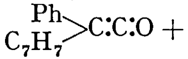
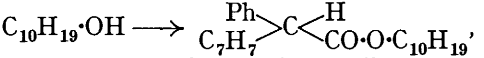
225. *The Action of Optically Active Alcohols on Ketens.*

By Alex. McKenzie and Edwin W. Christie.

Under the title " Ein Beitrag zur Frage der asymmetrischen Synthese," Weiss (*Monatsh.*, 1919, **40**, 301) describes the action of (—)menthol on phenyl-*p*-tolylketen,  $\overset{Ph}{\underset{C_7H_7}{}}\!\!>C{:}C{:}O$ +  $C_{10}H_{19}{\cdot}OH \longrightarrow \overset{Ph}{\underset{C_7H_7}{}}\!\!>C<\overset{H}{\underset{CO{\cdot}O{\cdot}C_{10}H_{19}}{}}$, where a new asymmetric atom is generated. The selection of phenyl-*p*-tolylketen was made because the (—)menthyl esters of the isomeric phenyl-*p*-tolylacetic acids had previously been investigated (McKenzie and Widdows, J., 1915, **107**, 702).

Weiss obtained a yellow syrup, b. p. 190—196°/1 mm., $[\alpha]_D$ — 45·4° in acetone. It could not be induced to crystallise, and gave on analysis C, 82·73; H, 8·11 (calc. for $C_{25}H_{32}O_2$: C, 82·36; H, 8·85%).

McKenzie and Widdows had already described (—)menthyl (+)phenyl-*p*-tolylacetate (I) as feathery needles, m. p. 53—54°, giving in acetone $[\alpha]_D^{14°}$ — 53·0°.

The discrepancy between the values for the specific rotatory power led Weiss to the following conclusions : (1) the action of (—)menthol on phenyl-*p*-tolylketen proceeds one-sidedly, the yellow syrup being optically pure (—)menthyl (+)phenyl-*p*-tolylacetate (I); (2) the action presents an example of asymmetric synthesis; (3) the crystalline ester of McKenzie and Widdows had obviously undergone partial racemisation, and was accordingly optically impure.

The experimental evidence which Weiss has submitted in support of those claims is far too slender to carry conviction, but he himself does not appear to have prosecuted any further experiments on his ingenious topic. Since the study of asymmetric synthesis, more particularly in its relationship to asymmetric induction, had been resumed by one of us and his colleagues within recent years, we have now extended the former observations on the (—)menthyl esters of *r*-, (+) and (—)phenyl-*p*-tolylacetic acids. The data recorded by McKenzie and Widdows for (I) were confirmed. Weiss's contention that the ester of McKenzie and Widdows was optically impure is incorrect. The diastereoisomeric (—)menthyl (—)phenyl-*p*-tolylacetate (II) had m. p. 57·5—58° and gave $[\alpha]_D^{21°}$ — 58·0° in acetone. The m. p. given by McKenzie and Widdows was 57—58°, but they did not record the rotatory power.

It is possible to distil (II) under diminished pressure without causing its rotatory power to be impaired.

(—)*Menthyl* dl-*phenyl*-p-*tolylacetate* (III) was obtained as a solid, m. p. 33—34°, by mixing equal amounts of the diastereoisomerides (I) and (II) in acetone. Its specific rotatory powers for λ 5893 and λ 5461 in acetone are in agreement with those calculated from the figures for (I) and (II) on the basis of the principle of optical superposition : thus, $[\alpha]_D$ found, − 55·5° (calc. − 55·5°); $[\alpha]_{5461}$ found, − 65·8° (calc. − 65·75°). There is no dubiety regarding the optical purity of these three esters.

(III) is resolvable into its diastereoisomerides (I) and (II) by several crystallisations from aqueous alcohol, optically pure (II) being obtained as the more sparingly soluble of the two esters.

