syntheses such as the classical Fischer indole[8] and the recent Gassman indole[9] syntheses do not provide regiocontrolled entry into the 4-substituted indoles[10] (except for the case of an electron-withdrawing group such as nitro in the latter approach) which are important intermediates toward ergot alkaloids attaches special merit to this approach.

Acknowledgment. We thank the National Science Foundation and the National Institutes of Health, General Medical Sciences, for their generous support of our programs. M.R. thanks the Deutsches Forschungsgemeinschaft for partial support. M.C. thanks the Science Research Council of the United Kingdom for a postdoctoral fellowship.

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(1) Cf. deWaard, E. R.; Rens, H. R.; Huisman, H. O. *Tetrahedron Lett.* **1973,** 4315. Oikawa, Y.; Yonemitsu, O. *J. Org. Chem.* **1976,** *41,* 1118.
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(3) **2**: NMR δ 1.54 (s, 3 H), 1.76 (s, 3 H), 1.95 (m, 4 H), 2.70 (t, J = 6 Hz, 2 H), 3.69 (s, 3 H), 6.42 (d, J = 3 Hz, 1 H), 6.61 (dd, J = 9, 3 Hz, 1 H), 7.40 (d, J = 9 Hz, 1 H). **3**: NMR δ 7.0 (d, J = 8 Hz, 1 H), 6.58 (m, 2 H), 5.62 (br t, J = 4 Hz, 1 H), 3.74 (s, 3 H), 2.68 (m, 2 H), 2.2 (m, 2 H), 1.98 (br s, 3 H). **5a:** NMR δ 1.54 (s, 3 H), 1.80 (s, 3 H), 1.70–2.10 (m, 4 H), 2.63 (m, 2 H), 5.82 (s, 2 H), 6.36 (s, 1 H), 7.0 (s, 1 H). **9**: NMR δ 1.48 (s, 3 H), 1.78 (m, 4 H), 1.97 (s, 6 H), 2.56 (m, 2 H), 3.56 (s, 3 H), 5.80 (m, 1 H), 5.90 (t, J = 3 Hz, 1 H), 6.41 (m, 1 H). **10:** NMR δ 1.60 (s, 3 H), 1.67–2.40 (m, 6 H), 2.38 (s, 3 H), 3.40 (s, 3 H), 6.03 (d, J = 3 Hz, 1 H), 6.39 (d, J = 3 Hz, 1 H), 7.09 (d, J = 8 Hz, 2 H), 7.46 (d, J = 8 Hz, 2 H). **12:** NMR δ 0.92 (d, J = 7 Hz, 6 H), 1.16–164 (m, 9 H), 1.80 (s, 3 H), 1.87 (s, 3 H), 2.40 (s, 3 H), 3.42 (s, 3 H), 4.04 (dd, J = 11, 4 Hz, 1 H), 5.72 (m, 1 H), 5.88 (t, J = 3 Hz, 1 H), 6.44 (t, J = 2 Hz, 1 H), 7.12 (d, J = 8 Hz, 2 H), 7.30 (d, J = 8 Hz, 2 H). **13:** NMR δ 0.98 (d, J = 8 Hz, 6 H), 1.64 (m, 3 H), 2.89 (br t, J = 8 Hz, 2 H), 3.80 (s, 3 H), 6.43 (d, J = 3 Hz, 1 H), 6.83 (apparent, t, J = 4 Hz, 1 H), 6.93 (d, J = 3 Hz, 1 H), 7.06 (apparent d, J = 4 Hz, 2 H). **15:** NMR δ 1.76 (s, 6 H), 3.52 (d, J = 8 Hz, 2 H), 3.76 (s, 3 H), 5.37 (t, J = 8 Hz, 1 H), 6.36 (d, J = 3 Hz, 1 H), 6.76 (apparent t, J = 4 Hz, 1 H), 6.86 (d, J = 3 Hz, 1 H), 7.00 (apparent d, J = 4 Hz, 2 H). New compounds have been fully characterized by spectral means and have satisfactory elemental composition.
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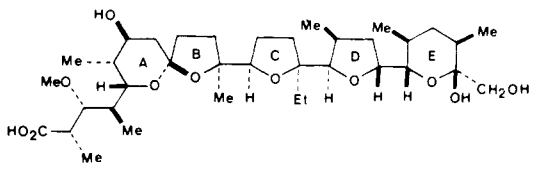
Total Synthesis of Monensin. 1. Stereocontrolled Synthesis of the Left Half of Monensin[1]

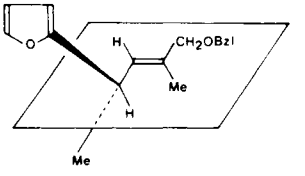
Sir:

Monensin (**1**),[2] produced by a strain of *Streptomyces cinnamonensis,* is perhaps the best known, most historical example from among a group of about 40 naturally occurring polyether antibiotics.[3] Monensin presents a formidable challenge to synthetic chemists; 17 asymmetric centers are present on the backbone of 26 carbon atoms, which means that in principle 131 072 stereoisomers exist for the antibiotic. In reporting the first total synthesis of monensin, we describe the synthesis of the left half of the antibiotic in this communication, the synthesis of the right half in the second,[4] and the total synthesis in the third.[5]



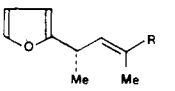
1 monensin

Wittig reaction of 2-(2-furyl)propionaldehyde[6] with carbethoxyethylidenetriphenylphosphorane in refluxing benzene afforded the trans ester **2**[7] (^{1}H NMR ($CDCl_3$) δ 1.38 (3 H, d, J = 7 Hz), 1.93 (3 H, d, J = 2 Hz), 6.70 (1 H, dq, J = 10, 2 Hz)) in 70% yield along with a small amount of the corresponding cis ester (<5% yield). Hydride reduction of **2** ($LiAlH_4$, Et_2O, RT), followed by benzylation ($C_6H_5CH_2Br$, KH, DMF-THF (1:4), 0 °C), gave the benzyl ether **3**[7] (^{1}H NMR ($CDCl_3$) δ 1.31 (3 H, d, J = 7 Hz), 1.75 (3 H, d, J = 1.5 Hz), 3.90 (2 H, br s), 4.43 (2 H, s), 5.43 (1 H, br d, J = 8 Hz)) in 95% overall yield. Hydroboration of **3** (B_2H_6, THF, 0 °C), followed by alkaline hydrogen peroxide workup, yielded the alcohol **4**[7] (^{1}H NMR ($CDCl_3$) δ 0.98 (3 H, d, J = 7 Hz), 1.29 (3 H, d, J = 7 Hz), 4.50 (2 H, s)) along with a small amount of its diastereomer in 85% yield. The ratio of **4** and its diastereomer was ~8:1. The structure assignment of **4** was made based on an example similar to this case.[8] The origin of the remarkable stereospecificity observed might be related to the conformational preference of **3**; based on the pioneering investigations by Wilson,[9] Herschbach,[10] Bothner-By,[11] and others,[12] the preferred conformation of **3** is assumed to be A. Therefore, hydroboration would take place preferentially from the sterically less hindered α face to yield **4**.

