stereochemistry (Figure 1), and the derived bond lengths agree with the high-spin electronic configuration. The Mn-P distance compares favorably with that found (2.625 Å) in $MnCl_2(LL)_2$, LL = *o*-phenylenebis(dimethylphosphine).[3a]

The reaction of $MnBr_2(dmpe)_2$ with excess $LiAlH_4$ in toluene gives a yellow diamagnetic Mn^I complex of stoichiometry $Mn(AlH_4)(dmpe)_2$. Infrared stretches at 1740, 1610, and 970 cm^{-1} may be assigned to various Al-H and Mn-H-Al modes.[6] In the ^1H NMR spectrum, a Mn*H*Al hydride resonance occurs at δ -15.02 broadened due to the quadrupole moments of manganese and aluminum. A terminal AlH signal at δ +5.05 is similarly broadened, although to a lesser extent; the ratio of bridging to terminal hydrides is 1:1 by integration. The dmpe ^1H and $^{13}C\{^1H\}$ NMR resonances indicate a cis-octahedral arrangement about manganese, while the $^{31}P\{^1H\}$ NMR spectrum is uninformative, again due to quadrupolar effects.

In view of the rarity of transitional-metal AlH_4 complexes, we have determined the X-ray crystal structure of $Mn(AlH_4)(dmpe)_2$ (Figure 2).[7] In the solid state the compound exists as a centrosymmetric dimer, $[Mn(AlH_4)(dmpe)_2]_2$, due to the formation of a $Mn(\mu\text{-}H_2)AlH(\mu\text{-}H)_2AlH_2(\mu\text{-}H)_2Mn$ bridge. The aluminum atoms have trigonal-bipyramidal geometries. The dihydride bridges are all formed from one axial and one equatorial hydrogen atom on each aluminum. The central $Al(\mu\text{-}H)_2Al$ unit is asymmetric, with the long and short Al-H distances differing by ca. 0.2 Å. Thus, the molecule can be thought of as a loosely bound dimer, and this is compatible with the monomeric structure implied by the solution NMR data. In the $Mn(\mu\text{-}H)_2Al$ units, the Mn-H distances are equal and shorter than the two Al-H distances by 0.2 Å, indicating a strong affinity of the hydrides for the manganese atom. The geometries about Mn are cis octahedral, with the Mn-P distances trans to the hydrides being slightly *shorter* than the Mn-P distances trans to each other.

Although this is the first example of a transition-metal AlH_4^- complex to be structurally determined, other complexes containing M-H-Al bridges have been examined crystallographically.[8] The structure of $[Ta(AlH_2(OCH_2CH_2OMe)_2)(dmpe)_2]_2$[8d] is similar to the manganese molecule described here, but as is often the case,[8b-e] the hydrogen atoms were not located.

Alkylation of $MnBr_2(dmpe)_2$ with $MgMe_2$ in diethyl ether gives red *trans*-$MnMe_2(dmpe)_2$. This complex is low spin (μ = 2.4 μ_B); evidently, the stronger ligand field strength of alkyls relative to halides is sufficient to effect spin pairing. This is substantiated by the X-ray crystal structure,[9] which shows that the Mn-P distances are ca 0.4 Å shorter than in *trans*-$MnBr_2(dmpe)_2$.

Alkylation of $MnBr_2(dmpe)_2$ with $MgEt_2$ in diethyl ether gives the yellow diamagnetic Mn^I complex *trans*-$MnH(CH_2{=}CH_2)(dmpe)_2$ presumably by β-hydride transfer in an intermediate ethyl compound. The NMR parameters are consistent with a trans-octahedral structure, with rotation of the ethylene being fast on the NMR time scale. Only two other ethylene complexes of manganese are known, both being carbonyl species.[10]

Acknowledgment. We thank C. G. Howard for helpful discussions, the SERC for support of the X-ray work, and the National Science Foundation for a NATO Postdoctoral Fellowship (G.S.C.).

Registry No. *trans*-$MnBr_2(dmpe)_2$, 87450-48-4; *trans*-$MnI_2(dmpe)_2$, 87450-51-9; $[Mn(AlH_4)(dmpe)_2]_2$, 87450-49-5; *trans*-$MnMe_2(dmpe)_2$, 87450-50-8; *trans*-$MnH(CH_2{=}CH_2)(dmpe)_2$, 87450-52-0.

