

NOTES.

1 : 2 : 3 : 4-Tetrahydroisoquinaldinic Acid. By W. SOLOMON.

isoQuinaldinic Acid.—1-Cyano-2-benzoyl-1 : 2-dihydroisoquinoline, obtained from *isoquinoline*, benzoyl chloride, and aqueous potassium cyanide (Reissert, *Ber.*, 1905, **38**, 3427), is best hydrolysed to *isoquinaldinic acid* by boiling with 10 vols. of 65% sulphuric acid for 2 hours (cf. Paddy and Lindwall, *J. Amer. Chem. Soc.*, 1945, **67**, 1269). The crude yield in the form of copper salt is 83%. The free acid is best crystallised from 7—8 parts of hot water. The yield of the acid so purified, calculated on the original cyano-compound, is 58%; m. p. 168—171° (froths).

1 : 2 : 3 : 4-Tetrahydroisoquinaldinic Acid.—*isoQuinaldinic acid* (24 g.) in glacial acetic acid (288 c.c.) at atmospheric pressure and *ca.* 50°, absorbed, in the presence of Adams's platinum oxide catalyst (1.6 g.), the calculated volume of hydrogen (6.5 l. at N.T.P.) in 13 days' intermittent shaking. The catalyst had to be highly active to effect even this rate of absorption. After filtration and removal of solvent under reduced pressure, the residue was triturated with alcohol and the resulting solid collected and washed with alcohol. Only 15.9 g. were obtained, the filtrate containing a further 10.5 g. of uncrystallisable material whose nature at present remains unknown. The solid, on crystallisation from a boiling mixture of alcohol (10 vols.) and water (20 vols.), furnished the *tetrahydro-acid* in colourless plates, m. p. 299° (decomp.) after softening (Found: C, 67.7; H, 6.3; N, 7.55. $C_{10}H_{11}O_2N$ requires C, 67.8; H, 6.3; N, 7.9%). The *N-benzoyl* derivative, obtained by the method of Steiger (*J. Org. Chem.*, 1944, **9**, 396), separated from alcohol in hard, dazzlingly white incrustations of colourless plates, m. p. 120° (decomp.) after sintering at 110° (Found: C, 72.4; H, 5.6; N, 4.9. $C_{17}H_{15}O_2N$ requires C, 72.6; H, 5.4; N, 5.0%). This derivative, on esterification with methanol and sulphuric acid, furnished *methyl N-benzoyl-1 : 2 : 3 : 4-tetrahydroisoquinaldinate*, large transparent prisms, m. p. 105—108°, from methanol, sparingly soluble in ether, but readily in other solvents (Found: C, 73.4; H, 5.8; N, 4.8. $C_{18}H_{17}O_3N$ requires C, 73.2; H, 5.8; N, 4.7%).

The author's thanks are due to Messrs. A. W. Stokes and H. Waddington for experimental assistance and to Mr. A. Bennett for the micro-analyses.—WELLCOME LABORATORIES OF TROPICAL MEDICINE, LONDON, N.W.1. [Received, April 18th, 1946.]

Diglycylethylenediamine. By T. L. COTTRELL and J. E. GILL.

PFEIFFER and SAURE (*J. pr. Chem.*, 1941, **157**, 116) obtained, by ammonolysis of bischloroacetylene-diamine under fairly drastic conditions, a compound which they considered to be diglycylethylenediamine. They reported a viscous oil, which on long standing gave hygroscopic crystals. No m. p. or analytical figures were given, and it was characterised as the picrate, m. p. 238—241°.

We have obtained diglycylethylenediamine as a crystalline, non-hygroscopic material in good yield. The difference between our method of preparation and that of Pfeiffer and Saure was in the use of milder conditions of ammonolysis (cf. Cheronis and Spitzmueller, *J. Org. Chem.*, 1941, **6**, 349), and in the method of isolation of the base from the hydrochloride. For this they used silver oxide, but we noted that the base tended to form a soluble silver complex.

