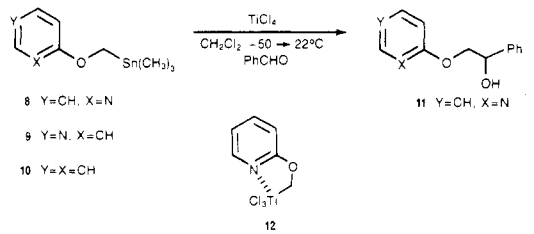
Scheme II



cluded that a discrete organotitanium species was produced from oxazole 1.[9]

The metalation of 4,5-diphenyl-2-[2-(trimethylstannyl)ethyl]oxazole-d_2 is shown in Scheme I.[10] Deuterated intermediates **4** and **5** can be directly observed by proton magnetic resonance and trapped by protonation to give oxazoles **6** and **7**. The deuterated oxazole **3** was prepared by synthesis of 4,5-diphenyl-2-(trideuteriomethyl)oxazole from benzoin, acetonitrile-d_3, and sulfuric acid-d_2 using the procedure of Jeffereys.[5b] Alkylation of the (trideuteriomethyl)oxazole afforded **3** in 85% isolated yield. When **3** was allowed to react with titanium tetrachloride in CD_2Cl_2, *only one* new singlet was observed at 3.12 ppm. When water was added to the reaction mixture, one 4,5-diphenyl-2-ethyloxazole-d_2 (**6**) (mp 32–34 °C) was isolated in 64% yield. The proton nuclear magnetic resonance spectrum of **6** showed only one broad singlet at 1.44 ppm. From this data, it was concluded that only one titanium reagent was derived from **3**, and the 4,5-diphenyl-2-ethyloxazole-d_2 (**6**) was produced from **3** by protonation of intermediate **4**. The metalation reaction did not proceed through a cyclopropyl intermediate.

In order to determine the need for a heteroatom in the substrate, three new compounds were prepared and submitted to the metalation reaction conditions (Scheme II).

Alkylation of 2-pyridone and 4-hydroxypyridine with (iodomethyl)trimethyltin and silver carbonate in pentane using the procedure of Hopkins[11] gave **8** and **9** as clear oils. The phenyl ether **10** was prepared by alkylation of phenol (NaH, DMF, 50 °C) with (iodomethyl)trimethyltin. When compounds **8**, **9**, and **10** were submitted to the metalation conditions ($TiCl_4$, 1.2 equiv, PhCHO, 1 equiv, CH_2Cl_2, −50 °C to 22 °C), only the pyridyl ether **8** afforded the addition product **11** in 50% yield. Compounds **9** and **10** did not react and only starting material was observed by TLC. The proton magnetic resonance spectrum (360 MHz) of **8** possessed a singlet at 4.16 ppm (^{118}Sn) and a doublet (J = 12.6 Hz, ^{117}Sn and ^{119}Sn) for the methylene protons. These peaks disappeared and a new singlet at 4.97 ppm was observed when titanium tetrachloride was added. Again, this result was indicative of the formation of an organotitanium intermediate (**12**). The preceding data

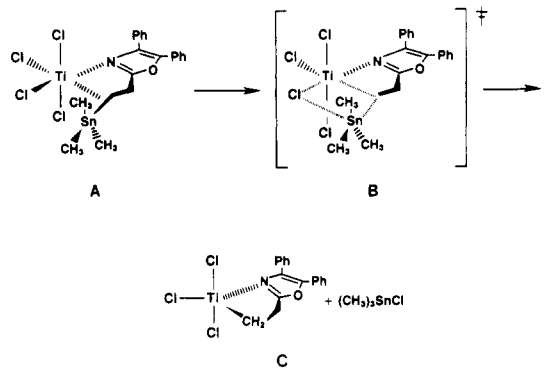


Figure 1. Reaction pathway of the metalation of 4,5-diphenyl-2-[2-(trimethylstannyl)ethyl]oxazole with titanium tetrachloride showing (a) the tin-oxazole–titanium tetrachloride complex, (b) the transition state, (c) the organotitanium product.

suggest that the pyridine and oxazole nitrogen was involved in the transition state for metalation. Furthermore, the metalation reaction did not proceed by an electronic effect due to the nitrogen atom as demonstrated by the unreactivity of isomer **9**. A mechanistic interpretation for this reaction is shown in Figure 1.