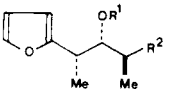


A

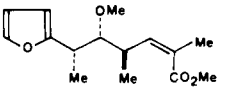
Methylation of **4** (CH_3I, KH, DMF-THF (1:4), 0 °C, followed by debenzylation (1 atm of H_2, 10% Pd/C, CH_3OH, RT), gave the alcohol **5**[7] (^{1}H NMR ($CDCl_3$) δ 0.96 (3 H, d, J = 7 Hz), 1.27 (3 H, d, J = 7 Hz), 3.21 (3 H, s)) in 88% overall yield. Optical resolution of **5** was achieved in a three-step sequence: (1) (−)-$C_6H_5CH(CH_3)N{=}C{=}O$, Et_3N at 50 °C; (2) separation of the resultant diastereomeric urethanes



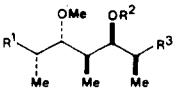
2 $R = CO_2C_2H_5$
3 $R = CH_2OCH_2C_6H_5$



4 $R^1 = H$, $R^2 = CH_2OCH_2C_6H_5$
5 $R^1 = CH_3$, $R^2 = CH_2OH$
6 $R^1 = CH_3$, $R^2 = CHO$



7



8 R^1 = 2-furyl, $R^2 = H$, $R^3 = CH_2OH$
9 R^1 = 2-furyl, $R^2 = CH_2C_6H_5$, $R^3 = CH_2OCH_2OCH_3$
10 $R^1 = CO_2CH_3$, $R^2 = CH_2C_6H_5$, $R^3 = CH_2OCH_2OCH_3$
11 $R^1 = CO_2CH_3$, $R^2 = CH_2C_6H_5$, $R^3 = CH_2OH$
12 $R^1 = CO_2CH_3$, $R^2 = CH_2C_6H_5$, $R^3 = CHO$

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by medium-pressure column chromatography (silica gel; hexane–methylene chloride–acetone (48:48:4)); (3) $LiAlH_4$ reduction of the separated diasteromeric urethanes to the levorotatory (α^{22}_D −11.07° (*c* 3.63, $CHCl_3$)) and dextrorotatory (α^{22}_D +11.13° (*c* 1.77,$CHCl_3$)) alcohols **5**, respectively.

Pyridinium chlorochromate oxidation[13] of the levorotatory alcohol **5** in methylene chloride at room temperature yielded the aldehyde **6**[7] (^{1}H NMR ($CDCl_3$) δ 1.11 (3 H, d, *J* = 7 Hz), 1.32 (3 H, d, *J* = 7 Hz), 3.28 (3 H, s), 9.41 (1 H, d, *J* = 1.8 Hz)) in 88% yield. Condensation of **6** in THF at −78 °C to −50 °C with the phosphonate anion prepared from $(MeO)_2P(O)CH(CH_3)CO_2CH_3$ gave exclusively[14] the cis ester **7**[7] (^{1}H NMR ($CDCl_3$) δ 1.05 (3 H, d, *J* = 7 Hz), 1.28 (3 H, d, *J* = 7 Hz), 1.85 (3 H, d, *J* = 1.2 Hz), 3.40 (3 H, s), 3.65 (3 H, s), 5.76 (1 H, dq, *J* = 10, 1.2 Hz)) in 73% yield. Hydride reduction ($LiAlH_4$, Et_2O, RT), followed by hydroboration ((1) B_2H_6, THF, 0 °C; (2) H_2O_2, aqueous 10% KOH–THF, RT), afforded the alcohol **8**[7] (^{1}H NMR ($CDCl_3$) δ 1.05 (6 H, d, *J* = 7 Hz), 1.33 (3 H, d, *J* = 7 Hz), 3.46 (3 H, s)) in 80% yield along with a small amount of its diastereomer in a ratio of 12:1. Based on the aforementioned reason (note the geometry of the olefinic bond), the structure **8** was tentatively assigned to the major product, which was later confirmed by comparison of **12** with the authentic sample prepared by an alternative route.[15] The alcohol **8** was converted to the methoxymethyl benzyl ether **9**[7] (^{1}H NMR ($CDCl_3$) δ 1.00 (3 H, d, *J* = 7 Hz), 1.06 (3 H, d, *J* = 7 Hz), 1.25 (3 H, d, *J* = 7 Hz), 3.05 (3 H, s), 3.35 (3 H, s)) in 2 steps ((1) $BrCH_2OCH_3$, $(CH_3)_2NC_6H_5$, CH_2Cl_2, 0 °C; (2) $C_6H_5CH_2Br$, KH, DMF–THF (1:4), 0 °C) in 68% overall yield. Ozonization of **9** (O_3, CH_3OH, −78 °C), followed by diazomethane esterification, gave the ester **10**[7] (^{1}H NMR ($CDCl_3$) δ 0.94 (3 H, d, *J* = 7 Hz), 1.05 (3 H, d, *J* = 7 Hz), 1.13 (3 H, d, *J* = 7 Hz), 3.25 (3 H, s), 3.35 (3 H, s), 3.67 (3 H, s); α^{22}_D +32.5° (*c* 1.36, $CHCl_3$)) in 55% overall yield. Acid treatment of **10** (concentrated HCl–CH_3OH (1:150), reflux) yielded the alcohol **11**[7] (^{1}H NMR ($CDCl_3$) δ 0.98 (6 H, d, *J* = 7 Hz), 1.13 (3 H, d, *J* = 7 Hz), 3.25 (3 H, s), 3.68 (3 H, s); α^{22}_D +23.6° (*c* 1.35, $CHCl_3$)) in 94% yield. Pyridinium chlorochromate oxidation of **11** furnished the unstable aldehyde **12**[7,15,17] (^{1}H NMR ($CDCl_3$) δ 0.93 (3 H, d, *J* = 7 Hz), 1.11 (3 H, d, *J* = 7 Hz), 1.15 (3 H, d, *J* = 7 Hz), 3.26 (3 H, s), 3.70 (3 H, s), 4.07 (1 H, dd, *J* = 6, 3 Hz), 4.57 (2 H, s), 9.77 (1 H, d, *J* = 2 Hz); α^{22}_D +74.2° (*c* 0.91, $CHCl_3$)) in ~95% yield.

Acknowledgment. We are appreciative of the efforts of Drs. Tatsumi Yamazaki and Donald S. Karanewsky in the early stages of this synthesis. Financial assistance from National Institutes of Health, National Science Foundation, and Hoffmann-La Roche Inc. is gratefully acknowledged.

