

STUDIES IN SESQUITERPENES

Part V. Syntheses of 3:8-Dimethylcadalene and 1:3:6-Trimethylnaphthalene

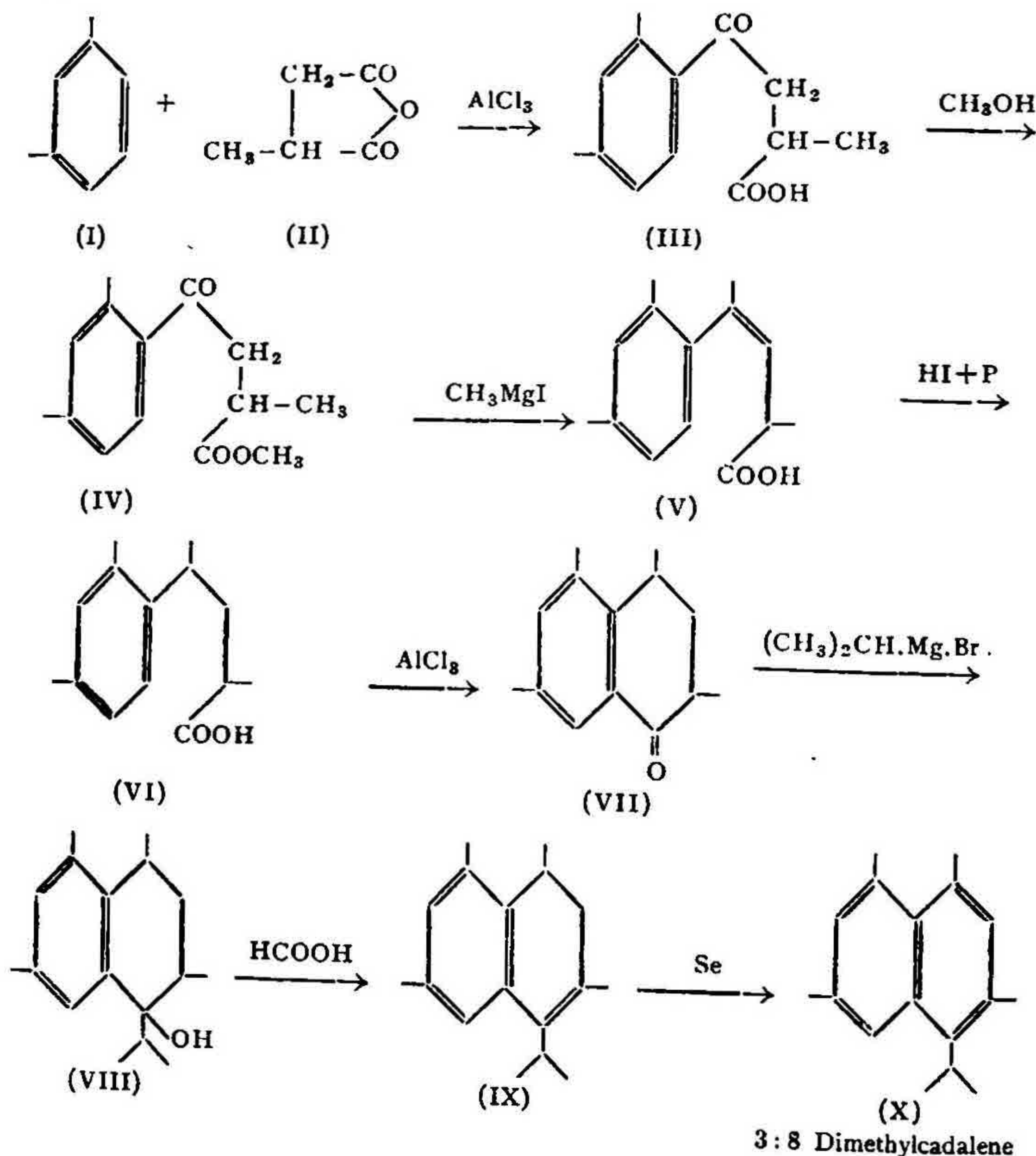
BY R. C. GUPTA AND M. S. MUTHANA

(Department of Organic Chemistry, Indian Institute of Science, Bangalore-3)

