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Pristimerin. Part I.

By R. C. Shah, A. B. Kulkarni, and V. M. Thakore.

[Reprint Order No. 5350.]

On the basis of elementary analyses and molecular-weight determinations, pristimerin, isolated by Bhatnagar and Divekar (*J. Sci. Ind. Res., India*, 1951, **10**, *B*, 56), has been assigned a provisional molecular formula $C_{28}H_{36}O_4$ (Kulkarni and Shah, *Nature*, 1954, **173**, 1237). Its quinonoid character is indicated by its rapid decolorisation by reducing agents and the reappearance of the colour on aeration, and has been confirmed by reductive acetylation. Its solubility in alcoholic sodium hydrogen sulphite and concomitant decolorisation suggest the presence of a β-quinonoid grouping (Fieser, *J. Amer. Chem. Soc.*, 1926, **48**, 2925). However, in view of a negative test with *o*-phenylenediamine an α-quinonoid structure cannot be excluded. It gives a positive test with boroacetic anhydride (Dimroth and Foust, *Ber.*, 1921, **54**, 3020; *Annalen*, 1925, **446**, 97; cf. Anderson *et al.*, *Analyt. Chim. Acta*, 1952, **7**, 226), suggesting the presence of a potential hydroxy-group probably *peri* to the quinone grouping. It contains one methoxy-group and gives no active hydrogen (Zerewitinoff), the last observation being confirmed by the absence of a hydroxyl band in the infrared spectrum. Methylated pristimerin contains three methoxy-groups, so during its preparation disproportionation has taken place; the ring containing the quinone grouping is aromatised and the two hydroxy-groups so formed are methylated (Sheshadri *et al.*, *Proc. Indian Acad. Sci.*, 1948, **27**, *A*, 245). This trimethyl ether forms a 2 : 4-dinitrophenylhydrazone and therefore has a keto-group which must presumably be present also in pristimerin. The presence of the keto-group is confirmed by the reduction of the trimethyl ether with lithium aluminium hydride to a compound $C_{30}H_{44}O_4$ which does not form a ketonic derivative and has an infrared hydroxyl band (3350 cm.$^{-1}$). Thus the nature of all the oxygen atoms in pristimerin is established. Titration with perbenzoic acid shows the presence of one double bond in the trimethyl ether.

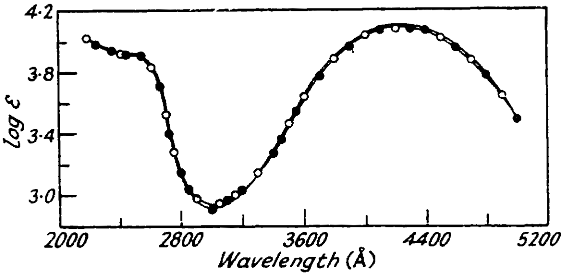

Fig. 1. *Ultraviolet absorption of* (○—○) *primisterin* (0·0263 *g./l.*) *and* (●—●) *methyl-celastrol* (0·03252 *g./l.*), *both in* 95% EtOH.

Pristimerin has the characteristic ultraviolet absorption of a quinone (Fig. 1), and this curve is identical with that of methylcelastrol (Gisvold, *J. Amer. Pharm. Assoc.*, 1939, **28**, 449; 1940, **29**, 12; 1942, **31**, 529; Fieser and Jones, *ibid.*, 1942, **31**, 315; Schechter and Haller, *J. Amer. Chem. Soc.*, 1942, **64**, 182). The identity of the substances is confirmed by the melting point and mixed melting point. The ultraviolet absorption curves of reductively acetylated pristimerin (Fig. 2*A*) and methylated pristimerin (Fig. 2*B*) show the presence of a substituted benzene ring system (cf. Fig. 2*C*; Morton and Sawires, *J.*, 1940, 1052; Campbell and Coppingen, *J. Amer. Chem. Soc.*, 1951, **73**, 2708) and not that of a substituted naphthalene (Fig. 2*D* and *E*) or a higher aromatic fused-ring system. These observations lead us to believe that pristimerin is a benzoquinone derivative (Brockmann and Budde, *Ber.*, 1953, **86**, 432). The molecular formula $C_{22}H_{30}O_3$ and the naphthaquinone structure assigned to celastrol, therefore, appear to be untenable.

Experimental.—*Purification of pristimerin.* Crude pristimerin (5 g.), m. p. 214°, crystallised from benzene–light petroleum (1 : 1) in orange-red stout needles (3·6 g.), m. p. 216—217°. For analysis it was crystallised six times, then having m. p. 219—220°, and its homogeneity was confirmed by chromatographic adsorption on silicic acid and quantitative elution therefrom

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[Found : C, 77·4, 77·5, 77·0; H, 8·4, 8·6, 8·9; OMe, 8·1; *C*-Me, 7·2%; *M*, (cryoscopic in C_6H_6) 391, (*X*-ray method) 429. $C_{28}H_{36}O_4$ requires C, 77·2; H, 8·3; OMe, 7·1; 2*C*-Me, 6·9%; *M*, 436]. The *compound* gives a greenish-brown colour with alcoholic ferric chloride; it is insoluble in alkali but its yellow alcoholic solution on addition of alkali or acid becomes deep red. It has absorption max. in 95% EtOH at 2440 (ε 8320), 2560 (ε 7890), and 4250 Å (ε 12,270).

Reductive acetylation. To a boiling solution of pristimerin (135 mg.) in acetic anhydride (25 c.c.) zinc dust was added until it became colourless. After filtration the excess of anhydride was removed under a vacuum and the residue was extracted with chloroform. The extract was washed with water, aqueous sodium carbonate, and water, dried (Na_2SO_4), and evaporated. The residual *acetate* crystallised from alcohol as colourless needles (85 mg.), m. p. 245—246° after two further crystallisations (Found : C, 74·0, 74·4; H, 8·2, 8·2; OMe, 5·9; Ac, 12·9, 13·3. $C_{32}H_{42}O_6$ requires C, 73·6; H, 8·1; OMe, 5·9; Ac, 16·5%), $[\alpha]_D^{32}$ +105·9° (*c* 0·0604 in $CHCl_3$), $\lambda_{max.}$ 2660—2760 Å (ε 775) in 95% EtOH.

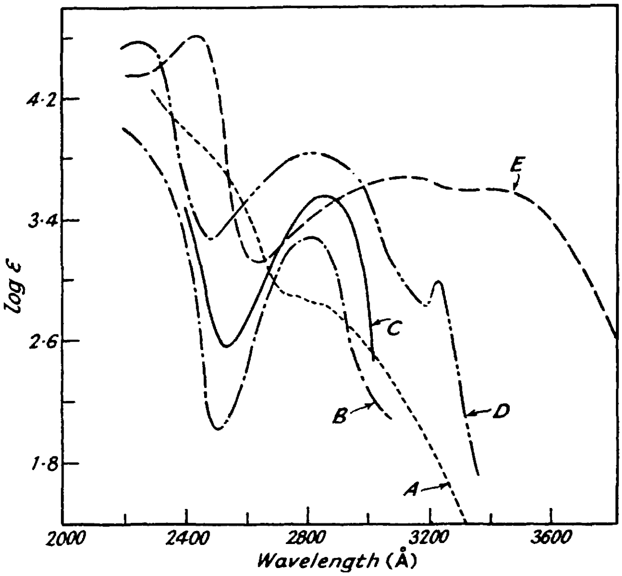

FIG. 2. *Ultraviolet absorption of* (*A*) *the product* (0·05017 *g./l.*) *of reductive acetylation of primisterin,* (*B*) *methylated primisterin* (0·0675 *g./l.*), (*C*) 1 : 2 : 4-*trimethoxybenzene* (0·0682 *g./l.*), (*D*) 1 : 2 : 4-*triacetoxynaphthalene* (0·0632 *g./l.*) (*A*—*D in* 95% EtOH), *and* (*E*) 1 : 2 : 4-*trihydronaphthalene* (from Daglish, *J. Amer. Chem. Soc.*, 1950, **72**, 4859).

Methylation. Pristimerin (140 mg.) was refluxed in acetone with methyl sulphate (2 c.c.) and potassium carbonate (1 g.) for 3 hr. Then more methyl sulphate (2 c.c.) was added and the solution was further refluxed for 3 hr. Acetone was removed, the mixture diluted with water, and the *ether* filtered off. It (130 mg.), m. p. 170—175°, was crystallised from dilute alcohol, giving long colourless needles (83 mg.), m. p. 184—185° (Found : C, 77·2; H, 9·6; OMe, 20·4; active H, 0. $C_{30}H_{42}O_4$ requires C, 77·3; H, 9·0; 3OMe, 19·9%). It consumes 0·77 atom-equiv. of oxygen on titration with perbenzoic acid, gives a negative ferric chloride test but a positive test with tetranitromethane, and has an absorption max. at 2840 Å (ε 1900) in 95% EtOH. The 2 : 4-*dinitrophenylhydrazone* forms needles (from alcohol), m. p. 206° (decomp.; shrinking at 189°) (Found : C, 66·8; H, 7·5; N, 7·9. $C_{36}H_{46}O_7N_4$ requires C, 66·6; H, 7·1; N, 8·7%).

Reduction of methylated pristimerin with lithium aluminium hydride. Methylated pristimerin (115 mg.) in ether (50 c.c.) was added to lithium aluminium hydride (120 mg.) in ether (50 c.c.) and then worked up as usual. The residual *alcohol* crystallised from alcohol as colourless needles (45 mg.), m. p. 162° (decomp.) (Found : C, 76·4; H, 10·1; OMe, 17·3. $C_{30}H_{44}O_4$ requires C, 76·8; H, 9·4; 3OMe, 19·9%).

The authors are grateful to Colonel S. S. Bhatnagar for supplying pristimerin, to Professor J. D. Bernal for determining the molecular weight by *X*-rays and to Mr. W. Manser, of Edg. Techn. Hochschule, Zurich, for checking and confirming some of the microanalytical results obtained at Poona. They also thank Professor Gisvold for a sample of methylcelastrol.

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[*Received, May* 3*rd*, 1954.
Revised, February 24*th*, 1955.]

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Organosilicon Compounds. Part XIV. The Reaction between Trisubstituted Silanes and Silver Perchlorate.*

By C. Eaborn.

[Reprint Order No. 6063.]

Triorganosilanes and silver perchlorate react in toluene solution with precipitation of silver and evolution of hydrogen. The material balance is represented roughly by:

$$R_3SiH + AgClO_4 \longrightarrow R_3SiClO_4 + Ag + \tfrac{1}{2}H_2 \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (1)$$

but deviations from this of as much as 20% in the yields of hydrogen and silver are common. The amount of silver formed is always low, but for a given silane is greater the greater the relative initial concentration of silver perchlorate (Runs 8 and 10, 14 and 15, 22 and 25); and when silver perchlorate is initially in excess the amount of hydrogen is lower the greater this excess (Runs 1—5, 6—12, 14—15). With an initial deficiency of silver salt the amount of hydrogen produced is usually more than equivalent to the silver salt (Run 1), and sometimes more than equivalent to the organosilane taken (Runs 16, 25, 26, 27).

Exact conclusions are impossible because apparently duplicate reactions sometimes gave amounts of hydrogen differing by as much as 15%, although the rates of gas evolution from such "duplicates" usually agreed well during the first 50—60% of reaction. The discrepancies seemed not to be due to traces of water, since addition of small quantities of water had no apparent effect. However, the hydrogen of the silane must almost certainly be initially liberated as atoms, and subsequent atom and radical reactions, possibly of the chain type, would be sensitive to traces of catalysts. The initial reaction is probably $AgClO_4 + R_3SiH \longrightarrow R_3SiClO_4 + AgH$, followed by the rapid decomposition $AgH \longrightarrow Ag + \cdot H$. [The two steps could be simultaneous, but the transitory existence of silver hydride is proposed because (i) silanes reduce copper salts to copper hydride, and (ii) when silanes are mixed with silver perchlorate in toluene, or silver nitrate in ethanol or aqueous acetone, a golden-yellow precipitate is immediately formed and rapidly becomes black as hydrogen is evolved.] Subsequent reactions such as $H\cdot + \cdot H \longrightarrow H_2$ (normally accounting for some 80—100% of the reaction), $Ag^+ + \cdot H \longrightarrow Ag + H^+$, $R_3SiH + \cdot H \longrightarrow R_3Si\cdot + H_2$, along with attack of atoms or radicals on the solvent, could account for the departures from the stoicheiometry of eqn. (1).

With triethylsilane, at a fixed initial concentration of silver salt, the initial rate of hydrogen evolution is roughly proportional to the initial concentration of silane (Runs 1—5), while at a fixed silane concentration (Runs 6—13) this rate is proportional to the square of the silver salt concentration up to 0·35M (but the fall in the rate of hydrogen evolution as reaction proceeds is usually markedly less than expected for a third-order reaction). Above this, increase in the silver salt concentration causes even greater rise in the initial rate than would be expected for an order of two with respect to this salt. Reaction is faster in the less polar solvent benzene (Runs 31 and 32).

