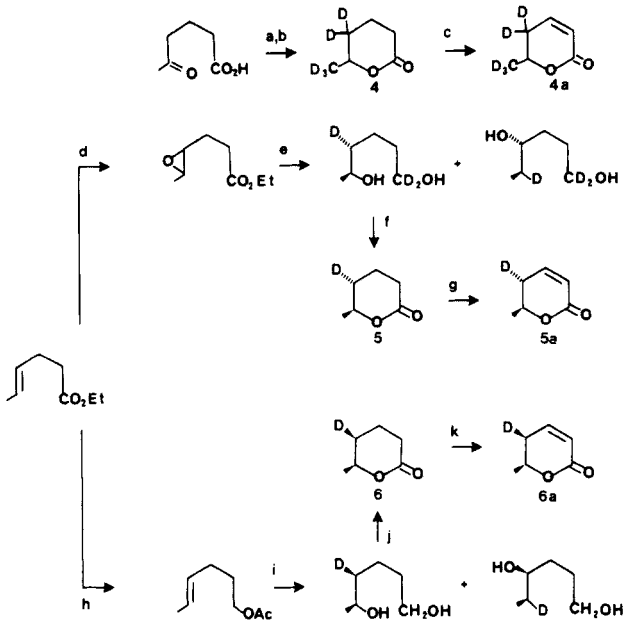
Table I. ^{1}H NMR Spectral Data for Compounds **2-6**[a]

compd	H-2	H-3	H-4 *pro-R*	H-4 *pro-S*	H-5	C-6 CH_3
2	2.5 (m)[b]	1.8-2.0 (m)	1.2-2.0 (m)	1.5 (m)	4.43 (m)	1.36 (d, 6.5)
3	5.94 (ddd, 1.19, 2.53, 9.82)	6.82 (ddd, 5.34, 2.68, 9.82)	2.28 (m)	2.28 (m)	4.51 (dqd, 4.46, 6.55, 10.72)	1.37 (d, 6.55)
4	2.5 (m)	1.8-2.0 (m)	*c*	*c*	4.5 (m)	*c*
5	2.5 (m)	1.8-2.0 (m)	*c*	1.51 (m)	4.42 (m)	1.36 (d, 6.28)
5a	5.98 (dd, 2.68, 9.82)	6.84 (dd, 2.38, 9.82)	*c*	2.25 (m, 2.38, 2.68, 11.76)	4.53 (m, 6.55, 11.76)	1.40 (d, 6.55)
6	2.5 (m)	1.8-2.0 (m)	1.89 (m)	*c*	4.4 (m)	1.35 (d, 6.16)
6a	6.0 (dd, 0.9, 9.53)	6.85 (dd, 5.66, 9.82)	2.33 (m, 0.9, 3.87, 5.66)	*c*	4.56 (m, 3.87, 6.55)	1.42 (d, 6.26)

[a] Spectra were determined at 90, 200, or 270 MHz in $CDCl_3$; assignments are given in parts per million relative to the $CHCl_3$ at δ 7.24 as the internal standard. [b] Signal multiplicities and assignable coupling constants (Hz) are given in parentheses. [c] No signal because of ^{2}H substitution.

Scheme II[a]



[a] (a) NaOD, D_2O/dioxane; (b) $NaBH_4$/dioxane; H^+; 77% combined yield; (c) LDA/THF, -78 °C; PhSSPh, $NaIO_4$, 110 °C; 69% yield; (d) mCPBA/CH_2Cl_2, 0 °C; 52% yield; (e) $LiAlH_4/Et_2O$, 0 °C; 52% yield of 1,5-diol and 98% combined yield; (f) Pt/O_2, $NaHCO_3$; H^+; 28% yield from epoxide; (g) same as (c); 60% yield; (h) $LiAlH_4/Et_2O$; Ac_2O, DMAP (catalyst), CH_2Cl_2; 80% yield; (i) THF:BD_3; H_2O_2/NaOH; 38% yield of 1,5-diol and 80% combined yield; (j) same as (f); 18% yield from olefin acetate; (k) same as (c); 51% yield.

