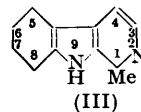
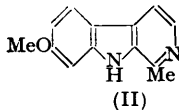
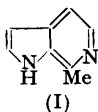


NOTES.

264. *Synthesis of 5 : 6 : 7 : 8-Tetrahydro-1-methyl- β -carboline.*

By G. R. CLEMO and R. J. W. HOLT

It is somewhat surprising that *apoharmine* (I) the important degradation product of *harmine* (II) has apparently not been synthesised directly although Lawson, Perkin, and Robinson (*J.*, 1924, 626) state that by degradation of synthetic methyldiveratroharmyrine enough *apoharmine* was obtained for a comparison of melting points and fluorescent properties.



We have prepared the 2-methyl-3-pyridylhydrazones of ethyl pyruvate and *cyclohexanone*, but so far have not cyclised the former by the Fischer method, although the latter readily gives the hitherto undescribed 5 : 6 : 7 : 8-tetrahydro-1-methyl- β -carboline (III) which has been dehydrogenated to *harman*.

This appears to be the first successful use of the Fischer indole reaction in the pyridine series and also of the synthesis of the *harman* system starting with its pyridine ring, and although our work is incomplete we record it in view of the work of Baumgarten and Su (*J. Amer. Chem. Soc.*, 1952, **74**, 3828).

Experimental.—6-Amino-2-methyl-3-nitropyridine. 6-Amino-2-picoline (81 g.) was added with stirring to nitric acid (50 c.c.; *d* 1.42); the solid nitrate was washed with acetone (50 c.c.). The dry nitrate (100 g.) was added to cooled concentrated sulphuric acid (400 c.c.) with stirring, the solution heated at 100° for 1 hour, then cooled, 20% oleum (30 c.c.) added, and the whole heated at 100° for a further hour. 6-Amino-2-methyl-3-nitropyridine (Siede, *J. Russ. Phys. Chem.*, 1918, **50**, 534) was obtained from the reaction mixture and converted into the 6-chloro-compound (Baumgarten and Su, *loc. cit.*).

3-Amino-2-methylpyridine (cf. Parker and Shive, *J. Amer. Chem. Soc.*, 1947, **69**, 63). 6-chloro-2-methyl-3-nitropyridine (40 g.) was shaken in methanol (1 l.) under hydrogen at room temperature and pressure with palladised charcoal (2 g.; 15%), the catalyst and methanol were removed and the 3-amino-2-methylpyridine (22 g.) was obtained from the residue by basification and extraction with hot benzene.

2-Methyl-3-pyridylhydrazine. 3-Amino-2-methylpyridine (10 g.) was dissolved in concentrated hydrochloric acid (25 c.c.) and cooled to -20°, solid sodium nitrite (7 g.) added during 2 hours, and the mixture kept at -20° for a further 2 hours and then added dropwise to a stirred solution of stannous chloride (50 g.) in concentrated hydrochloric acid (35 c.c.) at -20°. The

mixture was left overnight, the solid collected, and the 2-methyl-3-pyridylhydrazine liberated by basification and extraction with ether; it separated from benzene as yellow needles (2.5 g.; m. p. 130—131°) (Found: C, 58.25; H, 7.3. $C_6H_9N_3$ requires C, 58.5; H, 7.3%).

Ethyl pyruvate 2-methyl-3-pyridylhydrazone. The foregoing hydrazine (1 g.) and ethyl pyruvate (1 g.) were mixed and pyridine (2 c.c.) was added. The mixture was heated on a water-bath for 0.5 hour, and water (4 c.c.) added. The *hydrazone* separated on cooling and recrystallised from aqueous alcohol as almost colourless needles (1.4 g.), m. p. 119—120° (Found: C, 60.0, 59.9; H, 7.2, 7.2. $C_{11}H_{15}O_2N_3$ requires C, 59.8; H, 6.8%).

cycloHexanone 2-methyl-3-pyridylhydrazone. The hydrazine (1 g.) and cyclohexanone (1 g.) gave the hydrazone (1.5 g.), m. p. 128—129° (Found: C, 71.0; H, 8.6. $C_{12}H_{17}N_3$ requires C, 71.0; H, 8.4%).

5 : 6 : 7 : 8-Tetrahydro-1-methyl- β -carboline. *cycloHexanone 2-methyl-3-pyridylhydrazone* (1 g.), zinc chloride (5 g.), and dry ethanol (5 c.c.) were heated at 100° during 18 hours in a sealed tube; the reaction mixture was evaporated to small bulk, basified, and extracted with ether. The *carboline* (0.1 g.), crystallised from benzene-acetone and then sublimed at 160°/16 mm., had m. p. 233—235° (Found: C, 76.95; H, 7.7; N, 14.8%; *M*, 182.5. $C_{12}H_{14}N_2$ requires C, 77.4; H, 7.5; N, 15.0%; *M*, 186).

Harman. The carboline (0.01 g.), palladised charcoal (0.005 g., 15%), and Dowtherm (diphenyl ether 75%, diphenyl 25%) (0.2 c.c.) were refluxed for 1 hour, benzene was added, and the mixture extracted with 2*N*-hydrochloric acid. The acid solution showed blue-violet fluorescence in ultra-violet light. On basification and extraction, harman (0.007 g.) was obtained as colourless crystals (from benzene), m. p. 237—238°, depressed to 210° by the tetrahydro-compound but unchanged by admixture with an authentic specimen of harman (Found: C, 79.3; H, 6.0. Calc. for $C_{12}H_{10}N_2$: C, 79.0; H, 5.5%).

