

LXXV.—*The Racemisation of Phenyl-p-tolylacetic Acid.*

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It is well known that alkali often causes an interchange of groupings to occur in an optically active system. The catalytic racemisation thus induced, either partial or incomplete as the case may be, is accelerated by an elevation of temperature in such cases where the latter effect has actually been examined; for example, a solution of *l*-mandelic acid in potassium hydroxide is comparatively stable at the ordinary temperature so far as its rotatory power is concerned, even when the amount of the base present is considerably more than is necessary for the neutralisation of the acid. On the rise of temperature, however, the solution becomes less laevorotatory, and may, when sufficient alkali is present, become quite inactive (T., 1904, **85**, 378).

In the course of work on asymmetric synthesis, one of us had occasion to examine the behaviour of *l*-menthyl *l*-mandelate towards alcoholic potassium hydroxide, and it was found that, no matter under what conditions the saponification was effected, the resulting mandelic acid was invariably racemised to a very considerable extent (T., 1904, **85**, 1249); for example, when a dilute alcoholic solution of the ester was saponified at 25° by the calculated quantity of alkali, the resulting acid had the value $[\alpha]_D - 36.3^\circ$ (in aqueous solution), which is less than one-fourth of the value for the pure *l*-acid. For this reason, although unequal amounts of *l*-menthyl *d*-mandelate and *l*-menthyl *l*-mandelate were actually produced by the reduction of *l*-menthyl phenylglyoxylate, the acid obtained by the saponification of this mixture was optically inactive, and this difficulty had to be surmounted before the asymmetric synthesis of *l*-mandelic acid could be successfully accomplished (McKenzie and Humphries, T., 1909, **95**, 1105).

Now mandelic acid, $C_6H_5 \cdot CH(OH) \cdot CO_2H$, contains a hydrogen atom and a hydroxyl group, both attached to the asymmetric

carbon atom, and it is conceivable that the phenomena to which reference has been made may have been due to this cause. It was, accordingly, deemed desirable to examine some other acid where the hydroxyl group of mandelic acid had been substituted by a hydrocarbon residue, more especially since data are already available regarding the behaviour of atrolactic acid,



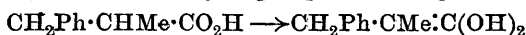
where the hydrogen atom of mandelic acid is displaced by a methyl group (T., 1904, **85**, 1249; 1906, **89**, 365). *r*-Phenyl-*p*-tolylacetic acid, $\text{C}_7\text{H}_7 \cdot \text{CHPh} \cdot \text{CO}_2\text{H}$, is readily accessible, and it was accordingly selected for the purpose in view.

The inactive acid was, first of all, resolved. The *d*-acid, which is obtained fairly readily by the agency of cinchonidine, melts at 83–84°, and has $[\alpha]_{\text{D}} + 14.6^\circ$ in acetone. Quinine was used for the preparation of the *l*-isomeride, but the resolution was troublesome, as it appeared that the quinine salts of the enantiomorphously related acids formed a solid solution. The *d*-acid undergoes partial racemisation when heated with aqueous alkali, the recovered acid having $[\alpha]_{\text{D}} + 9.1^\circ$ in acetone.

The method of Marckwald and McKenzie for resolving inactive compounds, depending on fractional esterification and fractional saponification, was next utilised, and, from the behaviour of the *r*-acid with *l*-menthol, on the one hand, and that of the *l*-menthyl *r*-ester towards alkali on the other, the conclusion was drawn that profound racemisation would take place during the saponification either of the *l*-menthyl *d*-ester or of the *l*-menthyl *l*-ester.

These esters were accordingly prepared separately, and the conclusion was verified. A similar behaviour was exhibited by the *l*-bornyl esters. It was also interesting to note that ethyl *d*-phenyl-*p*-tolylacetate gave an inactive acid on saponification with alcoholic potassium hydroxide. Finally, when the *d*-acid chloride was submitted to the Friedel-Crafts' reaction with benzene and aluminium chloride, the resulting ketone was the racemic form. These experiments showed conclusively that optically active phenyl-*p*-tolylacetic acid is more readily racemised than is mandelic acid under similar conditions.

