

# STUDIES IN SESQUITERPENES

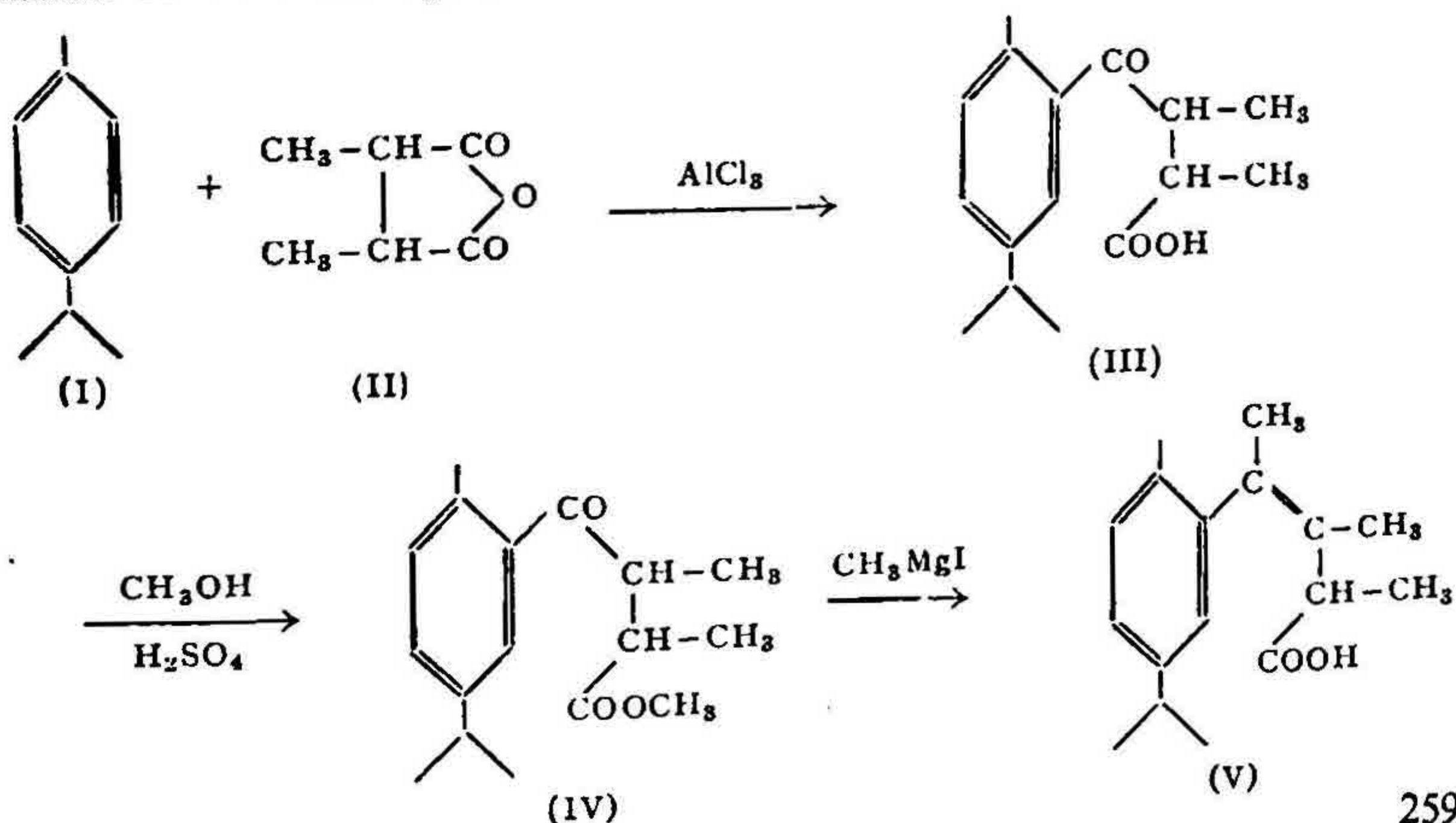
## Part II. Synthesis of 7:8-Dimethyl-Cadalene (1:6:7:8-Tetramethyl-4-isopropylnaphthalene)

