Compounds to Amines. *J. Am. Chem. Soc.* **1978**, *100*, 3969.
99. Grice, N.; Kao, S. C.; Pettit, R. Chemical Properties of Metallocarboxylic Acids of Transition Metals. *J. Am. Chem. Soc.* **1979**, *101*, 1627.
100. Pettit, R.; Cann, K.; Cole, T.; Mauldin, C. H.; Slegeir, W. Catalytic Reductions Using Carbon Monoxide and Water in Place of Hydrogen. *Adv. Chem. Ser.* **1979**, *No. 121*.
101. Bierschenk, T. R.; Pettit, R.; Nielsen, D. R. Ethylene Glycol. German Patent 2912956, 1979.
102. Cole, T.; Ramage, R.; Cann, K.; Pettit, R. Homogeneous Catalysts for Utilization of Synthesis Gas as a Reducing Agent. *J. Am. Chem. Soc.* **1980**, *102*, 6182.
103. Brady, R. C., III; Pettit, R. Reactions of Diazomethane on Transition-Metal Surfaces and Their Relationship to the Mechanism of the Fischer–Tropsch Reaction. *J. Am. Chem. Soc.* **1980**, *102*, 6161.
104. Pettit, R.; Cann, K.; Cole, T.; Mauldin, C. H.; Slegeir, W. Homogeneous Catalysts for Reduction Utilizing Carbon Monoxide and Water. *Ann. N.Y. Acad. Sci.* **1980**, *333*, 101.
105. Summer, C. E., Jr.; Riley, P. E.; Davis, R. E.; Pettit, R. Synthesis, Crystal Structure and Chemical Reactivity of Octacarbonyl-μ-Methylene-Diiron. *J. Am. Chem. Soc.* **1980**, *102*, 1752.
106. Pettit, R. Alcohol and Aldehyde Production Using Ruthenium Carbonyl Catalysts. U.S. Patent 4306084 A, 1981.
107. Brady, R. C., III; Pettit, R. Mechanism of the Fischer–Tropsch Reaction. The Chain Propagation Step. *J. Am. Chem. Soc.* **1981**, *103*, 1287.
108. Kao, S. C.; Lu, P. P. Y.; Pettit, R. Preparation and Properties of Bis(η^5-Cyclopentadienyl)-μ-Methylene-Diiron Tricarbonyl and Some of Its Derivatives. *Organometallics* **1982**, *1*, 911.
109. Osterloh, W. T.; Cornell, M. E.; Pettit, R. On the Mechanism of Hydrogenolysis of Linear Hydrocarbons and Its Relationship to the Fischer–Tropsch Reaction. *J. Am. Chem. Soc.* **1982**, *104*, 3759.

Methylenomycin B: An Efficient Synthesis from (2-Butyne)hexacarbonyldicobalt†

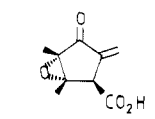
David C. Billington and Peter L. Pauson*

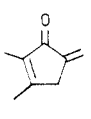
Department of Pure and Applied Chemistry, University of Strathclyde, Glasgow G1 1XL, Scotland

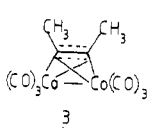
Received June 30, 1982

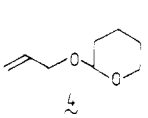
(2-Butyne)hexacarbonyldicobalt reacts at moderate temperatures with tetrahydro-2-(2-propenyloxy)pyran to give a trisubstituted cyclopentenone regiospecifically and in moderate yield. This cyclopentenone may be readily converted into the antibiotic methylenomycin B. This is the first example of regiospecificity, with respect to a simple alkene, in a cyclopentenone synthesis by this method.