For the silanes examined (except possibly the unreactive tri*iso*propylsilane and the very reactive tribenzylsilanes, which cannot be accurately studied) the plots of volume of hydrogen against log time are roughly superimposable, implying that the mechanism of the reactions does not seriously vary. The reactivities of the R_3SiH compounds, as revealed by the initial rate of hydrogen evolution, lie in the following series, the figures in parentheses showing the approximate relative reactivities within each set: (R_3 =) Et_3 (1) > Pr^n_3 (0·5) > Bu^n_3 (0·35) > Bu^i_3 (0·013) > Pr^i_3 (0·001); (p-$C_6H_4Me)Me_2$ (1·1) > Ph, Me_2 (1); (p-$C_6H_4Me)_3$ (3·8) > Ph_3 (1) > (p-$C_6H_4Cl)_3$ (0·2); (p-$Me\cdot C_6H_4\cdot CH_2)_3$ (1·2) > $(C_6H_4\cdot CH_2)_3$ (1) > (p-$C_6H_4Cl\cdot CH_2)_3$ (0·03); $(C_6H_4\cdot CH_2)_3$ (~200) > Ph, Me_2 (~40) > Et_3 (1) > Ph_3 (0·04).

The very low reactivity of the sterically hindered tri*iso*propylsilane implies that nucleophilic attack on silicon is involved in the initial (rate-determining) breaking of the Si–H bond, even though the strongest nucleophile present is perchlorate ion. However, the

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* Part XIII, *J.*, 1955, 2047.

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special effectiveness of silver ions in decomposing silanes strongly indicates that electrophilic attack on hydrogen is important, and since electron-release in R raises the reactivity of R_3SiH the electrophilic attack predominates in the transition state. Simultaneous attack of perchlorate ion on silicon and silver ion on hydrogen would account for the order of two with respect to silver perchlorate. The higher rate in a less polar solvent would be expected for such a reaction, involving disappearance of ionic charges.

Experimental.—Toluene was dried by long storage over phosphoric oxide. Silver perchlorate was dried at 120° for 24 hr., and weighed samples were re-dried at 120° for several hours immediately before use.

Triethylsilane and silver perchlorate. It was considered unsafe to attempt isolation of triethylsilyl perchlorate.

(i) A solution of silver perchlorate (41·5 g.) in toluene (350 ml.) was added during 6 hr. to a solution of triethylsilane (24 g.) in toluene (250 ml.). After an additional 20 hr. the mixture was stirred with water, and the silver (20 g., 90% based on triethylsilane) was filtered off. The toluene layer was washed with dilute alkali and water and then dried (Na_2SO_4), and the toluene was fractionally distilled from the mixture. The residue was distilled, to give 1·0 g. of liquid of b. p. 140—220° [$Et_3SiOH + (Et_3Si)_2O$ (?)], and 23 g. (90%) of hexaethyldisiloxane, b. p. 225—235°, n_D^{17} 1·4350, leaving a small residue (*ca.* 0·5 ml.) which ignited.

(ii) The gas from triethylsilane (0·01 mole) and silver perchlorate (0·015 mole) in toluene (20 ml.) was shown by mass-spectral analysis to contain 99 vol. % of hydrogen (the remaining 1% being reported as carbon dioxide).

Rate studies. The reactants were put into the separate arms of a twin-limbed vessel, which was immersed in a thermostat (23·2° ± 0·02°) and connected to a manometer; the solvent used in the reaction was used also as manometric liquid. When the system reached equilibrium (*ca.* ¼ hr.) the vessel was shaken in such a way that all the liquid ran into any one limb once every second. When gas evolution ceased the silver was filtered off and determined by titration after dissolution in nitric acid.

The following typical runs with triethylsilane (initially 0·00093 mole) show the rates of gas evolution at different initial silver perchlorate concentrations: (*a*) 0·00252, (*b*) 0·00155, (*c*) 0·000774 mole. The gas volume was measured over toluene at 18°/738 mm. The volume of the reaction mixture was 7 ml.

(*a*) Time (min.)	0	½	1	1½	2	3	4	5	7	10	15	26	∞
H_2 (ml.)	0	0·40	1·05	1·73	2·21	3·18	4·00	4·69	5·71	6·86	8·03	9·29	10·3

(*b*) Time (min.)	0	1	2	4	7	12	18	28	38	83	∞
H_2 (ml.) ...	0 *	0·27	0·68	1·47	2·52	3·97	5·20	6·69	7·85	10·36	12·0

* —0·1 when reactants were mixed.

(*c*) Time (min.)	0	1	2	4	8	16	28	41	63	98	142	183
H_2 (ml.)	0	0·05	0·16	0·36	0·76	1·58	2·71	3·77	5·10	6·48	7·54	8·31

The following list gives, in order, the number of the run (in parentheses), R_3 in R_3SiH, the initial amount of silane, the initial amount of perchlorate, the amount of hydrogen evolved, the amount of silver precipitated (all quantities in units of 10^{-5} mole) and (in italics) the initial rate of hydrogen evolution in ml. at N.T.P. per min. The volume of the reaction mixture was 7 ml. except for runs 23, 24, and 26—30, in which it was 12 ml.

(1), Et_3, 180, 155, 66, —, *0·75*; (2), Et_3, 90, 155, 48·1, —, *0·39*; (3), Et_3, 72, 155, —, —, *0·31*; (4), Et_3, 54, 155, 27·0, —, *0·19*; (5), Et_3, 36, 155, 14·2, —, *0·11*; (6), Et_3, 93, 337, 39·1, —, *2·94*; (7), Et_3, 93, 301, —, —, *2·03*; (8), Et_3, 93, 266, 40·6, 90·0, *1·51*; (9), Et_3, 93, 252, 40·8, —, *1·11*; (10), Et_3, 93, 216, 46·0, 85·0, *0·82*; (11), Et_3, 93, 155, 47·6, —, *0·40*; (12), Et_3, 93, 117, 48·0, —, *0·21*; (13), Et_3, 93, 77·2, —, —, *0·089*; (14), Bu^n_3, 100, 216, 52·3, 79·7, *0·32*; (15), Bu^n_3, 100, 301, 50·5, 89·3, *0·68*; (16), Pr^n_3, 100, 216, 53·5, 79·2; *0·43*; (17), Bu^i_3, 100, 301, —, —, *0·024*; (18), Pr^i_3, 100, 301, —, —, *ca. 0·0016*. In 22 hr., 4·3 × 10^{-5} mole of hydrogen and 17 × 10^{-5} g.-atom of silver were formed; the latter figure is probably high because of exposure of the reaction mixture to moisture during filtration; (19), Ph_3, 100, 301, 50·0, 90·2, *0·076*; (20), (p-$C_6H_4Me)_3$, 100, 301, 37·0, 95·7, *0·29*; (21), (p-$C_6H_4Cl)_3$, 100, 301, —, —, *0·015*; (22), $(C_6H_5{\cdot}CH_2)_3$, 100, 301, 50·0, 98·4, — (too fast to follow); (23), Ph,Me_2, 100, 155, 47·4, 78·8, *3·6*; (24), Et_3, 100, 155, 49·0, —, *0·085*; (25), $(C_6H_5{\cdot}CH_2)_3$, 100, 77·2,

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54·1, 75·8, *>5*; (26), $(C_6H_5{\cdot}CH_2)_3$, 100, 77·2, 60·0, —, *~4·5*; (27), $(p\text{-}Me{\cdot}C_6H_4{\cdot}CH_2)_3$, 100, 77·2, 55·2, —, *~5·6*; (28), $(p\text{-}C_6H_4Cl{\cdot}CH_2)_3$, 100, 77·2, —, —, *0·16*; (29), Ph, Me_2, 100, 77·2, —, —, *0·85*; (30), $(p\text{-}Me{\cdot}C_6H_4)Me_2$, 100, 77·2, —, —, *0·98*; (31), Et_3, 80, 119 (supersaturated), 47·7, —, *0·33* (in benzene); (32), Et_3, 80, 85·3, 46·0, —, *0·20* (in benzene).

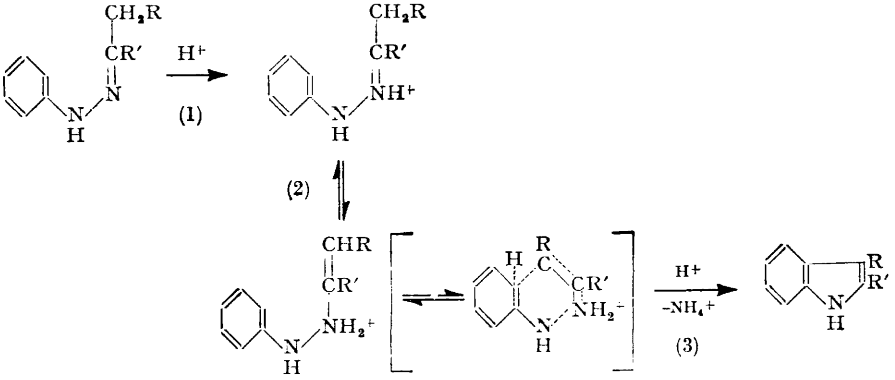
UNIVERSITY COLLEGE, LEICESTER. [*Received, January* 25*th*, 1955.]

Some Kinetic Observations on the Fischer Indole Reaction.

By JAMES MCLEAN, STEWART MCLEAN (in part), and ROWLAND I. REED.

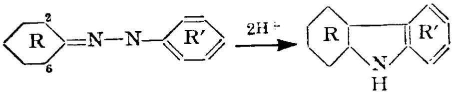
[Reprint Order No. 6100.]

THE suggested mechanism of the Fischer indole reaction (Carlin and Fisher, *J. Amer. Chem. Soc.*, 1948, **70**, 3421; Carlin, Wallace, and Fisher, *ibid.*, 1952, **74**, 990) is shown below in an abridged form. Carlin (*ibid.*, p. 1077) has further examined this mechanism with reference to Pausacker and Schubert's kinetic measurements (*J.*, 1950, 1814), and has considered the case in which reaction (3) is the slow, rate-determining stage.



The above sequence, with reaction (2) as the rate-determining process, is also consistent with the known kinetic evidence. Moreover it is not necessary that the slow stage be the same under all experimental conditions.

The measured first-order rate constants for the formation of a series of substituted tetrahydrocarbazoles in acetic acid are as follows



R	R′	[Hydrazone]	Temp.	10^5k_1 (sec.$^{-1}$)	R	R′	[Hydrazone]	Temp.	10^5k_1 (sec.$^{-1}$)
H	H	0·024	35·0°	2·62	H	H	0·089	35·0°	2·81
,,	,,	0·031	,,	2·80	,,	,,	0·188	,,	2·81 [a]

R	R′	[Hydrazone]	Temp.	10^5k_1 (sec.$^{-1}$)	$k_{(2)}$	$k_{(6)}$	R	R′	[Hydrazone]	Temp.	10^5k_1 (sec.$^{-1}$)
H	H	0·033	40·9°	4·59	2·30	2·30	H	*p*-MeO	0·033	40·0°	—
4-Me	,,	,,	,,	4·41	2·20	2·20	,,	*p*-Me	,,	,,	36·8
3-Me	,,	,,	,,	3·30	—	3·30	,,	H	,,	,,	4·07
2-Me	,,	,,	,,	40·8	36·4 [b]	4·4	,,	*o*-Me	,,	,,	7·67

[a] Value interpolated from Pausacker and Schubert's data (*J.*, 1950, 1814) is 2·58. [b] This product is tetrahydro-11-methylcarbazolenine.

$k_{(2)}$ and $k_{(6)}$ are the partial rate constants for position 2 and 6, respectively.

The ring-closure of 2-methyl*cyclo*hexanone phenylhydrazone in acetic acid as solvent gives largely tetrahydro-11-methylcarbazolenine, whilst with aqueous sulphuric acid there is about twice as much 1 : 2 : 3 : 4-tetrahydro-1-methylcarbazole as of this basic product. These results support those of Pausacker (*J.*, 1950, 621) which suggest that the ratio of possible products varies with the solvent. The heterogeneous nature of the reactions in

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aqueous sulphuric acid would not affect this conclusion if, as is probable, both reaction sequences have protonation as a common origin.

Experimental.—The kinetic measurements were made by dilatometric methods, tapless dilatometers (Benford and Ingold, *J.*, 1938, 925) being used, and ammonia estimations by the standard micro-Kjeldahl method (Pausacker and Schubert, *J.*, 1950, 1814). In view of the uncertainties attached to the former method, it was frequently checked by the second at one or more points. Generally the two methods agreed and the value determined from the dilatometric estimation (Guggenheim, *Phil. Mag.*, 1926, 538) was preferred. The extent of the reaction was also determined in many cases, the values lying between 60 and 80% of the theoretical.

Ring closure of the 2-methyl*cyclo*hexanone phenylhydrazone in aqueous sulphuric acid was by Pausacker's method (*J.*, 1950, 623). The yields of 1 : 2 : 3 : 4-tetrahydro-1-methylcarbazole and tetrahydro-11-methylcarbazolenine were 50% and 28%, respectively; the values for the experiment in acetic acid were 7% and 61% of the theoretical.

The ring-closure of the 3-methyl*cyclo*hexanone derivative, which could give rise to two products, was also examined. The product, removed by distillation in steam, was mainly 1 : 2 : 3 : 4-tetrahydro-2-methylcarbazole. A small quantity of an unidentified product was obtained, which was not a carbazole. This confirms Barclay and Campbell's findings (*J.*, 1945, 530).

Acetic acid (B.D.H. AnalaR grade) was refluxed (2 hr.) with chromium trioxide (1%by wt.), and then distilled. The fraction, b. p. 117—118°, was cooled to 15° (20 min.), the liquid decanted, and the solid retained for use.