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(3) Reviews on polyether antibiotics: J. W. Westley, *Adv. Appl. Microbiol.*, **22,** 177 (1977); B. C. Pressman, *Annu. Rev. Biochem.*, **45,** 501 (1976); J. W. Westley, *Annu. Rep. Med. Chem.*, **10,** 246 (1975).
(4) T. Fukuyama, C.-L. J. Wang, and Y. Kishi, *J. Am. Chem. Soc.*, following paper in this issue.
(5) T. Fukuyama, K. Akasaka, D. S. Karanewsky, C.-L. J. Wang, G. Schmid, and Y. Kishi, *J. Am. Chem. Soc.*, accompanying paper in this issue.
(6) We have studied several routes to 2-(2-furyl)propionaldehyde including the known method (U. Schmidt, J. Gombos, E. Haslinger, and H. Zak, *Chem. Ber.*, **109,** 2628 (1976)), and found that the following sequence of reactions is most practical for preparation of a large quantity of this substance: (1) methylation (*n*-BuLi (1.2 equiv), MeI, THF, −78 °C to RT) of (2-furyl)acetonitrile (K. Yu. Novitskii, Kh. Gresl, and Yu. K. Yur'ev, *Khim. Geterotsikl. Soedin.*, 829 (1966)); (2) hydrolysis (KOH, aqueous CH_3OH; reflux); (3) reduction ($LiAlH_4$, Et_2O, 0 °C); (4) oxidation (CrO_3PyHCl, CH_2Cl_2, RT).
(7) Satisfactory spectroscopic data (mass spectrum, ^{1}H NMR, IR, etc.) were obtained for this substance.
(8) T. Matsumoto, Y. Hosoda, K. Mori, and K. Fukui observed a highly stereospecific hydroboration on a very similar system to **3** (*Bull. Chem. Soc. Jpn.*, **45,** 3156 (1972)).
(9) R. W. Kilb, C. C. Lin, and E. B. Wilson, Jr., *J. Chem. Phys.*, **26,** 1695 (1957).
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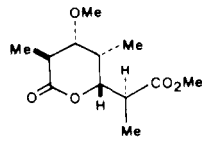
(11) A. A. Bothner-By, C. Naar-Colin, and H. Guenther, *J. Am. Chem. Soc.*, **84,** 2748 (1962).
(12) For example, see E. L. Eliel, N. L. Allinger, S. J. Angyal, and G. A. Morrison, "Conformational Analysis", Interscience Publishers, New York, 1965, p 19 ff.
(13) E. J. Corey and J. W. Suggs, *Tetrahedron Lett.*, 2647 (1975).
(14) *The amount of the corresponding trans ester, if any, should be <2%.* Related to the synthesis of the polyether and some other antibiotics, we have studied the Horner–Emmons modification of the Wittig reaction to optimize the formation of cis-α,β-unsaturated esters like **7**, and realized that the ratio of the cis and trans esters is sensitive to the structure of the phosphonate anion, solvent, and reaction temperature: G. Schmid, Y. Oikawa, and Y. Kishi, unpublished results. Attempted application of the oxido ylide method (see E. J. Corey and H. Yamamoto, *J. Am. Chem. Soc.*, **92,** 226, (1970)) for the synthesis of cis-allylic alcohol (cf. **7**) directly from **6** was not successful.
(15) We first investigated an alternative route to **12** involving aldol reaction of **6** with the zinc enolate of 2-methyl-2-hydroxy-3-pentanone. Thus, **12** was synthesized from **6** in eight steps ((1) aldol reaction; (2) $LiAlH_4$, Et_2O, 0 °C; (3) $NaIO_4$, aqueous CH_3OH, RT; (4) $CH(OCH_3)_3$–CH_3OH, CSA, RT; (5) $C_6H_5CH_2Br$, KH, DMF–THF (1:4), 0 °C; (6) O_3, CH_3OH, −78 °C; (7) CH_2N_2, Et_2O, 0 °C; (8) aqueous AcOH, RT) with 13% overall yield. A disadvantage of this sequence is the fact that the best stereospecificity of the aldol reaction was 1.8:1 in favoring the desired product. The stereochemistry of the major aldol was confirmed by transforming it to the lactonic ester i,[16]



i

one of the degradation products of monensin, in three steps ((1) O_3, CH_3OH, −78 °C; (2) H_5IO_6, dioxane, RT, 24 h; (3) CH_2N_2, Et_2O, 0 °C).
(16) We are indebted to Dr. Chamberlin, Eli Lilly & Co., for a sample of the lactonic ester i.
(17) We have recently developed a method to convert the lactonic ester i (see ref 15 and 16) to **12** in 11 steps: T. Fukuyama, K. Akasaka, and Y. Kishi, unpublished results.

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Total Synthesis of Monensin. 2. Stereocontrolled Synthesis of the Right Half of Monensin[1]

Sir:

Here, continuing from the preceding communication on the synthesis of the left half of monensin, we describe the synthesis of the right half of the antibiotic.

Monobenzylation of 2-allyl-1,3-propanediol[2] was efficiently carried out in two steps ((1) C_6H_5CHO, CSA, C_6H_6, azeotropic conditions; (2) $LiAlH_4$–$AlCl_3$ (1:4), Et_2O, RT) in 93% overall yield. Optical resolution of the monobenzyl ether **1**[3] was achieved in a three-step sequence: (1) (+)-1-$C_{10}H_7CH(CH_3)N{=}C{=}O$, Et_3N, RT; (2) separation of the resultant diastereomeric urethanes by medium-pressure column chromatography (silica gel; hexane–methylene chloride–ether (10:10:1)), (3) $LiAlH_4$ reduction of the separated diastereomeric urethanes to the levorotatory (α^{22}_D −12.1° (*c* 0.68, $CHCl_3$)) and dextrorotatory (α^{22}_D +13.6° (*c* 0.92, $CHCl_3$)) monobenzyl ethers **1**, respectively. The *S* configuration was assigned to the levorotatory alcohol **1** based on the following experiment: (−)-**1** was converted to (−)-2-methylpentanoic acid (α^{22}_D −21.4°) in four steps ((1) MsCl, Py, 0 °C; (2) $LiAlH_4$, Et_2O, RT; (3) H_2, 10% Pd/C, CH_3OH, RT; (4) Jones oxidation), while the rotation of (*S*)-2-methylpen-

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by medium-pressure column chromatography (silica gel; hexane–methylene chloride–acetone (48:48:4)); (3) $LiAlH_4$ reduction of the separated diasteromeric urethanes to the levorotatory (α^{22}_D −11.07° (*c* 3.63, $CHCl_3$)) and dextrorotatory (α^{22}_D +11.13° (*c* 1.77,$CHCl_3$)) alcohols **5**, respectively.

