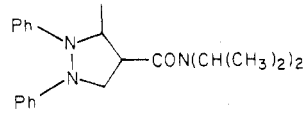
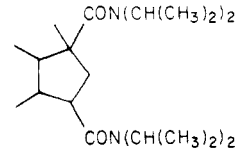
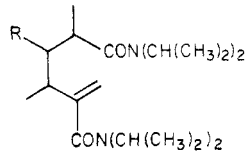
demonstrated by conversion of **9b**, obtained from **8** and azobenzene, to the dihydropyrazoline **15** in 22% yield and by the formation of **16**, in 72% yield, when a THF solution of **7** and 0.55 equiv of *sec*-butyllithium–tetramethylethylenediamine is allowed to warm to ambient temperature prior to quenching.[7] If the latter reaction is quenched at −78 °C, the acyclic amide **17**, the anion of which presumably is the precursor to **16**, is obtained in 40% yield.[7]



15



16

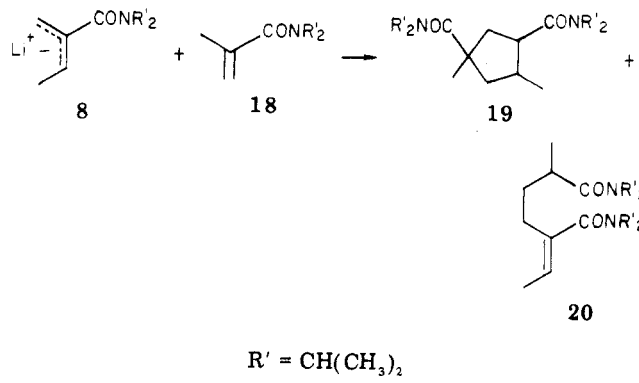


17, R = CH_3
21, R = H

Of greater interest is the addition of the anion **8** to **18** at −60 °C followed by warming to ambient temperature to give the cyclopentane derivative **19** in 59% yield along with a 16% yield of **20**.[7] If this reaction is quenched at −65 °C **21** is obtained in 60% yield.[7] This result, which establishes that the β'-lithio-α,β-unsaturated amides can be used in an addition–cyclization sequence, has important synthetic potential and its generalization is under further investigation.

This facile preparation of the novel β'-lithiomethacrylate synthon **1**, along with the classic enolate and addition chemistry well-known for this system under other basic conditions,[8] appears to substantially expand the possibilities for controlled syntheses with α,β-unsaturated carboxylic acid derivatives. For the β' metalations of secondary amides it was suggested[1,2] that additions and enolate formation were suppressed by initial proton removal from the nitrogen. The present results indicate that such deactivation at both the carbonyl and β positions can be accomplished through steric inhibition.[9] The implication of these results, that the tertiary amide is effective in directing metalation due to strong complexation with lithium, is consistent with the paramount position of this group as a director of aromatic lithiation[10] and with metalations similarly directed in allyl systems by the ionized secondary amide,[1] alkoxide,[2c,11] and the neutral dimethylamino[12] groups.

Conversion of 3 to 5. A stirred solution of *sec*-butyllithium (1.0 mL, 1.3 mmol) and *N,NN',N'*-tetramethylethylenediamine (0.2 mL, 1.3 mmol) in 5 mL of tetrahydrofuran was cooled in a dry ice/acetone bath and treated dropwise with 269 mg (1.29 mmol) of **3** in 5 mL of tetrahydrofuran. The resulting red-orange solution was stirred under N_2 for 5 min, treated with 0.2 mL (1.7 mmol)