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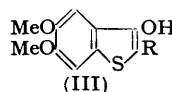
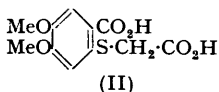
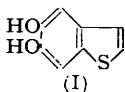
[Received, December 6th, 1952.]

265. The Synthesis of 5 : 6-Dihydroxythionaphthen.

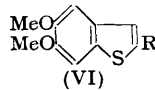
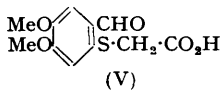
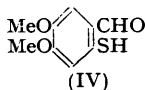
By D. G. BEW and G. R. CLEMO.

IN view of work in progress on the formation of melanin from 5 : 6-dihydroxyindole, 5 : 6-dihydroxythionaphthen (I) has been prepared and its oxidation examined.

6-Nitroveratric acid was converted *via* the derived amino-ester into the substituted thiosalicylic acid and thence into (2-carboxy-4 : 5-dimethoxyphenylthio)acetic acid (II), but the cyclisation of this by acetic anhydride (Hansch and Lindwall, *J. Org. Chem.*, 1945, 19, 383) and alkali fusion (Friedlander, *Annalen*, 1907, 351, 406) to the thioindoxyl (III; R = H) proved troublesome. The diethyl ester of (II), however, was readily cyclised by sodium in toluene to ethyl 5 : 6-dimethoxythioindoxyl-2-carboxylate (III; R = CO₂Et). This proved surprisingly resistant to both acid and alkaline hydrolysis.



Attention was then turned to the preparation of the 4 : 5-dimethoxy-2-mercaptobenzaldehyde (IV) by direct replacement from the 2-bromo-aldehyde (cf. Fries and Hemmecke, *Annalen*, 1927, 454, 126; Hemmecke, Diss., Braunschweig, 1929) but without success, and the thiol was ultimately obtained from 6-aminoveratraldehyde (cf. Bogert and Elder, *J. Amer. Chem. Soc.*, 1929, 51, 526) by diazotisation and coupling with potassium ethyl xanthate followed by hydrolysis. Condensation of (IV) in alkaline solution with chloroacetic acid gave (V) which on liberation cyclised spontaneously to 5 : 6-dimethoxythio-



naphthen-2-carboxylic acid (VI; R = CO₂H). This was decarboxylated by the method of Shepard, Winslow, and Johnson (*J. Amer. Chem. Soc.*, 1930, 52, 2083) to 5 : 6-dimethoxythionaphthen (VI; R = H). Demethylation by anhydrous pyridine hydrochloride (Prey,

Ber., 1941, **74**, 1221) gave the desired compound (I). This is markedly more stable to oxidation than its nitrogen analogue but its solution in 2*N*-sodium hydroxide rapidly becomes dark brown and gradually deposits a brown solid. Aeration in solution at pH 8 did not lead to the evolution of carbon dioxide (cf. Clemo, Duxbury, and Swan, *J.*, 1952, 3464).

Experimental.—*Ethyl 6-aminoveratrate*. The nitro-ester (Fetscher and Bogert, *J. Org. Chem.*, 1939, **4**, 71) (10 g.) and Raney nickel (5.5–6 g.) in ethanol (150 ml.) were stirred with hydrogen at 100°/100 atm. for 6 hours, then filtered and concentrated under reduced pressure, and the hydrochloride (8.1 g.; m. p. 201–203°) was precipitated with hydrochloric acid.

(2-Carboxy-4 : 5-dimethoxyphenylthio)acetic acid (II). To the above hydrochloride (5 g.) in water (50 ml.) and 2*N*-hydrochloric acid (15 ml.), sodium nitrite (3.0 g.) in water (10 ml.) was added dropwise with cooling. The diazonium solution was added slowly to a stirred solution of potassium ethyl xanthate (4.0 g.) and sodium carbonate (2.5 g.) in water (50 ml.) at 70°. On cooling, the dark brown oil which separated was extracted with ether and refluxed for 2 hours with sodium hydroxide (3.5 g.) in water (5 ml.) and methanol (40 ml.). A solution of chloroacetic acid (1.5 g.) in water (5 ml.) basified with sodium carbonate was added and refluxing continued for 2 hours. The methanol was removed, the solution treated with charcoal, and the acid (II) precipitated by hydrochloric acid. Sublimation or recrystallisation from alcohol gave a cream-coloured solid (1.8 g.; m. p. 229–230°) (Found: C, 48.6; H, 4.9; S, 11.7. C₁₁H₁₂O₆S requires C, 48.6; H, 4.4; S, 11.8%). The diethyl ester has m. p. 82–83° (Found: C, 54.8; H, 6.75. C₁₅H₂₀O₆S requires C, 54.9; H, 6.1%).

Ethyl 5 : 6-dimethoxythioindoxyl-2-carboxylate. The diester (0.7 g.) was refluxed with powdered sodium (0.25 g.) in toluene (20 ml.) for 3 hours, excess of sodium removed with alcohol, the solution acidified (hydrochloric acid) and taken to dryness, and the residue taken up in water (10 ml.) and extracted with ether, giving a pale brown ester which recrystallised from alcohol in plates (0.35 g.), m. p. 137–138° (Found: C, 55.3; H, 5.3. C₁₃H₁₄O₅S requires C, 55.3; H, 5.0%).

