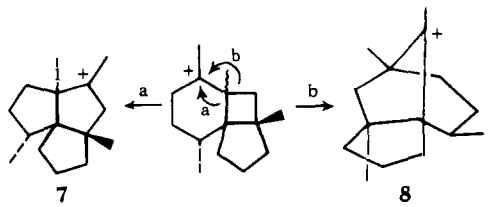
Scheme II



7 8

ϵ 1.50), tailing to 340 nm) as a waxy solid (mp 63–68 °C) in 77% yield. Detailed examination of the reaction product by ^{1}H NMR, ^{13}C NMR, LC, and GLC revealed the presence of only a single stereoisomer.

Although we were unable to induce **5** to undergo addition with a number of methylation reagents (MeLi, MeMgBr, $LiAlMe_4$) under a variety of conditions, seemingly owing to enolization,[6] it did react with methylenetriphenylphosphorane (2 equiv, Me_2SO, 70 °C, 3 days) to furnish hydrocarbon **6** (IR (neat) 1640 cm^{-1}). Upon treatment with *p*-toluenesulfonic acid (0.3 equiv, benzene, reflux, 1 h), **6** provided racemic isocomene in 98% yield (mp 60–62 °C), possessing spectral data (^{1}H NMR, ^{13}C NMR, IR, MS) identical with those contained in comparison spectra graciously supplied by Professor Zalkow.

While 1,2-alkyl shifts in cyclobutyl carbinyl cations have been studied,[7] there are examples in which both modes of rearrangement to relieve the cyclobutane strain are observed. These are illustrated in Scheme II with our substrate. Migration of the ring fusion bond in sense a, as observed in this work, provides **7** and thence isocomene, while migration in sense b results in **8**. Examination of molecular models suggests that migration in sense a, at least for a cis-fused bicyclo[4.2.0] system, would be disfavored, since the migrating bond lies in the nodal plane of the p orbital. An intriguing explanation for the observed behavior would be the obtention of trans-fused[8] product from the cycloaddition, in which the ring fusion bond is favorably disposed for migration.

In conclusion, the synthetic approach described here stereoselectively provides (±)-isocomene in seven steps from an abundant, inexpensive, starting material. It is noteworthy for its brevity, high yield (>40%), and, *with the photoaddition step, production of three contiguous, quaternary chiral centers exclusively with the stereochemistry necessary for the natural product.* Its efficiency is illustrated by the preparation of ~3 g of the natural product by this route. We are continuing in our investigations of rearrangements of cyclobutylcarbinyl cations, including the acid-catalyzed reaction[9] of **5**.

Acknowledgments. I thank the Fannie & John Hertz Foundation for financial support in the form of a fellowship, Professor C. H. Heathcock for providing laboratory space and supplies (U.S. Public Health Services Grant No. CA-12617), and Professor W. G. Dauben and Dr. Todd Brookhart for invaluable advice on the photochemical cyclization step.

References and Notes

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(5) Gen, A.; Wiedhaup, K.; Swoboda, J.; Dunathan, H.; Johnson, W. *J. Am. Chem. Soc.* **1973**, *95*, 2656.
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(7) A number of examples are found: (a) Hayano, K.; Ohfune, Y.; Shirahama, H.; Matsumoto, T. *Chem. Lett.* **1978**, 1301. (b) Duc, K.; Fetizon, M.; Kone, M. *Tetrahedron* **1978**, *34*, 3513. (c) Manh, D.; Fetizon, M.; Flament, J. P. *Ibid.* **1975**, *31*, 1897. (d) Ohfune, Y.; Shirahama, H.; Matsumoto, T. *Tetrahedron Lett.* **1976**, 2869.
(8) We thank S. Graham for suggesting this possibility. The formation of trans-fused bicyclo[4.2.0]octanones by photochemical addition of cyclohexenones is known: Corey, E.; Bass, J.; Le Mahieu, R.; Mitra, R. *J. Am. Chem. Soc.* **1964**, *86*, 5570. Experiments are currently underway to test this hypothesis.
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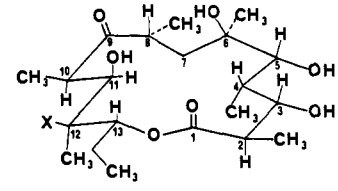
Total Synthesis of Erythromycins. 5. Total Synthesis of Erythronolide A