8 18 19 20

R' = $CH(CH_3)_2$

of benzyl chloride, and allowed to warm to ambient temperature. Extractive workup followed by separation by medium-pressure liquid chromatography and bulb-to-bulb distillation yielded 225 mg (58%) of pure **5** (E = $CH_2C_6H_5$): ^1H NMR (360 MHz) δ ($CDCl_3$) 1.1–1.6 (m, br d, 15 H), 1.63–1.71 (m, 1 H), 2.07–2.10 (m, 2 H), 2.29 (t, J = 12.4 Hz, 1 H), 2.76 (m, 1 H), 2.96 (d of d , J = 13.1, 3.3 Hz, 1 H), 3.3–3.5 (br d, 1 H), 4.2–4.4 (br d, 1 H), 5.73 (m, 1 H), 7.17–7.19 (m, 3 H), 7.25–7.28 (m, 2 H); IR (NaCl, film) 2940 (m), 1620 (s), 1435 (s), 1372 (s), 1325 (s) cm^{-1}; mass spectrum (70 eV), m/e (relative intensity) 299 (20.6), 256 (9.4), 208 (100) 199 (48.5), 198 (25.0), 91 (46.7), 43 (28.6), 41 (21.1). anal. Calcd for $C_{20}H_{29}NO$: C, 80.22; H, 9.76; N, 4.68. Found: C, 79.91; H, 9.75; N, 4.79.

Acknowledgment. We are grateful to the National Institute of Health–Institute of General Medicine for support of this work. We also acknowledge use of the Regional NMR facility at the University of Illinois at Champaign–Urbana supported in part by NSF CHE 79-16,100.

Dale J. Kempf, Kenneth D. Wilson, Peter Beak*
Department of Chemistry
University of Illinois
Urbana, Illinois 61801
Received November 6, 1981

Macrolide Synthesis: Narbonolide

Summary: Narbonolide, a 14-membered polyoxomacrolide, has been synthesized through two major steps: (i) condensation of the C_1–C_{10} and C_{11}–C_{15} fragments and (ii) macrolactonization using a phosphoric acid mixed anhydride intermediate.

Sir: Narbonolide (**1**),[1] isolated from fermentation broths of *Streptococcus venezuelae* MCRL 0376, is a metabolic intermediate leading to narbomycin (**2**)[2] and pikromycin (**3**),[3] both of which belong to the well-known family of 14-membered polyoxomacrolides.[4] The full stereostructures of narbonolide and narbomycin, which apparently

(7) The compounds **16**, **17**, **19**, and **21** are obtained as mixtures of diastereomers which are separated by medium-pressure liquid chromatography.

(8) (a) Majewski, M.; Mango, G. B.; Thomas, M. T.; Wu, A.; Snieckus, V. *J. Org. Chem.* **1981**, *46*, 2029 and references cited therein; (b) Savu, P. M.; Katzenellenbogen, J. A. *J. Org. Chem.* **1981**, *46*, 239 and references cited therein.

(9) The attempted metalation of *N,N*-diethyl-1-cyclohexenecarboxamide results in self-addition of the transient β'-lithiated species.

(10) Beak, P.; Brown, R. A. *J. Org. Chem.* **1982**, *47*, 34.

(11) (a) Cardillo, G.; Contento, M.; Sandri, S. *Tetrahedron Lett.* **1974**, 2215. (b) Sarkar, T. K.; Andersen, N. H. *Ibid.* **1978**, 3513.

(12) Fitt, J. J.; Gschwend, H. W. *J. Org. Chem.* **1981**, *46*, 3349.

(1) (a) Hori, T.; Maezawa, I.; Nagahama, N.; Suzuki, M. *Chem. Commun.* **1971**, 304. (b) Maezawa, I.; Hori, T.; Kinumaki, A.; Suzuki, M. *J. Antibiot.* **1973**, *26*, 771. (c) Maezawa, I.; Hori, T.; Suzuki, M. *Agric. Biol. Chem.* **1974**, *38*, 539.

(2) (a) For the first isolation of **2**, see: Corbaz, R.; Ettlinger, L.; Gäumann, E.; Keller-Schierlein, W.; Neipp, L.; Prelog, V.; Reusser, P.; Zähner, H. *Helv. Chim. Acta* **1955**, *38*, 1202. (b) Structural work on **2**, see: Prelog, V.; Gold, A. M.; Talbot, G.; Zamojski, A. *Ibid.* **1962**, *45*, 4.

