843. 1 : 2-*Dihydro-2-thianaphthalene Derivatives. Part III.** *Further Examples of the Conversion of* 1 : 2-*Dihydro-1-keto-2-thianaphthalenes into Indanones.*

By J. J. Brown and G. T. Newbold.

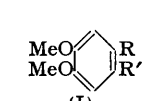
Reaction of 1 : 2-dihydro-1-keto-6 : 7-dimethoxy- and -6 : 7-methylenedioxy-2-thianaphthalene-3-carboxylic acid with Raney nickel give respectively 5 : 6-dimethoxy- and 5 : 6-methylenedioxy-indan-1-one. The latter compound has been obtained by the action of Raney nickel on hydrastal (6-vinylpiperonaldehyde).

Continuing the study of the conversion of 1 : 2-dihydro-1-keto-2-thianaphthalene-3-carboxylic acids into indanones (Dijksman and Newbold, *J.*, 1952, 13), we have turned to the action of Raney nickel on 1 : 2-dihydro-1-keto-6 : 7-dimethoxy- (II) and -6 : 7-methylenedioxy-2-thianaphthalene-3-carboxylic acid (V). These were selected because of the relationship between the expected products 5 : 6-dimethoxy- (III) and 5 : 6-methylenedioxy-indan-1-one (VI) to 4 : 5-dimethoxy-2-vinylbenzaldehyde (I; R = $CH{:}CH_2$, R′ = CHO), a degradation product of cryptopine (Perkin, *J.*, 1916, **109**, 815) and hydrastal (IV; R = $CH{:}CH_2$, R′ = CHO), obtained by degradation of hydrastine (Freund, *Ber.*, 1889, **22**, 2329) respectively.

The starting materials for the preparation of the required thianaphthalene acids were *m*-opianic acid (I; R = CO_2H, R′ = CHO) and 4 : 5-methylenedioxyphthalaldehydic acid (IV; R = CO_2H, R′ = CHO). *m*-Opianic acid has been synthesised by several

* Part II, *J.*, 1952, 13.

methods, of which none is of preparative use (Fargher and Perkin, *J.*, 1921, **119**, 1724; Perkin and Stoyle, *J.*, 1923, **123**, 3171; Chakravarti and Swaminathan, *J. Indian Chem. Soc.*, 1934, **11**, 715). *m*-Meconin, the lactone of (I; R = CO_2H, R′ = CH_2OH), is readily available, being formed, albeit in low yield, by the action of paraformaldehyde in hydrochloric acid on veratric acid (Edwards, Perkin, and Stoyle, *J.*, 1925, **127**, 195). These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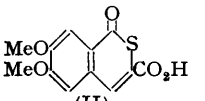
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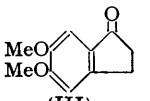
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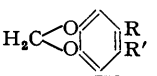
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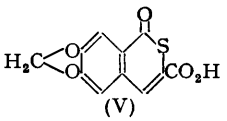
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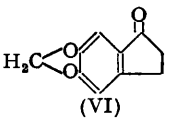
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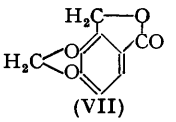
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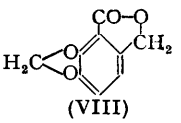
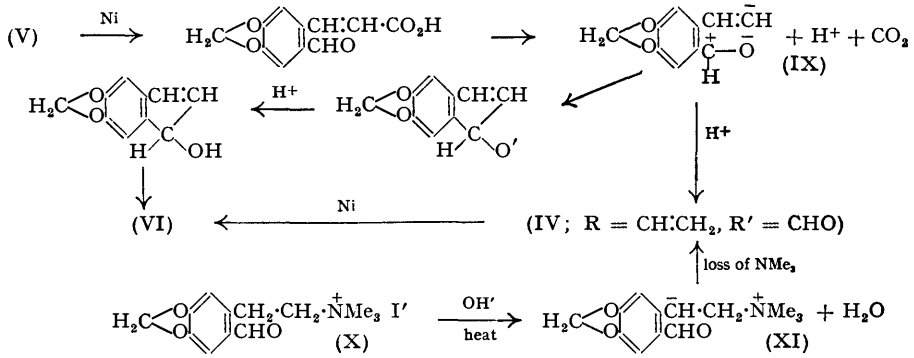

