THE RELATION BETWEEN OPTICAL PROPERTIES & CHEMICAL CONSTITUTION.

I. β BUTYLENE GLYCOL.

II. THE SYNTHESIS & RESOLUTION OF SEC: BUTYL CARBINOL.

by

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The work described in this thesis was carried out for the degree of Master of Science by me in the chemical laboratories of the Battersea Polytechnic under the supervision of J. Kenyon, B.Sc. (Lond.) F.I.C., to whom I wish to record my sincere thanks for his kindly advice and help.

The work has been carried out in spare time during the last four years.
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II. The synthesis and resolution of sec. 

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being a thesis submitted to the University of London 

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December, 1923.

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The possibility of obtaining \( n \)-butyl alcohol in large quantity as a result of the fermentation of starch, has led to its use recently as a starting point in many organic syntheses. The \( n \)-butyl alcohol, being a bye-product, (with acetone as the main product) can be obtained fairly cheaply, and has formed the starting point in the syntheses described herewith. It may be used, not only for the preparation of a number of \( n \)-amyl derivatives and derivatives of \( n \)-capric and \( n \)-valeric acids, (Adams and Marvel, J. Amer. Chem. Soc., 1920, 42, 310-320) but also for the synthesis of certain substances capable of exhibiting optical activity.

\( n \)-butyl alcohol forms a point from which \( d \)-compounds may be prepared and subsequently resolved into their \( d \)-and \( l \)-isomerides.

\( \beta \)-Butylene Glycol (sym. dimethylethylene glycol; 2,3 dihydroxy-butane).

If the formula of this body be examined, a semblance to that of tartaric acid will be observed, the difference being the presence of two methyl groups in place of two carboxyl groups.

Each contains two asymmetric carbon atoms, and the glycol should, like tartaric acid, be capable of existing in four forms, the \( d \)- and \( l \)-, the racemic and meso. forms. When the arrangement of the groups around the asymmetric carbon atoms is the same, so that the two carbon atoms reinforce one another, as far as \( d \)- or \( l \)-rotation is concerned, the molecule as a whole will exhibit a \( d \)- or \( l \)-rotation; whilst
will exist; (i.e., the internally compensated one) and the racemic form will be a mixture in equal proportions of the \(d\)- and \(l\)- forms, which should be resolvable. In addition to these features, somewhat unique for an alcohol, the fact that it is a dihydroxy alcohol makes \(
\beta\)-butylene glycol an interesting compound from an optical point of view. Considerable interest therefore attaches to the isolation of these four forms. Further, were the rotatory dispersion of \(
\beta\)-butylene glycol known, valuable additional evidence would be at hand which might definitely assign complex dispersion to some specific property of the carboxyl group. The relation between rotation and the wave length of the light employed was first embodied in an equation by Biot:

\[
(\text{Mem. Acad. Sci., 1817}, 2, 49, 57, 135)
\]

where the rotation for light of any colour was assumed to be inversely proportional to the square of its wave length. \(\alpha = \frac{\lambda}{\lambda^2}\). Later, this was modified by Drude to \(\alpha = \frac{K}{\lambda^2 - \lambda_n^2}\) where \(\lambda = \) wave length of the light employed, and \(\lambda_n\) represents the wave lengths of the ultra violet rotatory absorption bands possessed by some organic liquids. Where a compound exhibits the simple rotatory dispersion, \(i.e.,\) the dispersion ratio \(\frac{\alpha_{355}}{\alpha_{546}}\) does not fall below 1.577) an equation of only one term suffices to represent its properties, whilst if the compound exhibits complex dispersion, two terms in the Drude equation are necessary. From a study of a large number of secondary alcohols of simple chemical constitution, it has been found \(\) (Lowry, Pickard & Kenyon, \text{J.C.S. 1914, 105, 94}) that such compounds possess simple dispersive powers under widely varying conditions. Also, when the reciprocal of the rotation is plotted against the square of the wave length, linear curves are obtained, showing that the one term Drude equation expresses the relation between rotatory power of course in the case of the alcohols themselves.
However, esters and compounds containing a carboxyl group (or its equivalent) generally display complex rotatory dispersion, and require a Drude equation embracing two terms. This may be explained on the assumption that there are present, in an otherwise homogeneous substance, two dynamic isomerides of different dispersive power, and the complexity is attributed to a peculiar kind of association, in which the supplementary valencies of the oxygen atoms are exercised. Thus \( \gamma = \frac{\alpha}{\alpha - \lambda_0} \) (Smedley, J.C.S., 1909, 95, 231). Here are present two isomerides in equilibrium, each in itself exhibiting simple dispersion, and each therefore requiring a one term Drude equation, whilst as a whole a two term equation results.

