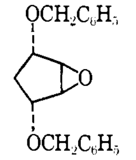
When the acid hydrolysis of **9** was preceded by acetylation and the resulting aldehyde oxidized with Jones reagent followed by alkaline hydrolysis, there was isolated after acidification in 90% yield the lactone **12**, identical with an authentic sample[17] by tlc, glc, and mass spectrum of its bistrimethylsilyl ether. Conversion of **12** into PGE$_2$ has been described,[17] and so has the conversion of PGE$_2$ into PGE$_1$ and PGF$_{1\alpha}$.[20] The preparation of **12**, therefore, also constitutes a synthesis of these three prostaglandins.



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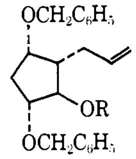
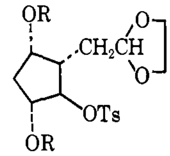
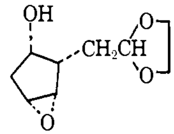


2, R = H
3a, R = Ts
3b, R = CONHCHCH$_3$C$_6$H$_5$



4, R = CH$_2$C$_6$H$_5$
5, R = H



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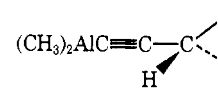

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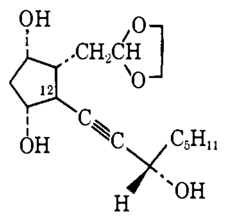

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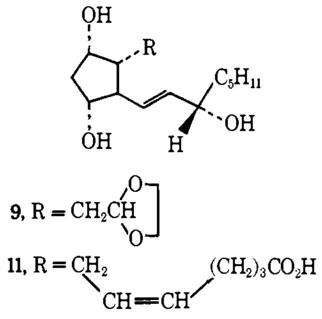
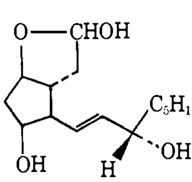


9, R =
11, R =



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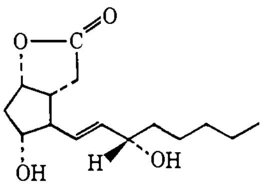

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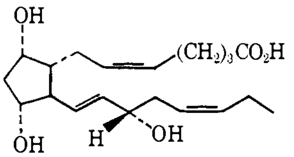

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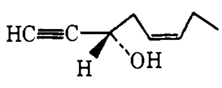

13

By an analogous sequence *rac*- and *nat*-PGF$_{3\alpha}$ (**14**) and their 15-epimers can be prepared in equivalent yields using *rac*- or (*S*)-*cis*-oct-5-en-1-yn-3-ol (**13**) in place of octyn-3-ol. *rac*-**13** was prepared from *cis*-3-hexenal[21] with ethynylmagnesium bromide in THF at 0° in 62% yield: bp 67–67.5° (6–7 mm). Resolution of **13** was achieved *via* the hemiphthalate ester (*S*)-(−)-α-phenethylamine salt:[10] mp 120–122°; $[\alpha]_D$ −27.2°. Pure (*S*)-**13** had $[\alpha]^{Et_2O}_D$ −3.7°.[22] *rac*-PGF$_{3\alpha}$ (**14**) prepared by the above procedure was shown to be identical with an authentic sample by its tlc mobility in three systems,[18] glc, and ir and nmr spectra, as well as the mass spectrum of its tristrimethylsilyl ether methyl ester. It is clear from the foregoing that by our method the intermediate corresponding to **9** but possessing a 17,18-cis double bond can be converted into the lactone corresponding to **12** and thence into PGE$_3$.[23]

Greater economy may be achieved by utilizing optically active **2** in the above syntheses. Resolution was performed with (+)-α-phenethylamine isocyanate, which yielded the (+)-urethane (**3b**), mp 102.5–103°, $[\alpha]_D$ +12°, from ether–hexane in 70% yield. On alkaline hydrolysis (+)-**3b** reverted to (+)-**2**, mp 70–71°, $[\alpha]_D$ +44°, possessing the absolute configuration shown.[24]

Acknowledgments. We are grateful for the generous support of this work by the National Institutes of Health (research grants AM 11499 and K6-AM-21846). Our thanks are due to Dr. John Pike of the Upjohn Co. for authentic samples of PGF$_{2\alpha}$, its racemate, and PGF$_{3\alpha}$, to Dr. Ned M. Weinshenker of the Alza Corp. for 15-epi-PGF$_{2\alpha}$, to Professor E. J. Corey for a sample of the lactone **12**, and to Drs. G. Ohloff and M. Winter of Firmenich and Co. for generous supplies of *cis*-3-hexenal dimethyl acetal.

