191. *Chemistry of Indanthrone. Part VIII.** 3 : 3′-*Dimethyl Derivatives of Indanthrone and Flavanthrone.*

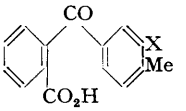
By William Bradley and Harry E. Nursten.

Both in its properties and the methods available for its preparation 3 : 3′-dimethylindanthrone resembles indanthrone and differs from 3 : 3′-di-*tert.*-butylindanthrone.

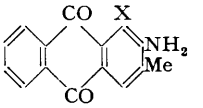
In Part V (*J.*, 1951, 2170) we described the preparation and properties of 3 : 3′-di-*tert.*-butylindanthrone and mentioned several unexpected aspects of its chemistry. The unusual features were considered to result from the presence of *tert.*-butyl groups as 3 : 3′-substituents and this view has now been tested by a study of the dimethyl analogue.

Heated with concentrated nitric acid at the boiling point *o*-(*p*-toluoyl)benzoic acid gave mainly the 3′-nitro-derivative (I; X = NO_2), but *o*-(4-methyl-2-nitrobenzoyl)benzoic acid and *p*-nitrotoluene were formed in small amounts. Under the same conditions *o*-(*p*-*tert.*-butylbenzoyl)benzoic acid gave a higher yield of *o*-(4-*tert.*-butyl-2-nitrobenzoyl)benzoic acid and *p*-nitro-*tert.*-butylbenzene.

Reduction of the 3′-nitro-acid gave *o*-(3-amino-4-methylbenzoyl)benzoic acid (I; X = NH_2), and from this 2-amino-3-methylanthraquinone (II; X = H) was obtained in low yield, together with 1-amino-2-methylanthraquinone, by heating with sulphuric acid. The use of the methyl ester of the 3-amino-acid did not improve the yield, but a better result was obtained with methyl *o*-(3-diacetylamino-4-methylbenzoyl)benzoate. The 3′-amino-acid yielded a triacetyl derivative (III); this also proved difficult to convert



(I)



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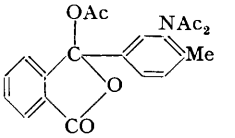


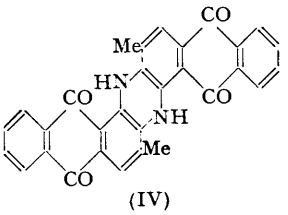
(III)

into a derivative of anthraquinone. Unlike 2-amino-3-*tert.*-butylanthraquinone the 3-methyl analogue was easily substituted by bromine, 2-amino-1-bromo-3-methylanthraquinone (II; X = Br) being formed. When heated with potassium hydroxide at 220° 2-amino-3-methylanthraquinone gave 3 : 3′-dimethylindanthrone (IV) in small yield; there was no indication of the formation of a flavanthrone derivative, nor did the latter result at 300°. In contrast the 3-*tert.*-butyl analogue afforded a flavanthrone derivative in small yield at the lower temperature and readily at the higher. The same 3 : 3′-dimethylindanthrone resulted also when 2-amino-1-bromo-3-methylanthraquinone was heated with cupric acetate and sodium acetate. Heated with antimony pentachloride in nitrobenzene 2-amino-3-methylanthraquinone afforded 3 : 3′-dimethylflavanthrone (V). 2-Amino-3-*tert.*-butylanthraquinone did not react under these conditions. Thus in the reactions with both potassium hydroxide and antimony pentachloride 2-amino-3-methylanthraquinone resembles 2-aminoanthraquinone, and the exceptional properties of 2-amino-3-*tert.*-butylanthraquinone must be attributed to the *tert.*-butyl group. A product described as 3 : 3′-dimethylindanthrone has been prepared by the oxidation of 2-amino-3-methylanthraquinone and by the elimination of hydrogen bromide from 2-amino-1-bromo-3-methylanthraquinone (D.R.-P. 238,979). Preparations of 3 : 3′-dimethylflavanthrone are given in D.R.-P. 599,246 and 599,914.