We have for each isomeride a one term equation
\[
\alpha = \frac{\kappa_2}{\lambda^2 - \lambda^3} \quad \alpha = \frac{\kappa_2}{\lambda^2 - \lambda^3}
\]
which on adding we get
\[
(\alpha_2 + \alpha_1) = \frac{\kappa_2}{\lambda^2 - \lambda^3} + \frac{\kappa_2}{\lambda^2 - \lambda^3}
\]
There is perhaps not sufficient evidence to decide whether complex dispersion is due to some specific property of the carboxyl group as such, or to the juxtaposition of two oxygen atoms, one Ketonic and the other hydroxyl or ethereal, with the possibility of the exercise of latent valencies. Butylene glycol should form a link in that chain of evidence. Compounds containing one carboxyl group exhibit complex dispersion; e.g., the esters of simple aliphatic alcohols. Those compounds containing two carboxyl groups are markedly complex, e.g., the esters of dibasic acids (Hall, J.C.S., 1923, 123, 32). That the complexity is not due to the presence of one oxygen atom alone has been shown in the case of the \( n \) aliphatic ethers of \( d-\beta \) octanol; (Kenyon & McNicol, J.C.S., 1923, 123, 14), the \( n \)-alkyl ethers of \( d-\beta \) Benzylic Methyl Carbinol, (Kenyon & Phillips; J.C.S., 1923, 123, 22); and of course in the case of the alcohols themselves.
still results in simple dispersion, e.g., Di-β-octyl formal \( \overset{0}{\underset{o}{C}}\overset{0}{\underset{o}{C}}_{\text{octyl}} \) exhibits simple dispersion.

(Thesis to Univ. of London, H. Hunter, June 1921).

In di-β octyl carbonate, \( \overset{0}{\underset{o}{C}}\overset{0}{\underset{o}{C}}_{\text{octyl}} \) which shows simple dispersion, there are two ethereal oxygen atoms, symmetrically placed with respect to the Ketonic oxygen. The simple dispersion can be accounted for by assuming that owing to the proximity of these two ethereal oxygen atoms to the Ketonic oxygen, the balance of forces is such that neither of them exerts latent valencies.

Similar remarks apply to di-β Octyl sulphite, which also exhibits simple dispersion (private communication from author), if we assume that the \(-\overset{\text{S}}{\overset{\text{O}}{\text{C}}=0}\) group behaves like a \(\overset{\text{C}}{\overset{\text{O}}{\text{C}}=0}\) group. Ethyl tartrate has been shown recently to exhibit complex dispersion over a wide range of wave length, (Lowry and Cutter, J.C.S. 1922, 121, 532) and it would appear that complexity of dispersion is due to a specific property of the carboxyl group, namely the ketonic oxygen in juxtaposition to the ethereal oxygen with the exercise of latent valencies.

Finally it remains to examine β butylene glycol, which differs from tartaric acid only in the presence of two methyl groups in place of two carboxyl groups.

**EXPERIMENTAL.**

The synthesis of β Butylene glycol was carried out in the following steps:

I. The dehydration of n-butyl alcohol to \( \overset{\text{C}}{\overset{\text{O}}{\text{C}}}_{\text{butylene}} \) (King, J.C.S., 1919, 115, 1404) and conversion to \( \overset{\text{C}}{\overset{\text{O}}{\text{C}}}_{\text{butylene diacetate}} \).

II. The preparation of \( \overset{\text{C}}{\overset{\text{O}}{\text{C}}}_{\text{butylene diacetate}} \) from \( \overset{\text{C}}{\overset{\text{O}}{\text{C}}}_{\text{butylene dibromide}} \) (Sainbridge, J.C.S. 1914, 105, 2291.)

III. The hydrolysis of \( \overset{\text{C}}{\overset{\text{O}}{\text{C}}}_{\text{butylene diacetate}} \) to \( \overset{\text{C}}{\overset{\text{O}}{\text{C}}}_{\text{butylene glycol}} \). (ibid).
APPARATUS FOR MAKING & LIQUEFying

