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The Stereochemistry of Hydrogenation and Hydrogenolysis. VIII.[1] The Stereochemistry of the Reduction of 2-Acetoxy-1-tetralone and 3-Acetoxy-4-chromanone[*1]

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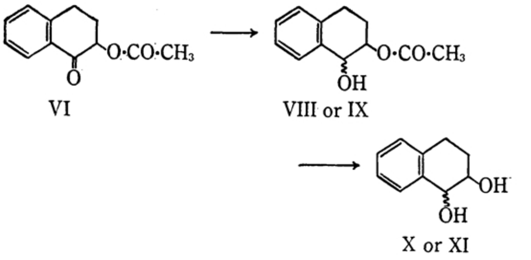
2-Acetoxy-1-tetralone (VI) and 3-acetoxy-4-chromanone (VII) were reduced with a metal hydride complex and by catalytic hydrogenation; the main products of the reduction were found to be *cis*-forms. These results indicate that, in the catalytic hydrogenation, the acetoxyl groups at the C-2 position of VI and at the C-3 position of VII hinder these carbonyl compounds from being adsorbed on the catalyst; also, in the reduction with metal hydride complex, the acetoxyl groups exert a steric hindrance upon the approach of the hydride ion to the carbonyl carbon atom.

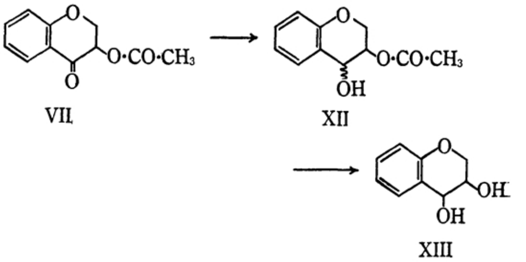
The stereochemistry of the reduction of 2-phenyl-1-tetralone (I)[2] and 2-methyl-1-tetralone (II)[3] has been investigated and described in previous papers of this series. The catalytic hydrogenation of I yielded *cis*-2-phenyl-1-tetralol (III) in a high yield, but the catalytic hydrogenation of II gave a mixture of equivalent quantities of *cis*-2-methyl-1-tetralol(IV) and *trans*-2-methyl-1-tetralol (V). These results suggest that, on the catalytic hydrogenation, the phenyl group hinders the carbonyl group of I from being adsorbed on the catalyst, while such steric hindrance does not occur when the 2-substituent is a methyl group. The reduction of I and II with a metal hydride complex gave III and V as the main products respectively. These results suggest that the phenyl group sterically protects the carbonyl carbon atom of I from the attack of the hydride ion, but the methyl group of II does not exert any such steric hindrance.

In order to obtain further information on the stereochemistry of the reduction of cyclic ketones, the reduction of 2-acetoxy-1-tetralone (VI) and 3-acetoxy-4-chromanone (VII) were investigated.

The reductions of VI and VII were carried out by catalytic and metal hydride methods. In both cases, the stereoisomeric composition was examined after the reduction products had been converted into diols by hydrolysis[*2] in a methanolic potassium hydroxide solution at room temperature. When VI was reduced with sodium borohydride or lithium aluminum hydride, the main product was a diol (X) (mp 101—102°C), accompanied by a small amount of a diol (XI) (mp 111—113°C). The catalytic hydrogenation of VI over a Raney nickel or Palladium-charcoal-B catalyst at an ordinary temperature and under an ordinary pressure yielded the diol (X) as the main product, along with small amounts of the epimeric diol (XI) and an oily product.


VI VIII or IX X or XI

The reduction of VII with sodium borohydride yielded only the diol (XIII) (mp 133—135°C). The catalytic hydrogenation of VII over a Raney nickel or Palladium-charcoal-B catalyst at an


VII XII XIII

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[1] Part VII: K. Hanaya, *Nippon Kagaku Zasshi (J. Chem. Soc. Japan, Pure Chem. Sect.)*, **87**, 995 (1966).

[*1] A part of this study was presented at the Tohoku Local Meeting of the Chemical Society of Japan, Kōriyama, October, 1963.

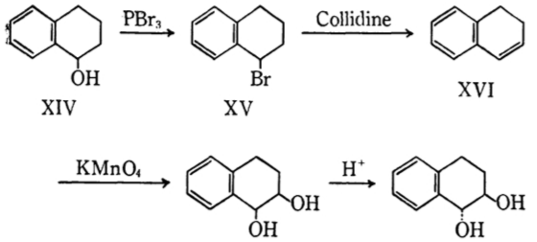
[2] K. Hanaya, *Nippon Kagaku Zasshi, (J. Chem. Soc. Japan, Pure Chem. Sect.)*, **87**, 745 (1966).

