NOTES.

174. *The Reaction of 9-Chlorophenanthridine and Related Compounds with Tertiary Amines.*

By C. B. Reese.

An attempt was made to quaternize 9-chlorophenanthridine (I) with excess of trimethylamine to obtain trimethyl-9-phenanthridinylammonium chloride (II), so that its ultraviolet absorption spectrum could be compared with those of other quaternary phenanthridine derivatives.[1] Preparation of the quaternary salt, and isolation as the derived iodide, had been described by Morgan and Walls,[2] who supported the structure by an iodine analysis. However, attempts to repeat this experiment under the same conditions with ethanolic trimethylamine, or at the lower temperature of 120° with pure trimethylamine, yielded a crystalline iodide which has been shown to be tetramethylammonium iodide. Unfortunately, 9-chlorophenanthridine reacted at a negligible rate with trimethylamine at 37°, perhaps partly owing to its relative insolubility at this temperature.

As some difficulty had been encountered in obtaining the other product of this reaction in a pure state, the reaction between 9-chlorophenanthridine and the tertiary amine, 4-methylmorpholine was investigated. 9-Morpholinophenanthridine (III) and 4 : 4-dimethylmorpholinium chloride were obtained quantitatively.

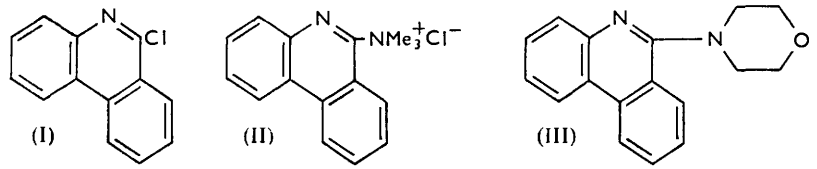
2-Chloroquinoline and 1-chloro*iso*quinoline were both reactive chloro-compounds, like 9-chlorophenanthridine. Further, the 1-position of *iso*quinoline was likely to be hindered to the same extent as the 9-position of phenanthridine. Both the compounds had the advantage of being freely soluble in trimethylamine at room temperature. When the former was heated with an excess of 4-methylmorpholine at 180°, 2-morpholinoquinoline and 4 : 4-dimethylmorpholinium chloride were the exclusive products. However, quaternization of 2-chloroquinoline with pure trimethylamine at 40°, followed by addition of iodide, gave trimethyl-2-quinolylammonium iodide in moderate yield. The structure of this compound was confirmed by alkaline hydrolysis to 2-quinolone. Therefore, at a lower temperature, it was possible to quaternize 2-chloroquinoline normally. The product obtained at a higher temperature may have been formed by reaction of quaternary compound with excess of amine.

1-Chloro*iso*quinoline with excess of 4-methylmorpholine at 180—200° gave 4 : 4-dimethylmorpholinium chloride as the only salt isolated. With an excess of pure trimethylamine at 35° (30 days) it afforded a very small quantity of water-soluble material, and tetramethylammonium iodide was obtained when the aqueous solution was treated with

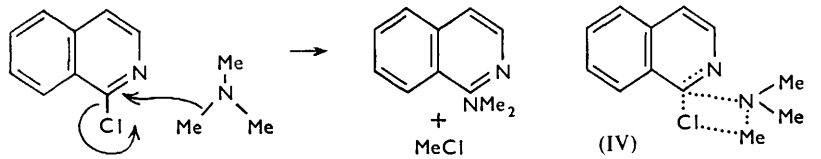
[1] Reese, preceding paper.
[2] Morgan and Walls, *J.*, 1938, 389.

iodide. Thus the normal quaternary compound was not even obtained at this low temperature.

There are, at least, two reasonable interpretations of this observation. One is that the normal quaternary product might be formed initially and be sufficiently reactive at 35° to methylate some of the excess of trimethylamine present. A second is that it might



be sterically impossible for the nitrogen atom of the bulky trimethylamine molecule to get within bonding distance of the 1-position of the *iso*quinoline nucleus. There is then the possibility of demethylation of the attacking trimethylamine by the departing chloride ion, to yield 1-dimethylamino*iso*quinoline and methyl chloride, which is then converted into tetramethylammonium chloride. This second mechanism is indicated in the annexed formulæ.



The transition state (IV) was at least as likely to regenerate the starting materials as it was to yield the products. No accurate rate measurements were made, but this reaction was noticeably slower than quaternization of 2-chloroquinoline under similar conditions. This was difficult to explain solely by electronic theory. If a steric factor operated in the case of 1-chloro*iso*quinoline, then it would be expected also to have done so in the case of 9-chlorophenanthridine (I).

Experimental.—M. p.s are corrected.

Reaction between 9-chlorophenanthridine and trimethylamine. (*a*) 9-Chlorophenanthridine (1 g.) was heated with 33% alcoholic trimethylamine (2·5 c.c.) in a sealed tube at 160° for 4 hr. Adding an excess of aqueous potassium iodide to an aqueous extract of the products, gave colourless crystals (*ca.* 0·03 g.) which, recrystallized from methanol, did not melt below 350°. Their aqueous solution had no absorption maximum in the region 220—320 mμ and analysis corresponded to that of tetramethylammonium iodide (Found, in material dried at 80°: C, 24·1; H, 6·0; N, 6·8. Calc. for $C_4H_{12}NI$: C, 23·9; H, 6·0; N, 7·0%).

(*b*) 9-Chlorophenanthridine (0·5 g.) was heated with pure trimethylamine (*ca.* 4 g.) in a sealed tube at 120° for 10 hr. The excess of amine was allowed to evaporate at room temperature and the residue was washed with dry benzene. The colourless crystals which remained were converted into the iodide and purified as above (Found: C, 24·3; H, 6·3%).

(*c*) 9-Chlorophenanthridine (0·7 g.) was allowed to react with excess of trimethylamine (*ca.* 5 g.) at 37° for 14 days. The products were treated as above, but only *ca.* 0·001 g. of crystalline material remained after the benzene extraction. This was dissolved in water and had no absorption peak in the range 220—300 mμ.

Reaction between 9-Chlorophenanthridine and 4-methylmorpholine. 9-Chlorophenanthridine (0·5 g.) was heated with an excess of 4-methylmorpholine (3 c.c.) at 200° for 5 hr. Crystals separated from the cooled products. Dry benzene (10 c.c.) was added to the mixture, which was then filtered. The residue recrystallized from ethanol–ethyl acetate as a colourless, extremely hygroscopic substance which decomposed above 330°, without melting. When treated with silver oxide, its aqueous solution gave a strongly alkaline reaction. Elementary analysis confirmed that this compound was 4 : 4-*dimethylmorpholinium chloride* (Found, in material dried at 50°: C, 47·5; H, 8·8; N, 9·1. $C_6H_{14}ONCl$ requires C, 47·5; H, 9·2; N, 9·2%).

The filtrate (above) was evaporated to yield a semicrystalline gum, which was recrystallized

from ethanol as colourless plates, m. p. 92°. This was redistilled in a " cold-finger " apparatus at 110°/0·5 mm. to give 9-*morpholinophenanthridine*, m. p. 94—96° (Found: C, 77·2; H, 6·2; N, 10·9. $C_{17}H_{16}ON_2$ requires C, 77·3; H, 6·1; N, 10·6%).

Both the crude products were obtained quantitatively.

Reaction between 2-chloroquinoline and 4-methylmorpholine. 2-Chloroquinoline (0·58 g.) was treated, in the same way, with excess of 4-methylmorpholine (3 c.c.) at 180° for 5 hr. The products were washed with dry benzene to leave a quantitative residue of 4 : 4-dimethylmorpholinium chloride (Found: C, 47·7; H, 9·3; N, 9·3%). The benzene washings, when evaporated, yielded crystals which, recrystallized from light petroleum (b. p. 40—60°) and resublimed (70°/0·5 mm.), gave 2-*morpholinoquinoline*, m. p. 91° (Found: C, 72·8; H, 6·4; N, 13·2. $C_{13}H_{14}ON_2$ requires C, 72·9; H, 6·5; N, 13·1%).

Reaction between 2-chloroquinoline and trimethylamine at 40°. 2-Chloroquinoline (3·2 g.) was allowed to react with a large excess of trimethylamine (*ca.* 10 g.) at 40° for 48 hr., crystals separating. The excess of trimethylamine was allowed to evaporate and benzene (20 c.c.) was added. The mixture was filtered and the residue was dissolved in water (2 c.c.). Saturated aqueous potassium iodide (1 c.c.) was then added. Crystals (0·21 g.) which were precipitated, when twice recrystallized from water, yielded cream-coloured plates of *trimethyl-2-quinolylammonium iodide*, m. p. 168° (Found, in material dried at 100°: C, 45·6; H, 4·6; N, 9·2. $C_{12}H_{15}N_2I$ requires C, 45·9; H, 4·8; N, 8·9%).

A solution of this compound (0·018 g.) in water (2 c.c.) was made alkaline (*ca.* pH 12) with sodium hydroxide and heated at 100° for 6 hr., then allowed to cool; fine needles separated. They were sublimed at 150°/0·2 mm. The sublimate (*ca.* 0·002 g.) had an infrared spectrum identical with that of 2-hydroxyquinoline.

Reaction between 1-chloroisoquinoline and 4-methylmorpholine at 180°. 1-Chloro*iso*quinoline (0·8 g.) was heated with excess of 4-methylmorpholine (4 c.c.) at 180° for 6 hr. 4 : 4-Dimethylmorpholinium chloride was isolated quantitatively as before (Found, in the purified product: C, 47·3; H, 9·0; N, 9·5%).

Reaction between 1-chloroisoquinoline and trimethylamine at 30—35°. A solution of 1-chloro-*iso*quinoline (1·3 g.) in excess of trimethylamine (*ca.* 10 g.) was kept in a sealed tube at 30—35° for 30 days, during which a small quantity of crystals separated. The excess of trimethylamine was then allowed to evaporate. The residue was washed with benzene, and the material remaining was dissolved in water (0·1 c.c.) and added to a saturated solution of potassium iodide (0·1 c.c.). The crystalline precipitate, obtained immediately, recrystallized from methanol as colourless prisms (*ca.* 0·003 g.). The infrared spectrum (in Nujol) of this substance was identical with that of tetramethylammonium iodide.

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175. *Some Anilinoquinones and* N-*Substituted* 2-*Hydroxy*-1 : 4-*naphthaquinone Imines.*

By M. Z. BARAKAT, S. K. SHEHAB, and M. M. EL-SADR.

WE believe that in its reaction [1,2] with *p*-benzoquinone in aqueous acetic acid one molecule of a primary aromatic amine adds at the ethylenic double bond of the quinone, and not at a C=O group, to form an additive product which is then oxidised by a second molecule of the quinone to produce the anilinoquinone. This explains why toluquinone yields only a monoanilide and *sym*-xyloquinone yields none [3,4] (steric hindrance).