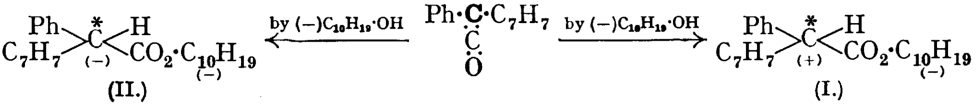
The product of McKenzie and Widdows from the action of (—)menthol on *dl*-phenyl-*p*-tolylacetyl chloride was obtained by them at first as an oil. This gradually solidified, and the solid ester, m. p. 54—55°, $[\alpha]_D$ − 59·2° in acetone, is designated by them as (—)menthyl *r*-phenyl-*p*-tolylacetate. The possibility of resolution into diastereoisomerides was recognised at the time, but the conclusion drawn that the ester is partially racemic is wrong, as we now find; resolution had actually occurred during the manipulation, but McKenzie and Widdows had missed detecting this. The original laboratory record of Miss Widdows states that the crude oil had solidified slowly on keeping for several weeks and that the solid had been separated from the adhering oil by draining the latter on a porous plate. This solid after one crystallisation from alcohol actually consisted of nearly pure (II), and was practically unchanged in rotatory power after crystallisation. This mistake made by McKenzie and Widdows is easily understood; the resolution of a *dl*-ester from an oil without the use of a solvent is an unusual phenomenon.

Following the experimental procedure described by Weiss, we then carried out the action of (—)menthol on phenyl-*p*-tolylketen. The keten was prepared on Staudinger's lines from *dl*-phenyl-*p*-tolylchloroacetyl chloride, which is obtained from *r*-phenyl-*p*-tolylglycollic acid, a convenient method for preparing this acid being described. The product from the synthesis with the keten was (III), and there was no evidence to support the contention of Weiss that the action had proceeded one-sidedly with the formation of (I). The oil obtained by Weiss was clearly insufficiently purified, and was doubtless contaminated with some by-product from the keten synthesis. Similarly, when (—)borneol was used in place of (—)menthol, (—)bornyl *dl*-phenyl-*p*-tolylacetate was obtained as an oil, which was identical with the compound prepared from the interaction of (—)borneol and *dl*-phenyl-*p*-tolylacetyl chloride.

Even if Weiss had been successful in proving that the action of (—)menthol on phenyl-*p*-tolylketen had proceeded one-sidedly with the formation of (I), such an action would not constitute a true asymmetric synthesis. In the experience of Weiss the acid resulting from the saponification of his oil was devoid of optical activity; it consisted of *r*-phenyl-*p*-tolylacetic acid. Had the oil consisted of (I), the same result would have been arrived at, since McKenzie and Widdows had shown that (I) is particularly susceptible to racemisation with alcoholic alkali. It seems necessary to emphasise the point that an asymmetric synthesis was not experimentally realised, inasmuch as this erroneous claim had been accepted by others. Thus, *inter alia*, in the *Ann. Reports*, 1920, **17**, 74, the reviewer states with reference to the action in question " This represents one of the simplest and least unexceptionable examples of asymmetric synthesis which has been placed on record." Unfortunately, the error is not only repeated but accentuated in statements made in three recent text-books, namely, those of Wittig (" Stereochemie," 1930, p. 40), of Freudenberg [" Stereochemie," 1932 (Section by Ebel, p. 582)], and of Goldschmidt (" Stereochemie," 1933, p. 29), where each of these authors reports that Weiss had actually obtained an optically active phenyl-*p*-tolylacetic acid from the keten synthesis, a claim which was never made even by Weiss himself.

A tentative criticism of the research of Weiss is submitted by P. D. Ritchie in his recent comprehensive monograph on " Asymmetric Synthesis and Asymmetric Induction " (*St.*

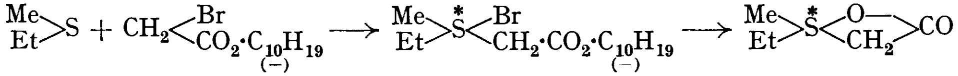
Andrews University Publication XXXVI, Oxford University Press, 1933). On theoretical grounds it is suggested by Ritchie that it is rather unlikely that the action could in reality have taken place one-sidedly. In the scheme



$$\underset{\text{(II.)}}{\begin{matrix}\text{Ph}\\ \text{C}_7\text{H}_7\end{matrix}\!>\!\overset{*}{\underset{(-)}{\text{C}}}\!<\!\begin{matrix}\text{H}\\ \text{CO}_2\cdot\underset{(-)}{\text{C}_{10}\text{H}_{19}}\end{matrix}} \xleftarrow{\text{by }(-)\text{C}_{10}\text{H}_{19}\cdot\text{OH}} \begin{matrix}\text{Ph}\cdot\textbf{C}\cdot\text{C}_7\text{H}_7\\ \text{C}\\ \text{O}\end{matrix} \xrightarrow{\text{by }(-)\text{C}_{10}\text{H}_{19}\cdot\text{OH}} \underset{\text{(I.)}}{\begin{matrix}\text{Ph}\\ \text{C}_7\text{H}_7\end{matrix}\!>\!\overset{*}{\underset{(+)}{\text{C}}}\!<\!\begin{matrix}\text{H}\\ \text{CO}_2\cdot\underset{(-)}{\text{C}_{10}\text{H}_{19}}\end{matrix}}$$