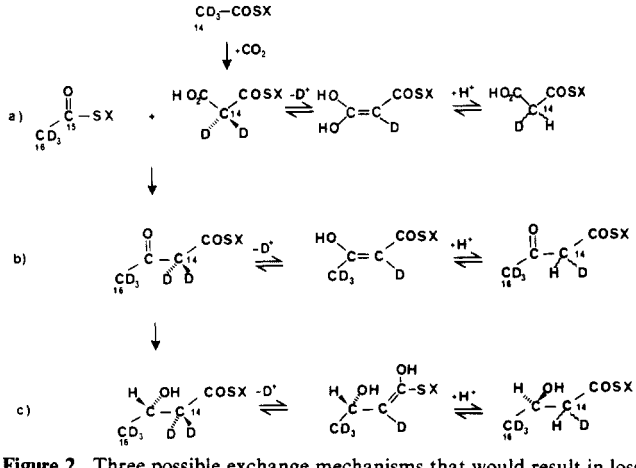


Figure 2. Three possible exchange mechanisms that would result in loss of ^{2}H during the incorporation of [^{2}H]acetate into **1** in vivo. The numbering of intermediates in (a), (b), and (c) corresponds to the positions of **1** that would be labeled by the acetate; X = coenzyme A or enzyme.

primarily at the level of the malonate intermediates and probably nonenzymatically. Malonyl thio esters would be likely candidates since their α-hydrogens are known to be exchangeable easily at physiological pH's.[2a,7,8a] Thus among the three possibilities shown in Figure 2 for proton (deuteron) exchange involving thio ester intermediates, we favor (a). Further hydrogen exchange might occur during the reduction of enoyl thio ester intermediates by analogy to observations made for fatty acid biosynthesis.[8] For brefeldin A, however, this possibility must have a very minor importance since all the positions labeled by [$^2H_3$]acetate (excluding the C-16 methyl group) exhibited a similar amount of ^{2}H loss, including the two, C-6 and C-8, where reduction of enoyl thio esters was postulated to occur.[9]

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Novel Hypervalent (10-I-2) Iodine Structures

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Studies of hypervalent iodine species have focused chiefly on iodinane (10-I-3), periodonium (10-I-4), and periodinane (12-I-5) systems.[1,2] With the exception of the trihalide anions, examples of stable 10-I-2 compounds are rare. The metal-halogen exchange reaction, discovered independently by Gilman[3] and Wittig,[4] has been the subject of numerous studies and mechanistic speculation,

(1) (a) Nguyen, T. T.; Martin, J. C. *Comprehensive Heterocyclic Chemistry*; Katritzky, A. R., Rees, C. W., Eds.; Pergamon Press: New York, 1984; p 563. (b) Koser, G. F. *The Chemistry of Functional Groups, Supplement D*; Patai, S., Rappoport, Z., Eds.; Wiley: New York, 1983; Chapter 18.

(2) For a description of the N-X-L classification scheme as it relates to hypervalency, see: Perkins, C. W.; Martin, J. C.; Arduengo, A. J.; Lau, W.; Alegria, A.; Kochi, J. K. *J. Am. Chem. Soc.* **1980**, *102*, 7753 and references therein.

(3) (a) Gilman, H.; Jacoby, A. L. *J. Org. Chem.* **1938**, *3*, 108. (b) Gilman, H.; Langham, W.; Jacoby, A. L. *J. Am. Chem. Soc.* **1939**, *61*, 106.

(4) Wittig, G.; Pockels, U.; Dröge, H. *Ber.* **1938**, *71*, 1903.

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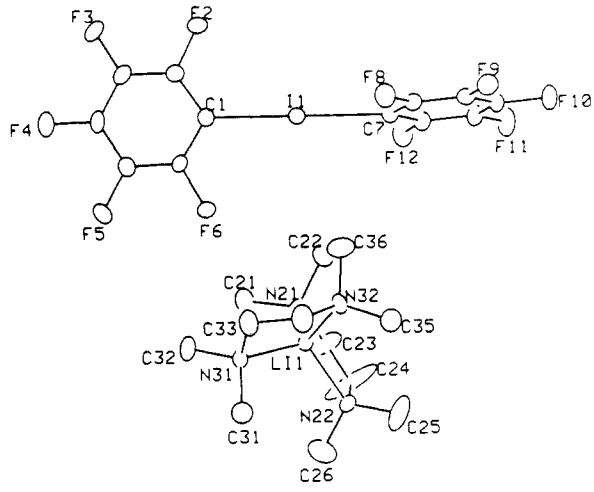

Figure 1.