5 : 6-Dimethoxythionaphthen-2-carboxylic acid. To 6-aminoveratraldehyde (4.1 g.) and sodium nitrite (1.7 g.) in aqueous ethanol, a solution of sulphuric acid (4.3 ml.) in water (30 ml.) was added with cooling. The red solution was added to potassium ethyl xanthate (4.0 g.) and sodium carbonate (3.5 g.) in water (30 ml.) at 70°, the whole extracted with ether, and the dark brown oil obtained on removal of the solvent refluxed with sodium hydroxide (3.0 g.) in water (5 ml.) and methanol (20 ml.) for an hour. A solution of chloroacetic acid (1.8 g.) in water (5 ml.) made alkaline with sodium carbonate was then added and refluxing continued for an hour. The methanol was removed, the solution acidified, and the crude acid recrystallised from alcohol (0.6 g.; m. p. 255–257°) (Found: C, 55.7; H, 4.6; S, 13.3. C₁₁H₁₀O₄S requires C, 55.4; H, 4.25; S, 13.5%).

5 : 6-Dimethoxythionaphthen. The acid (VI; R = CO₂H) (0.6 g.), quinoline (7 ml.) and copper powder (0.1 g.) were heated at 200–220° for 40 min. whilst a slow stream of nitrogen was passed in. The solution was acidified (sulphuric acid), and 5 : 6-dimethoxythionaphthen isolated by steam-distillation as a white solid of characteristic odour (0.3 g.; m. p. 89–91°) (Found: C, 61.6; H, 5.3. C₁₀H₁₀O₂S requires C, 61.9; H, 5.2%).

5 : 6-Dihydroxythionaphthen. 5 : 6-Dimethoxythionaphthen (0.2 g.) and pyridine hydrochloride (0.6 g.) were heated at 140–150° for 20 min. with exclusion of moisture. The temperature was then raised to 180–190° and heating continued for 30 min. Water (10 ml.) was added and the solution treated with charcoal and extracted with ether, and the dihydroxythionaphthen recrystallised from ether–light petroleum (19 mg.; m. p. 134–137°) (Found: C, 57.9; H, 4.2. C₈H₆O₂S requires C, 57.8; H, 3.65%).

One of us (D. G. B.) thanks D.S.I.R. for a Maintenance Grant.

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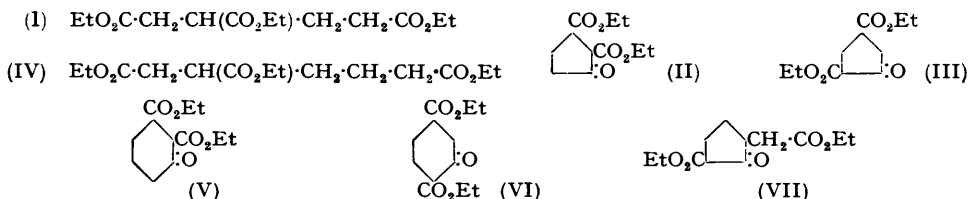
266. Course of Cyclisation in the Formation of Alicyclic Rings. Part II.* A Paradoxical Case of Dieckmann Cyclisation.

By R. N. CHAKRAVARTI.

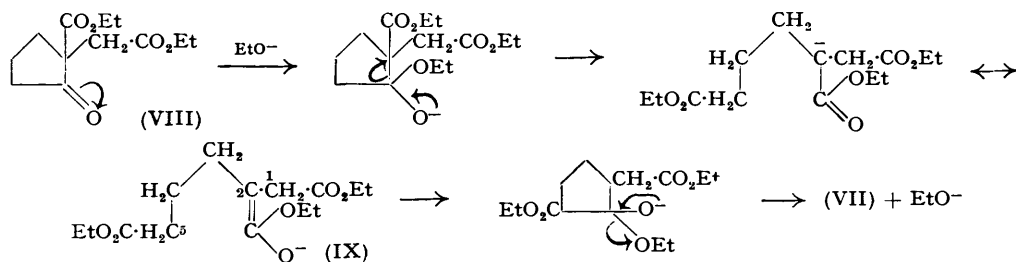
In Part I (cf. *Experientia*, 1947, **3**, 149) it has been established that an alkyl group attached to the β-carbon atom of a polycarboxylic ester has a deactivating influence on the α-methylene group. From this it may be inferred that, owing to its negative character, a carbethoxy-group attached to the β-carbon atom of a polycarboxylic ester has an activat-

* Part I, *J.*, 1947, 1028.

ing influence on the α -methylene group. This is supported by the fact that Dieckmann cyclisation of ethyl butane-1 : 2 : 4-tricarboxylate (I) leads to a mixture of (II) and (III) in which (II) largely predominates.



Dobson, Ferns, and Perkin (*J.*, 1909, **95**, 2010) found that Dieckmann cyclisation of ethyl pentane-1 : 2 : 5-tricarboxylate (IV) followed by hydrolysis affords 3-ketocyclohexanecarboxylic acid. Chatterjee, Das, and Barpujari later (*J. Indian Chem. Soc.*, 1940, **17**, 161) observed that ethyl 1-carbethoxy-2-ketocyclopentylacetate (VIII) is transformed by hot alcoholic sodium ethoxide into the cyclopentanone ester (VII). The last authors (cf. also N. K. Chakravarty and Banerjee, *ibid.*, 1946, **23**, 377) considered this to occur by



way of (IV) and erroneously concluded (cf. Atwood, Stevenson, and Thorpe, *J.*, 1923, **123**, 1758; von Braun, *Ber.*, 1928, **61**, 441; Chakravarti, *J. Indian Chem. Soc.*, 1943, **20**, 393) that the five-membered ring is almost invariably formed in preference to the six-membered ring when the two possibilities exist.

