cm^{-1}; mass spectrum m/e 396 (M^+). Elution with benzene–hexane (2:1) afforded 12 mg of the starting material.

28-Hydroxy-24-isopropylcholesteryl Acetate (10).—A solution of 250 μl of methyl iodide in 1 ml of dry ether was added dropwise to 96 mg of magnesium turnings under nitrogen atmosphere. After the spontaneous reaction began, another 5 ml of dry ether was added, and the mixture was stirred for 45 min. To the solution 800 mg of **12** in 5 ml of ether was added dropwise in 15 min and the solution was refluxed for 1.5 hr. After the usual work-up, the product was acetylated with excess acetic anhydride and pyridine and chromatographed on silica gel. Elution with benzene–hexane (2:1) afforded 237 mg of the starting material. Elution with benzene–hexane (10:1) afforded 28-hydroxy-24-isopropylcholesteryl acetate (**10**, 387 mg): mp 132–135° (from acetone); nmr (CCl_4) δ 0.62 (s, 3), 0.73–1.00 (m, 12), 1.07 (s, 6, C-29 CH_3, C-30 CH_3), 1.89 (s, 3), 4.50 (m, 1), 5.30 (m, 1); mass spectrum m/e 426.3849 (M^+ − AcOH) (calcd 426.3861).

24,28-Epoxy-28-methylstigmast-5-en-3β-yl Acetate (9).—To the solution of 150 mg of **10** in 3 ml of pyridine, 0.3 ml of phosphorus oxychloride was added, and the mixture was allowed to stand overnight at room temperature. After the usual work-up, the product was dissolved in 10 ml of chloroform and treated with 35 mg of *m*-chloroperbenzoic acid at 0° for 10 min. The product was chromatographed on silica gel. Elution with benzene–hexane (1:10) afforded 82 mg of 24-isopropylcholesta-5,28-dien-3-ol acetate (**5**): mp 128–131° (from acetone); nmr (CCl_4) δ 0.63 (s, 3), 0.80–1.03 (m, 12), 1.53 (s, 3), 1.90 (s, 3), 4.55 (m, 1), 4.59 (s, 1, C-29 H), 4.70 (s, 1, C-29 H), 5.33 ppm (m, 1); mass spectrum m/e 408.3724 (M^+ − AcOH) (calcd 408.375). Elution with benzene–hexane (3:1) afforded 48 mg of **9**: mp 103–105° (amorphous); nmr (CCl_4) δ 0.67 (s, 3), 0.83–1.13 (m, 12), 1.22 (s, 3), 1.26 (s, 3), 1.95 (s, 3), 4.55 (m, 1), 5.30 ppm (m, 1); mass spectrum m/e 424.3671 (M^+ − AcOH) (calcd 424.3704).

Reaction of 9 with Boron Trifluoride Etherate.—**9** (30 mg) in 6 ml of benzene was treated with boron trifluoride etherate (30 μl) for 10 sec at room temperature. After the usual work-up, the product was chromatographed on silica gel. Elution with benzene–hexane (1:3) afforded 6.6 mg of 24-acetyl-24-methylcholesteryl acetate (**16**): mp 115–120° (from methanol); nmr ($CDCl_3$) δ 0.67 (s, 3), 0.80 (s, 3), 0.90 (s, 6), 1.00 (s, 6), 1.97 (s, 3), 2.00 (s, 3, C-24 Ac), 4.60 (m, 1), 5.40 ppm (m, 1); ir 1690, 1715 cm^{-1}; mass spectrum m/e 424.3671 (M^+ − AcOH) (calcd 424.3704).

24-Ethylcholesta-5,24,28-trien-3β-ol Acetate (17).—A solution of 1 g of **6** and 65 mg of *p*-toluenesulfonic acid in 30 ml of benzene was refluxed for 30 min. After usual work-up of the mixture, the crude product was chromatographed on silica gel. The fraction eluted with benzene–hexane (1:1) gave 487 mg of **17**: mp 109–111°; nmr ($CDCl_3$) δ 0.69 (s, 3), 1.02 (s, 6), 1.83 (m, 6, C-26 and C-27 CH_3), 2.02 (s, 3), 4.60 (m, 1), 4.80–5.06 (m, 2, C-29 H_2), 5.38 (m, 1, C-28 H), 5.64 ppm (m, 1); uv max 235.5 nm (ε 18,600); mass spectrum m/e 452.3677 (M^+) (calcd 452.3654).