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[20] E. J. Corey and R. K. Varma, *J. Amer. Chem. Soc.*, **93**, 7319 (1971).

[21] M. Winter, *Helv. Chim. Acta*, **46**, 1792 (1963).

[22] The absolute configuration of **13** was determined by catalytic reduction (Pd/C) to 3-octanol, $[\alpha]_D$ −9.5°, which according to Brewster's rules has the *R* configuration. (−)-**13** therefore possesses the *S* configuration.

[23] E. J. Corey, H. Shirahama, H. Yamamoto, S. Terashima, A. Venkateswarlu, and T. K. Schaaf, *J. Amer. Chem. Soc.*, **93**, 1490 (1971).

[24] The absolute configuration of (+)-**2** was established as follows. Catalytic reduction of the tosylate (+)-**3a**, $[\alpha]_D$ +17°, with Pd/C afforded the corresponding dihydrodiol tosylate, $[\alpha]_D$ +59°, which was converted to the hydroxy epoxide, $[\alpha]_D$ −8.4°, with KOH in methanol, and thence into the keto epoxide, $[\alpha]_D$ −91°. The latter was related to the known (*S*)-2-methylcyclopentanone, *a* = +23(CH$_3$OH), by its negative Cotton effect, *a* = −23(CH$_3$OH); *cf.* ref 1, p 42. We thank Dr. M. M. Mehra for this resolution.

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Regiospecific Epoxide Opening with Acetylenic Alanes. An Improved Total Synthesis of E and F Prostaglandins

Sir:

In the preceding communication[1] we have described a total synthesis of the prostaglandins, which suffered from a single low-yield reaction (25–30%), caused by lack of regioselectivity in the epoxide opening of the trimethylsilyl ether of **6**[2] with (*S*)-(−)-3-trimethylsilyloxy-1-octynyldimethylalane (**7**). Similar problems were encountered by Corey and Noyori[3] in the reaction of the epoxide I with 1,3-bis(methylthio)allyllithium,

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[1] J. Fried, C. H. Lin, J. C. Sih, P. Dalven, and G. F. Cooper, *J. Amer. Chem. Soc.*, **94**, 4342 (1972).

[2] The arabic boldface numerals refer to the formulas of the preceding communication, the Roman numerals to those of the present one.

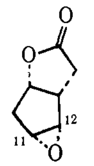
[3] E. J. Corey and R. Noyori, *Tetrahedron Lett.*, 311 (1970).

Table I. Isolated Yields and Ratios of Substitution at C-11 and C-12

Epoxide	$(CH_3)_2AlC{\equiv}C\underset{OSi(CH_3)_3}{CH}C_5H_{11}$ Substitution yield, % 11	12	11/12	$(CH_3)_2AlC{\equiv}C\underset{OC(CH_3)_3}{CH}C_5H_{11}$ Substitution yield, % 11	12	11/12
IIa				50	10	5.0
IIa–bistrimethylsilyl ether	45	15	3.0	51	19	2.7
IIb–trimethylsilyl ether	47	13	3.6			
6	22	23	1.0	26	21	1.2
6–trimethylsilyl ether	43	27	1.6	32	22	1.5
IIIa	7	35	0.2	0	60	0
IIIb	36	14	2.6			
VI				10	50	0.2
VII	4	20[a]	0.2			

[a] This low overall yield is the result of problems in the isolation of the water-soluble pentols.

which led to indiscriminate opening of the epoxide at positions 11 and 12 (prostaglandin numbering). This communication reports a solution to this problem, which we believe to be of general synthetic utility.