Supplementary Material Available: Atom coordinates, anisotropic temperature factors, bond lengths, and bond angles for $MnBr_2(dmpe)_2$ and $[Mn(AlH_4)(dmpe)_2]_2$ (5 pages). Ordering information is given on any current masthead page.

(6) Nakamoto, K. "Infrared and Raman Spectra of Inoganic and Coordination Compounds", 3rd ed.; Wiley-Interscience: New York, 1978.

(7) Monoclinic, crystals from light petroleum, space group $P2_1/n$, with a = 9.313 Å, (2) Å, b = 13.515 Å, (3) Å, c = 16.912 (3) Å, β = 97.01 (2)°, V = 2121.5 Å^3, Z = 2 dimeric units, R_y = 0.0415, (R_w = 0.0455) for 3131/3716 observed data [$F_o > 3\sigma(F_o)$]. All the hydrogen atoms were experimentally located and freely refined with individual isotropic thermal parameters.

(8) (a) Guggenberger, L. J.; Tebbe, F. N. *J. Am. Chem. Soc.* **1973**, *95*, 7870-7872. (b) Rettig, S. J.; Storr, A.; Thomas, B. S.; Trotter, J. *Acta Crystallogr., Sect. B* **1974**, *B 30*, 666-673. (c) Forder, R. A.; Prout, K. *Ibid.* 1974, *B30*, 2312-2317. (d) McNeese, T. J.; Wreford, S. S.; Foxman, B. M. *J. Chem. Soc., Chem. Commun.* **1978**, 500-501. (e) Kopf, J.; Vollmer, H.-J.; Kaminsky, W. *Cryst. Struct. Commun.* **1980**, *9*, 985-9880.

(9) Monoclinic, crystals from light petroleum, space group $P2_1/n$, with a = 9.576 Å, (2) Å, b = 12.642 Å, (3) Å, c = 8.953 (2) Å, β = 90.13 (2)°, V = 1083.8 Å^3, Z = 2, R = 0.12 for 1234/1907 observed data. Refinement has been hindered due to severe disorder of the dmpe ligands, and the results must be considered preliminary. In spite of the problems, the centrosymmetric trans structure is well-defined, and we consider the Mn-P and Mn-C distances of 2.241 (5)-2.251 (4) and 2.20 (2) Å to be reliable.

(10) (a) Fischer, E. O.; Kogler, H. P. *Z. Naturforsch.* **1960**, *16*, 676. (b) Fischer, E. O.; Ofele, K. *Angew. Chem.* **1961**, *73*, 581. (c) Green, M. L. H.; Nagy, P. L. I. *J. Organomet. Chem.* **1963**, *1*, 58-69. (d) Angelici, R. J.; Loewen, W. *Inorg. Chem.* **1967**, *6*, 682-686.

α-Substitution-Spiroannulation of Saturated Ketones

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The elaboration of molecular architecture around a carbonyl group constitutes the most important approach for the synthesis of complex molecules. Substitution at the α-position and replacing the C-O bonds by C-C bonds, normally only one but occasionally both C-O bonds,[1,2] forms the heart of this approach. Improving the efficiency and selectivity of this strategy represents an important goal. Based upon the concept of small strained rings as pseudofunctional groups and their ease of introduction at a carbonyl group,[2] we envisioned a stereocontrolled approach for the replacement of both C-O bonds of the carbonyl group (i.e., a geminal alkylation) and simultaneous introduction of substituents at the position α to a carbonyl group as shown in eq 1.

(1)

Vinylcyclopropanols are readily available from saturated ketones by a straightforward process. Reacting the ketones with cyclopropyldiphenylsulfonium fluoroborate and powdered potassium hydroxide in Me_2SO at room temperature produces oxaspiropentanes in virtually quantitative yield.[3] Extraction of the Me_2SO solution with pentane followed by exposure of the oxaspiropentane solution to lithium diethylamide generates the vinylcyclopropanol in 70-90% isolated yield as shown in Scheme I for cyclopentanone.[3,4] Chemoselective addition of an electrophile to the double bond of **1** should initiate ring expansion to the cyclobutanone.[5-7] Since secosulfenylation[8] and secobromination[9] (a

(1) For reviews, see: Martin, S. F. *Tetrahedron*, **1980**, *36*, 419. Krapcho, A. P. *Synthesis*, **1974**, 383.