The methyl*cyclo*hexanones (Glaxo Ltd.) were dried ($MgSO_4$) and distilled. Phenylhydrazones, prepared by standard methods, were recrystallised from aqueous ethanol, dried under reduced pressure, and stored under nitrogen. M. p.s agreed with those of the literature to within 2°, except for *cyclo*hexanone *p*-methoxyphenylhydrazone which was not obtained pure.

THE UNIVERSITY, GLASGOW. [*Received, February 7th,* 1955.]

The Hydrolysis of Acetamide and Acethydrazide in Hydrochloric Acid of Various Concentrations.

By J. T. EDWARD, H. P. HUTCHISON, and S. C. R. MEACOCK.

[Reprint Order No. 6147.]

IN connection with a problem in protein chemistry, the stability of acethydrazide to hydrochloric acid at 61° has been compared with that of acetamide. The hydrolysis of both compounds in excess of acid followed first-order kinetics. The hydrazide was hydrolyzed more slowly than the amide in acid weaker than about 2·5N but more rapidly in stronger acid (see Table).

The greater stability of acethydrazide in weak acid probably comes in part from the fact that it exists in the protonated form, $Ac{\cdot}NH{\cdot}NH_3^+$ (Lindgren and Niemann, *J. Amer. Chem. Soc.*, 1949, **71**, 1504), the positive charge of which repels hydrogen ions and so protects the compound from acid-catalysed hydrolysis (cf. Butterworth, Eley, and Stone, *Biochem. J.*, 1953, **53**, 30). As the ionic strength increases, this effect operates less strongly (La Mer, *Chem. Rev.*, 1932, **10**, 179).

First-order rate constants for the hydrolysis of acethydrazide (H) *and acetamide* (A) *in hydrochloric acid.*

Normality of acid	1·0	1·5	2·0	2·5	3·0	3·5	4·0	5·0	7·0	8·0
H : 10^2k (min.$^{-1}$)	0·49	1·08	1·53 [a]	2·62 [b]	2·69 [a]	—	—	—	6·5	—
A : 10^2k (min.$^{-1}$)	1·27 [c]	1·66	—	2·20	2·30	2·11	1·91 [d]	1·71	—	— [e]

[a] Mean of two determinations. [b] Mean of three determinations.

Interpolation of Arrhenius plots of Rabinovitch and Winkler's results (*Canad. J. Res.*, 1942, **20**, *B*, 73) gives [c] $k = 1{\cdot}32 \times 10^{-2}$ min.$^{-1}$; in the same way, [d] $k = 1{\cdot}90 \times 10^{-2}$ min.$^{-1}$, and [e] $k = 0{\cdot}52 \times 10^{-2}$ min.$^{-1}$.

The maximum rate for the hydrolysis of acetamide at 61° was found in about 3N-hydrochloric acid, the concentration found previously for maximum rates at 50° (Taylor, *J.*, 1930, 2741) and 25° (Krieble and Holst, *J. Amer. Chem. Soc.*, 1938, **60**, 2976; Taylor, *loc. cit.*).

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Experimental.—*Materials.* Acetamide was recrystallized from acetone to a constant m. p. of 82°, and acethydrazide (Curtius and Hofmann, *J. prakt. Chem.*, 1896, **53**, 524) from chloroform to a constant m. p. of 67°.

Analytical method for acethydrazide. This was based on the blue complex formed between cupric ion and hydrazides (Aggarwal, Darbari, and Rây, *J.*, 1929, 1941; Fallab and Erlenmeyer, *Helv. Chim. Acta*, 1953, **26**, 6). The blue colour given by acethydrazide in 0·5M-cupric nitrate was measured in a Lange colorimeter against the cupric nitrate solution as a blank, using a white-light source. Beer's law was obeyed for concentrations of acethydrazide up to 0·031M. When the cupric nitrate was 0·5N with respect to hydrochloric acid, hydrazine or acetic acid in concentrations up to 0·036M did not interfere with the determinations.

Rate measurements. (*a*) Acethydrazide. Acethydrazide in a thin glass bulb was added to hydrochloric acid (50 ml.) in a stoppered flask in a thermostat at 61·0° ± 0·2°. The mixture was stirred vigorously to break the bulb and cause the acethydrazide to dissolve. At intervals samples (*ca.* 6 ml.) were withdrawn and cooled rapidly. To an aliquot part (5 ml.), standard sodium hydroxide solution was added to bring the acid strength down to 0·5N; 0·5M-cupric nitrate in 0·5N-hydrochloric acid (30 ml.) was added, and sufficient 0·5N-hydrochloric acid to give a final volume of 70 ml. The optical densities were measured and the concentrations of acethydrazide calculated by reference to an empirical calibration curve. Two individual runs are illustrated:

In N-hydrochloric acid; acethydrazide 0·366M.

Time (min.)	9	21	40	74	98	121
Hydrolysis (%)	2·2	5·5	15·1	27·7	36·9	56·6

$k = 0{\cdot}49 \times 10^{-2}$ min.$^{-1}$.

In 2N-hydrochloric acid; acethydrazide 0·405M.

Time (min.)	5	19	32	44	56
Hydrolysis (%)	8·7	27·3	40·0	49·0	58·0

$k = 1{\cdot}54 \times 10^{-2}$ min.$^{-1}$.

(*b*) Acetamide. The same procedure was followed as for acethydrazide, the hydrolysis being followed by formol titration (Northrop, *J. Gen. Physiol*, 1926, **9**, 767) of the ammonia produced.

We are grateful to Professor W. Cocker for his constant encouragement, and one of us (S. C. R. M.) thanks the government of the Republic of Ireland and the Medical Research Council of Ireland for maintenance grants.

Chemical Laboratory, Trinity College, Dublin. [*Received, February 17th*, 1955.]

The Preparation of [^{14}C]*Ethylenediamine Dihydrochloride from* [1-^{14}C]*Ethanol.*

By D. S. Popplewell and R. G. Wilkins.

[Reprint Order No. 6179.]

For exchange studies of metal–ethylenediamine complexes, it was necessary to synthesise [^{14}C]ethylenediamine dihydrochloride. A highly active product was not desired and so it was possible to avoid synthesis on a small carrier-free scale with its attendent difficulties (Thomas and Turner, *Quart. Rev.*, 1953, **7**, 408).

Diluted [1-^{14}C]ethanol was catalytically dehydrated and [^{14}C]ethylene, obtained in 75—80% yields, absorbed in bromine to form 1 : 2-dibromo[^{14}C]ethane. Dehydration by any of the chemical methods (*e.g.*, hot syrupy phosphoric acid) gave poor yields (cf. Fries and Calvin, *J. Amer. Chem. Soc.*, 1948, **70**, 2235). [^{14}C]Ethylenediamine dihydrochloride was obtained from 1 : 2-dibromo[^{14}C]ethane by a modified Gabriel synthesis in hot *NN*-dimethylformamide (Sheehan and Bolhofer, *J. Amer. Chem. Soc.*, 1950, **72**, 2786) followed by the usual hydrazine hydrate treatment (Ing and Manske, *J.*, 1926, 2348). The use of the solvent in the formation of 1 : 2-diphthalimidoethane gave higher yields (80—85%)

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than the usual method (*e.g.*, Putochim, *Chem. Abs.*, 1930, **24**, 3756, reported 60%). The yield for the complete conversion averaged 50—55%.

[$^{14}C_2$]Ethylene has previously been obtained in excellent yields on a microscale by reduction of [$^{14}C_2$]acetylene (Arrol and Glascock, *J.*, 1949, 5335; Yattargolis, Klimenok, and Golsvina, *Doklady Akad. Nauk S.S.S.R.*, 1952, **86**, 313; Cox and Warne, *J.*, 1951, 1893).

Experimental.—1 : 2-*Dibromo*[^{14}C]*ethane.* [1-^{14}C]Ethanol (0·1 mc; 2·3 mg.; supplied by Radiochemical Centre, Amersham) was mixed thoroughly with dried redistilled inactive ethanol (2·86 g.) and heated gently in a 15-c.c. round-bottomed flask connected by a side-arm to a tube, 17″ long, packed with dried activated alumina (Type H, 100—200 mesh; Peter Spence and Sons Ltd.) and heated electrically at 360—400°. The emerging gas containing [^{14}C]ethylene passed into an absorption vessel containing bromine (12 g.) and fitted with a bubble-spiral so as to ensure good contact between the rising gas and the bromine. The time taken to evaporate the ethanol was about 150 min. and after this a slow stream of nitrogen was passed through the apparatus for about 5 min. The product in the absorption vessel was shaken thoroughly with several portions of 2N-sodium hydroxide until the latter no longer showed a red colour. 1 : 2-Dibromo[^{14}C]ethane remained (8·8 g.) and was dried and used in the next stage.

1 : 2-*Diphthalimido*[^{14}C]*ethane.* 1 : 2-Dibromo[^{14}C]ethane (8·3 g.), recrystallised potassium phthalimide (20 g.), and dimethylformamide (90 c.c.) were heated on a steam-bath for 4 hr. with occasional swirling. The bulk of the solvent was removed and the residue cooled in ice. The solid was filtered off and washed well with water, leaving an almost white solid (7·45 g.; m. p. 228—232°). A further amount of less pure product (4·3 g.; m. p. 195—215°) was obtained on concentration of the filtrate. The combined amount was boiled with carbon disulphide to extract any 2-bromo-1-phthalimidoethane and the residue (11·7 g.) used in the next stage. A small amount, recrystallised from absolute alcohol, had m. p. 233° (Found: C, 67·5; H, 3·7; N, 8·4. Calc. for $C_{18}H_{12}O_4N_2$: C, 67·7; H, 3·7; N, 8·8%). 1 : 2-Diphthalimidoethane prepared from ethylenediamine and phthalic anhydride (Wanag, *Ber.*, 1942, **75**, 719), had m. p. 233° alone or mixed with above product.

[^{14}C]*Ethylenediamine dihydrochloride.* Crude 1 : 2-diphthalimido[^{14}C]ethane (11·7 g.), suspended in absolute alcohol (300 c.c.), was treated with a slight excess of hydrazine hydrate (3·3 g.), and the suspension gently refluxed. After about 45 min. a clear solution was obtained and after a further 15 min. a white flocculent precipitate suddenly appeared in large amount. Heating was continued for a further 2—3 hr. The alcohol was evaporated, and the residual solid heated at about 100° for 15 min. under reduced pressure to remove any excess of hydrazine, and then refluxed with hydrochloric acid (1 : 1; 100 c.c.) for a further 3 hr. The acid was removed by heat under reduced pressure. The buff-coloured residue was lixiviated with small amounts of ice-cold water, the extract was evaporated to dryness, and the residue (4·9 g.) washed with a little hot absolute alcohol and recrystallised from concentrated hydrochloric acid (yield, 4·3 g.) (Found: C, 18·9; H, 7·65; Cl, 53·7. Calc. for $C_2H_{10}N_2Cl_2$: C, 18·1; H, 7·5; Cl, 53·4%). The picrate had m. p. and mixed m. p. 233°.

Radiochemical yield. Weighed amounts of the diluted [^{14}C]ethanol and [^{14}C]ethylenediamine dihydrochloride were separately quantitatively oxidised to [^{14}C]carbon dioxide by the Van Slyke–Folch combustion fluid (*J. Biol. Chem.*, 1940, **136**, 509). The evolved gas was collected in a small volume of carbon dioxide-free 2N-sodium hydroxide and converted into barium [^{14}C]-carbonate, weighed amounts of which were mounted on filter paper discs and their activity was measured. Standard counting equipment was used in conjunction with an end-window Geiger–Müller counter. Activities were reduced to those for an "infinitely thin" sample in the usual way (Cook and Duncan, "Modern Radiochemical Practice," Oxford Univ. Press, 1952, p. 234). It was found that under identical conditions the [^{14}C]barium carbonate activity was (from [^{14}C]-ethanol) 1·89 × 10^5 counts min.$^{-1}$ mmole^{-1} and (from [^{14}C]ethylenediamine dihydrochloride) 1·87 × 10^5, indicating that the overall radiochemical yield was the same as the chemical one, namely 52%.

One of the authors (D. S. P.) thanks the Department of Scientific and Industrial Research for a Maintenance Grant. The authors thank Dr. D. T. Elmore for helpful advice and are very grateful to Dr. B. A. Fry (of the Microbiological Department) for carrying out the determination of the radiochemical yield.

THE UNIVERSITY, SHEFFIELD, 10.

[*Received, February 28th*, 1955.]

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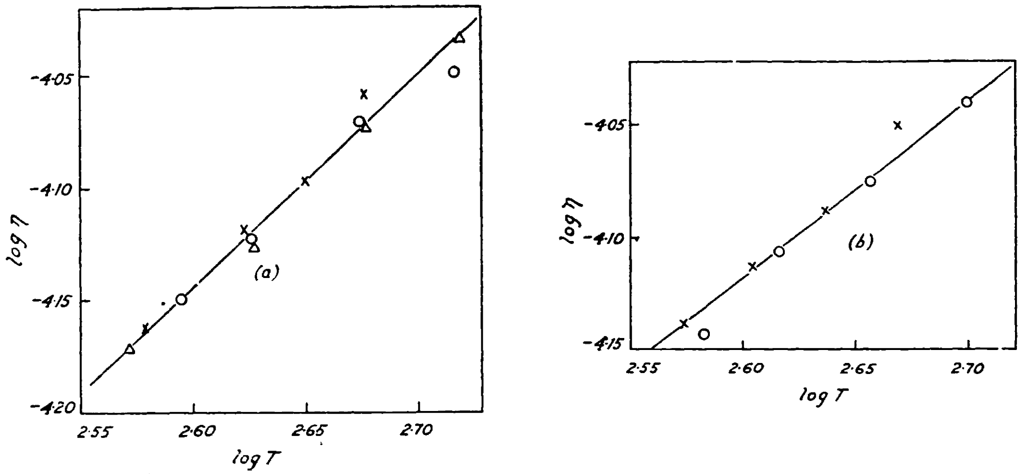
The Viscosity of the Vapours of n-*Octane and* 2 : 2 : 4-*Trimethylpentane.*

By G. A. McD. Cummings and J. C. McCoubrey.

