson, A. W.; Martin, J. O. *Chem. Ind. (London)* **1965**, 1726.
(7) Tewari, R. S.; Chaturvedi, S. C. *Tetrahedron Lett.* **1977**, 3843.
(8) (a) Mioskowski, C.; Solladie, G.; Ousset, J. B. *Tetrahedron Lett.* **1983**, 4419. (b) Mioskowski, C.; Solladie, G.; Ousset, J. B. *Synth. Commun.* **1983**, *13*, 1193.
(9) Broos, R.; Anteunis, M. J. O. *Bull. Soc. Chim. Belg.* **1988**, *97*, 271.
(10) A modification of the procedure reported by Oesch was used: Oesch, F.; Sparrow, A. J.; Platt, K. L. *J. Labelled Compd. Radiopharm.* **1983**, *20*, 1297. After the reaction mixture was heated for 3 days, the solvent was removed in vacuo and the residue taken up in CH_2Cl_2. This mixture was shaken with a solution (ca. 10 M) of $NaBF_4$ in water. The aqueous layer was washed twice with CH_2Cl_2, and the combined organics were dried through Na_2SO_4. Concentration in vacuo followed by trituration three times with dry THF resulted in allyltriphenylarsonium tetrafluoroborate as a white solid in 90% yield.

0022-3263/89/1954-3229$01.50/0

Scheme I. Reaction of Aldehydes and Arsonium Ylides Generated with KHMDS



Scheme II. Reaction of Aldehydes and Arsonium Ylides Generated with LiHMDS



in 76% yield. In contrast, when arsonium salt 1 was deprotonated with 1.1 equiv of lithium hexamethyldisilazide (LiHMDS) in THF at −65 °C and the resulting ylide treated with aldehyde 2, epoxide 4 was obtained in 81% yield along with a small amount of diene 3 (5%).

In order to investigate the generality of this unexpected observation, we examined the reaction of arsonium salt 1 with other aldehydes (see Table I). Deprotonation of 1 with LiHMDS followed by treatment with benzaldehyde, cyclohexanecarboxaldehyde, or octanal gave epoxides 5–7, respectively, in 55–71% yield as 2:1 trans/cis mixtures. Deprotonation of 1 with KHMDS followed by treatment with the same aldehydes gave *trans*-dienes 8–10 in 54–61% yield.

The observation that the reaction gives epoxides or olefins when either LiHMDS or KHMDS, respectively, is utilized appears to be general. In most instances, no product crossover was encountered (with the exceptions being the reactions of aldehyde 2 in the lithium case and octanal with the potassium-generated arsonium ylide, which gave 5% and 3% crossover product, respectively). Presumably, the most notable observation of our results, which may have significant bearing on the mechanistic considerations, lies in the fact that the epoxides were obtained in a 2:1 trans/cis-stereochemical mixture, whereas the dienes were obtained cleanly as their trans isomers.

For the mechanistic considerations of the results described above, a brief overview of the mechanistic work in the area of phosphorus and sulfur ylides may be warranted. Vedejs reported the first evidence for the presence of oxaphosphetane intermediates.[11] Maryanoff and coworkers extended this work by showing the existence of *cis*- and *trans*-oxaphosphetanes and their role in determining the stereochemical outcome of the Wittig reaction.[12] This study also showed that the *cis*-oxaphosphetanes have enhanced reversibility compared to *trans*-oxaphosphetanes. Although. direct evidence for the presence of a betaine intermediate in a Wittig reaction is lacking, betaine–lithium halide complexes have been generally assumed to be involved.[13] In 1987, Volatron and Eisenstein described theoretical calculations on phosphorus and sulfur ylides.[14] Their results indicate that betaine formation in a Wittig reaction is highly disfavored; however, it should be noted that their results are to be applied only to salt-free conditions, and incorporation of lithium into the medium could strongly stabilize a betaine intermediate.

Taking into account the work achieved in the phosphorus and sulfur ylide area as well as the results of Still,[2] it appears that our results may be consistent with the mechanism summarized in Schemes I and II. In the case of potassium-generated arsonium ylides (Scheme I), the *cis*-oxaarsetane, produced by the initial attack of the arsonium ylide on the carbonyl carbon of the aldehyde, is likely to be converted to the corresponding betaine. At this juncture the fate of the betaine is dependent on the substitution on the arsonium ylide. If R^2 is alkyl, i.e., an unstabilized ylide as in Still's case, the resultant betaine collapses to *trans*-epoxide products (pathway b). In contrast, if R^2 is allyl, i.e., a semistabilized ylide, an alternate pathway becomes compatible. Since the arsonium ylide is semistabilized, the betaine can revert back to allylide and aldehyde and recombine to form the more stable *trans*-oxaarsetane, which ultimately decomposes to *trans*-dienes and triphenylarsine oxide (pathway a).

