tended to heat up suddenly by heat of reaction. On the other hand, in FSO_3H–SbF_5 (1:1)–SO_2ClF solution benzene dissolved readily, was easily mixed with hydrogen peroxide, and gave phenol in 54% isolated yield.

Experimental Section

Hydroxylation of Aromatic Compounds. To a vigorously stirred solution of the corresponding aromatics in the appropriate superacidic solvent (FSO_3H–SO_2ClF, FSO_3H–SbF_5–SO_2ClF, CF_3SO_3H–SO_2ClF, HF–BF_3, or HF), a solution of 98% hydrogen peroxide (FMC Corp.) in the same solvent was added dropwise at the specified temperature (generally −78 °C), kept constant by external cooling. Some of the aromatics did not completely dissolve into acidic solvents and these reactions were carried out in the well-stirred heterogeneous systems. As the reactions proceeded, however, the media became homogeneous because formed product phenols are soluble in the acidic solvents. An aliquot of the resulting solution was analyzed by ^1H NMR at the same low temperature. After 30-min reaction time, the solution was quenched by dropwise addition to ice-cold aqueous sodium chloride solution. The mixture was extracted with ether. The ether extracts washed with 10% sodium bicarbonate solution to remove acid and phenols were then extracted by 10% sodium hydroxide or Claisen's alkali solution. The dried ether layer was rotary evaporated to remove the solvent, and residual products were analyzed by IR, GLC, and NMR, usually showing only unreacted aromatics. After acidification of the phenol extracts and ether extraction, the solvent was distilled and the products were analyzed either by GLC, after methylation by dimethyl sulfate in aqueous alkali solution, or after trimethyl silylation in the case of cresols [using a Perkin-Elmer Model 900 gas chromatograph equipped with 0.010 in. i.d. × 150 ft. stainless-steel capillary column, coated with MBMA (*m*-bis(*m*-phenoxy)benzene + apiezon L) and operated at a column temperature of 140 or 160 °C with 20 psi of He pressure]. Alternatively, products were isolated by vacuum distillation. The generally used quantities in analytical runs were 0.0027 mol of aromatics, 0.0030 mol of hydrogen peroxide, 2 mL of acid, and 1 mL of solvent. In preparative runs, 0.013 mol of aromatics was reacted with 0.015 mol of hydrogen peroxide. Acidic solvents used were FSO_3H–SO_2ClF or SO_2 at −78 °C, FSO_3H–SbF_5 (1:1)–SO_2ClF at −78 °C, HF–BF_3 at −78 °C, CF_3SO_3H–SO_2ClF at ca. −50 °C (its melting point), HF at −78 °C, CF_3CO_2H and CH_3CO_2H at room temperature.

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Stereochemistry of the Reductive Debromination of (*R*)-*meso*- and (*S*)-*meso*-3-Methyl-2,4-dibromopentane

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The reductive 1,3-dehalogenations of the stereoisomeric 3-methyl-2,4-dibromopentanes with zinc, chromous sulfate, or sodium have been shown to proceed by an inversion process at one carbon atom and by a nonstereospecific process at the other. (*R*)-*meso*-3-Methyl-2,4-dibromopentane gave only the trans isomer of 1,2,3-trimethylcyclopropane, while the (*S*)-*meso*-dibromide gave mixtures of the *cis*- and *trans*-cyclopropanes.

The reductive 1,3-dehalogenation synthesis of cyclopropanes was first reported by Gustavson[1,2] and Freund.[3] The method has been extensively used preparatively,[4] but mechanistic studies have been few. The present study provides a partial remedy for that deficiency by an investigation of the stereochemistry of the process with three different reducing agents.

Some stereochemical information was in the literature prior to the publication of the present work.[5-9] Most notable is the report of Fry and Britton[5] on reductions of stereoisomeric 2,4-dibromopentanes. They found that the meso and *dl* forms gave roughly the same mixture of *cis*- and *trans*-1,2-dimethylcyclopropanes upon electrochemical reduction in Me_2SO and that the 2*S*,4*S* isomer of the dibromide gave a mixture of the *cis*-cyclopropane and the (1*R*,2*R*)-cyclopropane with high optical purity. The results require a stepwise mechanism with loss of stereochemistry at one carbon and essentially complete inversion at the other. A similar result was obtained with sodium naphthalenide as reducing agent, but larger experimental errors made the conclusions less definitive.

A contrasting result was obtained by Trost[7] on the reactions of *meso*- and *dl*-2,4-dibromopentane with *n*-butyllithium in THF at low temperatures. The reactions were stereoselective, with the meso compound forming primarily *cis*-1,2-dimethylcyclopropane and the *dl* compound forming primarily the *trans*-cyclopropane. Since the experiment was not done with an optically active 2,4-dibromopentane, it cannot be determined if one of the carbons undergoes stereospecific inversion or retention in this experiment, nor can it be determined whether the predominant overall stereochemistry is double inversion or double retention. Several mechanistic possibilities must therefore be considered.