[Reprint Order No. 6187.]

McCoubrey, McCrea, and Ubbelohde have reported (*J.*, **1951**, 1961) measurements of the viscosity of a number of hydrocarbon vapours. The importance of the viscosity of C_8 isomers in fuel problems has prompted us to make fresh measurements on *n*-octane and 2 : 2 : 4-trimethylpentane, higher vapour pressures being used in the same apparatus in an attempt to obtain more accurate data for the viscosity of these vapours. The new data are combined with those already available (McCoubrey *et al.*, *loc. cit.*; Melaven and Mack, *J. Amer. Chem. Soc.*, 1932, **54**, 888) to obtain the best values.



(*a*) n-*Octane.* (*b*) 2 : 2 : 4-*Trimethylpentane.*

△ Melaven and Mack. × McCoubrey, McCrea, and Ubbelohde. ○ This work.

The combined measurements over the whole range of temperatures have been correlated by the following equations :

(1) log $\eta = s \log T + c$ with a standard deviation Δ, where η is the viscosity in c.g.s. units, T is the temperature in °K, and s and c are constants.

(2) $$\eta = 0{\cdot}086\rho\bar{c}/NA\ (1 + C/T)$$

where ρ is the density, $\bar{c}$ is the root-mean-square velocity, C is Sutherland's constant, and A is Sutherland's collision area in Å^2 (Chapman and Cowling, " Mathematical Theory of Non-uniform Gases," Cambridge Univ. Press, 1939).

(3) $$\eta = 266{\cdot}93(MT)(r_0)^{-2}\ V/W(2)$$

where M is the molecular weight, r_0 is the low-velocity collision diameter of the Lennard-Jones intermolecular potential

$$E(r) = 4\varepsilon[(r_0/r)^{12} - (r_0/r)^6]$$

and V and $W(2)$ are tabulated functions of ε, the depth of the potential well (Hirschfelder, Curtiss, and Bird, " Molecular Theory of Gases and Liquids," John Wiley, New York, 1954).

Values of the constants for the above equations obtained from calculated lines of closest fit are given in the Table. The Figures show the scatter of individual points from different experimental sources in the case of the log η–log T plots.

	n-Octane	2 : 2 : 4-Trimethylpentane		*n*-Octane	2 : 2 : 4-Trimethylpentane
s	0·944	0·915	A (Å^2) ...	31·5	31·6
c	−6·599	−6·501	ε/k	337	279
Δ	0·002	0·004	r_0 (Å)	7·38	7·48
C	376	342			

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No significant alteration in the conclusions drawn in the previous paper (McCoubrey *et al., loc. cit.*) is necessitated by the new measurements.

The authors thank Professor A. R. Ubbelohde for permission to publish these results obtained in his laboratory, and for advice on the problem.

QUEEN'S UNIVERSITY, BELFAST. [*Received, March 2nd,* 1955.]

Collision Diameters of Flexible Hydrocarbon Molecules in the Vapour Phase.

By G. A. McD. CUMMINGS and A. R. UBBELOHDE.

[Reprint Order No. 6188.]

THE diffusion coefficients of hydrocarbon molecules reported in a previous paper (*J.*, 1953, 3751) should have been multiplied by a factor 760/(atmospheric pressure in mm. Hg). With the various pressures prevailing during the experiments, this correction factor ranges from 0·97 to 1·03. Calculated collision diameters need correction by factors ranging from 0·985 to 1·015. Whilst this does not alter the conclusions previously reported, the corrected values may be of use in other connections. These are as given below; opportunity has been taken to include fresh experimental results for the values marked with an asterisk.

Compound	Carrier gas	Temp. (°K)	D_{760} (cm.²/sec.)	Compound	Carrier gas	Temp. (°K)	D_{760} (cm.²/sec.)
n-Hexane	H_2	288·7	0·288	*n*-Octane	H_2	*303·2	0·277
	N_2	288·6	0·0753		N_2	*303·1	0·0726
	O_2	288·6	0·0754		O_2	303·1	0·0687
	A	288·6	0·0662		A	303·0	0·0626
2 : 3-Dimethylbutane	H_2	288·8	0·299	2 : 2 : 4-Trimethylpentane	H_2	*303·1	0·292
	N_2	288·7	0·299		N_2	*303·1	0·0713
	O_2	288·4	0·0742		O_2	303·0	0·0672
	A	288·9	0·0652		A	303·0	0·0605
*cyclo*Hexane	H_2	288·5	0·319	*n*-Decane	H_2	363·8	0·293
	N_2	288·6	0·0746		N_2	*363·9	0·0763
	O_2	288·6	0·0731	2 : 3 : 3-Trimethylheptane	H_2	363·9	0·271
	A	288·7	0·0721		N_2	363·8	0·0681
Methyl*cyclo*pentane	H_2	288·5	0·312	*n*-Dodecane	H_2	399·6	0·311
	N_2	285·9	0·0758		N_2	399·4	0·0829
	O_2	287·1	0·0744				
	A	288·6	0·0715				

Apparent collision diameters of hydrocarbons (σ_2).

Carrier : Compound	H_2	N_2	$\Delta(\sigma_{H_2} - \sigma_{N_2})$	O_2	A
n-Hexane	6·78	6·51	+0·27	6·39	6·59
2 : 3-Dimethylbutane	6·60	6·53	+0·07	6·43	6·67
*cyclo*Hexane	6·30	6·58	−0·28	6·52	6·20
Methyl*cyclo*pentane	6·40	6·42	−0·02	6·46	6·18
n-Octane	7·31	6·94	+0·37	7·01	7·02
2 : 2 : 4-Trimethylpentane	7·05	7·02	+0·03	7·14	7·21
n-Decane	8·46	8·08	+0·38	—	—
2 : 3 : 3-Trimethylheptane	8·91	8·75	+0·16	—	—
n-Dodecane	8·91	8·37	+0·54	—	—

As pointed out in other publications, large " hydrogen effects " appear to be associated with molecular flexibility. In this connection, the rôle of ethylene is at present a matter for controversy, since diffusion diameters determined by different experimental techniques (Trautz and Müller, *Ann. Physik*, 1935, **22**, 350, 371; Boyd, Stein, Steingrimsson, and Rumpel, *J. Chem. Phys.*, 1951, **19**, 548) do not agree (see Table). On the other hand, the

Collision diameters for ethylene calculated from observed mass-diffusion experiments.

Carrier gas	Trautz and Müller	Boyd *et al.*
H_2	4·80	4·12
N_2	3·67	4·18
(H_2 − N_2)	+1·13	−0·06

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theoretical expectations for ethylene are not yet fully worked out. Hydrogen is markedly more efficient than nitrogen for promoting the transfer from translational to vibrational energy in collisions with ethylene. The number of collisions $Z_{\text{eff.}}$ for one act of transfer for hydrogen = 250, $Z_{\text{eff.}}$ for nitrogen >3500 (Richards and Reid, *J. Chem. Phys.*, 1934, **2**, 206; McGrath and Ubbelohde, *Proc. Roy. Soc.*, 1954, **227**, *A*, 1). However, for molecular encounters to show " roughness " in the Pidduck sense, thus affecting collision parameters for momentum or mass transfer, it seems probable that $Z_{\text{eff.}}$ must be still smaller than either of the above values. There should be no appreciable difference between the diffusion diameters of ethylene mixed with hydrogen or nitrogen if this expectation is correct. Further experiments on the mass diffusion of ethylene are required to clear up this point definitely.

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[*Received, March 2nd*, 1955.]

Syntheses of 8-Substituted Quinolines with Amide Groups in the Side Chain.

By M. Neeman.

[Reprint Order No. 6189.]

A number of new derivatives of 8-amino-6-methoxyquinoline with side chains containing amide groups attached to the 8 position (types I and II) have been prepared. In comparison with pamaquin, the secondary and the tertiary nitrogen atom of the side chain have

(I) Q·NH·CO·CRR'·NEt$_2$ Q·NH·CRR'·[CH$_2$]$_n$·CO·NEt$_2$ (II)

R$_1$, R$_2$ = alkyl or H; Q = 6-methoxy-8-quinolyl; n = 0—2.

severally been acylated. The substances of type (I) were prepared from 8-amino-6-methoxyquinoline by treatment with α-halogenoacyl halides and subsequently with diethylamine, and compounds of type (II) by condensing the diethylamides of α-, β-, or γ-halogeno-acids with 8-amino-6-methoxyquinoline at 100°. In these syntheses, the yields ranged from 50 to 70%.

Biological tests on a number of such compounds have been reported (Wiselogle, " A Survey of Antimalarial Drugs," J. W. Edwards, Ann Arbor, Mich., 1946; Coatney, Cooper, Eddy, and Greenberg, " Survey of Antimalarial Agents," Public Health Monograph No. 9, Federal Security Agency, U.S. Public Health Service, 1953). Our substances show toxicities of the order of that of quinine, and low or negligible antiplasmodial activity. *NN*-Diethyl-γ-(6-methoxy-8-quinolylamino)valeramide (II; R = H, R' = Me, n = 2) had a quinine equivalent of 0·2 in a suppressive test on ducks infected with *Plasmodium lophurae* (Wiselogle, *op. cit.*, SN 5883): *N*-acetylpamaquin (SN 12,448) also has a lower toxicity than pamaquin, and negligible antiplasmodial activity.

Experimental.—8-(α-Halogenoacylamido)-6-methoxyquinolines were prepared by the action of α-halogenoacyl chlorides or bromides (1 equiv.) on 8-amino-6-methoxyquinoline (1 equiv.) in chloroform with cooling. The hydrohalides of the products were precipitated as yellow to reddish-brown substances and were either recrystallised as such or converted into the corresponding bases.

8-Chloroacetamido-6-methoxyquinoline crystallised as white needles (from ethanol or ligroin), m. p. 112° (U.S.P. 2,494,083 reported m. p. 110—111°).

8-α-*Bromopropionamido*-6-*methoxyquinoline monohydrobromide*, crystallised from 30% aqueous hydrobromic acid, had m. p. 180° (Found: N, 7·0. $C_{13}H_{13}O_2N_2Br,HBr$ requires N, 7·2%).

8-α-*Bromo*-β-*methylbutyramido*-6-*methoxyquinoline* crystallised from ethanol as white needles, m. p. 104° (Found: C, 53·5; H, 5·2. $C_{15}H_{17}O_2N_2Br$ requires C, 53·4; H, 5·1%). The *monohydrobromide* crystallised from 30% aqueous hydrobromic acid as yellow needles, m. p. 185° (Found: C, 43·5; H, 4·3; N, 6·7. $C_{15}H_{17}O_2N_2Br,HBr$ requires C, 43·1; H, 4·3; N, 6·7%).

8-(α-*NN*-Diethylaminoacylamido)-6-methoxyquinolines (I) were prepared by refluxing the

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corresponding 8-α-halogenoacylamido-6-methoxyquinolines with excess of diethylamine for 20—48 hr. Excess of amine was distilled off, and the residue was treated with aqueous sodium hydroxide, extracted with ether, and distilled under reduced pressure. Thus were obtained: 8-(α-*NN*-Diethylaminoacetamido)-6-methoxyquinoline (I; R = R′ = H), a yellow oil, b. p. 200—215°/1 mm. (U.S.P. 2,494,083 reported b. p. 260—263/35 mm.), n_D^{25} 1·5852 [the *dihydrochloride*, precipitated from acetone by concentrated aqueous hydrochloric acid, crystallised from ethanolic hydrochloric acid as brown needles, m. p. 214—216° (Found: C, 53·4; H, 6·3. $C_{16}H_{21}O_2N_3$,2HCl requires C, 53·3; H, 6·4%)]. 8-(α-NN-*Diethylamino*-β-*methylbutyramido*)-6-*methoxyquinoline* (I; R = H, R′ = Pr^i), white needles, m. p. 262° (decomp.) (Found: C, 69·6; H, 8·2; N, 12·5. $C_{19}H_{27}O_2N_3$ requires C, 69·3; H, 8·3; N, 12·75%).

The compounds (II) were prepared by the action of the diethylamides of the appropriate α-, β-, or γ-halogeno-acids in slight excess on 8-amino-6-methoxyquinoline at 100°, for 3—30 hr. and crystallised directly from the corresponding aqueous hydrohalogen acid or were isolated as base.