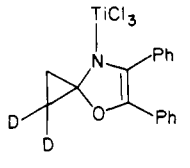
The metalation reaction involves the coordination of titanium tetrachloride with the carbon–tin σ bond and the nitrogen atom. The tin atom also coordinates with a chloride atom. It is hypothesized that the nitrogen atom and the carbon–tin σ bond form a chelate ring in the transition state. Since the organotitanium product possesses a chelate ring,[12] then the transition state must also experience enhanced stability (product development in the transition state). The decrease in entropy of activation obtained by chelation is a contributing factor for the metalation reaction to occur. The scope of this new reaction process is being developed.

Acknowledgment. The author would like to thank Dr. Stephen Spanton for recording the high-field proton magnetic resonance spectra and for valuable discussions during the course of this investigation.

Supplementary Material Available: High-field proton nuclear magnetic resonance spectra (360 MHz) for compounds **1**, **3**, **4**, **6**, **8**, and **12** are available (8 pages). Ordering information is given on any current masthead page.

(9) For recent reviews of organotitanium chemistry, see: (a) Reetz, M. *Top. Curr. Chem.* **1982**, *106*, 1. (b) Weidman, B.; Seebach, D. *Angew. Chem., Int. Ed. Engl.* **1983**, *22*, 31.

(10) If the formation of the organotitanium species proceeds through a cyclopropyl intermediate, then by symmetry, intermediate i must open to produce a one-to-one mixture of two titanium species, **4** and **5**. Secondary isotope effects should not effect this ratio.



i

(11) Hopkins, G. C.; Jonak, J. P.; Minnemeyer, H. J.; Tieckelmann, H. *J. Org. Chem.* **1967**, *32*, 4040.

(12) The crystal structure of methyl 3-(trichlorostannyl)propionate, which contains intramolecularly chelating ligands, has shown the tin atom to be occupying a trigonal bipyramidal geometry with the organic group in an equitorial site. Harrison, P. G.; King, T. J.; Healy, M. A. *J. Organomet. Chem.* **1979**, *182*, 17.

William R. Baker
Department of Medicinal Chemistry
Abbott Laboratories
Abbott Park, Illinois 60064
Received June 7, 1985

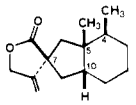
An Approach to the Bakkanes. A Short, Stereocontrolled Total Synthesis of (±)-Bakkenolide A[1]

Summary: A stereoselective total synthesis of (±)-bakkenolide A (fukinanolide) has been efficiently achieved in six steps.

(1) Presented in part at the Fourth French–Japanese Symposium, Antibes Sophia-Antipolis, Sept 1984 (A.E.G.).

0022-3263/85/1950-3943$01.50/0

Sir: Although the bakkane class of sesquiterpenes dates only from the isolation and structure elucidation of bakkenolide A (fukinanolide), reported in 1968 by two different groups,[3] it has grown rapidly so as now to include a number of more highly oxygenated members.[4] These novel spiro β-methylene-γ-butyrolactones, isolated primarily from several genera of Compositae,[3-5] are thought to be biogenetically related to the eremophilanes on the basis of their frequent cooccurrence in nature and the successful "biomimetic" conversion of fukinone to bakkenolide A (**1**).[6]