The principal interest of the present work is to emphasise the effect of *tert.*-butyl groups in promoting the formation of flavanthrone derivatives and in restraining the formation of the corresponding indanthrone compounds. In Part I (Bradley and Leete, *J.*, 1951, 2129) it was shown that the conversion of 2-aminoanthraquinone into indanthrone on fusion with alkali hydroxides depends on the intermediate formation of the anion (VI; R = H) and its further reaction with 2-aminoanthraquinone. That a 3-methyl substituent (VI;

* Part VII, *J.*, 1952, 3027.

R = Me) has little effect on the course of the change is not unexpected, but a 3-*tert.*-butyl substituent (VI; R = CMe_3) should reduce the rate by steric hindrance. The same effect would favour the alternative course of reaction which proceeds through the carbanion (VII; R = CMe_3) and results in the observed formation of 3 : 3′-di-*tert.*-butylflavanthrone (Part V).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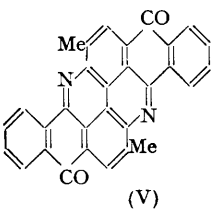
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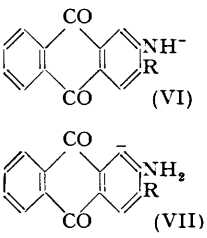
(VI) (VII)

3 : 3′-Dimethylindanthrone is less stable than indanthrone towards illumination in chlorobenzene but more stable than the 3 : 3′-di-*tert.*-butyl analogue; the progression follows that of ease of electron release in the series H, Me, CMe_3. The solubilities of the three compounds in chlorobenzene increase in the same order. Compared with *NN*′-dimethylindanthrone (Bradley and Leete, *loc. cit.*), 3 : 3′-dimethylindanthrone is much less soluble in organic solvents, a further confirmation of the occurrence of intermolecular hydrogen-bonding in indanthrone and its simple nuclear-substituted derivatives.

Both 1-amino-2-methyl- and 2-amino-3-methyl-anthraquinone afforded *N*-diacetyl derivatives with ease (cf. Sudborough, *Proc.*, 1901, **17**, 45), and 1-diacetylamino-2-methylanthraquinone yields 1-acetamido-2-methylanthraquinone when it is chromatographed on alumina from a cold solution in benzene.

Experimental

Methyl o-(4-*Methyl*-3-*nitrobenzoyl*)*benzoate*.—Nitration of *o*-(4-methylbenzoyl)benzoic acid using nitric acid and concentrated sulphuric acid essentially as in B.I.O.S. 987, p. 146, gave colourless leaflets, m. p. 208—209°, with some previous sintering (Found: C, 63·3; H, 3·5; N, 4·5. Calc. for $C_{15}H_{11}O_5N$: C, 63·2; H, 3·9; N, 4·9%). B.I.O.S. 987 (*loc. cit.*) states m. p. 196—198°; no analysis is recorded.

Methyl o-(4-*methyl*-3-*nitrobenzoyl*)*benzoate* crystallised from methanol in colourless rhombs, m. p. 108—109° (Found: C, 64·3; H, 4·4; N, 5·0. $C_{16}H_{13}O_5N$ requires C, 64·2; H, 4·3; N, 4·7%).

o-(4-*Methyl*-2-*nitrobenzoyl*)*benzoic Acid*.—A solution of *o*-(4-methylbenzoyl)benzoic acid (20 g.) in nitric acid (*d* 1·42; 100 c.c.) was refluxed for an hour. On cooling, the 3-nitro-derivative (21 g.) separated. The mother-liquor was distilled in steam; colourless crystals, m. p. 49—50° (0·2 g.), formed in the distillate. Crystallisation from methanol gave needles, m. p. 51—52°, not depressed by admixture with *p*-nitrotoluene. Evaporation of the methano mother-liquor gave a mixture of oil and crystals, and this, crystallised from toluene and then in turn from benzene, toluene, and alcohol–light petroleum (b. p. 60—80°), gave colourless, prismatic needles, m. p. 188—189·5°, which were not quite pure (Found: C, 62·5, 62·7; H, 3·8, 4·0; N, 4·8%). Admixture with the 3-nitro-compound depressed the m. p. to 170—185°.