(VIII)

authors, however, reported that oxidation of *m*-meconin with manganese dioxide in sulphuric acid gave only traces of *m*-opianic acid (I; R = CO_2H, R′ = CHO). An alternative method of oxidation was therefore desirable and was suggested by the experience of Hirshberg, Lavie, and Bergmann (*J.*, 1951, 1030) who showed that phthalide could be smoothly converted by aid of *N*-bromosuccinimide into 3-bromophthalide, which readily gives phthalaldehydic acid when heated with water (Racine, *Annalen*, 1887, **239**, 79). We find that bromination of *m*-meconin with *N*-bromosuccinimide followed by hydrolysis without isolation of the intermediate bromo-compound gives *m*-opianic acid in 65% yield. Similar treatment of 5 : 6-methylenedioxyphthalide, the lactone of (IV; R = CO_2H, R′ = CH_2OH), readily prepared from homopiperonylic acid after Stevens (*J.*, 1927, 178; Stevens and Robertson, *ibid.*, p. 2790), gave 4 : 5-methylenedioxyphthalaldehydic acid (IV; R = CO_2H, R′ = CHO) in 72% yield. Stevens and Robertson (*loc. cit.*) reported that (IV; R = CO_2H, R′ = CHO) could not be obtained from the lactone of (IV; R = CO_2H, R′ = CH_2·OH) by oxidation with manganese dioxide or lead dioxide in sulphuric or acetic acid or by use of chromium trioxide in acetic acid. 4 : 5-Methylenedioxyphthalaldehydic acid has been prepared by Chakravarti, Swaminathan, and Venkataraman (*J. Indian Chem. Soc.*, 1940, **17**, 264) by a similar route to that described by Chakravarti and Swaminathan (*loc. cit.*) for *m*-opianic acid. An attempt was made to prepare 5 : 6-methylenedioxyphthalide by the action of paraformaldehyde in hydrochloric acid on piperonylic acid (IV; R = CO_2H, R′ = H), though Edwards, Perkin, and Stoyle (*loc. cit.*) reported that piperonylic acid on long boiling with formaldehyde and hydrochloric acid gave a small yield of an easily oxidised substance of high molecular weight. We confirmed that the bulk of piperonylic acid was recovered after the reaction, but isolated a small quantity of a compound $C_9H_6O_4$, m. p. 176—178°, having the properties of a phthalide and whose ultra-violet light absorption (see Experimental) is similar to that of 5 : 6-methylenedioxyphthalide. We believe this compound to be 4 : 5-methylenedioxyphthalide (VII). The third isomer, 6 : 7-methylenedioxyphthalide (VIII), m. p. 233—234°, has been synthesised by Perkin and Trikojus (*J.*, 1926, 2925) and by Groenewoud and Robinson (*J.*, 1936, 199).

Dijksman and Newbold (Part I, *J.*, 1951, 1213) prepared rhodanine condensation products from the methyl esters of phthalaldehydic and opianic acid and then proceeded by alkaline treatment of these intermediates to the 1 : 2-dihydro-1-keto-2-thianaphthalene-3-carboxylic acids. In order to obviate the preparation of such methyl esters, the direct condensation of opianic acid with rhodanine in acetic acid in the presence of sodium acetate was examined; under these conditions 2-carboxyacetophenone gave 5-(*o*-carboxy-α-methylbenzylidene)rhodanine (*loc. cit.*). Surprisingly, opianic acid gave a monosodium salt of 5-(2-carboxy-3 : 4-dimethoxybenzylidene)rhodanine, from which the free acid could be liberated by dissolution of the salt in aqueous sodium carbonate followed by acidification with mineral acid. Both the sodium salt and the free rhodanine acid were converted into 1 : 2-dihydro-1-keto-7 : 8-dimethoxy-2-thianaphthalene-3-carboxylic acid by hot aqueous sodium hydroxide. Reaction of *m*-opianic acid and 4 : 5-methylene-

dioxyphthalaldehydic acid with rhodanine gave the sodium salts of the respective rhodanine derivatives (I; R = CO_2H, R' = CH:C·CO·NH·CS·S) and (IV; R = CO_2H, R' = CH:C·CO·NH·CS·S), from which the free rhodanine acids were liberated for charac terisation The respective sodium salts were directly converted into 1 : 2-dihydro-1-keto-6 : 7-dimethoxy- (II) and -6 : 7-methylenedioxy-2-thianaphthalene-3-carboxylic acid (V) by heating them with alkali; (II) and (V) were characterised as their methyl esters.