Received March 7, 1953

3:8-Dimethylcadalene

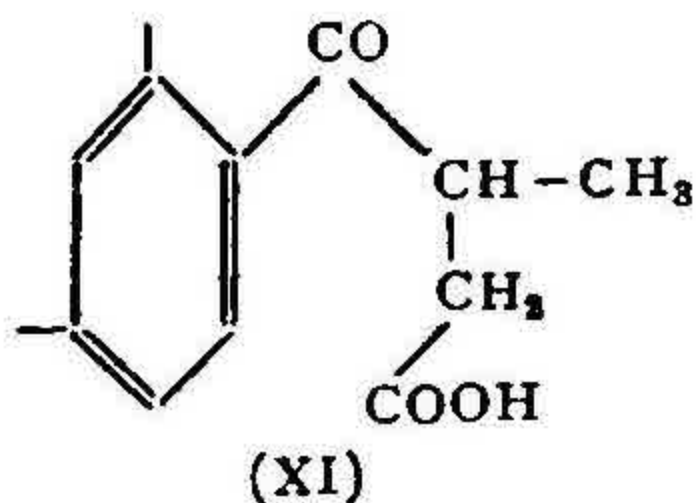
In continuation of this series of investigations (Gupta and Muthana, *J. Indian Inst. Sci.*, 1953, 35A, 308) the present paper deals with the synthesis of 3:8-dimethyl-cadalene. The scheme that was followed to synthesize this hydrocarbon has been schematically outlined below:



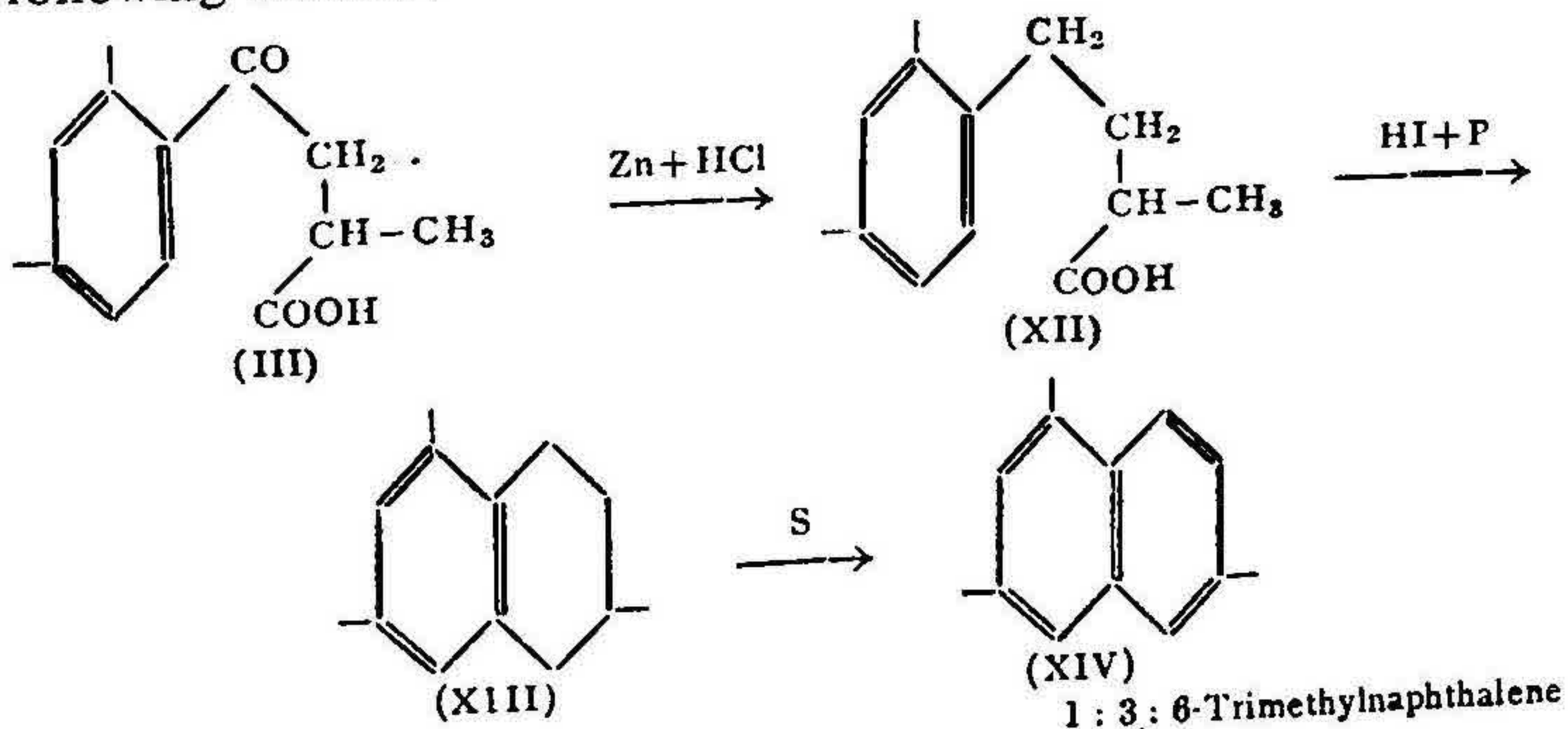
m-xylene (I) was condensed with methyl-succinic anhydride (II) in nitrobenzene solution in presence of anhydrous aluminium chloride and β -(*m*-xyloyl-2-)- α -methyl-propionic acid (III) thus obtained was esterified with methyl alcohol and sulphuric acid to yield methyl β -(*m*-xyloyl-2-)- α -methyl-propionate (IV). The latter was treated with methyl magnesium iodide (inverse addition) when γ -(*m*-xylyl-2-)- α - γ -dimethylvinyl-acetic acid (V) was isolated, which on reduction with hydriodic acid and red phosphorus furnished γ -(*m*-xylyl-2-)- α : γ -dimethyl-butyrac acid (VI). The acid (VI) was cyclised in presence of anhydrous aluminium chloride to 2:4:5:7-tetramethyl-tetralone-1 (VII) and the ketone on treatment with isopropylmagnesium bromide yielded a carbinol (VIII) which was dehydrated with formic acid to 1:3:6:8-tetramethyl-4-isopropyl-dihydronaphthalene (IX). The latter on dehydrogenation in presence of selenium furnished 3:8-dimethylcadalene.

1:3:6-Trimethylnaphthalene

The need to synthesize 1:3:6-trimethylnaphthalene arose to prove that the condensation of methyl-succinic anhydride (II), with *m*-xylene (I) gave β -(*m*-xyloyl-2-)- α -methyl-propionic acid (III) and not β -(*m*-xyloyl-2-)- β -methyl-propionic acid (XI). 1:3:6-Trimethylnaphthalene has been



previously synthesized by Ruzicka and Ehmann (*Helv. Chim. Acta.*, 1932, **15**, 154) and Sukh Dev (*J. Indian Chem. Soc.*, 1948, **25**, 323) by somewhat different methods. The present synthesis has been achieved according to the following scheme:



The keto acid (III), obtained by condensing *m*-xylene with methyl succinic anhydride, was reduced in presence of zinc and hydrochloric acid to γ -(*m*-xylyl-2-)- α -methyl-butyrac acid (XII). The latter was cyclised and reduced in one step by heating with hydroiodic acid and red phosphorus for 60 hours. The 1:3:6-trimethyltetralin (XIII) thus obtained was dehydrogenated in presence of sulphur to give 1:3:6-trimethylnaphthalene (XIV). The latter was characterised by its picrate, m.p. 114° C. and the mixed m.p. with an authentic sample remained undepressed.