Compound **17** (50 mg) was dissolved in 1 ml of acetic acid and hydrogenated over 5 mg of platinum dioxide. Three mole equivalents of hydrogen was absorbed over a period of 1 hr. After removal of the catalyst, the filtrate was made alkaline with NaOH solution and the precipitate crystallized from acetone, mp 123–126°. The melting point and ir and nmr spectra were identical with those of tetrahydrofucosteryl acetate prepared from fucosteryl acetate by the same procedure.

Compound **17** was unstable to light. After a 1-day exposure to light in the laboratory, the major part had decomposed, but it was stable when refrigerated in a dark bottle.

Dehydration of Saringosteryl Acetate.—A solution of 517 mg of saringosteryl acetate and 27 mg of *p*-toluenesulfonic acid in 15 ml of benzene was refluxed for 30 min. After the usual work-up, the crude product was chromatographed on silica gel. The fraction eluted with benzene–hexane (1:3) afforded prisms from acetone of mp 109–111°. The compound's melting point, mixture melting point, and nmr spectrum agreed with those of compound **17**.

Registry No.—**3**, 38863-83-1; **5**, 38863-84-2; **6**, 35458-70-9; **7**, 35458-74-3; **8**, 38863-87-5; **9**, 38863-88-6; **10**, 38863-89-7; **11**, 2665-04-5; **12**, 38863-91-1; **13**, 38863-92-2; **13** (24-hydroxymethyl derivative), 38863-93-3; **14**, 38863-94-4; **15**, 38863-95-5; **16**, 38863-96-6; **17**, 38863-97-7; fucosteryl acetate, 6035-62-7; boron trifluoride etherate, 109-63-7; 24-oxo-26-norcholesteryl acetate, 26308-99-6; 24-oxocholesteryl acetate, 20981-59-3.

Acknowledgments.—This work was supported by grants from The Ministry of Education and The Hoansha Foundation. We are grateful to Mr. Y. Shida, Tokyo College of Pharmacy, for the mass spectral measurements.

Stereospecific Synthesis of Cis and Trans Epoxides from the Same Diol

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From the benzaldehyde acetal of *meso*-2,3-butanediol, isomerically pure *cis*-2,3-epoxybutane was synthesized by treatment with *N*-bromosuccinimide in carbon tetrachloride, followed by treatment with potassium hydroxide; isomerically pure *trans*-2,3-epoxybutane was synthesized by treatment with *N*-bromosuccinimide in water, followed by treatment with *p*-toluenesulfonyl chloride, followed by treatment with potassium hydroxide. From these reactions and the treatment of other cyclic acetals with *N*-bromosuccinimide, the reaction was shown to be ionic, kinetically regiospecific, and specific for the acetal carbon.

The recently reported stereospecific syntheses of halohydrin esters and epoxides by Newman and Chen[2] prompt us to report our preliminary results on a related stereospecific epoxide synthesis. Treatment of the readily accessible acetal of benzaldehyde and *meso*-2,3-butanediol[3] with *N*-bromosuccinimide[4] (NBS) in carbon tetrachloride containing a trace of HBr followed by treatment of the resulting bromohydrin ester[5] with potassium hydroxide in ethylene glycol gives *cis*-2,3-epoxybutane isomerically pure by nmr (Scheme I). Treatment of the same acetal with NBS in water, followed by treatment of the tosylate derived from the resulting glycol monoester with potassium hydroxide in ethylene glycol and 1,2-dimethoxyethane, gives *trans*-2,3-epoxybutane isomerically pure by nmr (Scheme II).

(1) Participant in ACS Seed Catalyst Program, summer, 1971.

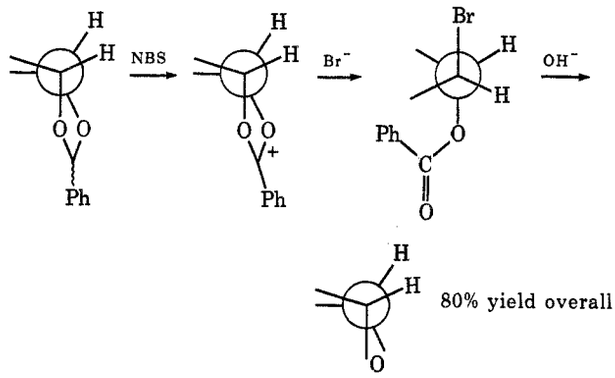
(2) M. S. Newman and C. H. Chen, *J. Amer. Chem. Soc.*, **94**, 2149 (1972).

