NOTES.

7-Methyl-4-isopropyl-1-hydrindone. By (MRS.) OTTILIE BLUM-BERGMANN.

COOK and his co-workers have described experiments on the synthesis of Diels's hydrocarbon ($C_{25}H_{24}$) from cholesterol (J., 1934, 1727). Some time ago the author was engaged in experiments with the same purpose and used nearly the same synthetic method. The initial material, 7-methyl-4-*iso*propyl-1-hydrindone, was made in a different way, which is reported here, as the experiments are not being continued.

3-Bromo-*p*-cymene (73 g.) in ether (300 c.c.) was boiled with magnesium turnings (8·4 g.), activated with iodine and methyl iodide, for 2—3 hours, ethyl orthoformate (67·5 c.c.) was then added, and the whole heated for 30 minutes; the ether was then distilled off, the residue heated for 2 hours, fresh ether, ice, and ammonium chloride added, and 5-methyl-2-*iso*propylbenzaldehyde diethylacetal isolated as an oil (19·3 g.), b. p. 135—145°/15 mm., 93—100°/0·85 mm.

The acetal (11 g.) was boiled with glacial acetic acid (20 c.c.) and dilute sulphuric acid (10 c.c.) for 2 hours and the crude aldehyde was isolated and heated with malonic acid (13 g.), pyridine (25 c.c.), and piperidine (1 c.c.) for 2 hours on the water-bath, then for 90 minutes over a direct flame. On acidification crystalline *5-methyl-2-isopropylcinnamic acid* was obtained, contaminated with an oily by-product, probably the stereoisomeric acid. Recrystallisation from petroleum (b. p. 80—100°) gave silky needles (4·5 g.), m. p. 145—146·5° (Found: C, 76·4; H, 8·1. $C_{13}H_{16}O_2$ requires C, 76·5; H, 7·8%).

The conversion into β-3-*p*-cymylpropionic acid was effected in quantitative yield by sodium amalgam (4%) in alkaline solution. When the reducing power towards potassium permanganate had disappeared, the solution was filtered and acidified. From light petroleum or, better, from a small amount of methyl alcohol, stout prisms, m. p. 66—68·5°, were obtained (Found: C, 75·4; H, 8·9. Calc. for $C_{13}H_{18}O_2$: C, 75·7; H, 8·7%). The ring closure was effected by stannic chloride in the way described by Cook and his co-workers. The m. p. of the 7-methyl-4-*iso*propyl-1-hydrindone (from methyl alcohol, long prisms) is somewhat higher than that reported by Cook.—THE DANIEL SIEFF RESEARCH INSTITUTE, REHOVOTH, PALESTINE. [*Received, April 1st,* 1935.]

The Preparation of 4-Methylthiazole-5-carboxylic Acid. By (MISS) M. L. TOMLINSON.

IT has been pointed out by Williams (*J. Amer. Chem. Soc.*, 1935, **57**, 229) that the compound $C_5H_5O_2NS$ obtained by Windaus by the oxidation of vitamin-B_1 (*J. Physiol. Chem.*, 1934, **27**, 288) is probably the 4-methylthiazole-5-carboxylic acid described by Wohmann (*Annalen*, 1890, **259**, 299). This acid and its ethyl and methyl esters have now been made by a new and improved method.

Ethyl 4-Methylthiazole-5-carboxylate.—Ethyl α-bromoacetoacetate (22 g.) (Conrad, *Ber.*, 1896, **29**, 1944) was mixed with thioformamide (10 g.) (Willstätter, *Ber.*, 1909, **42**, 1911), heat being developed. After cooling, the mixture was extracted with dilute hydrochloric acid, the extracts washed with a little ether, and the thiazole derivative liberated with ammonia, isolated by means

of ether, and distilled, b. p. 215—220°. The ester solidified to a mass of colourless prisms, m. p. and mixed m. p. with the substance prepared by Wohmann's method, 27—28° (yield, about 50%, calculated on the acetoacetic ester). The hydrochloride separated from alcohol in long colourless needles, m. p. 155° (decomp.). The ester was hydrolysed in the manner described by Wohmann; 4-methylthiazole-5-carboxylic acid crystallised from water in colourless prisms, m. p. 280° (decomp.) with previous softening at 270° (Wohmann cites m. p. 257°, decomp.) (Found: C, 42·3; H, 3·6. Calc. for $C_5H_5O_2NS$: C, 42·0; H, 3·5%).

Methyl 4-Methylthiazole-5-carboxylate.—4-Methylthiazole-5-carboxylic acid (1 g.) was refluxed for 5 hours with methyl-alcoholic hydrogen chloride, the solution evaporated to dryness, and the residue treated with aqueous ammonia, washed with water, and crystallised from light petroleum (b. p. 40—60°); the methyl ester separated in colourless prisms, m. p. 74—75° (Found: C, 46·0; H, 4·6. Calc. for $C_6H_7O_2NS$: C, 45·8; H, 4·5%).