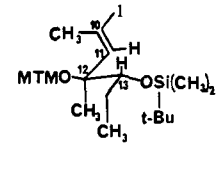
Sir:

The total synthesis of erythronolide B (**1**), the biosynthetic progenitor of all of the erythromycins, has previously been reported.[1,2] Herein we describe the first total synthesis of erythronolide A (**2**), the aglycone corresponding to the medically important antibiotic erythromycin A. The general strategy used for the synthesis of **2** is similar to that which led earlier to synthetic **1**, although there are major differences between the two syntheses with regard to segments of the synthetic plan and individual chemical steps. The construction of the erythronolide A molecule (**2**) involved the key optically active intermediates **3** (dextrorotatory form) and **4** (dextrorotatory form).

The synthesis of (+)-**3** in optically pure condition was accomplished as follows. Dehydration of 4-methyl-2-heptyn-4-ol (from reaction of 1-lithio-1-propyne and 2-pentanone in tetrahydrofuran (THF)) was effected by heating for 1 h at 100 °C with 0.1 equiv of *p*-toluenesulfonic acid monohydrate to afford after distillation a 93% yield of (*Z*)-4-methyl-4-hepten-2-yne (**5**) of 80% purity (^{1}H NMR and gas chromatographic analysis) along with the *E* isomer (10%) and 4-propyl-4-penten-2-yne (10%), bp 46 °C at 45 Torr.[3] Separation



1 X=H
2 X=OH



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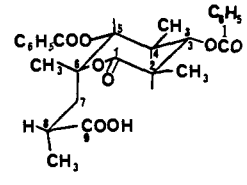

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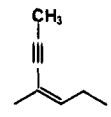
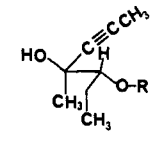
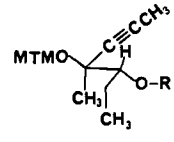


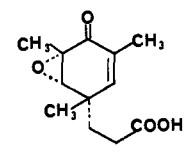
5



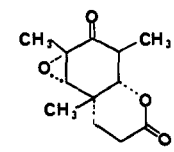
6 R=H
7 R=COCHC$_6$H$_5$ (OCH$_3$)



