

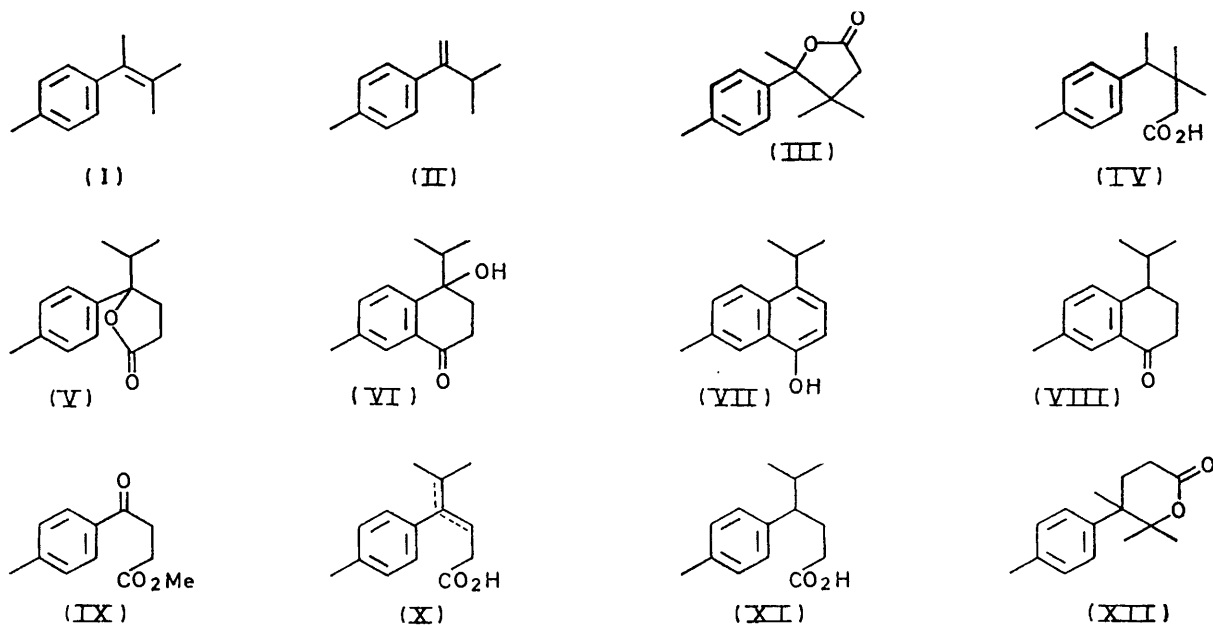
Carboxymethylation of $p,\alpha\beta\beta$ -Tetramethylstyrene by Manganese(III) Acetate. Reductive Cyclization during Treatment of the Derived γ -Aryl- γ -lactone with Polyphosphoric Acid to give 4-Isopropyl-7-methyl-1-tetralone

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Oxidation of $p,\alpha\beta\beta$ -tetramethylstyrene (I) with manganese(III) acetate gave a lactone mixture in which the presence of 4-isopropyl-4- p -tolylbutan-4-olide (V) as the major component was inferred from its n.m.r. spectrum. The formation of this lactone (V) is attributed to the addition of carboxymethyl radical [from manganese(III) acetate] to α -isopropyl- p -methylstyrene (II), arising from (I) by double-bond isomerisation. Treatment of the lactone mixture with polyphosphoric acid furnished in high yield 4-isopropyl-7-methyl-1-tetralone (VIII), identified by independent synthesis. This cyclization involves reduction by hydride transfer.