As stated above, owing to the influence of the carbethoxy-group attached to the β -carbon atom, (IV) may be expected to give (V) as major product, and (VI) and (VII) as minor products. Since both (V) and (VI) on hydrolysis give 3-ketocyclohexanecarboxylic acid the experimental results of Dobson *et al.* (*loc. cit.*) can be explained. As regards the experimental results of Chatterjee *et al.* (*loc. cit.*), the reaction mechanism shown in the annexed scheme (VIII \rightarrow VII) is now proposed. In other words, the latter reaction appears to proceed, not through (IV), but through the ester anion (IX).

SCHOOL OF TROPICAL MEDICINE, CALCUTTA.

[Received, July 24th, 1952.]

267. A New Synthesis of 2 : 5-Dihydroxyphenyl-DL-alanine adapted to Isotopic Scale.

By ALEXANDER T. SHULGIN and EMERY M. GAL.

THERE is apparently no record of the synthesis of 2 : 5-dihydroxyphenyl-DL-alanine by condensation of a 2 : 5-dimethoxybenzyl halide with either sodioacetamidomalonic ester or sodioacetamidocynoacetic ester, although the reactions of similar halides were extensively explored (Burckhalter and Stephens *J. Amer. Chem. Soc.*, 1951, **73**, 56), and tyrosine was obtained in excellent yields (Fields, Walz, and Rothchild, *J. Amer. Chem. Soc.*, 1951, **73**, 1000). The reported syntheses all employed free or substituted 2 : 5-dihydroxybenzaldehyde and acetylglycine (Hirai, *Biochem. Z.*, 1927, **189**, 88; Neuburger, *Biochem. J.*, 1948, **43**, 599; Lambooy, *J. Amer. Chem. Soc.*, 1949, **71**, 3758) or hippuric acid (Yakovlev,

Zhur. Obschei Khim., 1950, **20**, 361) condensation to the oxazole which is reduced with phosphorus and hydrogen iodide to 2 : 5-dihydroxyphenyl-DL-alanine. Lambooy claimed superior yields from 2 : 5-dihydroxybenzaldehyde with an overall yield of 26% whereas Yakovlev reported 40.7%.

The authors prepared diethyl α -acetamido- α -2 : 5-dimethoxybenzylmalonate and ethyl α -acetamido- α -cyano- α -2 : 5-dimethoxybenzylacetate. Unlike the derivatives described by Burchhalter *et al.* (*loc. cit.*), the above precursors failed to give 2 : 5-dihydroxyphenyl-DL-alanine on hydrolysis with 40 or 48% hydrogen bromide, in an inert or hydrogen atmosphere. Extensive charring resulted within a couple of hours. Alkaline hydrolysis was equally unsuccessful. Hydrolysis and decarboxylation with hydrogen iodide in glacial acetic acid in an inert atmosphere yielded 2 : 5-dihydroxyphenyl-DL-alanine, in overall yield of 45–49%. The chemically pure samples of 2 : 5-dihydroxyphenylalanine prepared by either this method or that of Yakovlev gave a second, weakly positive ninhydrin spot which moved ahead of the 2 : 5-dihydroxyphenylalanine in butanol-acetic acid-water.

DL-Tyrosine was similarly prepared through diethyl α -acetamido- α -*p*-methoxybenzylmalonate. The yield of ethyl α -cyano- α -*p*-methoxybenzylacetate was 70% in contrast to the 91% overall yield reported by Fields *et al.* (*loc. cit.*).

Experimental.—2 : 5-Dimethoxybenzyl bromide. The sample of 2 : 5-dimethoxybenzyl alcohol (2.8 g.), obtained in 75% yield through the lithium aluminum hydride reduction (Adams, Harfenist, and Loewe, *J. Amer. Chem. Soc.*, 1949, **71**, 1624) of 2 : 5-dimethoxybenzoic acid, distilling at 85–90°/25 \times 10⁻³ mm. was taken up in dry (P₂O₅) carbon tetrachloride (25 ml.). Phosphorus tribromide (1.5 g.) in carbon tetrachloride (10 ml.) was slowly added to the ice-cooled solution, which was then set aside overnight at room temperature, protected from moisture. The carbon tetrachloride solution was decanted from the separated phosphorous acid residue, which was extracted with carbon tetrachloride (2 \times 10 ml.), and the extracts and original solution were pooled. The solvent was evaporated from the combined original solution and extracts, and the residue was sublimed. 2 : 5-Dimethoxybenzyl bromide sublimed as white needles (3.29 g.; 85%; m. p. 75–76°) at 90–100° (bath-temp.)/1 mm. (Found : C, 46.9; H, 4.7; Br, 34.3. C₉H₁₁O₂Br requires C, 46.8; H, 4.8; Br, 34.6%). The alcohol was identified as its *p*-nitrobenzoate, m. p. 110° (Found : C, 60.1; H, 4.8; N, 4.4. C₁₆H₁₅O₆N requires C, 60.6; H, 4.8; N, 4.4%).