Pyridinium chlorochromate oxidation[13] of the levorotatory alcohol **5** in methylene chloride at room temperature yielded the aldehyde **6**[7] (^{1}H NMR ($CDCl_3$) δ 1.11 (3 H, d, *J* = 7 Hz), 1.32 (3 H, d, *J* = 7 Hz), 3.28 (3 H, s), 9.41 (1 H, d, *J* = 1.8 Hz)) in 88% yield. Condensation of **6** in THF at −78 °C to −50 °C with the phosphonate anion prepared from $(MeO)_2P(O)CH(CH_3)CO_2CH_3$ gave exclusively[14] the cis ester **7**[7] (^{1}H NMR ($CDCl_3$) δ 1.05 (3 H, d, *J* = 7 Hz), 1.28 (3 H, d, *J* = 7 Hz), 1.85 (3 H, d, *J* = 1.2 Hz), 3.40 (3 H, s), 3.65 (3 H, s), 5.76 (1 H, dq, *J* = 10, 1.2 Hz)) in 73% yield. Hydride reduction ($LiAlH_4$, Et_2O, RT), followed by hydroboration ((1) B_2H_6, THF, 0 °C; (2) H_2O_2, aqueous 10% KOH–THF, RT), afforded the alcohol **8**[7] (^{1}H NMR ($CDCl_3$) δ 1.05 (6 H, d, *J* = 7 Hz), 1.33 (3 H, d, *J* = 7 Hz), 3.46 (3 H, s)) in 80% yield along with a small amount of its diastereomer in a ratio of 12:1. Based on the aforementioned reason (note the geometry of the olefinic bond), the structure **8** was tentatively assigned to the major product, which was later confirmed by comparison of **12** with the authentic sample prepared by an alternative route.[15] The alcohol **8** was converted to the methoxymethyl benzyl ether **9**[7] (^{1}H NMR ($CDCl_3$) δ 1.00 (3 H, d, *J* = 7 Hz), 1.06 (3 H, d, *J* = 7 Hz), 1.25 (3 H, d, *J* = 7 Hz), 3.05 (3 H, s), 3.35 (3 H, s)) in 2 steps ((1) $BrCH_2OCH_3$, $(CH_3)_2NC_6H_5$, CH_2Cl_2, 0 °C; (2) $C_6H_5CH_2Br$, KH, DMF–THF (1:4), 0 °C) in 68% overall yield. Ozonization of **9** (O_3, CH_3OH, −78 °C), followed by diazomethane esterification, gave the ester **10**[7] (^{1}H NMR ($CDCl_3$) δ 0.94 (3 H, d, *J* = 7 Hz), 1.05 (3 H, d, *J* = 7 Hz), 1.13 (3 H, d, *J* = 7 Hz), 3.25 (3 H, s), 3.35 (3 H, s), 3.67 (3 H, s); α^{22}_D +32.5° (*c* 1.36, $CHCl_3$)) in 55% overall yield. Acid treatment of **10** (concentrated HCl–CH_3OH (1:150), reflux) yielded the alcohol **11**[7] (^{1}H NMR ($CDCl_3$) δ 0.98 (6 H, d, *J* = 7 Hz), 1.13 (3 H, d, *J* = 7 Hz), 3.25 (3 H, s), 3.68 (3 H, s); α^{22}_D +23.6° (*c* 1.35, $CHCl_3$)) in 94% yield. Pyridinium chlorochromate oxidation of **11** furnished the unstable aldehyde **12**[7,15,17] (^{1}H NMR ($CDCl_3$) δ 0.93 (3 H, d, *J* = 7 Hz), 1.11 (3 H, d, *J* = 7 Hz), 1.15 (3 H, d, *J* = 7 Hz), 3.26 (3 H, s), 3.70 (3 H, s), 4.07 (1 H, dd, *J* = 6, 3 Hz), 4.57 (2 H, s), 9.77 (1 H, d, *J* = 2 Hz); α^{22}_D +74.2° (*c* 0.91, $CHCl_3$)) in ~95% yield.

Acknowledgment. We are appreciative of the efforts of Drs. Tatsumi Yamazaki and Donald S. Karanewsky in the early stages of this synthesis. Financial assistance from National Institutes of Health, National Science Foundation, and Hoffmann-La Roche Inc. is gratefully acknowledged.

References and Notes

(1) Part 4 of the series Synthetic Studies on Polyether Antibiotics. For part 3, see T. Nakata and Y. Kishi, *Tetrahedron Lett.*, 2745 (1978).
(2) A. Agtarap, J. W. Chamberlin, M. Pinkerton, and L. Steinrauf, *J. Am. Chem. Soc.*, **89,** 5737 (1967); M. Pinkerton and L. K. Steinrauf, *J. Mol. Biol.*, **49,** 533 (1970); M. E. Haney, Jr., and M. M. Hoehn, *Antimicrob. Agents Chemother.*, 349 (1967); W. M. Stark, N. G. Knox, and J. E. Westhead, *ibid.*, 353 (1967); A. Agtarap and J. W. Chamberlin, *ibid.*, 359 (1967); M. Gorman, J. W. Chamberlin, and R. L. Hamill, *ibid.*, 363 (1967); R. F. Shumard and M. E. Callender, *ibid.*, 369 (1967); W. K. Lutz, F. K. Winkler, and J. D. Dunitz, *Helv. Chim. Acta*, **54,** 1103 (1971).
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(4) T. Fukuyama, C.-L. J. Wang, and Y. Kishi, *J. Am. Chem. Soc.*, following paper in this issue.
(5) T. Fukuyama, K. Akasaka, D. S. Karanewsky, C.-L. J. Wang, G. Schmid, and Y. Kishi, *J. Am. Chem. Soc.*, accompanying paper in this issue.
(6) We have studied several routes to 2-(2-furyl)propionaldehyde including the known method (U. Schmidt, J. Gombos, E. Haslinger, and H. Zak, *Chem. Ber.*, **109,** 2628 (1976)), and found that the following sequence of reactions is most practical for preparation of a large quantity of this substance: (1) methylation (*n*-BuLi (1.2 equiv), MeI, THF, −78 °C to RT) of (2-furyl)acetonitrile (K. Yu. Novitskii, Kh. Gresl, and Yu. K. Yur'ev, *Khim. Geterotsikl. Soedin.*, 829 (1966)); (2) hydrolysis (KOH, aqueous CH_3OH; reflux); (3) reduction ($LiAlH_4$, Et_2O, 0 °C); (4) oxidation (CrO_3PyHCl, CH_2Cl_2, RT).
(7) Satisfactory spectroscopic data (mass spectrum, ^{1}H NMR, IR, etc.) were obtained for this substance.
(8) T. Matsumoto, Y. Hosoda, K. Mori, and K. Fukui observed a highly stereospecific hydroboration on a very similar system to **3** (*Bull. Chem. Soc. Jpn.*, **45,** 3156 (1972)).
(9) R. W. Kilb, C. C. Lin, and E. B. Wilson, Jr., *J. Chem. Phys.*, **26,** 1695 (1957).
(10) D. R. Herschbach and L. C. Krisher, *J. Chem. Phys.*, **28,** 728 (1958).
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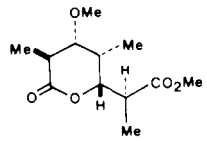
(12) For example, see E. L. Eliel, N. L. Allinger, S. J. Angyal, and G. A. Morrison, "Conformational Analysis", Interscience Publishers, New York, 1965, p 19 ff.
(13) E. J. Corey and J. W. Suggs, *Tetrahedron Lett.*, 2647 (1975).
(14) *The amount of the corresponding trans ester, if any, should be <2%.* Related to the synthesis of the polyether and some other antibiotics, we have studied the Horner–Emmons modification of the Wittig reaction to optimize the formation of cis-α,β-unsaturated esters like **7**, and realized that the ratio of the cis and trans esters is sensitive to the structure of the phosphonate anion, solvent, and reaction temperature: G. Schmid, Y. Oikawa, and Y. Kishi, unpublished results. Attempted application of the oxido ylide method (see E. J. Corey and H. Yamamoto, *J. Am. Chem. Soc.*, **92,** 226, (1970)) for the synthesis of cis-allylic alcohol (cf. **7**) directly from **6** was not successful.
(15) We first investigated an alternative route to **12** involving aldol reaction of **6** with the zinc enolate of 2-methyl-2-hydroxy-3-pentanone. Thus, **12** was synthesized from **6** in eight steps ((1) aldol reaction; (2) $LiAlH_4$, Et_2O, 0 °C; (3) $NaIO_4$, aqueous CH_3OH, RT; (4) $CH(OCH_3)_3$–CH_3OH, CSA, RT; (5) $C_6H_5CH_2Br$, KH, DMF–THF (1:4), 0 °C; (6) O_3, CH_3OH, −78 °C; (7) CH_2N_2, Et_2O, 0 °C; (8) aqueous AcOH, RT) with 13% overall yield. A disadvantage of this sequence is the fact that the best stereospecificity of the aldol reaction was 1.8:1 in favoring the desired product. The stereochemistry of the major aldol was confirmed by transforming it to the lactonic ester i,[16]



