# 97. *The Constituents of Some Indian Essential Oils. Part XXVII. A Synthesis of* dl-α-*Curcumene.*

By F. D. Carter, J. L. Simonsen, and H. O. Williams.

By the action of methylmagnesium iodide on *methyl* δ-p-*tolyl*-n-*hexoate* (III; R = Me) the *alcohol* (IV) was prepared, which gave on dehydration dl-α-*curcumene*, a mixture of the two hydrocarbons (I) and (II), characterised by the preparation of the *nitrosate*, decomp. 114°. Attempts to resolve the *acid* (III; R = H) into its optical enantiomorphs were unsuccessful. Two methods for the preparation of the acid are described.

*l*-α-Curcumene is, as was shown recently (J., 1939, 1504), a mixture of *l*-ζ-*p*-tolyl-β-methyl-$\Delta^{\beta}$-heptene (I) and *l*-ζ-*p*-tolyl-β-methyl-$\Delta^{\alpha}$-heptene (II). For the synthesis of this mixture, methyl δ-*p*-tolyl-*n*-hexoate (III; R = Me) was obviously a convenient starting material, since it should give on treatment with methylmagnesium iodide the alcohol (IV), from which by dehydration the required hydrocarbons would result.

$$\underset{\text{(I.)}}{C_6H_4Me{\cdot}CHMe{\cdot}CH_2{\cdot}CH_2{\cdot}CH{:}CMe_2} \qquad \underset{\text{(II.)}}{C_6H_4Me{\cdot}CHMe{\cdot}CH_2{\cdot}CH_2{\cdot}CH_2{\cdot}CMe{:}CH_2}$$

$$\underset{\text{(III.)}}{C_6H_4Me{\cdot}CHMe{\cdot}CH_2{\cdot}CH_2{\cdot}CH_2{\cdot}CO_2R} \qquad \underset{\text{(IV.)}}{C_6H_4Me{\cdot}CHMe{\cdot}CH_2{\cdot}CH_2{\cdot}CH_2{\cdot}C(OH)Me_2}$$

The dl-*alcohol* (IV), b. p. 164°/117 mm., was readily prepared by the method outlined above and gave on dehydration with potassium hydrogen sulphate dl-α-*curcumene*, which, like the natural hydrocarbon, was a mixture of (I) and (II), ozonolysis showing the latter to be present in the larger amount. The acid (III; R = H) could not be resolved into its optical enantiomorphs, since the salts which it formed with the various alkaloids all dissociated on recrystallisation and stronger bases, such as phenylethylamine, were not available. There can, however, be little doubt as to the structural identity of the natural and the synthetic hydrocarbon, since their physical constants are in close accord and, like the natural hydrocarbon, *dl*-α-curcumene yields a crystalline *nitrosate*, decomp. 114°.

δ-p-*Tolyl*-n-*hexoic acid* (III; R = H), b. p. 197°/112 mm., was prepared by two methods. In the first, and probably the more convenient method, although involving a larger number of stages, *ethyl* dl-γ-p-*tolyl*-n-*valerate* (V) (cf. Rupe and Steinbach, *Ber.*, 1911, **44**, 584) was reduced with sodium and alcohol to δ-p-*tolyl*-n-*amyl alcohol* (VI), b. p. 151°/116 mm., which was converted *via* the *chloride* and nitrile into (III; R = H). In the second method

$$\underset{\text{(V.)}}{C_6H_4Me{\cdot}CHMe{\cdot}CH_2{\cdot}CH_2{\cdot}CO_2Et} \longrightarrow \underset{\text{(VI.)}}{C_6H_4Me{\cdot}CHMe{\cdot}CH_2{\cdot}CH_2{\cdot}CH_2{\cdot}OH} \longrightarrow \text{(III)}$$

$$\underset{\text{(VII.)}}{C_6H_4Me{\cdot}CO{\cdot}CH_2{\cdot}CH_2{\cdot}CH_2{\cdot}CO_2H} \longrightarrow \underset{\text{(VIII.)}}{C_6H_4Me{\cdot}CMe{:}CH{\cdot}CH_2{\cdot}CH_2{\cdot}CO_2H} \longrightarrow \text{(III)}$$