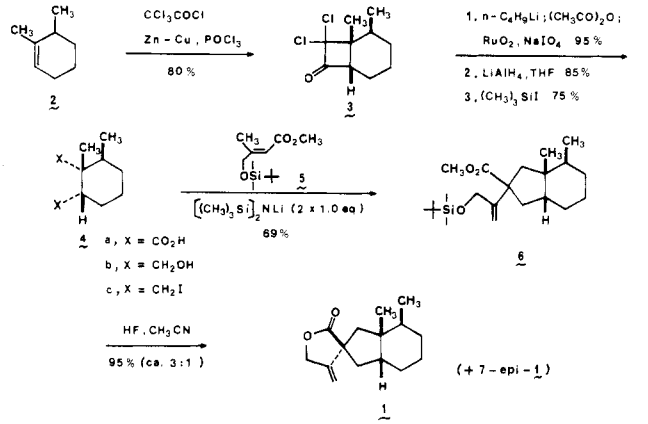
1

Bakkenolide-A

The unusual structural features of these compounds together with the confirmed level of selective cytotoxic activity of bakkenolide A (on cell lines derived from human carcinomas H.Ep.2 and HeLa vs. HeLu)[7] have served to engender remarkably little synthetic effort to date. The first *and only* success at total synthesis in this class belongs to Evans, Andrews, and Sims, who accomplished in 1973 a novel 13-step synthesis of racemic **1** in ca. 1.5% yield.[8] In this communication, we illustrate a potentially general approach to many of the bakkanes and their derivatives through a very brief total synthesis of (±)-bakkenolide A (**1**). The approach features a new procedure for stereospecific olefin dicarboxylation and a novel method for β-methylene-γ-butyrolactone construction.

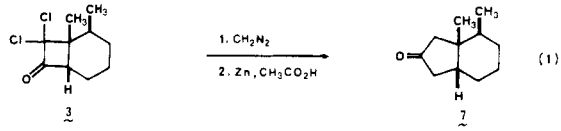
The starting material for the synthesis, commercially available 1,6-dimethylcyclohexene (**2**, Scheme I), underwent smooth cycloaddition with dichloroketene[9] to afford

Scheme I



2 **3** **4** **5** **6** **1**

regio- and stereoselectively (≥90%) the desired α,α-dichlorocyclobutanone **3**[10] in 80% yield. That the requisite relative stereochemistry had been produced could be readily established through conversion[11] of **3** to the previously described hydrindanone **7** (eq 1, 72%), a degra-



3 **7** (1)

dation product from both bakkenolide A and fukinone.[3a,12] The high degree of selectivity in this cycloaddition reaction reflects the known[9] preference for axial ketene carbonyl bond formation at the less substituted olefin carbon through a transition state involving a chair-like conformation; transition states leading to isomers of **3** are electronically, stereoelectronically, and/or sterically much less favorable than that which produces **3**.

A one-pot conversion of dichlorocyclobutanone **3** to the succinic acid derivative **4a**[10] was accomplished in 95% yield through sequential treatment of **3** with *n*-butyllithium (→ α-chloro enolate), acetic anhydride (→ enol acetate), and ruthenium(IV) oxide–sodium periodate.[13] Diol **4b**,[10] obtained from diacid **4a** in 85% yield by reduction with lithium aluminum hydride, was smoothly transformed to the corresponding diiodide **4c**[10] through prolonged exposure to trimethylsilyl iodide in chloroform at ambient temperature (75%).[14]

(2) (a) Université de Grenoble (LEDSS). (b) Universidade Federal de São Carlos.

(3) (a) Abe, N.; Onoda, R.; Shirahata, K.; Kato, T.; Woods, M. C.; Kitahara, Y. *Tetrahedron Lett.* **1968**, *9*, 369–373. (b) Shirahata, K.; Kato, T.; Kitahara, Y.; Abe, N. *Tetrahedron* **1969**, *25*, 3179–3191 and 4671–4680 (*Petasites japonicus* Maxim.). (c) Naya, K.; Takagi, I.; Hayashi, M.; Nakamura, S.; Kobayashi, M.; Katsumura, S. *Chem. Ind. (London)* **1968**, 318–320. (d) Naya, K.; Hayashi, M.; Takagi, I.; Nakamura, S.; Kobayashi, M. *Bull. Chem. Soc. Jpn.* **1972**, *45*, 3673–3685 (*Petasites japonicus* Maxim.).

(4) Abe, N.; Onoda, R.; Shirahata, K.; Kato, T.; Woods, M. C.; Kitahara, Y.; Ro, K.; Kurihara, T. *Tetrahedron Lett.* **1968**, *9*, 1993–1997. Shirahata, K.; Abe, N.; Kato, T.; Kitahara, Y. *Bull. Chem. Soc. Jpn.* **1968**, *41*, 1732–1733, and ref 3b–d. Naya, K.; Kawai, M.; Naito, M.; Kasai, T. *Chem. Lett.* **1972**, 241–244. Harmatha, J.; Samek, Z.; Synackova, M.; Novotny, L.; Herout, V.; Sorm, F. *Collect. Czech. Chem. Commun.* **1976**, *41*, 2047–2058.