(3) Brockmann, H.; Henkel, W. *Naturwissenschaften* **1950**, *37*, 138; *Chem. Ber.* **1951**, *84*, 284.

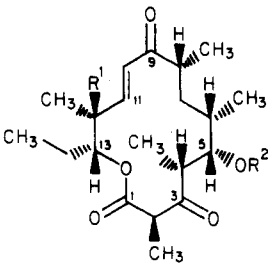
(4) For a recent review on the chemistry and biochemistry of macrolide antibiotics, see: Masamune, S.; Bates, G. S.; Corcoran, J. W. *Angew. Chem., Int. Ed. Engl.* **1977**, *16*, 585.

0022-3263/82/1947-1612$01.25/0

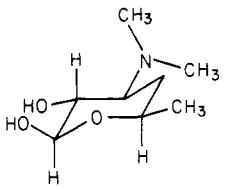
have not been formulated in the literature, can be deduced as shown in 1 and 2, respectively, from two lines of evidence: (a) enzymatic, oxidative conversion of 2 to 3, and that of 1 to pikronolide (4)[5] and (b) the now established stereochemistry of 3.[6] While the stereochemistry of 1 and 2 conforms to Celmer's model[7] and thus is similar to that of many polyoxomacrolides such as 6-deoxyerythronolide B,[8] it is the presence of the C_3-keto functionality (β to the C_5-hydroxy group and also β to the lactone group) that chemically distinguishes 2 as well as 3 from other members of the family. Thus, even under mild acidic and basic conditions, the elimination of desosamine from 2 and 3 readily takes place with the introduction of the C_4–C_5 double bond into the macroring.[2b,9] Also, the stereoselective construction and preservation of the chiral C_2 center presents another unique problem associated with this lactone framework as experienced in our earlier approach to the synthesis of 4.[10] We present herein the efficient synthesis of 1 that eliminates theses earlier drawbacks[10] and further incorporates newer, improved methodologies for macrolactonization and C_{10}–C_{11} double bond formation as applied in macrolide synthesis.

Two important intermediates (5 and 6) prepared in the recent synthesis of 6-deoxyerythronolide B[11] serve as major fragments of 1. Both intermediates, readily available through enantioselective aldol condensations,[11] comprise all the chiral centers necessary for the construction of 1. Thus, treatment of (−)-acid chloride 5 with the cuprate reagent prepared from [(trimethylsilyl)methyl]lithium[12] and CuI in ether provides quantitatively the α-(trimethylsilyl)methyl ketone 7, the lithium anion of which is then reacted (in tetrahydrofuran) at −78 °C with (+)-aldehyde 6 to afford an α,β-unsaturated ketone (8) in 95% yield (Scheme I). This result is remarkable in view of the base sensitivity of both reactants 6 and 7, as well as the product 8, and indeed the Peterson reaction is far superior in terms of both reaction time and yield to the Wittig reaction, using the corresponding α-ketomethylenephosphorane.[10] Removal of the triethylsilyl group with aqueous acetic acid at room temperature generates the C_{13}-hydroxy thiol ester 9 (100% yield).

Macrolactonization did not seem to be a fully solved problem. Compound 9 defied, in this particular instance, all attempts at direct cyclization through the activation



1, R^1 = H; R^2 = H
2, R^1 = H; R^2 = β-D-desosaminyl
3, R^1 = OH; R^2 = β-D-desosaminyl
4, R^1 = OH; R^2 = H



β-D-desosamine

of the thiol ester with a thiophilic metal cation,[13] and, therefore, a search was made for an alternative general method. Of the numerous methods for carboxyl activation examined thus far,[14] the phosphoric acid mixed anhydride has apparently escaped attention, despite the availability of the method for selectively converting a hydroxy carboxylic acid into the corresponding mixed anhydride (in the presence of the free hydroxyl group).[15] This activation technique has now been found to be simple and efficient as exemplified below by cyclization of the seco acid (10) derived from dimethylzearalenone ethylene glycol ketal (11).