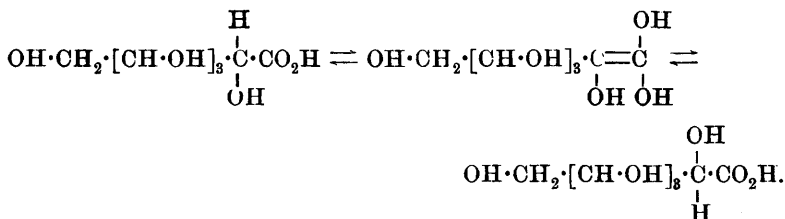
The hypothesis that racemisation may sometimes be attributed to desmotropic change with the concomitant disappearance of molecular asymmetry is not new. Kipping and Hunter (T., 1903, **83**, 1009) pointed out, with reference to α -benzylpropionic acid, that, from the fact that the asymmetric grouping is in the α -position relatively to the carboxylic group, the change:



would be expected to occur readily; in this case, however, there

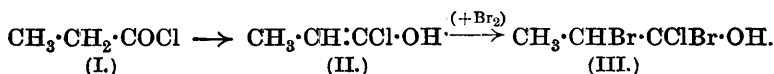
was no evidence of racemisation when the acid was heated (compare also Werner, "Lehrbuch der Stereochemie," 1904, 52, 80; Lowry, *British Association Report*, 1904). It would, however, be possible to interpret the racemisation observed by Kipping and Hunter with *d*-benzylpropionyl chloride to the desmotropism of this compound, and we do not doubt that, if the behaviour of the menthyl ester of the *d*-acid were studied, the phenomena exhibited would be similar to those of the menthyl esters of mandelic and phenyl-*p*-tolylacetic acids.

In the same connexion, E. Fischer's well-known observations on the transformation of polyhydroxy-acids of the sugar group by means of pyridine or quinoline are highly significant. In the interconversion, for instance, of *d*-gluconic and *d*-mannonic acids, inversion takes place only at the carbon atom in the α -position, a change which in the light of the above hypothesis would be interpreted as follows:



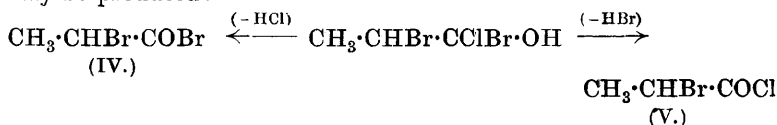
Similarly, the establishment of a condition of equilibrium between dextrose, *d*-mannose, and lævulose when any one of these sugars is treated with alkali has been ascribed by Wohl to the formation of a common enolic form.

Within recent years, data in favour of the interpretation of many cases of racemisation on the basis of desmotropism have been gradually accumulating. Incidentally, Aschan's views on the mechanism of the Hell-Volhard reaction (*Annalen*, 1912, **387**, 1; *Ber.*, 1912, **45**, 1913) merit special attention, even although they have not met with general acceptance (compare Lapworth, T., 1904, **85**, 30; Smith and Lewcock, *Ber.*, 1912, **45**, 2358; Meyer, *Ber.*, 1912, **45**, 2868; Michael and Scharf, *Ber.*, 1913, **46**, 136; Staudinger and Anthes, *Ber.*, 1913, **46**, 1417; Aschan, *Ber.*, 1913, **46**, 2162). The bromination of propionyl chloride is represented by this author as follows:



In the hypothetical compound (III) the hydrogen of the hydroxy-group may combine with chlorine or with bromine, so

that a brominated bromide (IV) and a brominated chloride (V) may be produced:



Since hydrogen has a greater affinity for chlorine than for bromine, the gas evolved should consist mainly of hydrogen chloride, and this has been found experimentally to be the case.

The question of the occurrence of desmotropic change during the racemisation of optically active ketols, such as *l*-benzoin and *d*-benzoylbenzylcarbinol in the presence of alkali, has been considered in former papers (T., 1910, **97**, 473; 1914, **105**, 1583; Wren, T., 1909, **95**, 1583, 1593; compare also Dakin, *Amer. Chem. J.*, 1910, **44**, 48, on the racemisation of hydantoins).

Applying the hypothesis to the case of active mandelic acid, as Lowry (*loc. cit.*) has already done, it will be seen how racemisation might occur:

$d\text{-OH}\cdot\text{CHPh}\cdot\text{CO}_2\text{H} \rightarrow \text{OH}\cdot\text{CPh}\cdot\text{C}(\text{OH})_2 \rightarrow r\text{-OH}\cdot\text{CHPh}\cdot\text{CO}_2\text{H}$,
and similarly with phenyl-*p*-tolylacetic acid and with isopropylmalonamic acid (Fischer and Brauns, *Sitzungsber. K. Akad. Wiss. Berlin*, 1914, 714), which is very easily racemised at the ordinary temperature when an excess of alkali is present.

