

Polycyclic Systems. Part XVI.¹ Synthesis of 1-Isopropyl-2,8-dimethylphenanthrene

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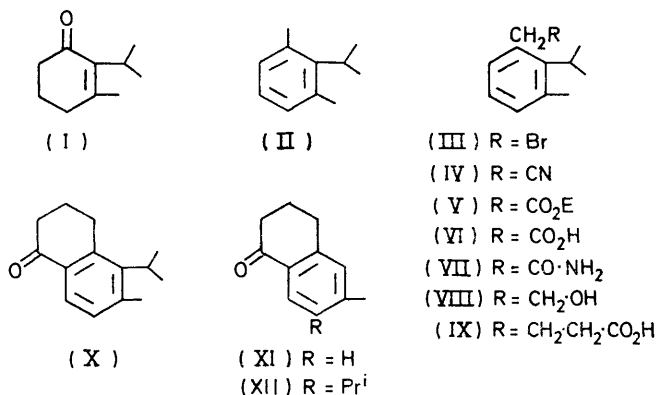
An unambiguous synthesis of 1-isopropyl-2,8-dimethylphenanthrene from 2-isopropyl-1,3-dimethylbenzene is described in which 3,4-dihydro-5-isopropyl-6-methylnaphthalen-1(2*H*)-one serves as a key intermediate. This hydrocarbon is different from one previously encountered by Short and Wang to which this formulation was ascribed. An error in the literature regarding the synthesis of this phenanthrene is corrected.

SHORT and WANG² in their attempt to synthesise a degradation product³ of the diterpene totarol, obtained a hydrocarbon, C₁₉H₂₀, m.p. 168.5–170°, by treatment of methyl 2-methoxy-8-methylphenanthrene-1-carboxylate with methylmagnesium iodide, which they formulated as 1-isopropyl-2,8-dimethylphenanthrene (XVI). The assignment was justified by the known propensity of a methoxy-group to be replaced by methyl during reaction of an adjacent hindered carbonyl group with methylmagnesium halide.⁴ Later, Bardhan and Nasipuri, during work on a general synthesis of alkylphenanthrenes,⁵ prepared what they believed to be this hydrocarbon by treatment of 3,4-dihydro-2,8-dimethylphenanthren-1(2*H*)-one with isopropylmagnesium iodide and subsequent dehydrogenation and found it to be different from that reported by Short and Wang. A reinvestigation, however, showed that the synthetic hydrocarbon was actually 1,7-dimethylphenanthrene, arising from reduction of the carbonyl group by isopropylmagnesium iodide, a common reaction of hindered ketones. Two other attempts to synthesise the title phenanthrene from 2-isopropyl-3-methylcyclohex-2-enone (I) also failed, this ketone being unreactive towards phenethylmagnesium bromide and also in attempted Reformatsky reactions with ethyl bromoacetate and with methyl γ -bromocrotonate. Meanwhile, a procedure for the preparation of 1,2-dialkyl-3-methylbenzenes from Hagemann's ester was developed in our laboratory.⁶ We now report an unambiguous synthesis of 1-isopropyl-2,8-dimethylphenanthrene (XVI) from 2-isopropyl-1,3-dimethylbenzene (II), prepared by this procedure.

2-Isopropyl-3-methylcyclohex-2-enone (I)⁷ was treated with methylmagnesium iodide and the product dehydrogenated to afford 2-isopropyl-1,3-dimethylbenzene (II) in 85% yield. The latter was submitted to a conventional series of reactions leading successively to the bromide (III), the cyanide (IV), the ester (V), and finally the crystalline acid (VI) in an overall yield of 42%. Each of the compounds including the amide (VII) obtained as a by-product in one of the reactions was characterised by n.m.r. spectra.

Bromination of the hydrocarbon (II) with *N*-bromosuccinimide also afforded 1,3-bisbromomethyl-2-isopropyl-

benzene in 12% yield, characterised by its n.m.r. spectrum. The ketone (I) was dehydrogenated to 2-isopropyl-3-methylphenol but an attempt to convert it into 1-bromo-2-isopropyl-3-methylbenzene by heating with triphenylphosphine dibromide⁸ failed, thus frustrating an alternative and possibly simpler approach to the alcohol (VIII). The ester (V) was reduced with lithium aluminium hydride to the corresponding phenethyl alcohol (VIII), and the latter converted into the arylbutyric acid (IX) by malonic ester synthesis. Cyclisation of the acid (IX) either by treatment of the derived acid chloride with anhydrous aluminium chloride or by heating



