NOTES.

427. *Degradation of α-Amino-acids to Aldehydes and Ketones by Interaction with Carbonyl Compounds.*

By RADWAN MOUBASHER.

IN addition to the forty ketones which are capable of degrading α-amino-acids to the corresponding aldehydes or ketones with one carbon atom less (Schönberg *et al.*, *J.*, 1948, 176), the nitrogen analogues of *o*- and *p*-quinones (*e.g.*, phenanthraquinone-imine, indophenol, and 2 : 6-dichlorophenol-indophenol) effect this change in boiling water. It is uncertain whether they act directly or after hydrolysis; *e.g.*, phenanthraquinone-imine is very easily hydrolysed to the quinone and it is possible that the observed reaction is due to this compound. However, even if they themselves react, they probably do so in a similar manner to the quinones (cf. Schönberg *et al.*, *loc. cit.*).

Recently, Moubasher (*J.*, 1951, 231) found that piperonaldehyde very slowly effected the same change in boiling water, and Baddar (*J.*, 1949, S 163) described a number of such degradations with nitrobenzaldehydes in 75% aqueous pyridine. It has now been found that fluorenone, which is inactive in neutral solution, degrades alanine, α-amino*iso*butyric acid, leucine, and valine in the same mixed solvent in good yield.

Experimental.—Action of phenanthraquinone-imine, indophenol, and 2 : 6-dichlorophenol-indophenol on leucine. The quinone-imine (0·5 g.), leucine (0·6 g.), and indophenol (0·5 g.) or 2 : 6-dichlorophenol-indophenol (0·6 g.) were mixed with water (50 c.c.) in a Claisen flask fitted with an upright condenser, to which were attached a Liebig condenser and a receiver. With a continuous current of carbon dioxide passing through it, the mixture was distilled until its volume was reduced to about 20 c.c. (1 hour). The distillate was collected in a receiver containing a solution of 2 : 4-dinitrophenylhydrazine (0·3 g. in 25 c.c. of alcohol). The contents of the receiver were treated with concentrated hydrochloric acid (5 c.c.) and cooled in ice; *iso*valeraldehyde 2 : 4-dinitrophenylhydrazone was obtained and identified by its m. p. and mixed m. p. With phenanthraquinone-imine the yield was about 10%, but with the other two compounds it was smaller.

Action of fluorenone on α-amino-acids in aqueous pyridine. The experiment was carried out as above but with fluorenone (1 g.) and alanine (0·5 g.), α-amino*iso*butyric acid (0·5 g.), leucine (0·5 g.), or valine (0·7 g.), and aqueous pyridine (50 c.c., 75% by vol.) for 3 hours; acetaldehyde, acetone, *iso*valeraldehyde, and *iso*butaldehyde, respectively, were obtained as their 2 : 4-dinitrophenylhydrazones, identified by m. p. and mixed m. p. The yield in each case was more than 30%.

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428. *Some Derivatives of Diacetyl.*

By H. C. Barany, E. A. Braude, and M. Pianka.

In connection with other work, the preparation and properties of some derivatives of diacetyl have been investigated. The results are briefly recorded here.

When diacetyl monoxime is treated with an equivalent of hydrazine hydrate in the cold, mainly diacetyl hydrazone oxime is obtained (Darapski and Spannagel, *J. prakt. Chem.*, 1915, **92**, 272) whereas on heating it with excess of hydrazine hydrate, replacement of the oximino- by a hydrazono-group occurs and diacetyl dihydrazone is produced. Similarly, the dihydrazone is formed by heating diacetyl dioxime with excess of hydrazine hydrate.

The direct reaction of diacetyl with hydrazine hydrate gives diacetyl monohydrazone and the azines (I) and (II) in proportions depending on the conditions (Diels and Pflaumer, *Ber.*, 1915, **48**, 226). The diazine (II) is also obtained by the reaction of diacetyl dihydrazone with diacetyl. The dioxime (III) is readily prepared from diacetyl dihydrazone and diacetyl monoxime, but no reaction occurred between the dihydrazone and diacetyl monohydrazone even on melting the two substances together. An alternative attempt to prepare the dihydrazone of (II) by heating (II) with hydrazine hydrate resulted in a breakdown of the azine chain, the only product obtained being diacetyl hydrazone oxime or diacetyl dihydrazone.