Treatment of 10 (0.1 mM) in 1 mL of tetrahydrofuran with triethylamine (0.1 mM) followed by diphenyl phosphochloridate (0.1 mM) at 0 °C immediately produces a white precipitate, which after 30 min of stirring is filtered. The filtrate, after dilution with 40 mL of benzene, is maintained at 5 °C and this cold diluent is added over a period of 8 h to 60 mL of stirred, warm (80 °C) benzene containing 4-(dimethylamino)pyridine (0.3 mM). After the addition has been completed, the resulting solution is kept at reflux for 13 h and is worked up in the usual manner. The yield of 11 is 90–95%. In applying this procedure to the present narbonolide synthesis, we first converted the thiol ester 9, with $Hg(CF_3CO_2)_2$ followed by aqueous $NaHCO_3$,[10] into the corresponding carboxylic acid 12 (97% yield). Treatment of acid 12 in the same manner as that described above[15] afforded the 14-membered lactone 13 and a dimeric product (14) in 32% and 25% yields, respectively. Although the ratio of 13 to 14, in principle, can be enhanced with a higher dilution, 12 particularly resists exclusive monocyclization with any of the currently available techniques, and a significant increase in the yield of cyclization may be achieved only at the expense of extensive structural modification of the seco acid 11.[16]

Brief treatment of 13 with trifluoroacetic acid (H_2O/acetonitrile, 1:1) generates the diol 15 (100%) and the regioselective oxidation of 15 presents a crucial problem

(5) Enzymatic oxidation very often is involved in a late stage of biosynthesis of macrolide antibiotics, and this oxidation normally proceeds with retention.

(6) (a) Richards, R. W.; Smith, R. M.; Majer, J. *Chem. Commun.* **1968**, 1049. (b) Muxfeldt, H.; Shrader, S.; Hansen, P.; Brockmann, H. *J. Am. Chem. Soc.* **1968**, *90*, 4748. (c) Hughes, R. E.; Muxfeldt, H.; Tsai, C.; Stezowski, J. J. *Ibid.* **1970**, *92*, 5267. (d) Anliker, R.; Dvornik, D.; Gubler, K.; Heuser, H.; Prelog, V. *Helv. Chim. Acta* **1956**, *39*, 1785. (e) Djerassi, C.; Halpern, O.; Wilkinson, D. I.; Eisenbraun, E. J. *Tetrahedron* **1958**, *4*, 369.

(7) Celmer, W. D. *Pure Appl. Chem.* **1971**, *28*, 413. For an exception to this rule, see Omura, S.; Matsubara, H.; Nakagawa, A. *J. Antibiot.* **1980**, *33*, 415.

(8) Egan, R. S.; Perun, T. J.; Martin, J. R.; Mitscher, L. A. *Tetrahedron* **1973**, *29*, 2525.

(9) (a) Brockmann, H.; Oster, R. *Chem. Ber.* **1957**, *90*, 605. (b) Anliker, A.; Gubler, K. *Helv. Chim. Acta* **1957**, *40*, 1768. Even at pH 6.5 (60 °C) pikromycin (3) is split into kromycin (pikronolide–H_2O) and desosamine. The antiperiplanar disposition of the C_4H and C_5 substituent in 2 and 3 is highly likely and is responsible for this facile elimination.

(10) Masamune, S. *Aldrichimica* **1978**, *11*, 23. The synthetic scheme previously reported for 4 involved the incorporation of a sensitive β-keto ester group in an early synthetic intermediate.