the acid with polyphosphoric acid led to a mixture of three tetralones (X)–(XII) as evidenced by g.l.c. Apparently the sterically hindered isopropyl group was partly lost and partly rearranged during acid-catalysed ring closure. The cyclisation was finally effected by replacing aluminium chloride with tin(IV) chloride in the above reaction and the tetralone (X) was obtained in 90% yield. The structure was confirmed by its n.m.r. spectrum, which showed an AB quartet for the two aromatic protons. The lability of the isopropyl group in the system precluded any conventional short synthesis by using the phenethyl bromide derived from alcohol (VIII). 1-Isopropyl-2,8-dimethylphenanthrene (XVI) was therefore synthesised by appropriate transformation of the well authenticated tetralone (X) (Scheme).

The structures of the acid (XIV), the ketone (XV), and the phenanthrene (XVI) were supported by n.m.r.

¹ Part XV, D. Nasipuri and A. Bhattacharya, *Indian J. Chem.*, 1972, **10**, 799.

² W. F. Short and H. Wang, *J. Chem. Soc.*, 1951, 2979.

³ For the synthesis of this degradation product, see D. Nasipuri and A. C. Chaudhuri, *J. Chem. Soc.*, 1958, 2579.

⁴ R. C. Fuson and R. Gaertner, *J. Org. Chem.*, 1948, **13**, 496; and earlier papers.

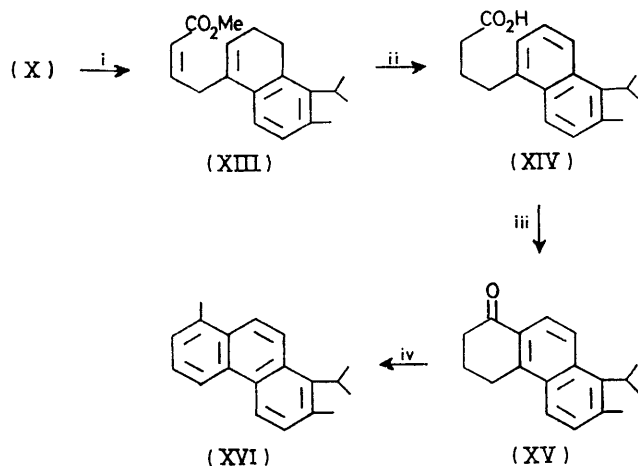
⁵ J. C. Bardhan and D. Nasipuri, *J. Chem. Soc.*, 1956, 350.

⁶ D. Nasipuri and I. De Dalal, *J.C.S. Perkin I*, 1973, 1754.

⁷ D. Nasipuri, G. Sarkar, R. Roy, and M. Guha, *J. Indian Chem. Soc.*, 1966, **43**, 383.

⁸ G. A. Wiley, R. L. Hershkowitz, B. M. Rein, and B. C. Chung, *J. Amer. Chem. Soc.*, 1964, **86**, 964

spectra. The phenanthrene (XVI) had m.p. 80.5–81°, formed a picrate, m.p. 176°, and a trinitrobenzene deriva-



SCHEME Reagents: i, $\text{BrCH}_2\text{CH}=\text{CH}\text{CO}_2\text{Me}$, Zn, C_6H_6 ; ii, heating with 10% Pd-C and hydrolysis; iii, PCl_5 followed by SnCl_4 in C_6H_6 ; iv, treatment with MeMgI , heating with 10% Pd-C

tive, m.p. 198°, and is entirely different from the hydrocarbon described by Short and Wang,² the structure of which thus remains uncertain.

EXPERIMENTAL

N.m.r. spectra were measured with a Varian T60 spectrometer for solutions in carbon tetrachloride (unless otherwise stated), with tetramethylsilane as internal standard. G.l.c. was carried out using a column (6 ft \times $\frac{1}{4}$ in) of 10% polyester of diethylene glycol adipate supported on Gas Chrom Z with nitrogen as carrier gas. I.r. spectra were measured for films (unless otherwise stated). Petroleum refers to the fraction of b.p. 40–60°. Solutions were dried over anhydrous sodium sulphate.