Diethyl α -acetamido- α -2 : 5-dimethoxybenzylmalonate. To the above bromide (2.38 g., 0.01 mole) an alcoholic solution of ethyl sodioacetamidomalonate (from 0.23 g. of sodium and 2.17 g. of ester; 0.01 mole) was added, the solution was refluxed for 3 hours, and the alcohol was removed under vacuum. The residue was washed with water (10 ml.) and the residue taken up in boiling water to which enough alcohol was added to complete dissolution. On cooling overnight white crystals (2.8 g., 75% when dried), m. p. 84–85° of the *ester* separated (Found : C, 58.6; H, 6.6; N, 3.9. C₁₈H₂₅O₇N requires C, 58.8; H, 6.85; N, 3.8%).

The *ester* obtained in a similar manner from the condensation of the bromide and ethyl acetamidocyanoacetate melted at 121° (Found : C, 60.0; H, 6.15; N, 8.9. C₁₆H₂₀O₅N₂ requires C, 60.0; H, 6.3; N, 8.7%).

2 : 5-Dihydroxyphenyl-DL-alanine. To freshly-distilled acetic acid (1.0 ml.) and freshly-distilled constant-boiling hydrogen iodide (0.8 ml.) the substituted malonic ester (250 mg.) was added, and the mixture was gently refluxed under a stream of nitrogen for 3 hours. (When necessary, small crystals of sodium hypophosphite were added until all iodine colour disappeared.) The mixture was then concentrated to dryness *in vacuo* at 50–55° (bath-temp.). The residue was dissolved in water (0.5 ml.) and again concentrated to dryness. A solution of the resulting solid (2 : 5-dihydroxyphenylalanine hydroiodide, m. p. 230–235°) in hot water (1.0 ml.) was carefully adjusted to pH 4.5 with ammonia solution, and left in the icebox for 3 days. The white crystals (95 mg., 65%) were shown to be free from glycine by paper chromatography. After recrystallization they contained 1 molecule of water of crystallisation (Found : C, 50.0; H, 6.0; N, 6.4. Calc. for C₉H₁₁O₄N.H₂O : C, 50.2; H, 6.1; N, 6.5%). The product, which melted over the range 230–250°, reduced phosphomolybdic acid in acid solution.

Diethyl α -acetamido- α -*p*-methoxybenzylmalonate. This was prepared, in 60% yield, as for the 2 : 5-dimethoxy-analogue; the *ester*, m. p. 50–51° (Found : C, 60.2; H, 6.8; N, 4.2. C₁₇H₂₃O₆N requires C, 60.5; H, 6.9; N, 4.1%). It gave DL-tyrosine in 80% yield on hydrolysis in glacial acetic acid and hydrogen iodide. Chromatography of the DL-tyrosine gave a single ninhydrin-positive spot of the correct R_F value.

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DEPARTMENT OF PHYSIOLOGICAL CHEMISTRY, SCHOOL OF MEDICINE, UNIVERSITY OF CALIFORNIA, BERKELEY 4, CALIFORNIA, U.S.A. [Received, December 1st, 1952.]

268. The Thermochromism of Diphenylmethylenanthrone.

By R. J. W. LE FÈVRE and (Miss) I. YOHOTSKY.

SCHÖNBERG, ISMAIL, and ASKER (*J.*, 1946, 442) attributed the thermochromic properties of diphenylmethylenanthrone (I) and a number of related substances to the increasing contribution, with rise of temperature, of betaine structures (*e.g.*, II) to the hybrid real states of the molecules. Since (II), if fully developed, should have a dipole moment of 25–30 D, it seemed of interest to compare the apparent polarities of cold (pale yellow) and warm (yellow-red) solutions in benzene.



Apparatus and techniques were those used for the thermochromic *spiropyrans* (Hukins and Le Fèvre, *J.*, 1949, 2088). Measurements are tabulated under conventional headings. The solute was prepared as noted by Padova (*Compt. rend.*, 1906, 143, 122; *Ann. Chim. Phys.*, 1910, 19, 386) and Clar and Müller (*Ber.*, 1930, 63, 869). Recrystallised from glacial acetic acid it had m. p. 205–207°.

Diphenylmethylenanthrone in benzene.

Temp. 25°.					Temp. 55°.				
$10^6 w_2$ *	ϵ^{25}	d_4^{25}	P_2 (c.c.)	n_D^{25}	$10^6 w_2$ *	ϵ^{55}	d_4^{55}	P_2 (c.c.)	
0	2.2725	0.87378	—	1.4972	0	2.2133	0.84180 ₅	—	
1,823	2.2817	0.87424	426	—	2,425	2.2235	0.84227	389	
2,425	2.2839	0.87439	403	—	3,924	2.2298	0.84238	397	
3,010	2.2868	0.87469	398	—	8,200	2.2480	0.84329	398	
3,924	2.2905	0.87476	387	—	9,840	2.2555	0.84387	400	
4,616	2.2926	0.87516	372	—	11,988	2.2652	0.84445	393	
15,060	2.3342	0.87830	351	1.4997					

* Subscript 2 indicates solute (see footnote in *J.*, 1952, 1932).