the carbon atom **C** is contained in a molecule which does not assume a disymmetrical environment until the combination with (—)menthol has actually occurred. There would thus appear to be no obvious reason why the additive reaction should favour the formation of either (I) or (II) at the expense of the other. The case is different from that investigated by Marckwald and McKenzie (*Ber.*, 1901, **34**, 469) where two diastereoisomeric esters were formed at different rates when *r*-mandelic acid was esterified by (—)menthol. Here, mandelic acid had an asymmetric carbon atom *before* combination with menthol took place. A comparison of Weiss's reaction with McKenzie's asymmetric syntheses from optically active α-ketonic esters reveals one significant difference. In the latter experiments the atom **C** which is to be rendered asymmetric is actually already a portion of a dissymmetric molecule, R·**C**O·CO·OR*; it is therefore under the directing or " inducing " influence of the optically active radical R* *before* it is itself transformed into a fixed asymmetric centre by the action either of Grignard agents or of reducing agents.

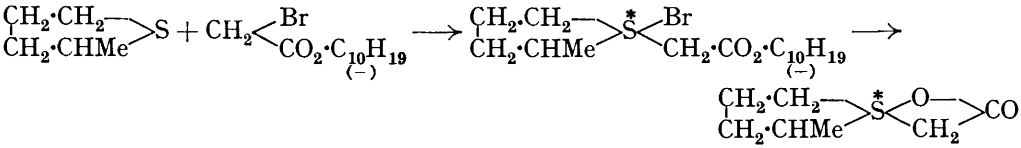
Further, Ritchie has attributed the failure of Smiles (J., 1905, **87**, 450) to effect an asymmetric synthesis of a quadrivalent sulphur compound to a similar cause. Smiles acted on methyl ethyl sulphide with (—)menthyl bromoacetate, and found that an optically inactive thetine was formed when the additive compound was saponified and the menthol removed:



$$\begin{matrix}\text{Me}\\ \text{Et}\end{matrix}\!>\!\text{S} + \text{CH}_2\!<\!\begin{matrix}\text{Br}\\ \text{CO}_2\cdot\underset{(-)}{\text{C}_{10}\text{H}_{19}}\end{matrix} \longrightarrow \begin{matrix}\text{Me}\\ \text{Et}\end{matrix}\!>\!\overset{*}{\text{S}}\!<\!\begin{matrix}\text{Br}\\ \text{CH}_2\cdot\text{CO}_2\cdot\underset{(-)}{\text{C}_{10}\text{H}_{19}}\end{matrix} \longrightarrow \begin{matrix}\text{Me}\\ \text{Et}\end{matrix}\!>\!\overset{*}{\text{S}}\!<\!\begin{matrix}\text{O}—\\ \text{CH}_2\end{matrix}\!>\!\text{CO}$$

(optically inactive)

A similar result was obtained recently by Menon and Guha (*Ber.*, 1931, **64**, 544) on the lines:



$$\begin{matrix}\text{CH}_2\cdot\text{CH}_2—\\ \text{CH}_2\cdot\text{CHMe}\end{matrix}\!>\!\text{S} + \text{CH}_2\!<\!\begin{matrix}\text{Br}\\ \text{CO}_2\cdot\underset{(-)}{\text{C}_{10}\text{H}_{19}}\end{matrix} \longrightarrow \begin{matrix}\text{CH}_2\cdot\text{CH}_2—\\ \text{CH}_2\cdot\text{CHMe}\end{matrix}\!>\!\overset{*}{\text{S}}\!<\!\begin{matrix}\text{Br}\\ \text{CH}_2\cdot\text{CO}_2\cdot\underset{(-)}{\text{C}_{10}\text{H}_{19}}\end{matrix} \longrightarrow \begin{matrix}\text{CH}_2\cdot\text{CH}_2—\\ \text{CH}_2\cdot\text{CHMe}\end{matrix}\!>\!\overset{*}{\text{S}}\!<\!\begin{matrix}\text{O}—\\ \text{CH}_2\end{matrix}\!>\!\text{CO}$$