Ultra-violet light absorption data for various diacetyl derivatives in ethanol solution are collected in the Table. In contrast to the observations made with monoazines (Barany, Braude, and Pianka, *J.*, 1949, 1898), diacetyl polyazines do not exhibit the usual bathochromic displacements of the characteristic maxima with increasing number of unsaturated groups, and effective conjugation does not appear to extend over the whole of the conjugated chain in these systems.

	M. p.	$\lambda_{max.}$, A.	$\varepsilon_{max.}$
O=CMe·CMe=N·OH	76°	2290	13,000
O=CMe·CMe=N·NH_2	67	2750	12,500
NH_2·N=CMe·CMe=N·NH_2	160	2650	17,000
(O=CMe·CMe=N·)$_2$ (I.)	39	2440	19,500
(HO·N=CMe·CMe=N·)$_2$	229	2510 2820	28,500 15,000
(O=CMe·CMe=N·N=CMe·)$_2$ (II.)	96	2590	36,000
(HO·N=CMe·CMe=N·N=CMe·)$_2$ (III.)	193	2510 2580 2810	31,500 29,500 22,500

Diacetyl Dihydrazone.—This compound was obtained in good yields by refluxing an excess of hydrazine hydrate with (i) diacetyl monohydrazone (Diels and Pflaumer, *Ber.*, 1915, **48**, 226) for 30 minutes, (ii) diacetyl monoxime for 8 hours, (iii) diacetyl hydrazone oxime for 10 hours, or (iv) diacetyl dioxime for 10 hours. It formed a dibenzylidene derivative, m. p. 125° (Darapski and Spannagel, *loc. cit.*, give m. p. 120°).

3 : 6 : 7 : 10-*Tetramethyl*-4 : 5 : 8 : 9-*tetra-azadodeca*-3 : 5 : 7 : 9-*tetraene*-2 : 11-*dione* (II) *and its Dioxime* (III).—The diazine (II) was obtained by the reaction of diacetyl in aqueous solution with (i) diacetyl monohydrazone (Diels and Pflaumer, *loc. cit.*) or (ii) diacetyl dihydrazone. After crystallisation from light petroleum (b. p. 40—60°) both samples had m. p. 96° (Found : N, 22·6. Calc. for $C_{12}H_{18}O_2N_4$: N, 22·4%) (Diels and Pflaumer, *loc. cit.*, give m. p. 105° for a distilled sample, possibly a stereoisomer). The dioxime (III) was prepared by shaking diacetyl dihydrazone (0·28 g.) with diacetyl monoxime (0·5 g.) in water (15 ml.). After two days the *dioxime* separated in pale yellow crystals, which were recrystallised from xylene and then had m. p. 193° (Found : C, 51·6; H, 7·0; N, 30·2. $C_{12}H_{20}O_2N_6$ requires C, 51·4; H, 7·1; N, 30·0%).

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429. *Synthesis of 6-Alkyl-2-thiouracils labelled with Radioactive Sulphur.*

By J. Bell and K. A. Macdonald.

The synthesis of thiourea and of 6-methyl-2-thiouracil labelled with radioactive sulphur, ^{35}S, has been reported by Ernsting and Nauta (*Landboukundig Tijdschrift*, 1949, **61**, 903) and of thiourea and 6-*n*-propyl-2-thiouracil by Bills and Ronzio (U.S. Atomic Energy Commission, A.E.C.U.—619) and Murray and Ronzio (A.E.C.U.—621). In the present work, undertaken before these reports were available, 6-ethyl- and 6-*n*-propyl-2-thiouracil labelled with radioactive sulphur were prepared by similar methods for use in studies of their distribution and metabolism.

Reduction of the precipitated barium sulphate to sulphide by hydrogen at 1000° proved more satisfactory than the reduction by carbon used by Ernsting and Nauta (*loc. cit.*) and by Peters (*Biochem. J.*, 1947, **41**, 370).

It was also found that separation of the thiourea in a pure condition was more readily effected if the hydrogen sulphide and cyanamide were allowed to react, at room temperature, in anhydrous ethyl alcohol, all reagents being rigorously dried.

On a 10-millimole scale the overall yield of thiourea from sulphate was 79—83% and that of the thiouracil from sulphate 53—57%.