8 R=COCHC$_6$H$_5$ (OCH$_3$)
9 R=H
10 R=Si(CH$_3$)$_2$ t-Bu



11



12

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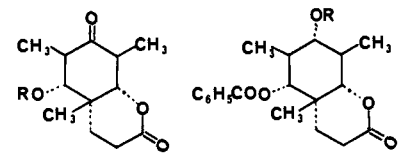
of these isomers was unnecessary since purification was easily accomplished after the next step, reaction of the mixture with 1.05 equiv of *N*-methylmorpholine *N*-oxide and 0.02 equiv of osmium tetroxide[4] in THF–water (1:1) at 25 °C for 70 h with vigorous stirring. The hydroxylation product was isolated by addition of ~0.01 mol equiv of sodium metabisulfite ($Na_2S_2O_5$) in a little water, filtration through Celite, concentration, addition of saturated NaCl, and extraction with ethyl acetate. The solid thus obtained was purified by two recrystallizations, first from 1:9 ether–pentane at −20 °C and then from 1:4 ether–pentane (cooling to −20 °C), to afford pure diol **6**, mp 97–98 °C, in 65% yield. The diol was converted into a mixture of diastereomeric mono esters **7** for resolution by reaction with a small excess of *O*-methyl mandelyl chloride (from (*S*)-(+)-mandelic acid)[5] and 4-dimethylaminopyridine in methylene chloride at 25 °C for 5–6 h. The diastereomeric mixture was readily separated by chromatography on silica gel using a Waters Associates "Prep 500" instrument with 15% ethyl acetate in hexane as eluant to give in 84% recovery the more polar diastereomer, $[\alpha]^{25}_D$ +68.5° (*c* 2.3, $CHCl_3$), which was demonstrated[6] to have the absolute configuration required for the synthesis (as depicted by **7**).[7] Treatment of **7** with excess acetic anhydride–dimethyl sulfoxide–acetic acid (8:8:1 by volume) at 25 °C for 72 h afforded the methylthiomethyl (MTM) ether[8] **8** quantitatively, and saponification of **8** using excess potassium hydroxide in methanol at 0 °C for 2 h gave the MTM-alcohol **9** as an oil in 87% yield. Reaction of **9** with 2.5 equiv of *tert*-butyldimethylsilyl chloride[9] and 5 equiv of 4-dimethylaminopyridine in dry dimethylformamide (DMF) at 50 °C for 30 h produced the silylated MTM ether **10** (99.5% yield) as a colorless oil, $[\alpha]^{25}_D$ +43.0° (*c* 1.2, $CHCl_3$). The conversion of **10** into the desired iodide **3** could not be accomplished efficiently using the method which had been successful in the synthesis of erythronolide B[1,2] and an alternative procedure had to be developed. The protected acetylenic diol **10** was hydroborated[10] using 1.2 equiv of dicyclohexylborane in THF at 0 °C for 5 h and the resulting vinylborane was oxidized by addition of trimethylamine *N*-oxide[11] to the vinylboronic ester which was transformed into the corresponding chloromercuri derivative by treatment with mercuric acetate followed by aqueous sodium chloride. After extractive isolation, the solid chloromercuri derivative was allowed to react with 1 equiv of iodine in dry pyridine[12] at 0 °C for 50 min to afford after chromatography on silica gel (5% ether in hexane as eluant) the vinyl iodide **3** (75% overall yield from **10**) as a colorless oil, $[\alpha]^{25}_D$ +27.9° (*c* 1.04 in ethanol).[13]

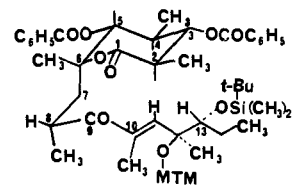
The synthesis of the lactone acid **4** was accomplished starting from the previously described[1] epoxy acid **11**, $[\alpha]^{28}_D$ −127° (CH_3OH),[14] via the epoxy lactone **12** which was prepared as outlined earlier.[1] Hydrogenation of **12** using palladium hydroxide on carbon catalyst in THF–HOAc (40:1) at 1 atm and 25 °C for 20–25 h afforded the hydroxy lactone **13** which was directly benzoylated using 2 equiv each of benzoic anhydride and 4-dimethylaminopyridine in a little pyridine at −20 °C for 3.5 h to give the corresponding keto benzoate **14.** Treatment of **14** with excess zinc borohydride in dimethoxyethane (DME) at −20 °C for 30 h produced, after recrystallization, the hydroxy benzoate **15,** mp 155–156.5 °C, $[\alpha]^{23}_D$ −17.1° (*c* 2.3, $CHCl_3$), in 65% overall yield from **12.** Benzoylation of **15** using benzoyl chloride–pyridine at 0–25 °C for 4 h yielded quantitatively the dibenzoate **16,** mp 203–205 °C, $[\alpha]^{24}_D$ −21.5° (*c* 1.6, $CHCl_3$).[15] The dibenzoate **16** was transformed into optically active lactone acid **4** by the procedures previously described.[1,2] The *p*-bromophenacyl ester of **4** had $[\alpha]^{24}_D$ +53 ± 1° (*c* 1.5, $CHCl_3$) and the free acid **4** had $[\alpha]^{20}_D$ +42° (*c* 0.7, $CHCl_3$).