$$C_6H_4Me{\cdot}CO{\cdot}CH_2{\cdot}CH_2{\cdot}CH_2{\cdot}CO{\cdot}C_6H_4Me \ \text{(IX.)}$$

toluene was condensed with glutaric anhydride to give γ-p-*toluoyl*-n-*butyric acid* (VII), m. p. 148—149°. The yield of the keto-acid was poor owing to the simultaneous formation of αγ-*di*-p-*toluoylpropane*, m. p. 110° (IX). On treatment with methylmagnesium iodide *methyl* γ-p-*toluoyl*-n-*butyrate* gave in excellent yield δ-p-*tolyl*-$\Delta^{\gamma}$-*hexenoic acid* (VIII), m. p. 80—81°, from which by catalytic hydrogenation (III; R = H) was prepared. The identity of the acids obtained by the two methods was confirmed by the preparation of their p-*phenylphenacyl* esters, m. p. 70°.

## EXPERIMENTAL.

dl-γ-p-*Tolyl*-n-*valeric Acid*.—The following method is more convenient than that described by Rupe and Steinbach (*loc. cit.*). A mixture of γ-*p*-tolyl-$\Delta^{\beta}$-butenecarboxylic acid (20 g.), amalgamated zinc (40 g.), and water (100 c.c.) was heated under reflux, and hydrochloric acid (60 c.c.) added, during 6 hours; the mixture was then heated for a further 10 hours. The cooled solution was extracted with ether, and the extract washed with aqueous sodium carbonate and evaporated, yielding unreduced lactone (4 g.). The sodium carbonate solution was acidified, and the acid (16 g.), m. p. 32°, b. p. 180°/14 mm., isolated by ether in the usual manner. The *ethyl* ester had b. p. 157°/19 mm. (Found : C, 76·4; H, 9·4. $C_{14}H_{20}O_2$ requires C, 76·4; H, 9·1%).

δ-p-*Tolyl*-n-*amyl Alcohol*.—A solution of the preceding ester (22 g.) in dried absolute alcohol (150 c.c.) was added as rapidly as possible to sodium (15 g.) and, after the initial reaction had subsided, the mixture was heated in an oil-bath at 130° for 1 hour. The ethyl alcohol was removed in steam, and the *alcohol* (12·5 g.) extracted from the cooled solution with ether. It was a viscid oil, b. p. 151°/16 mm. (Found : C, 81·0; H, 9·9. $C_{12}H_{18}O$ requires C, 80·9; H, 10·1%). The 3 : 5-*dinitrobenzoate* crystallised from methyl alcohol in prismatic needles, m. p. 80—81° (Found : C, 61·2; H, 5·7. $C_{19}H_{20}O_6N_2$ requires C, 61·3; H, 5·4%).

δ-p-*Tolyl*-n-*amyl Chloride*.—To a solution of the preceding alcohol (8·9 g.) in pyridine (3·95 g.) cooled in ice and mechanically stirred, thionyl chloride (6·8 g.) was gradually added. After 1 hour the mixture was heated on the water-bath for 3 hours, ice added to the cooled solution, and the oil extracted with ether. The extract was washed with dilute sulphuric acid, aqueous sodium carbonate, and water and dried, and the solvent evaporated. The *chloride* (9 g.) had b. p. 141—143°/17 mm.; it was redistilled for analysis, b. p. 141°/17 mm. (Found : Cl, 17·7. $C_{12}H_{17}Cl$ requires Cl, 18·1%).