The compound was strongly basic; its behaviour with copper hydroxide was similar to that of the compound described by Pfeiffer and Saure.

Experimental.—*Bischloroacetylene-diamine*. Bergell's method (*Z. physiol. Chem.*, 1922, **123**, 280) for the preparation of this compound gave only a 14% yield, so the following method was adopted. 22.7 G. of chloroacetyl chloride, dissolved in 60 ml. of dry chloroform, were added slowly with cooling and stirring to 14.7 g. of ethylenediamine in 100 ml. of dry chloroform. The solid was filtered off and extracted with hot absolute alcohol to give 15.2 g. of crude bischloroacetylene-diamine. This was recrystallised from absolute alcohol, giving 12.5 g. (59%) of pure compound, m. p. 175° (Bergell gives m. p. 171—172°). The compound could also be prepared from chloroacetic ester and ethylenediamine.

Diglycylethylenediamine. A mixture of 14.1 g. of the foregoing compound, 105 g. of ammonium carbonate in 90 ml. of water, and 120 ml. of ammonia (*d* 0.88) was kept at room temperature for 18 hours, heated to 55° for 4 hours, and then filtered. The clear filtrate was evaporated to dryness under reduced pressure and extracted with 300 ml. of absolute alcohol under reflux. The residue was dissolved in the minimum quantity of water, and poured into 200 ml. of absolute alcohol. The precipitate, which consisted of the crude hydrochloride, was filtered off (11.7 g., 70%). Recrystallised from aqueous alcohol, it had m. p. 246° (decomp.).

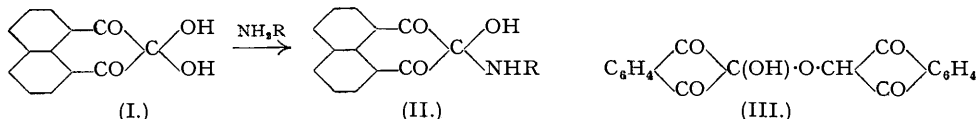
7 G. of the hydrochloride were converted into the base by adding 57 ml. of *N*-sodium hydroxide solution, evaporating to dryness, and extracting the residue with butanol. The base, crystallised from butanol, had m. p. 157—158° (yield theoretical) (Found: C, 41.3; H, 8.03; N, 31.4. Calc. for

$C_6H_{14}O_2N_4$: C, 41.3; H, 8.05; N, 32.2%) and formed non-hygroscopic needles. The picrate had m. p. 240° (decomp.). The acetyl derivative, recrystallised from aqueous alcohol or water, had m. p. 278—279° (Found: Ac, 32.6. Calc. for $C_{10}H_{18}O_4N_3$: Ac, 33.3%).

Attempts to prepare diglycylethylenediamine by condensation of ethylenediamine with glycol chloride or glycine were unsuccessful. From glycine ester a very small yield of the substance was obtained.—IMPERIAL CHEMICAL INDUSTRIES LIMITED, EXPLOSIVES DIVISION, RESEARCH DEPARTMENT, STEVENSTON, Ayrshire. [Received, April 25th, 1946.]

Derivatives of periNaphthindane-trione. By RADWAN MOUBASHER and (Mrs.) AKILA MOSTAFA.

ERRERA and SORGES (*Gazzetta*, 1913, **43**, ii, 625) stated that aniline reacts with *perinaphthindane-1 : 2 : 3-trione* hydrate to form a substance believed to be (II, R = Ph), but they did not describe the substance apart from stating that it decomposes on heating. We obtained this compound in intense yellow crystals and also the *p-chloroaniline* analogue. With benzidine a substance was obtained formed by condensation of equimolar amounts. Alkaline hydrolysis in the presence of air produced naphthalic acid and aniline, *p*-chloroaniline, or benzidine, respectively. Acid hydrolysis afforded the bases together with the trione hydrate.