[3] K. Hanaya, *ibid.*, **87**, 991 (1966).

[*2] W. Nagata *et al.* reported[4] that, on the hydrolysis of *cis*- and *trans*-6-methoxy-tetralin-1, 2-diol diacetate with sodium hydroxide, the configuration was not inverted.

ordinary temperature and under an ordinary pressure also afforded the same diol (XIII), but in this case a small amount of an oily product was also formed.

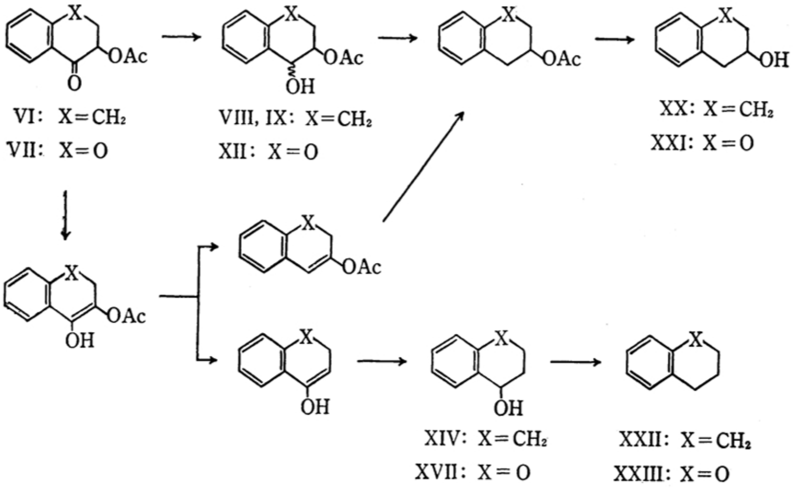
Compounds X, XI and XIII were identified as *cis*- and *trans*-tetralin-1, 2-diols and *cis*-chroman-3, 4-diol respectively by comparison with the authentic samples prepared by unequivocal syntheses.

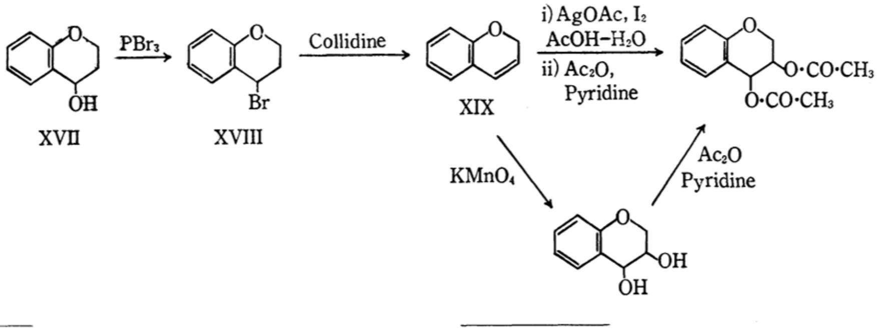


cis-Tetralin-1, 2-diol was synthesized by the hydroxylation[*3] of 3, 4-dihydronaphthalene (XVI) by potassium permanganate. The corresponding *trans*-diol was prepared by the isomerization of the *cis*-diol with acid, as has been reported in the literature.6)

The oily product produced by the catalytic hydrogenation of VI did not show the infrared absorption of a carbonyl group, and the absorption due to the OH stretching vibration is weaker than that of diols. From these results, the oily product was assumed to be a mixture of tetralin (XXII), 2-hydroxy-tetralin (XX), and 1-hydroxy-tetralin (XIV). XX may be produced by the hydrogenolysis of VIII and IX, because VIII and IX are both benzyl-type alcohols. XXII and XIV may be produced by the hydrogenolysis of the enol form of VI.

An authentic sample of *cis*-chroman-3, 4-diol was obtained by the hydroxylation of 3, 4-chromen (XIX) with potassium permanganate. The corresponding diacetate (mp 92.5—94°C) was obtained by treating the diol with acetic anhydride. The same diacetate (mp 93—95°C) was also obtained by a method reported by Woodward,5) namely, the hydroxylation of XIX in the presence of silver acetate and iodine in moist acetic acid, followed





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4) W. Nagata and T. Terasawa, *Chem. Pharm. Bull.*, **9**, 745 (1961).