The vinyl iodide **3** in THF solution at −78 °C was allowed to react with 2 equiv of *tert*-butyllithium[16] (0.5 M in pentane) for 5 min at −78 °C and then treated with a reagent prepared

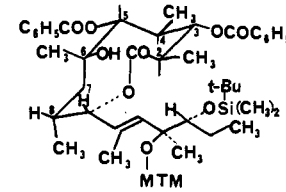


13 R = H
14 R = C_6H_5CO

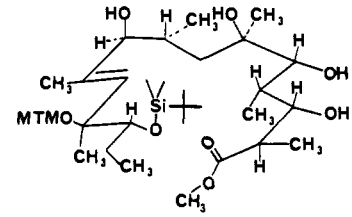
15 R = H
16 R = C_6H_5CO



17

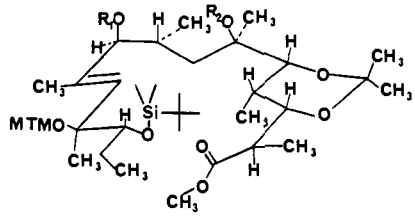


18

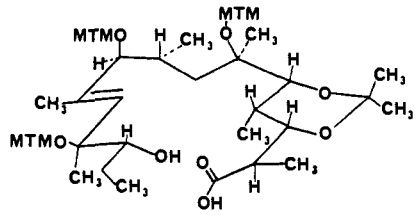


19

from 1 equiv each of 1-lithio-3-methoxy-3-methyl-1-butyne in hexane and pure cuprous iodide in dry THF at 0 °C, and the resulting bright yellow suspension was stirred for 10 min at −78 °C and then treated with a solution of the 2-pyridinethiol ester[18] of the lactone acid **4** (0.34 equiv) in cold (−20 °C), dry THF. The resulting mixture was stirred at −78 °C for 10 min and at −25 °C for 6 h and then quenched by the addition of aqueous ammonium chloride–ammonia (pH 7). Extractive isolation followed by chromatography on silica gel afforded 78% enone **17** as a colorless oil, $[\alpha]^{25}_D$ +14.5° (*c* 0.55, $CHCl_3$).[19] Reduction of the enone **17** in DME–ether (1:9) at 0 °C with 3.5 molar equiv of zinc borohydride[2] for 3 days afforded after isolation and chromatographic purification on silica gel 58% oily alcohol **18,** $[\alpha^{20}_D$ −35.3° (*c* 1.6, $CHCl_3$), and 14% C-9 epimeric alcohol, $[\alpha]^{20}_D$ +1.6° (*c* 1.5 in $CHCl_3$). Although the mixture of alcohols could in principle be used in the synthesis, in the present work pure **18** was carried through; the R_f values for **18** and its C-9 epimer on silica gel plates using 2% acetone in CH_2Cl_2 for development were 0.57 and 0.69, respectively.[20] Exposure of **18** to a solution of 3 equiv of lithium hydroxide, 11 equiv of hydrogen peroxide, and 30 equiv of 2,2′-dihydroxydiethyl sulfide in aqueous THF (1:3) at 0 °C for 5 h effected saponification of the ϵ-lactone function.[21] The reaction mixture was stirred with platinum wire to decompose excess hydrogen peroxide and concentrated in vacuo to remove most of the THF, then an excess of 1 N potassium hydroxide and DME (1:5 by volume) was added, and the resulting mixture was stirred at 60 °C for 24 h to effect cleavage of the benzoate groups. The reaction mixture was cooled to 0 °C and brought to pH 3.5 with oxalic acid and extracted with ethyl acetate, and the acid so obtained was treated with excess diazomethane in ether and chromatographed to afford the ester **19** (82% yield) as a colorless oil, $[\alpha]^{20}_D$ −5.8 ° (*c* 1.2, $CHCl_3$). The tetrahydroxy ester **19** was transformed into the 3,5-acetonide **20** by reaction with 10 equiv of 2-methoxypropene[2] and a catalytic amount of pyridinium tosylate in dry methylene chloride at 25 ° C for 12 h. Selective acetylation of **20** (acetic anhydride and 4-dimethylaminopyridine in pyridine at 5 °C for 20 h) afforded after chromatography the acetate **21** (83%) which was converted into the bis MTM ether **22** (92%) by