Reduction of (II) and (V) in boiling ethanol with Raney nickel gave respectively 5 : 6-dimethoxy- (III) and 5 : 6-methylenedioxy-indan-1-one (VI). The crude products in both cases gave a blue colour with concentrated sulphuric acid in acetic acid, a very sensitive and specific test for *o*-vinyl-aldehydes (Bick, Ewen, and Todd, *J.*, 1949, 2767; Bick and Todd, *J.*, 1950, 1606), though the intensity of the colour compared with that given by hydrastal (IV; R = CH:CH_2, R' = CHO) indicated the presence of only traces of such compounds; no 4 : 5-dimethoxy-2-vinylbenzaldehyde (I; R = CH:CH_2, R' = CHO) or hydrastal could be isolated in the two experiments. A mechanism was suggested in Part II of this series (*loc. cit.*) for the conversion of the thianaphthalenecarboxylic acids into indanones based on that suggested by Wiley and Hobson (*J. Amer. Chem. Soc.*, 1949, **71**, 2429) for the cyclisation of *o*-formylcinnamic acid to indan-1-one. In the 4 : 5-methylenedioxyphthalaldehydic acid series this would be as below :



Hydrastal could be formed from the ion (IX) by addition of a proton. There is no possibility of indanone formation during the preparation of hydrastal by application of the Hofmann elimination reaction to hydrastininium iodide (X) (Freund, *loc. cit.*) since, according to current views on the Hofmann elimination reaction (see Ingold and Hughes, *Trans. Faraday Soc.*, 1941, **37**, 657), loss of a proton from the 'onium hydroxide from (X) would give an intermediate (XI) which would lose trimethylamine to give hydrastal (IV; R = CH:CH_2, R' = CHO). We have found that hydrastal is isomerised to 5 : 6-methylenedioxyindan-1-one (VI) by boiling it in ethanol in the presence of Raney nickel; the reagent may effect the change from (IV; R = CH:CH_2, R' = CHO) to the ion (IX) by loss of a proton; the formation of (VI) could then occur by the scheme above. This direct conversion of (IV; R = CH:CH_2, R' = CHO) into (VI) suggests that the formation of indan-1-one by the action of Raney nickel on 1 : 2-dihydro-1-keto-2-thianaphthalene described in Part II (*loc. cit.*) may proceed by a similar mechanism, and that *o*-vinylbenzaldehyde could be an intermediate.

Catalytic reduction of hydrastal over palladium gives 6-ethylpiperonaldehyde (IV; R = Et, R' = CHO), isolated as its 2 : 4-dinitrophenylhydrazone (cf. Späth, Schmid, and Sternberg, *Ber.*, 1934, **67**, 2095, who reduced the vinyl group in the analogous norcotarnone).

Experimental

m-*Meconin.*—This compound was prepared from veratric acid according to Perkin (*J.*, 1925, **127**, 195) in 12% yield. A specimen crystallised from aqueous ethanol as needles, m. p. 158°, having light absorption in ethanol: Max. at 220 (ε = 24,100), 258 (ε = 9400), and 294 mμ (ε = 7200).

5 : 6-*Methylenedioxyphthalide.*—By the method given in *Org. Synth.*, Coll. Vol. II, p. 55, for

the azlactone of veratraldehyde, piperonal gave 5-(3 : 4-methylenedioxybenzylidene)-2-phenyloxazol-4-one, m. p. 196—197° (Kropp and Decker, *Ber.*, 1909, **42**, 1188, give m. p. 197°), in 90% yield; the latter was converted into ethyl homopiperonylate, b. p. 130°/2 mm. (Keimatsu, *J. Pharm. Soc. Japan*, 1933, **53**, 1070, gives b. p. 145—147°/8 mm.), in 50% yield by the method described for ethyl homoveratrate (*Org. Synth.*, Coll. Vol. II, p. 333). Hydrolysis gave homopiperonylic acid, m. p. 127° (95%) (Mauthner, *Annalen*, 1909, **370**, 368, gives m. p. 127°), which by the method of Stevens (*loc. cit.*) and Stevens and Robertson (*loc. cit.*) gave 5 : 6-methylenedioxyphthalide as needles, m. p. 188—189° (lit., m. p. 188—189°) from aqueous ethanol. It showed light absorption in ethanol : Max. at 220 (ε = 21,800), 256 (ε = 5400), and 298 mμ (ε = 7300).