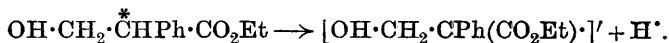
Now, such a transformation cannot take place with *l*-atrolactic acid, $\text{OH}\cdot\text{CPhMe}\cdot\text{CO}_2\text{H}$, as the labile hydrogen atom, which renders possible the formulation of a desmotropic structure, is absent. As has been shown very conclusively (T., 1904, **85**, 1249; 1906, **89**, 365), this acid is remarkably stable towards alkali, and in no case was there ever any evidence of racemisation. Moreover, although the menthyl esters of the *d*- and *l*-atrolactic acids were not prepared separately with the view of testing their behaviour towards alkali, the fact that an optically active acid was invariably obtained by the saponification under various conditions of a mixture of unequal quantities of these esters is a proof that the system is not prone to racemisation. These results have, however, escaped the notice of Rothe, who, in a recent paper (*Ber.*, 1914, **47**, 843), records the stability of active atrolactic acid towards alkali. It may also be observed that the description of the resolution of *r*-atrolactic acid as given by Rothe is imperfect; furthermore, this acid was resolved five years ago (McKenzie and Clough, T., 1910, **87**, 1016), in such a manner as to give the optically pure forms.

The behaviour of *d*-α-amino-α-methylbutyric acid (Fischer and Grävenitz, *Annalen*, 1914, **406**, 1) towards alkali is noteworthy.

As distinct from the commoner α -amino-acids, which are slowly racemised when heated with alkali at 100° , this acid exhibited no racemisation whatever under these conditions. Here, again, the mobile hydrogen atom, necessary for the assumption of desmotropism, is absent. Another instructive example is afforded by the stability towards alkali of the optically active alcohols of the type $\text{CHRR}'\cdot\text{OH}$; desmotropism is not possible with such compounds, which can be regenerated in an optically pure condition when their esters are treated with alkali (Pickard and Kenyon, T., 1911, **99**, 62, etc.).

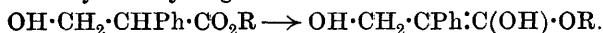
Again, Rupe and Häussler (*Annalen*, 1909, **369**, 324) found that d - β -phenylbutyric acid, $\text{CHPhMe}\cdot\text{CH}_2\cdot\text{CO}_2\text{H}$, could be obtained from its l -menthyl ester without the occurrence of racemisation during the process of saponification; similarly, the l -menthyl ester of the l -acid gave the unracemised acid. Now in the event of desmotropism taking place with these acids, the formation of the compound $\text{CHPhMe}\cdot\text{CH}:\text{C}(\text{OH})_2$ does not involve a disappearance of asymmetry, since the original asymmetric carbon atom is still asymmetric according to the latter formulation. The comportment of $\alpha\beta$ -diphenylpropionic acid, $\text{CH}_2\text{Ph}\cdot\text{CHPh}\cdot\text{CO}_2\text{H}$, under similar conditions is, however, different. If this acid, which is isomeric with phenyl- p -tolylacetic acid, undergoes transformation into the desmotropic form, $\text{CH}_2\text{Ph}\cdot\text{CPh}:\text{C}(\text{OH})_2$, a disappearance of asymmetry would result from the change. Now Rupe and Kerkovius (*Ber.*, 1912, **45**, 1398) have found that the optically active $\alpha\beta$ -diphenylpropionic acids are completely racemised by alcoholic potassium hydroxide, whilst the acid recovered from the saponification of the l -menthyl ester of the l -acid is sometimes quite inactive and sometimes only feebly active. This behaviour is, in fact, in the same category with that of mandelic and phenyl- p -tolylacetic acids.

Gadamer, who has shown that ethyl d -tropate is completely racemised at the ordinary temperature by alcoholic potassium hydroxide, emphasises the contrast between the ester and the free acid, which, so far as his observations go, is not racemised by alkali (*J. pr. Chem.*, 1913, [ii], **87**, 312). On the ground of this difference of behaviour, the assumption is made that the ester behaves as a pseudo-acid, and becomes ionised in the presence of hydroxyl ions:



The disappearance of optical activity is ascribed to the carbon atom C^* having only three groups attached to it in the anion, a condition which would involve a symmetrical arrangement owing to three groups falling into one plane with the carbon atom. In the association of the hydrogen ion and the anion by the reverse change,

the *d*- and *l*-esters would be produced in equal quantities. On the other hand, the free acid is assumed by Gadamer to undergo electrolytic dissociation either alone or under the influence of hydroxyl ions into the anion, $(\text{OH}\cdot\text{CH}_2\cdot\text{CHPh}\cdot\text{CO}\cdot\text{O}\cdot)'$, where the asymmetric carbon atom is still present. However, as Frankland (T., 1913, **103**, 725) has pointed out, the ester might be considered as undergoing isomeric change prior to ionisation, and the disappearance of asymmetry might be attributed to this cause:



