hydroxyallyl anion, it might be expected that **9** would be stabilized relative to **10** when metal cations such as Li^+ and Ca^{2+} are involved. These cations should form more covalent bonds with the oxygen atom than the more electropositive metal cations, thus allowing more favorable overlap of the β-carbanion with the π-electron system of the metal enolate.

Experimental Section[11]

General Procedure for the Metal–Ammonia Reduction of Octalone 1.[3c] Anhydrous liquid ammonia (300 mL, distilled from sodium) was distilled under nitrogen into a flame-dried three-necked flask fitted with a mechanical stirrer, an addition funnel, and a Claisen adaptor holding a dry-ice condenser and a gas inlet tube. Freshly cut metal, 0.022 g-atom of alkali metal or 0.011 g-atom of the alkaline-earth metal, was then added and the mixture was stirred until the metal had completely dissolved (15–45 min). A mixture of 1.78 g (0.010 mol) of octalone **1** and 0.74 g (0.010 mol) of *tert*-butyl alcohol in 70 mL of anhydrous ether (distilled from $LiAlH_4$) was added dropwise with stirring over 30 min at −33 °C. Stirring was continued for 3 h and then 3.14 g of solid ammonium chloride was added as rapidly as possible. The ammonia was allowed to evaporate and the residue was dissolved in 200 mL of a 1:1 ether–water mixture. The layers were separated and the aqueous layer was saturated with sodium chloride and extracted with three 50-mL portions of ether. The ethereal extracts were combined and dried over magnesium sulfate. After removal of the solvent in vacuo the residue was analyzed by GLC and distilled to give a mixture of decalones **3** and **4** in the yields given in Table I.

Pure samples of ketones **3** and **4** were collected by preparative GLC. Ketone **3** showed identical IR, ^1H NMR, and mass spectral properties and GLC behavior to an authentic sample.[4] Its ^{13}C chemical shifts are recorded in Table I. Compound **4** showed: mp 51.0–52.0 °C; IR (CCl_4) 1711, 1460, 1442, 1379, 1330, 1305, 1157, 1142, 1110 cm^{-1}; NMR (CCl_4) δ 0.89 (d, 3 H, J = 3.8 Hz), 1.25 (s, 3 H); MS (70 eV) *m/e* 180 (28), 109 (100).

Anal. Calcd for $C_{12}H_{20}O$: C, 79.94; H, 11.19. Found: C, 79.85; H, 11.18.

The ^{13}C chemical shifts of **4** are recorded in Table I. It formed a semicarbazone, mp 182.0–183.0 °C.

Anal. Calcd for $C_{13}H_{20}N_3O$: C, 65.79; H, 9.77. Found: C, 65.70; H, 9.81.

Preparation of Ketone 6. Ketone **6** was prepared in ~90% yield by lithium–ammonia reduction of the enone **5** according to the general procedure described for the enone **1**. Ketone **6** [bp 110–112 °C (0.1 mm); lit.[4b] 80 °C (0.01 mm)] showed identical IR, ^1H NMR, and mass spectral properties with those reported for the optically active material.[4b] It formed a semicarbazone: mp 203–204 °C (lit.[7] mp 202.5–203.0 °C). The ^{13}C chemical shifts are shown in Table I.

Catalytic Hydrogenation of Enone 1. To a solution of 0.32 g of octalone **1** in 6 mL of 95% ethanol was added 0.056 g of 10% palladium on carbon. The mixture was hydrogenated in a Parr apparatus for 2 h at 35 psi of hydrogen pressure. Removal of the catalyst by filtration and removal of the solvent in vacuo gave a mixture of decalones **3** and **4** [bp 110–115 °C (bath temperature) (0.1 mm)] in essentially quantitative yield. Analysis of the mixture by GLC showed that it contained ~65% **3** and ~35% **4**. A trace (<3%) of decalone **6** was also present.[5]