(3) D. Gagnaire and J.-B. Robert, *Bull. Soc. Chim. Fr.*, 3646 (1965).

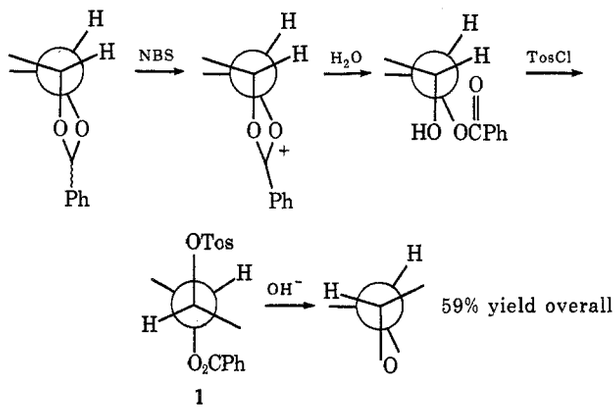
(4) For other examples of bromination of 1,3-dioxolanes, see ref 6 and papers cited therein; T. L. Hullar and S. B. Siskin, *J. Org. Chem.*, **35**, 225 (1970), and M. M. Ponpipom and S. Hanessian, *Can. J. Chem.*, **50**, 253 (1972), for uses in sugar and nucleoside chemistry; and D. H. R. Barton, L. Bould, D. L. C. Clive, P. D. Magnus, and T. Hase, *J. Chem. Soc. C*, 2204 (1971).

(5) Satisfactory ir, nmr, and low-resolution mass spectral data were obtained for each new compound. A satisfactory elemental analysis was obtained for compound **1**; all other compounds gave satisfactory high-resolution mass spectra.

SCHEME I



SCHEME II



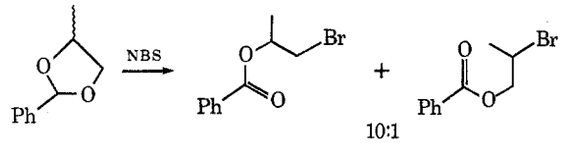
1

Hence either the cis or trans epoxide may be made at will from the same glycol.

That the oxidation of the dioxolane involves a dioxolenyl cation rather than radical is shown by the absence of bromo ester or 2-butyl benzoate in Scheme II and the absence of chloro ester in Scheme I.[6] When the acetal made from a mixture of 60% *dl*- and 40% *meso*-2,3-butanediol is treated with NBS in carbon tetrachloride, the erythro bromohydrin ester predominates.[7] When the acetal is treated with NBS in water, the threo glycol monoester predominates.[8] Hence there is no cis–trans isomerization of the dioxolane or dioxolenium rings before cleavage.

An explanation of the difference in the stereochemistry of the ring opening by water *vs.* bromide was advanced by Perst, as depicted in Scheme III.[9]

Regiospecificity similar to that of Newman and Chen[2] was observed on bromination of 4-methyl-2-phenyl-1,3-dioxolane in carbon tetrachloride with NBS and a trace of HBr at room temperature.[6] This ratio is apparently



kinetically controlled, since upon heating this reaction mixture or the 3:1 mixture of bromo benzoates resulting

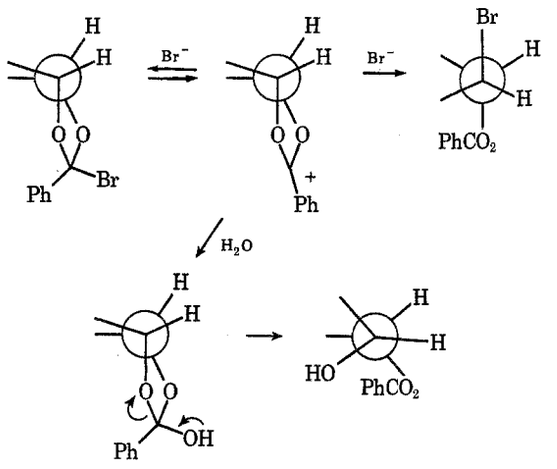
(6) *Cf.* J. D. Prugh and W. C. McCarthy, *Tetrahedron Lett.*, 1351 (1966).

(7) Assayed by nmr of the resultant epoxide: 40% cis and 60% trans.