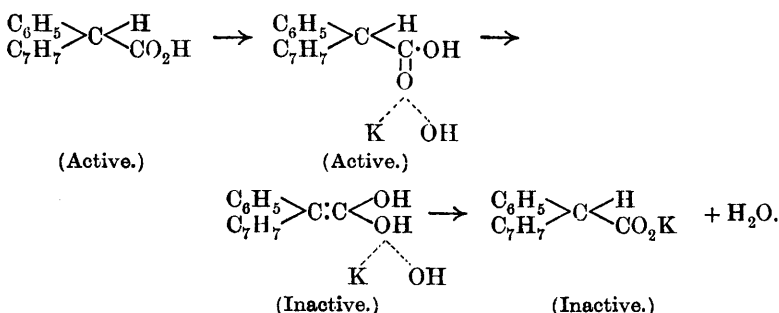
The occurrence of desmotropism appears, therefore, to be the most satisfactory interpretation of the racemisation of optically active compounds by means of alkali which has yet been adduced, and the experimental facts are in remarkable harmony with the idea.

Objection may be raised, however, on very valid grounds to one aspect, which is put forward in the preceding pages. As a convenient working hypothesis, the simplest expression of desmotropism has been employed throughout; the first phase in the process of racemisation by alkali has been represented as an isomeric change; thus, with phenyl-*p*-tolylacetic acid the dihydroxy-isomeride has been assumed to be formed in the first instance. Nevertheless, this conception that a complex of the latter type can have even an ephemeral existence in solution appears to us to be extremely improbable. The number of available acids which might undergo such a change is so large that, if the change did actually occur in any case, some definite evidence, either physical or chemical, would undoubtedly be forthcoming. In other words, then, we consider it unlikely that two forms of an optically active acid, such as phenyl-*p*-tolylacetic acid, which can be racemised by alkali, would exist alongside of one another as an equilibrated mixture as represented by $\text{C}_7\text{H}_7\cdot\text{CHPh}\cdot\text{CO}_2\text{H} \rightleftharpoons \text{C}_7\text{H}_7\cdot\text{CPh}\cdot\text{C}(\text{OH})_2$, comparable with the tautomerism exhibited by ethyl acetoacetate.

Bearing in mind, however, the reactivity of the carbonyl group,* we suggest that an additive compound is first formed with the catalyst, and that it is this unstable compound, and not the free acid itself, which undergoes desmotropic change. An assumption of this nature does not affect the arguments submitted in favour of the hypothesis of desmotropism during racemisation. The be-

* "Although it has been customary to regard carboxylic acids as compounds containing the free carboxylic radicle, the evidence that such is always the case is in no way sufficient, let alone conclusive. The behaviour of monocarboxylic acids, especially their recognised tendency to form double molecules, as in the case of acetic acid, is clear proof that the carboxylic radicle is far from being saturated" (Armstrong and Walker, *Proc. Roy. Soc.*, 1913, [4], **88**, 399).

haviour of active phenyl-*p*-tolylacetic acid towards alkali might, accordingly, be represented by some such scheme as the following, which postulates the addition of the base to the undissociated acid:



Other representations of an equally hypothetical character could, of course, be put forward. We desire, therefore, to emphasise the suggestion that addition precedes desmotropism.

The phenomena of racemisation may be divided broadly into three classes:

(1) Racemisation caused by heating. Werner (*loc. cit.*, pp. 49—50) has discussed this on a kinetic basis.

(2) Catalytic racemisation, by alkali, for example.

(3) Racemisation during reactions involving displacement of groupings.

With reference to this classification it should be observed that various compounds, which are not racemised by alkali, are, nevertheless, convertible by reactions of displacement into compounds which are either quite inactive or are not optically pure; for example, *L*-lactic acid gives *r*- α -chloro- α -phenylpropionic acid on treatment with hydrochloric acid (McKenzie and Clough, T., 1910, **97**, 1020); with phosphorus pentachloride, it gives a mixture of *r*- and *d*- α -chloro- α -phenylpropionic acids (McKenzie and Clough, T., 1910, **97**, 2564). Again, *d*- α -amino- α -methylbutyric acid is converted into *r*- α -hydroxy- α -methylbutyric acid by means of nitrous acid (Fischer and Grävenitz, *loc. cit.*). It is possible that the interpretation of catalytic racemisation which has been dealt with in this paper may also be serviceable in connexion with reactions of displacement, such as the Walden inversion.