By suitable selection of solvent and temperature, it is possible to make *p*-benzoquinone react with 1 or 2 mols. of a primary aromatic amine.[1] With various substituted anilines

[1] Suida and Suida, *Annalen*, 1918, **416**, 113.
[2] Martynoff and Tstsas, *Bull. Soc. chim. France*, 1947, 52.
[3] Shetsov and Shemyakin, *J. Gen. Chem.* (*U.S.S.R.*), 1949, **19**, 480.
[4] Cowdrey and Hinshelwood, *J.*, 1946, 1036.

we have obtained anilinoquinones in *ca.* 20% yield by reaction in very dilute aqueous acetic acid at <5°; these can be separated by means of light petroleum from the prevailing dianilinoquinones. At room temperature (25°) the product is entirely the dianilinoquinone.

Since naphthaquinone derivatives [5] have antibacterial properties,[5] including a curative effect on avian tuberculosis in white mice, we prepared some new *N*-substituted 2-hydroxy-1 : 4-naphthaquinone imines for evaluation as chemotherapeutic agents, using interaction of sodium 1 : 2-naphthaquinone-4-sulphonate with *p*-, *m*-, and *o*-chloroaniline and *o*-aminophenol.

Experimental.—All the anilinoquinones were insoluble in cold 10% alkali and gave purple colours in concentrated sulphuric acid. The tests for hydrogen peroxide and quinol in the filtrate of the reaction mixtures were positive in all cases.

Reaction of p-*benzoquinone with aniline.* (*a*) *p*-Benzoquinone (2·16 g.) was dissolved in hot distilled water (200 ml.), and the solution filtered from undissolved quinone, and cooled in ice. Freshly distilled aniline (0·93 g., 0·01 mol.) was suspended in distilled water (75 ml.), and glacial acetic acid was stirred in until dissolution was complete. This solution was added in portions (about 5 ml.) to the cold quinone solution with continuous shaking. Maroon-coloured crystals began to be deposited. The mixture was kept in ice for 15 min. and filtered. The solid monoanilino-quinone, recrystallised from light petroleum (b. p. 60—80°), had m. p. 139° (decomp.) (lit., m. p. 119°) (Found: C, 72·4; H, 4·45; N, 7·15. Calc. for $C_{12}H_9O_2N$: C, 72·4; H, 4·5; N, 7·0%) (yield, 0·4 g.). In concentrated sulphuric acid, it gave a purple-violet colour. The filtrate gave a positive test for peroxide with potassium iodide–starch and acetic acid, and on evaporation and recrystallisation of the residue from water gave quinol (mixed m. p.).

(*b*) The same reactants, but 2 mols. of aniline, when shaken at 25°, at once deposited red-violet crystals. After 30 minutes' shaking, filtration gave the dianilinoquinone which, recrystallised from nitrobenzene, had m. p. 224° (decomp.) (Found: C, 74·4; H, 4·8; N, 9·65. Calc. for $C_{18}H_{14}O_2N_2$: C, 74·5; H, 4·8; N, 9·7%) (yield 1·48 g.).

The following were similarly prepared and crystallised: 2-o-*chloro*-, brick red, m. p. 110—111° (decomp.) (Found: C, 62·2; H, 3·5; N, 6·5; Cl, 15·6. $C_{12}H_8O_2NCl$ requires C, 61·7; H, 3·4; N, 6·0; Cl, 15·2%), and 2-m-*chloro-anilino*-1 : 4-*benzoquinone*, violet-black, m. p. 106° (decomp.) (Found: C, 62·0; H, 3·7; N, 5·8; Cl, 15·9%); 2 : 5-*di*-o-*chloro*-, brick-red (cryst. from alcohol), m. p. 220—222° (decomp.) (Found: C, 60·4; H, 3·6; N, 7·4; Cl, 19·6. $C_{18}H_{12}O_2N_2Cl_2$ requires C, 60·2; H, 3·3; N, 7·8; Cl, 19·8%), 2 : 5-*di*-m-*chloro*-, maroon, m. p. 270—272° (decomp.) (Found: C, 59·8; H, 3·2; N, 8·25; Cl, 19·9%), and 2 : 5-*di*-p-*bromo-anilino*-1 : 4-*benzoquinone*, violet-black, m. p. >300° (Found: C, 48·7; H, 2·9; N, 7·0; Br, 34·4. $C_{18}H_{12}O_2N_2Br_2$ requires C, 48·2; H, 2·7; N, 6·25; Br, 35·7%).

Naphthaquinones. The products were free from sulphur and dissolved in 10% alkali.

Solutions of *p*-chloroaniline (1·275 g.) in ethanol (40 ml.) and of sodium 1 : 2-naphthaquinone-4-sulphonate (5·20 g.) in water (200 ml.), when mixed and kept for 10 min., deposited 2-*hydroxy*-1 : 4-*naphthaquinone* p-*chlorophenylimine*, red-brown (from acetone), m. p. 280—282° (decomp.) (Found: C, 68·1; H, 3·2; N, 4·9; Cl, 12·7; active H, 0·43. $C_{16}H_{10}O_2NCl$ requires C, 67·7; H, 3·5; N, 4·9; Cl, 12·5; 1H, 0·35%) (yield 2·60 g.).

Similar reactions gave the m-*chlorophenylimine*, brownish-red, m. p. 292—294° (Found: C, 67·7; H, 3·4; N, 4·3; Cl, 12·55%), o-*chlorophenylimine*, brick-red, m. p. 266° (decomp.) (Found: C, 67·6; H, 3·7; N, 5·0; Cl, 12·6%), and o-*hydroxyphenylimine*, brick-red, m. p. 246—248° (decomp.) (Found: C, 72·7; H, 4·3; N, 5·55. $C_{16}H_{11}O_3N$ requires C, 72·45; H, 4·15; N, 5·3%) (positive test with phosphotungstic acid indicating more than one phenolic group).

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CAIRO UNIVERSITY, GIZA, CAIRO, EGYPT. [*Received, May 27th,* 1957.]

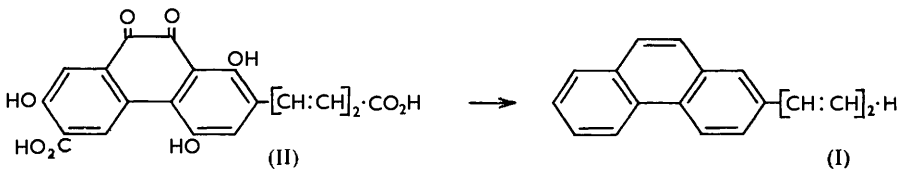
[5] Rubstov, *J. Gen. Chem.* (*U.S.S.R.*), 1946, **16**, 221.

176. *Researches on Polyenes. Part VI.* The Synthesis of* trans-1-2′-*Phenanthrylbuta*-1 : 3-*diene.*

By B. B. Millward and M. C. Whiting.

During degradations of the fungus pigment telephoric acid, Kögl, Erxleben, and Jänecki [1] isolated a hydrocarbon, $C_{18}H_{14}$, formed in good yield (~15%) by zinc-dust distillation of the triacetate. It gave 2-phenanthroic acid on oxidation. Since hexahydrotelephoric acid gave adipic acid on oxidation, the $C_{18}H_{14}$ hydrocarbon was formulated as 1-2′-phenanthrylbuta-1 : 3-diene (I) rather than the 2-compound. These results were part of the evidence on which structure (II) was advanced for telephoric acid.

The preparation of a series of 1-arylbut-2-en-1-ols,[2] including the 2-naphthyl and 9-phenanthryl derivatives, and the dehydration of several substituted 1-phenylbut-2-en-1-ols to the corresponding phenylbutadienes [3] suggested a straightforward synthesis of 1-2′-phenanthrylbuta-1 : 3-diene (I). Indeed, 2-bromophenanthrene [4] was converted into the corresponding arylbutenol by the interaction of its Grignard reagent, prepared in the presence of an equimolecular amount of ethylmagnesium bromide, with crotonaldehyde,[2] although careful purification of the bromide proved necessary. Dehydration



(II) (I)

as described by Braude, Jones, and Stern [3] was unsatisfactory, however, for both the phenanthrylbutenol and the 2-naphthyl analogue. It is noteworthy that despite the ease with which 1-phenylethanol is dehydrated, Price and Halpern [5] were unable to obtain the 2-, 3-, or 9-vinylphenanthrene by treating the corresponding 1-arylethanols with potassium hydrogen sulphate or thionyl chloride and pyridine. After several methods had been unsuccessful—although all gave spectroscopically detectable amounts of the required diene along with much polymer—toluene-*p*-sulphonic acid in benzene at 80° proved satisfactory. Optimal reaction times, roughly determined spectroscopically, were about 15 minutes and 1 minute for the 2′-naphthyl- and 2′-phenanthrylbutenols. The two dienes were rather unstable solids, m. p. 92—94° and 107—109°, respectively.

During the dehydration work, 1-2′-phenanthrylbut-2-en-1-ol was rearranged in good yield to the corresponding 4-arylbut-3-en-2-ol by sulphuric acid in aqueous dioxan. The rate constant was of the same order as that reported for other arylbutenols.[3]

The infrared spectra of the new dienes were similar, and, in particular, each showed bands at 892 and 1000 cm.$^{-1}$, attributable to a vinyl group, and at 945 cm.$^{-1}$, attributable to a *trans*-1 : 2-disubstituted ethylenic linkage. The best proof of structure, however, is the ultraviolet absorption spectra (Figs. 1 and 2), which can be compared with those of the corresponding phenyl compounds,[2] the analogy then becoming convincing.

Kögl, Erxleben, and Jänecki report only the melting point (125°) for their hydrocarbon; and Professor Kögl has informed us [6] that no sample has survived. In view of the difficulty of isolating telephoric acid, the situation remains unsatisfactory. It seems unlikely, though possible, that our diene was a low-melting polymorph. The naturally-derived hydrocarbon might be the *cis*-isomer, if that were (*a*) stable under pyrolytic conditions and (*b*)

* Part V, *J.*, 1957, 537.

[1] Kögl, Erxleben, and Jänecki, *Annalen*, 1930, **482**, 105.
[2] Braude, Jones, and Stern, *J.*, 1947, 1087.
[3] Braude, Fawcett, and Newman, *J.*, 1950, 793.
[4] Mossettig and de Kamp, *J. Amer. Chem. Soc.*, 1930, **52**, 3704; Bachmann and Boatner, *ibid.*, 1936, **58**, 2097, 2194; Dice and Smith, *J. Org. Chem.*, 1949, **14**, 179.
[5] Price and Halpern, *J. Amer. Chem. Soc.*, 1951, **73**, 818.
[6] Personal communication from Prof. F. Kögl.

higher melting than the *trans*-form. Finally, the hydrocarbon, m. p. 125°, may not have been 1-2′-phenanthrylbuta-1 : 3-diene; but in that case we can neither suggest an alternative formula for it based on structure (II) for telephoric acid, nor propose another structure for telephoric acid consistent with the published evidence.