[*3] It has been reported5) that the oxidation of olefines by potassium permanganate in an alkaline solution is *cis* hydroxylation.

5) F. D. Gunstone, "Advances in Organic Chemistry," Methods and Results, Vol. I, Interscience, New York (1960), pp. 103—147.

6) P. H. Hermans, *Ber.*, **57**, 827 (1924).

by acetylation. The examination of the melting point and the IR spectra confirmed that XIII is the *cis*-diol.

The oily product obtained by the catalytic hydrogenation of VII was assumed to be a mixture of chroman(XXIII), 3-hydroxychroman (XXI), and 4-hydroxychroman (XVII) on the basis of spectral evidence similar to that obtained with the oil from VI. The results are summarized in Tables 1 and 2.

TABLE 1. PRODUCTS OF THE REDUCTION OF 2-ACETOXY-1-TETRALONE (VI)

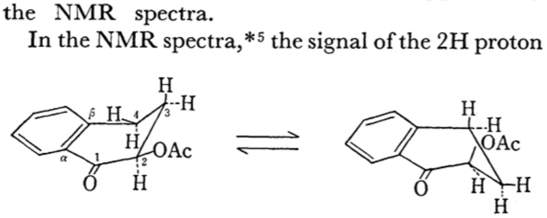
	Products, %		
	Diol X (mp 101—102°C)	Diol XI (mp 111—113°C)	Oily product
$LiAlH_4$	65	5	—
$NaBH_4$	80	5	—
Raney Ni	60	5	small amount
Pd-C-B	40	15	small amount

TABLE 2. PRODUCTS OF THE REDUCTION OF 3-ACETOXY-4-CHROMANONE (VII)

	Product, % Diol XIII (mp 133—135°C)	Oily product
$NaBH_4$	80	—
Raney Ni	75	small amount
Pd-C-B	70	small amount

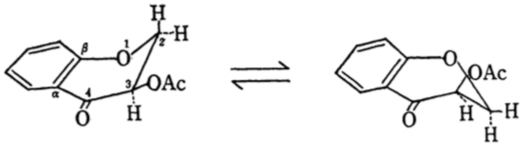
VI and VII are considered to have the steric structure shown in Figs. 1 and 2. In VI, C_1, C_2, C_4, C_α, and C_β exist on the same plane; only C_3 is slightly out of the plane. O_1, C_3, C_4, C_α, and C_β in VII exist on the same plane; only C_2 is slightly out of this plane. The conformation of the acetoxyl group in the 2-position of VI and in the 3-position of VII are assumed to be quasi-equatorial, as usual. These assumptions concerning the conformation of VI and VII are supported by the NMR spectra.

In the NMR spectra,*5 the signal of the 2H proton of VI appears as a quartet at $\delta=5.51$ ppm from TMS ($J_{2,3a}+J_{2,3e}=18.5$ cps), and the signal of the 3H proton of VII appears as a quartet at $\delta=5.65$ ppm ($J_{3,2a}+J_{3,2e}=17.0$ cps). Consideration from the Karplus relationship[8] suggests that the acetoxyl group exists in a quasi-equatorial conformation; that is, the preferable conformations of VI and VII are the (A) forms of Figs. 1 and 2.



(A) (B)

Fig. 1. Steric structure of VI.



(A) (B)

Fig. 2. Steric structure of VII.*4

In the case of the catalytic hydrogenation over Raney nickel and Palladium-charcoal-B catalysts, VI afforded the *cis*-diol as the main product, while VII gave only the *cis*-diol. These findings agree with the results of the reduction of I,[2] they indicate that the carbonyl group was hydrogenated on the catalyst surface from the opposite side of the acetoxyl group. The bulky acetoxyl groups hinder the molecules of VI and VII from being adsorbed on the catalyst surface from the side of the acetoxyl groups. On the other hand, when the adsorption takes place from the side opposite to the acetoxyl groups, the molecules of VI and VII can be easily adsorbed on the catalyst surface without any steric hindrance, and they are easily hydrogenated.

The enolization is possible with VI and VII. If the enol forms of VI and VII are hydrogenated, *cis*-tetralindiol and *cis*-chromandiol may be expected. A part of the X and XIII produced may arise from the hydrogenation of these enol forms.