Catalytic Hydrogenation of Enone 5 in Acidic Medium. To a solution prepared from 0.80 g of octalone **5**, 1.5 mL of 3.2 N hydrochloric acid, and 15 mL of 95% ethanol was added 0.15 g of 5% palladium on carbon. The mixture was hydrogenated in a Parr apparatus for 2 h at 35 psi of hydrogen pressure. On removal of the catalyst by filtration and removal of the solvent in vacuo, GLC analysis of the residue showed that it was composed of a 5:95 mixture of decalones **6** and **7**. Distillation of the mixture under reduced pressure gave 0.403 g (49%) of pure **7**: bp 108–112 °C (0.10 mm); IR (film) 1713, 1462, 1447, 1430, 1379, 1355, 1340, 1284, 1266, 1243, 1217, 1185, 1155, 1133, 1109, 1072, 1022, 1005, 934, 826, 755 cm^{-1}; NMR (CCl_4) δ 0.81 (d, 3 H, J = 6.6 Hz), 1.06 (s, 3 H); MS (70 eV) *m/e* 180 (37), 109 (100), 108 (88), 95 (65), 81 (53), 67 (54), 55 (84), 41 (79); semicarbazone mp 202.0–203.0 °C (lit.[7] 202.2–202.5 °C).

Registry No.—**1**, 64281-61-4; **4** semicarbazone, 64215-98-1.

References and Notes

(1) This investigation was supported by Grant No. CA12193, awarded by the National Cancer Institute, DHEW. The research was also assisted by Institutional Research Grants from the National Science Foundation for the purchase of a mass spectrometer and a Fourier transform NMR spectrometer.

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(4) (a) The major reduction product **3** showed identical NMR, IR, and mass spectral properties and chromatographic behavior to an authentic sample of racemic **3** which had identical spectral and chromatographic properties to the optically active material obtained by oxidative degradation of dihydroeudesmanol (ref 4b). We are grateful to Dr. B. Maurer for providing us with a generous supply of authentic racemic **3**. (b) B. Maurer, M. Frachebound, A. Grieder, and G. Ohloff, *Helv. Chim. Acta*, **55**, 2371 (1972).
(5) A trace (<3%) of the decalone **6** was obtained in the catalytic reduction of **1**. This product may have arisen because **1** was slightly contaminated with the trans isomer **5** or a slight amount of isomerization of **1** into **5** may have occurred under the reaction conditions.
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(11) Melting points and boiling points are uncorrected. Infrared spectra were taken on a Perkin-Elmer Model 457 infrared spectrophotometer. The ^1H NMR spectra were obtained on a Varian T-60 NMR spectrometer and the ^{13}C NMR spectra were determined at 25 MHz with a Jeol Fourier transform spectrometer, Model PFT-100. The chemical shifts are expressed in δ values (ppm) to Me_4Si as an internal standard. The mass spectra were obtained with a Hitachi (Perkin-Elmer) Model RMU-7. Gas–liquid chromatography was carried out using a Perkin-Elmer 881 or an Aerograph A-90-P3 gas chromatograph. A 6 ft × 0.125 in. aluminum column packed with 20% Carbowax K-20M on acid washed Chromosorb W was employed for analytical work and a 10 ft × 0.25 in. stainless steel column containing the same packing material was used for preparative work. Microanalyses were obtained by Atlantic Microlab, Inc., Atlanta, Ga.

A Convenient Method for the Stereoselective Reduction of Alkynes to Alkenes by the New Reagents MgH_2–CuI and MgH_2–CuO-*t*-Bu

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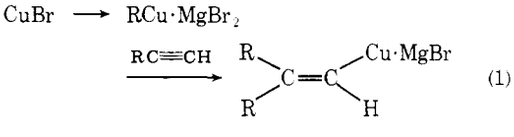
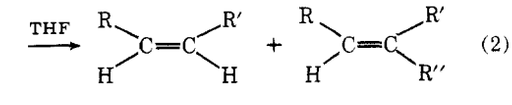
The most common method of reducing alkynes to cis olefins is by catalytic hydrogenation, whereas the most common method of reducing alkynes to trans olefins is by liquid ammonia reduction.[1] In catalytic hydrogenation, usually some trans olefin is also produced with the cis olefin and quite often the two isomers are difficult to separate completely. A more recent method of reducing alkynes to cis olefins is based on the work of Normant.[2,3] Normant has shown that organocopper reagents (RMgBr + CuBr) add to unactivated terminal alkynes (eq 1) to produce the alkyl addition product. More



(1)

recently, Crandall reported that when the reagent 2RMgX–CuI is added to disubstituted alkynes, reduction is the predominant reaction (eq 2).[4] These reactions are potentially important because of their stereospecificity and versatility in organic synthesis.[5–10] However, the main re-



(2)

