the addition (0.5 hr.) and for an additional 0.5 hr. Stirring at *ca.* 28° was maintained for 19 hr. after which time the reaction mixture was quenched with an ice–water mixture. The acetic acid was neutralized with sodium carbonate solution and the aqueous phase was extracted four times with ether. The combined extracts were washed with water and dried over magnesium sulfate.

The ether was carefully removed and a low-boiling fraction (3.4 g.) boiling at 50–65° (25 mm.) was collected. Gas chromatography of this fraction on a 6 ft. × 0.25 in. column of Carbowax 20 *M* at 145° showed three peaks: trioxane, ether V, and norbornyl acetate in the approximate ratios 10:90:10. Trioxane was identified by retention time. Norbornyl acetate was identified by retention time and comparison of infrared spectrum with a known sample. The infrared spectrum of the ether peak showed some weak carbonyl absorption. This impurity was removed by reduction with lithium aluminum hydride followed by gas chromatography. The ether was obtained as a volatile white solid, m.p. 64–65° (sealed capillary, uncor.), in about 16% yield based on the g.c. analysis above.

Anal. Calcd. for $C_8H_{12}O$: C, 77.37; H, 9.74. Found: C, 77.27; H, 9.79.

The infrared spectrum was consistent with the assigned structure and showed strong bands at 7.70, 9.15, 9.75, 9.80, 10.35, 10.75, and 11.40 μ. The n.m.r. spectrum exhibited a triplet at 6.1 τ (J = 2.5 c.p.s.) of relative area 1, a multiplet centered at 6.4 τ of area 2, a broad singlet at 7.9 τ of area 3, and a complex absorption of area 6 in the high-field region.

The high-boiling residue (23.8 g.) was essentially a mixture of diacetates VI and VII. The yield calculated on this basis is 75%. The gas chromatogram on a 5 ft. × 0.25 in. column of silicone SE 30 at 170° showed one main broad peak which was collected for analysis.

Anal. Calcd. for $C_{12}H_{18}O_4$: C, 63.70; H, 8.02. Found: C, 63.93; H, 7.94.

The n.m.r. spectrum of this product showed at least four peaks near 8 τ indicating that this material was a mixture of acetates.

Reduction of Diacetates with Lithium Aluminum Hydride.—The diester fraction (10 g.) was reduced with 3.0 g. of lithium aluminum hydride in ether to give 4.4 g. of a yellow oil. Gas chromatography did not prove feasible due to long retention times.

Oxidation of Diols.—The crude diols (1.0 g., *ca.* 0.007 mole) in 10 ml. of ether was stirred with a solution of 4.45 g. (0.03 mole) of potassium permanganate in 40 ml. of 20% aqueous potassium hydroxide solution. After 1.75 hr. at ice bath temperatures, the excess permanganate and manganese dioxide were destroyed by addition of sodium bisulfite. The reaction mixture was then acidified with hydrochloric acid and extracted with seven 30-ml. portions of ether. The combined extracts were dried and carefully evaporated. Ten milliliters of boron trifluoride–methanol reagent[5] was added and the resulting solution was kept at *ca.* 28° for 1 hr. After dilution with 100 ml. of water, the products were extracted into three 30-ml. portions of ether. The extracts were washed with sodium bicarbonate solution and water and dried. Evaporation of the ether gave 0.38 g. (34%) of the mixture of lactone VIII and diester IX. The yield calculation is based on the results of gas chromatographic analysis of this mixture on a 6 ft. × 0.25 in. column of Craig polyester at 190°. Only two peaks were observed and the retention times corresponded with known samples. Infrared spectra of the collected peaks also corresponded well with those of the authentic materials. The molar ratio of VIII to IX was determined by computation from known mixtures and was 3:2.

The lactone (VIII) was prepared according to Beckmann and Geiger[3] from nortricyclene carboxylic acid and had m.p. 118–118.5°, lit.[3] m.p. 120–121°. Diester IX was prepared by esterification of an authentic sample of 1,3-*cis*-cyclopentanedicarboxylic acid[6] with boron trifluoride–methanol reagent,[5] $\lambda_{max}^{C=O}$ 5.77 μ. The diacid could be regenerated unchanged (infrared) from the ester.