The antibiotics methylenomycin A and methylenomycin B were first isolated from *Streptomyces violaceoruber* by Haneishi et al.[1] in 1974. X-ray crystallographic determination[2] of the structure (1) for the first compound was followed in 1977 by synthetic confirmation by Scarborough and Smith;[3] several further syntheses have been reported.[4] The correct structure (2) of methylenomycin B was established by Jernow et al.[5] in 1979, by means of an unambiguous synthesis. Other syntheses have appeared,[6] but all require relatively inaccessible starting materials or many steps. We report here a brief new synthesis of methylenomycin B (2) involving as the key step a regiospecific reaction between (2-butyne)hexacarbonyldicobalt (3) and tetrahydro-2-(2-propenyloxy)pyran (4).

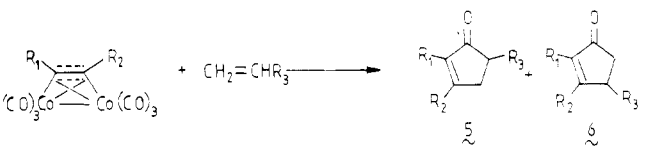

1


2


3


4

Scheme I


5 6

The reaction of (alkyne)cobalt complexes analogous to compound **3** with alkenes has previously been shown to be a general route to substituted cyclopentenones[7] (Scheme I). Its synthetic utility has, however, been limited by both the lack of regiospecificity observed[8] when simple unsym-

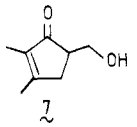
† Dedicated to the memory of R. Pettit.

(1) Haneishi, T.; Kitahara, N.; Takiguchi, Y.; Arai, M.; Sugawara, S. *J. Antibiot.* **1974**, *27*, 386. Haneishi, T.; Terahara, A.; Arai, M.; Hata, T.; Tamura, C. *Ibid.* **1974**, *27*, 393.
(2) Haneishi, T.; Terahara, A.; Hamano, K.; Arai, M. *J. Antibiot.* **1974**, *27*, 400.
(3) Scarborough, R. M., Jr.; Smith, A. B., III *J. Am. Chem. Soc.* **1977**, *99*, 7085.
(4) Takahashi, Y.; Isobe, K.; Hagiwara, H.; Kosugi, H.; Uda, H. *J. Chem. Soc., Chem. Commun.* **1981**, 714 and references therein.
(5) Jernow, J.; Tautz, W.; Rosen, P.; Williams, T. H. *J. Org. Chem.* **1979**, *44*, 4212.
(6) (a) Takahashi, Y.; Kosugi, H.; Uda, H. *J. Chem. Soc., Chem. Commun.* **1982**, 496. (b) Newton, R. F.; Reynolds, D. P.; Eyre, T. *Synth. Commun.* **1981**, *11*, 527.
(7) See Pauson, P. L.; Khand, I. U. *Ann. N. Y. Acad. Sci.* **1977**, *295*, 2. Newton, R. F.; Pauson, P. L.; Taylor, R. G. *J. Chem. Res., Synop.* **1980**, 277; *J. Chem. Res., Miniprint* **1980**, 3501 and references therein.
(8) Khand, I. U.; Pauson, P. L. *J. Chem. Res. Synop.* **1977**, 9; *J. Chem. Res., Miniprint* **1977**, 168.

0276-7333/82/2301-1560$01.25/0

metrical alkenes are employed (e.g., when R = C_6H_{13} in Scheme I, the ratio of **5**:**6** ≈ 1:1) and the relatively low reactivity displayed by simple alkenes. In contrast to the earlier examples we find that reaction with the alkene **4** proceeds under significantly milder conditions (80 °C) and with high regioselectivity. With use of the butyne complex **3**, the product, formed in 30–35% yield, is apparently exclusively the 2,3,5-substituted cyclopentenone (**5**, R^1 = R^2 = CH_3, R^3 = CH_2OTHP); no evidence for the presence of the expected 2,3,4-substituted isomer (**6**, R^1 = R^2 = CH_3, R^3 = CH_2OTHP) could be detected in the single frequency off resonance decoupled ^{13}C NMR spectrum of the product.

Mild acid hydrolysis readily converted this acetal (**5**, R^1 = R^2 = CH_3, R^3 = CH_2OTHP) into the free alcohol **7**.