4 : 5-*Methylenedioxyphthalide*.—Piperonylic acid (45 g.) was heated with hydrochloric acid (200 c.c.; *d* 1·19) and formaldehyde (45 c.c.; 40%) on the steam-bath for 12 hours. The reaction mixture was diluted with an equal volume of water and filtered from unchanged piperonylic acid (40 g.). The filtrate gradually deposited a solid (1·0 g.), m. p. *ca.* 135°, which after five crystallisations from aqueous ethanol gave 4 : 5-*methylenedioxyphthalide* (100 mg.) as long fine needles, m. p. 176—178°, depressed to 145—150° on mixture with 5 : 6-methylenedioxyphthalide [Found: C, 60·7; H, 3·5%; *M* (Rast), 192. $C_9H_6O_4$ requires C, 60·7; H, 3·4%; *M*, 178]. Light absorption in ethanol : Max. at 224 (ε = 25,100), 270 (ε = 6250), and 294 mμ (ε = 4900). The compound is more soluble in water than the 5 : 6-isomer, but dissolves in 5% aqueous potassium hydroxide on warming and is precipitated from the cold solution on acidification with hydrochloric acid. It dissolves in aqueous sodium carbonate on warming, crystallising out on cooling.

m-*Opianic Acid*.—A solution of *m*-meconin (10 g.) in dry benzene (250 c.c.) was distilled until 50 c.c. of distillate were collected and then treated successively with dry carbon tetrachloride (200 c.c.) and *N*-bromosuccinimide (18·5 g.). The mixture was heated under reflux on the steam-bath for 2 hours while irradiated with a 60-watt lamp adjacent to the flask. The cooled reaction mixture was filtered from succinimide, and the filtrate evaporated under reduced pressure to give a yellow oil, which was stirred with water (250 c.c.) on the steam-bath for 1 hour. The yellow solution was decanted from tar, heated on the steam-bath, and treated with aniline, added in portions until an excess was present. Methanol (50 c.c.) was added, and the mixture allowed to cool. The aniline compound was separated, washed with methanol (20 c.c.), and dried (13·5 g.; m. p. 213—214°; Fargher and Perkin, *loc. cit.*, give m. p. 213—214°). The aniline compound was hydrolysed by heating it with hydrochloric acid (100 c.c.; 3N) on the steam-bath for 30 min. The crude *m*-opianic acid which separated on cooling was purified by digestion with saturated aqueous sodium carbonate, filtration, and acidification of the filtrate (Congo-red) with 3N-hydrochloric acid, giving *m*-opianic acid (6·9 g., 65%; m. p. 183°). A specimen, once crystallised from water (charcoal), separated as needles, m. p. 187—188° (Fargher and Perkin, and Chakravarti and Swaminathan, *locc. cit.*, give m. p. 187—188°) (Found : C, 57·4; H, 5·0%; equiv., 208. Calc. for $C_{10}H_{10}O_5$: C, 57·15; H, 4·8%; equiv., 210). Light absorption in ethanol : Max. at 224 (ε = 18,400), 243 (ε = 11,100), and 292 mμ (ε = 7200).

4 : 5-*Methylenedioxyphthalaldehydic Acid*.—5 : 6-Methylenedioxyphthalide was treated with *N*-bromosuccinimide, and the product hydrolysed. The crude acid was isolated as the aniline compound (m. p. 185—186°; Chakravarti, Swaminathan, and Venkataraman, *loc. cit.*, give m. p. 187°) which after treatment as described above gave 4 : 5-methylenedioxyphthalaldehydic acid, m. p. 164—166° (72% yield). A sample crystallised from water in needles, m. p. 167° (*idem, ibid.*, give m. p. 167°) (Found : C, 55·9; H, 3·2%; equiv., 198. Calc. for $C_9H_6O_5$: C, 55·7; H, 3·1%; equiv., 194). Light absorption in ethanol : Max. at 224 (ε = 18,800), 240 (ε = 4300), 260 (ε = 4600), and 300 mμ (ε = 6400).