(optically inactive)

Finally, Weiss's choice of an *aromatic* keten was in our opinion unfortunate. A conclusive proof that the action had proceeded either totally one-sidedly or at least partially so, would have been supplied by the isolation of a substituted acetic acid in an optically active state. Such a proof is practically excluded when phenyl-*p*-tolylketen is chosen, since the esters of the optically active phenyl-*p*-tolylacetic acids undergo racemisation on saponification with alcoholic alkali, containing as they do two *aromatic* groups attached to the asymmetric carbon atom and at the same time there is a hydrogen atom in the α-position to the $-\text{CO}_2\cdot\text{C}_{10}\text{H}_{19}$ group.

In an attempt to settle the point Dr. P. D. Ritchie in this laboratory acted on methylethylketen with (—)menthol. The crude (—)menthyl α-methyl-*n*-butyrate obtained gave *optically inactive* α-methyl-*n*-butyric acid when saponified by alcoholic potash. Now, if the (—)menthyl ester either of the (+) or of the (—)acid had been formed exclusively in the synthesis from the keten, or if a mixture of the two menthyl esters in unequal quantities had been formed, the effect of saponification would still have been to give an optically active acid in either of these cases, since, although in $\begin{matrix}\text{Me}\\ \text{Et}\end{matrix}\!>\!\overset{*}{\text{C}}\!<\!\begin{matrix}\text{H}\\ \text{CO}_2\cdot\text{C}_{10}\text{H}_{19}\end{matrix}$ there is a hydrogen atom in the α-position to the $-\text{CO}_2\cdot\text{C}_{10}\text{H}_{19}$ group, there are two *aliphatic* groups attached to the asymmetric carbon atom, and such a system, as is known from the work of one of us on catalytic racemisation, undergoes no racemisation under the influence of alcoholic alkali. It appears, therefore, that this reaction produced the (−)menthyl (+)ester and the (−)menthyl (−)ester in equal quantities. It was not found possible to purify completely the crude ester from the additive reaction by repeated distillation (prior to saponification) owing to the presence of by-products. But on one occasion an almost pure specimen with about 96% of the optical activity of the (−)menthyl ester of optically inactive α-methyl-*n*-butyric acid was obtained.

In the three examples, therefore, which have been studied where a keten is acted on by an optically active alcohol, the evidence points to the formation of the ester of the *dl*-acid in each case. With these results before us, the suggestion made by Ritchie in his criticism of Weiss's work receives some confirmation.

Experimental.

r-*Phenyl*-p-*tolylacetyl Chloride.*—The chloride used in previous work by McKenzie and Widdows (*loc. cit.*) and by McKenzie, Roger, and McKay (J., 1932 2597) was an oil, which has now been obtained crystalline. 20 G. of *r*-phenyl-*p*-tolylacetic acid (1 mol.) were warmed for 2 hours with 32 g. of thionyl chloride (3 mols.), purified by dimethylaniline (Besthorn, *Ber.*, **1909, 42,** 269). The excess of thionyl chloride was removed under diminished pressure at the ordinary temperature, and the resulting brownish oil was kept under diminished pressure over soda–lime for 2 days. The solid which had separated was removed from the adhering oil and crystallised from light petroleum (b. p. 60—80°), yielding 7 g. of *r*-phenyl-*p*-tolylacetyl chloride in hexagonal prisms, m. p. 74—75° (Found : Cl, 14·5. Calc. for $C_{15}H_{13}OCl$: Cl, 14·5%).