The polarisations tabulated under P_2 have been calculated by Sugden's mixture rule (*Trans. Faraday Soc.*, 1934, 30, 720). To obtain values at infinite dilution the observed changes of dielectric constant or density from solvent to solutions have been fitted by the method of least squares to power series in w_2 , thus:

$$\text{At } 25^\circ \begin{cases} (\epsilon_{12} - \epsilon_1)w_2 = 4.74w_2 - 43w_2^2 \\ (d_{12} - d_1)w_2 = 0.269_5w_2 + 2.0w_2^2 \end{cases}$$

$$\text{At } 55^\circ \begin{cases} (\epsilon_{12} - \epsilon_1)w_2 = 4.11w_2 + 18w_2^2 \\ (d_{12} - d_1)w_2 = 0.126w_2 + 7.9w_2^2 \end{cases}$$

The coefficients of w_2 were taken as the $\alpha\epsilon_1$ or βd_1 needed for the equation: ${}_\infty P_2 = M_2 [p_1(1-\beta) + C\alpha\epsilon_1]$ (*cf. J.*, 1937, 1805; *Trans. Faraday Soc.*, 1950, 46, 1). Our results, after computation of standard errors, appear as follows:

Temp.	$\alpha\epsilon_1$	β	p_1 (c.c.)	C	${}_\infty P_1$ (c.c.)
25°	4.74 ± 0.06	0.308 ± 0.009	0.3409	0.1881	404 ± 5
55°	4.11 ± 0.02	0.150 ± 0.013	0.3421	0.2007	400 ± 3

The refractive indexes of the first five solutions (25° set) were indistinguishable from that of benzene (on the Abbé refractometer available) whence R_2 follows as $M_2 r_1 = 120$ c.c. However, from the strongest solution an R_2 of 113 c.c. is calculable and, being nearer the value expected (108 c.c., from anthrone 57.5 c.c., benzene 26.1 c.c., hydrogen 1.1 c.c., and carbon 2.4 c.c.), has been used in estimation of the moments. These emerge respectively as 3.77 ± 0.03 D at 25° and 3.93 ± 0.02 D at 55°.

Comment.—Despite the experimental uncertainties there is thus a slight sign that μ^{55} is greater than μ^{25} .

We originally intended the measurements in benzene to be preliminary to others with solvents with which higher temperatures could be reached. We did not proceed with this, however, after the appearance of a paper by Grubb and Kistiakowsky (*J. Amer. Chem. Soc.*, 1950, **72**, 419). These authors reported spectra of (I \leftrightarrow II) in decalin from 28° to 153° and observed the (single) band at 3550 Å to cover an area which is independent of temperature although a widening and flattening of the over-all absorption curve occurred as the temperature rose. This they explain on the Franck-Condon principle, and conclude that thermochromism is here due "to a trivial cause, the broadening of a near-ultra-violet absorption region by changing distribution of molecules among vibrational states." The same hypothesis probably covers the otherwise puzzling case of the *spiropyrans* (Hukins and Le Fèvre, *loc. cit.*; cf. however, Knott, *J.*, 1951, 3028).

The value now recorded for the moment at 25° (3.7₇ D) itself indicates marked conjugative modification of the carbonyl group (compare *cyclohexanone*, $\mu = 2.75$ D, with 3:5-dimethylcyclohex-5-enone, $\mu = 3.79$ D, or menthone, $\mu = 2.8$ D, with piperitone, $\mu = 3.8$ D; * indeed, where mesomeric shifts of the type $>C \overset{\curvearrowright}{=O}$ are concerned, it puts diphenylmethylenanthrone beyond anthrone in the series: Ph₂C:C:O, $\mu = 1.7_6$, Ph₂C:O, $\mu = 2.9_5$, anthrone, $\mu = 3.4_6$, diphenylmethylenanthrone, $\mu = 3.7_7$ D.

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UNIVERSITY OF SYDNEY, N.S.W., AUSTRALIA.

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269. Reactions of Sodium Carbonate and Sodium Hydroxide with Dinitrogen Tetroxide.

By C. C. ADDISON and J. LEWIS.

Reactions with Sodium Carbonate.—The observations of Oswald (*Ann. Chim.*, 1914, **1**, 44) that sodium carbonate reacts with nitrogen dioxide to give a mixture of sodium nitrate and nitrite, and of Briner, Lugin, and Monnier (*Helv. Chim. Acta*, 1930, **13**, 64) that calcium carbonate gives calcium nitrate only on reaction with liquid dinitrogen tetroxide, would imply that the reactions differ in the liquid and in the gaseous state. This is not in agreement with conclusions reached from the study of reactions of metal oxides (Addison and Lewis, *J.*, in the press), and the reactions of sodium carbonate have therefore been reinvestigated.

Sodium carbonate was dried to constant weight at 600°. On addition of liquid dinitrogen tetroxide to the cold solid, there was no immediate visible reaction; on long standing, nitric oxide was produced in sufficient amount to turn the tetroxide clay-brown, and the liquid froze to a pale blue solid.