(11) (a) Masamune, S.; Hirama, M.; Mori, S.; Ali, Sk. A.; Garvey, D. S. *J. Am. Chem. Soc.* **1981**, *103*, 1568. (b) Masamune, S.; Choy, W.; Kerdesky, F. A. J.; Imperiali, B. *Ibid.* **1981**, *103*, 1566.

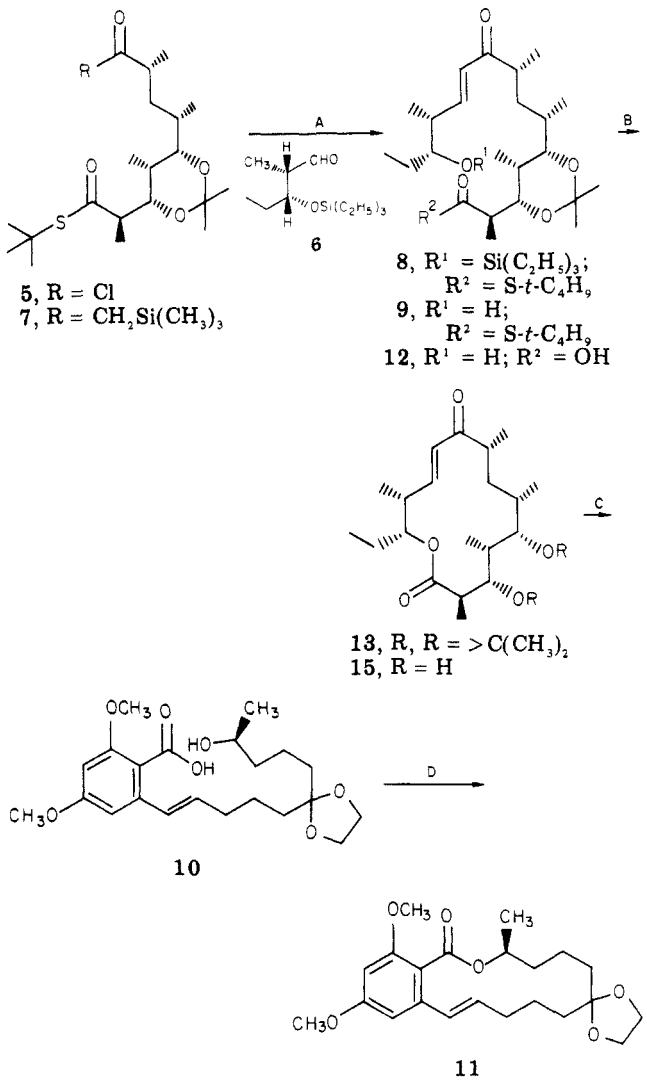
(12) (a) Ruden, R. A.; Gaffney, B. L. *Synth. Commun.* **1975**, *5*, 15. (b) Demuth, M. *Helv. Chim. Acta* **1978**, *61*, 3136. (c) Lappert, M. F.; Pearce, R. *J. Chem. Soc., Chem. Commun.* **1973**, 25. (d) For the preparation of α,β-unsaturated esters using α-silylated enolates, see Larchevêque, M.; Debal, A. *Ibid.* **1981**, 877 and references quoted therein.

(13) This method has been used successfully in a number of macrolide syntheses: (a) Masamune, S.; Yamamoto, H.; Kamata, S.; Fukuzawa, A. *J. Am. Chem. Soc.* **1975**, *97*, 3513. (b) Masamune, S.; Kamata, S.; Schilling, W. *Ibid.* **1975**, *97*, 3515. (c) Masamune, S.; Hayase, Y; Chan, W. K.; Sobczak, R. L. *Ibid.* **1976**, *98*, 7874. (d) Masamune, S. Hayase, Y.; Schilling, W.; Chan, W. K.; Bates, G. S. *Ibid.* **1977**, *99*, 6756. (e) Huang, J.; Meinwald, J. *Ibid.* **1981**, *103*, 861. (f) Tatsuta, K.; Amemiya, Y.; Maniwa, S.; Kinoshita, M. *Tetrahedron Lett.* **1980**, *20*, 2837. Also see ref 11a.