i

one of the degradation products of monensin, in three steps ((1) O_3, CH_3OH, −78 °C; (2) H_5IO_6, dioxane, RT, 24 h; (3) CH_2N_2, Et_2O, 0 °C).
(16) We are indebted to Dr. Chamberlin, Eli Lilly & Co., for a sample of the lactonic ester i.
(17) We have recently developed a method to convert the lactonic ester i (see ref 15 and 16) to **12** in 11 steps: T. Fukuyama, K. Akasaka, and Y. Kishi, unpublished results.

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Received September 22, 1978

Total Synthesis of Monensin. 2. Stereocontrolled Synthesis of the Right Half of Monensin[1]

Sir:

Here, continuing from the preceding communication on the synthesis of the left half of monensin, we describe the synthesis of the right half of the antibiotic.

Monobenzylation of 2-allyl-1,3-propanediol[2] was efficiently carried out in two steps ((1) C_6H_5CHO, CSA, C_6H_6, azeotropic conditions; (2) $LiAlH_4$–$AlCl_3$ (1:4), Et_2O, RT) in 93% overall yield. Optical resolution of the monobenzyl ether **1**[3] was achieved in a three-step sequence: (1) (+)-1-$C_{10}H_7CH(CH_3)N{=}C{=}O$, Et_3N, RT; (2) separation of the resultant diastereomeric urethanes by medium-pressure column chromatography (silica gel; hexane–methylene chloride–ether (10:10:1)), (3) $LiAlH_4$ reduction of the separated diastereomeric urethanes to the levorotatory (α^{22}_D −12.1° (*c* 0.68, $CHCl_3$)) and dextrorotatory (α^{22}_D +13.6° (*c* 0.92, $CHCl_3$)) monobenzyl ethers **1**, respectively. The *S* configuration was assigned to the levorotatory alcohol **1** based on the following experiment: (−)-**1** was converted to (−)-2-methylpentanoic acid (α^{22}_D −21.4°) in four steps ((1) MsCl, Py, 0 °C; (2) $LiAlH_4$, Et_2O, RT; (3) H_2, 10% Pd/C, CH_3OH, RT; (4) Jones oxidation), while the rotation of (*S*)-2-methylpen-

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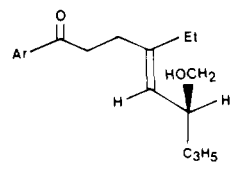
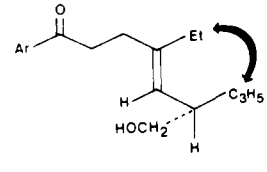
tanoic acid is known as α_D +21.4°.[4] The levorotatory monobenzyl ether **1** was converted to the *p*-methoxyacetophenone derivative **2**[3] (^{1}H NMR ($CDCl_3$) δ 1.01 (3 H, t, J = 7 Hz), 3.85 (3 H, s); α^{22}_D +4.0° (c 0.20, $CHCl_3$)) in 31% overall yield in eight steps ((1) CrO_3PyHCl,[5] CH_2Cl_2, RT; (2) $CH_3CH_2C(=CH_2)MgBr$, THF, 0 °C; (3) $CH_3C(OEt)_3$, $CH_3CH_2CO_2H$, 140 °C; (4) $LiAlH_4$, Et_2O, RT; (5) CrO_3PyHCl, CH_2Cl_2, RT; (6) *p*-$MeOC_6H_4MgBr$, Et_2O, 0 °C; (7) Jones oxidation; (8) BCl_3, CH_2Cl_2, 0 °C). The dextrorotatory monobenzyl ether **1** was also transformed to **2** with the same absolute configuration as that derived from the levorotatory monobenzyl ether **1** in 30% overall yield in 10 steps ((1) $BrCH_2OCH_3$, $(CH_3)_2NC_6H_5$, CH_2Cl_2, RT; (2) Li, liquid NH_3; (3-9) follow the steps 1-7 for the levorotatory series; (10) concentrated HCl, CH_3OH, 60 °C)—note the symmetry element of **1**.

We anticipated that epoxidation of **2** should afford the epoxide **3** as the major product, since the transition state A would experience less steric hindrance than the alternative transition state B (note the arrow in B), assuming that this epoxidation involves first complexation of an oxidant with the hydroxyl group of **2**. Indeed, *m*-chloroperbenzoic acid in methylene



A



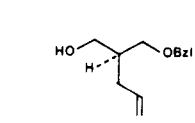
B

chloride-aqueous sodium bicarbonate (two phase) at room temperature gave almost quantitatively a single,[6] unstable[7] epoxide **3** (^{1}H NMR ($CDCl_3$) δ 1.05 (3 H, t, J = 7 Hz), 3.90 (3 H, s)). After tosylation (TsCl, Py, 0 °C), **3** was stereospecifically converted to the tetrahydrofuran **4** (^{1}H NMR ($CDCl_3$) δ 0.94 (3 H, d, J = 7 Hz), 0.95 (3 H, t, J = 7 Hz), 3.68 (3 H, s); α^{22}_D +18.8° (c 1.20, $CHCl_3$)) by the method ((1) $LiAlH_4$, Et_2O, 0 °C; (2) CSA, CH_2Cl_2, RT) recently developed in our laboratory.[8] The best ratio of **4** and its diastereomer was 7:2.[9] Periodate-osmium tetroxide oxidation of **4** in aqueous dioxane at room temperature yielded the lactol **5** (^{1}H NMR ($CDCl_3$) δ 1.00 (3 H, t, J = 7 Hz), 1.01 (3 H, d, J = 7 Hz), 3.76 (3 H, s); α^{22}_D +19.2° (c 2.62, $CHCl_3$)) in 36% overall yield from **3**.