(2) For an approach based upon small ring conjuctive reagents, see: Trost, B. M. *Acc. Chem. Res.* **1974**, *7*, 85. *Pure Appl. Chem.* **1975**, *43*, 563. For some recent related work, see: Halazy, S.; Lucchetti, J.; Krief, A. *Tetrahedron Lett.* **1978**, 3971. Cohen, T.; Matz, J. R. *Ibid.* **1981**, *22*, 2455. Trost, B. M.; Keeley, D. E.; Arndt, H. C.; Bogdanowicz, M. J. *J. Chem. Soc.* **1979**, *99*, 3088.

(3) (a) Trost, B. M.; Bogdanowicz, M. J. *Tetrahedron Lett.* **1972**, 887; (b) *J. Am. Chem. Soc.* **1973**, *95*, 5311.

(4) Trost, B. M.; Bogdanowicz, M. J. *J. Am. Chem. Soc.* **1973**, *95*, 289. Trost, B. M.; Kurozumi; S. *Tetrahedron Lett.* **1974**, 1929. Trost, B. M.; Hishimura, Y.; Yamamoto, K. *J. Am. Chem. Soc.* **1979**, *101*, 1328. Girard, C.; Amice, P.; Barnier, J. P.; Conia, J. M. *Tetrahedron Lett.* **1974**, 3329. Girard, C.; Conia, J. M. *J. Chem. Res.* **1978**, 183. Salaun, J.; Ollivier, J. *Nouv. J. Chim.* **1981**, *5*, 587.

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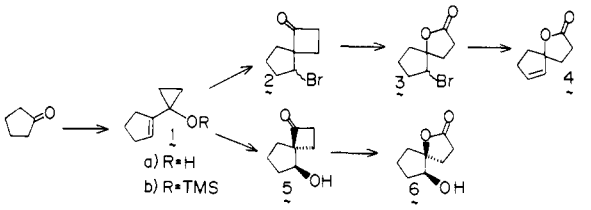
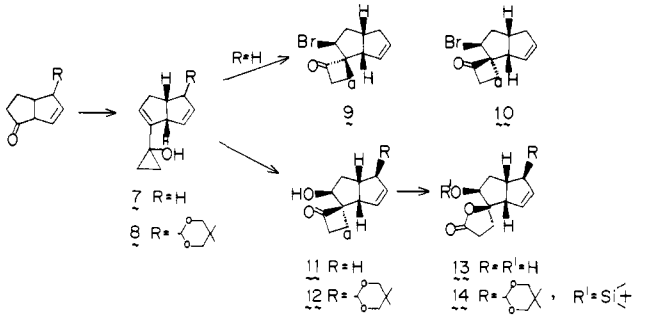
Scheme I. α-Substitution–Spiroannulation of Cyclopentanone



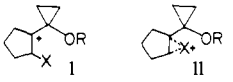
Scheme II



haloform-type) converts cyclobutanones into two chemodifferentiated alkyl groups, the conversion of **1** to **2** constitutes an equivalent of a substitution–spiroannulation and consequently geminal alkylation as shown in eq 1. Whether stereocontrol could be exercised in such an electrophilically initiated ring expansion is an unanswered but important question.

Reacting **1b** with dioxane–bromine complex effects ring expansion to the bromocyclobutanone **2**[10] as a 1:1 stereoisomeric mixture. The lability of **2** led us to treat it with 1 equiv of MCPBA to give the bromolactone **3** in 84% yield also as a 1:1 stereoisomeric mixture. Elimination of the elements of HBr from **3** (DBU, PhH, reflux) completes a conversion of a saturated ketone to an unsaturated γ-butyrolactone **4**.[10]

The lack of stereochemical control in the rearrangement of **1** to **2** presumably reflects the fact that the intermediate is an open ion as shown in I. If a bridged or partially bridged species such

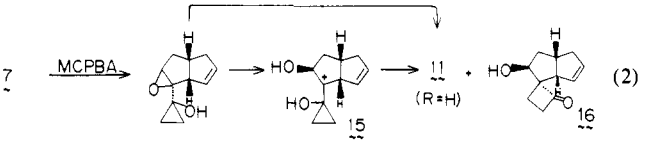


as II, regardless of how unsymmetrical the bridge might be, were involved, ring expansion may accompany opening of the bridged ion to give stereochemical control. A protonated epoxide would be such a case. Indeed, treatment of **1** with *tert*-butyl hydroperoxide in the presence of a vanadium catalyst[11] [$VO(acac)_2$ or $(Ph_3SiO)_3VO$][12] in toluene at −10 °C to room temperature leads to a unique cyclobutanone **5**, which has also been converted to its lactone **6**. The facility of the rearrangement precludes even detecting the presumed epoxide intermediate.