On catalytic hydrogenation, VII afforded only *cis*-chromandiol, while VI gave *cis*-tetralindiol with *trans*-tetralindiol. These results correspond with the findings on the catalytic hydrogenation of flavanone (XXIV)[9] and of 3-phenyl-1-tetralone (XXV)[1] reported in a previous paper; that is to say, the catalytic hydrogenation of XXIV gave only flavan-4β-ol, whereas the catalytic hydrogenation of XXV over a Raney nickel catalyst yielded a mixture of the epimers of 3-phenyl-1-tetralol. These results seem to indicate that the states of adsorption on the catalyst surface are different between the tetralone ring containing a methylene bond and the chromanone ring containing an ether bond.

On reduction with a metal hydride complex, VI gave *cis*-tetralindiol as the main product, while

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*4 The conformation of the chromanone ring has been reported[7] by Phillibin and Wheeler.

7) E. M. Phillibin and T. S. Wheeler, *Proc. Chem. Soc.*, **1958**, 167.

*5 The NMR spectra were measured at 60 Mc/sec on a modified Varian Model A-60 spectrometer. The sample was dissolved in $CDCl_3$ containing TMS (tetramethylsilane) as the internal reference.

8) M. Karplus and C. F. Conroy, "Advances in Organic Chemistry," Method and Results, Vol. II, Interscience, New York (1960), pp. 308—311.

9) S. Mitsui and A. Kasahara, *Nippon Kagaku Zasshi (J. Chem. Soc. Japan, Pure Chem. Sect.)*, **81**, 1583 (1960).

VII yielded only *cis*-chromandiol. These results, parallel with the findings on I, indicate that the attack of the hydride ion on the carbonyl carbon atom takes place from the side opposite to the acetoxyl group. On reduction with a metal hydride complex, the steric structure near the carbonyl group influences the reaction rather than the whole steric structure of the molecule. On the carbon adjacent to the carbonyl, a quasi-axial hydrogen atom and a quasi-equatorial acetoxyl group exist. When a hydride ion attacks the carbonyl carbon atom, the acetoxyl group is expected to exert a steric hindrance. According to Barton's generalization,10) when the steric hindrance is large in the reduction of alicyclic ketones, an axial hydroxy group is produced. The mechanism proposed by Dauben *et al.*11) states that when a sterically-hindered carbonyl group is reduced, the reaction depends upon "the steric approach control."

The above findings can be summarized as follows. In the reduction of VI and VII, the steric effect of the acetoxyl group of C-2 or C-3 is overwhelming even if they exist in a quasi-equatorial conformation, and both the catalytic hydrogenation and the metal hydride reduction yield *cis* compounds as the main products.

Experimental

2-Acetoxy-1-tetralone (VI). VI was prepared from the reaction between α-tetralone and lead tetraacetate under reaction conditions similar to those used in the case of VII. Recrystallization from methanol gave colorless crystals, mp 73—75°C (lit. mp 74.5—75°C12); mp 72—73°C13)).

Found: C, 70.25; H, 5.75%. Calcd for $C_{12}H_{12}O_3$: C, 70.57; H, 5.92%.

3-Acetoxy-4-chromanone (VII). VII was prepared by the procedure reported in the literature.14)

Catalytic Hydrogenation. One hundredth mol of the carbonyl compounds, 0.4 g of 5% Pd-C-B or 2 g of Raney nickel, and 150 m*l* of ethanol were stirred in hydrogen at an ordinary temperature and under atmospheric pressure. After the theoretical amount of hydrogen had been absorbed, the catalyst was filtered off and the reduction products were hydrolyzed by treatment with a 15% potassium hydroxide solution (12 m*l*) at room temperature for 24 hr. Water (100 m*l*) was added, and then the ethanol was removed under reduced pressure. The residual solution was continuously extracted with ether for 24 hr, and the ether solution was dried over anhydrous sodium sulfate. Then the ether was removed by distillation, and the residue was chromatographed on silica gel. The results are summarized in Tables 3 and 4.