EXPERIMENTAL.

A modification of the method described by Gyr (*Ber.*, 1908, **41**, 4321) for the preparation of phenyl-*p*-tolylacetic acid was adopted.

One hundred and thirty grams of stannic chloride ($1\frac{1}{2}$ mols.) were added gradually to a boiling solution of *r*-mandelic acid (50

grams, 1 mol.) in 250 c.c. of toluene. After two and a-half hours the evolution of hydrogen chloride had practically ceased, and the liquid was then cooled and shaken with an excess of water. The toluene layer was separated, the acid contained in it extracted by sodium carbonate, the alkaline solution filtered, and then acidified by hydrochloric acid. The crude acid, obtained by extraction with ether, was viscous, and became only partly solid by keeping. It was crystallised from dilute acetic acid, from which solvent, as well as from others, it separated as an oil, which, however, readily solidified on being sown with a nucleus. The melting point was 115—116°, whereas Zincke (*Ber.*, 1877, 10, 997) gives 115°. The yield was 32 grams.

Resolution of r-Phenyl-p-tolylacetic Acid.

Cinchonidine was found to be a suitable alkaloid for this purpose. When 6.5 grams of the alkaloid (1 mol.) were dissolved in a solution of 5 grams of the acid (1 mol.) in 160 c.c. of ethyl alcohol, 8.5 grams of crystals separated; these were crystallised twice from ethyl alcohol, and the resulting 4 grams gave 1.5 grams of acid with $[\alpha]_D + 10^\circ$ in acetone. On the other hand, when 5 grams of the *r*-acid were dissolved in 90 c.c. of alcohol and combined with 3.25 grams of the alkaloid ($\frac{1}{2}$ mol.), the crystals, which separated, amounted to 4 grams, and gave 1.7 grams of acid with $[\alpha]_D + 7.9^\circ$ in acetone. It was, therefore, advantageous to employ the acid and the alkaloid in molecular quantities.

Fifty grams of the *r*-acid (1 mol.) were dissolved in 2 litres of boiling ethyl alcohol, and 65 grams of cinchonidine (1 mol.) were added. Crystallisation proceeded during two days in an ice-chest. The 54 grams of salt which separated were crystallised as before from 900 c.c. of alcohol, and, after five additional crystallisations, the salt (24 grams), which separated in needles, was homogeneous. It melted and decomposed at 204—205°, and, after being dried at the ordinary temperature, it gave the following values when dissolved in chloroform; $l=2$, $c=3.025$, $\alpha_D^{16} - 2.12^\circ$, $[\alpha]_D^{16} - 35^\circ$. It was decomposed by shaking with an excess of dilute sulphuric acid, and the organic acid was then extracted with ether. Yield of acid, 9.2 grams.

d-Phenyl-p-tolylacetic acid, $C_7H_7 \cdot CHPh \cdot CO_2H$, separates from aqueous alcohol or from dilute acetic acid as an oil, which solidifies gradually to form feathery needles. It is very soluble in ethyl alcohol, acetone, benzene, chloroform, and acetic acid. It melts at 83—84° with slight preliminary softening. For analysis, it was dried in a vacuum over sulphuric acid:

0.175 gave 0.5096 CO₂ and 0.0982 H₂O. C=79.4; H=6.2.

C₁₅H₁₄O₂ requires C=79.6; H=6.2 per cent.

Its specific rotation was determined in acetone:

$$l=2, c=4.214, \alpha_D^{19.4} + 1.23^\circ, [\alpha]_D^{19.4} + 14.6^\circ.$$

Owing to the small rotatory power of the acid both in acetone and in other solvents, polarimetric measurements of the cinchonidine salts obtained from each separate crystallisation are of little value as an indication of the progress of the resolution. In order to establish the purity of the acid as prepared by the method just described, the filtrate from each crop in another resolution was decomposed by mineral acid, and the resulting organic acid examined. Thirty-nine grams of cinchonidine were dissolved in a solution of 30 grams of the *r*-acid in 1200 c.c. of ethyl alcohol, the progress of the separation being shown as follows:

	Cinchonidine salt.	Alcohol.	Acid from filtrate.	$[\alpha]_D^{19.4}$ in Acetone.*
1	36 grams	600 c.c. }	14.0 grams	-4.3°
2	29 "	500 "		
3	23 "	380 "	1.3 "	+1.6
4	21 "	345 "	0.8 "	7.1
5	18 "	300 "	0.6 "	9.9
6	16 "	250 "	0.5 "	11.7
7	14 "	230 "	0.5 "	14.6
8	12.5 "	225 "	0.3 "	not examined.
9	11.0 "	210 "	0.3 "	14.4
10	10.5 "	190 "	0.3 "	14.2
11	9.0 "	170 "	0.4 "	14.6
12	7.0 "	(gave an acid with $[\alpha]_D + 14.5^\circ$).		