Oxidation of Ether V to Lactone VIII.[3]—A solution of 1.0 g. of crude ether in 60 ml. of acetone was cooled in an ice bath and treated with a solution of 5.0 g. of chromium trioxide in 19 ml. of water containing 4.5 ml. of concentrated sulfuric acid. The resulting mixture was stirred at 28° overnight and then treated with sodium bisulfite to destroy the excess oxidant. Dilution with 500 ml. of water was followed by extraction with five 50-ml. portions of ether. The combined extracts were washed with sodium bicarbonate solution and dried. Evaporation of the ether gave 0.76 g. of an oil whose infrared and n.m.r. spectra were identical with those of the known material. Gas chromatography of the crude product showed starting material as the only other component.

Control Experiment.—A sample of the diacetate mixture was subjected to the Prins reaction conditions (60–70° for 24 hr.) to determine whether ether V is formed as a primary product. The acetates could be recovered in *ca.* quantitative yield. The small amount of V present in the starting mixture was still present at the end of the experiment.

Acknowledgment.—We wish to thank the National Science Foundation for funds toward purchase of the n.m.r. spectrometer and the National Institutes of Health for a research grant, no. R.G. 8701.

(5) Obtained from Applied Science Laboratories, State College, Pa.

(6) J. D. Roberts, C. C. Lee, and W. H. Saunders, Jr., *J. Am. Chem. Soc.*, **76**, 4501 (1954).

Steroid Hormone Analogs. II.[1] Transformations in the C-Nor-D-homosteroid Series[2]

S. MORRIS KUPCHAN, TADASHI MASAMUNE, AND G. W. A. MILNE

Department of Pharmaceutical Chemistry, University of Wisconsin, Madison, Wisconsin

Received September 11, 1963

As part of a continuing study of the synthesis of C-nor-D-homosteroid hormone analogs, experiments were carried out, as outlined below, with a view to synthesizing a cortisone analog.

The readily available veratrum alkaloid jervine[3] (I) was the starting material for this investigation. Degradation of jervine to II was effected by the fragmentation reaction developed in the course of the structure elucidation of the alkaloid.[4,1] The secondary alcoholic group in II could not be oxidized without concomitant oxidative cleavage of the 17,20-double bond when chromium trioxide in acetone or pyridine was used. However, Oppenauer oxidation with aluminum isopropoxide in toluene and cyclohexanone afforded an excellent yield of $\Delta^{4,12,17(20)}$-17-ethyletiojervatriene-3,11-dione (IV).

Treatment of the diketone (IV) with a large excess of monoperphthalic acid in ether for 20 hr. at room temperature afforded a 70% yield of the monoepoxide (III). This epoxide did not prove to be of value in the proposed synthesis, because it could not be caused to open with exclusive fission of the C-17 to oxygen bond. Catalytic hydrogenation gave rise to multicomponent mixtures which could be only partially separated by chromatography. Similarly, treatment with lithium aluminum hydride, lithium in liquid ammonia, or boron trifluoride etherate yielded intractable mixtures.

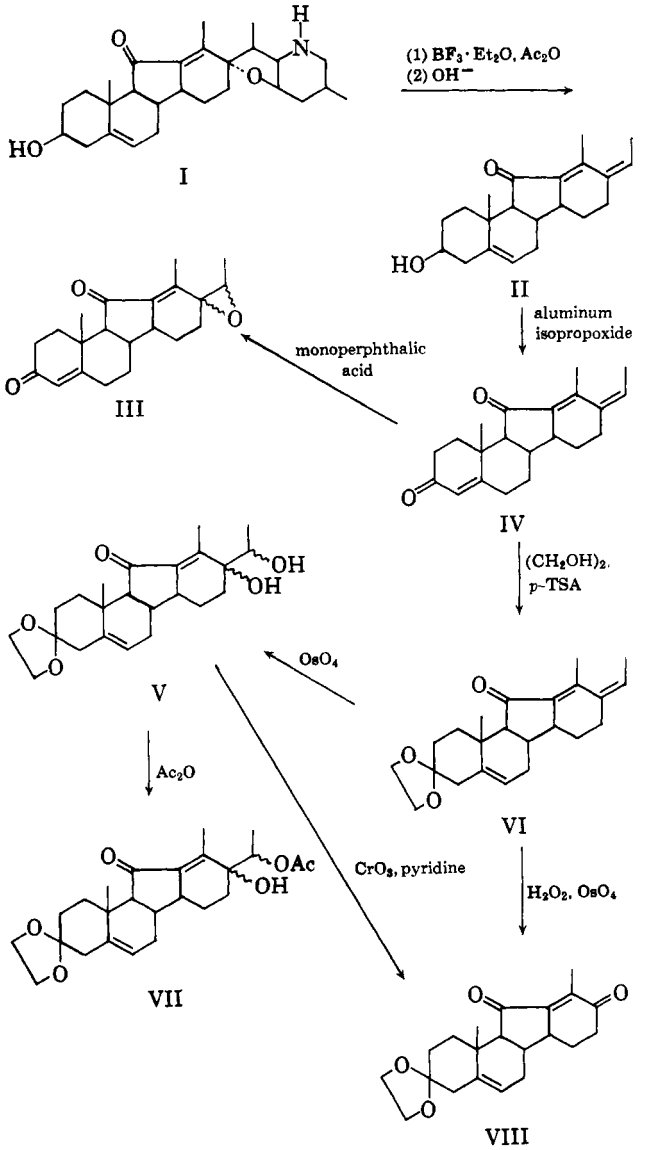
The 3-ethylene ketal derivative (VI) was formed selectively upon treatment of IV with ethylene glycol in the presence of *p*-toluenesulfonic acid, indicative