FIG. 1. FIG. 2.

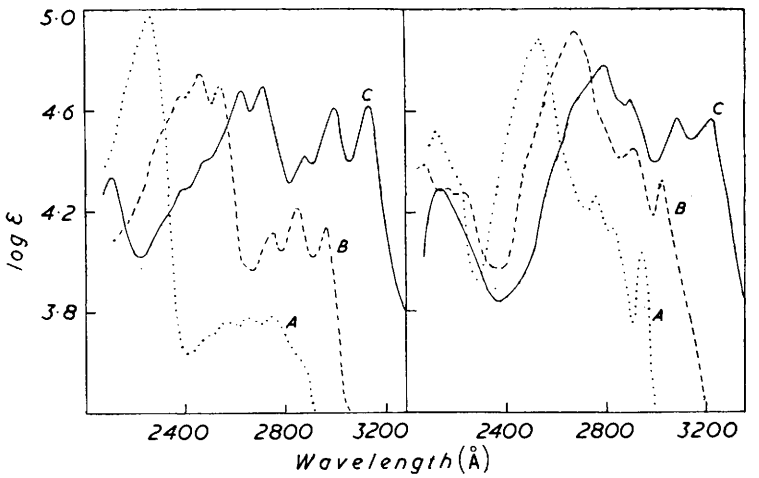


FIG. 1. *A*, 1-2′-*Naphthylbut*-2-*en*-1-*ol*; *B*, 4-2′-*naphthylbut*-3-*en*-2-*ol*; *and C*, 1-2′-*naphthylbuta*-1 : 3-*diene*.
FIG. 2. *A*, 1-2′-*Phenanthrylbut*-2-*en*-1-*ol*; *B*, 4-2′-*phenanthrylbut*-3-*en*-2-*ol*; *and C*, 1-2′-*phenanthrylbuta*-1 : 3-*diene*.

Experimental.—" Alumina " refers to Peter Spence, Grade H. Ultraviolet and infrared spectra were determined in ethanol and carbon disulphide, respectively. M. p.s were determined on a Kofler block.

trans-1-2′-*Naphthylbuta*-1 : 3-*diene*. (*a*) *trans*-1-2′-Naphthylbut-2-en-1-ol [3] (50 mg.), toluene-*p*-sulphonic acid (5 mg.), and benzene (25 c.c.) were heated under reflux, the reaction being followed spectroscopically. After 30 min.—beyond the point of optimal yield—the mixture was cooled, washed with sodium hydrogen carbonate solution, and evaporated under reduced pressure. The residue was extracted with methanol; addition of water gave the *diene* (18 mg., 45%) as plates, m. p. 91—94° (Found: C, 93·0; H, 6·8. $C_{14}H_{12}$ requires C, 93·3; H, 6·7%).

(*b*) *trans*-4-2′-Naphthylbut-3-en-2-ol [3] (133 mg.) was similarly dehydrated with toluene-*p*-sulphonic acid (14 mg.) in boiling benzene (50 c.c.), with the exclusion of light. Isolation of the product gave a solid, m. p. 87—94° (114 mg., 94%) which after chromatographic purification and crystallisation had m. p. 92—94°.

trans-1-2′-*Phenanthrylbut*-2-*en*-1-*ol*. A mixture of 2-bromophenanthrene [4] (3·0 g.), ethyl bromide (0·9 c.c.), benzene (15 c.c.), ether (30 c.c.), and magnesium (0·7 g.) was heated under reflux for 7 hr., then cooled to 0° whilst crotonaldehyde (2·0 g.) in ether (20 c.c.) and benzene (20 c.c.) was added dropwise. After 15 min. saturated ammonium chloride solution was added, and the aqueous solution extracted with benzene. Evaporation under reduced pressure gave a residue which, in light petroleum–benzene (3 : 2), was chromatographed on alumina. Elution with benzene containing 2% of methanol gave a residue which was extracted with pentane; evaporation and crystallisation (from aqueous ethanol) gave the *alcohol* as needles, m. p. 92—95° (Found: C, 86·9; H, 6·5. $C_{18}H_{16}O$ requires C, 87·1; H, 6·5%).

trans-4-2′-*Phenanthrylbut*-3-*en*-2-*ol*. The above alcohol (174 mg.) was dissolved in 0·01M-sulphuric acid in 60% dioxan. After 20 hr. addition of water and crystallisation from benzene–light petroleum gave the rearranged *alcohol* (130 mg., 75%) as prisms, m. p. 137—139° (Found: C, 86·8; H, 6·5%).

trans-1-2′-*Phenanthrylbuta*-1 : 3-*diene*. To toluene-*p*-sulphonic acid (21 mg.) in boiling benzene (50 c.c.), 1-2′-phenanthrylbut-2-en-1-ol (206 mg.) was added. After 1 min. the mixture was rapidly chilled and the solution was washed with sodium hydrogen carbonate solution. After evaporation under reduced pressure at 20° the residue, in benzene–light petroleum (1 : 20),

was chromatographed on alumina. Evaporation at 20° and crystallisation from methanol gave the required diene (62 mg., 32%), m. p. 107—109° (Found: C, 93·9; H, 6·0. $C_{18}H_{14}$ requires C, 93·9; H, 6·1%). The diene polymerised during 2 months at −30° in the absence of bright light. Irradiation with ultraviolet light rapidly reduced the intensity of the absorption maxima at 3230 and 3090 Å.

Analyses and spectrographic measurements were by Mr. E. S. Morton and Mr. H. Smith, and by Miss W. Peadon and Mrs. J. Hopkins, respectively.

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[7] Cf. Grummitt and Christolph, *J. Amer. Chem. Soc.*, 1951, **73**, 3479.

177. *A Synthesis of* 3-O-β-D-*Galactopyranosyl*-D-*galactose.*

By D. H. BALL and J. K. N. JONES.

THE isolation of the 1 : 6- and 1 : 3-β-linked isomers of *O*-D-galactopyranosyl-D-galactose from gums,[1] wood polysaccharides,[2] and galactogen [3] has recently been described. The former isomer was prepared several years ago by Freudenberg and his co-workers [4] and we now describe the synthesis of the latter.

A survey of the literature indicated that this synthesis might be achieved *via* 4 : 6-*O*-ethylidene-1 : 2-*O*-*iso*propylidene-D-galactose (*A*), first described by Foster *et al.*[5] However, in the first stage of this preparation, *viz.*, the condensation of D-galactose with paraldehyde, we obtained a crystalline 4 : 6-*O*-ethylidene-D-galactose and not a syrup as described by these workers. The crystalline compound condensed with acetone in the presence of zinc chloride to form a syrupy *iso*propylidene derivative, which was purified *via* its crystalline toluene-*p*-sulphonate. This ester had a high positive specific rotation (+119°) and was converted into the desired derivative by reduction with lithium aluminium hydride. Methylation with silver oxide and methyl iodide then gave a syrupy *O*-methyl derivative which on hydrolysis yielded a crystalline 3-*O*-methyl-D-galactose, proving that the compound (*A*) has a free hydroxyl group at position 3.

The compound previously thought to be the 3-*O*-toluene-*p*-sulphonate of compound (*A*) had a negative specific rotation [5] (−67°) and is believed to be 3 : 4-*O*-ethylidene-1 : 2-*O*-*iso*propylidene-D-galactose 6-*O*-toluene-*p*-sulphonate. This compound was isolated on acylation of the substance formed when 4 : 6-*O*-ethylidene-D-galactose is condensed with acetone in the presence of phosphoric oxide (details of this work will be given later).

Condensation of acetobromo-D-galactose with compound (*A*) by the method of Haskins *et al.*[7] gave a syrup which was heated with an excess of sodium hydroxide solution to saponify acetyl groups and to destroy reducing sugars. The mixture was then deionised and heated with acetic acid in order to hydrolyse *O*-ethylidene and *O*-*iso*propylidene groups. The mixture of sugars was fractionated on a cellulose column, and crystalline 3-*O*-β-D-galactopyranosyl-D-galactose was obtained.

Experimental.—Paper chromatography was carried out by the descending method [8] on Whatman No. 1 filter paper, the following solvent systems being used: (*a*) butan-1-ol–ethanol–water (3 : 1 : 1); (*b*) butan-1-ol–pyridine–water (10 : 3 : 3); (*c*) ethyl acetate–acetic acid–water (9 : 2 : 2); and (*d*) ethyl acetate–acetic acid–formic acid–water (18 : 3 : 1 : 4) (all v/v). The positions of the sugars on the chromatograms were determined by spraying either with silver nitrate in acetone followed by sodium hydroxide [9] in ethanol or with *p*-anisidine hydrochloride

[1] Jackson and Smith, *J.*, 1940, 79; Hirst and Perlin, *J.*, 1954, 2622.
[2] White, *J. Amer. Chem. Soc.*, 1942, **64**, 302; Bouveng and Lindberg, *Acta Chem. Scand.*, 1956, **10**, 1515.
[3] Weinland, *Z. physiol. Chem.*, 1956, **305**, 87.
[4] Freudenberg, Wolf, Knopf, and Zaheer, *Ber.*, 1928, **61**, 1743.
[5] Foster, Overend, and Stacey, *J.*, 1951, 980.
[6] Cf. Bouveng and Lindberg, *Acta Chem. Scand.*, 1956, **10**, 1283.
[7] Haskins, Hann, and Hudson, *J. Amer. Chem. Soc.*, 1941, **63**, 1724.
[8] Partridge, *Biochem. J.*, 1948, **42**, 238.
[9] Trevelyan, Procter, and Harrison, *Nature*, 1950, **166**, 444.

in butan-1-ol.[10] The rates of movement of the sugars are quoted relative to that of galactose (R_{gal}) on the same chromatogram. Optical rotations were determined at 23° ± 3° (unless otherwise stated, solution was in water and the figures given are equilibrium values). Solvents were removed under reduced pressure.

