In view of Wynberg's observation that an aryl substituent seemed essential for the dehydrogenation of dihydrofurans,[2] it is probable that the aryl substituents permit dehydrogenation of II. We do not intend to pursue this investigation further.

Experimental

2,3-Diphenylbutane-1,4-diol (III).—A mixture of *meso*-2,3-diphenylsuccinic acid[5] (m.p. 227–229°, 27 g., 0.10 mole) and lithium aluminum hydride (7.6 g., 0.20 mole) in dry ether (300 ml.) was boiled under reflux for 12 hr. Excess lithium aluminum hydride was destroyed by dropwise addition of wet ethanol to the stirred cooled slurry. The mixture was then shaken with cold aqueous 5% phosphoric acid and the layers separated. The aqueous layer was washed several times with methylene chloride and the combined organic extracts were dried over magnesium sulfate and evaporated to dryness. Recrystallization of the solid residue from benzene afforded colorless crystals, m.p. 142–143.5° (20 g., 83%).

Anal. Calcd. for $C_{16}H_{18}O_2$: C, 79.31; H, 7.49. Found: C, 79.21; H, 7.42.

The infrared spectrum in Nujol mull included absorption at 3.0, 6.24, and 9.6 μ.

3,4-Diphenyltetrahydrofuran (IV).—The diol III (8.0 g., 0.033 mole) was dissolved in hot benzene (100 ml.) and *p*-toluenesulfonic acid monohydrate (3.0 g., 0.016 mole) was added. The solution was boiled under reflux and the evolved water was collected in a Dean–Stark trap. After 4 hr., 0.75 ml. (0.042 mole, 86%) of water had collected. An additional 2 hr. of boiling did not afford any more water. The mixture was cooled, washed once with water, once with dilute aqueus sodium bicarbonate, dried over magnesium sulfate, filtered, and evaporated to dryness on a rotary evaporator. The white, crystalline residue was recrystallized once from aqueous ethanol to give colorless needles m.p. 86–86.5° (7.2 g., 97%).

Anal. Calcd. for $C_{16}H_{16}O$: C, 85.68; H, 7.19. Found: C, 85.39; H, 7.19.

The infrared spectrum in dichloromethane solution had no absorption at 2.5–3.2 μ, but included a strong band at 9.5 μ.

3,4-Diphenylfuran (II).—A mixture of the tetrahydrofuran IV (1.0 g., 4.5 mmoles) and sulfur (1.0 g., 31 mmoles) was melted and heated uuder a slow steam of nitrogen. No gas evolution was detected until the temperature reached 200°. Gas bubbles appeared and the odor of hydrogen sulfide then became evident. Heating was continued at 200–210° for 5 hr. The mixture was cooled and the crystalline mass was extracted several times with boiling ether. The ether extracts were concentrated on the steam bath, cooled, filtered, and the filtrate was evaporated to dryness. The residue was twice recrystallized from 95% ethanol to give pale yellow needles (0.25 g., 25%), m.p. 108–111° (dec. 109–110.5° [1]).

The infrared spectrum exhibited absorption at 6.24, 6.50, 9.50, and 11.40 μ in dichloromethane solution.

---

(5) A. Lapworth and J. A. McRae, *J. Chem. Soc.*, **121**, 1709 (1922).

Formation of Tetrahydrofuran Derivatives from 1,4-Diols in Dimethyl Sulfoxide[1]

BERNARD T. GILLIS AND PAUL E. BECK

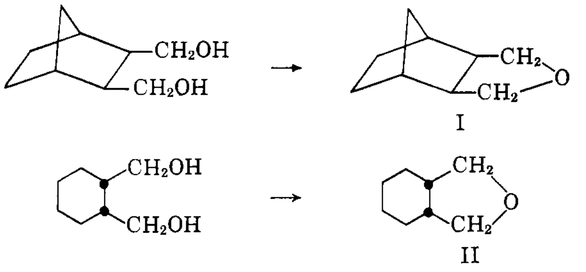
Department of Chemistry, Duquesne University, Pittsburgh 19, Pennsylvania

Received December 6, 1962

Three methods are prominent for the preparation of tetrahydrofuran derivatives from primary, secondary, and tertiary 1,4-diols. These are strong acid,[2] sulfonyl chloride–organic base,[3] and dehydration over alumina.[4] These methods, however, generally suffer from low yields and a mixture of products.