(1) Part I in the series: S. M. Kupchan and S. D. Levine, *J. Am. Chem. Soc.*, **86**, 701 (1964).

(2) This investigation was supported in part by research grants from the Squibb Institute for Medical Research and the National Institutes of Health (H-2275).

(3) We thank Riker Laboratories, Inc., for a generous gift of a jervine-rich alkaloidal extract.

(4) J. Fried and A. Klingsberg, *J. Am. Chem. Soc.*, **75**, 4929 (1953).



of the considerable steric hindrance to reaction of the carbonyl group at C-11. In the ketal (VI), the 17,20-double bond proved to be more reactive than those at 4,5 and 12,13, as evidenced by the rapid reaction of VI with osmium tetroxide to afford, after decomposition of the initially formed osmate ester, an 85% yield of $\Delta^{5,12}$-17-ethyletiojervadiene-3,11-dione-17,20-diol 3-ethylene ketal (V). Treatment of V with acetic anhydride and pyridine gave the 20-monoacetate (VII). Oxidation of the glycol (V) with chromic acid–pyridine (and a variety of other oxidizing agents) afforded only the diketone (VIII), which also was isolated after attempted reduction of V with lithium in liquid ammonia. Similarly, treatment of the diketone monoketal (VI) with hydrogen peroxide and osmium tetroxide,[5] or with phenyl iodosoacetate and osmium tetroxide,[6] led in both cases to VIII. Intractable mixtures were obtained from the reaction of VI with lead tetracetate.[7] The 12,13-double bond in V and VI could not be hydrogenated under a variety of conditions.

(5) *E.g.*, K. Miescher and J. Schmiden, *Helv. Chim. Acta*, **33**, 1840 (1950).

(6) *E.g.*, J. A. Hogg, P. F. Beal, A. H. Nathan, F. H. Lincoln, W. P. Schneider, B. J. Magerlein, A. R. Hanze, and R. W. Jackson, *J. Am. Chem. Soc.*, **77**, 4436 (1955).

(7) *E.g.*, J. von Euw, J. Lardon, and T. Reichstein, *Helv. Chim. Acta*, **27**, 1287 (1944).

Experimental

Melting points were determined on a Fisher-Johns melting point apparatus. Values of $[\alpha]$D have been approximated to the nearest degree. Ultraviolet absorption spectra were determined in ethanol on a Model 11 MS Cary recording spectrophotometer. Infrared spectra were determined in chloroform on a Model 5 Beckman double beam infrared recording spectrophotometer. Microanalyses were carried out by Dr. S. M. Nagy, Cambridge, Massachusetts.