A = Copper tube 5' x 1/2" diam:
B = Iron air bath 4' x 4" diam:
C = Vessel receiving unchanged alcohol and water.
D = Device for maintaining equilibrium of pressure in tube and
E = Pumice soaked in phosphoric acid.
F = Bottle containing 75% H₂SO₄ cooled in freezing mixture.
The apparatus described by King was modified somewhat, and is represented by diagram opposite. A copper tube, (5' x 1\(\frac{1}{2}\)" internal diam.) packed with pumice soaked in phosphoric acid, was surrounded by a cylindrical iron air bath, (4' x 4" diam.) and heated to 350° C. by a row of bunsen burners. The \(\eta\)-butyl alcohol was dropped into the tube from a tap funnel, the rate being about one drop per second. Unchanged alcohol collected in vessel C, along with water produced in the reaction. The \(\beta\) butylene passed on and was absorbed in bromine contained in a series of wash-bottles cooled in ice. The product obtained by dehydrating \(\eta\)-butyl alcohol in this manner, consists mainly of \(\beta\) butylene. Traces of the other isomerides were separated by fractional distillation of the dibromides. Two boiling points are quoted in the literature for \(\beta\) butylene dibromide, the so-called cis form 156° C., trans. 161° (King, J.C.S., 1919, 115, 1407). These correspond to possible meso. and racemic forms, and attempts were made to separate the two by fractional distillation using a long column. Little success was attained; the whole of the dibromide distilled whilst the temperature rose steadily through two degrees (60°-62° C. at 27 mm. density 1.313 at 0°C.) Refractionation yielded no further evidence of separation, and the experiment was abandoned, the dibromide with these constants being used for the next operation.

For the preparation of \(\beta\) butylene glycol from the dibromide, conversion to diacetae and subsequent hydrolysis appeared to be the best available method. (Bainbridge, J.C.S., 1914, 105, 2291). The use of alcoholic potash for the removal of the two bromine atoms merely results in the removal of one, as hydrogen bromide, leaving an unsaturated body. Aqueous potash
soluble glycol from the aqueous liquor. Boiling with aqueous potassium carbonate (Ehrth's method) was also not tried on account of this difficulty of separation. For the conversion to diacetate silver acetate was used. Potassium acetate removes the elements of hydrogen bromide, leaving trans \( \beta \) brom. pseudo butylene, \( \text{CH}_2\text{CBr}_2=\text{CH} \cdot \text{CH}_3 \) only very small quantities of the diacetate being produced. With silver acetate, however, much more diacetate is produced together with only traces of the unsaturated compound. A yield of 31% of diacetate was obtained by Bainbridge. In one experiment 80 gms. of silver acetate were heated with 50 gms. of \( \beta \) butylene dibromide and 20 cc. of glacial acetic acid. (This is not sufficient acetic acid to dissolve the silver acetate even when hot.) The heating was carried out in an oil bath at 140°-150° for six hours. The liquid was then distilled from the solid, under reduced pressure. The product (64 gms.) was reheated with 50 gms. of \( \beta \) butylene dibromide, 90 gms. silver acetate and 30 cc. glacial acetic acid for a further 7½ hours at the same temperature. The liquid was again distilled off under diminished pressure, and the distillate (151 gms.) on fractionation yielded 25 gms. of a somewhat viscous liquid, B. Pt. 83°-85° C. at 15 mm. (Yield 31% of theory).

The lower fractions of acetic acid, on pouring into water, gave a small quantity of oil, presumably trans \( \beta \) brom. pseudo butylene, which was not examined.

The following constants of the diacetate were determined:

\[
\begin{align*}
\text{Density } \rho_{21^\circ} &= 1.0309, \\
\mu_{5893} &= 1.4274
\end{align*}
\]

From which, using the Lorentz and Lorenz formula the molecular refractivity becomes:-
\[
\left[ \frac{R}{L} \right]_{5896}^{21^\circ} = \frac{1.03747 \times 174.14}{4.03747 \times 1.0308} = 42.452
\]

Calculated, using Eisenlohr's figures for atomic refractivities:

\[
\begin{align*}
C_8 &= 8 \times 2.418 = 19.344 \\
H_4 &= 14 \times 1.100 = 15.400 \\
O_2 &= 2 \times 1.348 = 3.286 \text{ (Ethereal)} \\
O_2 &= 2 \times 2.211 = 4.422 \text{ (Carboxyl)} \\
\end{align*}
\]

Whence

\[
\left[ \frac{R}{L} \right]_{5896}^{21^\circ} = 42.452 \text{ (observed)} \quad \Delta = +2\frac{1}{2}\%
\]

Later it was found that the yield of diacetate could be improved by heating the materials in a boiling water bath for 3-7 hours. In one case, from 200 gm. dibromide was obtained, 94 gms. of diacetate (B.Pt. 89°-95° C. at 20 mm.), a yield of 62% of theory.