Recently, Traynelis, *et al.*,[5] have reported that secondary and tertiary alcohols are dehydrated to olefins when heated in dimethyl sulfoxide.

In an attempt to prepare 2,3-dimethylene[2.2.1]bicycloheptane, *endo-cis*-bicyclo[2.2.1]heptane-2,3-dimethanol was heated for thirteen hours at 156–166° in dimethyl sulfoxide. Instead of the desired diene, the cyclic ether, 2-oxatetrahydro-*endo*-dicyclopentadiene (I), was formed in 98% yield.



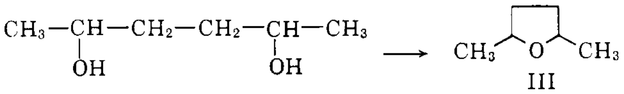
I

II

In view of this result, a study was undertaken to determine the scope of this facile dehydration using primary, secondary and tertiary 1,4-diols. A one to twelve ratio of diol to dimethyl sulfoxide was used.[6]

When *cis*-hexahydrophthalyl alcohol was heated in dimethyl sulfoxide at 159–161° for fourteen hours a 66% yield of *cis*-hexahydrophthalan (II) was obtained.

Similarly, the secondary diol, 2,5-hexanediol, when heated at 180° for eighteen hours in dimethyl sulfoxide furnished 2,5-dimethyltetrahydrofuran (III) in 68% yield.



III

Utilization of the tertiary diols, 2,5-dimethyl-2,5-hexanediol and 3,6-dimethyl-3,6-octanediol, resulted in 52% and 70% yields of products which contained the tetrahydrofuran derivatives, 2,2,5,5-tetramethyltetrahydrofuran (IV) and 2,5-diethyl-2,5-dimethyltetrahydrofuran (V), respectively.

The former diol leading to IV was heated at 167° for seventeen hours in dimethyl sulfoxide. Investigation of liquid product by gas chromatography showed it to be a mixture with the composition of 75.5%, 9.1%, and 15.5%, respectively. The infrared spectrum of this product was devoid of —OH bands but contained a very small carbon–carbon double bond stretching band at 6.05 μ. That the 15.5% component was

---

(1) This research was carried out under grant G17836 from the National Science Foundation, whose support is gratefully acknowledged.

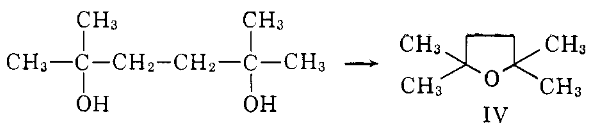
(2)(a) S. F. Birch, R. A. Dean, and E. V. Whitehead, *J. Org. Chem.*, **19**, 1449 (1954); (b) G. A. Haggis and L. N. Owen, *J. Chem. Soc.*, 389 (1953); (c) Y. S. Zal'kind and V. Markaryan, *J. Russ. Phys. Chem. Soc.*, **48**, 538 (1916); (d) T. A. Favorskaya and N. P. Ryzkova, *Zh. Obshch. Khim.*, **26**, 423 (1956); (e) T. A. Favorskaya and O. V. Sergievskaya, *ibid.*, **25**, 150 (1955); (f) E. Pace, *Atti. Accad. Lincei*, **7**, 757 (1928); (g) I. L. Kotlyarevskii, M. S. Shvartsberg, and Z. P. Trotsenko, *Zh. Obshch. Khim.*, **30**, 440 (1960).

(3)(a) K. Alder and W. Roth, *Ber.*, **88**, 407 (1955); (b) D. D. Reynolds and W. O. Kenyon, *J. Am. Chem. Soc.*, **72**, 1593 (1950).

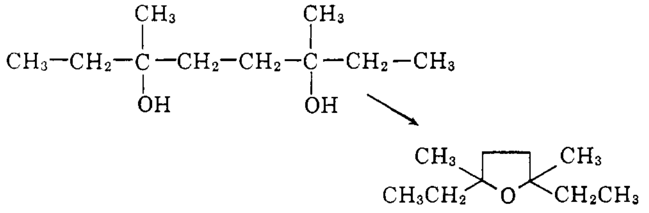
(4)(a) E. L. Wittbecker, H. K. Hall, Jr., and T. W. Campbell, *ibid.*, **82**, 1218 (1960); (b) R. C. Olberg, H. Pines, and V. N. Ipatieff, *ibid.*, **66**, 1096 (1944); (c) see ref. 2b.