The required diethylamides were prepared at −5° by the action of α-, β-, or γ-halogenoacyl chlorides or bromides in dry ether on 2 equivs. of diethylamine. After 3 hr., the diethylamine hydrochloride was filtered off, and the filtrate freed from solvent and distilled under reduced pressure, yielding *NN*-diethyl-α-chloroacetamide, b. p. 133°/30 mm. (Jacobs and Heidelberger, *J. Biol. Chem.*, **1915**, **21**, 145, reported b. p. 126·5—128·5°/21 mm.; Hahn and Loos, *Ber.*, 1918, **51**, 1436, reported b. p. 190—195°/25 mm.), n_D^{21} 1·4690 (Found: Cl, 23·4. Calc. for $C_6H_{12}ONCl$: Cl, 23·7%), -β-*chloropropionamide*, b. p. 92°/2 mm., n_D^{16} 1·4698, d^{15} 1·0451, $[M_R]_D$ 43·69 (calc., 43·34) (Found: Cl, 22·0. $C_7H_{14}ONCl$ requires Cl, 21·7%), and -α-*bromo*-α-*methylpropionamide*, b. p. 86°/2·5 mm., n_D^{12} 1·4878, d^{13} 1·255, $[M_R]_D$ 50·95 (calc., 50·86) (Found: Br, 35·7. $C_8H_{16}ONBr$ requires Br, 36·0%).

NN-*Diethyl*-γ-*chlorovaleramide*. *NN*-Diethylævulamide was reduced by aluminium *iso*propoxide in propan-2-ol (Haskelberg, *J. Amer. Chem. Soc.*, 1948, **70**, 2830), and the product was treated with thionyl chloride in benzene. After 1 hour's refluxing, excess of thionyl chloride and solvent was removed. The product distilled as a colourless oil, b. p. 94°/2 mm. (Wohlgemuth, *Ann. Chim.*, 1914, **2**, 302, reported b. p. 139—140°/17 mm.) (Found: C, 56·0; H, 9·3. Calc. for $C_9H_{18}ONCl$: C, 56·4; H, 9·5%).

NN-*Diethyl*-α-(6-*methoxy*-8-*quinolylamino*)*acetamide dihydrochloride* (II; R = R′ = H, *n* = 0), crystallised from dilute aqueous hydrochloric acid, had m. p. 230° (decomp.) (Found: C, 53·3; H, 6·0. $C_{16}H_{21}O_2N_3$,2HCl requires C, 53·3; H, 6·4%). The base was obtained as white crystals, m. p. 228° (U.S.P. 2,456,911 reported b. p. 175—180°/48 mm.). The *monopicrate* crystallised from ethanol as dark yellow crystals, m. p. 198° (Found: N, 16·2. $C_{16}H_{21}O_2N_3$,$C_6H_3O_7N_3$ requires N, 16·3%).

NN-*Diethyl*-α-(6-*methoxy*-8-*quinolylamino*)*propionamide* (II; R = Me, R′ = H, *n* = 0) crystallised as white needles (from butanol), m. p. 202° (Found: N, 13·6. $C_{17}H_{23}O_2N_3$ requires N, 13·9%). The *dihydrochloride* crystallised in orange crystals (from aqueous-ethanolic hydrochloric acid), m. p. 217° (Found: C, 54·8; H, 6·5. $C_{17}H_{23}O_2N_3$,2HCl requires C, 54·55; H, 6·7%).

NN-Diethyl-β-(6-methoxy-8-quinolylamino)propionamide (II; R = R′ = H, *n* = 1), b. p. 250°/2 mm., yielded the *dihydrochloride* by precipitation from a solution in ethyl acetate by ethanolic hydrochloric acid and recrystallisation from water as orange crystals, m. p. 230° (Found: C, 54·5; H, 6·5%).

NN-Diethyl-α-(6-methoxy-8-quinolylamino)-α-methylpropionamide (II; R = R′ = Me, *n* = 0) crystallised in colourless hexagonal plates (from benzene), m. p. 220°. The *monohydrochloride* crystallised as brown needles (from dilute aqueous hydrochloric acid), m. p. 244° (decomp.) (Found: N, 12·2. $C_{18}H_{25}O_2N_3$,HCl requires N, 11·9%).

NN-*Diethyl*-γ-(6-*methoxy*-8-*quinolylamino*)*valeramide* (II; R = Me, R′ = H, *n* = 2) distilled as a yellow viscous oil, b. p. 225—230°/0·06 mm., 160°/0·01 mm., which crystallised from light petroleum as yellow needles, m. p. 79° (Found: C, 68·9; H, 7·9; N, 13·0. $C_{19}H_{27}O_2N_3$ requires C, 69·3; H, 8·3; N, 12·75%). The *hydrochloride* prepared from the base by addition of aqueous hydrochloric acid recrystallised from water formed a hydrate, m. p. 128°, which lost water at 100°/30 mm. over phosphoric oxide. The resulting salt had m. p. 167° (Found: C, 62·5; H, 8·0. $C_{19}H_{27}O_2N_3$,HCl requires C, 62·4; H, 7·7%).

The author expresses his gratitude to the late Dr. L. Haskelberg of the Daniel Sieff Research Institute, Rehovoth, for his advice and help.

RESEARCH COUNCIL OF ISRAEL, JERUSALEM. [*Received, March 2nd*, 1955.]

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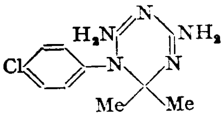
1 : 2-*Dihydro*-2 : 2-*dimethylquinazolines. The Condensation of Acetone with Anthranilamide Derivatives.*

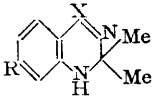
By H. C. Carrington.

[Reprint Order No. 6227.]

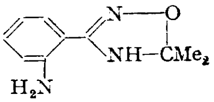
In connexion with the active metabolite (I) of the antimalarial drug Paludrine (see Carrington, Crowther, and Stacey, *J.*, 1954, 1017), dihydroquinazolines (II; $X = NH_2$), also containing the unit $Ar{\cdot}N{\cdot}CMe_2{\cdot}N{:}C{\cdot}NH_2$ have been prepared for the first time. They



(I)



(II)



(III)

are readily obtained by condensing *o*-aminobenzamidines with acetone in acid aqueous solution. Similarly anthranilamide and acetone give 1 : 2-dihydro-4-hydroxy-2 : 2-dimethylquinazoline (II; $R = H$, $X = OH$) (alternatively formulated as 1 : 2 : 3 : 4-tetrahydro-2 : 2-dimethyl-4-oxoquinazoline). The corresponding thioamide gives the 4-thiol (II; $R = H$, $X = SH$). The relation between these compounds is demonstrated by the following reactions. The compound (II; $R = H$, $X = NH_2$) is converted by acid hydrolysis into the hydroxy-compound (II; $R = H$, $X = OH$). The thiol (II; $R = H$, $X = SH$) with methyl iodide gives the methylthio-derivative (II; $R = H$, $X = SMe$), which is converted by alcoholic ammonia into the amine (II; $R = H$, $X = NH_2$).

o-Aminobenzamidine was prepared from *o*-aminobenzonitrile by addition of hydroxylamine to give the amidoxime (Pinnow and Sämann, *Ber.*, 1896, **29**, 623) and reduction of this. The amidoxime does not react with acetone in a similar way to the other anthranilic acid derivatives, but behaves in the way common to amidoximes, giving the oxadiazole (III).

4-Amino-7-chloro-1 : 2-dihydro-2 : 2-dimethylquinazoline (II; $X = NH_2$, $R = Cl$) was similarly prepared. Neither it nor its parent showed antimalarial activity.

Experimental.—1 : 2-*Dihydro*-4-*mercapto*-2 : 2-*dimethylquinazoline.* A solution of 2-aminothiobenzamide (Reissert and Grube, *Ber.*, 1909, **42**, 3710) (1·52 g.) in 3·5% hydrochloric acid (20 c.c.) and acetone (20 c.c.) was heated under reflux on the steam-bath for 18 hr. The yellow crystalline solid which separated on cooling recrystallised from aqueous methanol, to give the *quinazoline derivative* (1·8 g.), m. p. 151—152° (Found: C, 62·4; H, 6·05; N, 14·5. $C_{10}H_{12}N_2S$ requires C, 62·6; H, 6·25; N, 14·6%).

1 : 2-*Dihydro*-2 : 2-*dimethyl*-4-*methylthioquinazoline.* 1 : 2-Dihydro-4-mercapto-2 : 2-dimethylquinazoline (2 g.) in ether (150 c.c.) was allowed to stand overnight with methyl iodide (2 c.c.). The gum which separated was extracted with water, and the extract was clarified and made alkaline to Brilliant-yellow with ammonia. The yellow precipitate was washed with water, dried, and crystallised from light petroleum (b. p. 40—60°), giving the *methylthio-derivative* (1 g.), m. p. 62—64° (Found: C, 64·4; H, 6·6; N, 13·8. $C_{11}H_{14}N_2S$ requires C, 64·1; H, 6·8; N, 13·6%).

o-*Aminobenzamidine.* *o*-Aminobenzamidoxime (8 g.) in ethanol was reduced by hydrogen in presence of Raney nickel at 65°/30 atm. for 5 hr. After cooling and removal of the catalyst the hydrochloride of the product was precipitated by dry hydrogen chloride. The crude product (4·6 g.), m. p. 236—242°, could not readily be purified, and was used directly for the next stage. The *picrate*, from an aqueous solution of the hydrochloride and picric acid and crystallised from ethanol, had m. p. 222—224° (Found: C, 43·0; H, 3·4; N, 22·2. $C_7H_9N_3,C_6H_3O_7N_3$ requires C, 42·9; H, 3·3; N, 22·0%).

4-*Amino*-1 : 2-*dihydro*-2 : 2-*dimethylquinazoline hydrochloride.* (*a*) *o*-Aminobenzamidine hydrochloride (8·5 g.), hydrochloric acid (*d* 1·18; 4·3 c.c.), acetone (50 c.c.), and water (100 c.c.) were heated under reflux for 15 hr. After evaporation to a small bulk under reduced pressure, the yellow solid was separated and crystallised from ethanol, to give the *quinazoline hydrochloride* (3·4 g.), m. p. 255—256° (Found: C, 56·6; H, 6·4; N, 19·3. $C_{10}H_{13}N_3,HCl$ requires C, 56·7; H, 6·6; N, 19·9%).

(*b*) 1 : 2-Dihydro-2 : 2-dimethyl-4-methylthioquinazoline (5 g.) was heated with saturated ethanolic ammonia (50 c.c.) at 150° for 6 hr. After evaporation, the residual oil was dissolved in

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ethanol (20 c.c.) and dry hydrogen chloride was passed into the solution until it was acid to Congo-red. Addition of ether precipitated the hydrochloride of the aminoquinazoline, which after crystallisation had m. p. 255—256° (1·9 g.) and was identical with that described under (*a*).

1 : 2-*Dihydro-4-hydroxy-2* : 2-*dimethylquinazoline*.—(*a*) Anthranilamide (2·7 g.), 3·5% hydrochloric acid (40 c.c.), and acetone (40 c.c.) were heated under reflux for 15 hr. The excess of acetone was removed under reduced pressure, the residual solution was cooled, and the solid crystallised from methanol, giving the *hydroxyquinazoline* as colourless plates, m. p. 262° (Found : C, 67·9; H, 6·8; N, 16·2. $C_{10}H_{12}ON_2$ requires C, 68·2; H, 6·8; N, 15·9%).

(*b*) 4-Amino-1 : 2-dihydro-2 : 2-dimethylquinazoline hydrochloride (5·0 g.) in 20% hydrochloric acid (50 c.c.) was heated under reflux for 4 hr. After cooling, the solution was made alkaline to Brilliant-yellow with ammonia, and the precipitated solid recrystallised from methanol; it had m. p. 262°, and was identical with the material described under (*a*).

3-o-*Aminophenyl-4* : 5-*dihydro-5* : 5-*dimethyl-1* : 2 : 4-*oxadiazole*. *o*-Aminobenzamidoxime (2 g.), acetone (25 c.c.), and water (50 c.c.) were heated under reflux for 24 hr. After evaporation under reduced pressure the oily residue was triturated with acetone, and the solid *product* recrystallised from acetone–ethanol–light petroleum (b. p. 40—60°). It had m. p. 214—216° (Found : C, 63·2; H, 6·8; N, 22·3. $C_{10}H_{13}ON_3$ requires C, 62·85; H, 6·8; N, 22·0%).

2-*Amino-4-chlorobenzamidoxime*. To a mixture of 2-amino-4-chlorobenzonitrile (13·8 g.) (McKee, McKee, and Bost, *J. Amer. Chem. Soc.*, 1947, **69**, 940) in ethanol (30 c.c.) and hydroxylamine hydrochloride (10 g.) in water (20 c.c.) was added a solution of sodium (3·6 g.) in ethanol (55 c.c.) and the whole was heated under reflux for 8 hr. The ethanol was removed under reduced pressure and the residue was made alkaline to Clayton-yellow with dilute aqueous sodium hydroxide. After thorough shaking, the mixture was filtered, the filtrate was neutralised with acetic acid and cooled, and the solid product was separated. The *amidoxime*, crystallised from aqueous ethanol, had m. p. 128—130° (10·2 g.) (Found : C, 45·2; H, 4·4; N, 22·8. $C_7H_8ON_3Cl$ requires C, 45·3; H, 4·3; N, 22·6%).

2-*Amino-4-chlorobenzamidine dihydrochloride*. 2-Amino-4-chlorobenzamidoxime (10 g.) in ethanol (10 c.c.) was hydrogenated as above. The *dihydrochloride*, crystallised from ethanol–light petroleum, had m. p. 280—281° (11 g.) (Found : C, 34·6; H, 4·3; N, 17·8. $C_7H_8N_3Cl,2HCl$ requires C, 34·6; H, 4·1; N, 17·3%).