(−)*Menthyl* (+)*Phenyl*-p-*tolylacetate* (I).—The preparation of this ester from (+)phenyl-*p*-tolylacetic acid obtained by the resolution of the *r*-acid with cinchonidine was repeated. After three crystallisations of the crude ester from aqueous alcohol, (−)menthyl (+)phenyl-*p*-tolylacetate was obtained as rosettes of feathery needles, m. p. 52—53°, and its rotatory power was determined in acetone ($l = 2$, $c = 5·0445$) : $\alpha_{\mathrm{D}}^{20^\circ}$ −5·35°, $[\alpha]_{\mathrm{D}}^{20^\circ}$ − 53·0°; $\alpha_{5461}^{20^\circ}$ − 6·33°, $[\alpha]_{5461}^{20^\circ}$ − 62·7°. McKenzie and Widdows give $[\alpha]_{\mathrm{D}}^{14^\circ}$ − 53·0° for $c = 5·746$, the m. p. recorded being 53—54°. The influence of temperature on the rotatory power of its solution in acetone is only very slight within the range 2—33°. In carbon disulphide ($l = 2$, $c = 4·5425$) : $\alpha_{\mathrm{D}}^{20^\circ}$ − 3·98°, $[\alpha]_{\mathrm{D}}^{20^\circ}$ − 43·8°; $\alpha_{5461}^{20^\circ}$ − 4·71°, $[\alpha]_{5461}^{20^\circ}$ − 51·8°. In ethyl alcohol ($l = 2$, $c = 4·251$) : $\alpha_{\mathrm{D}}^{20·5^\circ}$ − 5·72°, $[\alpha]_{\mathrm{D}}^{20·5^\circ}$ −67·3°; $\alpha_{5461}^{20·5^\circ}$ −6·74°, $[\alpha]_{5461}^{20·5^\circ}$ − 79·3°.

(−)*Menthyl* (−)*Phenyl*-p-*tolylacetate* (II).—(−)Phenyl-*p*-tolylacetic acid was prepared by the resolution of the *r*-acid with quinine. The crude ester was crystallised twice from rectified spirit, from which it separated in long hexagonal prisms, m. p. 57·5—58°, whereas McKenzie and Widdows give 57—58°. In acetone ($l = 2$, $c = 5·1915$) : $\alpha_{\mathrm{D}}^{21^\circ}$ −6·02°, $[\alpha]_{\mathrm{D}}^{21^\circ}$ − 58·0°; $\alpha_{5461}^{21^\circ}$ − 7·14°, $[\alpha]_{5461}^{21^\circ}$ −68·8°. In carbon disulphide ($l = 2$, $c = 4·487$) : $\alpha_{\mathrm{D}}^{20^\circ}$ − 4·61°, $[\alpha]_{\mathrm{D}}^{20^\circ}$ − 51·4°; $\alpha_{5461}^{20^\circ}$ − 5·46°, $[\alpha]_{5461}^{20^\circ}$ − 60·8°. In ethyl alcohol ($l = 2$, $c = 5·323$) : $\alpha_{\mathrm{D}}^{20^\circ}$ − 7·36°, $[\alpha]_{\mathrm{D}}^{20^\circ}$ − 69·1°; $\alpha_{5461}^{20^\circ}$ − 8·76°, $[\alpha]_{5461}^{20^\circ}$ − 82·3°.

The rotatory power is not recorded by McKenzie and Widdows, but the following details are available from the laboratory record of Miss Widdows. In acetone ($l = 2$, $c = 4·716$) : α_{D} − 5·45°, $[\alpha]_{\mathrm{D}}$ − 57·9°, a value practically identical with that just recorded.

A specimen was distilled at 210—212°/4 mm.; the colourless distillate began to solidify very quickly, and the m. p. and rotatory power were unaltered.

Since, like its diastereoisomeride, it is very susceptible towards traces of alcoholic potash, which cause asymmetric catalytic racemisation, the importance of taking the necessary precautions during the preparation of these esters is emphasised. Thus, when two drops of alcoholic potash (0·841*N*) were added to a solution of the ester (II) in ethyl alcohol which gave $[\alpha]_{5461}^{20^\circ}$ − 82·6° ($c = 5·323$), the activity fell from $\alpha_{5461}^{20^\circ}$ − 8·80° to − 8·48° after 68 hours, whence $[\alpha]_{5461}^{20^\circ}$ − 79·6°. Some transformation into the isomeric ester had occurred. The product after removal of the solvent melted indefinitely between 33° and 54°. It had a distinct odour of menthol, so that " Umesterung " had occurred, as well as asymmetric catalytic racemisation.

When (I) was treated similarly, the observed rotation increased from $\alpha_{5461}^{20^\circ}$ − 6·72° to $\alpha_{5461}^{20^\circ}$ − 6·98° ($c = 4·2510$). The product consisted mainly of (III), the m. p. being 30—34°, and the odour of menthol was again detected.