* The influence of temperature on the rotatory power between 12° and 33° was found to be very slight.

A portion of the acid with $[\alpha]_D + 14.5^\circ$ was converted into the calcium salt, from the aqueous solution of which two separate fractions of crystals were withdrawn; the acids obtained from these fractions gave in each case the value $[\alpha]_D + 14.4^\circ$.

Since the pure acid does not have a sharp melting point, tends to separate as an oil from aqueous alcohol, and does not crystallise readily from other solvents, some such proof of its homogeneity as that just given was rendered necessary. It may also be added that the separation of the pure *d*-acid by crystallising a mixture of it and the *r*-acid from aqueous alcohol is not practical, even when the proportion of the *r*-acid present is small.

For the preparation of the *l*-acid, the various amounts of the levorotatory acid mixture, obtained from the mother liquors of the first crystallisations during the isolation of the *d*-acid by cinchonidine, were united, dissolved in alcohol, and combined with quinine. The separation of the pure quinine *l*-salt is not, however, accomplished readily. Thus 34.8 grams of the levorotatory acid

mixture were dissolved in 170 c.c. of ethyl alcohol and combined with 24.7 grams of quinine. Fine needles (35 grams) separated on cooling, and a portion on decomposition with mineral acid gave an acid with $[\alpha]_D - 8.3^\circ$ in acetone. Nevertheless, even after ten crystallisations the pure quinine *l*-salt was not obtained, since the acid resulting from the crystals (10 grams) had only $[\alpha]_D - 11.5^\circ$, a value which is about 3° too low. A better result was obtained in another experiment, where 121 grams of a levorotatory acid mixture were combined with 86 grams of quinine. After seven crystallisations from alcohol, the salt amounted to 47 grams, whilst the acid obtained from it had $[\alpha]_D - 13.9^\circ$ in acetone, and was therefore almost pure.

The difficulty in preparing the *l*-acid is to be attributed in all probability to the formation of mixed crystals of the quinine salts of the enantiomorphously related acids. The separation of such a product must necessarily be tedious; compare, for example, Schütz and Marckwald (*Ber.*, 1896, **29**, 52) on the resolution of *dl*-valeric acid, and Perkin, Pope, and Wallach (*T.*, 1909, **95**, 1789) on the resolution of 1-methylcyclohexylidene-4-acetic acid.

Action of Aqueous Potassium Hydroxide on the d-Acid.

1.7238 Grams of *d*-phenyl-*p*-tolylacetic acid were heated at 100° for one hour with 34 c.c. of aqueous potassium hydroxide, the amount of alkali present being twice that necessary for neutralisation. The acid was then recovered, and was found to have undergone partial racemisation; it melted indefinitely, and gave the following value in acetone:

$$l=2, c=5.591, \alpha_D + 1.02^\circ, [\alpha]_D + 9.1^\circ.$$

Activation of the r-Acid by Fractional Esterification.

Five grams of the *r*-acid (1 mol.) were heated with 3.45 grams of *l*-menthol (1 mol.) for three hours at 150° . The product was manipulated as described by Marckwald and McKenzie (*Ber.*, 1899, **32**, 2130) in connexion with the esterification of mandelic acid with menthol. 3.4 Grams of unesterified acid were recovered, and this was slightly dextrorotatory, a solution of 1.75 grams made up to 10 c.c. with acetone giving $\alpha_D + 0.11^\circ$ in a 2-dcm. tube. Very little esterification had, however, taken place, since only 0.25 gram of acid (inactive) was recovered by saponifying the esters formed.