The introduction of a mechanical stirrer failed to increase the yield further, probably owing to the large quantities of acetic acid which had to be added, in order to render the mixture sufficiently mobile to stir.

By combining the various preparations of diacetate, a quantity of about 375 grams, was accumulated for hydrolysis to glycol. The procedure adopted for the hydrolysis was a slight modification of the method of Bainbridge. In a trial experiment 2.3 gm. of sodium was dissolved in 50 cc. of ordinary so-called absolute alcohol \( (d_{15^\circ}^{15^\circ} = .7863 \text{ corresponding to } 99\% \text{ ethyl alcohol}) \) and 17.4 gm. of ester was slowly added. The reaction mixture was heated three hours on a water bath so that the alcohol refluxed. A quantity of ammonium chloride sufficient to react with the sodium ethoxide was then added, and the mixture heated on a water bath, till the
The residual liquid was distilled under diminished pressure. The product, a colorless liquid, more viscous than the diacetate, had the following constants:

- B.P.T. 77°-83° C. @ 13 mm. 
- d₁₀ = 1.4358
- n₅₀ = .9991

Using the Lorentz and Lorenz formula

\[
\frac{R}{L} = \frac{n^2 - 1}{n^2 + 2} \cdot \frac{d}{R^2 + 2}
\]

\[
\frac{R}{L} = \frac{21^o}{5396} = \frac{1.03152}{4.03152} = 0.2557
\]

The calculated value of the constant is 23.722. Hence, the theoretical quantity of butylene glycol was larger than the observed.

Larger quantities of glycol prepared in similar fashion boiled over greater temperature range. Since refractometric yield no definite separation, these quantities (d₁₀ = .9987) were taken to be reasonably pure glycol and were converted to the hydrogen phthalic ester.

Formation of Hydrogen phthalate by interaction with Phthalic Anhydride.

Butylene glycol, being a dihydric alcohol should be capable of forming two acid esters; one in which only one hydroxyl group has been esterified and that in which both have been esterified. Also, there is the possibility of the formation of a closed ring compound and a body of the phthalein type. These latter are weight approximating the last seven years.
It has been found that, when glycol and phthalic anhydride are heated together in an oil bath at 110° for 2-3 hours, both the mono- and the di-acid esters are produced. Even when the quantities of phthalic anhydride were near the theoretical quantities for either the mono- or di-ester, it was found that both were produced. Thus, the di-acid ester was obtained in small yield, against the expectation that the molecular weight of the ester, with larger quantities of phthalic anhydride, by titration (determined by titration with N caustic soda) varied between 254 and 193, ultimately falling in several cases from 234 to 193. (Theoretical value for mono-ester = 237, for di-ester = 383, appearing in calculations as monoster as 193). Also it was observed, experimentally, that when the phthalic anhydride solution that in preparation of the hydrogen phthalic ester, including conclusions to crystallise the diester which a white compound crystallised out from the chloroform can be extracted with water, being this was a whilst being dried with calcium chloride, and that the small quantity of a viscous viscous ester was obtained, compound left after the evaporation of the dry

For mono-molecular weight 237 (determined by titration with chloroform was invariably a thick gum). On examination of these two compounds, the crystalline solid M.Pt. 150° of glycol phthalocyanin = 391. Further this material (not sharp) could be crystallised from chloroform or glacial acetic acid giving a product with a lower melting point (90°) and a molecular weight more nearly approaching 193, and was probably di-acid ester, whereas the viscous

m.Pt. and a molecular weight approaching 233 but never pure.

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Several metallic salts were made to discover if any separation could be effected by their aid. The Zinc, Magnesium and calcium salts were made, but of these only the zinc salt was insoluble in water. In one experiment, the removal of the zinc salt resulted in a rise in the molecular weight to 237, possibly indicating that the di-acid ester might be separated by means of the zinc salt, but on the whole no concordant results were obtained and the method was abandoned.

In order that one of the esters might be obtained pure, identified and characterised, the mono-acid ester was prepared by an alternative method, which does not admit of the formation of the di-acid ester.

From 2-butylene was prepared 2-butylene bromhydrin; by converting this into its hydrogen phthalic ester, and removing the bromine atom with moist silver oxide, pure mono-hydrogen phthalate of 2-butylene glycol was obtained.