(5) Novotny, L.; Kotva, K.; Toman, J.; Herout, V. *Phytochemistry* **1972**, *11*, 2795–2799. Hayashi, K.; Nakamura, H.; Mitsuhashi, H. *Ibid.* **1973**, *12*, 2931–2933. Ishizaki, Y.; Tanahashi, Y.; Moriyama, Y.; Takahashi, T.; Koyama, H. *Ibid.* **1974**, *13*, 674–675. Naya, K.; Miyoshi, Y.; Mori, H.; Takai, K.; Nakanishi, M. *Chem. Lett.* **1976**, 73–76. Bohlmann, F.; Ehlers, D.; Zdero, C.; Grenz, M. *Chem. Ber.* **1977**, *110*, 2640–2648. Bohlmann, F.; Zdero, C.; Mahanta, P. K. *Phytochemistry* **1977**, *16*, 1769–1771. Ito, K.; Iida, T.; Tanaka, H. *Yakugaku Zasshi* **1977**, *97*, 1374–1376; *Chem. Abstr.* **1978**, *88*, 60132w. Shibata, H.; Shimizu, S. *Agric. Biol. Chem.* **1978**, *42*, 1427–1428. Ito, K.; Iida, T.; Takeichi, C. *Yakugaku Zasshi* **1978**, *98*, 1592–1596; *Chem. Abstr.* **1979**, *90*, 135082g. Ito, K.; Iida, T.; Funatani, T. *Yakugaku Zasshi* **1979**, *99*, 349–353; *Chem. Abstr.* **1979**, *91*, 52694c. Bohlmann, F.; Zdero, C.; Berger, D.; Suwita, A.; Mahanta, P.; Jeffrey, C. *Phytochemistry* **1979**, *18*, 79–93.

(6) Hayashi, K.; Nakamura, H.; Mitsuhashi, H. *Chem. Pharm. Bull.* **1973**, *21*, 2806–2807. See also ref 3c,d.

(7) Jamieson, G. R.; Reid, E. H.; Turner, B. P.; Jamieson, A. T. *Phytochemistry* **1976**, *15*, 1713–1715. "Antitumor Compounds of Natural Origin: Chemistry and Biochemistry"; Aszalos, A., Ed., CRC Press: Boca Raton, FL, 1981. See also: Kano, K.; Hayashi, K.; Mitsuhashi, H. *Chem. Pharm. Bull.* **1982**, *30*, 1198–1203.

(8) Evans, D. A.; Sims, C. L. *Tetrahedron Lett.* **1973**, *14*, 4691–4694. Evans, D. A.; Sims, C. L.; Andrews, G. C. *J. Am. Chem. Soc.* **1977**, *99*, 5453–5461.

(9) Krepski, L. R.; Hassner, A. *J. Org. Chem.* **1978**, *43*, 2879–2882 and 3173–3179. Hassner, A.; Krepski, L. R. *Ibid.* **1979**, *44*, 1376–1379.