A more decided effect was attained by esterifying 10 grams of the *r*-acid with an excess of menthol (30 grams) in the presence of 3 grams of sulphuric acid, the mixture being heated at 100° for four hours. The unesterified acid amounted in this case to

2.1 grams; 0.64 gram of it, when made up to 25 c.c. with acetone, gave $\alpha_D + 0.19^\circ$ in a 4-dm. tube. It appeared, therefore, that *l*-phenyl-*p*-tolylacetic acid is esterified by *l*-menthol slightly more quickly than is the *d*-isomeride. The ester mixture, obtained after the removal of the unesterified acid and the excess of menthol, amounted to about 8 grams, and consisted of *l*-menthyl *d*-ester and *l*-menthyl *l*-ester, the latter being slightly in excess. The saponification was conducted by dissolving the oil in 180 c.c. of alcoholic potassium hydroxide containing twice the calculated amount of alkali, and allowing to remain at the ordinary temperature for one and a-half days. 3.5 Grams of acid were recovered, and it was optically inactive. Accordingly, since the mixture of esters mentioned above did not, when saponified, give a levorotatory acid, complete racemisation had taken place during the process of saponification. The individual esters were subsequently prepared, and their behaviour towards alkali examined.

Action of Alkali on the Menthyl Esters.

By means of thionyl chloride, *r*-phenyl-*p*-tolylacetic acid was converted into its acid chloride, which was then acted on by menthol in the presence of benzene and pyridine. Yield of ester, 75 per cent.

l-Menthyl *r*-phenyl-*p*-tolylacetate boils at $250^\circ/12$ mm. It was blue when freshly distilled, but the colour disappeared gradually. The oil solidifies slowly. The solid ester melts at $54-55^\circ$, and separates from aqueous alcohol in rectangular crystals. Its rotatory power was unaltered when it was crystallised from aqueous alcohol. Apparently it was partially racemic, and did not undergo resolution into its diastereoisomerides under the temperature conditions employed in its crystallisation from aqueous alcohol:

0.2921 gave 0.8836 CO_2 and 0.2296 H_2O . $\text{C}=82.5$; $\text{H}=8.8$.

$\text{C}_{25}\text{H}_{32}\text{O}_2$ requires $\text{C}=82.4$; $\text{H}=8.9$ per cent.

The determination of the specific rotation was made in acetone: $l=2$, $c=5.625$, $\alpha_D^{15.8} - 6.66^\circ$, $[\alpha]_D^{15.8} - 59.2^\circ$. On submitting 12 grams of this ester to fractional saponification, three different fractions of acid were obtained, and these were all feebly levorotatory.

l-Menthyl *d*-phenyl-*p*-tolylacetate, prepared from *d*-phenyl-*p*-tolylacetyl chloride, separates from aqueous alcohol in feathery needles and melts at $53-54^\circ$:

0.1988 gave 0.6000 CO_2 and 0.1530 H_2O . $\text{C}=82.3$; $\text{H}=8.6$.

$\text{C}_{25}\text{H}_{32}\text{O}_2$ requires $\text{C}=82.4$; $\text{H}=8.9$ per cent.

In acetone solution:

$l=2$, $c=5.746$, $\alpha_D^{14} - 6.09^\circ$, $[\alpha]_D^{14} - 53.0^\circ$.

Four grams of this ester were boiled for one hour and twenty minutes with 100 c.c. of alcoholic potassium hydroxide containing slightly more than the quantity of alkali required for complete saponification. The alcohol was distilled off, and the residue submitted to distillation in steam in order to separate the free menthol, and then extracted with ether to remove unsaponified ester. The acid (0.8 gram), isolated from the potassium salt, exhibited no optical activity. Bearing in mind the slowness with which the esterification of the *r*-acid by direct heating with menthol occurred, it was not surprising that the saponification of the ester was also a slow process, and was, on this account, incomplete when conducted under the conditions quoted; in fact, no less than 2.2 grams of unsaponified ester were recovered. The value for the rotatory power of this latter product was $[\alpha]_D -54.7^\circ$ in acetone, a result perhaps not devoid of significance, indicating as it does that the ester is in part catalytically racemised by alkali prior to its undergoing saponification. This unsaponified ester was next boiled for one and a-half hours with 100 c.c. of alcoholic potassium hydroxide containing slightly more alkali than the amount requisite for complete saponification. The acid (0.3 gram) obtained from the potassium salt was practically inactive; when made up to 10 c.c. with acetone it gave $\alpha_D +0.06^\circ$ in a 2-dcm. tube. The residual ester (1.2 grams) was heated as before with alcoholic potassium hydroxide, and the resulting acid was inactive.

l-Menthyl *l*-phenyl-*p*-tolylacetate, prepared from *l*-phenyl-*p*-tolylacetyl chloride, melts at 57—58°. It was crystallised from aqueous alcohol:

0.1863 gave 0.5615 CO₂ and 0.1441 H₂O. C=82.2; H=8.7.