When the sodium carbonate had been dried at 250°, the temperature recommended for its drying for analytical purposes (see, *e.g.*, Vogel, "Quantitative Inorganic Analysis," 1st edn., Longmans, p. 281), the solid reacted vigorously, evolving nitric oxide and carbon dioxide and giving a product containing sodium nitrite also. The nitrite did not arise from adsorbed nitrogen dioxide, since the reaction product was heated at 100° for 24 hours before hydrolysis. The Table gives typical experimental results. For dry sodium carbonate,

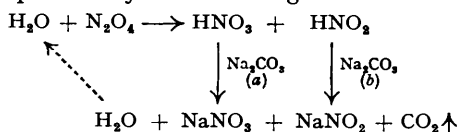
Reaction of liquid dinitrogen tetroxide with sodium carbonate

	(1) Dried at 250°		(2) Dried at 600°	
Period of contact (hours)	19	24	19	24
Conversion, %, into nitrate	49	64	10.2	14.6
Conversion, %, into nitrite	10	12.3	0.0	0.0

the reaction may be represented as $Na_2CO_3 + 2N_2O_4 = 2NaNO_3 + CO_2 + N_2O_3$. Comparisons in the table illustrate the extreme sensitivity of this reaction to traces of moisture,

* For references see the M.I.T. Tables. The value for piperitone is from Le Fèvre and Maramba (*J.*, 1952, 235) who, when writing their paper were unaware of a previous determination (omitted from the M.I.T. Tables) by Naves and Papazian (*Helv. Chim. Acta*, 1942, **25**, 1053).

which caused a considerable increase in the quantity of nitrate produced as well as introducing nitrite. This is explained by the following scheme of reactions :



From the Table, the quantities of nitrate and nitrite (formation of which may be attributed to the moisture present) are seen to be in the approximate molar ratio 4 : 1, rather than the equimolar amounts which would result if reactions (a) and (b) in the above scheme proceeded with equal readiness. The predominance of reaction (a) is in accord with the known properties of nitric and nitrous acids. In media of low dielectric constant the HNO_3 molecule is largely covalent; ionic dissociation can give only the H^+NO_3^- ion-pair. Nitrous acid retains its covalent character even in aqueous solution, so ionic dissociation under these conditions is much less probable. When this does occur, the formation of the NO^+OH^- ion-pair is as likely as that of the H^+NO_2^- form, and there is no apparent reason why the former should undergo reaction with sodium carbonate.

Sodium carbonate (dried at 600°) was found to react with nitrogen dioxide gas according to the equation $\text{Na}_2\text{CO}_3 + 3\text{NO}_2 = 2\text{NaNO}_3 + \text{CO}_2 + \text{NO}$; 33% conversion into nitrate occurred after 7 hours' contact at 250° . No nitrite was produced at any temperature. The increased reaction rate at high temperature is not due to thermal dissociation products of nitrogen dioxide, since experiments at temperatures up to 280° and periods of contact up to 3 hours showed that sodium carbonate was quite inert to nitric oxide. Nitrogen dioxide is therefore the only gaseous oxide of nitrogen to react with sodium carbonate, since it was observed during analysis of sodium hyponitrite (*J.*, 1952, 338) that the reaction $\text{Na}_2\text{N}_2\text{O}_2 + \text{CO}_2 = \text{Na}_2\text{CO}_3 + \text{N}_2\text{O}$ proceeds rapidly in the forward direction.

Reaction with Sodium Hydroxide.—This reaction has some points of analogy with the above. Sodium hydroxide was dried by fusing it in a silver boat at 320° for 3 hours in a current of dry oxygen. On addition of the dried hydroxide (1 g.) to 10 ml. of liquid dinitrogen tetroxide, reaction was vigorous, causing boiling of the tetroxide, and the green coloration of dinitrogen trioxide developed round the solid. Next morning the liquid was evaporated. In an attempt to remove the remaining traces of tetroxide, the white solid product was heated at 100° for a few minutes, and the evolved nitrogen dioxide removed by a current of dry oxygen. This is usually adequate, in the case of sodium salts, to remove adsorbed tetroxide, but in this reaction it was necessary to repeat this process several times before the atmosphere above the solid was free from nitrogen dioxide. This behaviour is attributed to decomposition of nitrous (and/or nitric) acid adsorbed on the solid. Analysis of this product showed 94% conversion into sodium nitrate, and 2.5% conversion into nitrite, the remainder being sodium hydroxide. The reaction may be considered as an ionic exchange: $\text{Na}^+\text{OH}^- + \text{NO}^+\text{NO}_3^- \longrightarrow \text{Na}^+\text{NO}_3^- + \text{ON}^+\text{OH}^-$. The small quantity of sodium nitrite in the reaction product indicates that the nitrous acid molecule reacts only slightly with sodium hydroxide the decomposition of nitrous acid under these conditions being responsible for the green colour observed in the liquid during reaction.

THE UNIVERSITY, NOTTINGHAM.

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270. *The Use of Iodine and Potassium Acetate in the Dehydrogenation of Tetrahydroisoquinoline. The Synthesis of 7-Nitroisoquinoline.*

By M. D. POTTER and E. P. TAYLOR.

7-NITROISOQUINOLINE has recently been prepared (McCoubrey and Mathieson, *J.*, 1951, 2851) by the nitration of 3 : 4-dihydroisoquinoline and catalytic dehydrogenation of the product. The overall yield of crude product was poor (21%), and we have found that this falls to 8–10% on purification. Moreover, the starting material, 3 : 4-dihydroisoquinoline, can itself be prepared only in very low yields by the Bischler–Napieralski reaction [Späth, Berger, and Kuntara, *Ber.*, 1930, **63**, 134 (18%); Snyder and Werber, *J. Amer. Chem. Soc.*, 1950, **72**, 2962 (31%)].