(5) V. J. Traynelis, W. L. Hergenrother, J. R. Livingston, and J. A. Valicenti, *J. Org. Chem.*, **27**, 2377 (1962).

(6) Dr. Vincent Traynelis of the University of Notre Dame has found that primary 1,4-, 1,5-, and 1,6-diols are dehydrated to the cyclic ethers in dimethyl sulfoxide (private communication).



IV



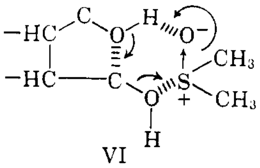
V

2,5-dimethyl-2,4-hexadiene was shown by the ultraviolet spectrum of the product which exhibited $\lambda_{\max}^{\mathrm{C_2H_5OH}}$ 242 mμ (ε 3590) or 16.7% of the conjugated diene. Retention time of 2,5-dimethyl-2,4-hexadiene and the 15.5% component were identical on the gas chromatogram. Quantitative hydrogenation of the product gave a total diene content of 27.3%. The 9.1% component is an unconjugated diene such as 2,5-dimethyl-1,4-hexadiene.

The latter diol when heated at 170° for 17.5 hours in dimethyl sulfoxide led to V. Gas chromatography of this product gave five peaks with the composition of 61.4%, 24.7%, 5.5%, 4.7%, and 3.6%, respectively. The first two peaks correspond to the *cis* and *trans* forms of 2,5-diethyl-2,5-dimethyltetrahydrofuran, while the latter three peaks are due to contaminating diene components. The infrared spectra showed no trace of —OH bands and a very small peak at 6.0 μ (C=C). The liquid exhibited an ultraviolet spectrum $\lambda_{\max}^{\mathrm{C_2H_5OH}}$ 239 mμ (ε 3470) and $\lambda_{\max}^{\mathrm{C_2H_5OH}}$ 245 mμ (ε 3620). Quantitative hydrogenation showed the total diene content to be 15.05%.

Thus, the method has been shown to offer a simple, convenient procedure for the preparation of tetrahydrofuran derivatives in good yields from primary, secondary, and tertiary 1,4-diols and is potentially superior to previous methods.[2-4]

The success encountered with 1,4-diols, quite naturally led to the postulation of a cyclic transition state (VI).



VI

An attempted formation of 2,5-dihydrofuran from *cis*-butene-1,4-diol under these conditions gave only starting diol (40%) and polymeric material.

Experimental[7]

Dimethyl Sulfoxide.—Dimethyl sulfoxide, obtained from either Crown Zellerbach Corp.,[8] Stepan Chemical Co., or Eastman Organic Chemicals, was allowed to stand over sodium hydroxide pellets and then distilled through a Vigreux column, b.p. 86° (18 mm.), n^{26}_{D} 1.4753 (lit.,[5] b.p. 83° (17 mm.), n^{20}_{D} 1.4795).

Bicyclo[2.2.1]hept-5-ene-2,3-dimethanol[9] was recrystallized three times from ether to a constant melting point of 85–86°. This material corresponded to the *endo–cis* compound (lit.,[10] m.p. 86°).

***endo–cis*-Bicyclo[2.2.1]heptane-2,3-dimethanol** was prepared by hydrogenation of unsaturated *endo–cis* diol in ethanol over palladium-on-charcoal catalyst and melted 63–64° when crystallized from ether (lit.,[10] m.p. 62°).

2-Oxatetrahydro-*endo*-dicyclopentadiene (I). *endo–cis*-Bicyclo[2.2.1]heptane-2,3-dimethanol (8.0 g., 0.051 mole) and 48.0 g. (0.615 mole) of dimethyl sulfoxide were heated under a reflux condenser at 156–166° for 13 hr. On cooling, 150 ml. of water was added and the reaction mixture extracted twice with 100-ml. portions of petroleum ether (b.p. 30–60°). The combined petroleum ether extracts were dried over calcium sulfate. Upon filtration, the petroleum ether was removed by distillation and the residue solidified on standing to give 6.95 g. (98%) of the saturated cyclic ether I, m.p. 104–107°. Recrystallization from hexane gave material melting at 109–110° (reported[3a] m.p. 110°). The infrared spectrum (chloroform solvent) was devoid of OH bands and exhibited absorption at 9.2 μ, which is characteristic of tetrahydrofuran and its derivatives.[11]

***cis*-Hexahydrophthalyl alcohol** was prepared in the following manner. 1,2-Cyclohexanedicarboxylic anhydride[12] was converted to the diester by the method of Price and Schwarcz.[13] The diester was then reduced to the *cis*-diol by the method of Bailey and Golden[14] using lithium aluminum hydride, and melted at 42–43°.