The specimens were sent to Professor A. Windaus, who has very kindly reported as follows: " I consider your preparation to be identical with our degradation product from vitamin-B_1. Our ester melted at 74—75°, the synthetic ester melts at 75·5—76·5°, and the mixture has m. p. 75—76°. Our acid melts with decomposition above 268°, whereas the synthetical acid begins to decompose at 269°." The decomposition point of the acid depends to some extent on the rate of heating.—Dyson Perrins Laboratory, Oxford University. [*Received, June 12th*, 1935.]

The Condensation of Naphthalene with Phthalic Anhydride. By E. de Barry Barnett and N. R. Campbell.

Contrary to the statement of Graebe (*Annalen*, 1905, **340**, 250), o-β-*naphthoylbenzoic acid* is formed in considerable quantity by the condensation of naphthalene with phthalic anhydride in the presence of aluminium chloride, although the experiments of Groggins and Newton (*Ind. Eng. Chem.*, 1930, **22**, 157) indicate that the amount is only small when the temperature is kept at or below 0°. When 64 g. of naphthalene were added during 30 minutes to a solution of 74 g. of phthalic anhydride and 150 g. of aluminium chloride in 450 c.c. of tetrachloroethane, the temperature rose to 28°. After being kept for 2½ hours at the ordinary temperature, the product was worked up in the usual way and the crude phthaloylic acids were converted into their ammonium salts. By fractional crystallisation a less soluble salt was obtained, from which *o*-β-naphthoylbenzoic acid was liberated. Recrystallised from dichloroethylene (yield, 30 g.), this was obtained colourless, m. p. 166°, unaltered after repeated crystallisation from toluene (Found: C, 78·2; H, 4·6. $C_{18}H_{12}O_3$ requires C, 78·2; H, 4·4%). It gave a deep olive-green solution in concentrated sulphuric acid, and was precipitated as a hydrate, m. p. 135° (decomp.), when a solution of one of its salts was poured into cold dilute hydrochloric acid (Found: loss at 110°, 6·3. $C_{18}H_{12}O_3,H_2O$ requires H_2O, 6·1%). It is a much more powerful sternutator than the α-isomeride. When 2 g. were heated for 8 hours at 60° with 2 g. of boric acid and 20 c.c. of concentrated sulphuric acid, a mixture of quinones was obtained, of which the main component was 1 : 2-benzanthraquinone. This was isolated by recrystallisation from glacial acetic acid and from alcohol and was identified by comparison with an authentic sample.

o-β-Naphthoylbenzoic acid was easily reduced to ω-β-*naphthyl*-o-*toluic acid* by heating on the water-bath for 12—16 hours with zinc dust (activated by copper sulphate), caustic soda, and ammonia. After crystallisation from toluene this melted at 135° (Found: C, 82·3; H, 5·4. $C_{18}H_{14}O_2$ requires C, 82·4; H, 5·3%).

Like other phthaloylic acids, both *o*-naphthoylbenzoic acids are readily decarboxylated by heating with " copper chromite " (Adkins and Connor, *J. Amer. Chem. Soc.*, 1931, **53**, 1092) without a solvent. This reaction frequently provides a convenient route to the phenyl aryl ketones.—Sir John Cass Technical Institute, Jewry Street, London, E.C. 3. [*Received, June 6th*, 1935.]

An Improved Method for the Synthesis of Coumarins by v. Pechmann's Method. By Herbert Appel.

Alcoholic hydrogen chloride (compare Crabtree, Robinson, and Turner, J., 1918, **113**, 879) may be used with advantage in cases where the v. Pechmann synthesis (v. Pechmann and Duisberg, *Ber.*, 1883, **16**, 2119) or its past modifications (*e.g.*, 73% sulphuric acid, hydrogen chloride in glacial acetic acid, zinc chloride in boiling alcohol, phosphorus oxychloride) give indifferent results. The advantages of the new method are the avoidance of sulphonation of aromatic

nuclei, the prevention of saponification of the β-keto-ester, and improved yields (exceeding 90%) and purer products. In the cases, however, where little or no reaction can be effected with concentrated sulphuric acid (phenol, β-naphthol, quinol; Robertson, Sandrock, and Hendry, J., 1931, 2427), the new method also gives bad results.

A solution of the phenol and the β-keto-ester in absolute alcohol was saturated with hydrogen chloride at room temperature (cooling with ice-water) and kept in a well-stoppered flask for 20 hours. It was then poured into water, and the coumarin collected after an hour. One recrystallisation from dilute alcohol usually sufficed for purification.