(8) Assayed by glc (10% SE-30, 100°) of the acetonides of the glycols resulting from saponification of this ester: ~70% threo and 30% erythro.

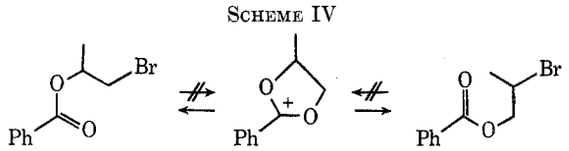
(9) H. Perst, "Oxonium Ions," Academic Press, New York, N. Y., 1971, p 80 ff.

SCHEME III



from reaction of benzoyl bromide with practical 1-bromo-2-propanol (consisting of 75% 1-bromo-2-propanol and 25% 2-bromo-1-propanol) in carbon tetrachloride at 70° for 12 hr, no significant change in the ratio of isomers is observed by nmr; *i.e.*, the reverse reactions (Scheme IV) do not occur under the reaction conditions.

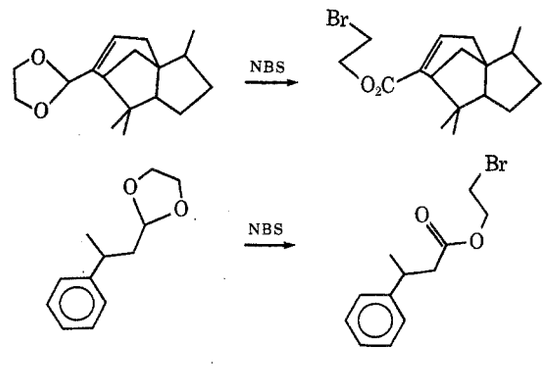
SCHEME IV



Note that, since there is no crossover of *dl*-2,3-butanediol-derived products to *meso*-2,3-butanediol-derived products, or vice versa, the conversion of either *d*- or *l*-2,3-butanediol to epoxide *via* Scheme I would result in no racemization and would give the enantiomerically pure epoxide.

The chemical specificity of this bromination is demonstrated in the reaction of cedrenaldehyde and 3-phenylbutyraldehyde ethylene acetals with NBS in carbon tetrachloride (Scheme V). In no case were any

SCHEME V



products resulting from the bromination of the allylic or benzylic positions detected by nmr.

One of the useful features of being able to generate either the cis or trans epoxide from a given diol is that the epoxides are intermediates for stereospecific deoxygenation to the olefins. We are now pursuing ways to generate cis or trans olefins at will directly from a given bromohydrin ester.

Experimental Section

Infrared spectra were recorded on a Perkin-Elmer 257 spectrometer. All nmr spectra were recorded on a Varian A-60A spectrometer. Mass spectra were recorded on a AEI MS-901/Digital PDP-8/I system. The elemental analysis was performed by Meade Microanalytical Laboratory, Amherst, Mass. Gas chromatographic analyses and preparations were made on a modified Wilkens Aerograph A-90-P/Varian Aerograph 700 gas chromatograph.

Cedren-15-aldehyde Ethylene Acetal.—A mixture of 5.57 g (25.6 mmol) of cedren-15-aldehyde,[10] 1.60 g (25.8 mmol) of ethylene glycol, 3.79 g (25.6 mmol) of triethyl orthoformate, and *ca.* 10 mg of *p*-toluenesulfonic acid was heated slowly to 140° while the volatile products were distilled through a short-path still at atmospheric pressure. When the head temperature reached 85° the remaining mixture was distilled *in vacuo* to give 3.0 g of mixture (70% acetal by gc[11]), bp 102–128° (0.10 mm), and 2.5 g of pure acetal, bp 128° (0.10 mm), in 68% yield (total): nmr (CCl_4) δ 0.90 (d, 3, J = 7 Hz), 0.98 (s, 3), 1.02 (s, 3), 1.2–2.3 (m, 11), 3.8 (m, 4), 5.05 (s, 1), 5.68 (t, 1, J = 3 Hz); *m/e* 262.1912 (calcd for $C_{17}H_{26}O_2$, 262.1932).