In the case of the lithium-generated arsonium ylides (Scheme II), addition of the ylide to the aldehyde initially forms the *cis*-oxaarsetane, which opens to the corresponding betaine through catalysis by the lithium salt present under these conditions.[12] This betaine can then follow two different pathways. It can immediately collapse to *trans*-epoxide products (pathway c) or can revert back to aldehyde and arsonium allylide (pathway d) and recombine to the *trans*-oxaarsetane. The *trans*-oxaarsetane in the presence of lithium salt can open to the corresponding betaine, which subsequently collapses to *cis*-epoxide products. Apparently, the 2:1 trans/cis-stereochemical ratio observed for the epoxide formation suggests that process c is only slightly favored over process d. The presence of lithium salt enhances the production of the betaine form compared to the potassium case, thus leading to the predominance of epoxide formation.

The results delineated above seem to be in accord with those reported by Mioskowski and co-workers.[8b] They reported the reaction of triphenylarsonium benzylide (generated by deprotonation with lithium diisopropylamide) with various carbonyl compounds. The reaction yielded epoxides exclusively when run in THF. When hexamethylphosphoramide (HMPA) was used as cosolvent, only olefin products were formed. Thus, the reaction gave epoxides when lithium coordination to the intermediate oxyanion was allowed, while olefins were formed when a more "naked" oxyanion was generated.

These results are also in accord with those reported by Broos and Anteunis.[9] These workers reacted triphenylarsonium benzylide (generated with phenyllithium) and benzaldehyde or acetaldehyde and obtained a predominance of epoxide over diene products. When the arsonium

(11) Vedejs, E.; Meier, G. P.; Snoble, K. A. *J. Am. Chem. Soc.* **1981**, *103*, 2823. See also: Vedejs, E.; Fleck, T.; Hara, S. *J. Org. Chem.* **1987**, *52*, 4637 and references cited therein.

(12) Maryanoff, B. E.; Reitz, A. B.; Mutter, M. S.; Inners, R. R.; Almond, H. R., Jr.; Whittle, R. R.; Olofson, R. A. *J. Am. Chem. Soc.* **1986**, *108*, 7664.

(13) Schlosser, M.; Christmann, K. F. *Justus Liebigs Ann. Chem.* **1967**, *708*, 1.

(14) Volatron, F.; Eisenstein, O. *J. Am. Chem. Soc.* **1987**, *109*, 1.

benzylide was generated by using sodium amide, a predominance of diene product was observed.

In summary, reactions of a semistabilized arsonium ylide were studied. Deprotonation of allyltriphenylarsonium tetrafluoroborate with either LiHMDS or KHMDS, followed by treatment with aldehydes, results in virtually exclusive epoxide or olefin formation, respectively. This appears to be the first case where the choice of the counterion of the base used for arsonium allylide generation is solely responsible for the observed product selectivity.

Experimental Section

General Procedures. Reactions were carried out under an atmosphere of dry nitrogen. Tetrahydrofuran was freshly distilled from sodium and benzophenone. Hexamethyldisilazane was distilled from calcium hydride and stored over potassium hydroxide pellets. Potassium hydride (35% dispersion in oil) and *n*-butyllithium (solution in hexane) were purchased from Aldrich. Flash column chromatography was carried out by using the method of Still.[15] Chromatography of the epoxides was carried out by using silica gel columns loaded as a slurry in hexane/EtOAc/triethylamine (10:5:1) and flushed with hexane. Lithium hexamethyldisilazide (LiHMDS) and potassium hexamethyldisilazide (KHMDS) were generated immediately prior to use.