(10) Cyclobutanone **3**: bp ~55 °C (0.05 torr, evaporative distillation); IR (film) 1800, 1460, 1380, 1020, 855 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.06 (d, J = 6.5 Hz, 3 H), 1.40 (s, 3 H), 3.5 (m, 1 H); mass spectrum, m/e 221 (M^+). Diacid **4a**: IR (film) 3200, 2650, 1705, 1290, 1250 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.01 (d, J = 6.8 Hz, 3 H), 1.26 (s, 3 H), 2.85 (t, J = 4.5 Hz, 1 H), 10.63 (br s, 2 H). Dimethyl ester of **4a**: IR (film) 1735, 1190 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.96 (d, J = 7 Hz, 3 H), 1.21 (s, 3 H), 2.73 (t, J = 5 Hz, 1 H), 3.63 (s, 3 H), 3.64 (s, 3 H); mass spectrum, m/e 228 (M^+). Anal. Calcd for $C_{12}H_{20}O_4$: C, 63.13; H, 8.83. Found: C, 62.93; H, 8.68. Diol **4b**: IR (film) 3280, 1460, 1040 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.83 (d, J = 6.3 Hz, 3 H), 0.94 (s, 3 H), 3.20–4.15 (m, 4 H), 4.30 (br s, 2 H); ^{13}C NMR ($CDCl_3$) δ 15.78, 18.37, 21.86, 26.61, 30.30, 32.99, 39.73, 43.67, 64.13, 68.96. Anal. Calcd for $C_{10}H_{20}O_2$: C, 69.72; H, 11.70. Found: C, 69.47; H, 11.89. Diiodide **4c**: 1450, 1380, 1310, 1230, 1180, 1140, 1110, 990 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.86 (d, J = 6.2 Hz, 3 H), 1.01 (s, 3 H), 2.9–3.7 (m, 4 H); ^{13}C NMR ($CDCl_3$) δ 8.60, 15.49, 19.91, 21.96, 22.76, 25.89, 30.62, 34.69, 39.69, 44.71; mass spectrum, m/e 392 (M^+). (±)-Bakkenolide A (**1**): mp 47–48 °C; IR (Nujol) 1765, 1665, 900 cm^{-1}; ^1H NMR (C_6D_6);[3a,b] mass spectrum, m/e 234 (M^+). Anal. Calcd for $C_{15}H_{22}O_2$: C, 76.88; H, 9.46. Found: C, 76.73; H, 9.46.

(11) Greene, A. E.; Deprês, J.-P. *J. Am. Chem. Soc.* **1979**, *101*, 4003–4005.

(12) Naya, K.; Takagi, I.; Kawaguchi, Y.; Asada, Y.; Hirose, Y.; Shinoda, N. *Tetrahedron* **1968**, *24*, 5871–5879. See also: Sarma, S.; Sarkar, B. *Indian J. Chem.* **1972**, *10*, 950–951, and ref 8.

(13) For other examples of vicinal dicarboxylation, see: Deprês, J.-P.; Coelho, F.; Greene, A. E. *J. Org. Chem.* **1985**, *50*, 1972–1973.

(14) Jung, M. E.; Ornstein, P. L. *Tetrahedron Lett.* **1977**, *18*, 2659–2662.

A new lactone synthesis[15] proved effective for the conversion of diiodide **4c** to bakkenolide A—viz., the methyl acrylate derivative **5** in DME at −58 °C on successive treatment with 1.0 equiv of lithium bis(trimethylsilyl)-amide in DME, 0.9 equiv of the diiodide in HMPA, and then once again with 1.0 equiv of the amide base furnished directly in 69% yield hydrindane **6** as a ca. 3:1 mixture (NMR) of C-7 epimers.[16] Deprotection–lactonization of **6** occurred on brief contact with aqueous hydrofluoric acid in acetonitrile[17] to produce in essentially quantitative yield the corresponding spiro β-methylene-γ-butyrolactones, from which pure racemic bakkenolide A (**1**),[10] mp 47–48 °C, was readily obtained by crystallization from cold pentane. This material was indistinguishable spectroscopically (IR, NMR, MS) and chromatographically (TLC, VPC) from an authentic sample of the natural product.

Work directed at extending this efficient approach to the synthesis of other bakkanes is planned.

Acknowledgment. We thank Professor A. Rassat and Dr. J.-L. Luche for their interest in this work and Professor T. Kato for a sample of natural bakkenolide A. Financial support from the C.N.R.S. (LA 332) and a fellowship award from the C.N.Pq. (to F.C.) are gratefully acknowledged.

(15) Greene, A. E.; Coelho, F.; Deprés, J.-P.; Brocksom, T. J. *J. Org. Chem.* **1985**, *50*, 1973–1975.