The vinylcyclopropanols **7** and **8**, available from their respective ketones as outlined above, extend the question of stereochemical control to more distal centers as well as raise the question of chemoselectivity. Treatment of **7** with 1 equiv of bromine–dioxane complex at −78 °C in methylene chloride gives a 75% yield of **9** and **10** as a 1:1 stereoisomeric mixture.[10] Anticipating that the Br^+ attacks from the convex face of the bicyclo[3.3.0]octane system, stereorandom migration would produce the two cyclobutanone isomers **9** and **10** (Scheme II). In accordance with our earlier correlation of ^{13}C chemical shifts for C(a) with stereochemistry at the spiro carbon,[13] **9** shows the signal for this carbon at δ 23.24; whereas, that for **10** appears at δ 17.80.

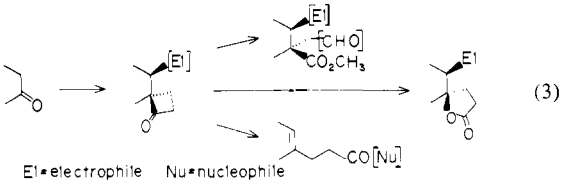
The vanadium-catalyzed epoxidation of both **7** and **8** chemoselectively effects hydroxyl-initiated ring enlargement to a single stereoisomer in each case (i.e., **11**[10] and **12**,[11] respectively) in 61–65% isolated yields. The δ 18.5 shift for C(a) in both products supports the stereochemistry of the spiro center depicted. In each case, the cyclobutanone was further characterized by the Baeyer–Villiger oxidation with basic hydrogen peroxide to the hydroxy lactones **13**[10] and **14**.[10] In the case of **12**, the yield improved from 46% to 92% if the free alcohol is silylated prior to the Baeyer–Villiger oxidation.

To show how sensitive the stereochemistry of this process is to reaction conditions, we compared the vanadium-catalyzed epoxidation to that of MCPBA even in the presence of buffer. With the latter, **7** gave a 2:1 stereoisomeric mixture of **11** (R = H) and **15** in contrast to the obtention of an isomerically pure product in the vanadium-catalyzed reaction. We attribute this observation to a competition between the direct rearrangement of the intermediate epoxide to **11** (R = H) and an acid-catalyzed ring opening to give an open cation **15**, which produces both stereoisomeric products (eq 2).



(2)

Thus, starting from saturated ketones, an electrophile can be introduced at the α carbon and the two C–O bonds of the carbonyl group be replaced by two C–C bonds simultaneously. Furthermore, such a transformation can be accomplished with high stereocontrol. In principle, a wide range of electrophiles including carbon electrophiles can be envisioned to participate in such a reaction. The facts that α-bromo and α-hydroxyketones are generally poor substrates for spiroannulation as well as their flexibility for further synthetic elaboration led us to concentrate on these two. It is interesting to note that ring opening of the cyclopropanol by the electrophile does not compete with attack of the electrophile on the double bond. The high reactivity of the double bond of the vinyl cyclopropanol toward electrophiles in comparison to other functionality raises interesting mechanistic questions in addition to its practical importance in terms of chemoselectivity. As summarized in eq 3, in addition to sub-



(3)

E¹ = electrophile Nu = nucleophile

(5) For pioneering work, see: Wasserman, H. H.; Hearn, M. J.; Cochoy, R. E. *J. Org. Chem.* **1980**, *45*, 2874 and earlier references therein.

(6) For proton-initiated ring expansion, see: Reference 3b. Salaun, J.; Garnier, B.; Conia, J. Lm. *Tetrahedron*, **1974**, *30*, 1413. Bourelli-Wargnier, F. *Tetrahedron Lett.* **1974**, 1589.

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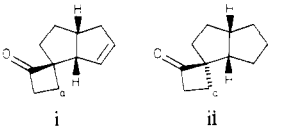
(10) All new compounds have been fully characterized by spectral means and elemental composition determined by high-resolution mass spectroscopy and/or combustion analysis.

(11) For a review, see: Sharpless, K. B.; Verhoeven, T. R. *Aldrichimica Acta* **1979**, *12*, 63.