(14) Setliou, K.; Szczygielska-Nowosielska, A.; Favre, A.; Poupart, M. A.; Hanessian, S. *J. Am. Chem. Soc.* **1980**, *102*, 7578, and also see references cited therein.

(15) Masamune, S.; Kamata, S.; Diakur, J.; Sugihara, Y.; Bates, G. S. *Can. J. Chem.* **1975**, *53*, 3693. The phosphoric acid anhydride intermediate is rather labile to heat and prone to disproportionate: $2RCO_2PO(OR')_2 \rightleftarrows (RCO)_2O + (CR'O)_2O$ [Sheehan, J. C.; Frank, V. S. *J. Am. Chem. Soc.* **1950**, *72*, 1312. Cramer, F.; Gärtner, K. G. *Chem. Ber.* **1958**, *91*, 704.] Therefore, the lactonization should not be performed at a temperature higher than 80 °C.

Scheme I



[a] (A) 5 → 7, $LiCu[CH_2Si(CH_3)_3]_2$ (ether), −78 °C, 25 min; 7 → 8, $LiN[Si(CH_3)_3]_2$ (THF), −78 °C, 45 min, and then 6. (B) 8 → 9, CH_3CO_2H (H_2O/THF, 1:3), room temperature, 16 h; 9 → 12, $Hg(CF_3CO_2)_2$ (CH_2Cl_2), room temperature, 20 min, and then aqueous $NaHCO_3$; 12 → 13, $(PhO)_2POCl$, Et_3N (THF), 0 °C, 30 min, and then DMAP (C_6H_6), 80 °C, 23 h. (C) 13 → 15, CF_3CO_2H (H_2O/CH_3CN, 1:1), room temperature, 3 h; 15 → 1, $RuCl_2(PPh_3)_3$ (C_6H_6), room temperature. (D) Same as that for 12 → 13.

in the final stage of the synthesis. Of the many known oxidants examined, many tend to favor the attack at the C_5-hydroxy group and in some cases the undesired C_5-keto compound (16) is the exclusive product.[17] Only two reagents provide reasonable quantities of the C_3 ketone (1): $RuCl_2(PPh_3)_3$[18] (1:1 mixture of 1 and 16, total yield 92%) and $(CH_3)_2SO$/DCC/H_3PO_4/benzene[19] (55:45, 90%). Fortunately, however, recovery of 15 from 16 with the use of $NaBH_4$ and then DDQ proceeds in 70% yield, and with this recycling the transformation of 15 to 1 is achieved at minimum 65% yield. Direct comparison of 1, mp 125–126 °C, with natural narbonolide generously supplied by Professor Suzuki confirms the identity of these two specimens as well as the correctness of the stereochemistry deduced above for 1. Two features of the synthesis that is outlined above may be worth emphasizing: (a) the generation of the C_3-keto group in the very final stage of the sequence has resolved the complications that were encountered in the earlier synthesis[10] and (b) a useful and simple lactonization technique has been developed. The application of this technique to tylonolide seco acid derivatives and related compounds has already been made and will be documented in due course.[20]

Acknowledgment. We thank Professor M. Suzuki, Meijo University, Japan, for a gift of narbonolide and the National Institute of Health (Grant AI 15403) and Hoffmann-LaRoche for financial support. T.K. is on leave from Mitsui Toatsu Chemicals Inc. Japan. High-resolution mass spectra were provided by the facility, supported by the National Institutes of Health (Grant RR 00317; the principal investigator, Professor K. Biemann), from the Biotechnology Resources Branch, Division of Research Resources.