THE recently discovered carboxymethylation of olefins, including styrenes, by manganese(III) acetate leading to γ -lactones,¹ and our interest in its application to terpenoid transformations,² prompted us to examine the action of manganese(III) acetate on $p,\alpha\beta\beta$ -tetramethylstyrene (I). We hoped thus to obtain 3,3,4-trimethyl-4- p -tolylbutan-4-olide (III), as the corresponding acid (IV) is a key intermediate in the synthesis of the naturally occurring sesquiterpenoid ketone, β -cuparenone.³

From the isopropylmethyl doublets in the n.m.r. spectrum of this mixture and their intensity [δ 0.88 (dd, J 7 Hz)], the presence in major amount of a γ -lactone, probably (V), besides the lactone (III), was inferred. The formation of the lactone (V) can be explained on the basis of addition of the carboxymethyl radical¹ arising from manganese(III) acetate to the styrene (II) formed from (I) by double-bond isomerisation. In order to confirm the presence of this lactone



Grignard reaction of isopropylmagnesium iodide with p -methylacetophenone followed by dehydration furnished the tetramethylstyrene (I), the various methyl groups of which were clearly assigned from its n.m.r. spectrum, in the light of Sternhell's work on trimethylstyrenes.⁴

The reaction of the styrene (I) with manganese(III) acetate furnished a γ -lactonic product (λ_{\max} 1776 cm^{-1}) which proved to be an inseparable mixture (overlapping bands obtained on preparative t.l.c. with various solvent

(V), we treated the lactone mixture with polyphosphoric acid in the hope of isolating the naphthol (VII), formed from (V) by cyclodehydration which could occur *via* the ketol (VI). However the product was in fact the tetralone (VIII) (λ_{\max} 1678 cm^{-1}), obtained in high yield and identified from its n.m.r. spectrum and comparison with material synthesised independently as follows.

Methyl 4-oxo-4- p -tolylbutyrate⁵ (IX) on inverse

¹ (a) J. B. Bush, jun., and H. Finkbeiner, *J. Amer. Chem. Soc.*, 1968, **90**, 5903; (b) E. I. Heiba, R. M. Dessau, and W. I. Koehl, *ibid.*, p. 5905.

² M. E. N. Nambudiry and G. S. Krishna Rao, *Indian J. Chem.*, in the press.

³ R. B. Mane and G. S. Krishna Rao, *J.C.S. Perkin I*, 1973, 1806.

⁴ G. F. Newsoroff and S. Sternhell, *Austral. J. Chem.*, 1966, **19**, 1667.

⁵ S. Dev, *J. Indian Chem. Soc.*, 1948, **25**, 315.

Grignard reaction⁶ with isopropylmagnesium iodide and work up with ice-cold dilute hydrochloric acid gave the unsaturated acid (X). Its reduction (nickel-aluminium alloy-sodium hydroxide) to the saturated acid (XI) followed by its cyclization with polyphosphoric acid gave 4-isopropyl-7-methyl-1-tetralone (VIII), identical (i.r. spectra and mixed m.p.s of 2,4-dinitrophenylhydrazones) with the tetralone originating from (I). The formation of (VIII) from the other isomeric γ -lactones [(III) and its isomer, 3,4,4-trimethyl-3-*p*-tolylbutan-4-olide], resulting from direct addition to the styrene (I) is mechanistically improbable.

The formation of the tetralone (VIII) from the γ -lactone mixture presumably occurs by hydride transfer to the C-4 carbocation derived from the tertiary carbinol (VI). There are precedents for similar reductions of carbocations by hydride transfer during treatment with polyphosphoric acid, although the hydride donor does not in all cases appear to have been identified.⁷ In certain heterocyclic systems also, acid-catalysed intermolecular hydride transfer by disproportionation has been observed.⁸

The intervention of the lactone (V) in the path (I) \rightarrow [(II)] \rightarrow (V) \rightarrow (VIII) was independently demonstrated as follows. The unsaturated acid (X) was lactonised (by acetic acid-concentrated hydrochloric acid) to give a two-component mixture [λ_{\max} 1775 (γ -lactone) and 1750 cm^{-1} (δ -lactone)], expected to be a mixture of (V) and (XII), formed by lactonisation at the benzylic carbon and the isopropyl carbon, respectively, of (X) which could not be separated. Treatment of the lactone mixture with polyphosphoric acid afforded neutral material consisting of two components, the major one of which (separated by preparative t.l.c.) was identical with 4-isopropyl-7-methyl-1-tetralone (VIII).