Formation of (−)*Menthyl* dl-*Phenyl*-p-*tolylacetate* (III) *from its Diastereoisomerides.*—A mixture of 0·4828 g. of (I) with an equal weight of (II) was made up to 20 c.c. with acetone, and the rotation determined ($l = 2$, $c = 4{\cdot}828$) : $\alpha_{\mathrm{D}}^{21\cdot5^\circ} - 5{\cdot}36^\circ$, $[\alpha]_{\mathrm{D}}^{21\cdot5^\circ} - 55{\cdot}5^\circ$; $\alpha_{5461}^{21\cdot5^\circ} - 6{\cdot}35^\circ$, $[\alpha]_{5461}^{21\cdot5^\circ} - 65{\cdot}8^\circ$. The solvent was then removed under diminished pressure at the ordinary temperature; the oil solidified in the course of several days. (—)Menthyl *dl*-phenyl-*p*-tolylacetate (III) forms clusters of radiating needles, m. p. 33—34°.

This ester was also obtained by esterifying *r*-phenyl-*p*-tolylacetic acid by heating with (—)menthol for 12 hours on the steam-bath in the presence of hydrogen chloride. By fractionation of the crude product, an oil with $[\alpha]_{\mathrm{D}}^{20^\circ} - 55{\cdot}5^\circ$ and $[\alpha]_{5461}^{20^\circ} - 66{\cdot}4^\circ$ ($c = 5{\cdot}6$) in acetone was obtained. These values agree with those just recorded.

The Resolution of (—)Menthyl dl-*Phenyl*-p-*tolylacetate* (III).—The preceding oil gradually solidified. The product showed signs that it had undergone resolution, since, when it was crystallised from aqueous alcohol, the value after three crystallisations rose to $[\alpha]_{\mathrm{D}} - 57{\cdot}5^\circ$ ($c = 1{\cdot}383$).

A solution of 23 g. of *r*-phenyl-*p*-tolylacetyl chloride (1 mol.) in benzene was added gradually to a solution of a mixture of 14·7 g. of (—)menthol (1 mol.) and 11·1 g. of pyridine (1·5 mols.) in benzene. A white solid separated, which was possibly an addition compound of the acid chloride and pyridine (cf. McKenzie and Gow, J., 1933, 705). The mixture was boiled for 1 hour and distilled in steam, the residue extracted with ether, the ethereal solution shaken with aqueous sodium bicarbonate to remove phenyl-*p*-tolylacetic acid, the ether expelled from the dried solution, and the oil distilled under diminished pressure, giving a blue ester. The fraction, b. p. 240—245°/12 mm., crystallised from aqueous alcohol in colourless feathery needles, m. p. 30—32°. On several crystallisations from aqueous alcohol, the m. p. of successive crops gradually rose, as also did the rotatory power. After four crystallisations, the ester had $[\alpha]_{\mathrm{D}}^{20^\circ} - 58{\cdot}6^\circ$ and $[\alpha]_{5461}^{20^\circ} - 68{\cdot}9^\circ$ for $c = 0{\cdot}6315$ in acetone, and after one additional crystallisation the m. p. was 57—58°, alone or mixed with an authentic specimen of (II).

r-*Phenyl*-p-*tolylglycollic Acid*.—In preference to Weiss's method (*loc. cit.*) we adopted the following : *r*-Mandelic acid was converted into benzoylformic acid by oxidation with alkaline permanganate. The Grignard reagent prepared from 104 g. of *p*-bromotoluene (3 mols.) was added with mechanical stirring within an interval of 3 hours to an ethereal solution of 30 g. of benzoylformic acid (1 mol.). A bulky yellow solid, which gradually assumed a reddish tint, separated. After 3 hours' boiling, and decomposition of the additive complex with ice and dilute sulphuric acid, the product from the ethereal layer was distilled in steam to remove *p*-ditolyl, and the hot aqueous layer was decanted from the undissolved residue. On cooling, colourless needles of *r*-phenyl-*p*-tolylglycollic acid separated, and additional quantities were obtained by passing steam several times over the semi-solid residue and decanting the aqueous extracts. The various crops were united and crystallised from water. Yield, 27 g. The acid tends to separate from glacial acetic acid as an oil, but may be crystallised as rosettes of needles from light petroleum (b. p. 80—100°)-acetone. It gave a blood-red coloration when dissolved in concentrated sulphuric acid, and after drying in a vacuum at 85° it had m. p. 133—134°, whereas Weiss gives 131—133°. The acid may also be prepared from ethyl benzoylformate, but this method does not appear to present any advantage over that described.