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Table I. Reduction of Alkynes by MgH_2–CuI and MgH_2–CuOBu-*t* in THF[a]

Alkyne	Registry no.	Reagent	Recovered starting material, %	Products, %		
			1-Hexyne	1-Hexene		Hexane
1-Hexyne	693-02-7	A[b]	0	80		0
		B[c]	5	78		0
				2-Hexene		Hexane
			2-Hexyne	cis	trans	
2-Hexyne	764-35-2	A	0	80	0	0
		B	7	81	0	0
			1-Octyne	1-Octene		Octane
1-Octyne	629-05-0	A	5	84		0
		B	0	92		0
			Phenylacetylene	Styrene		Phenylethane
Phenylacetylene	536-74-3	A	0	98		0
			Diphenylacetylene	Stilbene		1,2-Diphenylethane
				cis	trans	
Diphenylacetylene	501-65-5	A	0	95	0	0

[a] Mole ratio of MgH_2/CuI(CuOBu-*t*)/alkyne = 1.00:1.00:0.25 and the reaction time was 48 h except in the case of phenyl- and diphenylacetylene when the reaction time was 24 h. [b] Reagent A, MgH_2–CuI. [c] Reagent B, MgH_2–CuOBu-*t*.

duction product is accompanied by a side alkylation product, sometimes in substantial yield. This report encourages us to report our own findings using the reagent MgH_2–CuI and MgH_2–CuOBu-*t* which reduces alkynes stereoselectively to the corresponding cis olefins in the complete absence of trans olefin or alkane by-product. The advantages of this method over catalytic hydrogenation lie in the purity of the product formed and in the convenience of the method once the reagent is prepared.

Results and Discussion

Results of alkyne reduction by the reagents MgH_2–CuI or MgH_2–CuOBu-*t* are summarized in Table I. The terminal alkynes, 1-hexyne, 1-octyne, and phenylacetylene, were reduced to the corresponding alkene with 100% selectivity (0% alkane) in 80–98% yield (eq 3). The internal alkynes, 2-hexyne and diphenylacetylene, were reduced to the cis alkene as the only product (no trans alkene or alkane was detected) in 80–95% yield. The alkene, 1-octene, was not affected by either reagent. The high stereospecificity of the reaction of MgH_2–CuI (or CuOBu-*t*) reveals that these reagents are very promising for the conversion to alkynes to alkenes, especially interal alkynes to cis alkenes.

$$RC{\equiv}CH \xrightarrow[MgH_2\text{–}CuOBu\text{-}t]{MgH_2\text{–}CuI} RCH{=}CH_2 \quad (80\text{–}90\%\ \text{yield}) \qquad (3)$$

(where R = *n*-C_4H_9, *n*-C_6H_{13}, or Ph)

$$RC{\equiv}CR' \xrightarrow[\text{or } MgH_2\text{–}CuOBu\text{-}t]{MgH_2CuI} \underset{H}{\overset{R}{}}\!\!>C{=}C<\!\!\overset{R'}{}_{H} \quad (80\text{–}95\%\ \text{yield}) \qquad (4)$$

(where R = *n*-C_4H_9 and R′ = CH_3 or R = R′ = C_6H_5)

$$n\text{-}C_8H_{17}\text{–}CH_2{=}CH_2 \xrightarrow[48\ h]{MgH_2\text{–}CuI} \text{no reaction} \qquad (5)$$

The Normant reagent (RMgBr + CuBr) is believed to have a composition expressed by the empirical formula RCu·$MgBr_2$. By analogy one might propose that the reagent MgH_2–CuI has a similar composition, namely, CuH–HMgI; however, we have no evidence to support this idea and it would be difficult to obtain support. For example, the MgH_2 and CuI are mixed at −78 °C in THF. The solution does not become clear and a brownish mixture results. The alkyne is then added and the solution allowed to warm to room temperature, at which time the mixture turns black. Reagent decomposition is obviously taking place at room temperature, since H_2 is being slowly evolved; thus, a spectroscopic analysis of the reaction mixture is not possible.

Experimental Section

Apparatus. All operations were performed under a nitrogen atmosphere using either a nitrogen-filled glove box equipped with a special recirculating system to remove oxygen and moisture[11] or on the bench using Schlenk tube techniques.[12] All glassware were flash flamed and flushed with dry nitrogen prior to use.