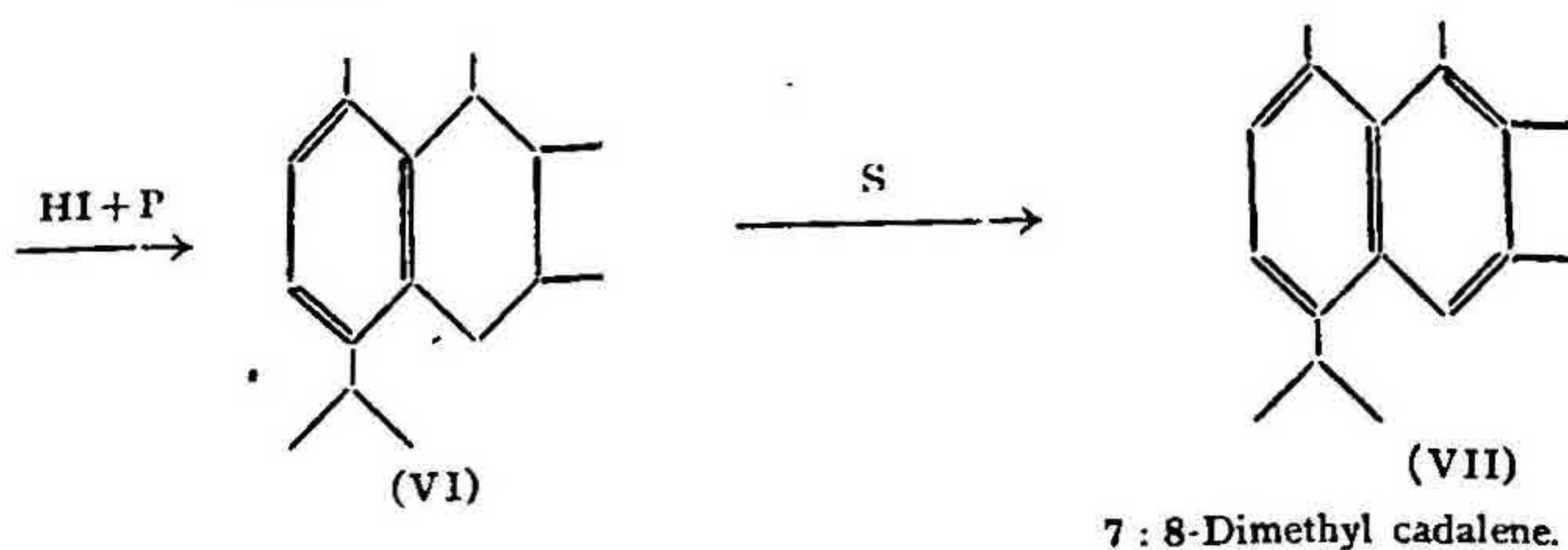
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During the synthesis of various alkyl naphthalenes often, a  $\gamma$ -arylbutyric acid, obtained through a series of reactions, is subjected to intramolecular condensation, yielding the corresponding tetralone, which is reduced to hydrocarbon and the latter on dehydrogenation furnishes the required alkyl naphthalene (Harvey, Heilbron and Wilkinson, *J. Chem. Soc.*, 1930, p. 423, 2537; Wilkinson, *ibid.*, 1931, p. 1333; Ruzicka *et al.*, *Helv. Chim. Act.*, 1932, **15**, 140; 1933, **16**, 314; 1936, **19**, 370; Barnett and Sanders, *J. Chem. Soc.*, 1933, p. 434; Rapson and Short, *ibid.*, 1933, p. 128; Brunner and Grof, *Montash*, 1934, **64**, 28; Sukh Dev and Guha, *J. Ind. Chem. Soc.*, 1948, **25**, 38). Aryl-butyrac acid is also obtained by the reduction of the corresponding  $\beta$ - $\gamma$ -unsaturated acid, obtained by the action of alkylmagnesium halide on methyl- $\beta$ -aroyl propionate.