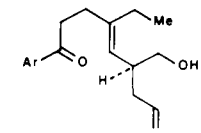
Baeyer-Villiger oxidation of *cis*-3,5-dimethylcyclohexanone,[10] followed by aqueous potassium hydroxide workup, gave the hydroxy acid **6**.[3] Optical resolution of **6** was achieved by fractional crystallization (eight times from $CHCl_3$-Et_2O) of its (+)-α-methylbenzylamine salt.[3] The 3*R* configuration was tentatively assigned to the dextrorotatory hydroxy acid **6**, since (+)-**6** yielded (+)-3,5-dimethylhexan-1-ol (α^{22}_D +8.65° (c 0.45, $CHCl_3$)) in three steps ((1) CH_2N_2, Et_2O, 0 °C; (2) MsCl, Py, 0 °C; (3) $LiAlH_4$, Et_2O, RT), while (*R*)-(+)-3,7-dimethyloctan-1-ol is known to have α_D +4.20°.[11] The dextrorotatory hydroxy acid **6** was transformed to the bromide **7**[3] (^{1}H NMR ($CDCl_3$) δ 1.03 (6 H, d, J = 7 Hz); α^{22}_D −15.0° (c 0.71, $CHCl_3$)) in 10 steps ((1) H_2SO_4, EtOH, reflux; (2) $BrCH_2OCH_3$, $(CH_3)_2NC_6H_5$, CH_2Cl_2, RT; (3) $LiAlH_4$, Et_2O, RT; (4) MsCl, Py, 0 °C; (5) C_6H_5SNa, DMF, RT; (6) CH_3CO_3H, AcONa, AcOH-CH_2Cl_2, 0 °C; (7) Δ, $CaCO_3$, decaline; (8) concentrated HCl, EtOH, reflux; (9) MsCl, Py, 0 °C; (10) LiBr, DMF, 100 °C). Treatment of **7** with triphenylphosphine in DMF at 120 °C gave the phosphonium salt **8**[3] (^{1}H NMR ($CDCl_3$) δ 0.83 (3 H, d, J = 7 Hz), 1.02 (3 H, br d, J = 7 Hz)). The overall yield from **6** to **8** was 36%.

Wittig reaction of **5** and **8** ($Me_2SO^-Na^+$, Me_2SO, RT) afforded the cis olefin **9**[3] (^{1}H NMR ($CDCl_3$) δ 0.94 (6 H, d, J = 7 Hz), 0.95 (3 H, d, J = 7 Hz), 3.79 (3 H, s); α^{22}_D +10.3° (c 0.71, $CHCl_3$)) in 78% yield along with a small amount of the corresponding trans olefin (<2% yield). NBS bromination[12] of **9** in acetonitrile at room temperature gave a single bromide **10**[3] (^{1}H NMR ($CDCl_3$) δ 0.98 (6 H, d, J = 7 Hz), 1.00 (3 H, d, J = 7 Hz), 1.03 (3 H, t, J = 7 Hz), 3.78 (3 H, s); α^{22}_D +1.3° (c 0.38, $CHCl_3$)) in 57% yield. The structure **10** was assigned for the product, based on our extensive studies in the lasalocid A synthesis.[13] Treatment of **10** with superoxide anion in Me_2SO containing crown ether[14] gave the alcohol **11**[3] (^{1}H NMR ($CDCl_3$) δ 0.95 (3 H, d, J = 7 Hz), 0.98 (3 H, t, J = 7 Hz), 1.02 (6 H, d, J = 7 Hz), 3.78 (3 H, s); α^{22}_D +19.5° (c 0.36, $CHCl_3$)) in 47% yield. Byproducts of this reaction were olefins formed from elimination of hydrogen bromide.

Functionalization of the vinyl group of **11** was accomplished in 53% overall yield by protection of the secondary alcoholic group as its trichloroacetate (Cl_3CCOCl, Py, 0 °C), osmylation (OsO_4, Py-THF, RT), monobenzoylation (C_6H_5COCl, Py-CH_2Cl_2, RT), Jones oxidation, and then hydrolysis of the trichloroacetyl and benzoyl groups (NaOMe, CH_3OH, RT). As a single hemiketal **12**[3] (^{1}H NMR ($CDCl_3$) δ 3.78 (3 H, s); α^{22}_D +74.7° (c 0.17, $CHCl_3$)) was produced on the base hydrolysis, the stereochemistry at C(25)[15] was concluded as indicated—note the stereochemistry of this center of monensin. The hemiketal group in **12** was protected as its methyl ketal **13**[3] (^{1}H NMR ($CDCl_3$) δ 3.26 (3 H, s), 3.76 (3 H, s); α^{22}_D



1



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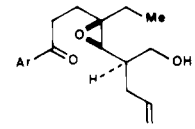

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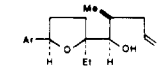

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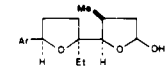

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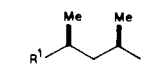
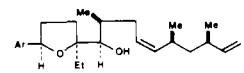


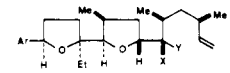
6 R^1=CH_2OH, R^2=CH_2CO_2H

7 R^1=CH_2Br, R^2=CH=CH_2

8 R^1=$CH_2P^+(C_6H_5)_3Br^-$, R^2=CH=CH_2

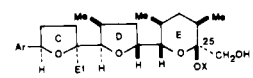


9



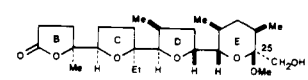
10 X=Br, Y=H

11 X=H, Y=OH

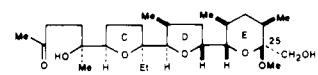


12 X=H

13 X=CH_3



14



15

Ar = p-$CH_3OC_6H_4$

+85.5° (*c* 0.18, $CHCl_3$)) under the standard conditions ($CH(OCH_3)_3$-CH_3OH, CSA, CH_2Cl_2, RT) quantitatively.