o-(3-*Amino*-4-*methylbenzoyl*)*benzoic Acid*.—A solution of the 3-nitro-acid (10 g.) in aqueous ammonia (*d* 0·880; 250 c.c.) was added to ferrous sulphate crystals (75 g.) in water (100 c.c.). The mixture was boiled for 15 minutes, then filtered. The filtrate, evaporated to small volume and then acidified with acetic acid, gave an oil which crystallised partly (8·8 g.). Repeated crystallisation from toluene gave pale yellow crystals of o-(3-*amino*-4-*methylbenzoyl*)*benzoic acid*, m. p. 197·5° (decomp.) (Found: C, 70·7; H, 5·1; N, 5·8. $C_{15}H_{13}O_3N$ requires C, 70·6; H, 5·1; N, 5·5%). In B.I.O.S. 987, p. 147, a product, m. p. 127—130°, is stated to be the 3-amino-acid. It was prepared by reduction of the 3-nitro-acid with hydrogen and nickel.

Methyl o-(3-*amino*-4-*methylbenzoyl*)*benzoate*, obtained by esterifying the 3-amino-acid, m. p. 197·5°, or by reducing methyl *o*-(3-nitro-4-methylbenzoyl)benzoate with iron and hydrochloric acid in aqueous methanol, formed colourless prisms, m. p. 116·5—117·5° (Found: C, 71·3; H, 5·5; N, 5·6. $C_{16}H_{15}O_3N$ requires C, 71·4; H, 5·6; N, 5·2%). Acetylation with acetic anhydride and pyridine at the b.p., followed by cooling, afforded *methyl* o-(3-*diacetylamino*-4-

methylbenzoyl)benzoate, m. p. 127—127·5° (Found: C, 67·7; H, 5·5; N, 3·7. $C_{20}H_{19}O_5N$ requires C, 68·0; H, 5·4; N, 4·0%). It crystallised from alcohol in colourless tablets. When the acetylation mixture was added to water an oil separated which later solidified. Recrystallisation from alcohol–light petroleum (b. p. 60—80°) gave colourless needles of *methyl* o-(3-*acetamido*-4-*methylbenzoyl*)*benzoate*, m. p. 209—210° (Found: C, 69·1; H, 5·2; N, 4·6. $C_{17}H_{15}O_4N$ requires C, 68·7; H, 5·1; N, 4·7%). When the acetylation was continued for 7 hours the product which separated on cooling was a *triacetyl* derivative (III) (yield 78%). After repeated crystallisation from alcohol–light petroleum (b. p. 60—80°) this was obtained as colourless crystals, m. p. 182° (Found: C, 66·1, 66·3; H, 5·2, 4·9; N, 3·7, 3·9. $C_{21}H_{19}O_6N$ requires C, 66·2; H, 5·0; N, 3·7%).

1-*Amino*-2-*methylanthraquinone and* 2-*Amino*-3-*methylanthraquinone*.—A solution of the triacetyl derivative (3 g.) in sulphuric acid (30 c.c.) was heated at 175° for 10 min., then cooled and added to water. The precipitate after extraction with boiling 5% sodium carbonate solution gave an insoluble product (1·5 g.). This was chromatographed in benzene on alumina, and 1-amino-2-methylanthraquinone was isolated from the more mobile zone as silky red needles, m. p. 207—207·5° (0·17 g.) (Found: C, 76·0; H, 4·7; N, 5·9. Calc. for $C_{15}H_{11}O_2N$: C, 76·0; H, 4·6; N, 5·9%). (Roemer and Link, *Ber.*, 1883, **16**, 695, state m. p. 202°.) From the less mobile band 2-amino-3-methylanthraquinone was obtained as orange needles, m. p. 261—262° (0·25 g.) (Found: C, 75·7; H, 4·6; N, 6·2%). G.P. 281,010 states m. p. 258—259°, but no analysis is recorded.