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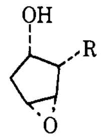
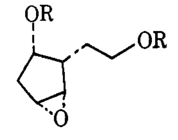
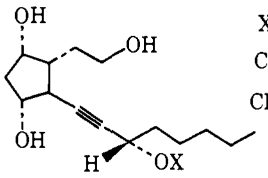


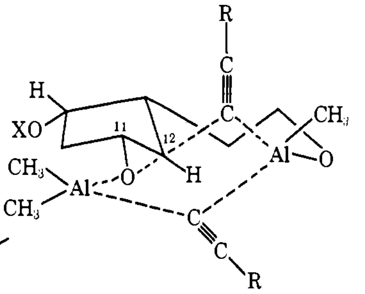
IIa, R = $(CH_2)_7OH$
b, R = $CH_2CH{=}CH_2$



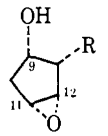
IIIa, R = H
b, R = $Si(CH_3)_3$



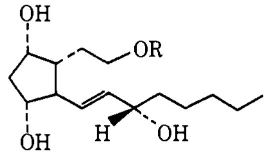
IVa, X = H
b, X = $C(CH_3)_3$



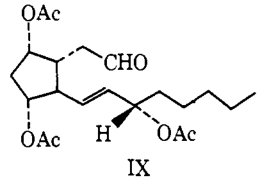
V



VI, R = $(CH_2)_3OH$
VII, R = $CH_2\underset{H\ \ OH}{C}CH_2OH$



VIIIa, R = H
b, R = trityl
c, R = trityl; H = acetyl
d, R = H; H = acetyl



IX

When applied to the synthesis of $PGF_{2\alpha}$ the overall yield reported from 3,5-cyclopentenediol was increased from 2.6 to 4.1%.

Aluminum alkyls are strong Lewis acids with great proclivity to form adducts with oxygen bases.[4] This property, which is shared by the dialkylalkynylalanes,[5] is held to be responsible for the facility with which these reagents effect epoxide cleavage.[6] It was reasoned, therefore, that the desired reaction could be made the kinetically preferred one by placing an oxygen atom into appropriate position relative to the epoxide ring so that complexing of that oxygen with the alane (*e.g.*, **7**) would produce a cyclic transition state V favoring bond formation involving C-12. The acetal grouping of **6** employed in the preceding communication[1] was intended as such a device, but the reaction of **6** with the alane **7** afforded alkynylation products in a ratio of 1.6:1 in favor of the undesired C-11 substituted isomer. Nevertheless, this constituted an improvement over the ratios obtained with the TMS ethers of IIa[7] and IIb,[8] which do not possess oxygen in the requisite position (Table I). Evidently, complexing with the acetal oxygens was not sufficient to suppress attack by the acetylide at C-11. Not until the acetal was replaced by a carbinol group capable of forming a covalent aluminum-oxygen bond[9] was the desired regiospecificity achieved. Thus, when the primary alcohol IIIa was employed in the reaction with **7**, followed by desilylation with 90% acetic acid, a product ratio of 5:1 in favor of the desired product IVa was obtained. Substituting the *tert*-butyl for the trimethylsilyl protecting group in **7** gave *exclusively* IVb. These results suggest that the favored transition state in this reaction may indeed be formulated as in V, which can be constructed with little strain from Dreiding models.[10] As predicted, silylation of IIIa (IIIb) prior to reaction with the alane caused reversion to the undesirable ratio of 2.6:1 favoring the 11 isomer. On the other hand, the homolog of IIIa (VI)[11] and the glycol VII[11] produced

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(4) R. Köster and P. Binger, *Advan. Inorg. Chem. Radiochem.*, **7**, 284 (1965).

(5) G. Wilke and H. Müller, *Justus Liebigs Ann. Chem.*, **629**, 222 (1960).

(6) J. Fried, C. H. Lin, and S. H. Ford, *Tetrahedron Lett.*, 1379 (1969).

(7) J. Fried, C. H. Lin, M. M. Mehra, W. L. Kao, and P. Dalven, *Ann. N. Y. Acad. Sci.*, **180**, 38 (1971).

(8) This epoxide was prepared from **3a** in 53% overall yield by first protecting the double bond by bromination in CCl_4 at −20°, followed by debenzylation with BBr_3 in CH_2Cl_2 at −78° for 2 min, debromination with Zn dust in hot 10% acetic acid, and epoxide ring closure with 0.5 *N* KOH in methanol.