(16) This favorable selectivity, although somewhat less than had been hoped for, was expected on the assumption that the ester dienolate would preferentially react through a "U-shape" and in such a way as to avoid bringing the bulky $-CH_2OSi(CH_3)_2(C_4H_9)$ group and the C-5 methyl group into proximity. See: Cainelli, G.; Cardillo, G.; Contento, M.; Trapani, G.; Umani Ronchi, A. *J. Chem. Soc., Perkin Trans. 1* **1973**, 400–404, and references cited therein. The use of sodium bis(trimethylsilyl)amide in place of the lithium amide, THF in lieu of DME, or smaller amounts of HMPA (70 → <40% of the final volume) has a deleterious effect on the isomer ratio.

(17) Newton, R. F.; Reynolds, D. P.; Finch, M. A. W.; Kelley, D. R.; Roberts, S. M. *Tetrahedron Lett.* **1979**, *20*, 3981–3982.

Andrew E. Greene,*[2a] Jean-Pierre Deprés[2a]
Fernando Coelho,[2a] Timothy J. Brocksom[2b]
Departments of Chemistry
Université de Grenoble (LEDSS)
38402 St. Martin d'Hères Cedex, France, and
Universidade Federal de São Carlos
13.560-São Carlos, S.P., Brazil
Received May 29, 1985

Alkylation of Aromatic Compounds with Optically Active Lactic Acid Derivatives: Synthesis of Optically Pure 2-Arylpropionic Acid and Esters

Summary: The alkylation of benzene with (*S*)-methyl 2-[(chlorosulfonyl)oxy]- or 2-(mesyloxy)propionate, in the presence of aluminum chloride, affords (*S*)-methyl 2-phenylpropionate in good chemical (50–80%) and excellent optical yield (≥97% as determined by rotation), with inversion of configuration at the attacking carbon atom.

Sir: Generally Friedel–Crafts alkylation proceeds with a high degree of racemization (40–100%) when an optically active alkylating reagent is used.[1] When an optically active product is recovered, a partial inversion of configuration, as a normal result, is observed. Some examples of highly stereospecific reactions have, however, been reported such as the alkylation of benzene with (*R*)-1,2-epoxypropane and (*R*)-1,2-epoxybutane (optical yield ~ 100% with inversion of configuration)[2a,b] and with (*R*)-2-chloro-1-phenylpropane (o.y. ~ 96% with retention of configuration).[2c] These results have been explained on the basis of the cyclic nature of the alkylating reagents or as the result of the formation of cyclic intermediates. When a low stereospecificity in this type of reaction is found, it may be due either to the formation of a free carbonium ion intermediate or to the racemization of the starting material[1h] and/or of the final product.[3,4]

Here we report the first example of a Friedel–Crafts alkylation reaction, using acyclic alkylating reagents, that proceeds with high stereospecificity (≥97%, Table I) and inversion of configuration. The reaction conditions are similar to procedures reported in patents[5a,b] where racemic reagents have been used.

It is of note that the alkylation reaction also works in the presence of basic inorganic and organic compounds such as calcium carbonate, pyridine, poly(vinylpyridine), or imidazole, giving the same optical yields but lower chemical yields. Exploratory experiments with different Lewis acids gave no improvement or low yields.

When we tried to extend this reaction to other aromatic substrates such as toluene, isobutylbenzene, tetralin, anisole, naphthalene, 2-methoxynaphthalene, we obtained mixtures of isomeric alkylation products and/or byproducts. At the present, we are unable to improve the reaction as reported in some patterns.[5c–h] However, after careful purification, by flash chromatography (eluent 7/3 hexane/ethyl acetate), of the mixture obtained in the reaction of isobutylbenzene and optically pure (*S*)-2-(mesyloxy)propionic acid, a sample of (*S*)-2-(4-isobutylphenyl)propionic acid (Ibuprofen) having $[\alpha]^{25}_D$ +58.5° (ethanol 95%, *c* 2) [maximum specific rotation reported $[\alpha]^{25}_D$ +60° (ethanol 95%, *c* 2)][7] was recovered.