Schönberg and Moubasher (*J.*, 1944, 366) showed that triketohydrindene is photochemically reduced in sunlight by *isopropyl* alcohol to the colourless product (III; see Ruhemann, *J.*, 1911, **99**, 797), and we find that *perinaphthindane-trione* behaves similarly, giving a colourless product (isolated as a *dihydrate*) believed to be of analogous structure, although a symmetrical constitution, $>C(OH)\cdot C(OH)<$, is not excluded.

Action of periNaphthindane-1 : 2 : 3-trione Hydrate on Bases.—(a) *Aniline.* The hydrate (1 g.), dissolved in water at room temperature, was treated dropwise with aniline (6 g.). Yellow needles were formed almost at once, and after standing for a short time the 2-anilino-2-hydroxyperinaphthindane-1 : 3-dione (II, R = Ph) was filtered off and crystallised from 50% alcohol; m. p. about 230° (decomp.), depending on the rate of heating; yield, 1.3 g. (Found: C, 75.6; H, 4.4; N, 4.7. Calc. for $C_{15}H_{13}O_3N$: C, 75.2; H, 4.3; N, 4.6%).

(b) *p-Chloroaniline.* The 2-*p-chloroanilino*-analogue, similarly prepared, formed yellow crystals, m. p. 220°; yield, 1.5 g. (Found: C, 66.9; H, 3.5; N, 3.9; Cl, 10.5. $C_{15}H_{12}O_3NCl$ requires C, 67.5; H, 3.6; N, 4.1; Cl, 10.5%).

(c) *Benzidine.* The reaction was carried out in a mixture of equal volumes of water and alcohol, containing *perinaphthindane-1 : 2 : 3-trione* (1 g.) and benzidine (0.82 g.). 2-Benzidino-2-hydroxyperinaphthindane-1 : 3-dione (II, R = $C_6H_4\cdot C_6H_4\cdot NH_2$) was crystallised from ethyl alcohol; m. p. 270° (decomp.); yield, 1.4 g. (Found: C, 75.6; H, 4.6; N, 7.0. $C_{25}H_{18}O_3N_2$ requires C, 76.1; H, 4.6; N, 7.1%).

The first two compounds were soluble in benzene and alcohol, and the last in the hot solvents. The colours given in concentrated sulphuric acid were, respectively, an intense violet, green, and red.

Hydrolysis of Condensation Products.—(a) *In acid solution.* 1 G. of the substance was refluxed with a mixture of 25 c.c. of hydrochloric acid (*d* 1.1) and 25 c.c. of water for 15 minutes. On cooling, colourless crystals of the trione hydrate were obtained, which after crystallisation had m. p. and mixed m. p. 273°. The solution contained aniline, *p*-chloroaniline, or benzidine.

(b) *In alkaline solution.* 1 G. of the substance was refluxed for 15 minutes with aqueous sodium hydroxide solution (10%; 50 c.c.), and the blue solution was cooled and decolorised by shaking with air. The mixture was extracted with ether, and the extract, on evaporation, yielded aniline, *p*-chloroaniline, or benzidine. The aqueous solution in each case on acidification yielded naphthalic acid (m. p. and mixed m. p. 274° after crystallisation from benzene).