A preliminary survey of the distribution of 6-*n*-propyl-2-thiouracil when injected into rats has shown a significantly increased concentration of radioactive sulphur in the thyroid gland, but 90% of the sulphur administered as thiouracil was excreted within 24 hours, in agreement with recent observations on the distribution of labelled thiourea (Schulman and Keating, *J. Biol. Chem.*, 1950, **183**, 215; Schulman, *ibid.*, 1950, **186**, 717) and 6-methyl-2-thiouracil (Bezem, Brunnekruft, Ernsting, Lever, and Nauta, *Acta Endocrinol.*, 1949, **3**, 151). Of the excreted sulphur, 67·2% was in the form of the unchanged thiouracil, 18·8% as organic metabolites, 3·8% as ethereal sulphates, and 10·2% as inorganic sulphate.

Experimental.—Reduction of sulphate to sulphide. Radioactive sulphur (1 mc.), as soluble sulphate, was diluted by the addition of anhydrous sodium sulphate (1·5 g.) and the total sulphate precipitated as barium sulphate. The washed and dried precipitate was inserted, in a porcelain boat, into a silica tube. A stream of hydrogen was passed through the tube which was heated during 2 hours to 1000° and kept at that temperature for 1·5—2 hours. Parallel experiments on non-isotopic material showed that under these conditions 99·8% of the sulphate was reduced to sulphide.

Preparation of thiourea. The thiourea was prepared by the method basically described by Baumann (*Ber.*, 1875, **8**, 26). The reaction vessel, a gas trap protected by a phosphoric oxide drying tube, was charged with cyanamide (0·444 g., 10 millimoles) in anhydrous ethyl alcohol (12 c.c.) and immersed in liquid air. Dry ammonia [from ammonium chloride (1 g.) and excess of calcium oxide] was led into the reaction vessel, followed by hydrogen sulphide generated by the action of dilute hydrochloric acid on the barium sulphide mixed with aluminium turnings (3 g.) and dried over phosphoric oxide. The inlet and outlet tubes of the reaction vessel were then sealed and the vessel was set aside, with occasional shaking, at room temperature for 8 days. The vessel was then again immersed in liquid air, re-opened, and hydrogen sulphide removed by gentle boiling in a slow stream of hydrogen and determined by absorption in iodine solution. The contents of the vessel were evaporated until thiourea began to crystallise and were then cooled. The thiourea was filtered off and recrystallised from dry alcohol (yield, 0·634 g., 79%; m. p. 179—180°).

Condensation of thiourea with keto-esters. The method described by Robinson and Tomlinson (*J.*, 1935, 1283) and by Anderson *et al.* (*J. Amer. Chem. Soc.*, 1945, **67**, 2197) was adapted to the use of small quantities of material.

(*a*) 6-Ethyl-2-thiouracil. Labelled thiourea (0·695 g., 9 millimoles), ethyl β-ketovalerate (1·32 g.), and sodium (0·213 g.) were heated in anhydrous ethyl alcohol (4·6 c.c.) for 5 hours. After evaporation to dryness the residue was dissolved in boiling water (9 c.c.), and the ethylthiouracil precipitated by the addition of concentrated hydrochloric acid (1·28 c.c.) and acetic acid (0·9 c.c.), dried at 120°, and recrystallised from alcohol (yield, 0·98 g., 68·6%; m. p. 228°).

(*b*) 6-*n*-Propyl-2-thiouracil. This was prepared by the method described above by the condensation of labelled thiourea (0·6 g., 8 millimoles) and ethyl 3-ketohexanoate ($CO_2H = 1$) (1·25 g.), and recrystallised from aqueous alcohol (yield, 0·96 g., 71·3%; m. p. 218°).

We are grateful to Drs. R. Schoental and S. C. Curran who supervised the animal experiments and the assay of radioactive sulphur respectively, and one of us (K. A. M.) is indebted to the Department of Scientific and Industrial Research for a Maintenance Allowance.

University of Glasgow. [*Received, February 12th*, 1951.]

430. *Anomalous Reactions of Phenetole Halides.*

By MAXWELL GORDON.

WE have confirmed Grignard's observation (*Compt. rend.*, 1904, **138**, 1048) that neither 2-bromo- nor 2-chloro-ethyl phenyl ether gives a Grignard reagent, since no β-phenoxypropionic acid is obtained on carboxylation. Thus the compound titrated by Gilman and McCracken (*Rec. Trav. chim.*, 1927, **46**, 469) was evidently phenoxymagnesium chloride. Abnormal results were also obtained in the reaction with sodium cyanide, which with 2-bromoethyl phenyl ether gave a 30% yield of 1 : 2-diphenoxyethane, m. p. 94—95° (Found : .C, 78·8, 78·5; H, 6·7, 6·4. Calc. for $C_{14}H_{14}O_2$: C, 78·5; H, 6·6%), the identity of which was proved by its mixed m. p. with an authentic specimen and by its infra-red spectrum.