Concerning the mechanism, it is reasonable to think that cyclic intermediates are involved in which the COOR and OX groups strongly coordinate with aluminum, though it cannot, at present, be established which atoms are actually bonded. Benzene is expected to attack the chiral carbon atom from the backside of the leaving group, analogously to what has been previously reported.[1d–l,2a,b] No free Lewis acid should be present to racemize the starting material, even if a molar ratio of Lewis acid to ester of 2 is used (compare ref 1h) and/or the rate of the alkylation should be appreciably faster than the scrambling of the OX group. The latter hypothesis is, in our opinion, less probable since

(1) (a) Price, C. C.; Lund, M. *J. Am. Chem. Soc.* **1940**, *62*, 3105. (b) Burwell, A. L., Jr.; Archer, S. *Ibid.* **1942**, *64*, 1032. (c) Streitwieser, A., Jr.; Stang, P. G. *Ibid.* **1965**, *87*, 4953. (d) Brauman, J. I.; Pandell, A. J. *Ibid.* **1967**, *89*, 5421. (e) Brauman, J. I.; Solladié-Cavallo, A. *J. Chem. Soc., Chem. Commun.* **1968**, 1125. (f) Suga, S.; Nakajima, T.; Nakamoto, Y.; Matsumoto, K. *Tetrahedron Lett.* **1969**, 3283. (g) Spanninger, P. A.; von Rosenberg, J. L. *J. Am. Chem. Soc.* **1972**, *94*, 1973. (h) Nakajima, T.; Masuda, S.; Nakashima, S.; Kondo, T.; Nakamoto, Y.; Suga, S. *Bull. Chem. Soc. Jpn.* **1979**, *52*, 2377. (i) Masuda, S.; Segi, M.; Nakajima, T.; Suga, S. *J. Chem. Soc., Chem. Commun.* **1980**, 86. (j) Suga, S.; Sagi, M.; Kitano, K.; Masuda, S.; Nakajima, T. *Bull. Chem. Soc. Jpn.* **1981**, *54*, 3611. (k) Segi, M.; Takebe, M.; Masuda, S.; Nakajima, T.; Suga, S. *Ibid.* **1982**, *55*, 167. (l) Taylor, S. K.; Haberkamp, W. C. *J. Heterocycl. Chem.* **1983**, *20*, 1745.

(2) (a) Nakajima, T.; Suga, S.; Sugita, T.; Ichikawa, K. *Tetrahedron* **1969**, *25*, 1807. (b) Nakajima, T.; Nakamoto, Y.; Suga, S. *Bull. Chem. Soc. Jpn.* **1975**, *48*, 960. (c) Masuda, S.; Nakajima, T.; Suga S. *J. Chem. Soc., Chem. Commun.* **1974**, 954.

(3) Eliel, E. L.; Wilken, P. H.; Fang, F. T. *J. Org. Chem.* **1957**, *22*, 231.

(4) Menicagli, R.; Piccolo, O. *J. Org. Chem.* **1980**, *45*, 2581.

(5) (a) Jpn. Kokai Tokkyo Koho 58 08 045; *Chem. Abstr.* **1983**, *98*, 143138*k*. (b) Jpn. Kokai Tokkyo Koho 7979246; *Chem. Abstr.* **1980**, *92*, 6253*f*. (c) Jpn. Kokai Tokkyo Koho 79 19 932; *Chem. Abstr.* **1979**, *91*, 20125*b*. (d) Jpn. Kokai 78 12 837; *Chem. Abstr.* **1978**, *89*, 23975*y*. (e) Jpn. Kokai Tokkyo Koho 81 145 241; *Chem. Abstr.* **1982**, *96*, 68650*z*. (f) Jpn. Kokai Tokkyo Koho 78 149 945; *Chem. Abstr.* **1979**, *90*, 168303*h*. (g) Jpn. Kokai 78 44 537; *Chem. Abstr.* **1978**, *89*, 108693*h*. (h) Jpn. Kokai 77 131 551; *Chem. Abstr.* **1978**, *88*, 104920*h*.

(6) Pracejus, H. *Liebigs Ann. Chem.* **1960**, *634*, 9.

(7) Kaiser, D. G.; Vangiessen, G. J.; Reische, R. J.; Wechter, W. J. *J. Pharm. Sci.* **1976**, *65*, 269.

0022-3263/85/1950-3945$01.50/0