4-*Amino-7-chloro-1* : 2-*dihydro-2* : 2-*dimethylquinazoline*. 2-Amino-4-chlorobenzamidine dihydrochloride (5 g.), acetone (30 c.c.) and water (60 c.c.) were heated under reflux for 24 hr. After evaporation under reduced pressure the residue was made just alkaline to Clayton-yellow with dilute aqueous alkali. The yellow precipitate crystallised from aqueous ethanol, giving the *quinazoline derivative*, m. p. 198—200° (4·1 g.) (Found : C, 56·9; H, 5·8; N, 19·9. $C_{10}H_{12}N_3Cl$ requires C, 57·1; H, 5·7; N, 20·0%).

I thank Mr. J. H. Sherwood for expert technical assistance.

IMPERIAL CHEMICAL (PHARMACEUTICALS) LTD., HEXAGON HOUSE,
BLACKLEY, MANCHESTER, 9.

[*Received, March 11th*, 1955.]

The Heat of Formation of Nickel Carbonyl.

By K. W. SYKES and S. C. TOWNSHEND.

[Reprint Order No. 6236.]

RECENT survey of the very discordant values so far obtained for the heat of formation of nickel carbonyl (Spice, Staveley, and Harrow, *J.*, 1955, 100) included the result of an indirect determination communicated privately by the Mond Nickel Company. A brief description of this work may be useful.

We measured the rate of formation of nickel carbonyl from carbon monoxide and nickel powder at a series of temperatures. The metal was prepared by reduction of the oxide in hydrogen and contained 0·022% of added sulphur, a known catalyst for the carbonyl reaction. A gas containing 95% of carbon monoxide was passed at 5 l. (760 mm.; 18°) per hour over nickel powder (7·86 g.) resulting in the following conversions :

Temp.	50°	104°	114°	125°	136°
Ni converted (g./hr.)	1·60	0·60	0·36	0·20	0·06

It was important to find out whether these figures represented rates of reaction or equilibrium concentrations. The only method available was to calculate $\Delta E_0{}^0$ as follows. A

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lower limit, C, for the equilibrium constant $K = p_{\mathrm{Ni(CO)_4}}/p_{\mathrm{CO}}{}^4$ was calculated from the expression $C = x(1{\cdot}053 - \frac{3}{4}x)^3/(1 - x)^4P^3$, where x is the fraction of carbon monoxide which has reacted and P is the total pressure (1 atm.). Free-energy functions $G^0 - E_0{}^0$ then available ("Selected Values of Chemical Thermodynamic Properties," Nat. Bur. Standards; Crawford and Cross, *J. Chem. Phys.*, 1938, **6**, 525) gave the following figures:

Temp.	50°	104°	114°	125°	136°
C (atm.$^{-3}$)	0·871	0·093	0·046	0·023	0·062
$\Delta(G^0 - E_0{}^0)/T$ (cal.)	91·81	92·90	93·09	93·27	93·41
$-\Delta E_0{}^0$ (kcal.)	29·57	33·25	33·66	34·13	34·08

The increase of the calculated energy of formation from 50° to 114° indicated that equilibrium, though not attained, was approached more closely as the temperature was raised; its constancy, within the experimental accuracy, at 125° and 136° suggested that equilibrium was effectively achieved at those temperatures. $\Delta E_0{}^0$ was thus estimated to be −34·1 kcal. and the corresponding standard heat of formation of gaseous nickel carbonyl to be given by ΔH^0 (298° K) = −36·5 kcal. for this system. Though the lower limit should be more reliable than the upper one because equilibrium was approached only from the carbon monoxide side, the probable error is thought to be ±0·8 kcal., owing chiefly to an uncertainty of 2% in the free-energy function for nickel carbonyl. The difference of 0·2 kcal. from Spice, Staveley, and Harrow's value (*loc. cit.*) arises from the fact that the inert gas in the carbon monoxide was not previously taken into account.

Experimental.—Nickel oxide (0·038% Fe, 0·004% S), prepared by oxidising in air at 750° nickel powder (particle size 9 μ) obtained by decomposition of the carbonyl, was mixed with 0·2% of powdered $NiSO_4,7H_2O$. 10 g. of the mixture, contained as a layer 5" long in a 13 mm. Pyrex tube, were reduced in hydrogen at 370°. Process gas (92% CO) was purified in a train consisting of a nickel tube at 220°, alkaline pyrogallol, potassium hydroxide, calcium chloride, and anhydrone; the product contained 95% of carbon monoxide, the remainder being nitrogen and hydrogen. This gas was passed over the reduced nickel powder at the specified temperature and the carbonyl determined by decomposition in a weighed nickel tube maintained at 220°.

UNIVERSITY COLLEGE OF SWANSEA, UNIVERSITY OF WALES.
THE MOND NICKEL COMPANY LIMITED, CLYDACH.

[*Received, March 14th*, 1955.]

The Direct Interaction of N-*Bromosuccinimide and Benzoyl Peroxide.*

By M. C. FORD.

[Reprint Order No. 6238.]

THE homolytic chain reaction first proposed by Bloomfield (*J.*, 1944, 118) as a mechanism for the allylic bromination of olefins with *N*-bromosuccinimide requires the initial presence of a small concentration of free succinimidyl radicals, $(C_4H_4O_2)N\cdot$, these being assumed to arise by thermal or photochemical dissociation of the bromo-imide. Karrer and Schmid (*Helv. Chim. Acta*, 1946, **29**, 573) showed that traces of benzoyl peroxide catalyse the reaction, it being now generally assumed that this effect is due to the much more efficient initial generation of succinimidyl radicals by a metathetic process:

$$(Ph{\cdot}CO_2)_2 \longrightarrow Ph\cdot + CO_2 + Ph{\cdot}CO_2\cdot \qquad (1)$$

$$(C_4H_4O_2)N{\cdot}Br + Ph\cdot \longrightarrow (C_4H_4O_2)N\cdot + Ph{\cdot}Br \qquad (2)$$

Although there seems to be no direct evidence for the above sequence of reactions in the case of benzoyl peroxide, the mechanism by which aliphatic azo-compounds, $RR'CX{\cdot}N{:}N{\cdot}CXRR'$ (R and R′ = alkyl, X = CN or CO_2Me), catalyse allylic bromination (Ford and Waters, *J.*, 1952, 2240) has been elucidated by independently showing that the radicals, $RR'CX\cdot$, derived from this class of compound were able to abstract the halogen from *N*-bromosuccinimide and other "positive" halogen compounds in a manner which is analogous to that postulated in equation (2) for phenyl radicals (Ford and Waters, *loc. cit.*; Ford, Hunt, and Waters, *J.*, 1953, 3529).

The present experiments were undertaken to demonstrate the occurrence of processes (1) and (2) by isolating the products formed in the reaction between equimolar quantities of *N*-bromosuccinimide and benzoyl peroxide; the use of a solvent was dispensed with, for no

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common solvent would remain unattacked. The controlled decomposition of an intimate mixture of the reactants at temperatures not exceeding 100° afforded bromobenzene (54%), succinimide (20%), benzoic acid (16%), and carbon dioxide, together with intractable material.

The isolation of bromobenzene shows that phenyl radicals do indeed abstract bromine from *N*-bromosuccinimide, and thus definitely establishes the nature of the initiation process in benzoyl peroxide catalysed allylic bromination. The conversion of succinimidyl and benzoyloxy-radicals into succinimide and benzoic acid is of some interest; no obvious hydrogen donor is present in the system, though it can be suggested that the $\cdot CH_2\cdot CO\cdot$ grouping, which is known to be susceptible to dehydrogenation by free radicals, might be responsible for the transformation of the radicals in question into stable products.

Experimental.—*N*-Bromosuccinimide and benzoyl peroxide were recrystallised samples, having purities (iodometric) of 98% and 99%, respectively.

A finely powdered mixture of the bromo-imide (1·78 g., 0·01 mole) and the peroxide (2·42 g., 0·01 mole) was contained in a 10-ml. long-necked distillation flask which was very slowly heated with a naked flame. After 1 hr. a slurry was formed from which carbon dioxide began to be evolved; the heating was then continued in such a way that after 30 min. a golden-yellow melt resulted. By keeping the mixture just molten, at 90—100°, a slow and steady evolution of gas was maintained, the reaction being complete (negative potassium iodide–starch test) after a further 1·5 hr. The mixture was very thoroughly stirred by hand throughout the whole operation, for local overheating, particularly at the outset, led to violent explosions.

Direct distillation of the product afforded bromobenzene (0·85 g., 54%), b. p. 70°/65 mm., characterised by conversion into *p*-bromonitrobenzene, m. p. and mixed m. p. 126°. The residue was dissolved in chloroform and repeatedly shaken with aqueous sodium hydrogen carbonate. Acidification of the combined aqueous extracts followed by isolation with ether gave a brown gum; sublimation at atmospheric pressure and crystallisation of the sublimate from light petroleum (b. p. 50—60°) afforded benzoic acid (0·2 g., 16%), m. p. and mixed m. p. 121°.

In another experiment the initial product, after trituration with light petroleum, was repeatedly extracted with 20-ml. portions of boiling carbon tetrachloride; the solid which separated on each occasion was washed with ether, and the combined material was recrystallised from benzene giving succinimide (0·2 g., 20%), m. p. and mixed m. p. 124°.

The University, Old Aberdeen. [*Received, March 15th*, 1955.]

6-*Methoxy*-2-*naphthaldehyde.*

By R. P. Gandhi, V. S. Gaind, and S. M. Mukherji.

[Reprint Order No. 6239.]

6-METHOXY-2-NAPHTHALDEHYDE has been prepared in 53% yield from 2-bromo-6-methoxynaphthalene. The method is an improvement on that of Horeau and Ormancy (*Compt. rend.*, 1953, **236**, 826).

Experimental.—The Grignard reagent from 2-bromo-6-methoxynaphthalene (28·4 g.; 0·12 mole) was activated by means of ethyl bromide and then cooled in ice, and ethyl orthoformate (29·6 g.; 0·2 mole) was added during 15 min. The ether was removed and the mixture refluxed for 5 hr., cooled, and decomposed with hydrochloric acid (15%; 150 c.c.). The organic layer was washed with water, and the solvent removed under reduced pressure. The residue was gently refluxed with hydrochloric acid (20%; 100 c.c.) for 10 hr., the organic layer separated, and the aqueous layer extracted with benzene. The combined organic layers were washed twice with water and dried (K_2CO_3), and the solvent removed. 6-Methoxy-2-naphthaldehyde distilled at 140—145°/5 mm. and was purified through the bisulphite compound. The aldehyde [12 g.; 53%; from light petroleum (b. p. 60—80°)] had m. p. 81—82° (Found: C, 77·2; H, 5·2. Calc. for $C_{12}H_{10}O_2$: C, 77·4; H, 5·4%). The *oxime* had m. p. 154—155° (Found: N, 7·2. $C_{12}H_{11}O_2N$ requires N, 7·0%), the *semicarbazone*, m. p. 215° (decomp.) (Found: N, 17·2. $C_{13}H_{13}O_2N_3$ requires N, 17·3%), and the 2 : 4-dinitrophenylhydrazone, m. p. 270—271° (Found: N, 15·0. $C_{18}H_{14}O_5N_4$ requires N, 15·3%).

Panjab University, Hoshiarpur, India. [*Received, March 15th*, 1955.]

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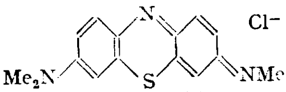
The Crystal Structure of Methylene-blue.

By J. O. Warwicker.

[Reprint Order No. 6240.]



(I)

In connection with an X-ray investigation of the combination of basic dyes with acidic oxycelluloses some measurements have been made on crystals of methylene-blue (I). X-Ray examination showed that the unit cell is monoclinic, with the dimensions: $a = 9{\cdot}63 \pm 0{\cdot}02$, $b = 31{\cdot}1 \pm 0{\cdot}1$, $c = 6{\cdot}96 \pm 0{\cdot}02$ Å; $\beta = 97°$. The space group is $P2_1/c$. These results are in general agreement with those reported by W. H. Taylor (*Z. Krist.*, 1935, **91**, 450; *Chem. and Ind.*, 1935, 732), but the cell dimensions differ slightly from his values.

On the assumption that the unit cell contains four dye molecules, the cell constants and the measured density of the crystals (1·31 g. cm.$^{-3}$) lead to a molecular weight of 408, which is close to the value (410) for a pentahydrate. The water content corresponding to this composition agrees closely with that obtained by drying a portion of the dye used in the X-ray work, and with the results of moisture determinations and chemical analyses previously made in these laboratories on a number of other recrystallized samples (Davidson, *J. Text. Inst.*, 1947, **38**, T408). On the other hand, Taylor concluded from his crystallographic data and observed density (1·29 g. cm.$^{-3}$) that his crystals contained 4 mols. of water and in the literature the dye has been formulated with from 1 to 5 mols. These discrepancies might be explained if methylene-blue chloride were capable of forming a number of hydrates stable within different humidity ranges.

It was found that within the range 0—50% r.h. the moisture content of the dye increased continuously with increasing humidity, the relation being similar to the typical adsorption isotherm. At 50% r.h. the moisture content is about 2·5 mols. of water; between 50 and 60% r.h. it rises abruptly to 5 mols., and it remains constant at this value over the range 60—96% r.h. Thus it appears that at above 60% r.h. the stable form of the dye is a pentahydrate. In drier atmospheres the equilibrium moisture content is less than that of the pentahydrate, but no evidence of the existence of a tetrahydrate, or other lower hydrate, has been obtained.