2-Isopropyl-3-methylcyclohex-2-enone (I).—2-Isopropyl-3-methylcyclohexenone (I), b.p. 95–100° at 12 mmHg, was obtained by alkylating Hagemann's ester with isopropyl iodide and hydrolysing the product with alkali.⁷ The unhydrolysed 1-alkylated product was left as a high boiling fraction (ca. 20%).⁹ The ketone (I) showed a single peak on g.l.c. and had n_D^{20} 1.4880; ν_{max} 1 670 cm^{-1} ; τ 7.00 (1 H, m, J 7 Hz, CHMe_2), 7.69 (4 H, m, 4- H_2 and 6- H_2), 8.02 (3 H, s, 3-Me), 8.05 (2 H, m, 5- H_2), and 8.85 (6 H, d, J 7 Hz, CMe_2).

2-Isopropyl-1,3-dimethylbenzene (II).—The foregoing ketone (24.3 g, 0.16 mol) was treated with methylmagnesium bromide (0.52 mol) in ether (250 ml) for 10 h under reflux. The cooled solution was decomposed with aqueous ammonium chloride and the product after the usual work-up afforded 2-isopropyl-1,3-dimethylcyclohexadiene (21.1 g, 88%), b.p. 73–75° at 10 mmHg. This was heated with powdered sulphur (5.1 g, 0.16 mol) at 210–220 °C for 6 h and the dark liquid distilled in steam. The organic material was separated, dried, and distilled over sodium to give 2-isopropyl-1,3-dimethylbenzene (II) as a liquid (20 g, 85%), b.p. 200–201° at 760 mmHg (Found: C, 88.7; H, 10.5. $\text{C}_{11}\text{H}_{16}$ requires C, 89.2; H, 10.8%); n_D^{20} 1.5032; τ 3.22 (3 H, s, ArH), 6.62 (1 H, m, J 7 Hz, CHMe_2), 7.67 (6 H, s, 2 \times Me), and 8.67 (6 H, d, J 7 Hz, CMe_2). It showed a single peak on g.l.c.

2-Isopropyl-3-methylphenol.—2-Isopropyl-3-methylcyclohex-2-enone (I) (7.8 g) was heated with 10% palladium-charcoal (0.78 g) in *p*-cymene (16 ml) for 5 h under nitrogen. The product on extraction with aqueous sodium hydroxide followed by acidification afforded 2-isopropyl-3-methylphenol (4.0 g), b.p. 150° at 20 mmHg; m.p. 73–74° (from petroleum) (Found: C, 80.1; H, 9.5. $\text{C}_{10}\text{H}_{14}\text{O}$ requires C, 80.0; H, 9.3%); τ (CDCl_3) 2.90–3.60 (3 H, m, ArH), 5.37 (1 H, s, OH), 6.70 (1 H, m, J 7 Hz, CHMe_2), 7.66 (3 H, s, 3-Me), and 8.66 (6 H, d, J 7 Hz, CMe_2).

Attempted Preparation of 1-Bromo-2-isopropyl-3-methylbenzene.—Triphenylphosphine dibromide, prepared from triphenylphosphine (3.93 g, 0.015 mol), bromine, and acetonitrile (13 ml) was freed from solvent under vacuum and mixed with the above phenol (1.5 g, 0.01 mol) and heated at 200 °C for 2 h. The product after usual work-up gave back the original phenol quantitatively.

2-Isopropyl-3-methylbenzyl Bromide (III).—2-Isopropyl-1,3-dimethylbenzene (14.8 g, 0.1 mol), *N*-bromosuccinimide (17.8 g, 0.1 mol), and benzoyl peroxide (0.1 g) in carbon tetrachloride (45 ml) were heated under reflux for 1 h. The monobromide (III) was obtained as an oil (15.8 g, 70%), b.p. 105–110° at 10 mmHg (Found: 57.8; H, 6.3; Br, 34.8. $\text{C}_{11}\text{H}_{15}\text{Br}$ requires C, 58.1; H, 6.6; Br, 35.2%). Some unchanged hydrocarbon was recovered as a lower boiling fraction which was re-brominated; the final yield of the bromide was 78%. The dibromide, b.p. 160° at 10 mmHg, m.p. 84–85° (Found: C, 42.5; H, 4.7; Br, 52.8. $\text{C}_{11}\text{H}_{14}\text{Br}_2$ requires C, 43.1; H, 4.6; Br, 52.3%), was obtained in 12% yield; τ (CDCl_3) 2.70 (3 H, m, ArH), 5.33 (4 H, s, 2 \times CH_2Br), 6.43 (1 H, m, J 7 Hz, CHMe_2), and 8.50 (6 H, d, J 7 Hz, CMe_2).