4 : 6-O-*Ethylidene*-D-*galactose*. To a suspension of finely powdered D-galactose (60 g.) in redistilled paraldehyde (220 ml.) was added concentrated sulphuric acid (0·6 ml.), and the mixture was shaken at room temperature for 24 hr. The solid was collected, washed with cold ethanol, and extracted with boiling ethanol which contained sufficient ammonia to neutralise residual acid. The hot solution was filtered to remove galactose and allowed to cool. The product (40 g., 58%) moved at the rate of rhamnose (solvent *a*) and contained traces of galactose. After two recrystallisations from ethanol, it had m. p. 185° and $[\alpha]_D$ +122° (20 min.) ⟶ +96° (4 hr., constant) (*c* 2·0). The *compound* therefore crystallises in the α-form (Found: C, 46·8; H, 6·8. $C_8H_{14}O_6$ requires C, 46·6; H, 6·8%). If the condensation is carried out in the presence of greater amounts of sulphuric acid as catalyst, a syrupy mixture of ethylidene derivatives results. Toluene-*p*-sulphonylation of this material gave, in one case, a crystalline compound thought to be 1 : 2-3 : 4-*di*-O-*ethylidene*-D-*galactose* 6-O-*toluene*-p-*sulphonate*. It had m. p. 119—122° and $[\alpha]_D$ −68° (*c* 1·0 in $CHCl_3$) (Found: C, 53·0; H, 5·7; S, 8·0. $C_{17}H_{22}O_8S$ requires C, 52·8; H, 5·7; S, 8·3%).

4 : 6-O-*Ethylidene*-D-*galactose* p-*nitrophenylhydrazone* was prepared by heating 4 : 6-*O*-ethylidene-D-galactose for 1 hr. with alcoholic *p*-nitrophenylhydrazine. It had m. p. 248° (decomp.) (Found: C, 49·1; H, 5·5; N, 12·5. $C_{14}H_{19}O_7N_3$ requires C, 49·2; H, 5·6; N, 12·6%).

Condensation of 4 : 6-O-*ethylidene*-D-*galactose with acetone*. The ethylidene compound (20 g.) was ground and suspended in acetone (500 ml.). Granular zinc chloride (50 g.) was added and the mixture was shaken. After 70 hr., a further portion (10 g.) of zinc chloride was added. After a further 45 hr., the mixture was homogeneous and the colourless solution was poured into a stirred solution of sodium carbonate (70 g.) in water (2 l.). The precipitated zinc salts were removed and extracted twice with boiling acetone. The combined filtrate and extracts were concentrated to remove acetone, and the residual aqueous solution (*ca.* 400 ml.) was then extracted with chloroform (5 × 50 ml.). The extracts were dried (Na_2SO_4) and concentrated to a syrup (8·9 g.). The condensation product gave one spot on paper chromatograms at R_F 0·8 (solvent *a*). It gave a yellow colour with the *p*-anisidine spray.

The syrupy condensation product (8·9 g.) was treated with toluene-*p*-sulphonyl chloride (7·6 g., 1·1 equiv.) in dry pyridine (40 ml.). The solution was left overnight at 20°, then heated at 80° for 20 min., cooled, and poured into ice-water (1 l.). The product separated as a gum which rapidly solidified. The crude light brown powder (12·5 g.) crystallised from hot ethanol and after further recrystallisation from methanol 4 : 6-O-*ethylidene*-1 : 2-O-iso*propylidene*-D-*galactose* 3-*toluene*-p-*sulphonate* had m. p. 116—118°, $[\alpha]_D$ +119° (*c* 1·0 in $CHCl_3$) (Found: C, 54·1; H, 6·0; S, 7·8. $C_{18}H_{24}O_8S$ requires C, 54·0; H, 6·0; S, 8·0%).

3-O-*Methyl*-D-*galactose*. The preceding ester (3·0 g.) was dissolved in a mixture of sodium-dried benzene (4 ml.) and sodium-dried ether (8 ml.). The solution was boiled under reflux and powdered lithium aluminium hydride (0·60 g.) was added in three portions during 36 hr. After 60 hr., the mixture was cooled and poured on ice, and the 4 : 6-*O*-ethylidene-1 : 2-*O*-*iso*propylidene-D-galactose (1·7 g.) was isolated by chloroform extraction of the aqueous solution. A portion of the syrup (0·40 g.) was methylated with sodium hydroxide and methyl sulphate in the usual way; the product (0·35 g.), purified by distillation, had b. p. 110—120° (bath temp.)/0·04 mm., n_D^{20} 1·4640. The syrup was heated in N-sulphuric acid at 100° for 1 hr. The solution was neutralised (Amberlite mixed-bed resin MB-3) and concentrated to a syrup which crystallised readily when nucleated with an authentic specimen of 3-*O*-methyl-D-galactose. The product, recrystallised from ethanol–acetone, had m. p. and mixed m. p. 139—143°. It was indistinguishable from 3-*O*-methylgalactose on paper chromatograms (solvents *a*, *b*, *c*, and *d*) and on paper electrophoretograms.[6]

Synthesis of 3-O-β-D-*galactopyranosyl*-D-*galactose*. 4 : 6-*O*-Ethylidene-1 : 2-*O*-*iso*propylidene-D-galactose (from the 3-*O*-toluene-*p*-sulphonate) (1·7 g., 0·007 mole) was dissolved in dry, alcohol-free chloroform (15 ml.) and to the solution was added Drierite (10 g.), silver oxide (5 g.), and glass beads. The mixture was shaken in the dark. After 1 hr., acetobromo-D-galactose (2·88 g., 0·007 mole) in dry, alcohol-free chloroform (10 ml.) and iodine (0·5 g.) were added and the shaking was continued. After 4 days, a test for ionisable bromine was negative and the above additions were repeated. The mixture was shaken for a further 4 days and then

[10] Hough, Jones, and Wadman, *J.*, 1950, 1702.

filtered and to the cooled filtrate was added a solution of sodium methoxide in methanol (10 ml.). A precipitate of galactose was removed and the filtrate concentrated to a syrup. This was taken up in water and extracted continuously with chloroform to remove unchanged acetals of galactose. The aqueous solution was then deionised and concentrated to a syrup (1·5 g.) which was fractionated on filter paper (Whatman No. 3MM). The main fraction was non-reducing and moved slightly faster than rhamnose. This material was isolated from the paper, and the acetal groups were removed by boiling it with dilute acetic acid for 3 hr. Concentration of the acidic solution gave a syrup which contained galactose and a disaccharide. These were separated on filter paper (Whatman No. 3MM), and the disaccharide fraction (0·16 g.) crystallised when nucleated with authentic 3-*O*-β-D-galactopyranosyl-D-galactose. After recrystallisation from aqueous methanol containing a little butan-1-ol, the crystals had m. p. 163—170° undepressed by admixture with an authentic specimen, and $[\alpha]_D$ +75° (5 min.) ⟶ +60° (2 hr., const.) (*c* 2·0). The synthetic disaccharide was indistinguishable on paper chromatograms from authentic material, and infrared analysis indicated that the synthetic and authentic materials were identical.

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178. *Search for Chemotherapeutic Amidines. Part XV.* 2-Methoxy- and 2-Hydroxy-derivatives of* 1 : 5-*Di*-p-*amidinophenoxypentane.*

By M. DAVIS.

THE trypanocidal activity of 4 : 4′-diamidinostilbene (" Stilbamidine ") is retained on introduction of a 2-methoxy-group into one ring, and is increased on the introduction of a 2-hydroxy-group.[1] Some mono- and di-substituted αω-di-*p*-amidinophenoxyalkanes have also been prepared,[2] but none of these contained a single 2-methoxy- or 2-hydroxy-group. Corresponding monosubstituted derivatives of " Pentamidine " (III; R = H) are now described.

Condensation of 4-cyano-2-methoxyphenol[3] (I; R = OMe) with 5-*p*-cyanophenoxypentyl bromide[2] gave the dinitrile (II; R = OMe) in high yield, which was converted into the diamidine (III; R = OMe) in the usual way.[4]

It is known that 4-nitrocatechol can be preferentially alkylated in the 1-position[5] and it seemed likely that 4-cyanocatechol[6] could be similarly converted into a 1-monoether. In the event, condensation of 4-cyanocatechol (I; R = OH) with 5-*p*-cyanophenoxypentyl

(I) (II); R′ = CN (III); R′ = C(:NH)·NH$_2$

bromide gave a mixture of the required dinitrile (II; R = OH) and the trinitrile (II; R = O·[CH$_2$]$_5$·O·C$_6$H$_4$·CN-*p*). The phenolic component was readily isolated as the crystalline sodium salt; its orientation was confirmed by methylation to the dinitrile (II; R = OMe). Its conversion into the diamidine (III; R = OH) proceeded normally.

Biological tests showed that the two diamidines possessed trypanocidal and antibacterial properties similar to those of " Pentamidine ". Thus, the LD_{50} (mg./g., subcutaneously in mice) for the diamidines (III; R = OMe) and (III; R = OH) were

* Part XIV, *J.*, 1957, 3089.

[1] Ashley and Harris, *J.*, 1946, 567.
[2] Berg and Newbery, *J.*, 1949, 642.
[3] Marcus, *Ber.*, 1891, **24**, 3654.
[4] Ashley and MacDonald, *J.*, 1957, 1668.
[5] Cardwell and Robinson, *J.*, 1915, 255.
[6] Ewins, *J.*, 1909, 1482.

respectively 0·175 and 0·075 (" Pentamidine ", 0·166). The corresponding CD_{50} against *T. rhodesiense* were respectively 0·0025 and 0·003 (" Pentamidine ", 0·002). Neither compound was curative against *T. congolense* in mice.

Experimental.—1-(4-*Cyano*-2-*methoxyphenoxy*)-5-p-*cyanophenoxypentane*. 4-Cyano-2-methoxyphenol (29·8 g.) and 5-*p*-cyanophenoxypentyl bromide (53·6 g.) were added successively to sodium hydroxide (8 g.) in water (10 ml.) and 2-ethoxyethanol (100 ml.). The mixture was refluxed for 20 hr., cooled, and diluted with water. The *dinitrile* (55·25 g., 82%) had m. p. 115—117° after recrystallisations from ethanol (Found: N, 8·4. $C_{20}H_{20}O_3N_2$ requires N, 8·3%).

1-(4-*Cyano*-2-*hydroxyphenoxy*)-5-p-*cyanophenoxypentane*. Potassium hydroxide (6·1 g.) in water (10 ml.) and 2-ethoxyethanol (10 ml.) was added during 1·5 hr. to a refluxing solution of 4-cyanocatechol (14·75 g.) and 5-*p*-cyanophenoxypentyl bromide (29·3 g.) in 2-ethoxyethanol (50 ml.). After another 3·5 hr. the mixture was cooled, shaken with chloroform and dilute hydrochloric acid, and filtered. The *dinitrile* (4·8 g.) had m. p. 141—143° after recrystallisations from ethanol and from toluene (Found: C, 70·7; H, 5·9; N, 8·8. $C_{19}H_{18}O_3N_2$ requires C, 70·8; H, 5·6; N, 8·7%). More (7·7 g., m. p. 140—142°) of the product was obtained by treatment of the chloroform solution with dilute sodium hydroxide solution, separation of the crystalline sodium salt, and acidification. Its structure was confirmed by methylation with methyl iodide and potassium carbonate in acetone. The 2-methoxy-compound had m. p. 114—115° and mixed m. p. 114·5—115·5° with authentic material. The chloroform solution, after removal of the sodium salt, was washed, dried, and evaporated. The residue, in benzene, was filtered through alumina and the eluate on evaporation yielded 1-[4-*cyano*-2-(5-p-*cyanophenoxypentyloxy*)-*phenoxy*]-5-p-*cyanophenoxypentane* (7·4 g.), m. p. 81—83° [from acetone–light petroleum (b. p. 40—60°)] (Found: C, 72·9; H, 6·2; N, 8·1. $C_{31}H_{31}O_4N_3$ requires C, 73·1; H, 6·1; N, 8·2%).