Condensation of Opianic Acid and Rhodanine (with D. J. Dijksman).—Opianic acid (10·0 g.), rhodanine (6·0 g.), fused sodium acetate (12·0 g.), and glacial acetic acid (30 c.c.) were heated together under reflux for 30 minutes, and the hot reaction mixture was poured into cold water (500 c.c.). The yellow solid (16·0 g.) which separated was insoluble in the common organic solvents but crystallised from water, to give the *tetrahydrate* of a monosodium salt of 5-(2-carboxy-3 : 4-dimethoxybenzylidene)rhodanine as yellow needles, decomposing at *ca.* 220° (Found : C, 39·55; H, 4·5%; equiv., 420. $C_{13}H_{10}O_5NS_2Na,4H_2O$ requires C, 39·45; H, 4·5%; equiv., 419). A solution of the sodium salt in cold 10% aqueous sodium carbonate was poured into excess of dilute hydrochloric acid, and the precipitate crystallised from aqueous ethanol, to give 5-(2-*carboxy*-3 : 4-*dimethoxybenzylidene*)*rhodanine* as small, light yellow prisms, m. p. 237—240° (decomp.) (Found : C, 47·8; H, 3·5%; equiv., 167. $C_{13}H_{11}O_5NS_2$ requires C, 48·0; H, 3·4%; equiv., 162·5). Light absorption in water : Max. at 270 (ε = 9400) and 286 mμ

(ε = 9800); in 0·1N-sodium hydroxide: Max. at 374 (ε = 17,800) and inflection at 258 mμ (ε = 8100); cf. light absorption of 1 : 2-dihydro-1-keto-7 : 8-dimethoxy-2-thianaphthalene-3-carboxylic acid in 0·1N-sodium hydroxide: Max. at 329 mμ (ε = 15,000).

1 : 2-*Dihydro*-1-*keto*-7 : 8-*dimethoxy*-2-*thianaphthalene*-3-*carboxylic Acid*.—(*a*) The sodium salt above (1·0 g.) was heated on the steam-bath for 30 minutes with 15% sodium hydroxide solution (10 c.c.), and the cooled reaction mixture poured into excess of 3N-hydrochloric acid. Crystallisation of the precipitate from ethanol gave the thianaphthalene acid (0·5 g.) as small needles, m. p. 257—258°, undepressed by a specimen prepared as described in Part I (*loc. cit.*) (Found: C, 54·3; H, 3·7. Calc. for $C_{12}H_{10}O_5S$: C, 54·1; H, 3·8%). (*b*) 5-(2-Carboxy-3 : 4-dimethoxybenzylidene)rhodanine under the same conditions as in (*a*) gave the thianaphthalene acid (50%) as small needles (from ethanol), m. p. 256—257°, undepressed by preparation (*a*) (Found: C, 54·0; H, 3·5%).

5-(2-*Carboxy*-4 : 5-*dimethoxybenzylidene*)*rhodanine*.—*m*-Opianic acid (4·0 g.), rhodanine (2·6 g.), and fused sodium acetate (8·0 g.) in glacial acetate acid (50 c.c.) were heated under reflux for 30 minutes. The solution was poured into water (300 c.c.); the precipitated sodium salt (4·3 g.) was separated, and a portion dissolved in 20% aqueous sodium carbonate in the cold, filtered, and acidified (Congo-red) with 3N-hydrochloric acid. Crystallisation of the precipitate from ethanol gave 5-(2-*carboxy*-4 : 5-*dimethoxybenzylidene*)*rhodanine* as yellow needles, m. p. 260° (decomp.) (Found: C, 48·0; H, 3·1. $C_{13}H_{11}O_5NS_2$ requires C, 48·0; H, 3·4%). Light absorption in ethanol: Max. at 215 (ε = 18,500), 252 (ε = 14,200), 268 (ε = 12,900), 290 (ε = 11,500), and 386 mμ (ε = 22,000).