Taylor (*loc. cit.*) also found the bromide of methylene-blue and of its selenium analogue to be isomorphous with methylene-blue chloride. In view of this, it is interesting that he concluded that the bromides crystallized with 5 molecules of water.

Experimental.—Methylene-blue chloride was salted out with sodium chloride from a concentrated aqueous solution of a commercial product, and then recrystallized twice from water; it was dried by exposure to the air at the ordinary temperature. Crystals for X-ray work were obtained by slow evaporation of a cold saturated aqueous solution of the purified dye. As was noted by Taylor, the crystals show twinning, but it was possible to cut untwinned fragments from the larger crystals.

The density of the crystals was determined by flotation with benzene–carbon tetrachloride. The value obtained (1·31 g. cm.$^{-3}$) was confirmed by pycnometric measurements in benzene at 20°.

The unit-cell dimensions were obtained from oscillation photographs by an extrapolation method based on that of Farquhar and Lipson (*Proc. Phys. Soc.*, 1946, **58**, 200); the angle β was obtained from a Weissenberg photograph.

The relation between the moisture content of the dye and the relative humidity was determined by first drying samples over phosphoric oxide and then exposing them to atmospheres of known relative humidity at 20° until the weight was constant. The relative humidity was controlled by means of solutions of sulphuric acid (Wilson, *J. Ind. Eng. Chem.*, 1921, **13**, 326). At 60% r.h. the moisture content was 21·4% and in the range 70—96% r.h. it varied between 21·9 and 22·2% (Calc. for $C_{16}H_{18}N_3SCl,5H_2O$: H_2O, 22·0%).

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[*Received, March 16th,* 1955.]

Published on 01 January 1955. Downloaded by University of Sussex on 14/09/2015 20:48:42.

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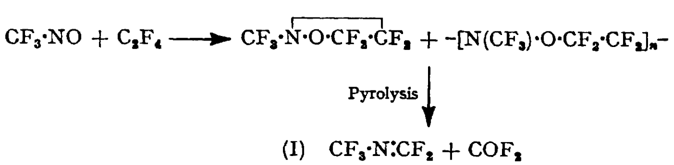
Perfluoroalkyl Derivatives of Nitrogen. Part II. Bisperfluoroalkylamines.*

By D. A. Barr and R. N. Haszeldine.

[Reprint Order No. 6248.]

A general method for the conversion of perfluoroalkylnitroso-compounds into perfluoro(alkylalkyleneamines) was described in Part I *, *e.g.* :



$$CF_3\cdot NO + C_2F_4 \longrightarrow CF_3\cdot N\cdot O\cdot CF_2\cdot CF_2 + -[N(CF_3)\cdot O\cdot CF_2\cdot CF_2]_n-$$

$$\big\downarrow \text{Pyrolysis}$$

$$\text{(I)}\quad CF_3\cdot N{:}CF_2 + COF_2$$

The availability of perfluoro(alkylalkyleneamines) now opens up a convenient general route to bisperfluoroalkylamines, and particularly to (perfluoroalkyl)trifluoromethylamines, since the C:N in the system $-CF_2\cdot N{:}CF-$ reacts readily with anhydrous hydrogen fluoride :

$$CF_3\cdot[CF_2]_n\cdot N{:}CF\cdot[CF_2]_m\cdot CF_3 \xrightarrow{HF} CF_3\cdot[CF_2]_n\cdot NH\cdot CF_2\cdot[CF_2]_m\cdot CF_3$$

$$CF_3\cdot[CF_2]_n\cdot N{:}CF_2 \xrightarrow{HF} CF_3\cdot[CF_2]_n\cdot NH\cdot CF_3$$

$$e.g.,\quad \underset{\text{(I)}}{CF_3\cdot N{:}CF_2} + HF \longrightarrow (CF_3)_2NH$$

The chemistry of unsubstituted alkylalkyleneamines has been investigated only in outline. They are said to combine readily with bromine or iodine to give solids believed to be dihalides : $R\cdot CH{:}NR' \xrightarrow{X_2} R\cdot CHX\cdot NXR'$ (X = Br or I; R = alkyl; R′ = alkyl or H), but no proof of structure is available (Franchimont and Van Epps, *Rec. Trav. chim.*, 1896, **15**, 169; Berg, *Bull. Soc. chim. France*, 1925, **37**, 637; Turcan, *ibid.*, 1932, **51**, 486; Dains and Lehmann, *Trans. Kansas Acad. Sci.*, 1931, **34**, 297; *Chem. Abs.*, 1932, **26**, 5270; Shelton, U.S.P. 2,393,271; *Chem. Abs.*, 1946, **40**, 2273). Delépine (*Bull. Soc. chim. France*, 1903, **29**, 1200) showed that hydrogen cyanide reacted by addition with the compound $EtN{:}CHMe$ to give $Et\cdot NH\cdot CHMe\cdot CN$, but the reaction of hydrogen halides with alkylene-alkylamines has apparently not been investigated. Pearlson and Hals (U.S.P. 2,643,267; *Chem. Abs.*, 1954, **48**, 6461) have recently briefly stated that hydrogen fluoride reacts with "fluorocarbon azomethines," *i.e.*, perfluoro(alkylalkyleneamines), to give *sec.*-perfluoro-amines, but details of conditions, yields, or products have not yet been released.

Perfluoro(methylmethyleneamine) (I) fails to react with chlorine at room temperature, and is recovered unchanged when heated with iodine. This sharp contrast with unsubstituted alkylalkyleneamines is not unexpected in view of the marked differences between addition reactions of olefins and the corresponding perfluoro-olefins (*e.g.*, $CH_3\cdot CH{:}CH_2$ and $CF_3\cdot CF{:}CF_2$). Reaction of perfluoro(methylmethyleneamine) with anhydrous hydrogen fluoride proceeds smoothly and almost quantitatively at 150°, however, and yields bistrifluoromethylamine (b. p. −6·7°). This is the first bisperfluoroalkylamine to be prepared by an unambiguous route, although the same compound was believed to be formed during the reaction of iodine pentafluoride with iodine cyanide (Ruff and Willenberg, *Ber.*, 1940, **73**, 724). The hydrogen for this last reaction was presumably supplied as hydrogen fluoride by moisture entering the reaction as impurity and combining with the iodine pentafluoride. The boiling point of the by-product obtained by Ruff and Willenberg (−6·2°) is in fact close to that of pure bistrifluoromethylamine; but, if the two compounds are identical, the mechanism of formation of bistrifluoromethylamine from iodine cyanide is, at first sight, obscure.

Bistrifluoromethylamine is a colourless gas, whose infrared spectrum shows a strong N–H stretching absorption at 2·89 μ (see Barr and Haszeldine, *J.*, 1955, in the press, for a discussion of the infrared spectrum). The gas is quite stable in absence of moisture, but

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* Part I, *J.*, 1955, 1881, where references to earlier related work are given.

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is rapidly converted by water into carbon dioxide and fluoride and ammonium ions; this is essentially hydrolysis under acid conditions. Decomposition in alkaline solution also causes complete breakdown of bistrifluoromethylamine, but the nitrogen appears as cyanate ion and not as ammonium ion. Perfluoro(methylmethyleneamine) gives analogous products, *i.e.*, ammonium ion in acid solution, cyanate ion in alkaline solution, and it is thus probable that bistrifluoromethylamine decomposes by initial loss of hydrogen fluoride to give perfluoro(methylmethyleneamine). Cyanate ion is converted into ammonium ion and carbon dioxide in acid solution, so a common mechanism can be written for both acid and base hydrolyses:

$$(CF_3)_2NH \longrightarrow HF + CF_3{\cdot}N{:}CF_2 \xrightarrow{H_2O} CF_3{\cdot}NH_2 + COF_2$$

$$\begin{tikzcd}
CF_3{\cdot}NH_2 \arrow[r, "-HF"] & CF_2{:}NH \arrow[r, "-HF"] \arrow[d, "OH^-"] & FCN \arrow[r, "OH^-"] & HOCN \arrow[d, leftrightarrow] \\
 & HNCO & & HNCO
\end{tikzcd}$$

$$HNCO + H_2O + H^+ \longrightarrow CO_2 + NH_4^+$$

If Ruff and Willenberg's by-product (which also yielded cyanate ion in alkaline solution) is in fact bistrifluoromethylamine, then a possible route to it is by reversal of the hydrolysis reaction, *i.e.*, by reaction of trifluoromethylamine with carbonyl fluoride produced by oxidative breakdown of iodine cyanide:

$$IF_5 \xrightarrow{H_2O} HF + IOF_3$$

$$ICN \xrightarrow{IOF_3} COF_2$$

$$ICN \xrightarrow{IF_5} FCN \overset{2HF}{\rightleftharpoons} CF_3{\cdot}NH_2 \xrightarrow{COF_2} CF_3{\cdot}N{:}CF_2 \xrightarrow{HF} (CF_3)_2NH$$

Confirmation of this must await the synthesis of trifluoromethylamine.

Experimental.—Perfluoro(methylmethyleneamine) was prepared by reaction of trifluoronitrosomethane with tetrafluoroethylene, followed by pyrolysis of the products (Part I, *loc. cit.*); its purity was checked by infrared spectroscopic examination.

Attempted addition reactions with perfluoro(methylmethyleneamine). (*a*) Perfluoro(methylmethyleneamine) (0·050 g., 0·00038 mole) and anhydrous chlorine (0·024 g., 0·00034 mole) were immiscible at room temperature, and failed to react during 3 days in a sealed 5-ml. Pyrex tube.

(*b*) The unsaturated compound (0·066 g.) and iodine (0·120 g.), heated at 160° (20 hr.) in a sealed tube, underwent no reaction.

Bistrifluoromethylamine. Perfluoro(methylmethyleneamine) (12·15 g., 0·0914 mole) and anhydrous hydrogen fluoride (1·75 g., 0·0875 mole) in a 20-ml. steel autoclave (pretreated with anhydrous hydrogen fluoride) were heated at 150° (15 hr.). Fractionation of the volatile products *in vacuo* gave *bistrifluoromethylamine* (12·4 g., 0·0810 mole, 89%) (Found: C, 15·8; H, 0·6; N, 9·2%; *M*, 154. C_2HNF_6 requires C, 15·7; H, 0·65; N, 9·2%; *M*, 153), unchanged perfluoro(methylmethyleneamine) (0·007 g., 0·05%), and negligible amounts of carbon dioxide, hydrogen fluoride, and silicon tetrafluoride. The formation of bistrifluoromethylamine is probably quantitative, since slight losses occurred during manipulation.

The vapour pressure of bistrifluoromethylamine, measured over the temperature range −66° to −8°, is given by the equation $\log_{10} p = 7{\cdot}896 - 1335/T$ (p in mm., T in °K), whence the b. p. is calculated as −6·7°, Trouton's constant is 22·9, and the latent heat of vaporisation is 6100 cal./mole.

Hydrolysis of bistrifluoromethylamine. (*a*) The amine (0·050 g., 0·000325 mole) and water (0·5 ml.) reacted immediately in a sealed 5-ml. Pyrex tube. After 12 hr., fractionation of the volatile products gave carbon dioxide (0·028 g., 0·000652 mole, 100%) (Found: *M*, 44. Calc. for CO_2: *M*, 44). The aqueous solution contained fluoride and ammonium ions.

(*b*) The amine (0·103 g., 0·00067 mole) and 10% aqueous sodium hydroxide (5 ml.), shaken in a sealed 25-ml. Pyrex tube at room temperature (4 hr.), gave only fluoride, carbonate, and cyanate ions. Ammonia was not detectable as gaseous product. Cerous nitrate–acetic acid was used to test for fluoride, and copper sulphate–pyridine for the cyanate test.

Alkaline hydrolysis of perfluoro(methylmethyleneamine). A rapid reaction ensued when

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perfluoro(methylmethyleneamine) (0·062 g., 0·00047 mole) and 10% aqueous sodium hydroxide (5 ml.) were sealed in a 25-ml. Pyrex tube and shaken at room temperature (5 hr.). No volatile products were found, and in particular ammonia was absent. Tests on the aqueous solution revealed the presence of fluoride, carbonate, and cyanate ions.

One of us (D. A. B.) is indebted to Imperial Chemical Industries Limited, Plastics Division, for a Maintenance grant.

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Published on 01 January 1955. Downloaded by University of Sussex on 14/09/2015 20:48:42.

Attempted Synthesis of 9 : 10-*Dihydro*-7 : 8 : 2′ : 3′-*tetramethoxy*-10-*methyl*-1 : 2-*benzophenanthridine by the Pschorr Reaction.*

By T. R. GOVINDACHARI and N. ARUMUGAM.

[Reprint Order No. 6254.]