2-Chloroethyl phenyl ether and magnesium afforded some phenoxymagnesium chloride and ethylene, but no phenoxypropionic acid after carboxylation. We also isolated approximately 20% of 1 : 4-diphenoxybutane, m. p. 97·5—98° (Found : C, 79·3; H, 7·4. Calc. for $C_{16}H_{18}O_2$: C, 79·3; H, 7·4%), the identity being proved by infra-red spectra and by depression of the m. p. of the 1 : 2-isomer. Grignard (*loc. cit.*) also obtained a small amount of 1 : 4-diphenoxybutane from 2-bromophenetole.

These reactions are being investigated further.

By contrast, 3-phenoxypropyl bromide reacts normally with cyanide, to give γ-phenoxybutyronitrile (Marvel and Tanenbaum, *J. Amer. Chem. Soc.*, 1922, **44**, 2645). The labile nature of alkyl–oxygen bonds in alkyl aryl ethers has been noted many times (Wheland, " Advanced Organic Chemistry," Wiley, 1949, pp. 555—561), but the reagents involved are usually strong acids and the products are usually alkylphenols and olefins. Thus, the isolation of 1 : 2-diphenoxyethane is of interest.

2-Phenoxyethyl halides thus represent a special case, perhaps not surprisingly inasmuch as the 1 : 4-disposition of reactive atoms often results in reactivity. Thus, for example, Crane and Rydon (*J.*, 1947, 766) and Mamalis and Rydon (*Nature*, 1950, **166**, 404) have found that compounds of the type $R_2\overset{+}{S}\cdot CH_2\cdot CH_2\cdot OPh$ are easily split by dilute alkali to give, initially, $R_2\overset{+}{S}\cdot CH{:}CH_2$ and sodium phenoxide.

The work described in this paper was sponsored by the U.S. Atomic Energy Commission, and the author was an Atomic Energy Commission Postdoctorate Research Fellow (1949—1950). Grateful appreciation is expressed to Prof. Melvin Calvin for providing facilities for this work, and to Dr. Norman K. Freeman for the infra-red spectra.

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431. *Chlorination of* 1-*Chloro*-2-*naphthol.*

By (MISS) P. M. JAMES and D. WOODCOCK.

ZINCKE (*Ber.*, 1888, **21**, 3378) suggested that chlorination of 1-chloro-2-naphthol in glacial acetic acid solution to 1 : 1-dichloro-1 : 2-dihydro-2-ketonaphthalene proceeds by way of the keto-1 : 2-dihydro-form. Addition of chlorine gives 1 : 1 : 3 : 4-tetrachloro-1 : 2 : 3 : 4-tetrahydro-2-ketonaphthalene from which by dehydrochlorination and further addition of one molecule of chlorine the 1 : 1 : 3 : 3 : 4-pentachloro-compound is obtained.

Since we required 1 : 6-dichloronaphthol in connection with work which will be reported later, an attempt was made to obtain it by the procedure of Ruggli *et al.* (*Helv. Chim. Acta*, 1929, **12**, 1051), *viz.*, slow chlorination in sunlight. In our hands, however, the oily product often failed to crystallise; in three cases out of twenty-three, crystalline 1 : 4-dichloro-2-naphthol,

m. p. 120—121° (cf. Burton, *J.*, 1945, 280), was obtained. When the acetic acid solution was kept for six days after chlorination, 1 : 3 : 4-trichloro-2-naphthol crystallised, whilst on one occasion the pentachloro-compound, m. p. 113°, was isolated, identical with that obtained by Fries and Schimmelschmidt (*Annalen*, 1930, **484**, 295) by chlorination of 2-hydroxy-3-naphthoic acid. The tetrachloro-compound has also been isolated, but was more reliably prepared by chlorination of 1-chloro-2-naphthol in carbon tetrachloride.