The cyclisation of methyl *o*-(3-amino-4-methylbenzoyl)benzoate under the same conditions gave 1-amino-2-methylanthraquinone (6%) and 2-amino-3-methylanthraquinone (12%). The use of the free acid gave low yields of impure material. Methyl *o*-(3-diacetylamino-4-methylbenzoyl)benzoate gave 7% of 1-amino-2-methylanthraquinone and 13% of 2-amino-3-methylanthraquinone after 10 min., and 13% and 24% of the two isomers, respectively, after an hour. Neither isomer gave a colour with methanolic potassium hydroxide in pyridine (cf. Bradley and Leete, *J.*, 1951, 2129).

1-*Diacetylamino*-2-*methylanthraquinone* resulted when 1-amino-2-methylanthraquinone (0·18 g.) was refluxed with acetic anhydride for an hour. The product, obtained by evaporation to small volume and cooling, separated as crystals (0·21 g.), and these, further purified from alcohol and then from acetic acid, gave pale yellow rhombs, m. p. 203·5—204·5° (Found: C, 71·3; H, 4·5; N, 4·7. $C_{19}H_{15}O_4N$ requires C, 71·0; H, 4·7; N, 4·4%).

1-*Acetamido*-2-*methylanthraquinone* was formed when 1-diacetylamino-2-methylanthraquinone (0·1 g.) was chromatographed in benzene on alumina. The single pale yellow band gave yellow needles (0·07 g.), m. p. 217° (Found: C, 73·0; H, 4·7; N, 4·8. $C_{17}H_{13}O_3N$ requires C, 73·1; H, 4·7; N, 5·0%). A mixture with 1-diacetylamino-2-methylanthraquinone melted below 180°. Roemer and Link (*loc. cit.*) describe a product, m. p. 176—177°, as 1-acetamido-2-methylanthraquinone, but it was light red and for this reason may have contained 1-amino-2-methylanthraquinone.

2-*Diacetylamino*-3-*methylanthraquinone* was prepared by refluxing 2-amino-3-methylanthraquinone with acetic anhydride for 5 hours. The product, crystallised from acetic anhydride, formed faintly yellow clusters, m. p. 209—210° (Found: C, 70·9; H, 4·9; N, 4·1. $C_{19}H_{15}O_4N$ requires C, 71·0; H, 4·7; N, 4·4%).

2-*Amino*-1-*bromo*-3-*methylanthraquinone*.—To a solution of 2-amino-3-methylanthraquinone (0·35 g.) in acetic acid (30 c.c.) were added water (6 c.c.) and then 12 c.c. of a solution of bromine (1 c.c.) in acetic acid (100 c.c.). The mixture was heated for 2 hours on the steam-bath and then added to water. The precipitate (0·43 g.) was chromatographed from benzene on alumina; it gave a single, orange, main zone. From this 2-*amino*-1-*bromo*-3-*methylanthraquinone* was eluted by means of acetone. Crystallisation from acetic acid gave rosettes of orange needles, m. p. 204—204·5° (Found: C, 57·2; H, 2·8; N, 4·7; Br, 25·15. $C_{15}H_{10}O_2NBr$ requires C, 57·0; H, 3·2; N, 4·4; Br, 25·3%). The compound formed a greenish-yellow solution in concentrated sulphuric acid. Its yellow-orange solution in pyridine became greener on the addition of methanolic potassium hydroxide. This compound is mentioned in D.R.-P. 238,979 but no preparation is given. Heated with benzoyl chloride and pyridine at the b. p. for 12 hours the amine afforded 1-*bromo*-2-*dibenzoylamino*-3-*methylanthraquinone*, which crystallised from alcohol as pale yellow needles, m. p. 243—244° (Found: C, 66·3; H, 3·6; N, 2·7; Br, 15·15. $C_{29}H_{18}O_4NBr$ requires C, 66·4; H, 3·4; N, 2·7; Br, 15·3%).