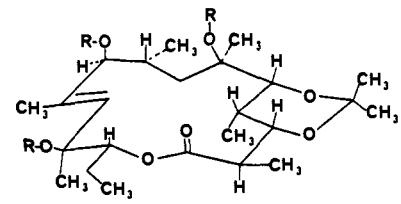
20 $R_1=R_2=H$
21 $R_1=Ac$, $R_2=H$
22 $R_1=Ac$, $R_2=MTM$
23 $R_1=R_2=MTM$



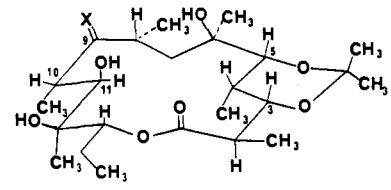
24

treatment with acetic anhydride–dimethyl sulfoxide–sodium acetate at 25 °C for 24 h. Acetate cleavage (K_2CO_3 in methanol at 25 °C for 15 h) and a second treatment with acetic anhydride–dimethyl sulfoxide–sodium acetate produced the tris MTM ether **23** (80% yield from **22**).[22] The methyl ester tris MTM ether **23** was saponified using a 5:1 mixture of methanol and 1 N sodium hydroxide (excess) at 55 °C for 1 h and the resulting carboxylic acid was desilylated by reaction with excess anhydrous tetra-*n*-butylammonium fluoride in THF at 25 °C for 0.5 h to afford in 70% yield the hydroxy acid–acetonide–tris MTM ether **24**, $[\alpha]^{25}_D$ −82.8° (*c* 0.43, methanol). Synthetic **24** was spectroscopically and chromatographically identical with material, $[\alpha]^{25}_D$ −81.7° (*c* 1.4, methanol), of the same structure produced by a series of transformations[23] starting from naturally derived erythronolide A.[24]

The cyclization of the hydroxy acid **24** to the 14-membered lactone **25** was accomplished using the double activation



25 R=MTM
26 R=H



27 X=O
28 X=NOH

method.[2,23] The acid **24** (azeotropically dried three times using dry toluene at reduced pressure) was allowed to react with 4-*tert*-butyl-*N*-isopropyl-2-imidazolyl disulfide[25] (2 equiv) and triphenylphosphine (2.1 equiv) in dry toluene at 25 °C for 1 h and the resulting solution of the thiol ester of **24** was added slowly by syringe (automatic drive, syringe maintained below 20 °C) over 1.5 h to dry toluene at reflux (under argon) and heating was continued for an additional 15 h. After chromatography the desired lactone (**25**) was obtained in 30% yield as a colorless oil, $[\alpha]^{25}_D$ −106° (*c* 0.03, $CHCl_3$), and was shown to be identical with a sample produced by functional modification of erythronolide A[23] by comparison of spectra, optical rotation, and TLC behavior in several different solvent systems.[26]