(12) We believe this is the first report of this reagent as an epoxidation catalyst. For the compound, see: Pauling, H. *Chimia*, **1973**, *27*, 383.

(13) Trost, B. M.; Scudder, P. *J. Am. Chem. Soc.* **1977**, *99*, 7601. This method was used to assign stereochemistry in all cases. As a benchmark the signal for C(a) in the ^{13}C nMR spectra of i, ii, and iii appears at δ 18.5, 19.9, and 26.7.



i ii

stitution–spiroannulation, when El = a leaving group, nucleophilic-promoted fragmentation can be achieved to constitute an alkylative elimination or secoalkylation sequence[14] from a saturated ketone.

Acknowledgment. We thank the National Science Foundation for their generous support of our programs.

Registry No. 1b, 37609-29-3; **2** (isomer 1), 86971-86-0; **2** (isomer 2), 86971-87-1; **3** (isomer 1), 86971-88-2; **3** (isomer2), 86971-89-3; **4**, 86971-90-6; **5**, 86971-91-7; **6**, 86971-92-8; **7**, 86971-93-9; **8**, 86971-94-0; **9**, 86971-95-1; **10**, 87037-57-8; **11**, 82517-58-6; **12**, 86971-96-2; **13**, 82517-59-7; **14**, 86971-97-3; **15**, 86971-98-4; **16**, 87037-58-9.

(14) Trost, B. M.; Bogdanowicz, M. J. *J. Am. Chem. Soc.* **1972**, *94*, 4777. Trost, B. M.; Bogdanowicz, M. J.; Frazee, W. J.; Salzmann, T. N. *Ibid.* **1978**, *100*, 5512.

Biomimetic Approach to Plumericin

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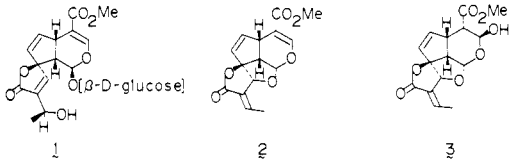
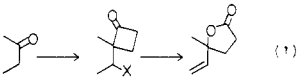
In 1951, Little and Johnstone isolated a compound that exhibited antifungal, antibacterial, and subsequently antitumor activity.[1] The compound, called plumericin, has been shown to possess the structure **2** by Albers-Schonberg and Schmid.[2] Closely related to plumericin is a hydrated analogue **3** known as allamandin,[3] a compound also possessing high antitumor activity. These densely functionalized molecules represent substantial synthetic challenges. A strategy emerges from the possibility that plumeride (**1**)[4,5] may be a biosynthetic precursor of plumericin.



1 2 3

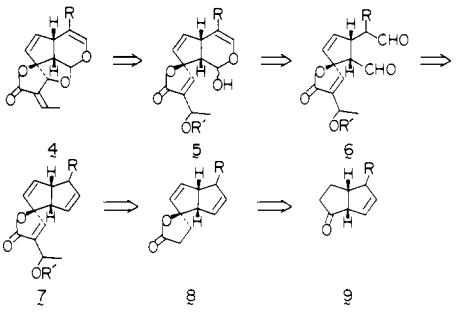
This suggestion led us to consider a conjugate addition–elimination approach for the formation of the tetrahydrofuran unit which simplifies the problem to **5** (see Scheme I). The dihydropyran ring of **5** represents a cyclized form of a dialdehyde such as **6**, which in turn, may derive from an oxidative cleavage of an olefin as in **7**. Anticipating that the butenolide substitution of **7** can evolve from the reactivity of the enolate of a saturated lactone as in **8**, a major structural simplification to the saturated ketone **9** is permitted by use of the concept of substitutive spiroannulation as embodied in eq 1. The establishment of the stereochemistry



(1)

of the five chiral centers of **4** factors to the stereochemistry of the conversion of **9** to **8** since only the α-anomer of **5** can geometrically reach to form **4**. While, at first glance, the need for the carbomethoxy group at C(4) of **2** tempts us to incorporate that carbon from the start, the fact that **9** (R = H) is a well-known