***cis*-Hexahydrophthalan (II).**—*cis*-Hexahydrophthalyl alcohol (8.55 g., 0.0594 mole) and 55.0 g. (0.71 mole) of dimethyl sulfoxide were heated at 159–161° for 14 hr. The mixture was cooled and 150 ml. of water added. The resulting mixture was extracted with two 100-ml. portions of petroleum ether. The combined petroleum ether extracts were dried over calcium sulfate and after filtration the petroleum ether was removed. The residual liquid was distilled and gave 4.96 g. (66%) of the ether II, b.p. 84° (29 mm.), n^{26}_{D} 1.4667 [reported[2a] b.p. 80° (28 mm.), n^{20}_{D} 1.4700]. The infrared spectrum (neat) showed no OH bands and the characteristic ether absorption was present at 9.13 μ.

2,5-Dimethyltetrahydrofuran (III).—2,5-Hexanediol[9] (10.0 g., 0.084 mole) and 78.0 g. (1.0 mole) of dimethyl sulfoxide were heated for 18 hr. at 180°. The apparatus was arranged with a Claisen head connected to a Dry Ice–acetone trap so that the product was collected immediately as it was formed. Distillation of the liquid that collected in the trap yielded 5.72 g. (68%) of III, b.p. 91–93°, n^{26}_{D} 1.4060 (lit.,[15] b.p. 92°, n^{23}_{D} 1.4045). The ether band at 9.25 μ was present in the infrared spectrum (neat) and alcohol bands were absent.

2,2,5,5-Tetramethyltetrahydrofuran(IV).—2,5-Dimethyl-2,5-hexanediol[12] (10.0 g., 0.069 mole) and 64.0 g. (0.82 mole) of dimethyl sulfoxide were heated at 167° for 17 hr. The reaction mixture was cooled, diluted with 150 ml. of water, and extracted with two 100-ml. portions of petroleum ether. The combined petroleum ether extracts were dried over calcium sulfate, filtered, and removed. Distillation of the residual liquid yielded 4.58 g. (52%) of product, b.p. 115–17°, $n^{25.5}_{\mathrm{D}}$ 1.4136 (lit.,[2d] b.p. 115.5–116.5°, n^{20}_{D} 1.4014). The infrared spectrum (neat) showed no OH absorption but a weak band at 6.05 μ (C=C) and the characteristic ether band at 9.23 μ.

Gas chromatography of the product showed three peaks, the composition being 75.5%, 9.1%, and 15.5%, respectively, as determined by the peak area method.[16]

---

[7] Boiling points and melting points are uncorrected. Spectra of the compounds were measured with a Beckman Model DU ultraviolet spectrophotometer and a Perkin-Elmer Model 137 double beam infrared spectrophotometer. Gas chromatographic analyses were performed on an F and M Scientific Corp. Model 21B dual heater gas chromatography apparatus using a 10 ft. long, 1/4-in. diameter Celite–silicone grease column.

[8] The authors wish to acknowledge the gift of a sample of dimethyl sulfoxide from Crown Zellerbach Corp., Camas, Wash.

[9] Purchased from Aldrich Chemical Co.

[10] K. Alder and W. Roth, *Ber.*, **87**, 161 (1954).

[11] G. Barrow and S. Searles, *J. Am. Chem. Soc.*, **75**, 1175 (1953).

[12] Purchased from Matheson Coleman and Bell Co.

[13] C. C. Price and M. Schwarcz, *J. Am. Chem. Soc.*, **62**, 2894 (1940).

[14] W. J. Bailey and H. R. Golden, *ibid.*, **75**, 4780 (1953).

[15] J. Cologne and A. Lagier, *Compt. rend.*, **224**, 572 (1947).