The bromhydrin was obtained in small yield, together with larger quantities 2-butylene dibromide, by blowing bromine vapour and butylene alternately through a large volume of water cooled in ice. The bromhydrin and dibromide were separated by heating with phthalic anhydride, when the first yields an acid ester, soluble in sodium carbonate solution, leaving the dibromide which can be extracted with ether. Working in this way a small quantity of a somewhat viscous mass was obtained, having molecular weight 307 (determined by titration with caustic soda). Theory for hydrogen phthalate of 2-butylene bromhydrin = 301. Further this material contained bromine and was completely soluble in alkali. On shaking in a bottle with excess of moist silver oxide for several days, a white crystalline body was isolated, M.Pt. 125°. This substance crystallised well from benzene, contained no bromine, had a molecular weight
pinnaiate of the glycol.

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observed in other cases of naturally occurring optically
active bodies e.g. terpene.

In our instance doubt has been cast upon the optical
purity of a body obtained by a natural process, e.g.
active glyceric acid, obtained by fermentation. (Frankland &
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Neuberg, J., 1894, 32, 153), but was later admitted to
be erroneous. (Neuberg & Silberman, Zeit. Chem., 1896, 41, 148). However it indicated Frankland and
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By this method it was found that, his /Frankland's inactive
Glyceric acid obtained by fermentation was optically
pure, thus setting at rest any doubts as to the optical
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to study the optical properties of a primary alcohol
comparing them with those of a secondary alcohol.

Of the early methods, adopted for the isolation of
active aryl alcohol from fusel oil, that due to Pasteur,
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sation of the barium, salt or aryl hydrogen suivate. The
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$\alpha_p = -3.5^\circ$ (1 in 1). Later, Le Petit quoted that by
subjecting fusel oil to the action of hydrochloric acid,
Butyl alcohol also forms a convenient starting point for the synthesis of sec. butyl carbinol. It was desired to prepare this alcohol and attempt its resolution by the method of Pickard & Kenyon (J.C.S., 1911, 99, 45). In this way it could be ascertained whether the naturally occurring alcohol, (about 16% in fusel oil) were of full optical activity or only partially active, as observed in other cases of naturally occurring optically active bodies e.g. terpineol.

In one instance doubt has been cast upon the optical purity of a body obtained by a natural process, e.g. active glyceric acid obtained by fermentation (Frankland & Appleyard, J.C.S., 1893, 63, 299). A higher value for the rotation of this was subsequently quoted (Silberman & Neuberg, Ber. 1904, 37, 339), but was later admitted to be erroneous. (Neuberg & Silberman, Zeit. physiol. Chem. 1905, 44, 146). However it stimulated Frankland and his co-workers to resolve inactive glyceric acid by a chemical means, namely by the crystallisation of its brucine salt. (Frankland & Done, J.C.S., 1905, 27, 613). By this method it was shewn that his (Frankland's) active glyceric acid obtained by fermentation was optically pure, thus setting at rest any doubts as to the optical purity of compounds obtained by fermentation. Further, amyl alcohol is the simplest primary alcohol capable of exhibiting optical activity, and it would appear desirable to study the optical properties of a primary alcohol and compare them with those of a secondary alcohol.

Of two early methods, adopted for the isolation of active amyl alcohol from fusel oil, that due to Pasteur, (C.R., 41, 296), consisted in the fractional crystallisation of the barium salt of amyl hydrogen sulphate. The alcohol, recovered from the more soluble barium salt by hydrolysis with dilute sulphuric acid, had a rotation \( \alpha_D = -3.55^\circ \) (\( l = 1 \)). Later, Le Bel showed that by subjecting fusel oil to the action of hydrochloric acid,
and, by repeating this operation several times, he obtained an alcohol of rotation $\alpha_D = -9^o (\ell = 2)$. By a modification of the method of Le Bel, namely heating fusel oil with fuming hydrochloric acid in sealed tubes, Rogers obtained an alcohol with the following constants $[\alpha]_D^{220} = -5.2^o$, $d^{220} = 0.818$, b.Pt. $138^o - 129^o$ (Rogers, J.C.S. 1893). This alcohol was considered by Rogers to be a mixture of active and inactive alcohol in such proportion that they are acted upon to equal extent by hydrogen chloride, and further treatment led to no increase in the rotatory power. McKenzie (J.C.S., 1901, 72 1135) has shown that on esterification of 3, nitrophthalic acid two esters may be obtained.

These figures are given later for comparison with those obtained in the present investigation. All the work not here recorded has dealt with the isolation and examination of active amyl alcohol from natural sources, a method tedious process requiring large quantities of material.