(16) As documented earlier (ref 4), the success of seco acid lactonization depends largely upon two factors: proper activation of the carboxyl group and the conformation of the seco acid. The significance of the latter effect, although obvious in hindsight, was first emphasized by the present author: Masamune, S.; Kim, C. U.; Wilson, K. E.; Spessard, G. O.; Georghiou, P. E.; Bates, G. S. *J. Am. Chem. Soc.* **1975**, *97*, 3512, and ref 4, p 591. The recent work on erythromycin A represents an excellent illustration: R. B. Woodward et al. *J Am. Chem. Soc.* **1981**, *103*, 3213.

(17) The C_{10}-methyl derivative of 15 which readily available from 6-deoxyerythronolide B (ref 11a) served as a model substrate for this selective oxidation. The ratios of the corresponding 3-keto vs. 5-keto compound are as follows: PCC, 1:9; $(CH_3)_2S$/NCS/$(C_2H_5)_3N$/CH_2Cl_2, 1:9; Me_2SO/$(CF_3CO)_2O$/$(C_2H_5)_3N$, 55:45; Me_2SO/DCC/C_5H_5N/CF_3CO_2H/C_6H_6, 45:55; Me_2SO/DCC/C_5H_5N/HCl, 34:66; Me_2SO/DCC/H_3PO_4, 3:2; Me_2SO/$(COCl)_2$/$(C_2H_5)_3N$, 1:1; $RuCl_2(PPh_3)_3$/benzene, 3:2; MoO$(O_2)(C_6H_5CONC_6H_5O)_2$/$C_2H_4Cl_2$, 0:100; Ag_2CO_3 on Celite/C_6H_6, 1:9; CrO_3/C_5H_5N, 1:9.

(18) Tomioka, H.; Takai, K.; Oshima, K.; Nozaki, H. *Tetrahedron Lett.* **1981**, 1605.

(19) Pfitzner, K. E.; Moffatt, J. G. *J. Am. Chem. Soc.* **1965**, *87*, 5661, 5670.