$\Delta^{4,12,17(20)}$-17-Ethyletiojervatriene-3,11-dione (IV).—A solution of $\Delta^{5,12,17(20)}$-17-ethyletiojervatriene-3β-ol-11-one (II, 6.408, m.p. 148–150°) in toluene (200 ml., redistilled) and cyclohexanone (60 ml., redistilled) was heated to distil about 50 ml. of toluene to dry the system. To the stirred, refluxing solution was added a solution of aluminum isopropoxide (3.30 g.) in toluene (50 ml., redistilled) over 5 min. The mixture was stirred and refluxed for 1 hr. before cooling to room temperature for the addition of a saturated aqueous solution of Rochelle salt (60 ml.). The homogeneous solution was steam distilled until 25 l. of distillate had been collected and the residue was then extracted with three 100-ml. portions of chloroform. After drying over anhydrous sodium sulfate, the solution was evaporated to dryness under reduced pressure to leave a crystalline residue. Recrystallization from acetone afforded $\Delta^{4,12,17(20)}$-17-ethyletiojervatriene-3,11-dione (IV) as yellow needles (4.49 g.), m.p. 191–193°. Three recrystallizations from acetone gave the analytical sample as yellow needles, m.p. 201–202°, $[\alpha]^{32}$D +150° (*c* 1.09, chloroform); λ_{max} 238 mμ (ε 16,000), 301 (27,000); 5.91, 6.01, 6.20, 6.30 μ.

Anal. Calcd. for $C_{21}H_{26}O_2$: C, 81.25; H, 8.44. Found: C, 81.45; H, 8.55.

$\Delta^{4,12}$-17-Ethyletiojervadiene-3,11-dione 17,20-Oxide (III).—To a solution of IV (3.64 g., m.p. 191–193°) in dry ether (1.2 l.) was added a 0.36 *M* solution of monoperphthalic acid in ether[8] (336 ml., 10 equiv.), and the mixture was allowed to stand for 24 hr. at room temperature. After washing with 10% sodium bicarbonate solution (2 l.) and water (2 l.), the solution was dried over anhydrous magnesium sulfate and concentrated to about 140 ml. Upon cooling, the product crystallized in small platelets. Three recrystallizations from ether afforded $\Delta^{4,12}$-17-ethyletiojervadiene-3,11-dione 17,20-oxide (III) as colorless platelets (2.49 g.), m.p. 182–184°, $[\alpha]^{33}$D +25° (*c* 0.86, chloroform); λ_{max} 252 mμ (ε 24,400); 5.85, 6.01, 6.15 μ.

Anal. Calcd. for $C_{21}H_{26}O_3$: C, 77.27; H, 8.03. Found: C, 76.47; H, 8.02.

$\Delta^{5,12,17(20)}$-17-Ethyletiojervatriene-3,11-dione 3-Ethylene Ketal (VI).—A solution of IV (7.00 g., m.p. 191–193°) in benzene (500 ml.) containing *p*-toluenesulfonic acid hydrate (350 mg.) and ethylene glycol (35 ml.) was stirred and was heated under reflux under a Dean–Stock apparatus for 9 hr. The solution was cooled, washed with 10% sodium bicarbonate solution (150 ml.), and dried over anhydrous magnesium sulfate. Removal of the solvent under reduced pressure left a crystalline residue. Two recrystallizations from ether gave $\Delta^{15,12,17(20)}$-17-ethyletiojervatriene-3,11-dione, 3-ethylene ketal (VI) as colorless needles (6.10 g.), m.p. 160–162°, $[\alpha]^{33}$D −8° (*c* 1.05, chloroform); λ_{max} 302 mμ (ε 24,200); 5.91, 6.31, 9.00, 9.20 μ.

Anal. Calcd. for $C_{23}H_{30}O_3$: C, 77.93; H, 8.53. Found: C, 77.98; H, 8.61.

$\Delta^{5,12}$-17-Ethyletiojervadiene-3,11-dione-17,20-diol 3-Ethylene Ketal (V).—A solution of VI (5.10 g., m.p. 160–162°) in benzene (60 ml.) was treated with osmium tetroxide (3.78 g.) and pyridine (4.3 ml.). The solid osmate ester separated in 10 min. and the mixture was allowed to stand at room temperature overnight. The solid was filtered, washed with benzene, dried, and dissolved in chloroform (350 ml.). This solution was shaken with 1% aqueous potassium hydroxide solution (700 ml.) containing mannitol (70 g.) for 10 hr. when it became colorless. The aqueous layer was rejected and the chloroform solution dried over anhydrous sodium sulfate. Evaporation of the chloroform left a crystalline residue which was recrystallized twice from acetone to yield $\Delta^{5,12}$-17-ethyletiojervadiene-3,11-dione-17,20-diol 3-ethylene ketal (V) as needles (4.67 g.), m.p. 236–239°, $[\alpha]^{33}$D −151° (*c* 1.16, chloroform); λ_{max} 251 mμ (ε 14,000); 2.80, 5.87, 6.12, 9.00, 9.20 μ.