7

This had been the final intermediate in the synthesis of methylenomycin B (**2**) developed by Jernow et al.,[5] and their method was successfully employed for the final dehydration step. The overall yield from complex **3** [itself formed in almost quantitative yield from 2-butyne and $Co_2(CO)_8$] was 23%.

The identity of the final product is clearly established by our spectral data and comparison to the spectral data reported by Jernow et al.[5] We found however that the compound **2** is considerably more stable than is suggested by these authors.

We are currently investigating the effects that lead to the observed regiospecificity in this case and extending the above methodology to related natural products.

Experimental Section

^1H NMR spectra were recorded at 90 MHz on a Perkin-Elmer R32 spectrometer and data refer to 5% samples in $CDCl_3$ referenced against Me_4Si. ^{13}C NMR spectra were recorded at 62.9 MHz on a Bruker WM 250 spectrometer. IR spectra were recorded on a Perkin-Elmer 257 spectrometer and refer to liquid films on sodium chloride plates. Mass spectra were obtained by using an AEI Kratos MS9 mass spectrometer fitted with a Mass Spectrometry Services Solid State Console, using a GEC 905 Computer system for data capture and processing. Allyl alcohol and 2-butyne were obtained commercially and used without purification. "Flash chromatography" refers to the method of Clark-Still[9] and was performed by using Merck Kiesel-gel 60 (230–400 mesh). Purity of products was confirmed by using TLC on Polygram 0.25 mm silica gel plates. All solvents were dried by standard methods and distilled before use. Petroleum ether refers to the fraction of bp 40–60 °C. Solvent removed in vacuo refers to the use of a Corning rotary film evaporator operating at 25 °C and 15 torr.

Tetrahydro-2-(2-propenyloxy)pyran. A solution of allyl alcohol (29 g, 0.5 mol), dihydropyran (50.4 g, 0.6 mol), and toluene-*p*-sulfonic acid (10 mg) in CH_2Cl_2 (150 mL) was stirred at room temperature for 15 h. The solution was washed with saturated $NaHCO_3$ solution (50 mL) and brine (50 mL), dried ($MgSO_4$) and fractionally distilled to give tetrahydro-2-(2-propenyloxy)pyran (60 g, 85%) as a colorless oil: bp 65–67 °C (20 torr) (lit.[10] 61–62 °C (15 torr)); NMR δ 1.6 (6 H, m), 3.2 (1 H, m), 4.0 (3 H, complex m), 4.65 (1 H, s), 5.2 (2 H, t), 5.9 (1 H, complex m).

(2-Butyne)hexacarbonyldicobalt (3). Following Greenfield et al.,[11] a solution of 2-butyne (2.8 mL, 1.9 g, 35 mmol) in petroleum ether (50 mL) was added over 0.5 h to a stirred solution of octacarbonyldicobalt (12 g, 35 mmol) in the same solvent (100 mL) at 10 °C under an atmosphere of nitrogen. The resulting red solution was stirred for 5 h at 10–15 °C and then filtered through celite. The solvent was removed in vacuo, and the residue chromatographed on neutral alumina by using petroleum ether as eluant, to give (2-butyne)hexacarbonyldicobalt (11.3 g, 94%) as a dark red oil, which crystallized on refrigeration.

Reaction between (2-Butyne)hexacarbonyldicobalt (3) and Tetrahydro-2-(2-propenyloxy)pyran (4). A solution of complex **3** (2.5 g, 7.3 mmol) and the acetal **4** (3 g, 22 mmol) in dry toluene (100 mL) under nitrogen was heated for 8 h under reflux. The resulting dark blue solution was filtered through celite, the solvent was removed in vacuo, and the residue was extracted with chloroform and with petroleum ether. The solvents were removed in vacuo, and the residue was purified by "flash chromatography" using petroleum ether and 70% ether/petroleum ether as eluants, to give dodecacarbonyltetracobalt (0.64 g, 56%), (2-butyne)-hexacarbonyldicobalt (0.25 g, 10%), and 2,3-dimethyl((5-tetrahydropyran-2-yloxy)methyl)cyclopent-2-en-1-one (**5**, R^1 = R^2 = CH_3, R^3 = CH_2OTHP; 0.43 g, 32%) as a colorless oil; NMR δ 1.6 (6 H, m), 1.7 (3 H, s), 2.1 (3 H, s), 2.6 (3 H, br s), 3.7 (4 H, m), 4.6 (1 H, s); IR 1700, 1650 cm^{-1}; mass spectrum, *m/e* found M^+ 224.1422, $C_{13}H_{20}O_3$ requires M 224.1412. A similar experiment conducted in benzene (8 h of reflux) gave the product **5** in 26% yield.