TABLE 3. THE PRODUCTS OF THE HYDROGENATION OF VI

Catalyst	*cis*-Diol (mp 101—102°C)	*trans*-Diol (mp 111—113°C)	Oily product
Raney Ni	0.99 g	0.08 g	small amount
Pd-C-B	0.65 g	0.24 g	small amount

TABLE 4. THE PRODUCTS OF THE HYDROGENATION OF VII

Catalyst	*cis*-Diol (mp 133—135°C)	Oily product
Raney Ni	1.25 g	small amount
Pd-C-B	1.16 g	small amount

Reduction of VI with $NaBH_4$. A solution of VI (2.04 g) in methanol (200 m*l*) was added over a 30-min period to a well-stirred mixture of sodium borohydride (1.5 g) in methanol (50 m*l*) at 0°C. After the mixture had then been allowed to stand for 24 hr at 0°C, water (100 m*l*) was added and the methanol was removed under reduced pressure. The residue was acidified with dilute acetic acid, the solution was continuously extracted with ether for 24 hr, and the ether solution was dried over anhydrous sodium sulfate. After the evaporation of the ether, the residue was chromatographed on silica gel, the fraction eluted with chloroform afforded *cis*-diol (mp 101—102°C) (1.31 g) and *trans*-diol (mp 111—113°C) (0.82 g).

Reduction of VII with $NaBH_4$. This reduction was carried out as in the case of VI; the *cis*-chroman-3, 4-diol (mp 133—135°C) (1.33 g) was thus obtained from VII (2.06 g).

Reduction of VI with $LiAlH_4$. To a well-stirred suspension of lithium aluminum hydride (0.6 g) in dry ether (150 m*l*), VI (2.04 g) in dry ether (200 m*l*) was added over a 30-min period at 0°C; the mixture was then stirred at 0°C for 5 hr. Water (30 m*l*) and 20% sulfuric acid (10 m*l*) were then added, and the ether layer was separated. The aqueous solution was extracted with ether, and the combined ether extracts were washed with water, dried over anhydrous sodium sulfate, and subjected to distillation in order to remove the ether. The residue was chromatographed on silica gel; the fraction eluted with chloroform afforded *cis*-diol (mp 101—102°C) (1.07 g) and *trans*-diol (mp 111—113°C) (0.08 g).

1, 2-Dihydronaphthalene (XVI). Phosphorus tribromide (47 g) was slowly stirred into a cooled solution of 1-hydroxy-tetralin (XIV) (56 g) in dry benzene (500 m*l*). The solution was then allowed to stand overnight at room temperature, refluxed for 4 hr, cooled, and then poured onto ice. The organic layer was separated, and the aqueous layer was extracted with a mixture of ether and benzene. The combined extracts were washed well with water and a 5% sodium carbonate solution and dried over anhydrous sodium sulfate, and the solvents were removed under reduced pressure. The residual oil was distilled under reduced pressure

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10) D. H. R. Barton, *J. Chem. Soc.*, **1953**, 1027.

11) W. G. Dauben, G. J. Fonken and D. S. Noyce, *J. Am. Chem. Soc.*, **78**, 2579 (1956).

12) F. Straus, O. Bernoully and P. Mautnen, *Ann.*, **444**, 179 (1925).

13) C. L. Stevens, J. J. Beereboom and K. G. Rutherford, *J. Am. Chem. Soc.*, **77**, 4590 (1955).

14) G. W. K. Cavill, F. M. Diean, A. McGookin, B. M. Marshall and A. Robertson, *J. Chem. Soc.*, **1954**, 4573.

to give 62.5 g of 1-bromotetralin (XV) (bp 102—104°C/28 mmHg). XV gave a positive Beilstein test, and its IR spectrum supported its identity. XV was mixed with collidine (275 m*l*), and the solution was refluxed for 4 hr. The mixture was cooled and poured into ice-cold 6 N hydrochloric acid (500 m*l*). The product was extracted with a mixture of ether and benzene, and the extract was washed with a 5% sodium carbonate solution, dilute hydrochloric acid, and water, and dried over anhydrous sodium sulfate. The solvents were removed under reduced pressure. The residual oil was then distilled under reduced pressure to give 12 g of XVI (bp 96—98°C/30 mmHg). The identity of XVI was ascertained by converting it into the dibromide (mp 68—69°C) (lit. mp 68—69°C[15]; mp 70—71°C).[16]