1-(4-*Amidino*-2-*methoxyphenoxy*)-5-p-*amidinophenoxypentane*. The dinitrile (30 g.) in dry chloroform (200 ml.) and ethanol (30 ml.) was treated with hydrogen chloride for 1 hr. at 0°. After 10 days at room temperature, the suspension was diluted with dry ether and the di-imidoate dihydrochloride was filtered off and dried. It was then added to saturated ethanolic ammonia (400 ml.) at 0° and the mixture was kept for 1·5 hr. at 0° and for 3 hr. at 60—70°, and filtered. The filtrate on cooling deposited the diamidine dihydrochloride (9·35 g.), which melts and effervesces above 165°. A second crop (19·7 g.) was obtained by concentrating the mother liquors *in vacuo*. The combined products yielded 1-(4-*amidino*-2-*methoxyphenoxy*)-5-p-*amidinophenoxypentane dihydrochloride sesquihydrate* (19·85 g.) (from ethanol), which slowly melted and effervesced above 155° (Found: C, 51·9; H, 6·6; N, 11·9; Cl, 15·1, loss at 110°/15 mm., 5·6. $C_{20}H_{26}O_3N_4,2HCl,1{\cdot}5H_2O$ requires C, 51·1; H, 6·6; N, 11·9; Cl, 15·1; H_2O, 5·7%).

1-(4-*Amidino*-2-*hydroxyphenoxy*)-5-p-*amidinophenoxypentane dihydrochloride*, similarly prepared, was purified by dissolution in very dilute hydrochloric acid and addition of concentrated hydrochloric acid. It separated as a *hydrate*, which slowly melted and effervesced above 201° (Found: N, 12·2; Cl, 15·55; loss at 100°/15 mm, 6·6; regain in air, 7·1. $C_{19}H_{24}O_3N_4,2HCl,1{\cdot}75H_2O$ requires N, 12·1; Cl, 15·4; H_2O, 6·8%).

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RESEARCH LABORATORIES,
MAY AND BAKER, LTD., DAGENHAM, ESSEX. [*Received, September 9th*, 1957.]

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179. *Certain Reactions of 4-Methoxydiphenyl.*

By W. H. LINNELL and H. J. SMITH.

A POSSIBLE synthesis of certain analogues of steroidal hormones [1] required 4'-methoxy-4-diphenylylacetic acid. Although this acid was finally prepared in good yield from 4'-methoxy-4-diphenylyl methyl ketone by a Kindler variation of the Willgerodt reaction initially the chloromethylation of 4-methoxydiphenyl was studied. Kosolapoff's method [2] yielded a solid containing 55% of chloromethyl compound which on reaction with cyanide

[1] Linnell and Smith, in the press.
[2] Kosolapoff, *J. Amer. Chem. Soc.*, 1946, **68**, 1670.

followed by alkaline hydrolysis gave an acid (m. p. 169—169·5°), isomeric with the required acetic acid (m. p. 188—188·5° [1]). Fieser and Bradsher [3] has described the Friedel–Crafts acylation of 4-methoxydiphenyl, substitution mainly occurring in the 4'-position, whereas nitration gives 4-methoxy-3-nitrodiphenyl.[4] Our acid, m. p. 169—169·5°, was therefore tentatively formulated as 4-methoxy-3-diphenylylacetic acid, this formulation being confirmed by independent synthesis.

A Gattermann reaction with 4-methoxydiphenyl yielded an aldehyde, oxidised to the known 4-methoxydiphenyl-3-carboxylic acid [5] by permanganate. This acid was converted by the Arndt–Eistert method into 4-methoxy-3-diphenylylacetic acid, identical with the acid prepared by chloromethylation of 4-methoxydiphenyl.

Experimental.—Chloromethylation of 4-methoxydiphenyl. 4-Methoxydiphenyl (17·85 g.), paraformaldehyde (2 g.), acetic acid (25 c.c.), hydrochloric acid (*d* 1·18; 28 c.c.), phosphoric acid (85%, 13·5 c.c.), and light petroleum (b. p. 60—80°, 50 c.c.) were refluxed with stirring for 20 hr. and then cooled and extracted with chloroform. The extract was washed free from acid, dried (Na_2SO_4), and evaporated to a solid (17·1 g.), m. p. 78·5—83°. The chloromethyl compound could not be isolated from this mixture by distillation or crystallisation. The solid was estimated to contain 55% of chloromethyl compound (monochloromethylation being assumed) by hydrolysis with alcoholic alkali and determination of the chloride ion by Volhard's method.

Reaction of chloromethyl compound with cyanide. Crude chloromethylated material (8·3 g.) in alcohol (70 c.c.) and sodium cyanide (6 g.) in water (8 c.c.) were refluxed for 13 hr.; aqueous potassium hydroxide was then added and refluxing was continued for 22 hr. The solution was then worked up to give *4-methoxy-3-diphenylylacetic acid* (4·35 g.), m. p. and mixed m. p. 169—169·5° (from aqueous alcohol) (Found: C, 74·1; H, 5·8%; equiv., 241. $C_{15}H_{14}O_3$ requires C, 74·4; H, 5·8%; equiv., 242·3). The amide was obtained as long white needles (from aqueous alcohol), m. p. and mixed m. p. 181·5—181·8°, and the *p*-bromophenacyl ester as white microneedles (from alcohol), m. p. 131·5° undepressed on admixture with authentic material (Found: C, 62·8; H, 4·45; Br, 17·9. Calc. for $C_{24}H_{21}O_4Br$: C, 62·9; H, 4·4; Br, 18·2%).

4-Methoxydiphenyl-3-aldehyde. Zinc cyanide (46·8 g.) and potassium chloride (5 g.) were added to 4-methoxydiphenyl (36·8 g.) in dry benzene (220 c.c.) and a rapid stream of dry hydrogen chloride passed in with stirring for 2½ hr. Aluminium chloride (40 g.) was then added and gas passed through the mixture at 40—50° for a further 4 hr. The benzene layer was separated, hydrochloric acid added, and the mixture refluxed for 1 hr. The upper layer which separated upon cooling was dried and the aldehydic fraction was isolated from this by decomposition of its semicarbazone (indicated 48% of aldehydic material present) with dilute sulphuric acid. Recrystallisation gave an *aldehyde*, m. p. 76·5—77° (Found: C, 79·45; H, 5·6; MeO, 14·2. $C_{14}H_{12}O_2$ requires C, 79·2; H, 5·7; MeO, 14·6%). The orange-red 2 : 4-*dinitrophenylhydrazone* had m. p. 230—231·5° (from aqueous acetic acid) (Found: C, 61·6; H, 4·2; N, 14·2. $C_{20}H_{16}O_5N_4$ requires C, 61·2; H, 4·1; N, 14·3%). The *semicarbazone* was obtained as pale yellow plates, m. p. 239·5—240° (from aqueous acetic acid) (Found: C, 66·8; H, 5·55; N, 15·9. $C_{15}H_{15}O_2N_3$ requires C, 66·9; H, 5·6; N, 15·6%).

4-Methoxydiphenyl-3-carboxylic acid. 4-Methoxydiphenyl-3-aldehyde (2·6 g.) was oxidised by a refluxing alkaline solution of potassium permanganate for 3 hr. Removal of manganese dioxide and addition of hydrochloric acid and a little sodium hydrogen sulphite gave a white precipitate (2·1 g.). Recrystallisation from ether gave pale yellow micro-crystals of the acid, m. p. 170—170·5° (lit.[3] gives m. p. 166—167°) (Found: C, 74·4; H, 5·4; MeO, 13·4%; equiv., 233·7. Calc. for $C_{14}H_{12}O_3$: C, 73·7; H, 5·3; MeO, 13·6%; equiv., 228·2).

4-Hydroxydiphenyl-3-carboxylic acid. 4-Methoxydiphenyl-3-carboxylic acid was quantitatively demethylated by acetic acid and 48% hydrogen bromide solution, to give white microcrystals of the hydroxy-acid, m. p. 214—214·5° (lit. gives m. p. 212—213°) (from *cyclo*hexane) (Found: C, 73·0; H, 4·8. Calc. for $C_{13}H_{10}O_3$: C, 72·9; H, 4·7%). The methyl ester was obtained as white micro-needles, m. p. 93—94° (lit.[3] gives m. p. 93—94°) (Found: C, 74·0; H, 5·1. Calc. for $C_{14}H_{12}O_3$: C, 73·7; H, 5·3%).

4-Methoxy-3-diphenylylacetic acid. 4-Methoxydiphenyl-3-carboxylic acid (3·2 g.) and freshly distilled thionyl chloride (25 c.c.) were refluxed for 1 hr. and excess of thionyl chloride then removed. The acid chloride in dioxan (20 c.c.) was added to ice-cold ethereal diazomethane (600 c.c.; prepared from 15 g. of methylnitrosourea), and left overnight. Removal

[3] Fieser and Bradsher, *J. Amer. Chem. Soc.*, 1936, **58**, 1738.
[4] Bell and Kenyon, *J.*, 1926, 3044.

of the ether was followed by addition of dioxan (100 c.c.), freshly prepared silver oxide (1 g.), and dioxan saturated with ammonia (100 c.c.). The suspension was stirred and heated at 80—100° for 3 hr., filtered, and evaporated to give micro-crystals, m. p. 169—175° (0·95 g.). Repeated recrystallisation from aqueous alcohol gave long white needles of *4-methoxy-3-diphenylylacetamide*, m. p. 180·5° (Found: C, 74·7; H, 6·5; N, 5·7. $C_{15}H_{15}O_2N$ requires C, 74·7; H, 6·6; N, 5·8%). Hydrolysis with alcoholic potassium hydroxide, and recrystallisation from aqueous alcohol, then from benzene–light petroleum (b. p. 60—80°) gave white needles, m. p. 170—171°, of *4-methoxy-3-diphenylylacetic acid* (Found: C, 74·2; H, 5·9%; equiv., 239·4. $C_{15}H_{14}O_2$ requires C, 74·4; H, 5·8%; equiv., 242·3). The *p-bromphenacyl ester* formed white micro-crystals (from alcohol), m. p. 131° (Found: C, 62·7; H, 4·4; Br, 18·0. $C_{24}H_{21}O_4Br$ requires C, 62·9; H, 4·4; Br, 18·2%).