Oxidation of the various crystalline products by alkaline potassium permanganate invariably gave phthalic acid and there was no evidence of substitution in the 6-position. Thus, whilst bromine substitutes in the 1- and then in the 6-position of 2-naphthol (Franzen and Stäuble, *J. pr. Chem.*, 1921, **103**, 352), the claim by Ruggli *et al.* (*loc. cit.*) to have prepared 1 : 6-dichloro-2-naphthol by the action of chlorine on the 1-chloro-compound has not been substantiated. Since no confirmation of orientation was offered there is some doubt about the identity of their product, m. p. 119·5°.

Experimental.—1 : 4-*Dichloro-2-naphthol.* A solution of 1-chloro-2-naphthol (9·5 g.) in glacial acetic acid was subjected to a stream of dry chlorine while illuminated by an ultra-violet lamp, and after an increase in weight of 1·8 g. had been recorded the product was isolated as described by Ruggli *et al.* The dark red oil on trituration with chloroform–light petroleum (b. p. 40—60°) gave a solid product which crystallised from light petroleum (b. p. 60—80°) (carbon) in prisms, m. p. 120—121° (Found : C, 56·2; H, 2·9; Cl, 33·3. Calc. for $C_{10}H_6OCl_2$: C, 56·3; H, 2·8; Cl, 33·3%). Admixture with an authentic specimen of 1 : 4-dichloro-2-naphthol, kindly supplied by Professor H. Burton, did not depress the m. p.

The identity was confirmed by the preparation of the acetate and the naphthyloxyacetic acid described below, neither of which depressed the m. p. of specimens prepared from Burton's 1 : 4-dichloronaphthol. The acetate crystallised from aqueous methyl alcohol in stout prisms, m. p. 85—85·5° (Found : C, 56·3; H, 3·4. Calc. for $C_{12}H_8O_2Cl_2$: C, 56·4; H, 3·2%). Zincke (*loc. cit.*) gives m. p. 90—91°. 1 : 4-*Dichloro-2-naphthyloxyacetic acid*, prepared by condensing the sodium salt of the naphthol with ethyl bromoacetate in ethyl alcohol, crystallised from acetic acid in prisms, m. p. 188—189° (Found : C, 53·3; H, 3·0; Cl, 25·9. $C_{12}H_8O_3Cl_2$ requires C, 53·1; H, 2·95; Cl, 26·2%).

Oxidation of the naphthol, prepared as described above, with alkaline potassium permanganate gave only phthalic acid, m. p. 204—205°.

1 . 1 : 3 : 3 : 4-*Pentachloro*-1 : 2 : 3 : 4-*tetrahydro-2-ketonaphthalene.* The product from one experiment carried out as above crystallised from light petroleum (b. p. 60—80°) in pale yellow prisms, m. p. 112—113° (Found : C, 38·1; H, 1·5; Cl, 55·7. Calc. for $C_{10}H_5OCl_5$: C, 37·7; H, 1·6; Cl, 55·3%), undepressed on admixture with an authentic specimen prepared according to Fries and Schimmelschmidt (*loc. cit.*).

1 : 3 : 4-*Trichloro-2-naphthol.* If chlorination was continued until the increase in weight was *ca.* 5·5 g. and the whole set aside for 6 days, a pale yellow solid was obtained which crystallised from aqueous methyl alcohol in prisms, m. p. 160—161° (Found : C, 48·7; H, 2·0; Cl, 42·5. Calc. for $C_{10}H_5OCl_3$: C, 48·5; H, 2·0; Cl, 43·0%). This product also gave phthalic acid on oxidation with alkaline potassium permanganate.

1 : 1 : 3 : 4-*Tetrachloro*-1 : 2 : 3 : 4-*tetrahydro-2-ketonaphthalene.* A slow stream of dry chlorine was passed through 1-chloro-2-naphthol (3·8 g.) dissolved in carbon tetrachloride (20 ml.), until there was no further gain in weight. The clear solution was diluted with light petroleum (b. p. 40—60°; 2 vols.) and set aside overnight at 0°, and the colourless crystalline product, m. p. 99—101°, was collected (Found : C, 42·3; H, 2·3; Cl, 49·8. Calc. for $C_{10}H_6OCl_4$: C, 42·2; H, 2·1; Cl, 50·0%). Zincke (*loc. cit.*) gives m. p. 102—103°. Oxidation gave phthalic acid and reduction with stannous chloride in hydrochloric acid gave a product, m. p. 69—72°, alone or mixed with authentic 1 : 3-dichloro-2-naphthol.