2-Isopropyl-3-methylbenzyl Cyanide (IV).—A mixture of 2-isopropyl-3-methylbenzyl bromide (37.5 g), sodium cyanide (26 g), potassium iodide (5.4 g), 95% ethanol (150 ml), and water (45 ml) was refluxed for 7 h. The product on usual work-up, afforded the cyanide (IV) (24.5 g, 86%), b.p. 135–140° at 10 mmHg (Found: C, 82.8; H, 8.8. $\text{C}_{12}\text{H}_{15}\text{N}$ requires C, 83.2; H, 8.7%); τ 2.95 (3 H, m, ArH), 6.33 (2 H, s, CH_2CN), 6.65 (1 H, m, J 7 Hz, CHMe_2), 7.59 (3 H, s, ArMe), and 8.62 (6 H, d, J 7 Hz, CMe_2).

Ethyl 2-Isopropyl-3-methyl-1-phenylacetate (V).—A solution of the above cyanide (22.6 g) in absolute ethanol (110 ml) cooled in ice was saturated with dry hydrogen chloride and the mixture was heated under reflux in a current of hydrogen chloride for 10 h. The solid that separated was partly dissolved in water and the mixture filtered. The filtrate was worked up for the ester (V), which was obtained as an oil (23.2 g, 81%), b.p. 143–145° at 10 mmHg (Found: C, 76.1; H, 9.2. $\text{C}_{14}\text{H}_{20}\text{O}_2$ requires C, 76.4; H, 9.1%). Hydrolysis with ethanolic sodium hydroxide afforded 2-isopropyl-3-methyl-1-phenylacetic acid (VI) (20.0 g), which crystallised from petroleum in needles (18.0 g), m.p. 81° (Found: C, 74.8; H, 8.3. $\text{C}_{13}\text{H}_{16}\text{O}_2$ requires C, 75.0; H, 8.3%); τ (CDCl_3) 0.37 (1 H, s, CO_2H), 2.90 (3 H, s, ArH), 6.24 (2 H, s, Ar CH_2), 6.65 (1 H, m, CHMe_2), 7.55 (3 H, s, Me), and 8.65 (6 H, d, CMe_2). The purified acid was re-esterified and used for reduction.

The solid collected by filtration crystallised from ethanol to give 2-isopropyl-3-methyl-1-phenylacetamide (VII), m.p. 124–125° (Found: C, 75.1; H, 9.1; N, 7.3. $\text{C}_{13}\text{H}_{17}\text{NO}$ requires C, 75.4; H, 8.9; N, 7.3%); τ (CDCl_3) 2.93 (3 H, m,

⁹ D. Nasipuri, K. Mitra, and S. Venkataraman, *J.C.S. Perkin I*, 1972, 1836.

ArH), 3.90br and 4.66br (2 H, d, NH₂), 6.37 (2 H, s, ArCH₂), 6.66 (1 H, m, CHMe₂), 7.57 (3 H, s, Me), and 8.67 (6 H, d, J 7 Hz, CMe₂). The amide was also hydrolysed to the acid (VI).

2-Isopropyl-3-methylphenethyl Alcohol (VIII).—The foregoing ester (18.4 g) was reduced with an excess of lithium aluminium hydride in ether to yield **2-isopropyl-3-methylphenethyl alcohol (VIII)** (14.2 g, 95%), b.p. 151—153° at 15 mmHg; n_D^{20} 1.5220 (Found: C, 80.5; H, 10.3. C₁₂H₁₈O requires C, 80.9; H, 10.1%). The alcohol (14.2 g, 0.081 mol) was treated with phosphorus tribromide (11.4 g, 0.042 mol) to yield the corresponding phenethyl bromide (17.1 g, 88%), b.p. 140—145° at 15 mmHg; n_D^{20} 1.544°.

γ -(2-Isopropyl-3-methyl-1-phenyl)butyric Acid (IX).—The preceding bromide (17.1 g) was condensed with diethyl malonate in the presence of ethanolic sodium ethoxide in the usual way to furnish **diethyl 2-isopropyl-3-methylphenethylmalonate** (19.4 g, 85%), b.p. 178—180° at 1.0 mmHg; n_D^{24} 1.4880 (found: C, 71.0; H, 9.0. C₁₉H₂₆O₄ requires C, 71.35; H, 8.75%). The ester (19.4 g) was hydrolysed with refluxing ethanolic 20% potassium hydroxide. The crude malonic acid (17.7 g) thus obtained was heated at 170—175° C to furnish **γ -(2-isopropyl-3-methyl-1-phenyl)butyric acid (IX)** (11.1 g), which crystallised from petroleum in white glistening needles (10.3 g, 76%), m.p. 80° (Found: C, 76.1; H, 9.5. C₁₄H₂₀O₂ requires C, 76.4; H, 9.1%).