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180. *Thermogravimetric Analysis of Ammonium Phosphomolybdate in vacuo.*

By S. J. GREGG and R. STOCK.

As a preliminary to the experimental study of the adsorptive properties [1] of ammonium phosphomolybdate it was necessary to ascertain the stability of the substance towards heat. Accordingly it was subjected to thermogravimetric analysis *in vacuo* in two stages by means of an electromagnetic sorption balance [2] connected through a liquid-oxygen trap to mercury-condensation and rotary pumps: the sample was first maintained at 180° till further loss in weight was negligible and was then raised in temperature at a rate of 1·2° per minute to 630°, after which it was rapidly heated to 830°.

The loss in weight at 180° was only 0·4%, probably due to adsorbed water since the trap contained no ammonia or nitric acid. Above 180° the rate of loss gradually increased to *ca.* 380°, when it sharply increased up to 470°, and then slowed down till 630° was reached (except for a curious notch in the curve at 540°, also reported by Duval [3] during thermogravimetric analysis in air); above this temperature the loss again accelerated and at 800° became too rapid to measure accurately.

The loss in weight between 180° and 470° was 6·60%, *i.e.*, 2·41% *in excess* of that to be expected for the reaction

$$(NH_4)_3PO_4,12MoO_3 \longrightarrow \tfrac{1}{2}P_2O_5,24MoO_3 + 3NH_3 + 1\tfrac{1}{2}H_2O \quad . \quad . \quad . \quad . \quad . \quad (1)$$

but the ammonia found in the contents of the trap corresponded to only 1·17%, *i.e.*, 1·55% *less than* the amount required by equation (1). The two discrepancies are accounted for by postulating that the " lost " ammonia has been oxidised by the MoO_3:

$$2NH_3 + 3O \text{ (from the } MoO_3) \longrightarrow 3H_2O + N_2 \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (2)$$

the 1·55% of ammonia would by this equation withdraw 2·20% of oxygen from the solid, which would be registered as an additional loss in weight; and this figure agrees within experimental error with the 2·41% found by experiment. The reduction of the solid is confirmed by the formation of a blue sublimate on the inside of the tube of the balance " case " just above the furnace.

Since the loss of weight between 180° and 380° (1·45%) was within experimental limits equal to that calculated for the loss of $1NH_3 + 0{\cdot}5H_2O$ (1·40%), the reduction only sets in above 380°.

The ammonium phosphomolybdate was prepared by addition of a solution of ammonium molybdate containing ammonium and nitrate ions to potassium dihydrogen phosphate at 50°, following the detailed procedure of Thistlethwaite.[4]

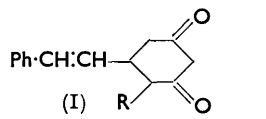
THE WASHINGTON SINGER LABORATORIES,
THE UNIVERSITY, EXETER. [*Received, October 14th*, 1957.]

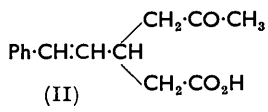
[1] Gregg and Stock, *Trans. Faraday Soc.*, 1957, **53**, 1355.
[2] Gregg, *J.*, 1955, 1498.
[3] Duval, " Thermogravimetric Analysis," Elsevier, Amsterdam, 1953, p. 130.
[4] Thistlethwaite, *Analyst*, 1947, **72**, 531.

181. cyclo*Hexane*-1 : 3-*diones. Part III.* Alkaline Hydrolysis of Ethyl* 2 : 4-*Dioxo*-6-*styryl*cyclo*hexanecarboxylate.*

By G. R. Ames and W. Davey.

In Part I [1] of this series, it was shown that hydrolysis of ethyl 2 : 4-dioxo-6-styryl*cyclo*hexanecarboxylate (I; R = CO_2Et) with hydrochloric acid did not yield the expected 5-oxo-3-styrylhexanoic acid (II), but gave instead the isomeric compound *trans*-5-oxo-3-phenethylhex-2-enoic acid (III), m. p. 127—128°. We have now found that when the dione-ester (I; R = CO_2Et) is refluxed with barium hydroxide solution, there is obtained a new acid, m. p. 89—90°, which, on evidence given below, is assigned structure (II). Ozonolysis of this acid gave benzaldehyde as the only steam-volatile product. The ultraviolet absorption spectrum of the new acid ($\lambda_{max.}$ 249·5 mμ; ε 19,500) was characteristic of a compound containing the styryl chromophore.[2] The infrared spectrum (in Nujol) contains a band at 1688 cm.$^{-1}$ (unconjugated acids [3] absorb at 1689—1754 cm.$^{-1}$; the acid (III) shows a band at 1679 cm.$^{-1}$); there is also a shoulder (1703 cm.$^{-1}$) due to the ketone group, and a band (970 cm.$^{-1}$) caused by the *trans* –CH=CH– system.[4]


(I)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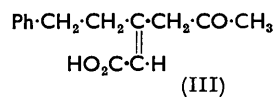
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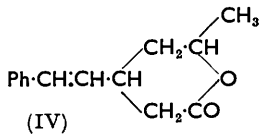
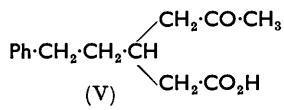
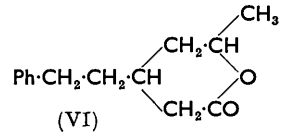

(IV)


(V)


(VI)

The esters of δ-keto-acids are cyclised by sodium alkoxides to *cyclo*hexane-1 : 3-diones.[5] Treatment of the methyl ester of the acid (II) with sodium methoxide yielded 5-styryl-*cyclo*hexane-1 : 3-dione (I; R = H). This observation confirms the assignment of structure (II).

Treatment of the acid (II) with potassium borohydride afforded the lactone (IV), which yielded benzaldehyde on ozonolysis. When the acid (II) was hydrogenated (palladised charcoal), 1 mol. of hydrogen was absorbed; the product, 5-oxo-3-phenethylhexanoic acid (V), was shown, by comparison of the 2 : 4-dinitrophenylhydrazones, to be identical with that obtained previously [1] by hydrolysis of ethyl 2 : 4-dioxo-6-phenethyl*cyclo*hexanecarboxylate. Hydrogenation of the acid (II) with a Raney nickel W7 catalyst gave the saturated lactone (VI); this is in contrast to the αβ-unsaturated acid (III), in which the double bond is not reduced under these conditions.[1] Attempts to prepare 3-styrylhexanoic acid by reduction of the keto-acid (II) by the Wolff–Kishner and the Clemmensen method were unsuccessful, as no crystalline product could be isolated. An attempt to isomerise the acid (II) by treatment with hydrochloric acid under the conditions used for the preparation of the acid (III), also yielded an uncrystallisable product.

Experimental.—Ultraviolet absorption spectra were determined for EtOH solutions, using a Unicam S.P. 500 spectrophotometer.

5-*Oxo*-3-*styrylhexanoic acid* (II). Ethyl 2 : 4-dioxo-6-styryl*cyclo*hexanecarboxylate (50 g.) and barium hydroxide (120 g.) in water (2·5 l.) were refluxed together for 20 hr. The mixture was acidified and decanted from an oil. Gradually 5-*oxo*-3-*styrylhexanoic acid* (16 g.) separated;

* Part II, *J.*, 1957, 3480.

[1] Ames and Davey, *J.*, 1956, 3001.
[2] Overberger and Tanner, *J. Amer. Chem. Soc.*, 1955, **77**, 369.
[3] Randall, Fowler, Fuson, and Dangl, "Infrared Determination of Organic Structures," Van Nostrand, New York, 1949, p. 20.
[4] Bellamy, "Infrared Spectra of Complex Molecules," Methuen, London, 1954, p. 31.
[5] Vorländer, *Annalen*, 1896, **294**, 253.

it formed prisms, m. p. 89—90°, from benzene–light petroleum (b. p. 60—80°) (Found: C, 72·2; H, 6·9. $C_{14}H_{16}O_3$ requires C, 72·4; H, 6·9%). The *semicarbazone*, prisms from ethyl acetate, had m. p. 165° (decomp.) (Found: C, 61·8; H, 6·5. $C_{15}H_{19}O_3N_3$ requires C, 62·3; H, 6·6%), and the *methyl ester* had b. p. 160—162°/1·2 mm., n_D^{21} 1·5353 (Found: C, 73·4; H, 7·5. $C_{15}H_{18}O_3$ requires C, 73·1; H, 7·4%).

Cyclisation of methyl 5-oxo-3-styrylhexanoate. The foregoing ester (2·9 g.) was added to a solution of sodium (0·3 g.) in methanol (50 c.c.) and the mixture refluxed for 3 hr. The solution was concentrated, diluted with water, and then washed with ether to remove any unchanged ester. Acidification of the aqueous layer afforded 5-styryl*cyclo*hexane-1 : 3-dione (1 g.), m. p. and mixed m. p. 183—184°.

5-Hydroxy-3-styrylhexanoic lactone (IV). A solution of 5-oxo-3-styrylhexanoic acid (3 g.) and potassium borohydride (6 g.) in water (100 c.c.) was set aside overnight. The mixture was acidified and the product isolated with ether. Distillation gave the *lactone* (2·6 g.), b. p. 188°/1·5 mm., n_D^{20} 1·5676 (Found: C, 77·6; H, 7·5. $C_{14}H_{16}O_2$ requires C, 77·7; H, 7·5%), which solidified on storage, having m. p. 54—55°, $\lambda_{max.}$ 250·5 mμ (ε 19,400), and infrared bands at 968 and 1721 cm.$^{-1}$ (in Nujol; 1726 cm.$^{-1}$ in $CHCl_3$).

Hydrogenation of 5-oxo-3-styrylhexanoic acid. (*a*) The acid (3 g.) in ethanol (150 c.c.) was shaken under hydrogen with 5% palladised charcoal (1 g.). Uptake of hydrogen ceased when 325 c.c. had been absorbed (1 mol.; 295 c.c.). The catalyst was removed, the solution evaporated, and the oily residue treated with Brady's reagent. The 2 : 4-dinitrophenylhydrazone thus obtained was identical (m. p. and mixed m. p. 147—148°) with that of 5-oxo-3-phenethylhexanoic acid (V) obtained previously.[1]

(*b*) A mixture of the acid (4 g.) in ethanol (150 c.c.), 2N-sodium hydroxide (20 c.c.), and Raney nickel (about 5 g.) was shaken under hydrogen until absorption ceased (vol. absorbed, 720 c.c.; $2H_2$ requires 780 c.c.). The filtered liquid was concentrated and then acidified, and the product was isolated with ether. *5-Hydroxy-3-phenethylhexanoic lactone* (VI) had b. p. 164°/0·5 mm., n_D^{23} 1·5311 (Found: C, 77·3; H, 8·6. $C_{14}H_{18}O_2$ requires C, 77·0; H, 8·3%).