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432. *Polyvinyl Alcohol as Indicator in Iodometry.*

By Samuel A. Miller and Arthur Bracken.

Starch, even acid-solubilised starch, is not an ideal indicator for iodine titrations. The chief disadvantages attending its use are its insolubility in cold water, the instability of its aqueous dispersions, the fact that the indicator cannot be added at the beginning of the titration, and the drift of the end-point when the solutions are dilute. Peate, Bourne, and Thrower (*Nature*, 1947, **159**, 810) proposed the use of sodium starch glycollate in which the ratio of glycollic acid to glucose units is approximately 1 : 10.

It has long been known that polyvinyl alcohol gives a blue colour with iodine, similar in many ways to that given by starch (Staudinger, Frey, and Starck, *Ber.*, 1927, **60**, 1782; Herrmann and Haehnel, *ibid.*, p. 1658; "Polyvinylalkohole," F. Kainer, Stuttgart, 1949, p. 50). We have now found that this blue colour is given only by completely deacetylated polyvinyl alcohol. Polyvinyl alcohol containing 10% or more of residual acetate groups gives a crimson colour, as indeed do also aqueous-alcoholic solutions of polyvinyl acetate. This crimson colour appears to be most sensitive with a polyvinyl alcohol containing about 20 mol.-% of residual acetate groups. At very high dilutions of iodine the colour is brownish-yellow and can be readily detected with the naked eye at iodine concentrations of 3×10^{-6}N. in potassium iodide solutions of concentration 0·002 g./l., and at iodine concentrations of 10^{-5}N. in potassium iodide solutions of concentration 0·0004 g./l. We were unable to obtain any visible colour with starch solutions at these concentrations, the blue colour becoming just detectable with about 10^{-5}N- and 2×10^{-5}N-iodine respectively.

Polyvinyl alcohol with 20 mol.-% of residual acetate groups readily gives a 1% solution in cold water and such a solution is stable on storage.

Experimental.—5-Ml. samples of approx. 0·01N-iodine were titrated with 4·0 ml. of approx. 0·01N-sodium thiosulphate, and then 0·5 ml. of a 1% solution of the polyvinyl alcohol was added and the titration continued to final discharge of the brownish-yellow colour. Successive titrations were 4·08, 4·09, 4·10, 4·09, 4·10, and 4·08 ml. In each case there was no doubt of the neutral point to 0·02 ml. In a parallel titration with the same materials but with starch as indicator, the titration figure was 4·06—4·08 ml., there being no apparent change on addition of a further 0·02 ml. after 4·06 ml.

It does not appear to be essential to add the indicator as above; addition of the indicator at the beginning gave the same result. Further, there was no drift of the end-point.

The feasibility of adding the indicator at the beginning of the titration and the lack of drift were confirmed for titrations of 0·1N-iodine with 0·1N-sodium thiosulphate.

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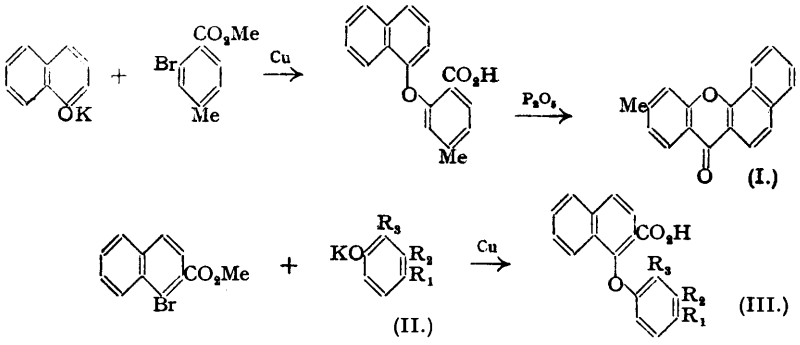
433. 3 : 4-*Benzoxanthens. Part II.* The Synthesis of* 5-, 6-, *and* 7-*Methyl*-3 : 4-*benzoxanthones.*

By Munir Gindy and Ibrahim M. Dwidar.