5-(2-*Carboxy*-4 : 5-*methylenedioxybenzylidene*)*rhodanine*.—By the above method 4 : 5-methylenedioxyphthalaldehydic acid (4·0 g.) gave the sodium salt (4·8 g., 70%). The free acid, 5-(2-*carboxy*-4 : 5-*methylenedioxybenzylidene*)*rhodanine*, separated from aqueous ethanol as needles, m. p. 256—257° (decomp.) (Found: C, 46·6; H, 2·3. $C_{12}H_7O_5NS_2$ requires C, 46·6; H, 2·3%). Light absorption in ethanol: Max. at 208 (ε = 18,300), 222 (ε = 18,500), 253 (ε = 13,400), 294 (ε = 14,500), and 385 mμ (ε = 13,400).

1 : 2-*Dihydro*-1-*keto*-6 : 7-*dimethoxy*-2-*thianaphthalene*-3-*carboxylic Acid*.—The sodium salt of 5-(2-carboxy-4 : 5-dimethoxybenzylidene)rhodanine (4·1 g.) was heated under reflux for 1 hour with 15% aqueous sodium hydroxide (60 c.c.). The cooled solution was poured into excess of dilute hydrochloric acid, and the precipitate separated. Crystallisation from ethanol gave 1 : 2-*dihydro*-1-*keto*-6 : 7-*dimethoxy*-2-*thianaphthalene*-3-*carboxylic acid* (3·35 g.) as fine yellow needles, m. p. 306—307° (Found: C, 53·8; H, 3·9; S, 11·8%; equiv., 262. $C_{12}H_{10}O_5S$ requires C, 54·1; H, 3·8; S, 12·0%; equiv.. 266). Light absorption in ethanol: Max. at 232 (ε = 13,700), 272 (ε = 36,500), 328 (ε = 7600), 350 (ε = 8750), and 366 mμ (ε = 7600). Esterification by ethereal diazomethane gave the *methyl* ester, which formed light yellow, felted needles, m. p. 212°, from methanol (Found: C, 55·9; H, 4·5; S, 9·8. $C_{13}H_{12}O_5S$ requires C, 55·7; H, 4·3; S, 10·2%). Light absorption in ethanol: Max. at 232 (ε = 10,400), 258 (ε = 26,400), 276 (ε = 34,100), 284 (ε = 30,100), 338 (ε = 8950), 352 (ε = 10,600), and 368 mμ (ε = 9650).

1 : 2-*Dihydro*-1-*keto*-6 : 7-*methylenedioxy*-2-*thianaphthalene*-3-*carboxylic acid*, prepared as above from the sodium salt of the corresponding rhodanine in 70% yield, formed needles, m. p. 335—336° (decomp.), from ethanol (Found: C, 52·7; H, 2·7. $C_{11}H_6O_5S$ requires C, 52·8; H, 2·4%). Light absorption in ethanol: Max. at 252 (ε = 27,000), 262 (ε = 21,300), 270 (ε = 22,800), 274 (ε = 23,500), 332 (ε = 5900), 350 (ε = 6400), and 364 mμ (ε = 5200). The *methyl* ester separated from ethanol as light yellow needles, m. p. 228—229° (Found: C, 54·5; H, 3·2; S, 11·9. $C_{12}H_8O_5S$ requires C, 54·5; H, 3·0; S, 12·1%). Light absorption in ethanol: Max. at 208 (ε = 8000), 255 (ε = 32,200), 271 (ε = 25,400), 276 (ε = 28,200), 288 (ε = 23,100), 352 (ε = 9100), and 370 mμ (ε = 7800).

5 : 6-*Dimethoxyindan*-1-*one*.—1 : 2-Dihydro-1-keto-6 : 7-dimethoxy-2-thianaphthalene-3-carboxylic acid (3·0 g.) was heated under reflux for 6 hours with a suspension of Raney nickel (34 g.; W.6, prepared according to *Org. Synth.*, **29**, 25) in ethanol (100 c.c.). After removal of the nickel and nickel sulphide, the filtrate and ethanol washings were evaporated to small bulk under reduced pressure, diluted with water (200 c.c.), and extracted with ether (4 × 50 c.c.). The combined ethereal extract was washed with 2N-sodium hydroxide and water and dried (Na_2SO_4). Removal of the ether gave a solid (300 mg.) which gave a blue colour in glacial acetic acid solution with concentrated sulphuric acid. Crystallisation of the solid from benzene–light petroleum (b. p. 40—60°) gave 5 : 6-dimethoxyindan-1-one as needles, m. p. 116—117°, undepressed when mixed with a specimen prepared as described by Perkin and Robinson (*J.*, 1907, **91**, 1080) (Found: C, 68·6; H, 6·3. Calc. for $C_{11}H_{12}O_3$: C, 68·7; H, 6·3%). Light absorption in ethanol: Max. at 230 (ε = 18,000), 268 (ε = 11,700), and 312 mμ (ε = 10,400).