Anal. Calcd. for $C_{23}H_{32}O_5$: C, 71.10; H, 8.30. Found: C, 70.70; H, 8.07.

(8) *Cf.*, G. B. Payne, *J. Org. Chem.*, **24**, 1354 (1959).

$\Delta^{5,12}$-17-Ethyletiojervadiene-3,11-dione-17,20-diol 3-Ethylene Ketal 21-Acetate (VII).—A solution of V (650 mg., m.p. 236–239°) in pyridine (15 ml.) and acetic anhydride (13 ml.) was allowed to stand at room temperature for 13 hr. The mixture was poured into iced water (100 ml.) and the product was extracted with two 100-ml. portions of chloroform. The chloroform solution was washed with two 100-ml. portions of water, dried over anhydrous sodium sulfate, and evaporated to dryness under reduced pressure. The solid residue was recrystallized twice from acetone to yield $\Delta^{5,12}$-17-ethyletiojervadiene-3,11-dione-17,20-diol 3-ethylene ketal 21-acetate (VII) as needles (660 mg.), m.p. 240–241°, $[\alpha]^{33}D$ −165° (*c* 0.59, chloroform); λ_{max} 251 mμ (ε 14,000); 2.83, 2.88, 5.78, 5.84, 6.12, 8.00, 9.00, 9.20 μ.

Anal. Calcd. for $C_{25}H_{34}O_6$: C, 69.74; H, 7.96. Found: C, 69.52; H, 8.07.

Oxidation of $\Delta^{5,12}$-17-Ethyletiojervadiene-3,11-dione-17,20-diol 3-Ethylene Ketal (V) to $\Delta^{5,12}$-Etiojervadiene-3,11,17-trione 3-Ethylene Ketal (VIII).—A solution of V (250) mg., m.p. 236–239°) in pyridine (5 ml.) was added to the complex prepared from chromium trioxide (300 mg.) and pyridine (15 ml.). The mixture was stirred for 30 min. at room temperature and then allowed to stand overnight in the refrigerator. The mixture was poured into ice–water (150 ml.) and extracted with two 75-ml. portions of ether. The ethereal extract was washed with 2 *N* hydrochloric acid (75 ml.), 1 *N* sodium hydroxide solution (50 ml.), water (50 ml.), and dried over anhydrous sodium sulfate. Evaporation to dryness yielded a solid residue, which was crystallized twice from acetone–isopropyl ether to yield $\Delta^{5,12}$-etiojervadiene-3,11,17-trione 3-ethylene ketal (VIII), 95 mg., m.p. 176–178°. The melting point was not depressed by admixture of an authentic sample,[1] and the ultraviolet and infrared spectra were superimposable upon those of the authentic sample.

The Dehydrohalogenation of S,S′-(β-Chloroethyl) Dithiolcarbonate[1]

C. G. OVERBERGER AND W. H. DALY

Department of Chemistry, Polytechnic Institute of Brooklyn, Brooklyn, New York

Received July 31, 1963

During a recent investigation of the cyclopolymerization of S,S′-divinyl dithiolcarbonate (I), a detailed study of the dehydrohalogenation of S,S′-(β-chloroethyl) dithiolcarbonate was conducted. Rigorous purification and identification of the reaction products has necessitated a revision in the physical constants previously reported[2] for I, and has revealed a sulfonium ion rearrangement occurring in competition with the expected dehydrohalogenation.

S,S′-(β-Chloroethyl) dithiolcarbonate (II) can be prepared by reaction of phosgene with ethylene sulfide.[2] Dehydrohalogenation of II with potassium *t*-butoxide yielded a mixture of S,S′-divinyl dithiolcarbonate (I), S-vinyl-O-*t*-butyl thiolcarbonate (III), S-(β-chloroethyl)-O-*t*-butyl thiolcarbonate (IV), S-β-(vinylmercapto)ethyl-S-vinyl dithiolcarbonate (V), and S-vinyl-S′-β-(chloroethyl) dithiolcarbonate (VI). The composition of the product mixture was dependent on the reaction conditions; the formation of V was favored by lower reaction temperatures as illustrated in Table I.