3,4-Dihydro-5-isopropyl-6-methylnaphthalen-1(2H)-one (X).—(a) The foregoing butyric acid (3.3 g, 15 mmol), phosphorus pentachloride (3.3 g, 16 mmol), and benzene (60 ml) were stirred at room temperature for 45 min and then warmed at 45° C for 10 min. A solution of tin(IV) chloride (4.5 ml) in benzene (15 ml) was dropped into the cooled mixture during 15 min. Stirring was continued for 1 h at room temperature and for 1 h at 45° C. The mixture was decomposed with cold dilute hydrochloric acid and the product extracted with benzene. The extract was washed with dilute alkali and finally distilled to afford **3,4-dihydro-5-isopropyl-6-methylnaphthalen-1(2H)-one (X)** (2.7 g, 90%), b.p. 145° at 1 mmHg (Found: C, 83.0; H, 9.3. C₁₄H₁₈O requires C, 83.2; H, 8.9%); it solidified to a low-melting solid (30—35°); ν_{\max} 1 685 and 1 612 cm⁻¹; τ 2.30 (1 H, d, J 8 Hz, 8-H), 3.03 (1 H, d, J 8 Hz, 7-H), 6.50 (1 H, m, J 7 Hz, CHMe₂), 7.02 (2 H, t, J 5 Hz, 4-H₂), 7.60 (3 H, s, 6-Me), 7.60 (2 H, m, 2-H₂), 7.92 (2 H, m, 3-H₂), and 8.64 (6 H, d, J 7 Hz, CMe₂); **dinitrophenylhydrazone**, m.p. 240° (from benzene-methanol) (Found: N, 14.7. C₂₀H₂₂N₄O₄ requires N, 14.6%). The ketone showed a single peak on g.l.c.

(b) The acid chloride from the acid (IX) (5.0 g) was treated with anhydrous aluminium chloride (4.0 g) in carbon disulphide (25 ml) in the cold. The dark red product was decomposed with dilute hydrochloric acid and then distilled in steam. The ketonic material was extracted with benzene and distilled to afford a sweet-smelling oil (3.6 g), b.p. 125—140° at 0.5 mmHg. G.l.c. showed it to be a ca. 2 : 5 : 3 mixture of three ketones (ν_{\max} 1 685 cm⁻¹; retention times 11, 20, and 25 min). The last peak corresponded to the tetralone (X). N.m.r. spectra of the mixture indicated partial loss of the isopropyl group. The first and the second components were thus possibly the tetralones (XI) and (XII).

(c) Treatment of the acid (IX) with polyphosphoric acid at 100° C for 1 h yielded a mixture very similar to that obtained in (b) (g.l.c.). In addition, there were two minor peaks in the chromatogram.

γ -(5-Isopropyl-6-methyl-1-naphthyl)butyric Acid (XIV).—A mixture of 3,4-dihydro-5-isopropyl-6-methylnaphthalen-

1(2H)-one (X) (3.62 g, 18 mmol), methyl γ -bromocrotonate (6.5 g, 36 mmol), zinc amalgam wool (3.0 g), and dry benzene (20 ml) was heated under reflux for 1 h. More zinc amalgam (2 g), methyl γ -bromocrotonate (4.4 g), and benzene (15 ml) were added and refluxing was continued for a further 3 h. The red mixture was decomposed with ice and hydrochloric acid, and the benzene layer was separated, washed, dried, and evaporated. The residue was distilled to yield methyl γ -(3,4-dihydro-5-isopropyl-6-methyl-1-naphthyl)crotonate (XIII) (3.0 g, 58%) as a viscous gum. The methyl ester (4.5 g) was intimately mixed with palladium black (0.3 g)¹⁰ and heated at 280—300° C under carbon dioxide for 3 h. The melt was extracted with hot benzene and filtered. The viscous residue left after removal of benzene was hydrolysed with ethanolic 10% potassium hydroxide to afford **γ -(5-isopropyl-6-methyl-1-naphthyl)butyric acid (XIV)** (3.3 g), which crystallised from benzene-petroleum in white plates (1.5 g), m.p. 80° (Found: C, 80.0; H, 8.3. C₁₈H₂₂O₂ requires C, 80.0; H, 8.1%); τ 2.00 (1 H, 2d, J 9 and 3 Hz, 4-H), 2.30 (1 H, d, J 9 Hz, 8-H), 2.84 (3 H, m, ArH), 6.20 (1 H, m, J 7 Hz, CHMe₂), 6.94 (2 H, t, J 7 Hz, ArCH₂), 7.50 (3 H, s, 6-Me), 7.52—8.26 (4 H, m, 2 \times CH₂), and 8.45 (6 H, d, J 7 Hz, CMe₂).