δ-p-*Tolyl*-n-*hexoic Acid*.—The chloride (35 g.) in methyl alcohol (100 c.c.) was digested with sodium cyanide (15 g.) and iodine (1 g.) for 10 hours. The crude nitrile, b. p. 150—160°/18 mm., isolated in the usual manner, was heated with an excess of ethyl-alcoholic potassium hydroxide until evolution of ammonia ceased (48 hours). After evaporation of the alcohol a little neutral oil was removed by ether extraction, the alkaline solution acidified, and the hexoic acid separated. The *acid* was a viscid oil, b. p. 197°/20 mm. (Found : C, 75·7; H, 8·9. $C_{13}H_{18}O_2$ requires C, 75·7; H, 8·7%). The *methyl* ester had b. p. 167°/17 mm. (Found : C, 76·5; H, 9·5. $C_{14}H_{20}O_2$ requires C, 76·4; H, 9·1%). The p-*phenylphenacyl* ester crystallised from methyl alcohol in leaflets, m. p. 70° (Found : C, 81·2; H, 7·1. $C_{27}H_{28}O_3$ requires C, 81·0; H, 7·0%).

*Condensation of Toluene and Glutaric Anhydride*.—To a solution of glutaric anhydride (4 g.) in toluene (5 c.c.) and tetrachloroethane (13 c.c.), aluminium chloride (10·4 g.) was added gradually (mechanical stirring). After 12 hours the mixture was heated on the water-bath until evolution of hydrogen chloride ceased. The cooled mixture was decomposed with ice and hydrochloric acid, the excess of hydrocarbon and tetrachloroethane removed in steam, and the deep brown residue collected. After digestion with aqueous sodium hydroxide the neutral gum (*A*) (1·5 g.) was removed by ether, and the alkaline solution acidified, the keto-acid (5 g.) separating as a brown crystalline powder. γ-p-*Toluoyl*-n-*butyric acid* crystallised from benzene (charcoal) in prismatic needles, m. p. 148—149° (Found : C, 70·2; H, 6·8. $C_{12}H_{14}O_3$ requires C, 69·9; H, 6·8%). The *semicarbazone* separated from ethyl alcohol in fine needles, decomp. 218° (Found : N, 15·8. $C_{13}H_{17}O_3N_3$ requires N, 16·0%). The *methyl* ester, b. p. 192—194°/18 mm., crystallised in long needles, m. p. 28—30° (Found : C, 70·5; H, 7·5. $C_{13}H_{16}O_3$ requires C, 70·9; H, 7·3%). The neutral gum (*A*) crystallised after removal of the ether; the brown solid was collected and washed with ether, which removed a resin, and *αγ-di*-p-*toluoylpropane* then crystallised from either benzene or alcohol in long colourless needles, m. p. 110° (Found : C, 81·6; H, 7·2. $C_{19}H_{20}O_2$ requires C, 81·4; H, 7·1%). The *bis*-2 : 4-*dinitrophenylhydrazone* separated from *cyclo*hexyl acetate in salmon-coloured prisms, m. p. 257° (Found : N, 17·0. $C_{31}H_{28}O_8N_8$ requires N, 17·5%).

δ-p-*Tolyl*-$\Delta^{\gamma}$-*hexenoic Acid*.—To a solution of methylmagnesium iodide (prepared from 4 g. of magnesium) in ether (100 c.c.), cooled in ice, an ethereal solution of methyl γ-*p*-toluoyl-*n*-butyrate (20 g.) was slowly added. The reaction was very vigorous and a gelatinous gum separated. After 12 hours the magnesium compound was decomposed with ice and ammonium chloride, and the ether separated, washed with aqueous sodium carbonate, dried, and evaporated. The residual oil gave on distillation at 17 mm. two fractions, (i) (2·5 g.), b. p. 160—180°, and

(ii) (2·1 g.), b. p. 192°. The latter fraction crystallised and consisted of the unchanged methyl ester; fraction (i) was a neutral oil and was not further examined. The sodium carbonate solution was acidified, and the liquid acid extracted with ether. Evaporation of the dried extract gave an oil (13 g.) which rapidly crystallised. After draining on porous porcelain to remove adhering oil, the *hexenoic acid* crystallised from light petroleum (b. p. 40—60°) in prismatic needles, m. p. 80—81° (Found: C, 76·4; H, 7·8. $C_{13}H_{16}O_2$ requires C, 76·5; H, 7·8%).