Interaction of Phenyl-p-*tolylketen and (—)Menthol*.—An ethereal solution of *dl*-phenyl-*p*-tolylchloroacetyl chloride (14 g., prepared from phosphorus pentachloride and *r*-phenyl-*p*-tolylglycollic acid) was acted on by zinc turnings (4·9 g.) under the conditions described by Weiss. An ethereal solution of (—)menthol was added to the ethereal solution of phenyl-*p*-tolylketen, the yellow colour of which persisted after 24 hours. The mixture was shaken with water, the ether expelled, and the unattacked menthol removed by distillation in steam. The residue was extracted with ether, and the ethereal solution shaken with aqueous potassium bicarbonate to remove the phenyl-*p*-tolylacetic acid formed by the action of water on unchanged keten. The ethereal solution was dried, the ether expelled, and the resulting brownish oil kept in a vacuum for 3 days. In acetone : $[\alpha]_{\mathrm{D}}^{20^\circ} - 46{\cdot}8^\circ$ ($c = 6{\cdot}3155$), whereas the product obtained by Weiss gave at the corresponding stage $[\alpha]_{\mathrm{D}}^{20^\circ} - 45{\cdot}37^\circ$ ($c = 8{\cdot}044$) in acetone. This impure ester with $[\alpha]_{\mathrm{D}}^{20^\circ} - 46{\cdot}8^\circ$ was distilled under diminished pressure three times, and a fraction, b. p. 195—203°/4 mm., was collected as a colourless oil, which solidified after several weeks. After one crystallisation from aqueous alcohol, feathery needles, m. p. 33—34°, were obtained (Found : C, 82·2; H, 8·9. $C_{25}H_{32}O_2$ requires C, 82·4; H, 8·9%). This ester was (—)*menthyl* dl-*phenyl*-p-*tolylacetate* (III). When mixed with the synthetic ester already described, there was no depression of the melting point. In acetone ($l = 2$, $c = 2{\cdot}3835$) : $\alpha_{\mathrm{D}}^{20\cdot5^\circ} - 2{\cdot}65^\circ$, $[\alpha]_{\mathrm{D}}^{20\cdot5^\circ} - 55{\cdot}6^\circ$; $\alpha_{5461}^{20\cdot5^\circ} - 3{\cdot}13^\circ$, $[\alpha]_{5461}^{20\cdot5^\circ} - 65{\cdot}7^\circ$. These values for the specific rotatory power are in close agreement with those already given for the synthetic ester.

(—)*Bornyl* dl-*Phenyl*-p-*tolylacetate*.—The rotatory power of this ester had not been determined by McKenzie and Widdows. The preparation from *dl*-phenyl-*p*-tolylacetyl chloride has accordingly been repeated, and the ester obtained as a colourless oil, b. p. 235°/12 mm. and $n_{\mathrm{D}}^{15°}$ 1·5447. In acetone ($l = 2$, $c = 6{\cdot}9605$) : $\alpha_{\mathrm{D}}^{20°}$ −3·52° $[\alpha]_{\mathrm{D}}^{20°}$ −25·3°; $\alpha_{5461}^{20°}$ −4·16°, $[\alpha]_{5461}^{20°}$ − 29·8°. After an additional distillation under diminished pressure, the oil gave in acetone $[\alpha]_{\mathrm{D}}^{20°}$ −25·9° and $[\alpha]_{5461}^{20°}$ − 30·2° for $c = 5{\cdot}8155$. This showed that no separation of the diastereoisomerides had occurred under the influence of heat.