An interesting stereoselectivity has been observed in the reductive debromination of *meso*- and *dl*-bis(α-bromobenzyl)

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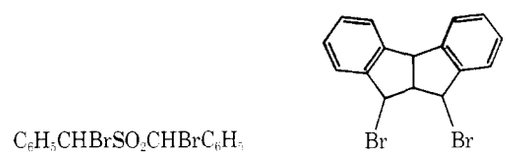
Table I. Product Yields and Composition[a] from the 1,3 Eliminations of (*R*)-*meso*-3-Methyl-2,4-dibromopentane

Product	Percent composition of products[b] Zn/PrOH-H_2O/ 0 °C	Cr^{2+}/ Me_2SO-H_2O/ RT[c]	Na/dioxane/ reflux
	95.7	87.6	55.5
	<0.8		<0.7
	3.5	12.4	27.7
			9.0
			7.1
Total yield[d]	60	26	42

[a] Uncorrected relative percent as determined by integration of the appropriate peak areas from vapor-phase chromatographic (VPC) analysis of the products. [b] Column headings list the reagent, solvent, and temperature used to effect 1,3 elimination. Results are the average of two independent runs. [c] RT = room temperature. [d] Percent yield based on dibromide assuming a product molecular weight of 84 g/mol, determined by VPC from the addition of an internal standard.

sulfone (**1**)[8] and a stereochemical dependence of the competition between debromination and reduction to a monobromide in the 2,8-dibromo-3,6-dibenzobicyclo[3.3.0]octadienes (**2**).[9] These rather special structural situations do not appear



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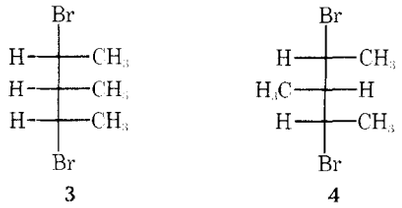
to provide unambiguous indications of the inherent stereochemical preferences or requirements of the simple reductive 1,3 elimination.

The substrates selected for the present investigation were (*R*)-*meso*- and (*S*)-*meso*-3-methyl-2,4-dibromopentane (**3** and **4**, respectively). These provide the same kind of stereochemical information as optically active 2,4-dibromopentane, but do so without the need for optical resolutions and without the potential errors in measurement of optical yield. The experimental analysis is basically just the determination of the cis/trans ratio in the product, 1,2,3-trimethylcyclopropane. Compounds **3** and **4** had been previously characterized in this laboratory[10] but had not been isolated as pure isomers. Dibromide **3** would give cis product from a double retention

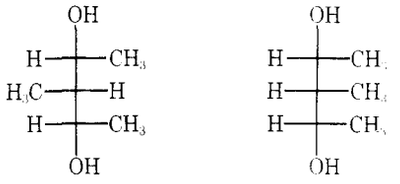


3 4

pathway and trans from double inversion or retention–inversion. Dibromide **4** would give cis product from double inversion and trans from double retention or retention–inversion. The reader will readily see that the *dl* isomer of **3** and **4** would not yield additional stereochemical information. It has therefore not been used in pure form as a substrate in this investigation.

Compounds **3** and **4** were prepared from the (*S*)-*meso*- and (*R*)-*meso*-diols **5** and **6**. Each of these was already available as a mixture with the *dl* isomer.[10] Separation of the high-boiling, viscous diols by fractional distillation was not convenient with the available equipment, so the mixtures were converted to the 1,3-dioxane derivatives with formaldehyde and then fractionated. The dioxanes were then individually converted to the diols by acid-catalyzed methanolysis.[11]

The conversions of **5** to **3** and **6** to **4** were done with triphenylphosphine dibromide in benzene. Under these condi-



5 6

tions, **5** [(*S*)-*meso*] gave a product which was 86% **3** [(*R*)-*meso*] and 14% *dl*. If tetra-*n*-butylammonium bromide was included in the reaction mixture to favor S_N2 over S_N1 processes, a 17% yield of **3** contaminated with only about 2–4% of the *dl* isomer was obtained.

The reaction of **6** [(*R*)-*meso*] with triphenylphosphine dibromide and tetra-*n*-butylammonium bromide gave only a 4% yield of **4** [(*S*)-*meso*], the main isolated product being allylic bromide **7**. A small sample of the product was purified to show that no (*R*)-*meso*- or *dl*-dibromide was present, but subsequent experiments were done on a mixture of **4** and **7**. It was established that **7** does not give any reduction products which interfere in the analysis of the *cis*- and *trans*-1,2,3-trimethylcyclopropanes.

$CH_3CH{=}C(CH_3)CHBrCH_3$

7

Stereochemical Results. The reaction conditions for three different reducing agents were worked out on a mixture of stereoisomers of 2,4-dibromo-3-methylpentane (to conserve the pure meso isomers). Subsequent reactions with the separated meso forms gave the results summarized in Tables I and II.