2,3-Dimethyl-5-(hydroxymethyl)cyclopent-2-en-1-one (7). A solution of the tetrahydropyranyl derivative (**5** R^1 = R^2 = CH_3, R^3 = CH_2OTHP; 0.23 g, 1 mmol) and one crystal of toluene-*p*-sulfonic acid (2 mg) in dry methanol (20 mL) was stirred at room temperature until TLC analysis showed no remaining starting material (19 h). The solvent was removed in vacuo, the residue extracted into ether (20 mL), and the solution washed with saturated $NaHCO_3$ solution (2 mL). The solvent was removed in vacuo, and the residue was purified by "flash chromatography" on silica gel using ether as eluant to give 2,3-dimethyl-5-(hydroxymethyl)cyclopent-2-en-1-one (**7**; 0.13 g, 92%) as a colorless oil: NMR δ 1.7 (3 H, s), 2.1 (3 H, s), 2.3–2.9 (3 H, complex m), 3.0 (1 H, s), 3.8 (2 H, m); IR 1675, 1635 cm^{-1}; mass spectrum, *m/e* found M^+ 140.0822, $C_8H_{12}O_2$ requires M 140.0837. These spectral properties are consistent with literature values.[5]

2,3-Dimethyl-5-(methylene)cyclopent-2-en-1-one, Methylenomycin B (2).[5] Following the method of Jernow et al.[5] a solution of alcohol **7** (0.13 g, 0.92 mmol) and dicyclohexylcarbodiimide (0.25 g, 1.2 mmol) in dry ether (20 mL) was stirred under nitrogen, and cuprous chloride (5 mg, 0.05 mmol) was added. The suspension was stirred under nitrogen for 15 h and then filtered. The solvent was removed in vacuo, and the residue was distilled in a Büchi Kugelrohr apparatus to give 2,3-dimethyl-5-(methylene)cyclopent-2-en-1-one (**2**; 0.091 g, 75%) as a colorless oil: bp 40 °C (oven temperature) (0.2 torr); NMR δ 1.8 (3 H, s), 2.1 (3 H, s), 3.1 (2 H, br s), 5.35 (1 H, d), 6.05 (1 H, d); IR 1690, 1662, 1630 cm^{-1}; mass spectrum, *m/e* found M^+ 122.0733, $C_8H_{10}O$ requires M 122.0732. In contrast to the reported instability[5] of this compound we find that it may be stored in petroleum ether solution at −20 °C for some time with no obvious decomposition.

Acknowledgment. We thank Dr. P. Bladon and his staff for the spectroscopic data.

Registry No. 2, 52775-77-6; **3**, 12282-08-5; **4**, 4203-49-0; **5** (R^1, R^2 = CH_3, R^3 = CH_2OTHP), 82891-98-3; **7**, 71719-44-3; allyl alcohol, 107-18-6; 2-butyne, 503-17-3; octacarbonyldicobalt, 15226-74-1.

(9) Clark-Still, W.; Kahn, M.; Mitra, A. *J. Org. Chem.* **1978**, *43*, 2923.
(10) Iwai, I.; Iwashige, T.; Asai, M.; Tomita, K.; Hiraokai, T.; Ide, J. *Chem. Pharm. Bull.* **1963**, *11*, 188.
(11) Greenfield, H.; Sternberg, H. W.; Friedel, R. A.; Wotiz, J. H.; Markby, R.; Wender, I. *J. Am. Chem. Soc.* **1956**, *78*, 120.