We thank Miss E. M. Tanner, Parke, Davis & Co., Hounslow, Middlesex, for determining the infrared spectra and for helpful suggestions on their interpretation.

THE POLYTECHNIC, 309 REGENT ST., LONDON, W.1. [*Received, November 4th*, 1957.]

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182. *Action of Acidic Reagents on 2 : 4 : 5-Trimethoxybenzyl and 2-Methoxy-4 : 5-methylenedioxybenzyl Alcohol.*

By T. R. GOVINDACHARI, K. NAGARAJAN, and P. C. PARTHASARATHY.

ALTHOUGH Harley-Mason and Jackson [1] noted the formation of a chlorine-free compound, m. p. 101°, by the action of thionyl chloride on 2 : 4 : 5-trimethoxybenzyl alcohol, its structure was not elucidated. During other work in this laboratory, it was found that the compound was formed from the alcohol in nearly quantitative yield by the action of thionyl chloride in chloroform or pyridine, of hydrogen chloride in benzene, or of aqueous 4N-hydrochloric acid. With the last reagent it was possible to demonstrate the formation of *ca.* 1 mol. of formaldehyde. Analyses suggested that the compound was 2 : 4 : 5 : 2′ : 4′ : 5′-hexamethoxydiphenylmethane. This was confirmed by comparison with a specimen synthesised as follows: 1 : 2 : 4-Trimethoxybenzene, in Friedel–Crafts reaction at 0—5° with 2 : 4 : 5-trimethoxybenzoyl chloride, gave a benzophenone which was reduced to the diphenylmethane derivative by hydrogen and pallidised charcoal in acetic acid containing perchloric acid. (Friedel–Crafts reaction at 70—80° gave 2 : 4 : 5 : 2′ : 4′ : 5′-hexamethoxydiphenyl.[2])

2-Methoxy-4 : 5-methylenedioxybenzyl alcohol likewise yielded 2 : 2′-dimethoxy-4 : 5—4′ : 5′-bismethylenedioxydiphenylmethane on treatment with thionyl chloride in the cold.

[1] Harley-Mason and Jackson, *J.*, 1954, 1168.
[2] Taylor, *J.*, 1954. 2636.

Experimental.—Ultraviolet measurements are for 95% ethanol solutions.

2 : 4 : 5-*Trimethoxybenzyl alcohol.* Asarylaldehyde (5 g.) in tetrahydrofuran (40 ml.) was added to a stirred suspension of lithium aluminium hydride (1·5 g.) in ether (30 ml.). Next morning the mixture was decomposed with water. The ether–tetrahydrofuran layer was decanted, dried, and evaporated. Crystallisation of the residue (4·5 g.) from light petroleum (b. p. 40—60°) gave 2 : 4 : 5-trimethoxybenzyl alcohol, plates, m. p. 73° (Harley-Mason *et al.*[1] report m. p. 70—71°).

2 : 4 : 5 : 2′ : 4′ : 5′-*Hexamethoxydiphenylmethane.* The foregoing alcohol (4·5 g.) in benzene (50 ml.) was treated with dry hydrogen chloride in the cold and left overnight. Next morning, the benzene solution was washed successively with water and aqueous sodium carbonate. Evaporation of the solvent left a solid (3·6 g.) which crystallised from aqueous alcohol as needles, m. p. and mixed m. p. 102° with 2 : 4 : 5 : 2′ : 4′ : 5′-hexamethoxydiphenylmethane, $\lambda_{max.}$ 290 mμ (log ε 3·93) (Harley-Mason *et al.*[1] report m. p. 101°) (Found: C, 65·5, 65·7; H, 6·8, 6·8; OMe, 50·5. Calc. for $C_{19}H_{24}O_6$: C, 65·5; H, 6·9; 6OMe, 53·4%).

2 : 4 : 5 : 2′ : 4′ : 5′-*Hexamethoxydiphenyl.* 2 : 4 : 5-Trimethoxybenzoyl chloride (1 g.) in benzene (40 ml.) containing 1 : 2 : 4-trimethoxybenzene (1·5 g.) was treated with aluminium chloride (1 g.) in small lots, then heated at 80° for 1 hr. and worked up as usual, the diphenyl (0·5 g.) being obtained as needles (from acetic acid), m. p. and mixed m. p. 178° with a synthetic specimen.[2]

2 : 4 : 5 : 2′ : 4′ : 5′-*Hexamethoxybenzophenone.* The foregoing reaction at 0—5° with carbon disulphide as solvent gave 2 : 4 : 5 : 2′ : 4′ : 5′-hexamethoxybenzophenone as lemon-yellow tablets (from methanol), m. p. 150—151° (Oskoläs[3] obtained it as a secondary product from 1 : 2 : 4-trimethoxybenzene and oxalyl chloride containing aluminium chloride and reported m. p. 147°).

2 : 4 : 5 : 2′ : 4′ : 5′-*Hexamethoxydiphenylmethane.* The foregoing benzophenone (0·2 g.) in acetic acid (10 ml.) containing 70% perchloric acid (0·2 ml.) was reduced (1 hr.) with hydrogen at 1 atm. at 50—60°, in presence of 5% palladised charcoal (0·2 g.). The catalyst was filtered off, and the filtrate concentrated *in vacuo*. The oily residue was taken up in ether, washed with water and dried (Na_2SO_4). Evaporation of the solvent gave 2 : 4 : 5 : 2′ : 4′ : 5′-hexamethoxydiphenylmethane (0·1 g.), needles (from alcohol), m. p. 102° (Found: C, 65·3; H, 6·7%).

2-*Methoxy*-4 : 5-*methylenedioxybenzyl alcohol.* Reduction of 2-methoxy-4 : 5-methylenedioxybenzaldehyde[4] (1 g.) by lithium aluminium hydride (1 g.) in ether (30 ml.) yielded 2-*methoxy*-4 : 5-*methylenedioxybenzyl alcohol*, needles (from light petroleum), m. p. 54—55° (Found: C, 59·2; H, 5·2. $C_9H_{10}O_4$ requires C, 59·3; H, 5·5%).

2 : 2′-*Dimethoxy*-4 : 5-4′ : 5′-*bismethylenedioxydiphenylmethane.* The foregoing alcohol (0·5 g.) in chloroform (5 ml.) with thionyl chloride (1 ml.) in the cold gave 2 : 2′-*dimethoxy*-4 : 5-4′ : 5′-*bismethylenedioxydiphenylmethane* (0·3 g.), needles (from alcohol), m. p. 140—141°, $\lambda_{max.}$ 301 mμ (log ε 3·97) (Found: C, 64·8; H, 5·3. $C_{17}H_{16}O_6$ requires C, 64·6; H, 5·1%).

We thank the Government of India for a senior research scholarship (to P. C. P.), and Mr. S. Selvavinayakam for analyses.

PRESIDENCY COLLEGE, MADRAS, INDIA. [*Received, November 12th,* 1957.]

[3] Oskoläs, *Acta Lit. Sci. Univ. Hung. Francisco-Josephinae, Sect. chem., min., phys.*, 1932, **2**, 165; *Chem. Abs.*, 1933, **27**, 1874.

[4] Campbell, Hopper, and Campbell, *J. Org. Chem.*, 1951, **16**, 1736.

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183. *Polynuclear Heterocyclic Systems. Part XII.* Further Examples of the Elbs Reaction with Heterocyclic Ketones.*

By G. M. BADGER and B. J. CHRISTIE.

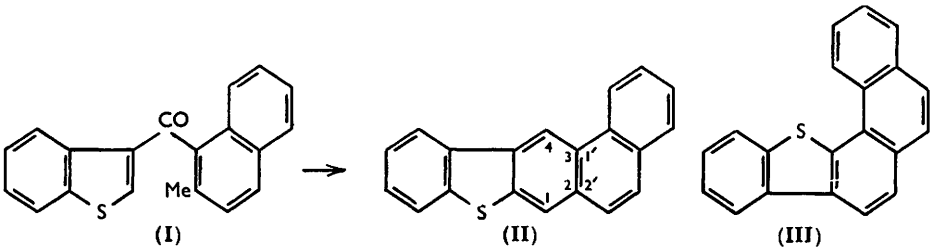
PYROLYSIS of 3-*o*-toluoylthionaphthen has been shown[1] to give 9-thia-1 : 2-benzofluorene and not the expected 9-thia-2 : 3-benzofluorene, and a possible mechanism for the rearrangement was advanced.[2] We now find that two analogues, (I) and (IV), are not rearranged in similar reactions.

* Part XI, *J.*, 1956, 3438.

[1] Badger and Christie, *J.*, 1956, 3435.

[2] Tilak, *Proc. Indian Acad. Sci.*, 1951, **33**, *A*, 131.

Cyclodehydration of 3-(2-methyl-1-naphthoyl)thionaphthen (I) occurred very readily, giving a good yield of product: if this had structure (II), it should give a 1 : 4-quinone on oxidation; if it had structure (III) it would give a 1 : 2-quinone. Chromic acid oxidation



of the product gave the known 1 : 4-quinone.[2] The product is therefore (II) and this is confirmed by the ultraviolet absorption spectrum, resembling that of 1 : 2-7 : 8-dibenzanthracene, with which it is isoelectronic [3] (Fig. 1).

FIG. 1. FIG. 2.

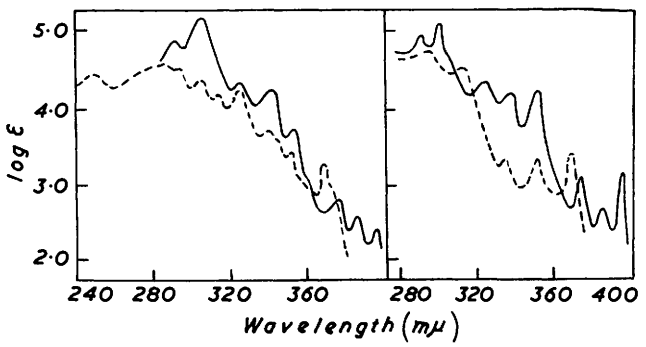
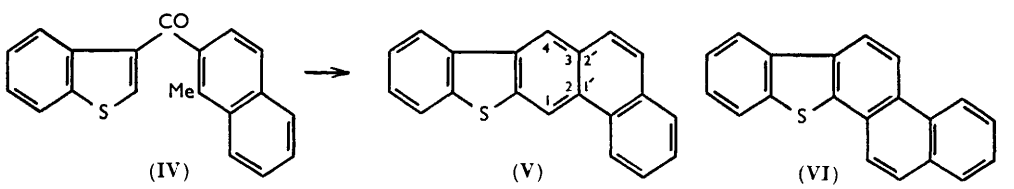


FIG. 1. *Ultraviolet absorption spectra of* (– – – –) *9-thianaphtho*(2′ : 1′-2 : 3)*fluorene* (II) *in* 95% EtOH *and of* (———) 1 : 2-7 : 8-*dibenzanthracene in* C_6H_6.[4]

FIG. 2. *Ultraviolet absorption spectra of* (– – – –) *9-thianaphtho*(1′ : 2′-2 : 3)*fluorene* (V) *in* C_6H_6 *and of* (———) 1 : 2-5 : 6-*dibenzanthracene in* C_6H_6.[4]

Cyclodehydration of 3-(1-methyl-2-naphthoyl)thionaphthen (IV) also proceeded readily, giving a product oxidised to a 1 : 4-quinone [2] and therefore having structure (V) and not (VI). The absorption spectrum resembles that of 1 : 2-5 : 6-dibenzanthracene, with which it is isoelectronic (Fig. 2).