The fact that no *cis*-1,2,3-trimethylcyclopropane, within the limits of detection, was obtained from any of the reducing agents and the (*R*)-*meso*-dibromide means that there was at least one inversion at carbon in every ring closure. The fact that both *cis*- and *trans*-cyclopropanes were obtained from the (*S*)-*meso*-dibromide means that the remaining carbon center underwent either inversion (to give cis) or retention (to give trans). Under the conditions in Table II, zinc in aqueous *n*-propyl alcohol at 0 °C favored double inversion over retention–inversion, while sodium in refluxing dioxane showed the opposite preference.

The loss of stereochemistry at one carbon suggests that under all three reducing conditions there is formed an intermediate radical, carbanion, or organometallic species, which does not preserve the original configuration, followed by an internal concerted homolytic or nucleophilic displacement of the second bromine with the expected clean inversion. Concerted 1,3 eliminations, which would presumably be stereospecific at both carbons, are thus not likely in the present systems.[12] The results are similar to those in the aforementioned electrochemical reductions by Fry but somewhat in contrast with the *n*-butyllithium reductions by Trost.

Experimental Section[13]

Infrared (IR) spectra were recorded on a Perkin-Elmer 137 Infracord using sodium chloride plates. Nuclear magnetic resonance

(NMR) spectra were recorded on Varian T-60, A-60A, EM-390, HA-100, or HR-220 instruments. Carbon-13 nuclear magnetic resonance (^{13}C NMR) spectra were recorded on a Jeol FX-60 Fourier transform spectrometer. Chemical shifts are expressed in parts per million relative to tetramethylsilane, which is used as an internal standard and assigned the value $\delta = 0$ ppm. Vapor-phase chromatography (VPC) was done on an F and M Model 300 for analytical separations, and preparative scale separations were made on a Varian Aerograph Model 700. Both instruments were equipped with differential thermal conductivity detectors. Helium was used as the carrier gas, and separations were effected with the following columns: (A) 12 ft × 0.25 in. 10% FFAP on 60–80 AW/DMCS Chromosorb G, (B) 6 ft × 0.25 in. 10% FFAP on 60–80 Chromosorb P, (C) 10 ft × 0.25 in. 15% Carbowax 20M on 60–80 Chromosorb G, (D) 12 ft × 0.25 in. 20% dioctylphthalate on 60–80 Chromosorb P, (E) 5 ft × 0.25 in. 5% 1,2,3-tris(2-cyanoethoxy)propane on 60–80 AW/DMCS Chromosorb G, (F) 20 ft × 0.25 in. 10% Apiezon L on 60–80 AW/DMCS Chromosorb P, (G) 13 ft × 3/8 in. 20% FFAP on 60–80 Chromosorb P, (H) 12 ft × 3/8 in. 20% Carbowax 20M on Anakrom ABS. All columns were made of coiled copper tubing. The compositions of any mixtures are reported, based on the integrated area under the appropriate chart peak, and are uncorrected for differences in thermal conductivity.

Melting points were determined on a Büchi "Schmeltzpunktbestimmungsapparat" and were uncorrected.

Materials. "Commercial" 3-methyl-2,4-pentanediol refers to that purchased from Baker Chemical Co. Otherwise, this compound was prepared by standard procedures.[4] Ether was distilled from sodium hydride under nitrogen prior to use, benzene was distilled from calcium hydride under nitrogen, tetrahydrofuran (THF) was distilled under nitrogen from sodium benzophenone ketyl, and dioxane was purified by refluxing with aqueous hydrochloric acid, followed by treatment with potassium hydroxide and distillation from sodium benzophenone ketyl under nitrogen. All other chemicals and solvents were reagent grade and were used without further purification. Ground glass joints were lubricated with Dow Corning high-vacuum silicone lubricant.

Mixed Isomers of 2,4-Dibromo-3-methylpentane. A stirred solution of 43.2 g (0.4 mol) of sodium bromide in 840 mL of DMF under nitrogen was heated to 55–60 °C. Then 85.2 g (0.2 mol) of 3-methyl-2,4-pentanediol ditosylate[10] (from commercial diol) was added to the solution and the resulting mixture stirred for 160 h at 55 °C. The reaction mixture was poured into 2100 mL of water and extracted with 4 × 100 mL portions of ether. The organic extract was washed with water to remove residual DMF and then dried over anhydrous potassium carbonate. The solvent was removed, and vacuum distillation of the crude product gave 15.1 g (31%) of 3-methyl-2,4-dibromopentane, bp 67–70 °C (4.5 mm) [lit.[10] bp 71 °C (4.6 mm)]. The product was identified by IR and NMR as well as VPC analysis on column B at 130 °C, which gave only one peak with a retention time of 11 min, characteristic of the dibromide.