On esterification of amyl alcohol by Fischer and Speier's method (Ber., 1895, 28, 3252), the main product was the $\alpha$ form, with some $\beta$ ester, and traces of the normal ester. If the esterification is carried out directly with 3-nitrophthalic anhydride, the $\alpha$ ester is the main product. Of the two carboxyl groups in 3-nitrophthalic acid, that in the $\alpha$-position to the nitro-group is the stronger. McKenzie has shown that the $\alpha$ ester, (in which the alcohol radicle is regarded as replacing the hydrogen of the stronger carboxyl group) is more difficult to hydrolyse than the $\beta$ ester, as would be expected on theoretical grounds. The method used for the esterification of amyl alcohol, described in this thesis, does not admit of the formation of two esters since the two carboxyl groups in phthalic acid are equal in value as far as acid properties are concerned, and no difficulty was encountered in hydrolysing the
(a) inactive iso amyl alcohol \((\text{CH}_3)\_\text{CH} \cdot \text{CH}_2 \cdot \text{CH}_2 \cdot \text{OH}\)

(b) active amyl alcohol (\(\ell\)-methyl ethyl carbinol) prepared by direct acetylation with \(\text{C}_4\text{H}_8\text{CHO}\) (acetic acid), yielding \(\text{C}_8\text{H}_{15}\text{COCH}_3\), which on crystallisation twenty times gave an ester of rotation,

starting with an alcohol \(\alpha_D = -5.95^\circ\) (\(\ell\) = 2) and esterifying by Fischer and Speier's method, the \(\beta\) ester.

(1-Amyl 3-nitrophthalic ester) was obtained. After in crystallisation from carbon bisulphide and benzene, an ester was obtained. M.P.: 113° - 114° C., \(\alpha_D = +6.5^\circ\).

This on hydrolysis with aqueous caustic soda yielded an alcohol \(\alpha_D = -5.90^\circ\). R.B.: 123° C. \(\delta_20^\circ = 0.816.

Marrick and McKenzie also give values for the rotation of the alcohol for lights of different wave length. These figures are given later for comparison with those obtained in the author's investigation. All the work so far recorded has dealt with the isolation and examination of active amyl alcohol from natural sources, a somewhat tedious process requiring large quantities of raw material. The synthesis and resolution of active amyl alcohol (\(\ell\)-sec. butyl carbinol) was first carried out by Cohen, Marshall and Woodman, (J.C.S., 1915, 107, 832).

The alcohol was prepared by the reduction of methyl ethyl ketone (Freundler & Damond, Compt. Rend. 1905, 141, 830). The sec. butyl alcohol bromide and a brucine salt which could be so obtained was converted to the corresponding bromide, crystallised from 9% ethyl alcohol, and this subjected to a Grignard reaction with trioxymethylene. Attempts at resolution by the method of Pickard and Kenyon, (J.C.S., 1911, 92, 45; 1912, 101, 620) failed, owing to the fact, that the hydrogen phthalic ester was obtained as a viscous mass, which gave a brucine salt, also a viscous mass, which solidified with difficulty and was too soluble in all ordinary solvents to recrystallise. The strychnine salt was obtained in crystalline form, but readily underwent
acid nature of the hydrogen phthalic ester, a stronger acid was used, i.e. 3-Nitrophthalic acid. The α ester, prepared by direct esterification with 3-nitrophthalic anhydride, yielded a brucine salt, which on crystallisation twenty times gave an ester of rotation, \[ \alpha = -2.67^\circ \]. The cinchonidine salt, likewise after about twenty crystallisations, gave an ester \[ \alpha = +2.65^\circ \]. Since further crystallisation brought about no change in the rotation, these were assumed to be the enantiomorphous forms of the ester, and were hydrolysed with 10% aqueous potassium hydroxide. The alcohol obtained from the \[ \beta \] ester had \[ \alpha = +3.28^\circ \] whilst that from the \[ \delta \] ester had \[ \alpha = -4.1^\circ \], indicating that partial racemisation had occurred during the hydrolysis.

The results obtained, which are described in this thesis, may be summarised as follows:

I. The hydrogen phthalic ester of \[ \text{dl-sec. butyl carbinol} \] was, when first prepared, a viscous mass, which solidified, after standing about eighteen months, to a white crystalline body, M.P. 54°C. It could be easily crystallised from petroleum ether (B.P. 40°C - 60°C).

II. The solid ester readily gave a well crystallised brucine salt which could be recrystallised from acetone, and a strychnine salt which could be crystallised from 96% ethyl alcohol.

III. The amount of decomposition of the strychnine salt, when boiled in 96% ethyl alcohol, was negligible, and did not in any way interfere with the resolution.

IV. Separation of the two enantiomorphous forms of the ester could be effected by the crystallisation of the brucine salt from acetone, or better still, the strychnine salt from 96% ethyl alcohol.