The unsaturated acid (5 g.) in alcohol was reduced catalytically with a palladium–norit catalyst, the absorption of hydrogen being rapid. The alcoholic solution of the saturated acid was mixed with an excess of aqueous sodium hydroxide, the alcohol removed on the water-bath, the solution acidified, and the acid extracted with ether. The acid (4·8 g.) had b. p. 193—194°/17 mm.; a portion of it was converted into the *p*-phenylphenacyl ester, which crystallised from methyl alcohol in leaflets, m. p. 70°, both alone and in admixture with the ester described above.

dl-β-*Hydroxy*-ζ-p-*tolyl*-β-*methylheptane*.—To a solution of methylmagnesium iodide (from magnesium, 10 g.) in ether (500 c.c.), methyl δ-*p*-tolyl-*n*-hexoate (23 g.) was gradually added, the reaction being somewhat vigorous. After 12 hours the Grignard product was decomposed with ice and hydrochloric acid, and the ether separated, washed with aqueous sodium carbonate, dried, and evaporated. The residual oil (20 g.) had b. p. 165—167°/19 mm. and on redistillation the *alcohol* was obtained as a somewhat viscid oil, b. p. 164°/17 mm. (Found: C, 81·6; H, 10·8. $C_{15}H_{24}O$ requires C, 81·8; H, 10·9%). The *xenylurethane* crystallised from light petroleum (b. p. 40—60°) in flat prisms, m. p. 84—85° (Found: C, 81·3; H, 7·9. $C_{28}H_{23}O_2N$ requires C, 81·0; H, 8·0%).

dl-α-*Curcumene*.—The above-mentioned alcohol (18 g.) was heated with potassium hydrogen sulphate (20 g.) at 170—180° for 3 hours. The hydrocarbon was collected in ether, the ethereal extract washed with aqueous sodium carbonate, and the oil (11 g.) remaining after the removal of the ether from the dried extract distilled twice over sodium. The *hydrocarbon* had b. p. 134°/16 mm., $d_{20°}^{20·6°}$ 0·8802, $n_D^{20°}$ 1·5002 (Found: C, 88·8; H, 11·0. $C_{15}H_{22}$ requires C, 89·1; H, 10·9%). The *nitrosate*, which was very sparingly soluble in alcohol, crystallised from acetone–methyl alcohol in fine needles, decomp. 114° (Found: N, 9·0. $C_{15}H_{22}O_4N_2$ requires N, 9·5%)

*Ozonolysis of* dl-α-*Curcumene*.—The hydrocarbon (2 c.c.) in methyl acetate (20 c.c.) was ozonised at 0°, the issuing gases being passed through water (*A*). After removal of the solvent under diminished pressure the ozonide was decomposed by heating with water (5 c.c.), the volatile ketone being trapped in aqueous *p*-nitrophenylhydrazine acetate (*B*). The aqueous solution (*A*) gave on treatment with dimedone the formaldehyde derivative, m. p. 181°. From (*B*), acetone-*p*-nitrophenylhydrazone (0·05 g.) separated, m. p. 148° both alone and in admixture. The aqueous solution from the decomposition of the ozonide was neutralised with sodium carbonate, and the neutral oil (1 g.) extracted with ether. The oil reacted rapidly with semicarbazide acetate; the *semicarbazone* of *dl*-methyl δ-*p*-tolylamyl ketone was collected, washed with ligroin to remove gum, and crystallised from methyl alcohol, from which it separated in leaflets, m. p. 133—134° (Found: N, 15·8. $C_{15}H_{23}ON_3$ requires N, 16·1%). The sodium carbonate solution was acidified; ether then extracted a liquid acid (0·1 g.).

We are indebted to Imperial Chemical Industries Limited for a grant.

UNIVERSITY COLLEGE OF NORTH WALES, BANGOR. [*Received, February 19th, 1940.*]