Rearrangement during pyrolysis of 3-acylthionaphthens is thus not a general characteristic.

Experimental.—*2-Methyl-1-naphthoic acid.* Carboxylation of 2-methyl-1-naphthylmagnesium bromide with anhydrous carbon dioxide [5] gave 2-methyl-1-naphthoic acid (71% yield), needles, m. p. 126—127° (from benzene), which was converted into the acid chloride in quantitative yield with excess of thionyl chloride.

3-(2-Methyl-1-naphthoyl)thionaphthen. Stannic chloride (27 g.) in thiophen-free benzene (75 c.c.) was added during 30 min., at room temperature, to a stirred solution of thionaphthen

[3] Badger and Christie, *J.*, 1956, 3438.
[4] Clar, " Aromatische Kohlenwasserstoffe," Springer-Verlag, Berlin, 2nd edn., 1952.
[5] Cf. Adams and Binder, *J. Amer. Chem. Soc.*, 1941, **63**, 2773.

(13·5 g.) and 2-methyl-1-naphthoyl chloride (20 g.) in thiophen-free benzene (200 c.c.). After refluxing for 3 hr. the mixture was poured on ice and hydrochloric acid. The benzene layer was washed with 10% hydrochloric acid, water, 10% aqueous sodium hydroxide, and water, dried (Na_2SO_4), and evaporated. The resulting 3-(2-*methyl*-1-*naphthoyl*)*thionaphthen* (24 g., 80%) crystallised from hexane in prisms, m. p. 160—161° (Found: C, 79·7; H, 4·75; S, 10·8. $C_{20}H_{14}OS$ requires C, 79·4; H, 4·7; S, 10·6%). It did not form a 2 : 4-dinitrophenylhydrazone or an oxime, but showed carbonyl absorption at 1639 cm.$^{-1}$.

9-*Thianaphtho*(2′ : 1′-2 : 3)*fluorene*. The above ketone (10 g.) was heated under reflux (bath-temp., 450°) for 3 hr., by which time evolution of water had ceased. A small amount of 2-methylnaphthalene was distilled off and characterised as the picrate, m. p. and mixed m. p. 115°. The residue was chromatographed in benzene on alumina. Elution with benzene, followed by evaporation and recrystallisation of the *product* from ethanol, gave leaflets (5·1 g., 54%), m. p. 141—142° (Found: C, 84·55; H, 4·3; S, 11·2. $C_{20}H_{12}S$ requires C, 84·5; H, 4·25; S, 11·3%). Its *dipicrate* crystallised from benzene in orange-red needles, m. p. 176—177° (Found: C, 52·0; H, 2·7; N, 10·9. $C_{32}H_{18}O_{14}N_6S$ requires C, 51·8; H, 2·4; N, 11·3%).

Chromium trioxide (0·3 g.) in water (10 c.c.) was added to a boiling solution of the above thiafluorene (0·2 g.) in glacial acetic acid (25 c.c.), and the mixture refluxed for 30 min. Pouring the whole into water gave an orange solid which was chromatographed in benzene on alumina. Recrystallisation from benzene gave the quinone as orange needles, m. p. 260—261°, recovered unchanged after being heated with *o*-phenylenediamine (Found: C, 76·35; H, 3·4; S, 10·3. Calc. for $C_{20}H_{10}O_2S$: C, 76·4; H, 3·2; S, 10·2%). Tilak [2] gives m. p. 261—262·5°.

1-*Methyl*-2-*naphthoic acid*. Cyclisation of ethyl α-phenethylacetoacetate (10 g.) with concentrated sulphuric acid (200 c.c.) at room temperature gave 3 : 4-dihydro-1-methyl-2-naphthoic acid (6 g., 75%) and not the fully aromatic compound as found by von Auwers and Möller.[6] It formed needles (from benzene), m. p. 127° (lit.,[6] 127°). Dehydrogenation was effected by 12 hours' refluxing with 10% palladium–charcoal in *p*-cymene. The resulting 1-methyl-2-naphthoic acid, m. p. 177—178° (lit.,[6] 177—178°), was converted into the acid chloride with excess of thionyl chloride.

3-(1-*Methyl*-2-*naphthoyl*)*thionaphthen*. Stannic chloride (9 g.) in thiophen-free benzene (30 c.c.), thionaphthen (4 g.), and 1-methyl-2-naphthoyl chloride (6 g.) in thiophen-free benzene, gave, as above, 3-(1-*methyl*-2-*naphthoyl*)*thionaphthen* (5·5 g., 61%), needles (from hexane), m. p. 119—120° (Found: C, 79·6; H, 4·7; S, 10·7%), $\nu_{max.}$ 1639 cm.$^{-1}$ (C=O).

9-*Thianaphtho*(1′ : 2′-2 : 3)*fluorene*. The above ketone (3 g.) was heated under reflux (bath-temp., 450°) for 4½ hr. The *product* (1·2 g., 43%) separated from benzene in needles, m. p. 322—323° (Found: C, 84·8; H, 4·2; S, 11·3%), and gave the 1 : 4-quinone, red needles (from benzene), m. p. 256° (lit.,[2] m. p. 255—256°), recovered unchanged after treatment with *o*-phenylenediamine.

Ultraviolet absorption spectra were determined with a Hilger Uvispek Spectrophotometer.

Microanalyses were carried out by the C.S.I.R.O. Microanalytical Laboratory, Melbourne. We also thank Dr. H. J. Rodda and Mr. A. G. Moritz for the infrared spectra. One of us (B. J. C.) has been working with an I.C.I.A.N.Z. Fellowship.

UNIVERSITY OF ADELAIDE, SOUTH AUSTRALIA. [*Received, September 16th*, 1957.]

[6] von Auwers and Möller, *J. prakt. Chem.*, 1925, **109**, 124.

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184. *Ethoxide–Hydroxide-ion Competition in Bimolecular Nucleophilic Substitutions in Alkaline Aqueous Ethyl Alcohol.*

By Y. POCKER.

IN the earlier investigation [1] of the reactions of *iso*propyl bromide in aqueous ethyl alcohol, the full amount of ethyl *iso*propyl ether formed under bimolecular conditions was possibly not revealed because of the difficulty of isolating products from the very dilute solutions used to obtain kinetic conditions. From a large-scale product analysis (*ca.* 4 l. of reaction mixture) it has now been possible to isolate, after the complete decomposition of *iso*propyl bromide in strongly alkaline 60% aqueous ethyl alcohol, an amount of ethyl *iso*propyl ether corresponding to 23·8 moles % of the total organic products.

[1] Hughes, Ingold, and Shapiro, *J.*, 1936, 225.

An independent check has shown that the recovery was 68%, indicating that under the above conditions the amount of ethyl *iso*propyl ether actually formed is *ca.* 35 moles % of the total organic products.

From the data given by Hughes, Ingold, and Shapiro [1] it is possible to show that, under the conditions used, the unimolecular reaction amounts to 4% and the total bimolecular reaction ($S_N2 + E2$) to 96%. The latter value comprises 55% of bimolecular elimination ($E2$) and 41% of bimolecular substitution (S_N2).

The amount of ethyl *iso*propyl ether formed under unimolecular conditions is not known but cannot be larger than that formed in the total unimolecular reaction. When the total amount of ethyl *iso*propyl ether formed in the reaction is corrected for this relatively small uncertainty one finds that $33 \pm 2\%$ of the total bimolecular reaction ($S_N2 + E2$) results in the formation of ether. This result means that *ca.* $80 \pm 5\%$ of the bimolecular substitution represents replacement of bromide by ethoxide ion.

Under the conditions used, the rate of bimolecular ethoxylation is thus about four times that of bimolecular hydroxylation. The relative anion concentrations $[EtO^-] : [OH^-]$ and the ratio of the corresponding second-order rate coefficients $k_2^{EtOH^-} : k_2^{OH^-}$, jointly contribute to this result, *i.e.*:

$$\left(\frac{\text{Ethoxylation rate}}{\text{Hydroxylation rate}}\right)_{S_N2} = \frac{[OEt^-]}{[OH^-]} \cdot \frac{k_2^{OEt^-}}{k_2^{OH^-}}$$

In the absence of a precise value for the equilibrium, $OH^- + EtOH = EtO^- + H_2O$, in 60% aqueous ethyl alcohol at 70°, the concentration ratio cannot be treated separately from the ratio of the corresponding second-order rate coefficients.

In conclusion, it should be noted that variations in temperature or solvent composition will change the above concentration ratio of ethoxide to hydroxide ions and thereby affect also the wider issue of bimolecular rates of substitution and elimination.

Experimental.—Materials. *iso*Propyl bromide (B.D.H.) was dried with phosphoric oxide and fractionated, the fraction of b. p. 60°/760 mm. being used for measurements. Commercial absolute ethyl alcohol was dried over lime and fractionated. The 60% aqueous ethyl alcohol was made by mixing 3 volumes of this absolute alcohol with 2 volumes of water.

Product analysis. (*a*) Isolation experiment. The reaction mixture comprising absolute ethyl alcohol (2·4 l.) water (1·6 l.), " AnalaR " sodium hydroxide (320 g.), and *iso*propyl bromide (400 g.) was heated in sealed bulbs for 10 hr. at 70°, then fractionated. The fraction boiling below 58° was collected, the remaining mixture diluted with water (4 vols.) and fractionated again, the fraction boiling below 58° collected. The mixed fractions were dried over potassium and distilled from it, yielding 70 g. of pure ethyl *iso*propyl ether, b. p. 54° (Found: C, 68·4; H, 13·6. Calc. for $C_5H_{12}O$: C, 68·1; H, 13·7%). A second experiment gave 66 g. of ether, b. p. 54° (mean, 68 g., 23·8 moles %).

(*b*) Recovery experiment. Absolute ethyl alcohol (2·4 l.), water (1·6 l.), and ethyl *iso*propyl ether (59 g.) were heated in sealed bulbs for 4 hr. at 70°, then treated as described above, affording 39 g. of pure ethyl *iso*propyl ether, b. p. 54°, *i.e.*, 66% recovery. A second experiment with 60 g. of ether gave 70% recovery.

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