Table I. Selected Bond Distances (Å) and Angles (deg) for 2

C(7)–I(1)	2.403 (6)	C(3)–C(4)	1.367 (7)
C(1)–I(1)	2.331 (5)	C(2)–F(2)	1.366 (5)
C(1)–C(2)	1.375 (7)	C(3)–F(3)	1.348 (6)
C(2)–C(3)	1.370 (7)	C(4)–F(4)	1.340 (6)
C(1)–I(1)–C(7)	175.2 (2)	C(2)–C(1)–C(6)	114.8 (5)
I(1)–C(1)–C(2)	123.6 (3)	C(3)–C(2)–F(2)	116.6 (5)
C(1)–C(2)–F(2)	119.5 (5)		

including the possible intermediacy of 10-X-2 species, since the late 1930's.[5] Iodinanide complexes (R_2I^- M^+), first suggested by Wittig and Schöllkopf,[6] were recently given supportive kinetic evidence by Reich and co-workers.[7] We wish to report the first isolation and structural characterization of this class of hypervalent iodine species which serves as a model for the lithium–halogen exchange transition state or intermediate.

Upon treatment with 1 equiv of tris(dimethylamino)sulfonium (TAS) perfluoro-*tert*-butyl carbanion,[8] perfluoro-*tert*-butyl iodide yields an adduct whose structure we formulate as **1** (eq 1).

$$TAS^+(CF_3)_3C^- + (CF_3)_3CI \rightarrow \underset{\mathbf{1}}{TAS^+(CF_3)_3C\text{–}I^-\text{–}C(CF_3)_3}$$

Elemental analyses, ^{19}F NMR, and products from several reactions[9] are consistent with this formulation. Since crystals of **1** suitable for X-ray analysis proved difficult to obtain, bis(pentafluorophenyl)iodinanide **2** was prepared by treatment of (pentafluorophenyl)lithium with pentafluorophenyl iodide at −78 °C (eq 2). The lithium salt of this anion may be isolated at −78 °C,

$$C_6F_5Li \xrightarrow[2.\ 2TMEDA]{1.\ C_6F_5I} \underset{\mathbf{2}}{(C_6F_5)_2I^-Li^+\cdot 2TMEDA}$$

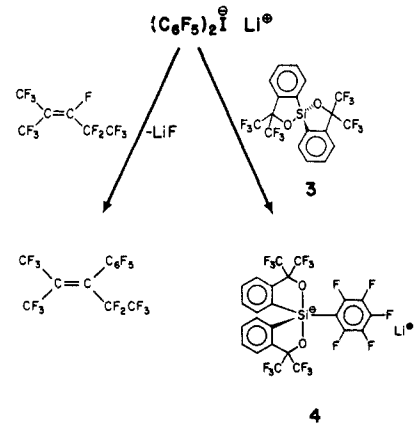

Figure 2.

but it undergoes vigorous exothermic decomposition at higher temperatures. Addition of 2 equiv of tetramethylethylenediamine (TMEDA) to the complex at −78 °C generates a more stable, complexed lithium salt which is isolable under an inert atmosphere and is stable for short periods at room temperature.[10] Although **2** decomposes in solution at 25 °C, suitable crystals were grown at −20 to −30 °C after rapid dissolution in ether at 25 °C.

Single-crystal X-ray diffraction analysis of **2** features a nearly linear C–I–C arrangement (∠C–I–C = 175°) with long carbon–iodine bond distances (2.331 (5), 2.403 (6) Å) (Figure 1, Table I).[11,12] These geometrical factors are readily understood in terms of a hypervalent 10-I-2 system in which the pentafluorophenyl groups serve as apical ligands in a three-center four-electron bonding scheme.[13,14] Each lithium ion is coordinated by two TMEDA molecules.[15]

Preliminary studies of adduct **2** show that it reacts with electrophiles, delivering a C_6F_5 group and liberating equimolar quantities of pentafluorophenyl iodide. For example, treatment of **2** with perfluoro-2-methyl-2-pentene yields perfluoro-2-

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(6) Wittig, G.; Schöllkopf, U. *Tetrahedron* **1958**, *3*, 91.

(7) Reich, H. J.; Phillips, N. H.; Reich, I. L. *J. Am. Chem. Soc.* **1985**, *107*, 4101.