[16] Retention time of the peaks were 7.27 min., 8.5 min., and 14.8 min., respectively. Flow rate of helium was 43 ml. per min. with the detector temperature 92° and the column temperature 80°. An authentic sample of 2,5 dimethyl 2,4-hexadiene[12] had a retention time of 14.8 min. under these conditions.

The ultraviolet spectrum exhibited $\lambda_{\max}^{C_2H_5OH}$ 242 mμ (ε 3590) and indicated that 16.7% of a conjugated diene was present.[17]

Quantitative hydrogenation at atmospheric pressure of a sample of the product in 95% ethanol over 10% palladium on charcoal showed a total diene content of 16.7%.

2,5-Diethyl-2,5-dimethyltetrahydrofuran (V).—A mixture of 8.5 g. (0.048 mole) of 3,6-dimethyl-3,6-octanediol (from Air Reduction Chemical Co.) and 45.5 g. (0.58 mole) of dimethyl sulfoxide was heated for 17.5 hr. at 170°. Water was added to the cooled reaction mixture which was then extracted with two 100-ml. portions of petroleum ether. The combined petroleum ether extracts were concentrated after drying over calcium sulfate. Distillation of the remaining liquid furnished 4.85 g. (70%) of product, b.p. 161–163°, n^{25}D 1.4378 (reported[2c] b.p. 162–165°, $n^{13.6}$D 1.4300). The infrared spectrum showed no trace of OH absorption and a very small peak at 6.0 μ (C=C). The characteristic band of cyclic ethers was present at 9.23 μ.

Gas chromatographic analysis of the product gave five peaks with the composition of 61.4%, 24.7%, 5.5%, 4.7%, and 3.6%, respectively, as determined by the peak area method.[18]

This liquid exhibited an ultraviolet spectrum $\lambda_{\max}^{C_2H_5OH}$ 239 mμ (ε 3470) and $\lambda_{\max}^{C_2H_5OH}$ 245 mμ (ε 3620).

Quantitative hydrogenation of a sample at atmospheric pressure in ethanol over 10% palladium-on-charcoal catalyst gave total diene content of 15.05%.

---

[17] Pure 2,5 dimethyl 2,4-hexadiene exhibits $\lambda_{\max}^{C_2H_5OH}$ 242 mμ (ε 21,500). E. A. Braude and J. A. Coles, *J. Chem. Soc.*, 1425 (1952).

[18] Retention times of the peaks were 9.9, 11.0, 11.8, 13.1, and 14.0 min., respectively. Flow rates of helium was 42.5 ml./min. with a detector temperature of 132° and column temperature 122°.

Steroids. CCXXXII.[1] One-step Rearrangement of 17α-Methyl-$\Delta^{1,4,6}$-androstatrien-17-ol-3-one to an 18-Norequilenin Derivative

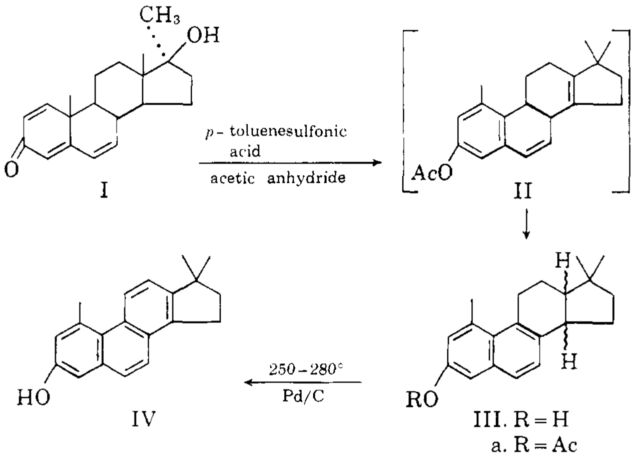
STEPHEN KAUFMANN

Research Laboratories of Syntex, S. A. Mexico, D. F.

Received November 5, 1962

Some time ago it was reported from these laboratories that the dienone–phenol rearrangement of $\Delta^{1,4,6}$-androstatrien-3-one derivatives leads to 1-methyl-Δ^6-estrogens.[2] We have now found that under the conditions used previously (heating with *p*-toluenesulfonic acid in acetic anhydride) 17α-methyl-$\Delta^{1,6,4}$-androstatrien-17-ol-3-one (I)[3] undergoes simultaneously a Wagner–Meerwein rearrangment of the 17-hydroxy and 13-methyl groups, dehydration and migration of the Δ^{13} double bond into ring B. Alkaline hydrolysis led to a crystalline substance (over-all yield, 21%), to which structure III (3′,3′,5-trimethyl-7-hydroxy-1,2-cyclopentano-1,2,3,4-tetrahydrophenanthrene) has been assigned, based on the following considerations.