Transformation of **13** to the lactone **14**[3] (^1H NMR ($CDCl_3$) δ 1.34 (3 H, s), 3.26 (3 H, s), 3.98 (1 H, d, J = 4 Hz); IR ($CHCl_3$) 1760 cm^{-1}; α^{22}_D +43.6° (*c* 1.69, $CHCl_3$)) was accomplished in seven steps ((1) Li, liquid NH_3, EtOH; (2) $CH(OCH_3)_3$-CH_3OH, CSA, CH_2Cl_2, RT; (3) O_3, CH_3OH, −78 °C; (4) $MgBr_2$, wet CH_2Cl_2, RT; (5) CH_3MgBr, Et_2O, RT; (6) O_3, CH_3OH, −78 °C; (7) concentrated HCl, CH_3OH, RT) in 22% overall yield. A few of these steps require a comment. First, magnesium bromide in wet methylene chloride (step 4) was found most satisfactory to form the enol ether of the β-ketoaldehyde. Second, highly stereospecific addition of a Grignard reagent to a ketonic group adjacent to a tetrahydrofuran (step 5) was demonstrated in our total synthesis of lasalocid A.[13] In this particular case **14** was the only product detected by NMR and TLC analysis. The structure of **14** was concluded from the following transformation; acid treatment of **14** (CSA, wet ether, RT), followed by periodate oxidation ($NaIO_4$, aqueous CH_3OH, 0 °C), gave the dilactone (i.e., the ring E[15] in the structure **14** is the δ-lactone), which was found to be identical with the authentic dilactone,[16,17] one of the degradation products of monensin, by comparison of spectroscopic (NMR, IR, α_D) and TLC data. Treatment of **14** with methyllithium in THF at −78 °C afforded the methyl ketone **15**[3] (^1H NMR ($CDCl_3$) δ 1.13 (3 H, s), 2.15 (3 H, s), 3.25 (3 H, s), 4.13 (1 H, d, J = 4 Hz); IR ($CHCl_3$) 1715 cm^{-1}; α^{22}_D +65.1° (*c* 1.78, $CHCl_3$)) almost quantitatively.

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References and Notes

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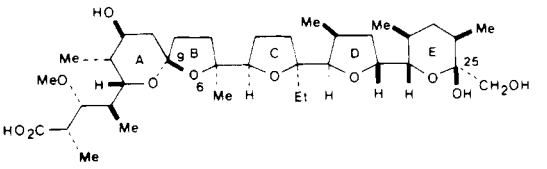
Department of Chemistry, Harvard University
Cambridge, Massachusetts 02138
Received September 22, 1978

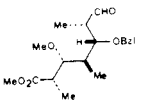
Total Synthesis of Monensin. 3. Stereocontrolled Total Synthesis of Monensin[1]

Sir:

Having completed the synthesis of the left and right halves **2** and **3** of monensin (**1**), we now need to develop a method of constructing the spiro ketal moiety of the antibiotic. We anticipated that the asymmetric center at the C(9)[2] position should stereospecifically be introduced by intramolecular ketalization of the corresponding dihydroxy ketone, because the configuration and conformation around this center of monensin (**1**) has been shown by X-ray analysis[3] as A, in which the C(9)-O(6)[2] bond takes the axial position with respect to the tetrahydropyran ring. Therefore, this configuration must be thermodynamically more stable than the alternative one owing to the anomeric effect well known in carbohydrate chemistry.



1 monensin



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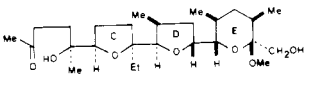

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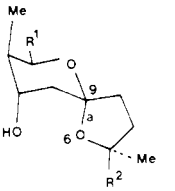
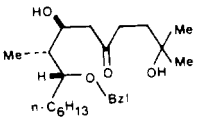


A

The proposed intramolecular ketalization, particularly its stereochemistry outcome, was investigated on the model compound **4**.[4,5] Hydrogenolysis of **4** (1 atm of H_2, 10% Pd/C, CH_3OH-AcOH (95:5), RT) yielded an ~1:1 mixture of spiro ketals **5**[5] and **6**[5] (Merck silica gel plate (0.25 mm), acetone-hexane (3:7); R_f 0.72 and 0.48, respectively). When this mixture was equilibrated with a catalytic amount of camphorsulfonic acid in methylene chloride at room temperature,



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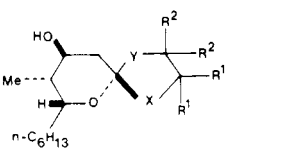

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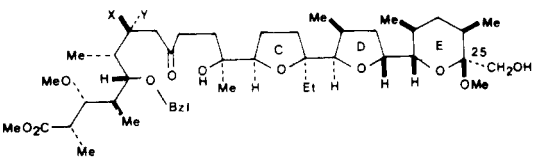

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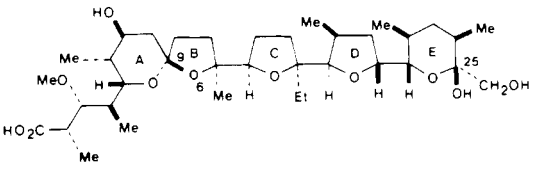

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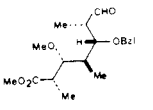

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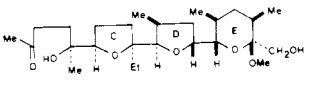

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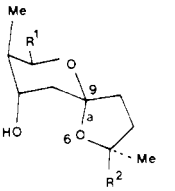

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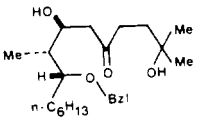

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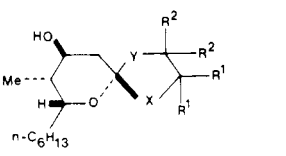

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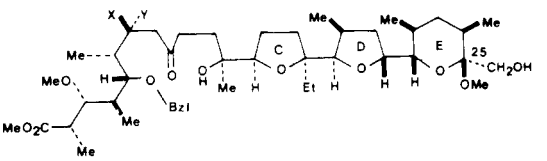

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a new mixture favoring the less polar isomer **5** by a ratio of at least 20:1 was produced. The spectroscopic studies on the spiro ketals and their acetates established the structure for **5** and **6** as indicated.[6]

Being encouraged by our successful total synthesis of lasalocid A,[7] we planned to form the crucial carbon–carbon bond between the left and right halves **2** and **3** by aldol reaction. After many unsuccessful attempts, we have found that this aldol reaction is nicely effected by freshly prepared $(i\text{-}C_3H_7)_2NMgBr$[8] in THF and furthermore that the ratio of the two diastereomeric aldols **7** and **8** is sensitive to the reaction temperature. The following ratios of **7** and **8** were observed at the indicated temperature: ~1:1 at 0 °C (71% yield; 90% yield based on the consumed ketone **3**), ~2:1 at −20 °C (60%; 91%), >5:1 at −50 °C (30%; 90%), and >8:1 at −78 °C (21%; 92%). The diastereomeric aldols **7**[5] (^{1}H NMR ($CDCl_3$) δ 3.25 (3 H, s), 3.27 (3 H, s), 3.68 (3 H, s), 4.60 (2 H, s), 7.31 (5 H, s); α^{22}_D +36.3° (*c* 0.95, CH_2Cl_2)[9]) and **8**[5] (^{1}H NMR ($CDCl_3$) δ 3.25 (6 H, s), 3.67 (3 H, s), 4.61 (2 H, a very close AB), 7.30 (5 H, s); α^{22}_D +46.1° (*c* 0.52, CH_2Cl_2)[9]) could be separated by preparative layer chromatography (Merck silica gel plate (0.5 mm), ether–pentane (5:4), five developments). Based on Cram's rule, the desired stereochemistry was tentatively assigned to the major aldol, which was later confirmed by successful transformation of **7** into monensin (**1**).