The conversion of **25** into erythronolide A was accomplished by a modification of the sequence used previously in the total synthesis of erythronolide B.[2] Treatment of **25** with excess potassium carbonate and methyl iodide in acetone–water (10:1) at 40 °C for 15 h effected removal[27] of the MTM groups to form **26** (80%) which underwent stereospecific epoxidation upon treatment with 4 equiv of *m*-chloroperoxybenzoic acid and 5 equiv of potassium carbonate in methylene chloride at 25 °C for 1 h to form quantitatively the corresponding 10,11-β-oxide[2,23] which could be oxidized by 3 equiv of pyridinium dichromate[28] in methylene chloride at 25 °C for 2 h to the 10,11-β-oxido 9-ketone (92%), $[\alpha]^{25}_D$ +18° (*c* 0.3, methanol). Hydrogenolysis of the C(10)–oxygen bond of the 9,10-β-oxide was effected in 89% yield by stirring with 10% palladium-on-charcoal catalyst in methanol containing sodium bicarbonate under 1 atm of hydrogen at 25 °C for 20 h to form the 3,5-acetonide of 10-*epi*-erythronolide A,[2,23] $[\alpha]^{25}_D$ +49° (*c* 0.19, methanol); this was etherified with 2-methoxypropene in methylene chloride containing a trace of $POCl_3$ as catalyst, epimerized at C(10) by exposure to 0.04% methanolic Triton B methoxide at 20 °C for 3 h, and deprotected after extractive workup by stirring for 1 h at 25 °C with 0.1 equiv of pyridinium tosylate in methanol to give in 25% overall yield the 3,5-acetonide of erythronolide A (**27**), $[\alpha]^{25}_D$ −42° (*c* 1.6, methanol), as a colorless oil.

The direct conversion of **27** into erythronolide A by acid-catalyzed hydrolysis using the conditions developed for the synthesis of erythronolide B from its 3,5-acetonide[2,23] could not be accomplished owing to the marked instability of erythronolide A under acidic conditions, and so an indirect process was necessary. The keto acetonide **27** was transformed into the corresponding 9-ketoxime (**28**) by heating at 60 °C with a concentrated solution of hydroxylamine hydrochloride (large excess) in pyridine under argon in a sealed tube and the crude ketoxime acetonide **28** was directly stirred with 3% methanol hydrogen chloride (from acetyl chloride and methanol) at 0 °C for 30 min to afford (54% yield overall) the oxime of erythronolide A, chromatographically and spectroscopically identical with a sample of oxime (mixture of syn and anti isomers) prepared from erythromycin A.[24] Finally, treatment[24] of a mixture of this oxime and a large excess of sodium nitrite (50 equiv) in methanol–water at 0 °C with 50 equiv of 1 N hydrochloric acid added by syringe drive over 3 h provided after isolation by extraction and recrystallization from acetone–hexane (1:2) fine, colorless needles of erythronolide A (76% yield), mp 168–172 °C (lit.[24] 172–173 °C), $[\alpha]^{25}_D$ −37° (*c* 0.9, methanol).

Although erythronolides A and B differ structurally by a single hydroxyl function, the synthesis of erythronolide A by the route described herein was successful only after a number of formidable and unique difficulties (not expected on the basis of previous experience with the synthesis of erythronolide B) were overcome. Specifically, steps **10** → **3**, **3** + **4** → **17**, **18** → **19**, **20** → **23**, **24** → **25**, and **27** → **2** all posed serious problems which required extensive experimentation.

With the synthesis of **1** and **2** completed their conversion into the corresponding erythromycins can now be addressed.[29]

References and Notes

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(2) Part 4: Corey, E. J.; Kim, S.; Yoo, S.; Nicolaou, K. C.; Melvin, L. S.; Brunelle,