V. The highest value obtained for the rotation of the hydrogen phthalic ester (known to be not
aqueous sodium hydroxide, an alcohol of rotation 

VII. The specific rotations of the alcohol for liquid light of several wavelengths compare favorably with those given by Harckwald and McKenzie (ibid). Hydrogen sulphide with a slight excess of hydrobromic acid solution (obtained by reduction of Bromine with sulphur dioxide), cooling half an hour and steam distilling, gave an obtained in fairly good yield. The Grignard reaction was carried out at 100°C. butyl carbinol was synthesised by the following series of operations:-

I. Conversion of n-butyl alcohol to β Butylene. (Kingsley, J.C.S., 1919, 115, 1404). slow heating

II. Absorption of β butylene in 75% sulphuric acid, giving butyl hydrogen sulphate. 200°C.

III. Treatment of butyl hydrogen sulphate with hydrobromic acid whereby sec butyl bromide is obtained in hours. It was found that, if trioxymethylene-

IV. hydrobromide A Grignard reaction is carried out with sec. butyl bromide and trioxymethylene yielding dl-sec. butyl carbinol. produced. In order to overcome this, the trioxymethylene was added to an alcohol solution of dl-

Carried out in ether for a period of 3 hours, the total weight of trioxymethylene added was only 15% of the required theoretical amount, since it is probable that, except for the total quantity of the reaction. (Gilman and Keynes, J. Am. Chem. Soc. 1923, 45, 1613).
butylene was produced, which was allowed to drop into a bottle containing 75% sulphuric acid, also cooled in a freezing mixture. In most of the experiments, 100 cc. of the acid were used and 50 gms. butylene condensed in the bottle. On corking tightly and agitating vigorously on a shaking machine, the butylene was absorbed with slight rise in temperature. The homogeneous liquid obtained in this way contained butyl hydrogen sulphate with excess sulphuric acid. On treating this butyl hydrogen sulphate with slight excess of hydrobromic acid solution (obtained by reduction of Bromine with sulphur dioxide), refluxing half an hour and steam distilling, sec-buty1 bromide was obtained in fairly good yield. The Grignard reaction was carried out using a mechanical stirrer. During the formation of the magnesium complex sec-buty1 bromide was dropped into the reaction mixture at such a rate that the reaction proceeded gently, ether refluxing slowly from the condenser. No cooling in ice was necessary, if the operation were carried out in this way. The rate of addition was such that 2 molecules (274 gms.) of sec-buty1 bromide were added gradually over a period of time of three hours. It was found that, if trioxymethylene be present in excess, or be added to the magnesium complex all at once, appreciable quantities of diamyl formal were produced. In order to overcome this, the trioxymethylene was added in small quantities at hourly intervals, the stirring and heating being carried out altogether for a period of about 38 hours. The total amount of trioxymethylene added was only 90% of the required theoretical amount, since it is probable that, in most cases, only 90% of the theoretical quantity of magnesium complex is produced in a Grignard reaction. (Gilman and Meyers, J. Amer. Chem. Soc., 1923, 45, 159).
with the production of quite inappreciable quantities of diaryl formal. This was the highest yield obtained in any case; the yield in an experiment in which excess of trioxymethylene was passed into the reaction mixture, in the form of vapor, (Zeigler, Ber. 1921, 54, [H] 737) being considerably below this, in addition to the formation of considerable quantities of diaryl formal (about 20% of theoretical amount). The alcohol obtained on decomposing the product from the Grignard reaction was fractionally distilled, that portion boiling at 125° - 130° being reserved for conversion to hydrogen phthalic ester.

The hydrogen phthalic ester was prepared in the usual manner, by heating the alcohol with slight excess of phthalic anhydride. (Pickard and Kenyon, J.C.S., 1911, 99, 45; 1912, 101, 620). The ester as prepared was a viscous mass, which solidified fairly readily when inoculated with some of the solid ester. The solid ester had been obtained by allowing some of the viscous mass to remain in a stoppered bottle for about eighteen months. After recrystallisation from light petroleum ether, the alcohol boiled at 125° - 130°. It had 4.4493 gm. of the ester required for neutralisation on treatment with p-nitrosoanil chloride in gr. NaOH.

The theoretical amount required = .0764 gm. NaOH.

The brucine salt was obtained when equimolecular quantities of ester and brucine were boiled in acetone. The salt could be recrystallised easily from acetone; after seven such crystallisations the M.Pt. of the salt had risen from 66° to 71° and the acid ester recovered from the seventh crop of crystals had [α]D +2.4° and M.Pt. 45°. To reach this point the weight of successive crops of crystals had been decreased enormously from 150 gms. to 13 gms.