Analyses. Gas analyses were carried out by hydrolyzing samples with hydrochloric acid on a standard vacuum line equipped with a Toepler pump. Magnesium was determined by EDTA titration, at pH 10, using Eriochrome Black as an indicator. Copper was determined electrolytically. GLPC analyses were performed on an F and M Model 720 or 700 gas chromatograph.

Materials. Tetrahydrofuran was distilled over $NaAlH_4$ prior to use. Diphenylacetylene, phenylacetylene, 2-hexyne, 1-octyne, 1-octene (Chemical Sample Co.), and 1-hexyne (Beacon Chemical Industries, Inc.) were purchased commercially and used without further purification.

Preparation of Cuprous *tert*-Butoxide.[13] Fifty millimoles of BuLi in *n*-hexane was added dropwise to a solution of *tert*-butyl alcohol (50 mmol) in THF and stirred for 1 h. This solution of 50 mmol of LiOBu-*t* was added to a slurry of cuprous chloride (4.95 g; 50 mmol) in THF and stirred for another hour, and the solvent was removed under vacuum. The residue was sublimed in vacuo at 160 °C (0.1 mm) to give yellowish crystals (yield 70%). Anal. Found: Cu/*t*-BuOH, 1.00:1.03.

Preparation of Active Magnesium Hydride in THF. When 15.0 mmol of $LiAlH_4$ solution in diethyl ether (30 mL) was added dropwise to a magnetically well-stirred solution of Et_2Mg (15.0 mmol) in diethyl ether (35 mL), an exothermic reaction occurred and an immediate precipitate appeared. This reaction mixture was allowed to stir for 1 h at room temperature followed by centrifugation of the insoluble white solid. The supernatant solution was separated by syringe and the insoluble white solid was washed with diethyl ether three to four times and finally made a slurry in THF. The analysis of this slurry showed that it contained Mg and H in ratios 1.00:2.02.

General Reaction. The experiments were carried out by the following procedure. A slurry of MgH_2 in THF was syringed into the mixture of alkyne and CuI (or CuOBu-*t*) at −78 °C. Then, the temperature was allowed to increase to room temperature by removing the cooling bath; a deep black color and slight gas evolution were observed at room temperature. After an indicated period (24 or 48 h), the reaction mixture was quenched with distilled water, dried over $MgSO_4$, and extracted with several portions of THF. Product analyses and percent yield were carried out either by NMR or GLC using an internal standard.

Acknowledgment. The authors thank the National Science Foundation (Grant MPS 7504127) for support of this work.

Registry No.—*t*-BuOH, 75-65-0; CuCl, 7758-89-6; CuOBu-*t*, 35342-67-7; $LiAlH_4$, 16853-85-3; Et_2Mg, 557-18-6; MgH_2, 7693-27-8; CuI, 7681-65-4.

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Facile Ring Cleavage of Prostaglandin Epoxy Ketones

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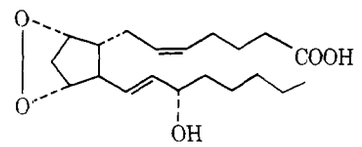
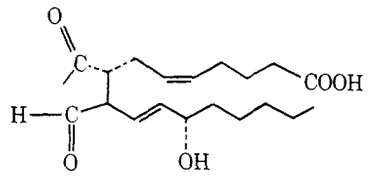
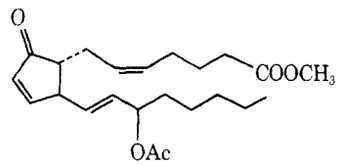
The suggestion of Salomon and Salomon[1] that prostaglandin endoperoxides (I) may rearrange to ring-opened keto aldehydes (II) prompts us to report another reaction in the prostaglandin field which we observed some years ago in connection with the epoxidation of (15*R*)-prostaglandin A_2 esters[2] [(15*R*)-PGA_2 esters, III], resulting in the facile opening of the 5-membered ring.