D. J.; Falck, J. R.; Trybuiski, E. J.; Lett, R.; Sheldrake, P. W. *J. Am. Chem. Soc.* **1978,** *100,* 4620.
(3) The structure of each synthetic intermediate was confirmed by appropriate spectroscopic analysis including proton magnetic resonance (^{1}H NMR), infrared, and mass spectra (using chromatographically homogeneous samples). All reactions involving air-sensitive components were conducted under argon.
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(5) (*S*)-(+)-Mandelic acid was converted into *O*-methylmandelic acid, $[\alpha]^{20}_D$ +151.7, $[\alpha]^{25}_D$ +148.7° (c 1.3, ethanol), by the method of W. A. Bonner (*J. Am. Chem. Soc.* **1951,** *73,* 3126) and thence to the acid chloride using an excess of pure thionyl chloride at reflux for 30 min. See Haller, R.; Schneider, H. J. *Arch. Pharm. (Weinheim, Ger.)* **1974,** *307,* 31.
(6) The more polar ester **7**, $[\alpha]^{25}_D$ +68.5°, was saponified to form dextrorotatory diol **6**, $[\alpha]^{25}_D$ +37.1° (c 0.7, in ethanol), which was converted into (*R*)-(+)-2-methyl-2,3-pentanediol by the following sequence: (1) benzoylation of 6 using benzoyl chloride–pyridine to the secondary mono benzoyl derivative, (2) oxidative cleavage by reaction with potassium permanganate–sodium periodate in aqueous *tert*-butyl alcohol to form 3-benzoyloxy-2-pentanone, (3) reaction with excess methylmagnesium bromide in ether to form the 3-benzoate of 2-methyl-2,3-pentanediol, and (4) saponification using potassium hydroxide in aqueous methanol to form dextrorotatory 2-methyl-2,3-pentanediol which is known to have the *R* configuration. See Manwaring, D. G.; Richards, R. W.; Smith, R. M. *Tetrahedron Lett.* **1970,** 1029.
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(14) The levo acid **11** was obtained using (+)-1-α-napthylethylamine for resolution. There is a typographical error in ref 1 which reports "(±)-1-α-naphthylethylamine" as the resolving agent.
(15) This route from the epoxy lactone **12** to the dibenzoate **16** differs from that previously used[1] with racemic intermediates. The present modification was found to be necessary for the preparation of optically active intermediates because of a pronounced tendency of optically active hydroxy lactone **13** to racemize readily under various conditions, including during its formation from epoxy lactone **12** when aluminum amalgam is used as the reductant (see ref 1). The facile racemization of the hydroxy lactone under mild conditions will be discussed in a separate paper. The palladium catalyst used for the presently described conversion of **12** into **13** was prepared according to Pearlman, W. M. *Tetrahedron Lett.* **1967,** 1663.
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(18) The 2-pyridinethiol ester was prepared by reaction of **4** with 1 equiv of triethylamine and 1 equiv of 2-pyridinethiol chloroformate in methylene chloride at 0 °C for 15 min, washing with water, drying, removal of methylene chloride, and azeotropically drying with toluene under reduced pressure three times. For method see Corey, E. J.; Clark, D. *Tetrahedron Lett.,* **1979,** 2875.
(19) The modified Mukaiyama coupling of **3** and **4** following an approach which had been very effective in the synthesis of erythronolide B failed completely with **3** as a component, probably as a result of the instability of the MTM group to some magnesium(II) species present after addition of magnesium bromide to lithiated **3**. To obtain successful coupling of **3** and **4** by the process described herein, *minimum* amounts of THF were used throughout the procedure and the final solvent was alkane–THF (ratio, 1.2:1; total volume, 25 mL/mmol of pyridinethiol ester). The hexane and pentane originated in the organolithium reagents used. The coupling process is very sensitive to changes from these reaction conditions or to the presence of impurities.
(20) For analogous stereochemistry and translactonization in the reduction of the corresponding enone in previous work see ref 2 and also Corey, E. J.; Brunelle, D. J.; Nicolaou, K. C. *J. Am. Chem. Soc.* **1977,** *99,* 7359.
(21) Unless the sulfide component was included in the reaction mixture a very complex assortment of products resulted after this step and ^{1}H NMR analysis indicated loss of the MTM group.
(22) For reasons which are unclear the tris MTM ether **23** could not be prepared directly from **20** in a single step, despite numerous attempts under a variety of conditions.
(23) The conversion of erythronolide A into **24** roughly parallels an analogous previously described sequence for the erythronolide B series. See Corey, E. J.; Nicolaou, K. C.; Melvin, L. S. *J. Am. Chem. Soc.* **1975,** *97,* 654. The details of the preparation of **24** from erythronolide A will be detailed in a separate publication.
(24) For a preparation of erythronolide A from erythronmycin A see Le Mahieu, R. A.; Carson, M.; Kierstead, R. W. *J. Med. Chem.* **1974,** *17,* 953.
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(29) The melting point of erythronolide A has been observed to vary from 171 to 200 °C (Dr. R. A. Le Mahieu, Hoffmann-La Roche Co., personal communication). It is possible that chemical change occurs during melting.
(30) This research was assisted financially by a grant from the National Institutes of Health. We are indebted to the Chas. Pfizer Co. for a generous gift of erythromycin A and to Dr. R. A. LeMahieu for a reference sample of erythronolide A. P.B.H. has been the holder of an NSF graduate fellowship.