C₂₅H₃₂O₂ requires C=82.4; H=8.9 per cent.

The *r*-acid was obtained by the saponification of this ester.

Action of Alkali on the Bornyl Esters.

l-Bornyl *dl*-phenyl-*p*-tolylacetate, prepared by the action of *l*-borneol on *dl*-phenyl-*p*-tolylacetyl chloride in the presence of benzene and pyridine, is an oil which boils at 249°/12 mm. When freshly distilled, it had a bright blue colour:

0.2460 gave 0.7456 CO₂ and 0.1814 H₂O. C=82.7; H=8.3.

C₂₅H₃₀O₂ requires C=82.8; H=8.3 per cent.

This ester was submitted to fractional saponification, and the specimens of acid obtained were optically inactive.

l-Bornyl *dl*-phenyl-*p*-tolylacetate is an oil, which boils at 240°/13 mm.:

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0.2394 gave 0.7270 CO_2 and 0.1764 H_2O . $\text{C}=82.8$; $\text{H}=8.2$.

$\text{C}_{25}\text{H}_{30}\text{O}_2$ requires $\text{C}=82.8$; $\text{H}=8.3$ per cent.

3.6 Grams of this ester were heated for one and a-quarter hours with 100 c.c. of alcoholic potassium hydroxide containing slightly more than the calculated quantity of alkali. 0.5 Gram of ester escaped saponification, whilst the recovered acid was optically inactive. When the saponification was conducted at the ordinary temperature during seven days, the recovered acid was only slightly dextrorotatory, having $[\alpha]_{\text{D}} +0.9^\circ$ in acetone.

Action of Alkali on the Ethyl d-Ester.

Ethyl d-phenyl-p-tolylacetate, prepared by esterifying the *d*-acid with ethyl alcohol and hydrogen chloride, separates from aqueous alcohol in feathery needles, and melts at $39-40^\circ$, whereas the inactive isomeride melts at 34° (Zincke, *loc. cit.*). It dissolves readily in the commoner organic solvents:

0.1900 gave 0.5590 CO_2 and 0.1256 H_2O . $\text{C}=80.2$; $\text{H}=7.4$.

$\text{C}_{17}\text{H}_{18}\text{O}_2$ requires $\text{C}=80.3$; $\text{H}=7.1$ per cent.

In acetone solution:

$l=2$, $c=8.231$, $\alpha_{\text{D}}^{15} +1.71^\circ$, $[\alpha]_{\text{D}}^{15} +10.4^\circ$.

2.5 Grams were heated for one hour with 50 c.c. of alcoholic potassium hydroxide, containing alkali in an amount just exceeding that necessary for complete saponification. The acid recovered was optically inactive when examined in acetone solution.

Conversion of the d-Acid into r-Phenyl-p-tolylacetophenone.

Ten grams of *r*-phenyl-*p*-tolylacetic acid were converted into the acid chloride by means of thionyl chloride. A solution of this acid chloride in carbon disulphide was added gradually to a mixture of 9 grams of aluminium chloride, 44 grams of benzene, and 18 grams of carbon disulphide, the action being conducted under diminished pressure for about one hour. After two days at the ordinary temperature, water and then dilute hydrochloric acid were added, and the benzene and carbon disulphide removed by steam. The residue was extracted with ether. When the ethereal solution was allowed to evaporate spontaneously, 1.4 grams of solid separated from an oil, and, on crystallising this from a mixture of benzene and light petroleum, 1 gram was obtained.

r-Phenyl-p-tolylacetophenone, $\text{C}_7\text{H}_7\cdot\text{CHPh}\cdot\text{COPh}$, separates from a mixture of benzene and light petroleum in hexagonal plates, and melts at $159-160^\circ$:

0.1258 gave 0.4058 CO_2 and 0.0696 H_2O . $\text{C}=88.0$; $\text{H}=6.2$.

$\text{C}_{21}\text{H}_{18}\text{O}$ requires $\text{C}=88.1$; $\text{H}=6.3$ per cent.

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On distilling the oil from which this solid had been withdrawn, a fraction was obtained which boiled at $120^{\circ}/15$ mm.; it separates from aqueous alcohol in transparent crystals, and melts at $28-29^{\circ}$.

Ten grams of the *d*-acid were submitted to the Friedel and Crafts' reaction, the conditions being similar to those just described. 1.4 Grams of crude ketone were obtained. This amount was crystallised from a mixture of benzene and light petroleum. The product was the racemic ketone, no optical activity being observed with its ethyl-alcoholic solution.

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[Received, April 8th, 1915.]