The strychnine salt also was obtained in crystalline form, and could be recrystallised from 96% ethyl alcohol with an inappreciable amount of decomposition. After
whilst the mother liquor from the last crystallisation gave an ester \([\alpha]_D^{20} = +3.5^\circ\) indicating that full activity had not yet been reached. Further crystallisation with this small quantity of material was not attempted satisfactorily with those obtained by Harrowfield and continued, for to do so would have so decreased its rotatory power in mind that the alcohols mentioned above in full action would have been insufficient to determine its rotatory power. The ester obtained of maximum rotation had M.Pt. 41° - 41.5°C, and 0.5182 gms. of it required 0.0380 gms. NaOH. Theory requires 0.0878 gms. NaOH. The mother liquors from the brucine and strychnine crystallisations were decomposed and the ester obtained had \([\alpha]_D^{20} = -1^\circ\).

Various alkaloidal salts of this were made in an attempt to isolate some fully active \(L\)-rotatory ester. The quinine, quinidine, cinchonine, and cinchonidene salts were all uncrystallizable viscous masses, and the attempt was abandoned. The slightly \(L\)-ester from these experiments was hydrolysed with dilute NaOH, steam distilled, extracted with ether and dried first over anhydrous potassium carbonate, then over barium oxide. On distillation, the alcohol boiled at 125° - 128°C, and had \([\alpha]_D^{20} = +1.2^\circ\). This partly \(d\)-alcohol yielded a \(p\)-nitrobenzoate, on treatment with \(p\)-nitrobenzoyl chloride in dry pyridine. This ester obtained as a viscous liquid, solidified on being kept in the ice chest, to a yellow crystalline solid M.Pt. 19°C. All attempts at recrystallisation failed owing to its extremely low M.Pt. (Rotation of \(d\)-rotatory \([\alpha]_D^{20} = -1^\circ\)).

The ester of maximum \(d\)-rotation, \([\alpha]_D^{20} = +4.2^\circ\) on hydrolysis, yielded an alcohol B.Pt. 126° - 129° \([\alpha]_D^{20} = -1.02^\circ (L = \frac{1}{2}).\) The amount obtained was insufficient to fill the smallest available pyknometer, and the density was therefore not determined, the value given by Markwald and McKenzie (\(d^{20}_4 = 0.916\)) being used to calculate the specific rotatory powers. The values obtained for the specific rotatory powers at 20°C, in \(\frac{1}{4}\) dm. tube, for light of four wave lengths were as follows:
whence $\frac{\kappa_{4359}}{\kappa_{5461}} = 1.69$ (cf. Lowry, Pickard and Kenyon, J.C.S., 1914, 105, 93) where the dispersion of active amy1 alcohol is given as 1.700. These values compare favorably with those obtained by Markwald and McKenzie, bearing in mind that the alcohol mentioned above is not fully active.

<table>
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<th>$\lambda$</th>
<th>4359</th>
<th>5106</th>
<th>5153</th>
<th>5210</th>
<th>5461</th>
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<tr>
<td>$\kappa_\lambda$</td>
<td>-4.42°</td>
<td>-5.90°</td>
<td>-7.44°</td>
<td>-8.03°</td>
<td>-11.76°</td>
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The following values for the refractive index of the partly $l$- alcohol were obtained

<table>
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<th>5153</th>
<th>5210</th>
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<tbody>
<tr>
<td>$n_{25.5^0}$</td>
<td>1.41736</td>
<td>1.41235</td>
<td>1.41166</td>
<td>1.41169</td>
<td>1.40782</td>
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<tr>
<td>$\lambda$</td>
<td>5790</td>
<td>5792</td>
<td>5790</td>
<td>5896</td>
<td>6708</td>
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<tr>
<td>$n^{\text{mr}}$</td>
<td>1.40958</td>
<td>1.40923</td>
<td>1.40947</td>
<td>1.40879</td>
<td>1.40673</td>
</tr>
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</table>

These values with one or two exceptions lie on a smooth curve.

In conclusion it may be stated that this work is being continued and it is hoped that the resolution will be completed shortly.

A. husa, Dec. 1923
ROTATION OF AMYL ETHER

VALUES OF MARCKNALL

REFRACTIVE INDEX

AMYL ALCOHOL

\[ \lambda \]

\[ 1.408 \]

\[ 1.412 \]

\[ 1.414 \]

\[ 1.416 \]

\[ 1.418 \]