***cis*-Tetralin-1, 2-diol (X).** A solution of potassium permanganate (9.0 g) and sodium hydroxide (1.92 g) in water (307 m*l*) was cooled to 0°C, and then quickly and vigorously stirred into a cold mixture (−10°C) of *t*-butyl alcohol (385 m*l*), water (77 m*l*), and cracked ice (190 g) containing XVI (5.0 g). After 5 min, most of the permanganate color had disappeared; sulfur dioxide was then added to ensure complete reduction of the permanganate. The manganese dioxide precipited was filtered, and the filtrate was concentrated to about 200 m*l* under reduced pressure with steam-bath heating. The solution was continuously extracted with ether for 48 hr, and the ether solution was dried over anhydrous sodium sulfate. The evaporation of the solvent gave 1.7 g of needle crystals, mp 101—102°C (lit. mp 101.5—102°C[17a]; mp 102.5—103.5°C[17b]; mp 102°C).[17c]:

Found: C, 73.17; H, 7.45%. Calcd for $C_{10}H_{12}O_2$: C, 73.14; H, 7.37%.

***trans*-Tetralin-1, 2-diol (XI).** XI was prepared by the isomerization of X with dilute sulfuric acid, a method reported in the literature.[6] The crude product was chromatographed on silica gel; the fraction eluted with chloroform afforded needle crystals, mp 111—113°C (lit. mp 111.8—112.4°C[17b]; mp 112—113°C).[17a,18]

Found: C, 72.87; H, 7.17%. Calcd for $C_{10}H_{12}O_2$: C, 73.14; H, 7.37%.

3, 4-Chromen (XIX). XIX (bp 84—86°C/8 mmHg) (17.0 g) was obtained *via* 4-bromochroman (XVIII) from 4-hydroxychroman (XVII) (43.0 g) by a method similar to that described above for XVI. The identity of XIX was ascertained by converting it into the dibromide (mp 124—125°C) (lit. mp 124—124.5°C)[19].

***cis*-Chroman-3, 4-diol (XIII).** (a) XIII (2.3 g) was prepared by the hydroxylation of XIX (5.0 g) with potassium permanganate under reaction conditions similar to those described above for the synthesis of X. Mp 133—135°C.

Found: C, 65.29; H, 6.27%. Calcd for $C_9H_{10}O_3$: C, 65.05; H, 6.07%.

The reaction of XIII (500 mg) with acetic anhydride-pyridine at 0°C for 24 hr gave, after crystallization from petroleum ether, the diacetate (620 mg) (mp 93—95°C).

Found: C, 62.63; H, 5.78%. Calcd for $C_{13}H_{14}O_5$: C, 62.39; H, 5.64%.

(b) XIX (1.0 g) was dissolved in glacial acetic acid (35 m*l*) in a three-necked flask equipped with a stirrer, a reflux condenser, and a thermometer. Silver acetate (2.9 g), and then finely-powdered iodine (2.0 g) in small portions, were added to the vigorously-stirred reaction mixture over a period of 30 min at room temperature. When all the iodine had been absorbed, aqueous acetic acid (3.5 m*l*, prepared by the dilution of 2.0 m*l* of water up to 50 m*l* with glacial acetic acid) was added; the reaction mixture was then heated in a boiling water-bath with vigorous stirring for 3.5 hr. After cooling, a saturated solution of sodium chloride was added, and the insoluble precipitates were removed by filtration. The precipitates were washed with hot benzene, the filtrate was extracted with benzene, and the combined benzene solution was dried over anhydrous sodium sulfate. After the evaporation of the solvent, the residual oil was allowed to react with acetic anhydride-pyridine at 0°C for 24 hr. The usual working-up and crystallization from petroleum ether yielded the diol diacetate, mp 92.5—94°C (0.6 g).

The author wishes to express his deep gratitude to Professor Sekio Mitsui of Tohoku University, and Assistant Professor Akira Kasahara of Yamagata University for their kind guidance and encouragement throughout this work.

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15) I. I. Chizhevskaya and Z. B. Idelchik, *Zhur. Obshchei Khim.*, **27**, 83 (1956); *Chem. Abstr.*, **51**, 12022 (1957).

16) F. Straus and L. Lemmel, *Ber.*, **46**, 237 (1913).

17) a) F. Straus and A. Rohrbacher, *Ber.*, **54**, 68 (1921); b) P. E. Verkade, J. Coops, C. J. Maan and F. A. Verkade-Sandbergen, *Ann.*, **467**, 227 (1928); c) J. Boeseken and H. G. Derx, *Rec. Trav. Chim.*, **40**, 523 (1921).

18) H. G. Derx, *ibid.*, **41**, 325 (1922).

19) P. Maitte, *Ann.*, **9**, 431 (1954); *Chem. Abstr.*, **49**, 6930 (1955).