EXPERIMENTAL

3:8-Dimethylcadalene

(i) β -(*m*-xyloyl-2-)- α -methylpropionic acid (III).—*m*-Xylene (1, 40.8 g., 1.1 mol.) was condensed with methylsuccinic anhydride (39.5 g., 1 mol.) in nitrobenzene (150 c.c.) in presence of anhydrous aluminium chloride (104 g., 2.2 mols.) for details *cf.* preparation of β -(*p*-cymoyl-2-)- α -methyl propionic acid (Gupta and Muthana, *J. Indian Inst. Sci.*, 1953, 35A, 131). The complex was decomposed with ice (200 g.), followed by concentrated hydrochloric acid (60 c.c.). The acid was obtained as colourless plates, m.p. 77° C. Yield 51 g. (Found: C, 70.4; H, 7.3; $C_{13}H_{16}O_3$ requires C, 70.91; H, 7.273 per cent.)

(ii) Methyl- β -(*m*-xyloyl-2-)- α -methylpropionate (IV).—The acid (III, 51 g.) was esterified with methyl alcohol (100 c.c.) and sulphuric acid (7 c.c.) by heating on water-bath for 12 hours. The ester was purified by distillation b.p. 170–3° C./6 mm. Yield 50 g.

(iii) γ -(*m*-xylyl-2-)- α : γ -dimethylvinyl-acetic acid (V).—A Grignard solution prepared from magnesium (2.917 g.; 1.6 mol.), methyl iodide (17 g.) and anhydrous ether (50 c.c.) was added to a solution of the ester (V, 17.5 g.; 1 mol.) in anhydrous ether (50 c.c.) (Inverse Grignard reaction) [for details *cf.* the preparation of γ -(*p*-cymyl-2-)- α : γ -dimethylvinyl acetic acid, Gupta and Muthana, *loc.cit.* The complex was decomposed with dilute hydrochloric acid (1:2; 50 c.c.). The acid was obtained as a slightly pale viscous liquid; b.p. 150–55° C./2 mm. Yield 15 g. (Found: C, 77.8; H, 9.04; $C_{14}H_{18}O_2$ requires C, 77.05; H, 8.256 per cent.)

(iv) γ -(*m*-xylyl-2-)- α : γ -dimethylbutyric acid (VI).—The unsaturated acid (V, 58 g.) was reduced with hydroiodic acid (290 g.) and red phosphorus (60 g.) by heating under reflux (130–40° C.) for 12 hours (*cf.* preparation of γ -(*p*-cymyl-2-)- α : γ -dimethyl-butyrac acid, Gupta and Muthana, *loc. cit.*). The acid was obtained as a thick viscous liquid, b.p. 145–50° C./2 mm. Yield 20 g. (Found: C, 75.9; H, 9.3; $C_{14}H_{20}O_2$ requires C, 76.37; H, 9.09 per cent.)

From the neutral fraction a ketone was isolated, b.p. 122–3° C./2 mm., which was identified as 2:4:5:7-tetramethyl-tetralone-1 (VII) by preparing its 2:4-dinitrophenyl hydrazone, m.p. 246–7° C. Mixed m.p. with an authentic sample remained undepressed.

(v) 2:4:5:7-Tetramethyl-tetralone-1 (VII).—The acid chloride, prepared from the acid (VI, 20 g., 1 mol.) by treating with phosphorus pentachloride (20.8 g., 1.1 mol.) in dry benzene (15 c.c.), was cyclised in presence of anhydrous aluminium chloride (13.36 g., 1.1 mol.) in dry and thiophene-free benzene solution (for details *cf.* preparation of 2:4:5-trimethyl-8-isopropyltetralone-1, Gupta and Muthana, *loc. cit.*). The complex was decomposed with ice (200 g.) and concentrated hydrochloric acid (40 c.c.). The ketone distilled as a colourless mobile liquid; b.p. 122–3° C./2 mm. Yield 8 g. (Found: C, 83.42; H, 9.01; $C_{14}H_{18}O$ requires C, 83.16; H, 8.91 per cent.).