(Z)-3-Methyl-3-penten-2-ol was prepared by the method of House and Ro[14] but was shown by its NMR spectrum to be contaminated with about 12% of the *E* isomer[14] (signal at δ 4.07). Fractional distillation failed to separate the alcohols, so the mixture was converted to the acetates for fractionation.

A solution of 374 mL (2.0 M, 0.774 mol) of *n*-butyllithium in hexane was stirred and cooled to 0 °C under a nitrogen atmosphere. A mixture of the (*Z*)- and (*E*)-3-methyl-3-penten-2-ols, 75.7 g (0.757 mol), was added slowly over a 3-h period while the temperature was maintained below 5 °C. Then 54.8 mL (0.77 mol) of acetyl chloride was added slowly, and after the addition was complete, the reaction mixture was stirred at 0 °C for 2 h. The reaction mixture was then poured into 400 mL of ice–water and the small amount of solid formed was removed by filtration. The aqueous phase was extracted with hexane and the combined hexane extracts were dried over anhydrous magnesium sulfate. The solvent was removed and the crude product was purified by vacuum distillation: bp 86–89 °C (85 mm) [lit.[15] bp 49–50 °C (14 mm)]; 73.88 g (69%). VPC on column C at 125 °C indicated a mixture of 77.4% (*Z*)-3-methyl-3-penten-2-ol acetate, 12.3% (*E*)-acetate, and 10.3% unreacted alcohol, identified by coinjection with authentic samples. Separation of the mixture was effected by fractional distillation (113 mm) through a 4-ft column packed with glass helices and equipped with a heated jacket. The first fractions of the distillate were mixtures of the (*Z*)-acetate and unreacted alcohol, which were easily separated by chromatography on silica gel eluted with 10% ether in hexane. The next fraction of the distillate was found to be pure (*Z*)-3-methyl-3-penten-2-ol acetate identified by VPC, NMR, and IR: NMR δ 1.23 (d, J = 6.7 Hz, 3 H), 1.64, (m, 6 H), 1.95 (s, 3 H), 5.22 (m, 1 H), 5.67 (q, J = 6.7 Hz, 1 H), in agreement with that of an authentic sample. The later fractions of the distillation were identified as mixtures of the (*Z*)- and (*E*)-acetates which could be further separated by preparative VPC on column H at 150 °C; the first compound eluted was the (*Z*)-acetate, followed by the *E* isomer.

Table II. Product Yields and Composition[a] from the 1,3 Eliminations of (S)-meso-3-Methyl-2,4-dibromopentane[b]

	Percent composition of products[c]		
Product	Zn/PrOH-H_2O/ 0 °C	Cr^{2+}/ Me_2SO-H_2O/ RT[d]	Na/dioxane/ reflux
	25.0	17.4	29.9
	56.3	18.2	19.2
	18.7	24.0	11.8
			18.7
		40.4	20.4
Total yield[e]	38	12	38

[a] Uncorrected relative percent as determined by integration of the appropriate peak areas from vapor-phase chromatographic (VPC) analysis of the products. [b] Mixture of 57% (*S*)-*meso*-3-methyl-2,4-dibromopentane and 43% 3-methyl-4-bromo-2-pentene by NMR. [c] Column headings list reagent, solvent, and temperature used to effect 1,3 elimination. [d] RT = room temperature. [e] Percent yield based on dibromide, assuming a product molecular weight of 84 g/mol, determined by VPC from addition of an internal standard.

A solution of 35.98 g (0.253 mol) of (*Z*)-3-methyl-3-penten-2-ol acetate in 360 mL of dry ether was added to a suspension of 6.72 g (0.177 mol) of lithium aluminum hydride in 225 mL of ether at a rate to maintain reflux. The mixture was refluxed for an additional 1.5 h and then 7 mL of water was added dropwise, followed by 7 mL of 15% sodium hydroxide and an additional 58 mL of water. The reaction mixture was filtered to remove solid hydroxides and the solid was washed with ether. The ether solution was concentrated to 200 mL and washed with water and brine. The aqueous washings were extracted twice with ether and the combined ether solutions were dried over anhydrous magnesium sulfate. The ether was evaporated and the crude product, 22.0 g (87%), was vacuum distilled to give 21.0 g (83%) of (*Z*)-3-methyl-3-penten-2-ol: bp 87–88 °C (90 mm) (lit.[14] bp 140–141 °C); NMR δ 1.16 (d, J = 6.5 Hz, 3 H), 1.61 (m, 6 H), 3.40 (variable, s, 1 H), 4.74 (q, J = 6.5 Hz, 1 H), 5.20 (m, 1 H). No *E* alcohol could be detected in the NMR spectrum.