*Interaction of Phenyl-*p*-tolylketen and* (−)*Borneol.*—A solution of *dl*-phenyl-*p*-tolylchloroacetyl chloride (6 g.) in 120 c.c. of anhydrous ether was gradually added to zinc turnings (2·5 g.), the action becoming vigorous on gentle warming. On completion of the reaction, which was conducted in an atmosphere of dry carbon dioxide, a solution of (−)borneol (4 g.) in 50 c.c. of anhydrous ether was added, and the mixture kept at the ordinary temperature for 44 hours. The unattacked keten was then decomposed by the addition of water, and the ethereal layer separated. After expulsion of the ether the borneol was removed from the oil by steam, the residue extracted with ether, the ethereal solution shaken with potassium bicarbonate solution to remove phenyl-*p*-tolylacetic acid, and dried with anhydrous sodium sulphate. The resulting reddish oil (5 g.) after drying in a vacuum for 3 days had $[\alpha]_{\mathrm{D}}^{20°}$ −23·9° ($c = 4{\cdot}799$) in acetone. On distillation a fraction was collected with $[\alpha]_{\mathrm{D}}^{20°}$ −25·1° ($c = 6{\cdot}3205$), and this on further distillation gave a colourless oil, b. p. 230—235°/9 mm., $n_{\mathrm{D}}^{15°}$ 1·5452 (Found : C, 83·0; H, 8·3. Calc. for $C_{25}H_{30}O_2$: C, 82·8; H, 8·3%). In acetone ($l = 2$, $c = 4{\cdot}8045$) : $\alpha_{\mathrm{D}}^{20°}$ − 2·40°, $[\alpha]_{\mathrm{D}}^{20°}$ − 25·0°; $\alpha_{5461}^{20°}$ − 2·87°, $[\alpha]_{5461}^{20°}$ − 29·9°. The product was thus (−)bornyl *dl*-phenyl-*p*-tolylacetate.

(−)*Menthyl* dl-α-*Methyl*-n-*butyrate.*—A solution of (−)menthol (15 g.) and *dl*-α-methylbutyryl chloride (10 g.) in 100 c.c. of anhydrous ether was kept at the ordinary temperature for 24 hours, and then gently warmed for 4 hours. After one distillation under diminished pressure, the oil from the ethereal solution gave the practically pure ester (12 g.). Two subsequent distillations brought the optical activity and the refractive index to constant values. (−)Menthyl *dl*-α-methyl-*n*-butyrate has b. p. 131—132°/18 mm. and $n_{\mathrm{D}}^{17°}$ 1·4492. It gave $\alpha_{\mathrm{D}}^{20°}$ −11·88° and $\alpha_{5461}^{20°}$ − 13·96° ($l = 0{\cdot}2$). In benzene ($l = 2$, $c = 10$) : $a_{\mathrm{D}}^{20°}$ − 12·89°, $[\alpha]_{\mathrm{D}}^{20°}$ − 64·4°; $\alpha_{5461}^{20°}$ − 15·13°, $[\alpha]_{5461}^{20°}$ − 75·6°. The rotation for λ 5893 is thus in close agreement with Rupe's value $[\alpha]_{\mathrm{D}}^{20°}$ − 63·97° in benzene (*Annalen*, 1909, **369**, 338).

dl-α-*Bromo*-α-*methylbutyryl Bromide.*—15·6 C.c. of bromine (4 mols.) were added very gradually to a mixture of 15 g. of *dl*-α-methyl-*n*-butyric acid (1 mol.) and 2 g. of red phosphorus (0·5 mol.). When the vigorous reaction had subsided, the mixture was heated on the steam-bath for 1½ hours, and the product distilled twice under diminished pressure. Yield, 33 g.

dl-α-*Bromo*-α-*methylbutyryl bromide* is a colourless mobile liquid which fumes strongly in air (Found : Br, 65·6. $C_5H_8OBr_2$ requires Br, 65·6%). It has $n_{\mathrm{D}}^{16°}$ 1·5101, and b. p. 70—71°/17 mm., and 96—97°/50 mm.

Interaction of Methylethylketen and (−)*Menthol.*—The keten was prepared by the action of zinc (38 g.) on an ethereal solution of *dl*-α-bromo-α-methylbutyryl bromide (68 g.) in the presence of a mixture of a little copper–bronze, magnesium, and aluminium turnings to act as an activator. The solution was acted on by (−)menthol (42 g.). The crude product was distilled in steam, and the ester obtained in the distillate together with menthol. The menthol was removed, and the residue fractionated, an oil being obtained with $n_{\mathrm{D}}^{12°}$ 1·4487, b. p. 158—164°/42 mm., and $\alpha_{5461}^{20°}$ − 13·34° ($l = 0{\cdot}2$). This is (−)menthyl *dl*-α-methyl-*n*-butyrate of about 96% optical purity, and after saponification with alcoholic potash, it gave optically inactive α-methyl-*n*-butyric acid with $n_{\mathrm{D}}^{14°}$ 1·4083 and b. p. 172—173°/756 mm.

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