2:4-Dinitrophenylhydrazone of the ketone was prepared by sulphuric acid method and crystallised from glacial acetic acid in bright red needles, m.p. 246–7° C.

(vi) 1:3:6:8-Tetramethyl-4-isopropyldihydronaphthalene (IX).—A solution of the ketone (VII, 6 g., 1 mol.) in anhydrous ether (25 c.c.) was added to a Grignard mixture prepared from magnesium (1.11 g., 1.6 mol.), isopropylbromide (5.563 g.) and anhydrous ether (25 c.c.) [*cf.* Preparation of 1:5:6:8-tetramethyl-4-isopropyldihydronaphthalene (Gupta and Muthana, *loc. cit.*)]. The crude carbinol (VIII) was dehydrated with formic acid (90%; 20 c.c.) and the hydrocarbon (IX) purified by repeatedly distilling over sodium, b.p. 102–3° C./1 mm. Yield 0.35 g.

(vii) 3:8-Dimethylcadalene (X).—The hydrocarbon (IX, 0.3 g.) was dehydrogenated with selenium (0.2 g.) by heating for 40 hours between 300–330° C. The dehydrogenated product was purified by distilling over sodium (twice); b.p. 115–6° C./1 mm. Yield 0.1 g. (Found: C, 89.84; H, 9.62; $C_{17}H_{22}$ requires C, 90.265; H, 9.735 per cent.).

Trinitrobenzene compound.—3:8-Dimethylcadalene was characterised by its trinitrobenzene compound, prepared by mixing alcoholic solutions of trinitrobenzene and the hydrocarbon. The derivative was crystallised from alcohol in bright yellow needles, m.p. 149–50° C. (Found: N, 9.27; $C_{23}H_{25}N_3O_6$ requires N, 9.52 per cent.)

1:3:6-Trimethylnaphthalene

(i) γ -(*m*-xylyl-2-)-*o*-methylbutyric acid (XII).—The keto acid (III, 11 g.) was reduced by refluxing for 40 hours with a mixture of zinc amalgam (20 g.),

concentrated hydrochloric acid (35 c.c.), water (20 c.c.) and toluene (20 c.c.), adding concentrated hydrochloric acid (10 c.c.) every 6 hours. The mixture was cooled, and toluene layer separated. After washing the toluene solution with water (once) toluene was removed on water-bath under suction and the acid purified by distillation; b.p. 150–55° C./1 mm. Yield 9 g. (Found: C, 75.38; H, 8.59; $C_{13}H_{18}O_2$ requires C, 75.72; H, 8.73 per cent.)

(ii) 1:3:6-*Trimethyltetralin* (XIII).—The reduced acid (XII, 9 g., 1 part) was cyclised and reduced simultaneously by heating with a mixture of phosphoric acid (syrupy, d. 1.75; 27 c.c., 3 parts), red phosphorus (9 g., 1 part) and iodine (5 g., 0.5 part), at 170–80° C. for 60 hours. The mixture was cooled, diluted with water and extracted with ether (4 times). The ether-extract was washed with water, sodium carbonate solution, water, sodium thiosulphate solution (to remove traces of iodine) and then with water successively. After drying over anhydrous sodium sulphate, ether was distilled off and the hydrocarbon purified by distillation, b.p. 91–3° C./2 mm. Yield 3. g.

(iii) 1:3:6-*Trimethylnaphthalene* (XIV).—The hydrocarbon (XIII, 2.6 g., 1 mol.) was dehydrogenated with sulphur (0.95 g.) by heating at 235° C. for 30 minutes and at 260° C. for further half an hour. The dehydrogenated product was purified by distilling over sodium, b.p. 104–8° C./1 mm. Yield (1.1 g.).

Picrate was prepared in the usual manner from alcoholic solution and crystallised in orange red needles, m.p. 114° C. Mixed m.p. with an authentic sample remained undepressed.

Our sincere thanks are due to Dr. B. H. Iyer for his kind interest in the work.