(9) Reaction of the free hydroxyl groups with the alane reagent was indicated by the evolution of methane upon mixing of substrate and reagent.

(10) The three-center Al–C–Al bond is preferred because of the tendency of alanes to form dimers involving such bonding; *cf.* ref 5.

(11) VI (mp 39–40°) and VII were prepared from **3a**, the former by

ratios of the same order as IIIa, whereas the diol IIa, in which the primary hydroxyl group is at the terminus of a seven-carbon chain, gave the highly unfavorable 5:1 ratio (Table I).

The diol epoxide IIIa was selected for completion of the synthesis. It was prepared by borohydride reduction in isopropyl alcohol of the ozonide[1] of **3a**, followed by hydrogenolysis of the benzyl groups with 10% Pd/C in moist ethyl acetate, and epoxide closure with 1.1 equiv of KOH in methanol (overall yield from **3a** 82%). Reaction of IIIa with *rac*-3-*tert*-butyloxy-1-octynyldimethylalane[12] (10 equiv, 60°, 2 hr) produced a mixture of *rac*-IVb and its racemic 15-epimer (60%), which was debutylated with trifluoroacetic acid at −15° for 4 hr (87%) to form IVa; the latter was reduced with $LiAlH_4$ in boiling THF for 5 hr (80%) to a mixture of *rac*-VIIIa and its 15-epimer. Selective monotritylation at 25° afforded the racemate VIIIb and its 15-epimer,[13] which proved the most easily separable mixture of 15-epimers encountered by us. The more polar isomer VIIIb was acetylated to form VIIIc and the latter detritylated with 90% acetic acid at 25° for 15 hr and the triacetate alcohol VIIId oxidized with $CrO_3 \cdot 2py$ in CH_2Cl_2 at 25° for 15 min. The aldehyde triacetate IX (85% overall yield from VIIIb) was shown to be identical with that described in the preceding communication[1] by tlc, glc, and ir and mass spectra. When IX was subjected to a Wittig reaction followed by hydrolysis with 2% aqueous KOH at 25°, *rac*-$PGF_{2\alpha}$ (**11**) was obtained in 55% yield and identified as previously described.[1] In a parallel sequence the less polar isomer of VIIIb was converted to *rac*-15-epi-$PGF_{2\alpha}$.

Oxidation of VIIId with Jones reagent at 25° for 15 min followed by hydrolysis with 1% NaOH (1:1 H_2O–CH_3OH) furnished the Corey lactone (**12**)[14] in 85% yield, identified as previously described[1] and by glc and the mass spectrum of the tristrimethylsilyl ether–trimethylsilyl ester of the corresponding acid.

The above experimental conditions are equally compatible with the functionality present in the PGE_3 and $F_{3\alpha}$ side chains. This improved procedure should therefore be applicable to these prostaglandins as well.

Acknowledgments. The authors are grateful for the generous support of this work by the National Institutes of Health (research grants AM 11499 and K6-AM 21846). We wish to thank Dr. John Gilmore for the preparation of VI and of its reaction product with 3-*tert*-butyloxyoctynyldimethylalane, and Mrs. Esther Chao for the preparation of intermediates.

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hydroboration and the latter by reaction with OsO_4 in pyridine, followed in both cases by debenzylation and epoxide ring closure (1 equiv of KOH in MeOH). The osmylation of **3a** furnished two glycols, epimeric at C-6 in a 4:1 ratio separable after debenzylation by tlc, of which only the more abundant one was convertible to the epoxide VII. Its 6-epimer furnished, instead, the isomeric tetrahydropyran derivative. This difference in the course of reaction was used to assign relative configuration at C-6. Molecular models of the tosylate precursor of VII clearly show that hydrogen bonding between the 6- and 9-hydroxyl groups prevents approach of the 5-hydroxyl group to C-12; thus, epoxide formation is preferred, whereas in its 6-epimer such hydrogen bonding forces the 5-hydroxyl group into position for bonding to C-12 leading to tetrahydropyran formation.