(S)-meso-4,5,6-Trimethyl-1,3-dioxane was prepared as a mixture with the *dl* isomer, as previously described.[10] The mixture was separated by fractional distillation through a 4-ft column packed with glass helices and equipped with a heated jacket; the *S*-meso isomer with bp 82.5–83.5 °C (96 mm) and estimated by VPC to be >99.5% pure was obtained, followed by the *dl* isomer at bp 93–94 °C (94 mm). The isomers were also readily separated on preparative VPC (column G). The NMR spectrum of the *S*-meso in CCl_4 showed δ 0.75 (d, J = 6.0 Hz, 3 H), 1.16 (d, J = 6.0 Hz, 7 H, obscures 1 H multiplet), 3.18 (d of q, J = 9.0 Hz, J' = 6.0 Hz, 2 H), 4.72 (AB quartet, J = 6.0 Hz, 2 H).

(R)-meso-4,5,6-Trimethyl-1,3-dioxane was prepared as a mixture with the *dl* isomer[10] and subjected to fractional distillation as for the *S*-meso form above, but because the original mixture contained only about 18% of the *R*-meso (from VPC analysis on column A), it was not possible to obtain the pure *R*-meso with the available equipment. An enriched fraction, bp 84–99 °C (123 mm), containing 41% *R*-meso was obtained as a forerun. This mixture was separated by preparative VPC on column G at 140 °C. The NMR spectrum of *R*-meso showed δ 0.91 (d, J = 6.6 Hz, 3 H), 1.14 (d, J = 6.6 Hz, 7 H, hides 1 H multiplet), 3.67 (q of d, J = 6.6 Hz, J' = 2.4 Hz, 2 H), 4.73 (AB quartet, J = 6.0 Hz, 2 H).

(S)-meso-3-Methyl-2,4-pentanediol (5). A solution of 27.83 g (0.21 mol) of (*S*)-*meso*-4,5,6-trimethyl-1,3-dioxane and 20 g (0.1 mol) of *p*-toluenesulfonic acid in 135 mL of methanol was heated to 88–90

°C for 216 h, after which time the theoretical amount of dimethoxymethane had distilled. The mixture was cooled and neutralized with 7.75 g (0.1 mol) of diethylamine and the methanol was then removed by evaporation. Then 120 mL of water was added to the crude product and the aqueous solution was continuously extracted with ether for 144 h, after which time the extract was dried over anhydrous magnesium sulfate and the solvent removed. Vacuum distillation of the crude product gave 19.5 g (79%) of (*S*)-*meso*-3-methyl-2,4-pentanediol: bp 91–93 °C (2.4 mm); NMR δ 0.74 (d, J = 7.0 Hz, 3 H), 1.13 (d, J = 6.5 Hz, 6 H), 1.38 (q of d, J = 7.0 Hz, J' = 2 Hz, 1 H), 3.63 (quintet, J = 6.5 Hz, 2 H), 5.14 (variable, s, 2 H) [lit.[11] NMR δ 0.73 (d, J = 6.5 Hz, 3 H), 1.12 (d, J = 6.5 Hz, 6 H), 1.35 (m, 1 H), 3.71 (m, 2 H)].

(*R*)-*meso*-3-Methyl-2,4-pentanediol (6). By the same procedure used for the preparation **5**, 4.89 g (37.56 mmol) of (*R*)-*meso*-4,5,6-trimethyl-1,3-dioxane and 3.51 g of *p*-toluenesulfonic acid in 24 mL of methanol for 120 h yielded 3.63 g (82%) of crude oil (solvent removed but product not distilled). The NMR spectrum indicated that the oil was sufficiently pure **6** to use without further purification: NMR δ 0.83 (d, J = 6 Hz, 3 H), 1.08 (d, J = 6 Hz, 7 H, hides 1 H multiplet), 3.82 (m, 2 H), 4.21 (variable, s, 2 H) [lit.[11] NMR δ 0.88 (d, J = 6.5 Hz, 3 H), 1.16 (d, J = 6.5 Hz, 7 H, hides 1 H multiplet), 4.03 (m, 2 H)].

(*R*)-*meso*-3-Methyl-2,4-dibromopentane (3). A solution of 36.46 g (0.139 mmol) of triphenylphosphine in 270 mL of dry benzene was stirred under nitrogen at 4 °C while a solution of 22.2 g (0.139 mol) of bromine in 10 mL of benzene was added slowly, followed by 13.54 g (0.042 mol) of tetra-*n*-butylammonium bromide in 125 mL of benzene. Then 8.2 g (0.069 mol) of (*S*)-*meso*-3-methyl-2,4-pentanediol in 85 mL of benzene was added rapidly. The mixture was heated to 60 °C for 40 min with a moderate flow of nitrogen through the solution. The reaction mixture was then cooled to 8 °C and filtered to remove triphenylphosphine oxide. The benzene was evaporated, the orange residue was extracted six times with low petroleum ether, and the extracts were washed with sodium bicarbonate and water and then dried over anhydrous magnesium sulfate. The solvent was removed and the crude product was purified by vacuum distillation [bp 69 °C (4.2 mm), 2.82 g (17%)], identified as (*R*)-*meso*-3-methyl-2,4-dibromopentane: NMR δ 1.22 (d, J = 6 Hz, 3 H), 1.74 (d, J = 6.5 Hz, 7 H, hides 1 H multiplet), 4.16 (q of d, J = 6.5 Hz, J' = 6.0 Hz, 2 H) [lit.[10] NMR δ 1.21 (d, J = 7 Hz, 3 H), 1.75 (d, J = 7 Hz, 6 H), 1.9 (m, 1 H), 4.19 (quintet, J = 6 Hz, 2 H)]. The NMR showed that contamination by the (*S*)-*meso*- or *dl*-dibromide could amount to no more than ~3%. The ^{13}C NMR spectrum contained the expected four resonances which were assigned by the aid of the partially coupled spectrum and in analogy to the ^{13}C NMR of *meso*-2,4-dichloropentane:[16] ^{13}C NMR δ 14.17 (q, C-6), 24.45 (q, C-1 and C-5), 48.77 (d, C-3), 54.33 (d, C-2 and C-4).