Sukh Dev (*J. Ind. Chem. Soc.*, 1948, **25**, 323) has developed a method which completes all the three steps, viz., reduction ring-closure and further reduction, in one operation. This method has been followed in the present synthesis of 7:8-dimethyl-cadalene according to the scheme outlined below:





*p*-Cymene (I) was condensed with  $\alpha$ : $\beta$ -dimethylsuccinic anhydride (II) in presence of anhydrous aluminium chloride to yield  $\beta$ -(*p*-cymoyl-2-)- $\alpha$ : $\beta$ -dimethyl-propionic acid (III). The latter was esterified with methyl alcohol and sulphuric acid and methyl- $\beta$ -(*p*-cymoyl-2-)- $\alpha$ : $\beta$ -dimethyl-propionate (IV) thus obtained was treated with methyl magnesium iodide (inverse addition) furnishing  $\gamma$ -(*p*-cymoyl-2-)- $\alpha$ : $\beta$ : $\gamma$ -trimethyl-acetic acid (V). The unsaturated acid (V) was heated under reflux with a mixture of iodine, red phosphorus and phosphoric acid (syrupy) for 70 hours. The substituted tetralin (VI) thus prepared was dehydrogenated with sulphur when 7:8-dimethyl-cadalene (VII), was obtained.

### EXPERIMENTAL

#### *Preparation of $\alpha$ : $\beta$ -Dimethyl succinic anhydride*

$\alpha$ : $\beta$ -Dimethyl succinic acid was prepared as follows by a newer method than found in literature (Fieser and Daudt, *J. Am. Chem. Soc.*, 1941, 63, 782; cf. Bonn and Sprankling, *J. Chem. Soc.*, 1899, 75, 839).

Malonic ester (1 mol.) was added in a thin stream under stirring to a mixture of molecular sodium (1 mol.) and toluene (1 lit.) taken in a 2-litre 3-necked flask fitted with a stirrer (mercury sealed), condenser and a dropping funnel. When the reaction subsided the contents were heated under reflux for 3 hours. After cooling to the room temperature  $\alpha$ -bromopropionic ester (1 mol.) was added dropwise under stirring during 2 hours. The mixture was then refluxed for 6 hours, diluted with water and toluene layer separated. The toluene solution was washed with water, dilute hydrochloric acid and water successively. Toluene was removed on water-bath under suction and the mixture heated to 170° to remove the unreacted products. The residue was fractionated under reduced pressure and the fraction boiling 130–60° at 12 mm. was collected and added to a mixture of molecular sodium (1 mol.) and toluene (1 lit.) under stirring. When the initial reaction subsided the contents were heated under reflux for 4 hours, cooled in ice, and methyl iodide (1.1 mol.) added dropwise under efficient stirring and cooling. After stirring for 3 hours the reaction mixture was left overnight

and warmed under reflux for 2 hours. The contents were diluted with water and the toluene layer separated, washed with dilute hydrochloric acid and water successively. After removing toluene on the water-bath under suction, the residue was hydrolysed with concentrated hydrochloric acid (800 c.c.) by heating under reflux till the oily layer disappeared (30 hours). On cooling,  $\alpha$ : $\beta$ -dimethyl succinic acid separated in pure form and filtered. Further concentration of the residual liquid on the water-bath yielded another crop of the acid; combined overall yield being 70 per cent. m.p. of the crude acid 198° C.

To  $\alpha$ : $\beta$ -dimethyl succinic acid (1 mol.) acetylchloride (2 mols.) was added and when the initial reaction subsided it was warmed on water-bath for 2 hours. After removing the low boiling fractions the residue was distilled under reduced pressure and the anhydride. b.p. 100–102/2 mm., collected in 60 per cent. yield.