3 : 3′-*Dimethylindanthrone*.—This was prepared from 2-amino-1-bromo-3-methylanthraquinone (0·5 g.) essentially as described in D.R.-P. 238,979 except that *o*-dichlorobenzene (30 c.c.) was employed as solvent and anhydrous sodium acetate (0·5 g.) with a small proportion of

cupric acetate as the condensing agent. After 24 hours' refluxing the insoluble material was washed with hot *o*-dichlorobenzene, methyl alcohol, water, and finally methyl alcohol. The product consisted of blue needles (0·25 g.). The following supplements the description given in the above patent. After extraction with boiling quinoline (250 c.c.) the insoluble material (Found: C, 75·8; H, 3·7; N, 5·8. Calc. for $C_{30}H_{18}O_4N_2$: C, 76·6; H, 3·8; N, 6·0%) gave a greenish-blue solution in 1-chloronaphthalene, which at a concentration of *ca.* 0·001% showed maximum light absorption at 770 ($\varepsilon = 2{\cdot}90 \times 10^4$) and 705 mμ ($\varepsilon = 2{\cdot}27 \times 10^4$). A similar solution of 3 : 3′-di-*tert.*-butylindanthrone (*J.*, 1951, 2170) showed maximum absorption at 796 ($\varepsilon = 3{\cdot}32 \times 10^4$) and 727 mμ ($\varepsilon = 2{\cdot}60 \times 10^4$). In concentrated sulphuric acid 3 : 3′-dimethylindanthrone gave a brown solution with the following maxima at *ca.* 0·001% concentration:

Max. (mμ)	235	299	335	410	468	840	889
$10^{-4}\varepsilon$	2·48	5·01	3·66	1·28	1·16	1·76	1·72

A solution in 1-chloronaphthalene became green on exposure to light, but the change was slower than with the 3 : 3′-di-*tert.*-butyl analogue. The blue solution in pyridine became green on the addition of methanolic potassium hydroxide and dull olive with excess of the reagent. The further addition of methyl alcohol restored the blue colour.

3 : 3′-Dimethylindanthrone also resulted when 2-amino-3-methylanthraquinone (0·2 g.) was heated with potassium hydroxide (5 g.) at 220° for 20 minutes. The cooled product was added to hot water (70 c.c.) containing a small proportion of sodium dithionite, the resulting suspension was filtered, and the filtrate aerated. The precipitate was collected, dried, and extracted with hot *o*-dichlorobenzene; the filtered extract afforded 3 : 3′-dimethylindanthrone (0·01 g.) on cooling.

3 : 3′-*Dimethylflavanthrone.*—A solution of antimony pentachloride (0·5 c.c.) in nitrobenzene (2 c.c.) was added to one of 2-amino-3-methylanthraquinone (0·2 g.) in an equal volume of the same solvent. The mixture was refluxed for an hour. The colour changed rapidly to brown and a solid separated. On cooling, this was collected, and washed in turn with nitrobenzene and alcohol. 3 : 3′-*Dimethylflavanthrone* (0·037 g.) formed bronze needles (Found: C, 80·9; H, 3·7; N, 6·2. $C_{30}H_{16}O_2N_2$ requires C, 82·6; H, 3·7; N, 6·4%) which dissolved in concentrated sulphuric acid with an orange colour, and in alkaline sodium dithionite forming a blue solution. Methanolic potassium hydroxide added to the pale yellow solution in hot pyridine caused a colour change to green, and with more of the reagent to blue.

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