(8) Smart, B. E.; Middleton, W. J.; Farnham, W. B., submitted for publication in *J. Am. Chem. Soc.*

(9) (a) Preparation of **1**: A mixture of TAS perfluoro-*tert*-butyl carbanion (385 mg, 1.0 mmol) and perfluoro-*tert*-butyl iodide (346 mg, 1.0 mmol) was dissolved in THF (4.0 mL) and allowed to stand for 0.5 h. Solvent was evaporated, and the residue was treated with ether (5.0 mL) and Freon-113 (5.0 mL). Evaporation provided 720 mg of white solid, mp 80–81 °C. ^{19}F NMR (THF-d_8): −56.97 (s). Anal. Calcd for $C_{14}H_{18}F_{18}N_3SI$: C, 23.06; H, 2.49; N, 5.76; F, 46.90; S, 4.40; I, 17.40. Found: C, 22.93; H, 2.77; N, 6.81; F, 47.14; I, 17.24. (b) Reactions of **1** (reagent, solvent, temperature, products): $CH_3OSO_2CF_3$, CH_2Cl_2, 25 °C, $(CF_3)_3CCH_3$ + $(CF_3)_3CI$ + TAS CF_3SO_3; $C_6H_5N_2$ PF_6, THF, 25 °C, $(CF_3)_3CNNC_6H_5$ + $(CF_3)_3CI$ + TAS PF_6.

(10) Preparation of **2**: (Pentafluorophenyl)lithium, prepared by dropwise addition of bromopentafluorobenzene (2.44 g, 10 mmol) to a solution of butyllithium (10 mmol) in 50/50 ether/petroleum ether (30 mL) at −78 °C, was treated dropwise with iodopentafluorobenzene (2.92 g, 10 mmol). The resulting slurry was treated with ether (30 mL) and then dropwise with tetramethylethylenediamine (3.05 mL, 20 mmol). The mixture was stirred for 1.5 h at −78 °C, transferred quickly to a drybox, and filtered to provide 6.36 g (90%) of off-white solid. Rapid dissolution in ether and cooling to −30 °C gave colorless needles, mp 77 °C dec. ^{19}F NMR (glyme-d_{10}, dissolved and recorded at −20 °C without F-11 internal standard): −122.05 (m, 2 F), −163.70 to −164.50 (overlapping m, 3 F). Anal. Calcd for $C_{24}H_{32}F_{10}N_4ILi$: C, 41.16; H, 4.61; N, 8.00; F, 27.13; I, 18.12. Found: C, 40.29; H, 4.39; N, 8.03; F, 28.55; I, 18.30.

(11) Crystal structure information for **2**: triclinic; space group $P\bar{1}$ (No. 2); a = 9.945 (1) Å, b = 16.982 (2) Å, c = 9.540 (1) Å, V = 1483.2 Å^3, Z = 2; T = −100 °C. Data collected on a Syntex R3 diffractometer, graphite monochromator, Mo Kα radiation, λ = 0.710 69 Å; 4655 reflections, 4.4° ≤ 2θ ≤ 53.0°, 3163 unique reflections with $I \geq 3.0\sigma(I)$. Structure solved by automated Patterson analysis (PHASE); full-matrix, least-squares refinement with scattering factors from *International Table for X-ray Crystallography*, Vol. IV, including anomalous terms for I. All hydrogens refined isotropically, other atoms, anisotropically. Final R = 0.035, R_w = 0.036 for 361 independent variables.

(12) Few C–I distances have been determined for polyfluorinated aromatic systems. We regard 1,4-diiodo-2,3,5,6-tetrafluorobenzene, wherein the C–I distance is 2.089 Å, as representative of this class. See: Chaplot, S. L.; McIntyre, G. J.; Mierzejewski, A.; Pawley, G. S. *Acta Crystallogr., Sect. B* **1981**, *B37*, 2210.

(13) Factors responsible for the unequal C–I bond lengths are not understood. Unequal bond distances for various trihalide ions (e.g., I_3^-) have been reported and explained on the basis of asymmetric crystal environments. See: Alcock, N. W. *Adv. Inorg. Chem. Radiochem.* **1972**, *15*, 1. Wiebenga, E. H.; Kracht, D. *Inorg. Chem.* **1969**, *8*, 738. Carpenter, G. B. *Acta Crystallogr.* **1966**, *20*, 330. Migchelsen, T.; Vos, A. *Acta Crystallogr.* **1967**, *23*, 796.

(14) The iodinanide is apparently stabilized by electron-withdrawing pentafluorophenyl groups. Our attempts to isolate lithium diphenyliodinanide from reaction of phenyllithium with iodobenzene have not been successful.