(*S*)-*meso*-3-Methyl-2,4-dibromopentane (4). A 3.6-g (30.46 mmol) sample of (*R*)-*meso*-3-methyl-2,4-pentanediol was allowed to react with triphenylphosphine dibromide (61.0 mmol) in the presence of tetra-*n*-butylammonium bromide (18.46 mmol), under identical conditions as employed for the reaction of the (*S*)-*meso*-diol above. A yield of crude product (2.19 g) was obtained and subjected to short-path vacuum distillation. The first fraction, bp <50 °C (4.5 mm), 0.85 g, was shown to be 3-methyl-4-bromo-2-pentene by comparison of its NMR spectrum with that of an authentic sample.[10] Fraction two, bp >50 °C (4.5 mm), 0.5 g, was shown by NMR to consist of ~57% (*S*)-*meso*-3-methyl-2,4-dibromopentane and ~43% 3-methyl-4-bromo-2-pentene. A small sample of the (*S*)-*meso*-dibromide was purified by preparative VPC on column E at 110 °C. The NMR spectrum showed that it was pure (*S*)-*meso*-3-methyl-2,4-dibromopentane and was contaminated by the (*R*)-*meso*- and *dl*-bromides to no more than a few percent: NMR δ 1.13 (d, J = 7.0 Hz, 3 H), 1.63 (d, J = 7.0 Hz, 6 H), 2.24 (m, 1 H), 4.28 (quintet, J = 7.0 Hz, 2 H) [lit.[10] NMR δ 1.15 (d, J = 6.5 Hz, 3 H), 1.67 (d, J = 7.5 Hz, 6 H), 2.27 (m, 1 H), 4.35 (quintet, J = 6.5 Hz, 2 H)].

Reaction of 3-Methyl-2,4-dibromopentane with Zinc. A 50-mL round-bottom flask was equipped with a mechanical stirrer, a nitrogen inlet, and an outlet attached to a collection apparatus, which consisted of two cold traps connected in series and cooled to −78 °C. The flask was charged with 0.9 g (13.77 mg-atoms) of zinc dust in 4 mL of a 3:1 1-propanol–water mixture and stirred at 0 °C. Then 1.12 g (4.59 mmol) of (*R*)-*meso*-3-methyl-2,4-dibromopentane was added and the reaction allowed to warm to room temperature over an 18–20-h period. The flask was then warmed to 50 °C and purged with nitrogen for 5–10 min, after which time the product that collected in the cold traps was dried over anhydrous magnesium sulfate. The product was analyzed by VPC on column D at 110 °C after the addition of *n*-pentane as an internal standard. The products were separated by preparative VPC on column D and identified from their IR and NMR spectra.[10,17] The results are shown in Table I.

An alternative procedure was used for the (*S*)-*meso*-dibromide because of the limited amount available. A breakseal tube was charged on one side with 0.08 g (1.22 mg-atoms) of zinc dust in 0.3 mL of a 3:1 1-propanol–water mixture and a small magnetic stirring bar and sealed under vacuum. The other side of the tube was charged with 0.13 g of a mixture of 57% (*S*)-*meso*-3-methyl-2,4-dibromopentane and 43% 3-methyl-4-bromo-2-pentene in 0.1 mL of the same solvent mixture and sealed under vacuum. The seal was broken and the reactants were allowed to mix. The tube was placed in an ice bath and the mixture was agitated by means of the small magnetic stirring bar. After 16 h, the tube was cooled to −78 °C and opened. The contents were distilled trap to trap at 1.0 mm in order to remove inorganic salts. A known amount of *n*-pentane was added to the product mixture as an internal standard and the mixture was analyzed by VPC on column D at 110 °C. The results are shown in Table II.

One set of control experiments showed that mixtures of *cis*- and *trans*-1,2,3-trimethylcyclopropane present in reactions of zinc with ethylene dibromide in 3:1 1-propanol–water at 0–50 °C did not change in composition beyond experimental error (1%).