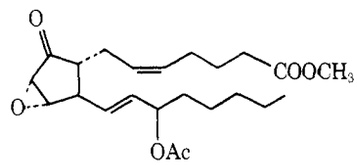
I



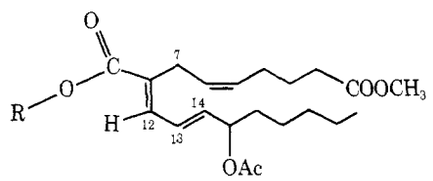
II



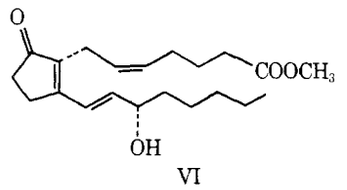
III



IV



Va, R = H
b, R = CH_3



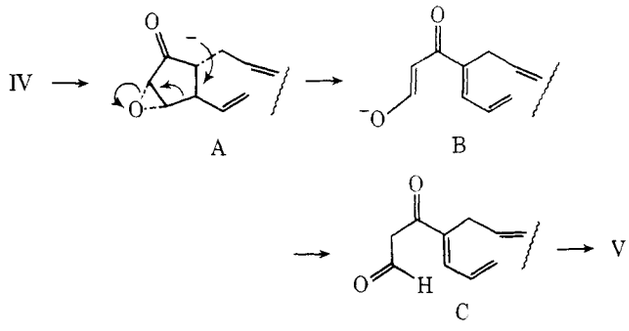
VI

The epoxidation of III to produce IV was accomplished by hydrogen peroxide and catalytic amounts of alkali metal hydroxides in cold methanol or other alcohols. If larger amounts of base or longer times are used for the reaction, an increasing amount of an acidic byproduct was formed which was shown to be the acid ester Va. The NMR spectrum of this showed the original C-1 methyl ester was still intact (OCH_3 at δ 3.67). This material was more easily isolated by chromatography as the diester Vb after diazomethane treatment, when it now showed an additional methyl ester function by NMR at δ 3.75.

The conjugated diene ester system for Vb was evident by the UV spectrum (λ_{max}(EtOH) 265 nm) and the NMR spectrum, which was particularly definitive in structure determination. It strongly resembled that of PGB_2 methyl ester VI except for an additional vinyl proton (C-12, PG numbering system) as a doublet at δ 7.15 (J = 11 Hz) coupled with the C-13 proton, now a doublet of doublets centered at δ 6.54 ($J_{12,13}$ = 11, $J_{13,14}$ = 14.5 Hz). The C-14 proton was also coupled to the proton at C-15 by 6.5 Hz at δ 5.96. By decoupling at 100 MHz, these couplings were shown to be correct, and also the presence of long-range coupling from C-15 to C-13 protons and from C-7 to C-12 protons was detected. The doubly allylic protons at C-7 occurred at δ 3.16 as a doublet with long-range coupling. The infrared and mass spectra were completely consistent with this formulation, the latter confirming the empirical formula $C_{22}H_{34}O_6$ for Vb and giving the expected fragmentation ions (see Experimental Section). The double bond at C-8(12) (PG numbering) is shown in the *E* configuration in structure V to show its relationship to its parent prostaglandin, and this seems consistent with its UV maximum.[3]

The same product, Vb, was formed when the epoxide mixture (IV and its 10β, 11β isomer)[2] was first isolated, freed of starting enone III by chromatography, and then retreated as above. The epoxide mixture used was about 5:1 α- to β-epoxides, but the epoxide recovered after the reaction (12%) was essentially all the 10β,11β-epoxide, perhaps reflecting a slower removal of the 8β-proton from the β-epoxide. These epoxides can be distinguished by NMR, the α-epoxide having a proton at δ 3.43 (d, J = 3 Hz) and the C-13,14 protons between δ 5.5 and 5.68. The β-epoxide has a proton at δ 3.38 (d, J = 3 Hz) with the C-13,14 protons between δ 5.65 and 5.88.

Structure V may arise by some such mechanism as below, followed by the cleavage of β-keto aldehyde by base.[7]



Experimental Section

Methyl (5*Z*,8*E*,10*E*,12*R*)-8-Carboxy-12-acetoxyheptadeca-5,8,10-trienoate. A solution of 4.0 g of (15*R*)-PGA_2 methyl ester acetate[2] in 75 mL of methanol was cooled to 0 °C, and then 5 mL of 30% H_2O_2 was added, followed over a period of 20 min by 10 mL of 1 N NaOH. The reaction mixture was stirred at 0 °C for 2.5 h, 12 mL of 1 N HCl was added, and the methanol was largely removed in vacuo. The products were extracted with ethyl acetate, and the extracts were washed with water and brine, dried with Na_2SO_4, and evaporated. The

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