(15) Structural features of the coordinated cation are similar to those of $Li^+(TMEDA)_2$ in an otherwise unrelated complex. See: Jonas, K.; Pörschke, K. R.; Krüger, C.; Tsay, Y. H. *Angew. Chem., Int. Ed. Engl.* **1976**, *15*, 621.

methyl-3-phenyl-2-pentene as the nearly exclusive (92%) product.[16] Addition of spiro silane **3** yields the pentafluorophenyl siliconate **4**[17] (Figure 2). While these reactions may involve the iodinanide directly, we have not ruled out the likelihood that "free" pentafluorophenyl lithium is responsible for the observed products.[18]

Supplementary Material Available: Tables of fractional coordinates and isotropic thermal parameters, anisotropic thermal parameters, interatomic and intermolecular distances, and intramolecular angles (4 pages). Ordering information is given on any current masthead page.

(16) Replacement of vinylic fluorine in perfluoro olefins by organolithium reagents is a known reaction. See: Hudlicky, M. *Chemistry of Organic Fluorine Compounds*; Ellis Horwood Ltd.: Sussex, England, 1976; Chapter 5.

(17) Stevenson, W. H., III; Wilson, S.; Martin, J. C.; Farnham, W. B. *J. Am. Chem. Soc.* **1985**, *107*, 6340.

(18) Although we have not isolated perfluoro-*n*-alkyl congeners of iodinanide **2**, our results suggest a reinterpretation of the finding by P. Johncock (Johncock, P. *J. Organomet. Chem.* **1969**, *19*, 257) that perfluoro-*n*-heptyllithium is stabilized by excess perfluoro-*n*-heptyl iodide. Formation of perfluoroalkyl iodinanide complexes at low temperature would handily account for the results of the earlier work. We thank Professor H. J. Reich for bringing this reference to our attention.

Total Synthesis of (+)-Latrunculin B

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In 1980 Kashman reported the isolation and structure elucidation of two novel toxins, termed latrunculin A and B (**1** and **2**, Scheme I), derived from the Red Sea Sponge, *Latrunculia magnifica* (Keller).[3] Colonies of this sponge, found in the Gulf of Eilat, grow completely exposed to the hostile sea environment.[3] The sponge, however, is not damaged or eaten by fish or other predators. Indeed, when disturbed the sponge emits a reddish fluid which causes nearby fish to flee the vicinity.[3] The structure of latrunculin A (**1**) including absolute stereochemistry was secured through a combination of X-ray analysis[3b,d] and chemical degradation,[3e] while the structure of latrunculin B (**2**) derived from spectroscopic comparison with that of latrunculin A (**1**).

Our interest in the latrunculins stemmed not only from their novel architecture but also from the report that the latrunculins induce a reversible reorganization of the cytoskeletal proteins.[4] We set as our goal the development of an advanced subtarget that would be amenable to the total synthesis of both latrunculin A and B, as well as possible structural analogues of biological interest.[5] We record here the first total synthesis of (+)-latrunculin B (**2**).

(1) Recipient of an ACS Division of Organic Chemistry Graduate Fellowship sponsored by Merck, Sharp & Dohme Research Laboratories (1984-1985).