5 : 6-*Methylenedioxyindan*-1-*one*.—1 : 2-Dihydro-1-keto-6 : 7-methylenedioxy-2-thianaphthalene-3-carboxylic acid (3·5 g.) and Raney nickel (35 g.) in ethanol (70 c.c.) were heated under reflux for 8 hours. The reaction mixture was worked up as in the previous experiment. The solid residue (1·0 g.) after removal of ether gave a blue colour in the sulphuric–acetic acid test. Crystallisation from benzene–light petroleum (b. p. 40—60°) gave prismatic needles, m. p. 156—158° (300 mg.), which on further crystallisation from the same solvent and sublimation at 120°/10^{-4} mm. gave 5 : 6-methylenedioxyindan-1-one, m. p. 164—165° (Found : C, 67·8; H, 4·8. Calc. for $C_{10}H_8O_3$: C, 68·1; H, 4·5%). Light absorption in ethanol : Max. at 208 (ε = 16,000), 229 (ε = 16,500), 265 (ε = 7500), and 315 mμ (ε = 10,000). It was undepressed on mixing with a specimen prepared from β-(4 : 5-methylenedioxyphenyl)propionic acid according to Perkin and Robinson (*loc. cit.*), which separated from benzene as prismatic needles, m. p. 164—165° (lit., m. p. 160°) (Found : C, 68·25; H, 4·7%). The compound gave a crimson colour with concentrated sulphuric acid. The 2 : 4-*dinitrophenylhydrazone* separated from benzene as bright red needles, m. p. 265—266° (decomp.) (Found : C, 54·3; H, 3·4; N, 15·7. $C_{16}H_{12}O_6N_4$ requires C, 53·9; H, 3·4; N, 15·7%). Light absorption in chloroform : Max. at 246 (ε = 18,300), 316 (ε = 7950), 334 (ε = 7950), and 404 mμ (ε = 32,700).

Preparation of Hydrastal from Cotarnine.—Hydrocotarnine. Freund and Dormeyer's procedure (*Ber.*, 1891, **24**, 2734) lacks detail; the following method proved satisfactory. A solution of cotarnine chloride (50 g.) in water (250 c.c.) was stirred vigorously for 6 hours with sodium amalgam (450 g.; 8%), the solution being kept acid (Congo-red) by frequent additions of 5N-sulphuric acid. The solution was made alkaline with 3N-sodium hydroxide and extracted with ether (3 × 150 c.c.), the combined extracts being washed with water (100 c.c.) and dried (Na_2SO_4). Removal of the ether gave hydrocotarnine (20·0 g.) as an oil which solidified when kept at 0° overnight. The product had m. p. 55—56° (lit., m. p. 55·5—56·5°) and gave a yellow colour with concentrated sulphuric acid in the cold, becoming deep purple on warming.

Hydrastinine hydriodide. In our hands the oxidation of hydrohydrastinine [prepared from hydrocotarnine according to Pyman and Remfry (*J.*, 1912, **101**, 1595) in 30% yield] by potassium dichromate and dilute sulphuric acid, as recommended by Freund and Will (*Ber.*, 1887, **20**, 2403), proved very unsatisfactory. The following method, a modification of that of Topchiev (*J. Applied Chem. U.S.S.R.*, 1933, **6**, 529), was used. Hydrohydrastinine (13·5 g.) and freshly fused sodium acetate (9·5 g.) were heated under reflux in ethanol (34 c.c.) and treated with a solution of iodine (21·6 g.) in ethanol (210 c.c.), added dropwise during 1 hour. The solution was kept overnight at room temperature, and the solid (22 g.) which separated was filtered off and added in small amounts to a solution of sodium dithionite (hydrosulphite) (7·0 g.) in water (50 c.c.). The solution was warmed and filtered, hydrastinine hydriodide (15 g.) separating as yellow needles, m. p. 231—233° (lit., m. p. 233—234°), on cooling.