(i)  $\beta$ -(*p*-Cymoyl-2-)- $\alpha$ : $\beta$ -dimethyl propionic acid (III).— $\alpha$ : $\beta$ -Dimethylsuccinic anhydride (II, 40 g., 1 mol.) was condensed with *p*-cymene (I, 46 g., 1.1 mol.) in nitrobenzene (125 c.c.) in the presence of anhydrous aluminium chloride (100 g.; 2.2 mols.). (For details see preparation of  $\beta$ -(*p*-cymoyl-2-)- $\alpha$ -methyl propionic acid. Sukh Dev and Guha (*J. Indian Chem. Soc.*, 1948, 25, 13). After removing nitrobenzene by steam distillation the oily layer was extracted with ether (thrice) and the ether extract washed (4 times) with water and dried over anhydrous sodium sulphate. Ether was distilled off and the reddish viscous liquid obtained was triturated with petroleum ether. Petroleum ether was removed and the reddish viscous acid (crude) was obtained in an overall yield of 21 g.

(ii) Methyl- $\beta$ -(*p*-cymoyl-2-)- $\alpha$ : $\beta$ -dimethyl propionate (IV).—The crude acid (III, 21 g.) was esterified by refluxing with methyl alcohol (40 c.c.) and concentrated sulphuric acid (3 c.c.). The ester was worked up in the usual manner and purified by distillation under reduced pressure. B.p. 148–9°/2 mm. Yield, 13 g. (Found: C, 73.2; H, 6.8;  $C_{17}H_{24}O_3$  requires C, 73.91; H, 6.90 per cent.).

(iii)  $\gamma$ -(*p*-cymoyl-2-)- $\alpha$ : $\beta$ - $\gamma$ -trimethylvinyl acetic acid (V).—A Grignard solution, prepared from magnesium (0.09 g.; 1.6 mol.), methyl iodide (4.5 g.; 1.6 mol.) and ether (20 c.c.) was added (inverse addition) to a solution of methyl- $\beta$ -(*p*-cymoyl-2-)- $\alpha$ : $\beta$ -dimethyl propionate (6 g.; 1 mol.) in ether (20 c.c.). (For details see the preparation of  $\gamma$ -(*p*-cymoyl-2-)- $\alpha$ : $\gamma$ -dimethylvinyl-acetic acid, Gupta and Muthana (*J. Ind. Inst. Sci.*, 1953, 35 A, 131). The magnesium complex was decomposed with dilute hydrochloric acid (1:2; 60 c.c.). Ether layer was removed, washed with water and extracted

with sodium carbonate solution (4 times). The alkaline extract was acidified (congo-red) and the liberated acid extracted with ether (4 times). The ethereal extract was washed with water and dried over anhydrous sodium sulphate. After removal of ether the unsaturated acid was used without further purification, since it showed signs of decomposition on distillation.

(iv) 1:6:7:8-*Tetramethyl-4-isopropyl-tetralin* (VI).—The unsaturated acid (V, 5 g., 1 part), phosphoric acid syrupy (15 g., 3 parts, d. 1.75), iodine (2.5 g., 0.5 part) and red phosphorus (5 g., 1 part) were heated under reflux for 70 hours at 170–80° C. The reaction mixture was cooled, diluted with water and extracted with ether (4 times). The ethereal extract was washed with water, dilute sodium carbonate solution (twice), water, sodium thio-sulphate solution, and then with water successively and dried over anhydrous sodium sulphate. Ether was removed and the residue purified by distillation over sodium, b.p. 104–07/1 mm. Yield, 2.9 g. (Found: C, 88.3; H, 11.12;  $C_{17}H_{26}$  requires C, 88.69; H, 11.31 per cent.).

(v) 7:8-*Dimethyl-cadalene* (VII).—The hydrocarbon (VI, 0.8 g.) and sulphur (0.25 g.) were heated in a metal bath at 230° C. for 30 minutes; the temperature was then raised to 260° for further half an hour. The dehydrogenated product was purified by distilling (twice) over sodium, b.p. 115–20° C./1 mm. Yield, 0.2 g. (Found: C, 89.73; H, 9.71;  $C_{17}H_{22}$  requires, C, 90.265; H, 9.735 per cent.).

*Trinitrobenzene compound*.—The trinitrobenzene compound of 7:8-dimethyl-cadalene was prepared by mixing the hot alcoholic solution of trinitrobenzene and the hydrocarbon and allowing to crystallise slowly. Bright yellow needles were obtained, which were crystallised (twice) from alcohol, m.p. 143° C. Further crystallisation did not raise the melting point.

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