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Preferential 1,4- vs. 1,6-Hydrogen Transfer in a 1,5 Biradical. Photochemistry of β-Ethoxypropiophenone

Sir:

We have obtained evidence that the 1,5 biradical generated photochemically from β-ethoxypropiophenone (**1**) undergoes internal disproportionation by two paths: the minor one is a 1,6-H transfer which regenerates starting ketone; the major one, surprisingly, is a 1,4-H transfer which generates the enol of starting ketone.

Irradiation of **1** produces only two products, the (*Z*)- and (*E*)-oxacyclopentanols **3**, which arise from δ-hydrogen abstraction by triplet ketone[1] (Scheme I). The quantum efficiency for this photocyclization is *lower* in Lewis base solvents than in hydrocarbons, in sharp contrast to the solvent effects observed on quantum efficiencies of product formation resulting from γ-hydrogen abstraction.[2,3] It is widely accepted that hydrogen bonding to solvent by 1-hydroxy-1,4 biradicals suppresses their internal disproportionation back to ground-state ketone. We speculated that in the analogous 1,5 biradicals a 1,4-hydrogen transfer might provide an alternative mode of internal disproportionation, one not affected by hydrogen bonding involving the OH group.

To test this idea we have studied the effect of α deuteration[4] on the photochemistry of **1**. A degassed benzene solution 0.05 M in **1**-α,α-d_2 (**1**-D) was irradiated to ~65% conversion. Unreacted ketone was isolated and analyzed by mass spectrometry. Comparison of isotopic distribution for the M − CH_3, M − CH_2CH_3, M − OCH_2CH_3, and $CH_2OH_2CH_3$ peaks indicated that 20% of the remaining ketone had undergone a deuterium shift specifically from the α to the δ carbon.[5] A similar result was obtained for solutions containing dioxane. This result is readily rationalized only as enolization of the 1,5-biradical intermediate **2**.

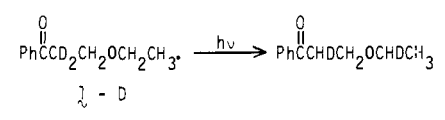

Table I lists *Z*/*E* product ratios and total quantum efficiencies for **1**-D and all protio-**1** (**1**-H) as a function of added *tert*-butyl alcohol or dioxane. As observed previously, added H-bond acceptors lower the overall quantum efficiency and drastically lower the relative yield of (*Z*)-**3**. As expected, if enolization is a major decay mode of the intermediate biradical, a primary isotope effect causes **1**-D to yield products with greater efficiency than does **1**-H.

It is possible to deduce relative values for the rate constants in Scheme I from the measured quantum efficiencies as listed in Table II. These values depend on the following assumptions: (1) that k_{-H} is negligibly small in *tert*-butyl alcohol; (2) that α deuteration affects only k_e; and (3) that biradical solvation

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