(12) J. Fried, M.M. Mehra, and W. L. Kao, *J. Amer. Chem. Soc.*, **93**, 5594 (1971).

(13) The yield of primary monotrityl derivatives was 55%. In addition, 20% of secondary monotrityl and 25% of ditrityl compound were obtained, which were detritylated with 90% acetic acid and recycled.

(14) E. J. Corey, N. M. Weinshenker, T. K. Schaaf, and W. Huber, *J. Amer. Chem. Soc.*, **91**, 5675 (1969).

The Structure of the Seven-Coordinate Cyano Complex of Vanadium(III)

Sir:

Seven-coordinate transition metal complexes containing simple monodentate ligands remain a rarity in chemistry.[1] While the classic example of seven coordination is IF_7,[2] metal complexes which have been found include the MF_7^{n-} species (M = Zr,[3] Nb,[4,5] U[6]) and UO_2F_5.[3–7] Among structures found are the pentagonal bipyramid (ZrF_7^{3-} [3,8]), the monocapped trigonal prism (NbF_7^{2-} [4]), and the tetragonal base–trigonal base structure ($Ph_4C_4Fe(CO)_3$[9]). The structure of the ZrF_7^{3-} ion described by Hurst and Taylor[3] is not unambiguous because of severe disordering. Brunton[8] has described the structure of $Rb_5Zr_4F_{21}$ in which both a pentagonal bipyramid and a distorted antiprism with one vacant position occur; however, these structures are not isolated units but instead are part of a ligand-bridged network. The structure of $Zr(acac)_3Cl$ has recently been reported to be derived from a pentagonal bipyramid.[10] Of late, there has been considerable interest in the cyano complex of vanadium(III),[11–13] the primary concern being a determination of the molecular formula and the coordination about the vanadium. The ir studies[11–13] on this compound have been restricted to the solid state; it has been shown, however, that structure determinations of cyano complexes on the basis of solid state ir evidence alone can be unreliable.[14] We now wish to report the results of a single crystal X-ray study of $K_4[V(CN)_7] \cdot 2H_2O$, potassium heptacyanovanadate(III) dihydrate, which contains a discrete seven-coordinate vanadium(III) ion.

Red crystals were prepared by a modification of the method of Locke and Edwards.[15] A nearly cubic-shaped crystal of dimensions of 0.20 × 0.22 × 0.24 mm was mounted into a thin-walled capillary tube under a nitrogen atmosphere. The compound crystallizes in the triclinic system, and the space group was

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(1) E. L. Muetterties and C. M. Wright, *Quart. Rev., Chem. Soc.*, **21**, 109 (1967).

(2) R. C. Lord, M. A. Lynch, Jr., W. C. Schumb, and E. J. Slowiski, Jr., *J. Amer. Chem. Soc.*, **72**, 522 (1950).

(3) H. J. Hurst and J. C. Taylor, *Acta Crystallogr., Sect. B*, **26**, 417 (1970).

(4) J. L. Hoard, *J. Amer. Chem. Soc.*, **61**, 1252 (1939).

(5) G. M. Brown and L. A. Walker, *Acta Crystallogr.*, **20**, 220 (1966).

(6) W. H. Zachariasen, *ibid.*, **7**, 792 (1954).

(7) W. H. Zachariasen, *ibid.*, **7**, 783 (1954).

(8) G. Brunton, *Acta Crystallogr., Sect. B*, **27**, 1944 (1971).

(9) R. P. Dodge and V. Schomaker, *Nature (London)*, **186**, 798 (1960).

(10) R. B. VonDreele, J. J. Stezowski, and R. C. Fay, *J. Amer. Chem. Soc.*, **93**, 2887 (1971).

(11) W. P. Griffith and G. T. Turner, *J. Chem. Soc. A*, 858 (1970).

(12) B. G. Bennett and D. Nicholls, *ibid.*, 1204 (1971).

(13) R. Nast and D. Rehder, *Chem. Ber.*, **104**, 1709 (1971).

(14) B. M. Chadwick and A. G. Sharpe, *Advan. Inorg. Chem. Radiochem.*, **8**, 830 (1966).

(15) J. Locke and G. H. Edwards, *Amer. Chem. J.*, **20**, 594 (1898).