3-Phenylbutyraldehyde Acetal.—A mixture of 2.00 g (13.5 mmol) of 3-phenylbutyraldehyde {prepared by reduction of ethyl 3-phenylbutyrate[12] with diisobutylaluminum hydride by the method of Zakharkin and of Khorlina[13], bp 83–84° (2.8 mm) [lit.[14] bp 115° (18 mm)] in 86% yield}, 1.3 g (21 mmol) of ethylene glycol, and 10 mg of *p*-toluenesulfonic acid in 50 ml of benzene was heated at reflux in a Dean–Stark apparatus for 15 hr. The mixture in the pot was diluted with 50 ml of ether, washed with 30 ml of saturated aqueous $NaHCO_3$ solution, dried over K_2CO_3, concentrated on a rotating evaporator, and distilled *in vacuo* to give 2.18 g (84%) of acetal: bp 88–94° (0.8 mm); nmr (CCl_4) δ 1.25 (d, 3, J = 7 Hz), 1.8 (m, 2), 2.93 (sextet, 1, J = 7 Hz), 3.76 (m, 4, A_2B_2), 4.56 (d × d, 1, J = 4, 6 Hz), 7.13 (s, 5); *m/e* 192.1169 (calcd for $C_{12}H_{16}O_2$, 192.1150).

Bromination of 4,5-Dimethyl-2-phenyl-1,3-dioxolane in CCl_4.—To a slurry of 21.0 g (0.118 mol) of *N*-bromosuccinimide (NBS) in 250 ml of CCl_4 cooled in an ice bath, 21.0 g (0.118 mol) of 4,5-dimethyl-2-phenyl-1,3-dioxolane[2] [prepared by the triethyl orthoformate method (above) in 98% yield from 2,3-butanediol (56% threo and 44% erythro by gc[15] of acetonide), bp 153–157° (56 mm)] was added slowly. The mixture was stirred in darkness for 16 hr at room temperature, after which all of the NBS was observed to have reacted (this reaction time varies, without apparent pattern, from 2 hr to 1 week). The reaction mixture was filtered, washed twice with 60 ml of saturated aqueous $NaHCO_3$ solution, dried with Na_2SO_4, and concentrated on a rotating evaporator to 33.7 g of yellow oil (111% of theory). A sample was purified by distillation *in vacuo* for analysis: bp 112–113° (1.6 mm); ir (neat) 1725 and 1270 cm^{-1}; nmr (CCl_4) δ 1.60 (d, 3, J = 6.5 Hz), 1.72 (d, 3, J = 7 Hz), 4.21 (m, 1), 5.17 (m, 1), 7.4 (m, 3), 8.0 (m, 2); *m/e* 258.0051 (calcd for $C_{11}H_{13}Br^{81}O_2$, 258.0078). The nmr spectrum of an analytical sample prepared from the bromination of 4,5-dimethyl-2-phenyl-1,3-dioxolane prepared from *erythro*-2,3-butanediol differs only in the multiplets at δ 4.12 and 5.17, which are simplified to 4.21 (d × q, 1, J = 4, 7 Hz) and 5.17 (d × q, 1, J = 4, 6 Hz).

Saponification of Crude 2-(3-Bromobutyl) Benzoate.—A mixture of 1.9 g (47 mmol) of NaOH and 5.32 (20.7 mmol) of 2-(3-bromobutyl) benzoate in 15 ml of ethylene glycol was gradually heated to 140° while the product was distilled through a short-path still, giving 1.19 g of clear liquid, bp 59° (740 mm), which was analyzed by nmr to be 35% *cis*- and 55% *trans*-2,3-epoxybutane and 10% ethylene glycol. The yield from 4,5-dimethyl-2-phenyl-1,3-dioxolane was 111% × 72% or 80%.

Bromination of 4,5-Dimethyl-2-phenyl-1,3-dioxolane in H_2O.—To a mixture of 13.51 g (76.1 mmol) of NBS, 1 drop of concentrated hydrobromine acid, and 130 ml of H_2O cooled in an ice bath, 13.51 g (76.1 mmol) of 4,5-dimethyl-2-phenyl-1,3-dioxolane (prepared from a mixture of *erythro*- and *threo*-2,3-butanediols) was added slowly. After being stirred for 1 hr, the reaction mixture was still red, so *ca.* 2 g of $NaHCO_3$ was added, and the mixture was stirred for 17 hr at room temperature, then extracted with 3 × 100 ml portions of ether which were combined, dried with Na_2SO_4, and concentrated to *ca.* 20 ml of yellow oil. The oil was distilled *in vacuo* to give 12.58 g (85%) of 2-(3-hydroxybutyl) benzoate: bp 108–115° (0.5 mm); ir (neat) 3450 and 1720 cm^{-1}; nmr ($CDCl_3$) δ 1.25 (d, 3, J = 7 Hz), 1.34 (d, 3, J = 5 Hz), 2.9 (s, 1), 3.95 (m, 1), 5.07 (m, 1), 7.45 (m, 3), 8.1 (m, 2); *m/e* 194.0964 (calcd for $C_{11}H_{14}O_3$, 194.0942).