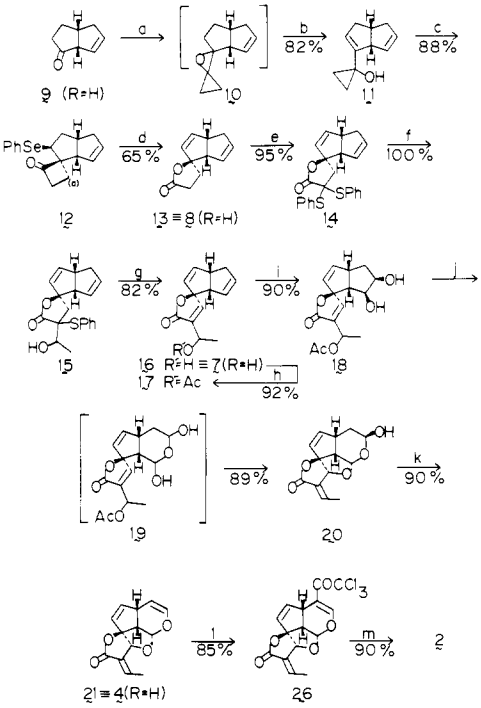
Scheme I



4 5 6

7 8 9

Scheme II[a]



[a] (a) ▷—$S^+Ph_2BF_4^-$, KOH, Me_2SO, room temperature; (b) LiN$(C_2H_5)_2$, pentane, room temperature; (c) PhSeBr (1.5 equiv), $(C_2H_5)_3N$ (2.0 equiv), CH_2Cl_2, −40 °C; (d) MCPBA, CH_2Cl_2, −78 → 0 °C then add $CH_2{=}CHOC_2H_5$, room temperature; (e) LDA, THF, then $PhSSO_2Ph$, THF, −78 °C → room temperature; (f) C_2H_5MgBr, ether, THF, 0 °C, then CH_3CHO; (g) MCPBA, CH_2Cl_2, −78 °C → room temperature, then CCl_4, $CaCO_3$, reflux; (h) Ac_2O, C_5H_5N, DMAP, 0 °C; (i) cat OsO_4,  $\cdot H_2O$ THF, H_2O, 0 °C; (j) $NaIO_4$ (3 equiv), ether, H_2O, room temperature, then add NaOAc; (k) Ac_2O, DMAP, $(i\text{-}C_3H_7)_2NC_2H_5$, CH_2Cl_2, room temperature, and distill crude through quartz tube at 500 °C; (l) CCl_3COCl (50 equiv), 2,6-$(t\text{-}C_4H_9)_2C_5H_3N$ (5 equiv), CH_2Cl_2, room temperature; $Mg(OCH_3)_2$, CH_3OH, THF, −45 °C; (n) All new compounds have been fully characterized by spectral means, and elemental composition was determined by combustion analysis and/or high-resolution mass spectroscopy.

compound both in the racemic[6] and optically active[7] form led us to gamble that, even though methodology did not exist for the carbomethoxylation of an enol ether at the start of this program, a method could be found to carbomethoxylate descarbometh-

(1) Little, J. E.; Johnstone, D. B. *Arch. Biochem.* **1951**, *30*, 445.
(2) Albers-Schonberg, G.; Schmid, G. *Helv. Chim. Acta* **1961**, *44*, 1447.
(3) Kupchan, S. M.; Dessertine, A. L.; Blaylock, B. T.; Bryan, R. F. *J. Org. Chem.* **1974**, *39*, 2477.
(4) Schmid, H.; Bickel, H.; Meijer, T. M. *Helv. Chim. Acta*, **1952**, *35*, 415. Halpern, O.; Schmid, H. *Ibid.* **1958**, *41*, 1105.
(5) Also see: Inoue, K.; Takeda, Y.; Nishimura, H.; Inouye, H. *Chem. Pharm. Bull.* **1979**, *27*, 3115.

(6) Available in 80% yield in 3 steps from 1,3-cyclooctadiene. Apparu, M.; Barrelle, M. *Tetrahedron* **1978**, *34*, 1541. Whitesell, J. K.; Matthews, R. S.; Wang, P. K. S. *Synth. Commun.* **1977**, *7*, 355. Crandall, J. K.; Banks, D. B.; Colyer, R. A.; Watkins, R. J.; Arrington, J. P. *J. Org. Chem.* **1968**, *33*, 423. LeBel, N. A.; Spurlock, L. A. *Tetrahedron* **1964**, *20*, 215.
(7) Kuritani, H.; Takaoka, Y.; Shingu, K. *J. Org. Chem.* **1979**, *44*, 452.
Note Added in Proof: An additional method for resolution of the alcohol precursor has been reported: Whitesell, J. K.; Minton, M. A.; Felman, S. W. *J. Org. Chem.* **1983**, *48*, 2193.

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