A control reaction in which 0.1 g (0.61 mmol) of 3-methyl-4-bromo-2-pentene was allowed to react with 0.08 g (1.22 mg-atoms) of zinc in the small-scale manner described above showed that the only product was 3-methyl-2-pentene, as determined by VPC.

Reaction of 3-Methyl-2,4-dibromopentane with Chromous Sulfate. A 100-mL round-bottom flask was fitted with a magnetic stirrer and an adaptor, which was equipped with a stopcock below a rubber septum cap. In the flask, 20 mL of Me_2SO was degassed with nitrogen for 45 min. Then 23 mL (0.51 N, 11.73 mmol) of chromous sulfate[18] was introduced through the septum and stopcock via syringe. Then a degassed solution of 0.7123 g (2.92 mmol) of (*R*)-*meso*-3-methyl-2,4-dibromopentane in 2 mL of Me_2SO was added via syringe. The stopcock was closed and the reaction mixture was stirred for 22 h at room temperature. The septum cap was removed and the flask connected to two cold traps in series, the first cooled to −8 °C and the second to −78 °C. The flask was cooled to 0 °C and the pressure in the system was reduced to ~40 mm. The reaction flask was then allowed to warm to room temperature over a 45-min period, and the product which collected in the cold traps was washed with water and dried over anhydrous magnesium sulfate. Cyclohexane was added as an internal standard and the mixture analyzed by VPC on column F at 110 °C. The products were identified by VPC and NMR as *trans*-1,2,3-trimethylcyclopropane, *cis*-1,2,3-trimethylcyclopropane, and 3-methyl-2-pentene in the ratios shown in Table I.

A small-scale procedure was used for the (*S*)-*meso*-dibromide. A breakseal tube was evacuated on one side and flushed with nitrogen four times, and then 1.81 mL (0.94 N, 1.69 mmol) of chromous sulfate was injected into the tube under nitrogen. The tube was then sealed under vacuum. The other side of the tube was charged with 0.13 g of 57% (*S*)-*meso*-3-methyl-2,4-dibromopentane and 43% 3-methyl-4-bromo-2-pentene in 2 mL of Me_2SO and evacuated and flushed with nitrogen four times. This side was then sealed under vacuum. The seal was broken and the reactants were mixed. The initially pale blue solution of chromous sulfate turned to a light green upon mixing with the dibromide. The reaction was agitated by means of the small magnetic stirring bar at room temperature for 24 h. The tube was then cooled to −78 °C and opened. The contents were placed in a small flask with 1 mL of toluene, and the mixture was stirred for 20 min. The toluene extract was washed three times with water, dried over anhydrous magnesium sulfate, and analyzed by VPC on column F at 85 °C after the addition of a known amount of cyclohexane as an internal standard. The products were *trans*-1,2,3-trimethylcyclopropane, *cis*-1,2,3-trimethylcyclopropane, 3-methyl-2-pentene, and 3-methyl-1,3-pentadiene in the ratios shown in Table II. The diene was probably formed from the 3-methyl-4-bromo-2-pentene present initially and was identified as 3-methyl-1,3-pentadiene by coinjection with an authentic sample on VPC and by comparison of its NMR and IR spectra to those of authentic samples.[10]

Two control reactions were run to show that the composition of a mixture of the two cyclopropanes did not change (beyond experimental error) in solution with a reacting system of chromous sulfate and ethylene dibromide at room temperature for 24 h.

Reaction of 3-Methyl-2,4-dibromopentane with Sodium. A 50-mL round-bottom flask was equipped with a magnetic stirrer, nitrogen inlet, and reflux condenser connected to two cold traps in series, cooled to −78 °C. Freshly cut sodium, 0.7 g (30.4 mg-atoms), in 10 mL of dry dioxane was placed in the flask and the mixture was stirred and heated to reflux. Then a solution of 0.91 g (3.7 mmol) of (*R*)-*meso*-3-methyl-2,4-dibromopentane in 5 mL of dioxane was

added and the reaction mixture was refluxed for 20 h. The system was purged with nitrogen for 1 h and the product which collected in the cold traps was analyzed by VPC on column F at 90 °C after the addition of a known amount of *n*-pentane as an internal standard. For two independent reactions, the overall yields of hydrocarbons averaged 42% and had the composition shown in Table I. The products were identified by VPC by peak enhancement upon coinjection of authentic samples and by separation via preparative VPC. The first eluted was *trans*-1,2,3-trimethylcyclopropane, identified by comparison of the NMR and IR spectra to those of authentic samples.[10] The second eluted was 3-methylpentane, identified by comparison of its IR and NMR spectra to those of an authentic sample.[17] The next compound eluted was identified as 3-methyl-2-pentene by comparison of its NMR to that of an authentic sample.[17] The fourth compound eluted was *cis*-1,2,3-trimethylcyclopropane, also identified by comparison of its NMR and IR spectra to those of authentic samples.[10] The last compound was identified as 3-methyl-1,3-pentadiene: NMR δ 1.68 (m, 6 H), 4.95 (m, 2 H), 5.55 (m, 1 H), 6.4 (m, 1 H) [lit.[10] NMR δ 1.7 (m, 6 H), 5.0 (m, 2 H), 5.5 (m, 1 H), 6.4 (m, 1 H)].