2-(3-Benzoyloxybutyl) *p*-Toluenesulfonate.—To 0.88 g (4.53 mmol) of 2-(3-hydroxybutyl) benzoate in 12 ml of pyridine, 1.74 g (9.11 mmol) of freshly recrystallized *p*-toluenesulfonyl chloride was added. The mixture was allowed to stand at room temperature for 24 hr, then was diluted with 50 ml of ether. The solution was washed successively with 3 × 10 ml of dilute (1:1) HCl solution, 2 × 10 ml of saturated aqueous $NaHCO_3$ solution, and 10 ml of H_2O, dried over $MgSO_4$, and concentrated on a rotating evaporator to a white solid which was recrystallized from ether and petroleum ether (bp 30–60°) to give 1.13 g (72%) of tosylate: mp 81–82° (uncorrected); nmr ($CDCl_3$) δ 1.30 (d, 3, J = 7 Hz), 1.38 (d, 3, J = 6.5 Hz), 2.31 (s, 3), 4.9 (m, 2), 7.0–8.0 (m, 9).

Anal. Calcd for $C_{18}H_{20}O_5S$: C, 62.05; H, 5.79. Found: C, 62.17; H, 6.04.

Saponification of 2-(3-Benzoyloxybutyl) *p*-Toluenesulfonate.—A mixture of 3.76 g (10.8 mol) of tosylate and 6.5 ml of *ca.* 1.4 *M* KOH in 1,2-dimethoxyethane (glyme) solution in 12 ml of glyme was stirred at room temperature for 1 hr and then distilled at room temperature *in vacuo* (50 mm) with a cold trap immersed in Dry Ice–acetone. After 14 hr at 50 mm the reaction pot was heated at 50° and the pressure was lowered to 25 mm for 1 hr. The contents of the trap (9.67 g) were analyzed by nmr to be 6.80 wt % 2,3-epoxybutane in glyme, a net yield of 97%.

Registry No.—Cedren-15-aldehyde ethylene acetal, 38739-76-3; cedren-15-aldehyde, 30960-40-8; ethylene glycol, 107-21-1; triethyl orthoformate, 122-51-0; 3-phenylbutyraldehyde ethylene acetal, 38739-78-5; 3-phenylbutyraldehyde, 16251-77-7; *N*-bromosuccinimide, 128-08-5; 4,5-dimethyl-2-phenyl-1,3-dioxolane, isomer A, 13165-94-1; 4,5-dimethyl-2-phenyl-1,3-dioxolane, isomer B, 4359-31-3; erythro-2-(3-bromobutyl) benzoate, 38822-42-3; threo-2-(3-bromobutyl) benzoate, 38739-82-1; *cis*-2,3-epoxybutane, 1758-33-4; *trans*-2,3-epoxybutane, 6189-41-9; *erythro*-2-(3-hydroxybutyl) benzoate, 38739-85-4; *threo*-2-(3-hydroxybutyl) benzoate, 38739-86-5; *erythro*-2-(3-benzoyloxybutyl) *p*-toluenesulfonate, 38739-87-6; *threo*-2-(3-benzoyloxybutyl) *p*-toluenesulfonate, 38739-88-7; *p*-toluenesulfonyl chloride, 98-59-9.

Acknowledgment.—We thank the donors of the Petroleum Research Fund, administered by the American Chemical Society, for support of this research.

(10) M. I. Goryaev and G. A. Tolstikov, *Izv. Akad. Nauk Kaz. SSR, Ser. Khim.*, 72 (1962); *Chem. Abstr.*, **59**, 6443*g* (1962).
(11) 10% SE-30 Chromosorb P AW-DMCS at 260°.
(12) V. K. Honwad and A. S. Rao, *Tetrahedron*, **21**, 2593 (1965).
(13) L. A. Zakharkin and I. M. Khorlina, *Tetrahedron Lett.*, 619 (1962).
(14) J. Colonge and A. Perrot, *Bull. Soc. Chim. Fr.*, 658 (1957).
(15) 10% SE-30 Chromosorb P AW-DMCS at 110°.