Hydrastinine methiodide. Hydrastinine (8·0 g.) was heated under reflux with methyl iodide (40 c.c.) for 1 hour. The excess of methyl iodide was removed under reduced pressure, and the residue crystallised twice from water to give hydrastinine methiodide (5·0 g.) as yellow needles, m. p. 262—264° (Freund, *loc. cit.*, gives m. p. 267°).

Hydrastal. Hydrastinine methiodide (5·0 g.) was heated on the steam-bath with 10% aqueous potassium hydroxide (90 c.c.) for 15 minutes; trimethylamine was evolved and an oil (2·7 g.) separated which solidified on cooling. Crystallisation from light petroleum (b. p. 60—80°) gave hydrastal (2·0 g.) as plates, m. p. 76—78° (Freund, *loc. cit.*, gives 78—79°). The compound gave an intense deep blue colour in acetic acid with concentrated sulphuric acid. It showed light absorption in ethanol : Max. at 206 (ε = 8600), 248 (ε = 27,700), 300 (ε = 6700), and 328 mμ (ε = 6700). The 2 : 4-*dinitrophenylhydrazone* separated from benzene as small red prisms, m. p. 227—228° (decomp.) (Found : C, 54·1; H, 3·6; N, 15·9. $C_{16}H_{12}O_6N_4$ requires C, 53·9; H, 3·3; N, 15·7%). Light absorption in chloroform: Max. at 250 (ε = 22,500), 314 (ε = 9000), and 396 mμ (ε = 47,900).

5 : 6-*Methylenedioxyindan*-1-*one from Hydrastal*.—A solution of hydrastal (500 mg.) in ethanol (10 c.c.) was heated under reflux with Raney nickel (4 g.) for 4 hours. The filtrate and washings from the catalyst were concentrated under reduced pressure to 5 c.c. and diluted with water (50 c.c.), and the mixture was extracted with ether (3 × 25 c.c.). The dried (Na_2SO_4) ethereal extract was evaporated, to give a colourless oil (450 mg.) which gave no colour with the sulphuric–acetic acid test, but gave a crimson colour with concentrated sulphuric acid. Since the product showed no signs of solidification, it was dissolved in methanol (10 c.c.) and treated with Brady's reagent, and the resulting precipitate (500 mg.) crystallised three times from benzene, to give 5 : 6-methylenedioxyindan-1-one 2 : 4-dinitrophenylhydrazone as fine red needles, m. p. 266—

267° (decomp.) alone or mixed with a specimen of the authentic derivative (Found: C, 54·3; H, 3·5. Calc. for $C_{16}H_{12}O_6N_4$: C, 53·9; H, 3·4%). Light absorption in chloroform: max. at 246 (ε = 17,000), 316 (ε = 7800), 332 (ε = 7800), and 404 mμ (ε = 29,400).

6-Ethylpiperonaldehyde 2 : 4-Dinitrophenylhydrazone.—A solution of hydrastal (500 mg.) in methanol (80 c.c.) was shaken for 15 minutes with previously reduced 3% palladium–calcium carbonate catalyst at room temperature and pressure with hydrogen, after which time 68 c.c. had been absorbed (Calc. for 1 mol.: 68 c.c.). The filtered solution was evaporated under reduced pressure to give a clear viscous oil, which gave a dark red colour rapidly assuming a green-brown hue with concentrated sulphuric acid on warming. With sulphuric–acetic acid similar behaviour was shown. A portion of the oil on treatment in methanol with Brady's reagent gave *6-ethylpiperonaldehyde 2 : 4-dinitrophenylhydrazone*, which separated from benzene as red needles, m. p. 236—237° (decomp.) (Found: C, 54·0; H, 4·3. $C_{16}H_{14}O_6N_4$ requires C, 53·6; H, 4·7%). Light absorption in chloroform: Max. at 246 (ε = 17,700), 312 (ε = 7450), and 388 mμ (ε = 28,700).

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