Following the conditions that we established in the model series, we subjected the aldol **7** to the following sequence of reactions: (1) 1 atm of H_2, 10% Pd/C, CH_3OH–AcOH (100:5), RT, 30 min; (2) CSA, wet CH_2Cl_2–Et_2O (3:1), RT, 1 h; (3) 1 N NaOH–CH_3OH (1:5), 60 °C, 1 h. Step 2 in this sequence was required to equilibrate the spiro ketal center and also to hydrolyze the tertiary methoxy group at the C(25)[2] position. Preparative layer chromatography (Merck silica gel plate (0.5 mm), ether, three developments) allowed isolation of synthetic monensin (**1**)[10] as its sodium salt. The overall yield from **7** to **1** was 53%. The synthetic substance was found to be identical with natural monensin in every respect (NMR, IR, α_D, mass spectrum, melting point, mixture melting point, TLC).

Acknowledgment. Financial assistance from National Institutes of Health, National Science Foundation, and Hoffmann-La Roche Inc. is gratefully acknowledged.

References and Notes

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(2) The numbering corresponds to that of monensin.
(3) For X-ray analysis of silver salt of monensin, see A. Agtarap, J. W. Chamberlin, M. Pinkerton, and L. Steinrauf, *J. Am. Chem. Soc.*, **89**, 5737 (1967), and M. Pinkerton and L. K. Steinrauf, *J. Mol. Biol.*, **49**, 533 (1970); for X-ray analysis of free acid of monensin, see W. K. Lutz, F. K. Winkler, and J. D. Dunitz, *Helv. Chim. Acta*, **54**, 1103 (1971).
(4) Compound **4** was synthesized by the aldol reaction analogous to **2** + **3** → **7** + (**8**): D. S. Karanewsky, T. Fukuyama, and Y. Kishi, unpublished results.
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(6) Details of the structure assignment for **5** and **6** will be reported later.
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(8) This base (1.5 M) was prepared from EtMgBr and diisopropylamine in THF at 80 °C and kept at ~50 °C. The aldol reaction was carried out as follows. The aldehyde **2** (prepared from 38.2 mg of the alcohol (see part 2 of this series) just before use) and ketone (21.5 mg) were dissolved in 10 mL of anhydrous THF under an argon atmosphere, and cooled to −50 °C. To this solution was added 100 μL of the freshly prepared base. At ~5-min intervals, additional base (9 × 25 μL) was added. The reaction was monitored by TLC after each addition of the base. After the base was quenched with saturated ammonium chloride solution at −50 °C, the products were extracted with ether and then with methylene chloride. Preparative layer chromatography (Merck silica gel (0.5 mm), ether–pentane (5:4), five developments) gave 11.1 mg of **7** (30% yield; 90% yield based on the consumed **3**), 2.0 mg of **8** (contaminated by an unknown compound), and 14.3 mg of the recovered ketone **3**.
(9) It takes some time for this substance to give the steady rotation, perhaps owing to the phenomenon similar to mutarotation known for carbohydrates.
(10) We are indebted to Dr. Chamberlin, Eli Lilly & Co., and Dr. Westley, Hoffmann-La Roche Inc., for samples of sodium salt of monensin.

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Synthesis of Monomeric Niobium- and Tantalum–Benzyne Complexes and the Molecular Structure of $Ta(\eta^5\text{-}C_5Me_5)(C_6H_4)Me_2$

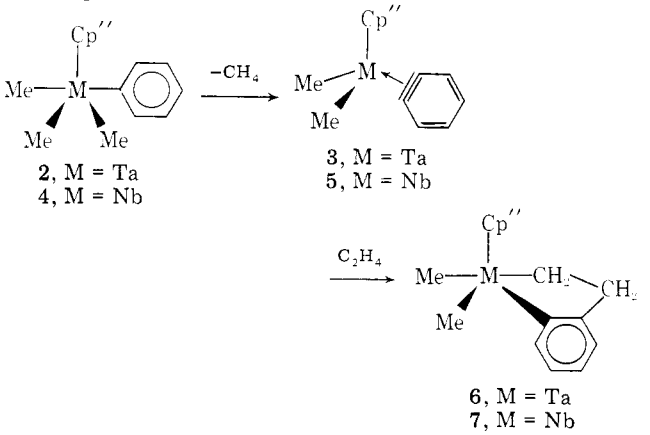
Sir:

Many transition metal complexes contain organic ligands which are highly reactive or unknown in the free state (e.g., cyclobutadiene,[1] trimethylenemethane,[2] carbenes,[3] and small-ring acetylenes[4]). A benzyne (C_6H_4) complex has been postulated as an intermediate in the thermal decomposition of $Ti(\eta^5\text{-}C_5H_5)_2(C_6H_5)_2$ on the basis of labeling and trapping experiments,[5] and recent results by Erker[6] support the formation of a benzyne intermediate, $Zr(\eta^5\text{-}C_5H_5)_2(C_6H_4)$, in the thermal exchange of aryl groups between $Zr(\eta^5\text{-}C_5H_5)_2(aryl)_2$ and aromatic solvents. To our knowledge, however, no compounds containing a benzyne molecule η^2 bonded to a single transition metal have been isolated.[7] Our studies of metallocyclopentane complexes[12] led us to develop a synthesis of tantalum–olefin complexes, $Ta(\eta^5\text{-}C_5Me_5)(CH_2{=}CHR)Cl_2$, by decomposition of thermally unstable dialkyl complexes, $Ta(\eta^5\text{-}C_5Me_5)(CH_2CMe_3)(CH_2CH_2R)Cl_2$ (R = H, Me).[13] We now report the extension of this principle, a form of the β-hydride elimination process by which many transition metal alkyl complexes decompose,[14] to the preparation of stable benzyne complexes.[15]

$Ta(\eta^5\text{-}C_5Me_5)(CH_2CMe_3)Cl_2$[13] reacts slowly (~24 h) with 1 equiv of $Zn(C_6H_5)_2$ in benzene to give neopentane and a dark brown solution containing $Ta(\eta^5\text{-}C_5Me_5)(C_6H_4)Cl_2$ (**1**); no intermediates can be observed by ^{1}H NMR. $Ta(\eta^5\text{-}C_5Me_5)(C_6H_4)Cl_2$ can be isolated as yellow crystals in 44% yield by removing the benzene in vacuo and recrystallizing the gummy residue from toluene at −30 °C. The ^{1}H NMR spectrum of **1** (τ, C_6H_6) shows a singlet for the $\eta^5\text{-}C_5Me_5$ group at 8.26 (relative area 15) and a symmetric AA′BB′ pattern consisting of two multiplets at 2.07 and 2.78 (relative area 4), consistent with its formulation as a benzyne complex. Since **1** is not soluble enough for ^{13}C NMR or a cryoscopic molecular weight determination, we sought a more soluble derivative.

Adding 1 mol of phenyllithium to a suspension of $Ta(\eta^5\text{-}C_5Me_5)Me_3Cl$[13] in ether at −78 °C initially produces a ho-

Scheme I



2, M = Ta
4, M = Nb

3, M = Ta
5, M = Nb

6, M = Ta
7, M = Nb

0002-7863/79/1501-0263$01.00/0