The investigation thus reveals double-bond isomerisation of a trisubstituted styrene during manganese(III) acetate oxidation and carbocation reduction during treatment of a γ -alkyl- γ -aryl- γ -lactone with polyphosphoric acid.

EXPERIMENTAL

p, α , β -Tetramethylstyrene (I).—A solution of *p*-methylacetophenone (25 ml) in dry ether (50 ml) was added dropwise with stirring at room temperature to isopropylmagnesium iodide [from isopropyl iodide (29 ml), magnesium (7 g), and dry ether (50 ml)]. The solution was then stirred for 1 h, left overnight, and added to crushed ice (150 g) and concentrated hydrochloric acid (20 ml). The organic layer was separated and the aqueous portion extracted twice with ether. The residue obtained on removal of ether was refluxed with ethanol (150 ml) and concentrated hydrochloric acid (30 ml) for 6 h. Ethanol was removed under reduced pressure and the residue extracted with ether. The crude product, containing some unchanged ketone, was treated with 2,4-dinitrophenylhydrazine reagent (7 g) and steam-distilled. Distillation of the steam-volatile hydrocarbon gave the pure styrene, b.p. 115–117° at 43 mmHg (24 g), (CCl_4) 1.56 (3H, m, β -Me *cis* to ring), 1.77br (3H, s, β -Me

⁶ S. Dev, *J. Indian Chem. Soc.*, 1948, **25**, 323, and references cited therein.

trans to ring), 1.90 (3H, m, α -Me), 2.30 (3H, s, ArMe), and 6.95 (4H, m, ArH) (Found: C, 90.0; H, 10.0. $\text{C}_{13}\text{H}_{16}$ requires C, 89.9; H, 10.1%).

Oxidation of the Styrene (I) with Manganese(III) Acetate.—A mixture of the styrene (I) (8 g), freshly prepared manganese(III) acetate^{1a} (26.8 g), acetic acid (350 ml), acetic anhydride (100 ml), and potassium acetate (150 g) was refluxed under nitrogen for 4 h.^{1b} The mixture was cooled and poured into water (1 l). The organic phase was extracted with ether. Distillation of the residue (11 g) obtained on removal of ether gave ν -lactonic material (6.2 g), λ_{\max} 1776 cm^{-1} , b.p. 145–160° at 2 mmHg.

Treatment of the Lactone Mixture from the Styrene (I) with Polyphosphoric Acid: Isolation of 4-Isopropyl-7-methyl-1-tetralone (VIII).—The mixture of lactones (0.8 g) was stirred with polyphosphoric acid [prepared from phosphorus pentoxide (10 g) and phosphoric acid (6 ml)] at 90–100° for 2.5 h. The mixture was cooled and decomposed with crushed ice (100 g) and the product extracted with light petroleum. Removal of the solvent and short-path sublimation (135–140° at 2 mmHg) furnished ketonic material (0.6 g), ν_{\max} (film) 1678 cm^{-1} , 2,4-dinitrophenylhydrazone, m.p. 166–167° (from ethanol-ethyl acetate), δ (CDCl_3) 0.87 (3H, d, *J* 7 Hz, MeCMe), 1.05 (3H, d, *J* 7 Hz, MeCMe), 2.42 (3H, s, ArMe), 1.5–2.8 (m, CH_2 and CH), 7.12 (2H, m, aromatic H-5 and -6), 7.92br (1H, s, H-8 *per* to C=O), 8.13 (1H, d, *J* 10 Hz, 2,4-dinitrophenyl H-6), 8.35 (1H, dd, *J* 10 and 3 Hz, 2,4-dinitrophenyl H-5), 9.11 (1H, d, *J* 3 Hz, 2,4-dinitrophenyl H-3), and 11.3br (1H, s, NH) (Found: C, 63.1; H, 5.6; N, 14.4. $\text{C}_{20}\text{H}_{22}\text{N}_4\text{O}_4$ requires C, 62.8; H, 5.8; N, 14.7%).