5-, 6-, and 7-Methyl-3 : 4-benzoxanthones have been prepared (forthcoming publication), in good yields, by oxidation of the corresponding 3 : 4-benzoxanthens (cf. Baddar and Gindy, *J.*, 1951, 64; *Nature*, 1946, **157**, 409; Gindy, *ibid.*, 1949, **164**, 577). 6-Methyl-3 : 4-benzoxanthone (I) was obtained in quantitative yield by cyclodehydration of 4-methyl-2-1′-naphthyloxybenzoic acid with phosphoric oxide. However, attempts to obtain this acid by heating methyl 2-bromo-4-methylbenzoate and potassium α-naphthyloxide with copper bronze (Knapp, *J. pr. Chem.*, 1936, **146**, 116) gave a very poor yield, so this method was impracticable for the preparation of other methyl-substituted 3 : 4-benzoxanthones.

* Part I, *J.*, 1951, 64.

A better method of preparing 5- and 7-methyl-3 : 4-benzoxanthones was to heat methyl 1-bromo-2-naphthoate (Boyes, Grieve, and Rule, *J.*, 1938, 1833) with the potassium salt of a cresol (II; *o*-, $R_1 = R_2 = H$, $R_3 = Me$; *p*-, $R_1 = Me$, $R_2 = R_3 = H$) in presence of copper



bronze to give 1-*o*- and 1-*p*-tolyloxy-2-naphthoic acid, (III; $R_3 = Me$, $R_1 = R_2 = H$) and (III; $R_1 = Me$, $R_2 = R_3 = H$), respectively. These were then cyclodehydrated quantitatively in dry benzene with phosphoric oxide to the corresponding methyl-3 : 4-benzoxanthones. The 1-*m*-tolyloxy-acid (III; $R_2 = Me$, $R_1 = R_3 = H$), prepared by heating methyl 1-bromo-2-naphthoate with potassium *m*-tolyloxide and copper bronze, however, gave on cyclisation a mixture of 6- and 8-methyl-3 : 4-benzoxanthones, but owing to lack of material these could not be separated.

Experimental.—(M. p.s are not corrected. Microanalyses are by Drs. Weiler and Strauss, Oxford).

4-Methyl-2-1'-naphthyloxybenzoic acid. To a stirred mixture of potassium α-naphthyloxide (4 g., 1 mol.) and methyl 2-bromo-4-methylbenzoate (5 g., 1 mol.) heated in an oil-bath at 180—185°, copper bronze (1 g.) was added. Stirring and heating were continued for a further 1½ hours. The product was extracted with acetone, the solvent evaporated, and the residue refluxed with alcoholic potassium hydroxide (70 c.c.; 20%) for 2 hours. The alcohol was evaporated, the residue dissolved in water (50—60 c.c.), and the solution filtered and acidified. The precipitate was digested with ether, and the acid product extracted with sodium carbonate solution. The alkaline layer (charcoal) was acidified, and the precipitate was dried and dissolved in hot benzene; the solution slowly deposited an acid (m. p. 184°) (under investigation) which was filtered off. The mother-liquor was evaporated to dryness and the residue crystallised from light petroleum (b. p. 60—80°), to give *4-methyl-2-1'-naphthyloxybenzoic acid* in colourless needles (0·05 g., 0·8%), m. p. 156° [Found : C, 77·9; H, 5·2%; *M* (Rast), 273. $C_{18}H_{14}O_3$ requires C, 77·7; H, 5·0%; *M*, 278].

1-Tolyloxy-2-naphthoic acids. (i) Potassium *p*-tolyloxide (2·75 g., 1 mol.) was stirred with methyl 1-bromo-2-naphthoate (5 g., 1 mol.) and copper bronze (1 g.) in a mercury-sealed tube at 200—210° and kept thereat for 2 hours. The cold product was worked up as above, and the acid precipitated on acidification of the sodium carbonate solution was filtered off and crystallised from dilute methyl alcohol, to give 1-p-*tolyloxy-2-naphthoic acid* in fine needles (0·8 g., 15%), m. p. 187—188° [Found : C, 77·5; H, 5·3%; *M* (Rast), 258. $C_{18}H_{14}O_3$ requires C, 77·7; H, 5·0%; *M*, 278]. It gave an olive-green colour with concentrated sulphuric acid. (ii) The corresponding o-*tolyloxy-acid*, prepared (oil-bath, 175—180°) and worked up similarly, crystallised from light petroleum (b. p. 60—80°) in rods, m. p. 188° (Found : C, 77·1; H, 5·1%) (yield, *ca.* 22%). (iii) The analogous m-*tolyloxy-acid* (nitrobenzene-bath; 2½ hours) crystallised from benzene–light petroleum (b. p. 60—80°) in long needles (*ca.* 10·5%), m. p. 186° (Found : C, 77·4; H, 4·8%).

