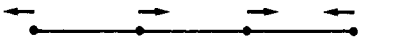
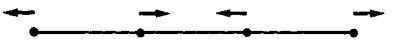
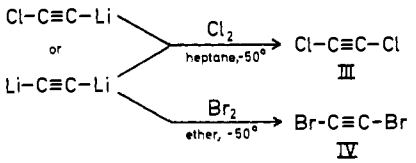
Table I. Observed Fundamental Frequencies (in cm^{-1}) and Vibrational Assignments of Dihaloacetylenes

ClC≡CBr I	ClC≡CCl II	ClC≡CCl III	BrC≡CBr IV	IC≡CI[c] V	Approximate motion XC≡CY	
2223	2191	2234[a,b]	2185[a,b]	2118[a,b]		-C≡C- str
923	886	988	832	720[a]		XC≡CY asym str
389	276[a,b]	477[a,b]	267[a,b]	190[a,b]		XC≡CY sym str
326[a,b]	325[a,b]	333[a,b]	311[a,b]	296[a,b]		XC≡CY bend
152	135	172	137	136[a]		XC≡CY bend

[a] Observed in solution. All other frequencies are vapor values. [b] In the Raman effect. [c] The spectral findings of diiodoacetylene are in good accordance with those of A. G. Meister and F. F. Cleveland, *J. Chem. Phys.*, **17**, 212 (1949); *J. Chim. Phys.*, **46**, 108 (1949), who measured all but the lowest band.

acetylide, prepared from acetylene with phenyllithium in ether, reacted (in heptane) with molecular chlorine to yield III; lithium chloroacetylide reacted similarly. In both cases phenyllithium was prepared from chlorobenzene. If the lithium base was made in the usual way from bromobenzene, the action of chlorine as well as bromine on dilithium acetylide gave dibromoacetylene (IV) exclusively.

Scheme II



When 1,2-dibromoethylene was treated with phenyllithium and iodine under similar conditions, the reaction failed to produce bromoiodoacetylene. Instead, diiodoacetylene (V) (mp 76.0°;[7] yield 18.2%) was isolated as the only reaction product.

All compounds can be gas chromatographed (except V) (Apiezon L, 50–90°). Samples were collected under helium at −80°, at which temperature the products crystallize as long needles.

The compounds have been identified by their mass spectra and by their vibration spectra. The five fundamental vibrations of the linear molecules, three stretching and two doubly denerate bending modes, have all been identified in the spectra. Table I gives the wave numbers and the assignments of the ir and Raman bands.[8]

Detailed descriptions of the preparative techniques and the vibrational spectra,[9] mass spectra, and photoelectron spectra will be published elsewhere.

(7) Several melting points varying from 74 to 82° are given in the literature.[2]

(8) The infrared spectra were recorded on Perkin-Elmer Model 225 and Beckman IR-9 spectrometers. A Michelson interferometer was employed in the far-infrared region. The Raman spectra were determined on a Cary 81 spectrometer with Spectra Physics Model 125 helium–neon laser.

(9) P. Klaboe, E. Kloster-Jensen, D. H. Christensen, and I. Johnsen, submitted for publication.

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Chemistry of Cephalosporin Antibiotics. XVII. Functionalization of Deacetoxycephalosporin. The Conversion of Penicillin into Cephalosporin

Sir:

We wish to report conversions which, taken together with previous work from this laboratory,[1] constitute a transformation of the penicillin system into the cephalosporin system.

Morin and coworkers reported[1] the conversion of penicillin V *via* its methyl ester sulfoxide **1** into deacetoxycephalosporin V methyl ester (**2**). We now describe the conversion of the latter compound into cephalosporin V (**7b**).

Mild, controlled hydrolysis of methyl ester **2** in 1:1 pyridine–water with 1 equiv of sodium hydroxide afforded 7-phenoxyacetamido-3-methyl-2-cephem-4-carboxylate[1b] (**3a**, Δ^2-deacetoxycephalosporin V), mp 183–184°, in yields ranging from 45 to 60%. Acid **3a** was transformed in 90% yield into its *p*-methoxybenzyl ester **3b**,[2] mp 112–114°, by treatment with dimethylformamide dineopentyl acetal[3] and *p*-methoxy-

(1) R. B. Morin, B. G. Jackson, R. A. Mueller, E. R. Lavagnino, W. B. Scanlon, and S. L. Andrews, *J. Amer. Chem. Soc.*, 85, 1896 (1963); (b) *ibid.*, 91, 1401 (1969).

(2) All new crystalline compounds afforded excellent spectral and microanalytical data.

(3) H. Brechbühler, H. Büchi, E. Hatz, J. Schreiber, and A. Eschenmoser, *Helv. Chim. Acta*, **48**, 1746 (1965).

benzyl alcohol in methylene chloride. The allylic methyl group of Δ^2 ester **3b** could be functionalized by azobisisobutyronitrile-initiated bromination using N-bromosuccinimide in hot carbon tetrachloride. Although no attempts were made to purify this bromination product, an nmr spectrum of the crude material displayed absorptions at δ 6.48 (crude doublet; C-2 vinyl H) and 4.14 (quartet, J = 8 Hz; methylene bearing bromine), relative areas *ca.* 1:2, consistent with allylic bromide **4**. The crude allylic bromide, in which the only significant contaminant was starting material **3b**, was immediately treated with potassium acetate in acetone. The newly formed species was separated from deacetoxy starting material (*ca.* 15%) by preparative tlc and was shown to be a mixture by nmr analysis. That this product (**5**), obtained in 30–40% yield, was an equilibrium mixture of cephalosporin V *p*-methoxybenzyl ester (30%) and its Δ^2 isomer (70%) was verified by nmr comparison with an authentic mixture.[4] Although the Δ^3 ester portion of mixture **5** did not appear to be readily separable from its Δ^2 isomer by chromatographic means,[5] the total ester mixture could be cleaved with trifluoroacetic acid in benzene to give a mixture containing cephalosporin V, as indicated by tlc and bioautography of a paper chromatogram.