5-Methyl-4-(p-tolyl)hexanoic Acid (XI).—An ethereal solution of isopropylmagnesium iodide [from magnesium (4.5 g) and isopropyl iodide (42 g) in dry ether (150 ml) under nitrogen] was added dropwise at room temperature under nitrogen to a solution of methyl 4-oxo-4-(*p*-tolyl)butyrate⁵ (IX) (52 g) in dry ether (125 ml) during 20 min. The mixture was then refluxed (4 h), left overnight, and decomposed by addition of ice-cold dilute hydrochloric acid (1:3 acid: water; 100 ml), and the ether layer was separated. The aqueous portion was thoroughly extracted with ether. The combined organic extract was washed with aqueous 5% sodium carbonate. The alkaline extract was washed with ether, cooled, and acidified (ice-cold hydrochloric acid) to give the unsaturated acid (X) (17.5 g) as a syrupy liquid, ν_{\max} (film) 3040–2590br (OH of CO_2H) and 1709 cm^{-1} (C=O of acid). To the unsaturated acid (10 g) dissolved in aqueous sodium hydroxide (10%; 330 ml), nickel-aluminium alloy powder (33 g) was added at 95° in small portions with stirring during 2 h. Heating and stirring were then continued for 1 h more. The Raney nickel was filtered off and the filtrate poured into concentrated hydrochloric acid (330 ml) and crushed ice (*ca.* 160 g) to furnish the saturated acid, b.p. 155–160° at 2 mmHg (8.5 g) (Found: C, 76.5; H, 9.2. $\text{C}_{14}\text{H}_{20}\text{O}_2$ requires C, 76.4; H, 9.1%).

4-Isopropyl-7-methyl-1-tetralone (VIII).—(a) *From the saturated acid (XI).* The acid (XI) (8.5 g) was stirred with polyphosphoric acid [from phosphorus pentoxide (17 g) and phosphoric acid (10 ml)] at 95° for 30 min. Work-up as described already gave the tetralone (6 g), b.p. 135–140° at 2 mmHg, ν_{\max} (film) 1678 cm^{-1} (C=O), δ (CCl_4) 0.94 (3H,

⁷ R. T. Conley and B. E. Nowak, *J. Org. Chem.*, 1962, **27**, 3196, and references cited therein.

⁸ V. N. Gogte, K. M. More, and B. D. Tilak, *Indian J. Chem.*, 1974, **12**, 327, and references cited therein.

d, J 7 Hz, MeCMe), 0.96 (3H, d, J 7 Hz, MeCMe), 2.33 (3H, s, ArMe), 1.9—2.9 (m, CH₂ and CH), 7.03—7.17 (2H, m, H-5 and -6), and 7.71br (1H, s, H-8) (Found: C, 83.3; H, 8.8. C₁₄H₁₈O requires C, 83.2; H, 8.9%).

(b) *From the unsaturated acid (X)*. A solution of the acid (X) (6 g) in acetic acid (20 ml) and concentrated hydrochloric acid (20 ml) was set aside for 36 h. Acetic acid was removed *in vacuo* and the organic residue was extracted with ether. The extract was washed several times with saturated aqueous sodium hydrogen carbonate to remove any unlactonised acid. Removal of solvent furnished neutral lactonic material, b.p. 160—165° at 2 mmHg (5 g), as a viscous yellowish oil, ν_{\max} (film) 1775s (γ -lactone) and 1750 cm⁻¹ (δ -lactone). T.l.c. (silica gel) showed two very close spots. The lactonic

material (1.6 g) was treated with polyphosphoric acid as described above and the neutral product sublimed at 145—150° and 3mmHg (1.3 g); ν_{\max} (film) 1678s cm⁻¹ (C=O). Preparative t.l.c. of the ketonic material gave two components. The major, less polar component was the tetralone (VIII) (i.r. spectrum).

The 2,4-dinitrophenylhydrazone prepared from the tetralone obtained by the above procedures was identical [m.p. (167°) (from ethanol-ethyl acetate), mixed m.p., and i.r. (Nujol) and n.m.r. (CDCl₃) spectra] with the 2,4-dinitrophenylhydrazone obtained from the tetralone formed in the reaction of the lactone mixture arising from (I) with polyphosphoric acid.

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