Tortorella, *et al.*,[4] have shown that the Wagner–Meerwein reaction of 17α-methyl-Δ^5-androstene-3β-17-diol and of 17α-methylandrostane-3β-17-diol gives rise to a double bond in position 13. The migration of the latter into ring B is facilitated by the presence of the Δ^6 double bond in an intermediate such as II. Structure III is confirmed by the ultraviolet spectrum (Fig. 1), which is similar to that of 1-methyldihydroequilenin,[2] as well as by the infrared and n.m.r. spectra.[5] In the latter the 17-*gem*-dimethyl group appears as two 3-proton singlets at 53.3 and 64.5 c.p.s., and the protons of the methyl of the aromatic ring resonate at 119.7 c.p.s. (singlet). Two broad unresolved multiplets equivalent, respectively, to two and one protons, are due to the benzylic protons at C-11 (*ca.* 209 c.p.s.) and at C-14 (*ca.* 255 c.p.s.). The aromatic protons at C-2 and C-4 both resonate close to 409 c.p.s., so that a broadened single peak is observed. Mutual long-range coupling between these two protons and between those at C-4 and C-6 may also be responsible for the broadening of this absorption. A typical AB quartet at 422.8, 431.3, 438.0, and 446.5 c.p.s. (J = 8.5 c.p.s.) appears for the adjacent protons at C-6 and C-7.



I

II

IV

III. R = H
a. R = Ac

Substance III contains two asymmetric centers at C-13 and C-14, which, though present in the starting material I, had been destroyed in the intermediate Δ^{13}-compound (*e.g.*, II). That no racemization had occurred was shown by the fact that III was optically active ([α] D + 43.5°). The stereochemistry of II was not established but we believe the substance to possess the thermodynamically more stable *cis* C/D-ring junction.[6]

The acetate of compound III is easily dehydrogenated with palladium–carbon at 250–280°. Subsequent alkaline hydrolysis yielded the fully aromatic optically inactive 3′,3′,5-trimethyl-7-hydroxy-1,2-cyclopentenophenanthrene (IV).

Experimental[7]

3′,3′,5-Trimethyl-7-hydroxy-1,2-cyclopentano-1,2,3,4-tetrahydrophenanthrene (III).—A solution of 10 g. of 17α-methyl-$\Delta^{1,4,6}$-androstatrien-17-ol-3-one (I)[3] in 150 ml. of acetic anhydride containing 3 g. of *p*-toluenesulfonic acid was heated on the steam bath for 5 hr. The solution after cooling was poured into 2 l. of water and the mixture was allowed to stand overnight. The oily precipitate was extracted with ether. The extract, after being washed with water and sodium bicarbonate solution,

---

[1] Paper CCXXXI. O. Halpern, R. Villotti, and A. Bowers, *Chem. Ind.* (London), in press.

[2] C. Djerassi, G. Rosenkranz, J. Romo, J. Pataki, and S. Kaufmann, *J. Am. Chem. Soc.*, **72**, 4540 (1950).

[3] British Patent 854,343.

[4] V. Tortorella, G. Lucente, and A. Romeo, *Ann. chim.* (Rome), **50**, 1198 (1960).

[5] We are indebted to Dr. Alexander Cross for the n.m.r. measurement and interpretations. The n.m.r. spectrum was taken with a *ca.* 5% solution in deuteriochloroform containing tetramethylsilane as an internal reference standard. A Varian A-60 spectrometer was used. Chemical shifts are presented as c.p.s. from the reference and are accurate to ±1 c.p.s. Coupling constants, J, are also expressed as c.p.s. and are accurate to ±0.5 c.p.s.

[6] *Cf.* L. F. Fieser and M. Fieser, "Steroids," Reinhold Publishing Co., New York, N. Y., 1959, pp. 461, 464.

[7] Melting points were determined in a Thomas-Hoover melting point apparatus and rotations have been recorded in chloroform. We are indebted to Dr. Claudio Zapata and his staff for the determination of all rotations and the recording of spectra.