Oxidation with *m*-chloroperbenzoic acid[6] in chloroform smoothly converted the Δ^2,Δ^3 sulfide mixture **5** into the Δ^3 sulfoxide **6**, mp 161–163°,[2] identical with authentic sulfoxide[7] according to physical measurements and mixture melting point. This oxidation–isomerization provides a means for converting all the cephalosporin material present to the potentially biologically active Δ^3 isomer (Δ^2-cephalosporins are essentially inactive). The explanation for this convenient conversion must involve electronic considerations favoring an α,β- over β,γ-unsaturated ester system as well as an allylic over a vinylic sulfoxide.[8] Other workers[9] have been unsuccessful in attempts to oxidize the Δ^2 sulfide ester system with oxidants milder than *m*-chloroperbenzoic acid, such as periodate.

Reduction of sulfoxide **6** in DMF by acetyl chloride–sodium dithionite[10] afforded *p*-methoxybenzyl 3-acetoxymethyl-7-phenoxyacetamido-3-cephem-4-carboxylate (**7a**, cephalosporin V *p*-methoxybenzyl ester),[2] mp 108–111°, in 55% yield after chromatographic purification. There was no other cephalosporin product. Cleavage of ester **7a** with trifluoroacetic acid in benzene containing some anisole gave 3-acetoxymethyl-7-phenoxyacetamido-3-cephem-4-carboxylic acid (**7b**, cephalosporin V), identical with authentic cephalosporin V by tlc, bioassay, and nmr comparison.

(4) Prepared by treatment of *p*-methoxybenzyl 3-acetoxymethyl-7-phenoxyacetamido-2-cephem-4-carboxylate,[2] mp 110–113°, at room temperature with potassium acetate in acetone.

(5) R. B. Woodward, *et al.* [*J. Amer. Chem. Soc.*, **88**, 852 (1966)] in their synthesis of the cephalosporin system separated a similar Δ^2,Δ^3 equilibrium mixture of the trichloroethyl esters of thiopheneacetamido-cephalosporanic acid by chromatography and then carried out ester cleavage to obtain the pure, biologically active Δ^3 acid.

(6) A discussion of this oxidation is in preparation by several members of this laboratory.

(7) Prepared by oxidation of *p*-methoxybenzyl 3-acetoxymethyl-7-phenoxyacetamido-3-cephem-4-carboxylate with *m*-chloroperbenzoic acid in chloroform.

(8) See, for example: D. E. O'Connor and W. I. Lyness, *J. Amer. Chem. Soc.*, **86**, 3480 (1964).

(9) J. D. Cocker, S. Eardley, G. I. Gregory, M. E. Hall, and A. G. Long, *J. Chem. Soc., C*, 1142 (1966); however, they could oxidize Δ^2 sulfide acids with sodium periodate to the Δ^3 sulfoxide, with some concomitant decarboxylation.

(10) A discussion and other examples of this type of reduction will be the subject of a later paper.

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Stereo-Controlled Synthesis of Prostaglandins $F_{2\alpha}$ and E_2 (*dl*)

Sir:

This communication describes a new approach to the synthesis of prostaglandins which was designed with the following objectives in mind: (1) control of stereochemistry, (2) the synthesis of all the primary prostaglandins and a variety of analogs from a single precursor, and (3) optical resolution at an early stage.[1-3]

Addition of cyclopentadienylsodium to a slight excess of chloromethyl methyl ether in tetrahydrofuran at −55° furnished after evaporation of solvent below 0° 5-methoxymethyl-1,3-cyclopentadiene,[4,5] which was

(1) For previous papers from these laboratories on the total synthesis of the primary prostaglandins E_1 and $F_{1\alpha}$, see (a) E. J. Corey, N. H. Andersen, R. M. Carlson, J. Paust, E. Vedejs, I. Vlattas, and R. E. K. Winter, *J. Amer. Chem. Soc.*, **90**, 3245 (1968); (b) E. J. Corey, I. Vlattas, N. H. Andersen, and K. Harding, *ibid.*, **90**, 3247 (1968); (c) E. J. Corey, I. Vlattas, and K. Harding, *ibid.*, **91**, 535 (1969).

(2) A group at the Upjohn Co. has recently described syntheses of racemic prostaglandins E_1, E_2, and $F_{2\alpha}$; see (a) W. P. Schneider, U. Axen, F. H. Lincoln, J. E. Pike, and J. L. Thompson, *ibid.*, **90**, 5895 (1968); (b) U. Axen, F. H. Lincoln, and J. L. Thompson, *Chem. Commun.*, 303 (1969); (c) W. P. Schneider, *ibid.*, 304 (1969).

(3) For a review on prostaglandins and the definition of primary prostaglandins, see S. Bergström, *Science*, **157**, 382 (1967).

(4) G. Kresze, G. Schulz, and H. Walz, *Ann. Chem.*, **666**, 45 (1963). This product is subject to facile isomerization to 1-methoxymethyl-1,3-cyclopentadiene.

(5) Infrared and nmr (at 60 MHz) spectra were in agreement with the assigned structure.