2·6 G. of acetoacetic ester, 2·2 g. of resorcinol, and 25 c.c. of alcohol gave 3·4 g. of 7-hydroxy-4-methylcoumarin (β-methylumbelliferone), m. p. 185—186°. Yield, 97%.

3·9 G. of benzoylacetic ester, 2·2 g. of resorcinol, and 25 c.c. of alcohol gave 4·4 g. of 7-hydroxy-4-phenylcoumarin (β-phenylumbelliferone), m. p. 242—244°. Yield, 92%.

3·0 G. of α-naphthol, 2·6 g. of acetoacetic ester, and 25 c.c. of alcohol, after 48 hours at room temperature, the product being washed with water and ether, gave 3·9 g. of 4-methyl-α-naphthacoumarin, m. p. 169·5—170·5°. Yield, 93% (after 20 hours, the yield is only 62%).

2·5 G. of hydroxyquinol, 2·6 g. of acetoacetic ester, and 25 c.c. of alcohol gave 3·6 g. of 6 : 7-dihydroxy-4-methylcoumarin (β-methylæsculetin). The product was precipitated from sodium carbonate solution with acid and recrystallised from dilute alcohol; m. p. 273—275°. Yield, 95%. Contrary to v. Pechmann and v. Krafft (*Ber.*, 1901, **34**, 423), who record m. p. 269—270° and yield 60—65%, this substance does not show fluorescence in aqueous or sulphuric acid solutions.

The author is grateful to Prof. R. Robinson, F.R.S., for his interest in the work.—The Dyson Perrins Laboratory, Oxford. [*Received, April 3rd*, 1935.]

Abnormal Reaction of an α-Bromo-ketone. By (Miss) S. N. McGeoch and T. S. Stevens.

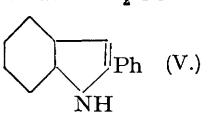
When ω-bromo-ω-benzylacetophenone (I) was treated with aniline, it yielded, in addition to the expected product (II), an isomeric substance for which the structure (III) was established by degradation and synthesis. A possibly analogous anomaly in the interaction of α-bromo*iso*-hexophenone and *p*-toluidine has been recorded by Wedekind and Bruch (*Annalen*, 1929, **471**, 108), who have kindly agreed to our continuing the study of this type of reaction. This formation of (III) from (I) may be related to the conversion of ω-anilinoacetophenone (IV) into 2-phenylindole (V) (compare Bischler, *Ber.*, 1892, **25**, 2860), and its mechanism will be discussed in a future communication.

(I.) $Ph{\cdot}CO{\cdot}CHBr{\cdot}CH_2Ph$

(II.) $Ph{\cdot}CO{\cdot}CH(NHPh){\cdot}CH_2Ph$

(III.) $Ph{\cdot}CH(NHPh){\cdot}CO{\cdot}CH_2Ph$

$Ph{\cdot}NH{\cdot}CH_2{\cdot}COPh$ (IV.)



(V.)

ω-Anilino-ω-benzylacetophenone (II).—ω-Bromo-ω-benzylacetophenone (Stevens, Creighton, Gordon, and McNicol, J., 1928, 3193) (pure, m. p. 58°; 1 mol.) was heated with aniline (2 mols.) at 60° for 4 days. The mixture was diluted with ether, filtered from aniline hydrobromide, and shaken with moderately dilute hydrochloric acid. The precipitated hydrochloride (A), treated with ammonia, yielded *ω-anilino-ω-benzylacetophenone*, pale yellow warts from alcohol, whose m. p., 106°, was depressed by admixture with (III) (Found : C, 83·8; H, 6·6; N, 4·6. $C_{21}H_{19}ON$ requires C, 83·7; H, 6·3; N, 4·7%). The base was reduced by heating on the water-bath with excess of zinc dust and 15% sulphuric acid for 1—2 hours. Extraction with ether then yielded ω-benzylacetophenone, identified as semicarbazone, m. p. and mixed m. p. 143°.

α-Anilinodibenzyl ketone (III) separated on basification of the aqueous filtrate from (A) and crystallised from alcohol in colourless needles, m. p. 125° (Found : C, 83·5; H, 6·5%). Reduced in the same way as its isomeride, it gave dibenzyl ketone semicarbazone, m. p. and mixed m. p. 145°. The yields of the isomeric bases were small, 20% and 5% respectively, and the ethereal filtrate from (A) contained much resin; variation in conditions effected no improvement.

Synthesis.—α-Bromodibenzyl ketone (Bourcart, *Ber.*, 1889, **22**, 1368) was heated with aniline (2 mols.) at 60° for ½ hour. Water was added, and the anilinodibenzyl ketone collected. After purification, it melted at 125°, alone or mixed with the product from ω-bromo-ω-anilino-acetophenone.—The University, Glasgow. [*Received, April 1st*, 1935.]