(20) All new compounds prepared in this work have been fully characterized by means of high-resolution mass spectra, 250-MHz ^1H NMR, and IR spectra. NMR signals ($CDCl_3$) of these compounds are expressed in δ (multiplicity, coupling constant (hertz), numbers of protons). 1: 0.93 (t, J = 7.4, 3 H), 0.93 (d, J = 7.0, 3 H), 1.10 (d, J = 7.0, 3 H), 1.14 (d, J = 7.0, 3 H), 1.15 (d, J = 7.0, 3 H), 3.02 (sext, J = 7.0, 1 H), 3.71 (q, J = 7.0, 1 H, H-2), 3.86 (br q, J = 4.8, 1 H, H-3), 5.16 (m, 1 H, H-13), 6.11 (dd, J = 16.5, 1.8, 1 H, H-10), 6.91 (dd, J = 16.5, 4.8, 1 H, H-11). 7: 0.10 (s, 9 H), 0.76 (d, J = 7.0, 3 H), 0.88 (d, J = 7.0, 3 H), 1.03 (d, J = 6.6, 3 H), 1.19 (d, J = 7.0, 3 H), 1.35 (s, 3 H), 1.37 (s, 3 H), 1.44 (s, 9 H), 1.89 (m, 1 H), 2.20 (s, 2 H), 2.62 (q, 7.0 1 H), 2.73 (dq, J = 9.9, 6.6, 1 H), 3.35 (d, J = 9.6, 1 H), 3.83 (d, J = 9.9, 1 H). 8: 0.60 (~q, J = 7.7, 6 H), 0.73 (d, J = 7.0, 3 H), 0.87 (d, J = 7.0, 3 H), 0.96 (t, J = 7.7, 9 H), 1.04 (d, J = 7.0, 3 H), 1.09 (d, J = 6.6, 3 H), 1.19 (d, J = 6.6, 3 H), 1.36 (s, 3 H), 1.38 (s, 3 H), 1.45 (s, 9 H), 2.06 (m, 1 H), 2.46 (sext, J = 6.6, 1 H), 2.73 (dq, J = 9.9, 6.6, 1 H), 2.86 (sext, J = 7.0, 1 H), 3.35 (dd, J = 9.6, 1.8, 1 H), 3.57 (dt, J = 6.3, 5.2, 1 H), 3.83 (dd, J = 9.9, 1.8, 1 H), 6.17 (dd, J = 15.8, 1.1, 1 H), 6.91 (dd, J = 15.8, 7.4, 1 H). 9: 0.74 (d, J = 6.6, 3 H), 0.87 (d, J = 7.0, 3 H), 0.97 (t, J = 7.3, 3 H), 0.99 (d, J = 6.3, 3 H), 1.1 (2 d, J = 7.0, 6 H), 1.19 (d, J = 6.6, 3 H), 1.36 (s, 3 H), 1.38 (s, 3 H), 1.45 (s, 9 H), 2.06 (m, 1 H), 2.43 (sext, J = 6.6, 1 H), 2.73 (dq, J = 9.9, 7.0, 1 H), 2.90 (sext, J = 7.0, 1 H), 3.36 (dd, J = 9.6, 1.8, 1 H), 3.50 (m, 1 H), 3.84 (dd, J = 9.9, 1.8, 1 H), 6.24 (dd, J = 15.8, 1.1, 1 H), 6.86 (dd, J = 15.8, 7.8, 1 H). 12: 0.77 (d, J = 6.6, 3 H), 0.83 (d, J = 6.6, 3 H), 0.97 (t, J = 7.4, 3 H), 1.10 (d, J = 7.0, 3 H), 1.11 (d, J = 7.0, 3 H), 1.24 (d, J = 6.6, 3 H), 1.41 (s, 6 H), 2.08 (m, 1 H), 2.45 (sext, J = 6.6, 1 H), 2.67 (dq, J = 9.9, 7.0, 1 H), 2.89 (sext, J = 7.0, 1 H), 3.40 (dd, J = 9.6, 1.8, 1 H), 3.51 (m, 1 H), 3.88 (dd, J = 9.2, 1.8, 1 H), 6.24 (dd, J = 15.8, 1.1, 1 H), 6.87 (dd, J = 15.8, 7.7, 1 H). 13: 0.91 (t, J = 7.4, 3 H), 0.97 (d, J = 7.4, 3 H), 0.98 (d, J = 6.6, 3 H), 1.09 (d, J = 6.3, 3 H), 1.14 (d, J = 7.0, 3 H), 1.18 (d, J = 6.6, 3 H), 1.43 (s, 3 H), 1.45 (s, 3 H), 1.87 (bq, J = 6.6, 1 H), 2.16 (m, 1 H), 2.78 (m, 2 H), 2.88 (m, 1 H), 3.77 (dd, J = 10.7, 1.5, 1 H), 3.98 (dd, J = 6.2, 1.8, 1 H), 5.12 (m, 1 H), 6.05 (dd, J = 16.5, 1.8, 1 H), 6.68 (dd, J = 16.5, 5.5, 1 H). 15: 0.93 (t, J = 7.4, 3 H), 0.95 (d, J = 7.0, 3 H), 1.01 (d, J = 7.0, 3 H), 1.12 (d, J = 7.0, 3 H), 1.12 (d, J = 7.0, 3 H), 1.25 (s, 3 H), 1.25 (s, 3 H), 2.56 (dq, J = 9.2, 7.0, 1 H), 2.65 (m, 1 H), 3.52 (m, 1 H), 3.64 (m, 1 H), 5.18 (m, 1 H), 6.11 (dd, J = 16.2, 2.1, 1 H), 6.98 (dd, J = 16.2, 4.8, 1 H).

Tatsuo Kaiho, Satoru Masamune,* Tatsuo Toyoda

Department of Chemistry
Massachusetts Institute of Technology
Cambridge, Massachusetts 02139

Received January 14, 1982