(*E*)-1-(2,6-Bis(methoxymethoxy)phenyl)-1,3-butadiene (3). Into a 250-mL round-bottomed flask was placed 1 (1.813 g, 4.18 mmol) in 50 mL of THF at −60 °C. To this was added KHMDS (7.58 mmol) in 10.0 mL of THF via cannula. The resulting orange solution was warmed to −50 °C over 45 min and then cooled down to −65 °C. Aldehyde 2 (0.999 g, 4.42 mmol) in 10.0 mL of THF was then added. The solution immediately became lighter in color and was allowed to warm to 25 °C over 3 h. The solution was stirred for 17 h at 25 °C and then quenched with 25 mL of H_2O. After removal of the solvent in vacuo, the mixture was extracted with CH_2Cl_2 (3 × 50 mL). The combined organics were dried through Na_2SO_4 and concentrated in vacuo to give a brown oil. Chromatography (hexanes/EtOAc, 9:1) of the crude product gave 3 (0.840 g, 76%) as a white solid: mp 53.0–54.0 °C; ^{1}H NMr (300 MHz, $CDCl_3$) δ 3.499 (6 H, s), 5.134 (1 H, d, J = 10.2 Hz), 5.226 (4 H, s), 5.290 (1 H, d, J = 17.8 Hz), 6.538 (1 H, dt, J = 10.2, 10.3, 16.8 Hz), 6.794 (2 H, d, J = 8.3 Hz), 6.889 (1 H, d, J = 16.1 Hz), 7.092 (1 H, t, J = 8.3 Hz), 7.233 (1 H, dd, J = 10.4, 16.1 Hz) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 56.2 (q), 95.1 (t), 108.9 (d), 116.3 (t), 117.0 (s), 124.1 (d), 128.1 (d), 134.4 (d), 139.5 (d), 156.2 (s) ppm; IR ($CHCl_3$) 3019 (m), 2976 (w), 2935 (w), 1592 (w), 1577 (w), 1471 (w), 1215 (s), 1153 (m), 1098 (w), 1082 (w), 1043 (s), 1011 (w), 923 (w), 770–758 (s), 669 (s) cm^{-1}; high-resolution MS calcd for $C_{14}H_{18}O_4$ 250.1205, found 250.1205. Anal. Calcd for $C_{14}H_{18}O_4$: C, 67.17; H, 7.26. Found: C, 67.06; H, 7.17.

***trans*-2-(2,6-Bis(methoxymethoxy)phenyl)-3-vinyloxirane (4).** Into a 50-mL round-bottomed flask was placed 1 (0.280 g, 0.65 mmol) in 10 mL of THF at −60 °C. To this was added LiHMDS (0.71 mmol) in 2.0 mL of THF via cannula. The resulting orange solution was warmed to −55 °C over 45 min and then cooled down to −65 °C. Aldehyde 2 (0.1061 g, 0.47 mmol) in 1 mL of THF was then added. The solution immediately became lighter in color and was allowed to warm to 25 °C over 3 h. The solution was stirred for 24 h at 25 °C and then quenched with 5 mL of H_2O. After removal of the solvent in vacuo, the mixture was extracted with CH_2Cl_2 (3 × 10 mL). The combined organics were dried through Na_2SO_4 and concentrated in vacuo to give an orange oil. Chromatography (hexanes/EtOAc, 9:1) of the crude product gave 4 (0.101 g, 81%) as faint yellow crystals. Recrystallization from cold hexanes gave faint yellow crystals: mp 45.0–45.5 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.503 (6 H, s), 3.818 (1 H, dd, J = 2.4, 7.5 Hz), 3.917 (1 H, d, J = 2.4 Hz), 5.207 (4 H, s), 5.352 (1 H, d, J = 10.2 Hz), 5.577 (1 H, d, J = 17.2 Hz), 5.781 (1 H, ddd, J = 7.4, 10.2, 17.2 Hz), 6.781 (2 H, d, J = 8.4 Hz), 7.191 (1 H, t, J = 8.3 Hz) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 54.4 (d), 56.1 (q), 58.9 (d), 94.9 (t), 108.7 (d), 115.2 (s), 118.7 (t), 129.6 (d), 136.3 (d), 157.2 (s) ppm; IR ($CHCl_3$) 3019 (s), 2976 (w), 1600 (w), 1473 (w), 1215 (s), 1155 (w), 1044 (w), 927 (w), 770–756 (s), 669 (s) cm^{-1}; high-resolution MS calcd for $C_{14}H_{18}O_5$ 266.1154, found 266.1140. Anal. Calcd for $C_{14}H_{18}O_5$: C, 63.14; H, 6.83. Found: C, 62.81; H, 6.82.