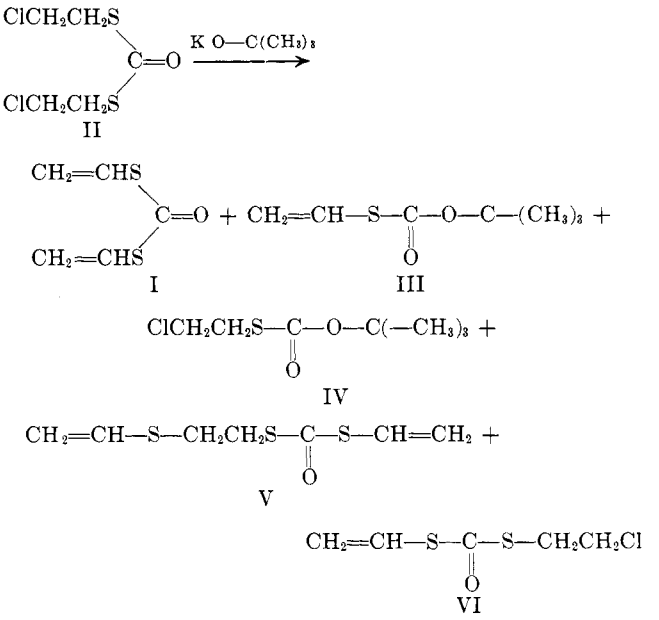


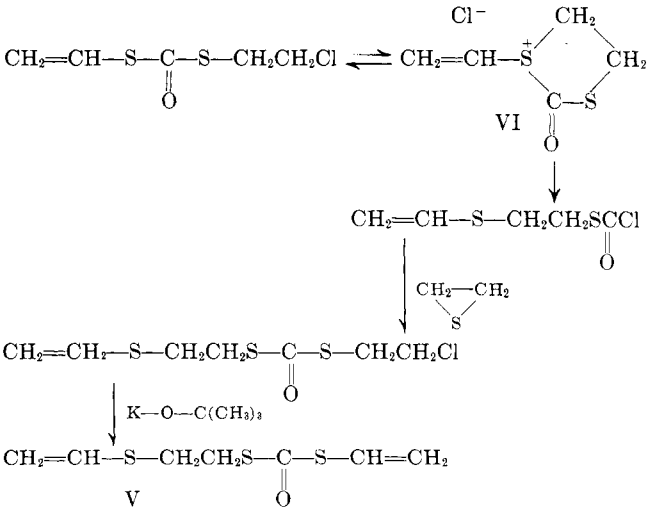
TABLE I

DEHYDROHALOGENATION OF S,S′-(β-CHLOROETHYL) DITHIOLCARBONATE (II)

Reaction conditions		Yield of products, %			
Pot temperature, °C.	Stirring[a] time, hr.	I	III	IV + VI	V
85	3	9.8	13.1	5.4	13.0
85	2	18.5	17.5	14.5	6.5
85	1	20.6	5.8	18.1	9.1
75	1	20.0	11.6	16.0	9.3
55	1	15.3	19.1	8.4	22.0

[a] After addition was completed.

Although the formation of V under the conditions of dehydrohalogenation was not anticipated, a mechanism for its formation can be proposed. The existence of cyclic sulfonium ions has been documented by Fuson and co-workers[3–5] and a similar intermediate should be applicable to this situation as illustrated.



The mechanism is indigent upon the presence of ethylene sulfide; however, ethylene sulfide is a by-product from the formation of S-vinyl-O-*t*-butyl thiol-

(1) This is the 26th in a series of papers concerned with new monomers and polymers: for the previous paper in this series, see C. G. Overberger, H. Kayé, and G. Walsh, *J. Polymer Sci.*, in press.

(2) H. Ringsdorf and C. G. Overberger, *Makromol. Chem.*, **44**, 418 (1961).

(3) R. C. Fuson, C. C. Price, and D. M. Burness, *J. Org. Chem.*, **11**, 475 (1946).

(4) R. C. Fuson and A. J. Speziale, *J. Am. Chem. Soc.*, **71**, 1582 (1949).

(5) R. C. Fuson and J. H. Koehneke, *J. Org. Chem.*, **14**, 706 (1949).