Methyl-3 : 4-benzoxanthones. (i) 4-Methyl-2-1'-naphthyloxybenzoic acid (0·05 g., 1 mol.), dissolved in dry benzene (3 c.c.), was warmed for 2 hours with phosphoric oxide (0·5 g.) in a flask fitted with a condenser protected by a calcium chloride tube. The thoroughly cooled product was decomposed with ice-cold water acidified with few drops of hydrochloric acid. The benzene layer was separated, washed with sodium carbonate solution, and dried. On evaporation of the solvent, the residue crystallised from acetone in colourless needles of *6-methyl-3 : 4-benzoxanthone* (yield, *ca.* 100%), m. p. 172° [Found : C, 82·6; H, 4·4%; *M* (Rast), 277. $C_{18}H_{12}O_2$ requires C, 83·1; H, 4·6%; *M*, 260]. (ii) The *5-methyl* and the *7-methyl* compound, prepared from the appropriate acids in the same way, crystallised from acetone in needles, m. p. 226° (yield, quantitative) [Found : C, 82·7; H, 4·6%; *M* (Rast), 284], and m. p. 166° [Found : C, 83·6; H, 4·6%; *M* (Rast), 251], respectively. (iii) 1-*m*-Tolyloxy-2-naphthoic acid, when similarly cyclised, gave a mixture of 6- and 8-methyl-3 : 4-benzoxanthones.

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434. *Synthesis of Deoxy*apo*xanthoxyletin.*

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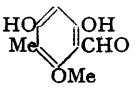
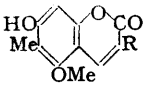
The orientation (II; R = H) derived for deoxy*apo*xanthoxyletin (*J.*, 1937, 286) has now been confirmed by its synthesis from 4 : 6-dihydroxy-2-methoxy-3-methylbenzaldehyde (I) which has recently become available (*J.*, 1950, 1882).

(I.)   (II.)

*Deoxy*apo*xanthoxyletin.*—A mixture of 4 : 6-dihydroxy-2-methoxy-3-methylbenzaldehyde (1 g.), 20% aqueous sodium hydroxide (20 ml.), and cyanoacetic acid (8 ml. of a solution prepared according to Phelps and Tillotson, *Amer. J. Sci.*, 1908, **26**, 267) was kept at room temperature for 24 hours, diluted with water (100 ml.), and acidified with concentrated hydrochloric acid. The resulting α-cyano-β-(4 : 6-dihydroxy-2-methoxy-3-methylphenyl)acrylic acid (1·1 g.) was a pale yellow, microcrystalline solid, m. p. 291° (decomp.), and on being hydrolysed with boiling 4% hydrochloric acid (35 ml.) for ½ hour gave *7-hydroxy-5-methoxy-6-methylcoumarin-3-carboxylic acid* (II; R = CO_2H) which formed greenish yellow, stout prisms (0·8 g.), m. p. 263—264°, readily soluble in aqueous sodium hydrogen carbonate giving a solution with a magnificent blue-violet fluorescence (Found: C, 57·6; H, 4·1. $C_{12}H_{10}O_6$ requires C, 57·6; H, 4·0%).

A mixture of the foregoing acid (0·5 g.), quinoline (15 ml.), and copper bronze (2 g.) was heated under reflux for 5 minutes, diluted with ether (750 ml.), filtered, washed with dilute hydrochloric acid and then with aqueous sodium hydrogen carbonate, dried, and evaporated. Crystallised from benzene, the residue gave 7-hydroxy-5-methoxy-6-methylcoumarin (II; R = H) in colourless needles (0·3 g.), m. p. 199—200° identical in every way with natural deoxy*apo*xanthoxyletin (Found: C, 64·0; H, 5·2. Calc. for $C_{11}H_{10}O_4$: C, 64·1; H, 4·9%). Ethylation of this coumarin (0·1 g.) with potassium carbonate (1 g.) and excess of ethyl iodide in boiling acetone (30 ml.) for 2 hours gave the 7-ethoxy-5-methoxy-6-methylcoumarin which separated from dilute alcohol in colourless needles (0·1 g.), m. p. 141°, identical with the ethyl ether of deoxy*apo*xanthoxyletin (Found: C, 66·9; H, 5·9. Calc. for $C_{13}H_{14}O_4$: C, 66·7; H, 6·0%).

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