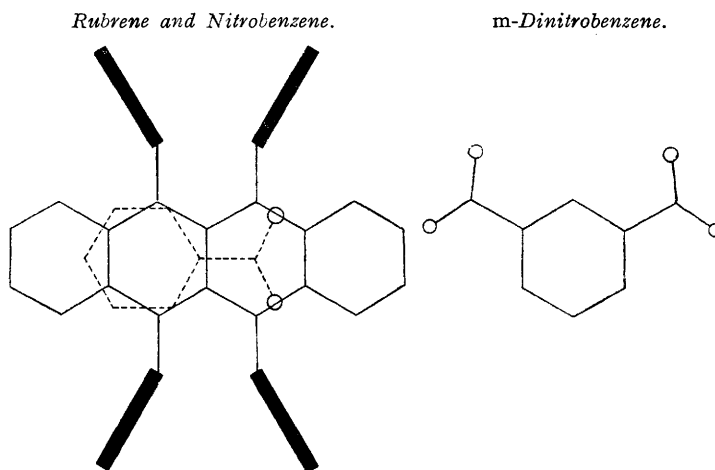
Photo-reduction of periNaphthindane-1 : 2 : 3-trione with isoPropyl Alcohol.—The trione (2 g.) was suspended in freshly distilled *isopropyl* alcohol (10 c.c.) in a sealed "Pyrex" tube, in an atmosphere of carbon dioxide. The tube was exposed to sunlight for a week (in April). The resulting yellow solid was filtered off, and the excess of alcohol evaporated in a vacuum. The solid mass recrystallised from benzene to form pale yellow needles of a *dihydrate* (1.1 g.), m. p. 220° (decomp.), soluble in alcohol and acetic acid (Found: C, 67.6; H, 3.9. $C_{26}H_{14}O_6\cdot 2H_2O$ requires C, 68.1; H, 3.9%).

The photo-product (0.5 g.) was refluxed with 25 c.c. of sodium hydroxide solution (20%) for 15 minutes. The blue solution was cooled, and shaken with air until decolorised; from this solution naphthalic acid (identified as above) was obtained. The same acid (m. p. and mixed m. p. 274°) was isolated as a colourless sublimate when the photo-product was heated with selenium in a stream of oxygen at 220° (bath temp.).—FOUAD I UNIVERSITY, CAIRO, EGYPT. [Received, April 26th, 1946.]

Stereo-effects and van der Waals Complexes. By E. J. BOWEN and E. COATES.

The quenching of the fluorescence of aromatic hydrocarbons in solution by other aromatic molecules is often due to the formation of comparatively stable van der Waals complexes (Bowen, Barnes, and Holliday, *Trans. Faraday Soc.*, 1946, to appear), and in other cases, where the life of the complex is very short, to collisions governed by diffusion. We find that the quenching of the fluorescence of rubrene

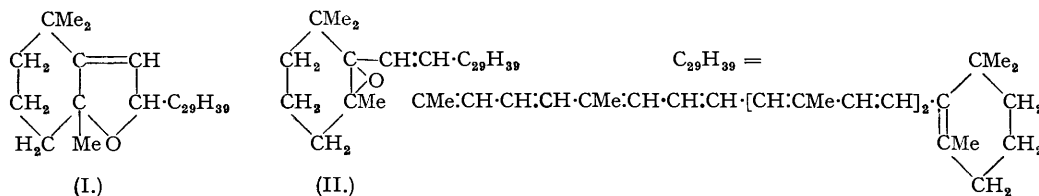
in hexane solution by nitrobenzene arises from complex formation with a heat of formation of 2.5 k.-cals./mole, and *m*-dinitro- and *s*-trinitro-benzene behave as collisional quenchers. The reason for this difference in behaviour, which is the opposite of that which would be expected at first sight from the work of Briegleb (*Z. physikal. Chem.*, 1932, *B*, **19**, 255; 1934, *B*, **26**, 63; 1935, *B*, **27**, 474; 1935, *B*, **31**, 58; 1936, *B*, **32**, 305) on the stability of hydrocarbon-nitro-compound complexes, is apparent from the figure. The nitrobenzene molecule can accommodate itself parallel to the naphthacene centre of



the rubrene molecule, but the polynitro-compounds cannot because of interference from the four phenyl groups which are not coplanar with the centre. This affords further evidence of the structure of hydrocarbon-nitro-compound complexes as parallel molecular orientations.—PHYSICAL CHEMISTRY LABORATORY, SOUTH PARKS ROAD, OXFORD. [Received, May 22nd, 1946.]

The Pro-vitamin-A Activity of Mutatochrome. By N. T. GRIDGEMAN, R. F. HUNTER, and N. E. WILLIAMS.