3,4-Dihydro-8-isopropyl-7-methylphenanthren-1(2H)-one (XV).—A mixture of the foregoing acid (1.62 g, 6 mmol) with phosphorus pentachloride (1.28 g, 6.1 mmol) in benzene (25 ml) was stirred at room temperature for 30 min, and then warmed at 50° C for 5 min. A solution of tin(IV) chloride (1.8 ml) in benzene (10 ml) was added at 5—10° C within 15 min and stirring was continued for 1 h at room temperature and for another 1 h at 45° C. The product on conventional work-up yielded a neutral material (1.26 g) which was passed through a column of activated alumina (benzene-petroleum as eluant). **3,4-Dihydro-8-isopropyl-7-methylphenanthren-1(2H)-one (XV)** was obtained as a gum (1.2 g, 80%) (Found: C, 85.9; H, 8.1. C₁₈H₂₀O requires C, 85.7; H, 7.9%); it gave a single spot on t.l.c. and showed ν_{\max} (CHCl₃) 1 680 cm⁻¹; τ 2.00 (2 H, ABq, 10- and 9-H), 2.55 (2 H, ABq, J 9 Hz, 5- and 6-H), 6.20 (1 H, m, CHMe₂), 6.75 (2 H, t, J 6 Hz, 4-H₂), 7.48 (3 H, s, 7-Me), 7.30—8.14 (4 H, m, 2 \times CH₂), and 8.50 (6 H, d, J 7 Hz, CMe₂); **dinitrophenylhydrazone**, m.p. 288° (from benzene-methanol) (Found: N, 13.1. C₂₄H₂₄N₄O₄ requires N, 13.0%).

1-Isopropyl-2,8-dimethylphenanthrene (XVI).—A solution of the preceding ketone (1.3 g) in benzene (40 ml) was heated with an excess of methylmagnesium iodide in ether. The product after the usual work-up furnished an alcohol, m.p. 130—135°, which was heated with 10% palladium-charcoal (0.7 g) at 300° C for 2 h. The hydrocarbon was taken up in petroleum and passed through an alumina column to yield a gum (700 mg). This was directly converted into the picrate, m.p. 170—173°, which in turn was eluted through an alumina column with ether to afford **1-isopropyl-2,8-dimethylphenanthrene (XVI)** as a crystalline solid (420 mg, 32%), m.p. 75—80°. It crystallised from benzene-petroleum or methanol to furnish shining flakes, m.p. 80.5—81° (Found: C, 91.7; H, 8.4. C₁₉H₂₀ requires C, 91.9; and H, 8.1%); τ 1.50—1.82 (2 H, m, 4- and 5-H), 1.90—2.40 (2 H, m, 9- and 10-H), 2.50—2.85 (3 H, m, ArH), 6.20 (1 H, m, CHMe₂), 7.30 (3 H, s, 8-Me), 7.46 (3 H, s, 2-Me), and 8.48 (6 H, d, J 7 Hz, CMe₂); **picrate**, m.p. 176° (from ethanol) (Found: 62.5; H, 5.0; N, 8.9. C₂₅H₂₃N₃O₇ requires C, 62.9; H, 4.8; N, 8.8%);

¹⁰ D. Nasipuri and A. K. Mitra, *J.C.S. Perkin I*, 1973, 285; J. W. Cook and R. Schoental, *J. Chem. Soc.*, 1945, 288.

trinitrobenzene derivative, m.p. 198° (from ethanol) (Found: C, 64.9; H, 5.2; N, 9.0. $C_{25}H_{23}N_3O_6$ requires C, 65.0; H, 5.0; N, 9.1%). Short and Wang report ² m.p.s 168.5—170° and 177—179° for their hydrocarbon and trinitrobenzene derivative, respectively.

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