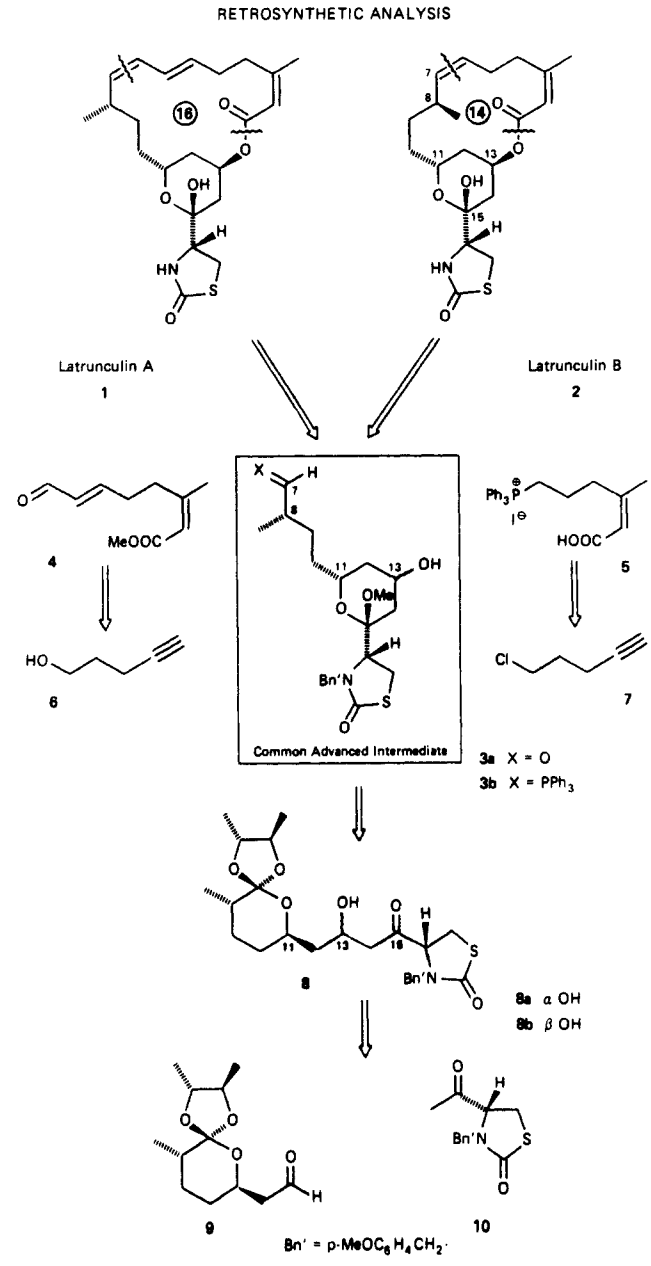
(2) Camille and Henry Dreyfus Teacher-Scholar, 1978-1983, NIH Career Development Awardee, 1980-1985, and J. S. Guggenheim Foundation Fellow, 1985-1986.

(3) (a) Neeman, I.; Fishelson, L.; Kashman, Y. *Mar. Biol.* **1975**, *30*, 293. (b) Kashman, Y.; Groweiss, A.; Shmueli, U. *Tetrahedron Lett.* **1980**, *21*, 3629. (c) Spector, I.; Shochet, N. R.; Kashman, Y.; Groweiss, A. *Science (Washington, D.C.)* **1983**, 493. (d) Groweiss, A.; Shmueli, U.; Kashman, Y. *J. Org. Chem.* **1983**, *48*, 3512. (e) Kashman, Y.; Groweiss, A.; Lidor, R.; Blasberger, D.; Carmely, S. *Tetrahedtron* **1985**, *41*, 1905.

(4) A recent study by Spector et al. on the effects of the latrunculins on cultured mouse neuroblastoma and fibroblast cells demonstrated that submicromolar amounts of the latrunculins induce changes in the cell morphology (cytoskeletal proteins) which proved reversible upon removal of the toxins.[3c]

(5) Preliminary accounts of this work were presented at the 1984 International Chemical Congress of Pacific Basin Societies, Honolulu, HI, 1984, ORGN 10E36, and the 189th National Meeting of the American Chemical Society, Miami, FL, 1985, ORGN 1.

Scheme I



From the retrosynthetic perspective, cleavage of the macrolide linkage and scission of the cis olefin led to an advanced southern hemisphere (aldehyde **3a** for latrunculin B or ylide **3b** for latrunculin A). The requisite northern hemispheres (**4** or **5**) were envisioned to derive from an appropriately functionalized acetylene; union via a Wittig reaction[6] would then be followed by macrocyclization.[7] Further simplification of advanced intermediate **3a** by ring opening and reorganization led to β-hydroxy ketone **8**, the aldol product of **9** and **10**.

We recognized that our strategy possessed considerable flexibility via-ã-vis the stereochemical outcome of the aldol process. If, for example, the C(13)-*R* configuration were to prevail, direct macrolactonization would be required.[7] Alternatively, if the *S* configuration at C(13) were to predominate, macrolactonization would require inversion.[8] Well aware of the general lack of diastereofacial selectivity observed for methyl ketone enolates,[9a]

(6) For reviews on the Wittig olefination process, see: Trippett, S. *Q. Rev. Chem. Soc.* **1963**, *17*, 406. Maercker, A. *Org. React.* **1965**, *14*, 270.

(7) Masamune, S.; Bates, G. S.; Corcoran, J. W. *Angew. Chem., Int. Ed. Engl.* **1977**, *16*, 585. Nicolaou, K. C. *Tetrahedron* **1977**, *33*, 683. Back, T. G. *Tetrahedron* **1977**, *33*, 3041.

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