MUTATOCHROME (I) (Karrer and Jucker, *Helv. Chim. Acta*, 1945, **28**, 27), which Euler, Karrer, and Walker (*ibid.*, 1932, **15**, 1507) originally supposed to be β -carotene epoxide (" β -carotene oxide ") (II), shows growth-promoting activity in rats not closely similar to that of β -carotene as stated by the original authors but appreciably less than that of α -carotene.



This result and the 1 : 2 ratio for biological activity of α - to β -carotene (Kuhn and Brockmann, *Klin. Wochenschr.*, 1933, **12**, 972; Kuhn, Brockmann, Scheunert, and Schieblich, *Z. physiol. Chem.*, 1933, **221**, 129; Wilkinson, *Biochem. J.*, 1941, **35**, 824) are consistent with the view that the conversion of β -carotene into vitamin-A which occurs *in vivo* involves the fission of the central double bond in the former (cf. Hunter, *Chem. and Ind.*, 1942, **61**, 89). Similar but less precise evidence on the same point is furnished by the earlier observations of Kuhn and Brockmann (*Ber.*, 1933, **66**, 1319) and Kuhn and Grundmann (*Ber.*, 1934, **67**, 593) that semi- β -carotenone and cryptoxanthin show growth-promoting activity in daily doses of 5—10 μ g. in contrast to β -carotene which is effective in doses of 2.5 μ g.

Experimental.—The following experiment on the preparation of mutatochrome is typical:

A solution of β -carotene (0.55 g.) in chloroform (100 c.c.) was treated with perbenzoic acid in the same solvent (1.2 mols.; 3.2 c.c.) and kept at 0° in an atmosphere of carbon dioxide for 42 hours. The solution was washed with aqueous sodium bicarbonate (5%), dried (Na_2SO_4), and evaporated under reduced hydrogen pressure with the usual precautions (Hunter and Scott, *Biochem. J.*, 1941, **35**, 31) at a temperature below 50°. The mutatochrome, which was separated by chromatography on alumina as a typical lemon-yellow zone, was rechromatographed and crystallised from acetone, from which it separated in small yellow-brown crystals, m. p. 158°, which showed absorption maxima at 487 and 456 μ in carbon disulphide and at 464 and 437 μ in chloroform ($\epsilon_{1\%}^{1\text{cm}}$ = 1910 and 2190, respectively, for latter solvent). It showed a transient band at 5950 Å. in the antimony trichloride reaction.

The yield of mutatochrome varied from 5 to 12% but attempts to increase this by variation of concentration of perbenzoic acid, temperature, and time proved unsuccessful (cf. Euler, Karrer, and Walker, *loc. cit.*).

Biological assay. Mutatochrome was dissolved in refined deodorised arachis oil containing 0.01% of quinol and the pro-vitamin-A activity of the solution in Wistar rats was compared with that of the International Standard preparation (1934) of β -carotene diluted with arachis oil. A total of 87 vitamin-A deficient rats, in 27 isogenic sets (11 tetrads, 11 triads, and 5 pairs), was used in a 4-point experimental design (Gridgeman, *Biochem. J.*, 1943, **37**, 127), with daily doses of (i) 0.54 μ g. mutatochrome, (ii) 0.72 μ g. β -carotene, (iii) 0.9 μ g. mutatochrome, and (iv) 1.2 μ g. β -carotene over a 3-week period. As group (i) grew less than group (ii) and group (iii) less than group (iv), it was at once obvious that the mutatochrome was appreciably less than 75% as potent as β -carotene. The actual assay, expressed as weight for weight activity of mutatochrome in terms of β -carotene, was 39%, the ($P = 0.95$) fiducial limits of error being 29 to 47%. As the International Standard preparation of β -carotene is known to be less than 100% pure, mutatochrome has certainly less than 47%, and probably less than 39%, of the pro-vitamin-A activity of β -carotene.

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RESEARCH DEPT., LEVER BROTHERS AND UNILEVER LTD., PORT SUNLIGHT. [*Received, May 1st, 1946.*]