Acknowledgment. We are grateful to the National Institutes of Health (ES-02851) for the support of this work.

(15) Still, W. C.; Kahn, M.; Mitra, A. *J. Org. Chem.* **1978**, *43*, 2923.
(16) Auge, J.; David, S. *Tetrahedron Lett.* **1984**, *4009*.
(17) Furuta, K.; Ikeda, Y.; Meguriya, N.; Ikeda, N.; Yamamoto, H. *Bull. Chem. Soc. Jpn.* **1984**, *57*, 2781.
(18) Ikeda, Y.; Ukai, J.; Ikeda, N.; Yamamoto, H. *Tetrahedron* **1987**, *43*, 723.
(19) Ishibashi, H.; Komatsu, H.; Ikeda, M. *J. Chem. Res., Synop.* **1987**, 296.

Single-Pot Reductive Conversion of Amino Acids to Their Respective 2-Oxazolidinones Employing Trichloromethyl Chloroformate as the Acylating Agent: A Multigram Synthesis

Lendon N. Pridgen* and J. Prol, Jr.[1]

Smith Kline & French Laboratories, Synthetic Chemistry Department, Chemical R&D, P.O. Box 1539, King of Prussia, Pennsylvania 19406-0939

Bruce Alexander and L. Gillyard

Smith Kline & French Laboratories, Chemical Engineering Department, Chemical R&D, P.O. Box 1539, King of Prussia, Pennsylvania 19406-0939

Received January 10, 1989

The emergence of the oxazolidinone ring system as the chiral auxiliary of choice in stereodifferentiating reactions owes its genesis principally to the pioneering work of the Evan's laboratory.[2] This amino acid based ring system has been so extensively exploited in recent years that it has been the subject of several reviews,[3,4] which all enumerate its capabilities in determining final product stereochemistry.

In continuing our research efforts in chiral Darzen's chemistry, wherein we utilized 2-oxazolidinones as our chiral auxiliary, we required large quantities of (4*S*)-4-phenyl-2-oxazolidinone (**5c**).[5] Existing synthesis methodologies for this very important class of compounds generally start with expensive optically active α-amino alcohols and use either diethyl carbonate or phosgene as the acylating agent. The Evan's diethyl carbonate procedure[2d] gave inconsistent results in our hands, and the alternative use of phosgene for large-scale preparations was not practical in this laboratory.

To circumvent using the expensive α-amino alcohol as a starting point, we simply needed to find efficient conditions for reducing α-amino acids. Our initial attempts at using the BF_3/borane methyl sulfide complex in refluxing THF as originally reported by Lane,[6] and later by

(1) Drexel University Co-op, 1986–1988.
(2) (a) Evans, D. A.; Takacs, J. M.; McGee, L. R.; Ennis, M. D.; Mathre, D. J.; Bartroli, J. *Pure Appl. Chem.* **1981**, *53*, 1109. (b) Evans, D. A.; Bartroli, J.; Shih, T. L. *J. Am. Chem. Soc.* **1981**, *103*, 2127. (c) Evans, D. A.; Ennis, M. D.; Mathre, D. J. *J. Am. Chem. Soc.* **1982**, *104*, 1737. (d) Evans, D. A.; Mathre, D. J.; Scott, W. L. *J. Org. Chem.* **1985**, *50*, 1830. (e) Evans, D. A.; Bartroli, J.; Shih, T. L. *J. Am. Chem. Soc.* **1981**, *103*, 2127. (f) Evans, D. A.; Weber, A. E. *J. Am. Chem. Soc.* **1986**, *108*, 6757.
(3) Evans, D. A. *Aldrichimica Acta* **1982**, *15*, 23.
(4) (a) Coppola, G. M.; Schuster, H. F. *Asymmetric Synthesis; Construction of Chiral Molecules Using Amino Acids*; Wiley: New York, 1987. (b) Meyers, A. I.; Yamamoto, Y. *Tetrahedron* **1984**, *40*, 2309.
(5) (a) Abdel-Magid, A.; Pridgen, L. N.; Eggleston, D. S.; Lantos, I. *J. Am. Chem. Soc.* **1986**, *108*, 4595. (b) Abdel-Magid, A.; Lantos, I.; Pridgen, L. N. *Tetrahedron Lett.* **1984**, *25*, 3273.
(6) Lane, C. F. U.S. Patent 3,935,280, 1976.

0022-3263/89/1954-3231$01.50/0