A small-scale procedure was used for the (S)-*meso*-dibromide. A dry combustion tube was charged with 0.08 g (3.5 mg-atoms) of freshly cut sodium in 0.6 mL of dry dioxane and cooled to −78 °C. To the cooled mixture, 0.13 g of a mixture of 57% (*S*)-*meso*-methyl-2,4-dibromopentane and 43% 3-methyl-4-bromo-2-pentene in 0.3 mL of dry dioxane was added. The tube was sealed under a vacuum and then heated at 125 °C in an oil bath for 17 h. The tube was cooled to −78 °C and opened. The contents were distilled trap to trap at 1.0 mm to remove inorganic salts, and a known amount of *n*-pentane was added as an internal standard. The mixture was analyzed by VPC on column F at 85 °C. The products were identified as above and were as shown in Table II.

Two control reactions were run under the conditions of the larger scale procedure to show that the composition of a mixture of the two cyclopropanes did not change (beyond experimental error) in the reaction mixture of sodium with ethylene dibromide in dioxane.

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Registry No.—**3**, 40814-61-7; **4**, 40814-60-6; **5**, 25618-03-5; **6**, 30781-40-9; (*E*)-3-methyl-3-penten-2-ol, 24652-51-5; acetyl chloride, 75-36-5; (*E*)-3-methyl-3-penten-2-ol acetate, 64683-04-1; (*Z*)-3-methyl-3-penten-2-ol acetate, 64683-05-2; (*Z*)-3-methyl-3-penten-2-ol, 64683-06-3; (*S*)-*meso*-4,5,6-trimethyl-1,3-dioxane, 28163-74-8; *dl*-4,5,6-trimethyl-1,3-dioxane, 40902-89-4; (*R*)-*meso*-4,5,6-trimethyl-1,3-dioxane, 26561-69-3.

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Competing Nucleophilic Processes in Haloalkynes. Carbanionic Attacks

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Carbanions (R_3C^-) derived from triphenylmethane and benzhydryl cyanide displace chloride ion from phenylchloroacetylene in KOH–glycol dimethyl ether (glyme) to give $PhC{\equiv}CCR_3$. Similarly, benzhydryl cyanide anion in glyme reacts with mercuric bis(chloroacetylide) to give the substitution product $Hg(C{\equiv}CCPh_2CN)_2$. In other cases, the "first" substitution products often react further: those of benzyl and benzhydryl cyanides are converted to dimers; cyclopentadiene and methylcyclopentadiene in KOH–dimethyl sulfoxide lead ultimately to phenylethynyl- and 1,1′-phenylethynylferrocenes; from fluorene and ethyl malonate in glyme or Me_2SO β,β adducts, e.g., β,β-difluorenylstyrene, are produced; with benzyl cyanide in Me_2SO a 1:2 adduct forms. As nucleophiles, the anions derived from diphenylmethane and dimethyl sulfoxide anions differ in that they abstract chlorine from phenylchloroacetylene—diphenyldiacetylene is the only isolated product. Given a carbanionic nucleophile and an activated haloalkyne, conditions which favor substitution and minimize addition and halogen abstraction are a relatively low p*K* of the parent carbon acid and an aprotic medium, e.g., glyme.

Based on success with several nucleophilic substitutions at an acetylenic carbon,[1] our plan was to develop syntheses according to eq 1. As written in ionic form, process 1 has little, perhaps no precedent; most organometallics (R_3CM), whether predominantly ionic or covalent, are largely aggregated in most organic solvents.

$$PhC{\equiv}CCl + R_3C^- \rightarrow PhC{\equiv}CCR_3 + Cl^- \qquad (1)$$

In this paper, examples of eq 1 are described. Since diversions to other products were typical, we became equally concerned with the competing processes involving carbanionic attacks on a haloalkyne. As a result, limitations in and conditions for the use of process 1 in syntheses can now be appreciated.

Now couplings between sp carbon and other carbon reagents, e.g., organometallics of Li, Na, Mg, Zn, Sn, Pb, have *sometimes* given the product of eq 1.[2] These syntheses, as well as ours with organosodiums to be described below, are probable examples of the use of aggregated nucleophiles. From a synthetic viewpoint, however, "organocopper reagents constitute a breakthrough in the synthesis of [these] carbon–carbon bonds"[2a] and obviously should be considered for any route to $R'C{\equiv}CCR_3$.

Three broad categories for nucleophilic substitution at an acetylenic carbon have emerged.[1] Ionic attacks on triphilic haloalkyne are delineated in Scheme I. Clearly, the intermediates **2–4** may be intercepted, e.g., by proton donors (HA), and the expected product never obtained. The second group of mechanisms involves aggregates, that is, polymeric species,

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