Attempts were first made to improve the preparation of the starting material. The dehydrogenation of 2-substituted 1 : 2 : 3 : 4-tetrahydro- to 3 : 4-dihydro-isoquinolines by iodine and potassium acetate has been achieved in a number of instances (see, *e.g.*, Kondo and Nakazato, *J. Pharm. Soc. Japan*, 1924, **507**, 326; Haworth and Perkin, *J.*, 1925, **127**, 1434; Haworth, Perkin, and Rankin, *ibid.*, p. 1444; Leonard and Leubner, *J. Amer. Chem. Soc.*, 1949, **71**, 3408; Clayson, *J.*, 1949, 2016), but when oxidation of a 1 : 2 : 3 : 4-tetrahydroisoquinoline containing a secondary nitrogen atom was attempted, only the corresponding isoquinolines resulted (see, *e.g.*, Schmidt, *Arch. Pharm.*, 1894, **232**, 136; 1899, **237**, 561; Buck and Perkin, *J.*, 1924, **125**, 1675; Haworth, Perkin, and Rankin, *ibid.*, p. 1686). However, by treating 1 : 2 : 3 : 4-tetrahydroisoquinoline with the quantity of iodine (1 mol.) necessary to remove only two atoms of hydrogen, we have obtained a mixture of tetrahydroisoquinoline, dihydroisoquinoline, and isoquinoline, from which the required 3 : 4-dihydroisoquinoline was separated *via* its picrate, albeit in low yield (20%).

McCoubrey and Mathieson (*loc. cit.*) were unable to dehydrogenate 1 : 2 : 3 : 4-tetrahydro-7-nitroisoquinoline under a variety of conditions. We have prepared 7-nitroisoquinoline in fair yield (35%) by oxidation of the tetrahydro-derivative with iodine and potassium acetate. The identity of the product was established by comparison with the 7-nitroisoquinoline prepared by McCoubrey and Mathieson's method and also by reduction to the known 7-aminoisoquinoline.

Experimental.—3 : 4-Dihydroisoquinoline. To a stirred mixture of 1 : 2 : 3 : 4-tetrahydroisoquinoline (6.6 g.), freshly fused potassium acetate (5.4 g.) and boiling, dry ethyl alcohol (50 ml.), was added iodine (12.7 g.) in dry ethyl alcohol (120 ml.) during 6 hours. After 3 hours' refluxing the mixture was concentrated to small bulk, then cooled, filtered, and evaporated to dryness under reduced pressure and the brown tarry residue triturated with dilute hydrochloric acid and ether. The clear yellow, aqueous portion was made alkaline with sodium hydroxide solution, and the oil which separated was extracted with benzene. After drying (Na_2SO_4), the benzene was evaporated off, leaving a light brown oil. To a solution of this in benzene was added excess of picric acid in benzene, and the precipitated solid was once recrystallised from alcohol (yield, 9.0 g.; m. p. 163—165°). Boiling water (approx. 600 ml.) dissolved the picrates of tetra- and di-hydroisoquinoline, leaving that of isoquinoline undissolved. The insoluble residue, after repeated recrystallisation from alcohol and acetone alternately, gave a small quantity of pure isoquinoline picrate, m. p. 222—223°. The aqueous extract above, on cooling, gave 7 g. of mixed picrates, m. p. 165—166°, which were recrystallised from alcohol, giving 5 g. of a picrate, m. p. 171—172°. Concentration of the alcoholic mother-liquor gave crystals, m. p. 185—187°, which on repeated recrystallisation from ethanol gave pure 1 : 2 : 3 : 4-tetrahydroisoquinoline picrate, m. p. 199—200°. The main crop of picrate was once more recrystallised from water, giving pure 3 : 4-dihydroisoquinoline picrate, m. p. 175—176° (4.2 g.). This was hydrolysed with aqueous ethanalamine (Kaye, Kogon, and Burlant, *J. Amer. Chem. Soc.*, 1950, **72**, 5752), and the 3 : 4-dihydroisoquinoline extracted with benzene. Drying (K_2CO_3) and evaporation of the benzene gave the pure base (1.2 g.), b. p. 108—110°/12 mm.

7-Nitroisoquinoline.—Iodine (33.5 g.) in dry alcohol (310 ml.) was added to 1 : 2 : 3 : 4-tetrahydro-7-nitroisoquinoline hydrochloride (14.0 g.; McCoubrey and Mathieson, *loc. cit.*), freshly fused potassium acetate (28.0 g.), and dry ethyl alcohol (240 ml.) under reflux, with stirring, during 5 hours. Refluxing was continued for a further 15 hours and the precipitated solid was filtered from the cooled mixture. The filtrate was evaporated to about half-bulk, a solution of concentrated hydrochloric acid (20 ml.) in water (80 ml.) added, and removal of alcohol completed under reduced pressure. The residual aqueous solution was diluted with water, filtered, and washed with ether. Addition of 20% sodium hydroxide solution until a deep orange colour just began to form, precipitated 7-nitroisoquinoline as a pale orange solid, which was filtered off. (If excess of alkali is added, a quantity of deep orange precipitate separates and is only removed from the product with difficulty, necessitating sublimation under reduced pressure.) The pale orange solid crystallised from light petroleum (b. p. 100—120°) as buff-coloured needles (4.0 g.), m. p. 176—177° alone or mixed with a specimen obtained by nitration and dehydrogenation of 3 : 4-dihydroisoquinoline (McCoubrey and Mathieson, *loc. cit.*).

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