As the first step in the synthesis named in the title, 1 : 2 : 3 : 4-tetrahydro-1-hydroxyimino-6 : 7-dimethoxynaphthalene (Haworth and Mavin, *J.*, 1932, 1485) was reduced to the 1-amine by sodium amalgam. When heated with formic acid this amine did not give the expected formyl derivative but, instead, the amino-group was eliminated with formation of a neutral nitrogen-free oil. The acetyl derivative of the amine was, however, easily obtained and was dehydrogenated by heating it in *p*-cymene with palladised charcoal to *N*-acetyl-6 : 7-dimethoxy-1-naphthylamine; a side reaction led to the simultaneous formation of 2 : 3-dimethoxynaphthalene. The amine obtained from the acetyl derivative by hydrolysis was formylated and then reduced by lithium aluminium hydride to 6 : 7-dimethoxy-*N*-methyl-1-naphthylamine, which condensed with 2 : 3-dimethoxy-6-nitrobenzoyl chloride to yield *N*-(2 : 3-dimethoxy-6-nitrobenzoyl)-6 : 7-dimethoxy-*N*-methyl-1-naphthylamine, though only in 30% yield. The amide was reduced catalytically to *N*-(6-amino-2 : 3-dimethoxybenzoyl)-6 : 7-dimethoxy-*N*-methyl-1-naphthylamine which was then submitted to the Pschorr reaction, under a variety of conditions. Careful chromatography of the products failed to yield any crystalline material.

Experimental.—1 : 2 : 3 : 4-*Tetrahydro*-6 : 7-*dimethoxy*-1-*naphthylamine.* Sodium amalgam (400 g.) was added in small portions to a solution of 1 : 2 : 3 : 4-tetrahydro-6 : 7-dimethoxy-1-hydroxyiminonaphthalene (20 g.) in alcohol (200 ml.) at 60°. The solution was kept acidic by intermittent addition of 50% acetic acid. After 3 hr. the mercury was removed and the alcohol distilled off *in vacuo.* The residue was made alkaline and extracted with ether. On removal of the ether from the dried extract, the base was obtained as an oil (18 g.). This was heated with acetic anhydride (15 ml.) and the *acetyl derivative* produced was recrystallised from benzene–light petroleum, yielding needles, m. p. 149° (Found: C, 67·7; H, 7·5; N, 5·3. $C_{14}H_{19}O_3N$ requires C, 67·5; H, 7·6; N, 5·6%).

N-*Acetyl*-6 : 7-*dimethoxy*-1-*naphthylamine.* The foregoing acetyl derivative (2 g.) was heated in *p*-cymene under reflux with 30% palladised charcoal (0·2 g.) for 8 hr. in a carbon dioxide atmosphere. The hot solution was filtered. The filtrate deposited, on cooling, white needles (1·2 g.) which on recrystallisation from benzene yielded N-*acetyl*-6 : 7-*dimethoxy*-1-*naphthylamine* (0·9 g.), m. p. 185° (Found: C, 68·3; H, 6·2; N, 5·8. $C_{14}H_{15}O_3N$ requires C, 68·6; H, 6·1; N, 5·7%). From the benzene mother-liquor undehydrogenated substance (0·3 g.) was recovered. The *p*-cymene filtrate yielded on concentration 2 : 3-dimethoxynaphthalene, m. p. 116° (Kauffmann and Beisswenger, *Ber.*, 1903, **36**, 569).

6 : 7-*Dimethoxy*-1-*naphthylamine.* The acetyl derivative (5 g.) in refluxing 20% sulphuric acid (200 ml.; 3 hr.) gave the *base*, m. p. 130° (from alcohol) (Found: C, 71·3; H, 6·1; N, 7·2. $C_{12}H_{13}O_2N$ requires C, 70·9; H, 6·4; N, 6·9%). This (5 g.) was heated with formic acid (6 ml.; 90%) for 3 hr. at 180°. The *formyl derivative*, crystallised from alcohol, melted at 175° (Found: C, 67·7; H, 5·4; N, 6·2. $C_{13}H_{13}O_3N$ requires C, 67·5; H, 5·6; N, 6·1%).

6 : 7-*Dimethoxy*-N-*methyl*-1-*naphthylamine.* The formyl derivative (2 g.) was added to lithium aluminium hydride (2 g.) in tetrahydrofuran (100 ml.). After 2 hours' stirring the excess of hydride was decomposed by water, and the solution decanted from the alumina, which was further washed with ether. The solvent was removed *in vacuo* and the residual *base* crystallised from methanol, yielding needles (1 g.), m. p. 154° (Found: C, 72·1; H, 6·4; N, 6·3. $C_{13}H_{15}O_2N$ requires C, 71·9; H, 6·9; N, 6·5%).

This amine (1·3 g.) in benzene (30 ml.) was treated with 10% potassium carbonate solution

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(30 ml.) and then with a solution of 2 : 3-dimethoxy-6-nitrobenzoyl chloride (1·8 g.) in benzene (30 ml.) with vigorous stirring. After an hour the benzene layer was separated, washed successively with dilute hydrochloric acid, dilute sodium hydroxide solution, and water, dried, concentrated to a small volume, and poured on to an alumina column, which was then eluted with benzene. From the eluate, the 2 : 3-*dimethoxy-6-nitrobenzoyl derivative* was obtained in 30% yield, m. p. 216° (Found : C, 62·1 ; H, 5·1 ; N, 6·3. $C_{22}H_{22}O_7N_2$ requires C, 62·0 ; H, 5·2 ; N, 6·6%).

N-(6-*Amino*-2 : 3-*dimethoxybenzoyl*)-6 : 7-*dimethoxy*-N-*methyl*-1-*naphthylamine*. The nitro-compound (1 g.) in alcohol (25 ml.) was reduced in the presence of Adams catalyst. The *product* (0·6 g.), crystallised from methanol, had m. p. 154° (Found : C, 67·2; H, 6·1; N, 7·0. $C_{22}H_{24}O_5N_2$ requires C, 66·7; H, 6·0; N, 7·1%). The *hydrochloride* crystallised from absolute alcohol and melted with decomposition at 215° (Found : C, 60·7; H, 6·3. $C_{22}H_{25}O_5N_2Cl$ requires C, 61·0; H, 6·5%).

We are grateful to the Government of India and to the East India Pharmaceuticals Works Ltd., Calcutta, for the award of a scholarship to one of us (N. A.), and to Mr. S. Selvavinayagam for the microanalyses.

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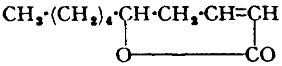
[*Received, March* 21*st*, 1955.]

Synthesis of (±)-Massoialactone.

By L. CROMBIE.

[Reprint Order No. 6279.]

MASSOI BARK (from *Cryptocarya massoia*, family Lauraceae) on steam distillation yields about 2% of an essential oil from which an optically active unsaturated lactone, massoia (or massoy)lactone, has been isolated (Abe, *J. Chem. Soc. Japan*, 1937, **58**, 246; Meijer, *Rec. Trav. chim.*, 1940, **59**, 191). Abe formulated it as (—)-7-methylnon-2-eno-5-lactone but Meijer, on the basis of oxidative degradation, has shown it to be (—)-dec-2-eno-5-lactone (I). Abe and Sato (*J. Chem. Soc. Japan*, 1954, **75**, 952) now concur with Meijer.



$$CH_3\cdot(CH_2)_4\cdot\underset{\displaystyle O}{CH}\cdot CH_2\cdot CH{=}\underset{\displaystyle CO}{CH}$$

(I)

A synthesis of (±)-dec-2-eno-5-lactone was recently described in connection with the preparation of deca-*cis*-2 : *trans*-4-dienoic acid (Crombie, *J.*, 1955, 1007). Through the intercession of Dr. Meijer, Dr. Boeknoogen has generously provided an authentic specimen of massoialactone; its infrared spectrum (liquid film) is identical with that of the synthetic material. Meijer's structure for the natural lactone is thus firmly established. As expected, the (—)-lactone in 0·01N-methanolic sodium methoxide has initially only pronounced end absorption, but gradually develops a maximum at 260 mμ. This is due to intramolecular elimination giving sodium deca-*cis*-2 : *trans*-4-dienoate. Data for massoialactone and synthetic (±)-dec-2-eno-5-lactone are summarised in the table.

						Infrared	
Natural (—)	B. p.	n_D^t	d_4^t	R_D^1	$[\alpha]_D^t$	C=O	C=C
Abe	122—123°/2 mm.	1·4718 (20°)	0·9859 (20°)	47·76	−97°[3]	—	—
Meijer	169·5—174/24 mm.	1·4714 (26)	0·9788 (27·5)	48·02[2]	−93[3]	—	—
Crombie[6] ...	103—104/0·5 mm.	1·4722 (21)	0·9800 (21)	48·09	−95·5[4]	1723 s[5]	1627 w
Synthetic (±)							
Crombie[7]......	85—86/0·07 mm.	1·4705 (21)	0·9785 (21)	48·01	0	1723 s[5]	1627 w

[1] Calc. molecular refractivity, 47·37 (data from Gilman, "Organic Chemistry," Wiley, 1943, Vol. II, p. 1751). [2] n_D corrected to 27·5° by —0·0004 per degree for this calculation. [3] Neat liquid. [4] *c*, 10·42% in ethanol. [5] Pinder, *J.*, 1952, 2236, gives 1725 cm.$^{-1}$ for hex-2-eno-5-lactone. [6] Dr. Boeknoogen's specimen had n_D^{18} 1·4727 and was redistilled. [7] *Loc. cit.*

Both the natural and the synthetic lactone have similar characteristic odours and irritate the skin. Massoi bark is used in native medicine in Dutch New Guinea and in view of the interesting physiological activity of hex-2-eno-5-lactone (see Haynes, *Quart. Rev.*, 1948, **2**, 48; *idem*, "Modern Methods of Plant Analysis," Vol. II, Springer, Berlin, 1955, p. 583) specimens are being tested by Dr. L. J. Haynes.

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[*Received, March* 30*th*, 1955.]

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The Preparation of Some Derivatives of 5 : 6-*Dimethoxyindole.*

By D. G. Harvey.

[Reprint Order No. 6299.]

During metabolic studies some derivatives of 5 : 6-dimethoxyindole were required. Oxford and Raper (*J.*, 1927, 417) prepared this by the ferrous sulphate reduction of 4 : 5-dimethoxy-2-nitrophenylpyruvic acid in poor yield. If, however, the concentration of ammonia was increased and the ferric oxide sludge thoroughly washed with aqueous ammonia, reasonable yields resulted. In addition, the pyruvic acid need not be isolated, but can be used as an ammoniacal solution of the potassium salt. Decarboxylation of 5 : 6-dimethoxyindole-2-carboxylic acid was effected smoothly in glycerol. Attempts to introduce an aldehyde group into 5 : 6-dimethoxyindole, including the Reimer–Tiemann, Gattermann, and gramine reactions, failed. However, the Gattermann reaction with ethyl indole-2-carboxylate gave (cf. Boyd and Robson, *Biochem. J.*, 1935, **29**, 555) the aldimine and thence the aldehyde. Attempts to decarboxylate this compound resulted in tars.

Experimental.—5 : 6-*Dimethoxyindole*-2-*carboxylic acid.* A suspension of the potassium derivative of ethyl 5 : 6-dimethoxy-2-nitrophenylpyruvate was prepared from 4 : 5-dimethoxy-2-nitrotoluene as described by Oxford and Raper (*loc. cit.*). This was shaken out with water (500 ml.) and the benzene–ether layer extracted with 7% aqueous ammonia (75 ml. × 10). A further quantity of ammonia (125 ml.; *d* 0·880) was added to the combined aqueous extracts. Hot ferrous sulphate solution (500 g. in 800 ml. of water) was added and the mixture heated on water-bath for 0·5 hr. and boiled for the same length of time. The ferric oxide sludge was boiled five times with 3·5% aqueous ammonia (1 l. per time). The combined filtrates were decolorised with charcoal at 80° and concentrated *in vacuo*. Acidification of the cold concentrate (Congo-red) with 5% sulphuric acid yielded practically colourless needles of the indole acid. Recrystallisation from ethanol or acetic acid gave colourless needles, m. p. 223° (decomp.) (20—23 g., 35—41% based on nitrotoluene) (Found : N, 6·3. Calc. for $C_{11}H_{11}O_4N$: N, 6·3%).

5 : 6-*Dimethoxyindole.* The 2-carboxylic acid (20 g.) was converted into the ammonium salt by dissolution in ammonia and ethanol and concentration. The dry salt was heated in glycerol (10 ml.) at 200—210° for 0·5 hr. The hot melt was poured into excess of aqueous sodium hydrogen carbonate and cooled at 0° for 6 hr. The crystalline product (15 g., 97%), recrystallised from benzene, had m. p. 142° (Oxford and Raper give 154°). Further crystallisations and vacuum-distillation failed to raise the m. p. (Found : N, 7·8. Calc. for $C_{10}H_{11}O_2N$: N, 8·1%).

Ethyl 5 : 6-*dimethoxyindole*-2-*carboxylate.* The acid (15 g.) was converted into the ammonium salt and thence into the silver salt which was dried in *vacuo* (H_2SO_4) (21 g., 95%), then boiled in dry benzene (100 ml.) with ethyl iodide (13·5 g.) for 0·5 hr. The iodide was filtered off and washed with hot benzene, and the filtrate and washings were concentrated to 20 ml. Light petroleum (b. p. 40—80°) (100 ml.) was added. Pale yellow needles of the ester crystallised at 0° (9—10 g., 53—59%). On recrystallisation from ethyl acetate it softened at 155° and had m. p. 160° (Found : N, 5·5. Calc. for $C_{13}H_{15}O_4N$: N, 5·7%). Perkin and Rubinstein (*J.*, 1926, 357) give 172°.

Treating the carboxylic acid with excess of ethanol containing 3% v/v of sulphuric acid gave the ester (10—20%) as pale yellow-brown needles, m. p. 162°.

Anil of 3-*formyl*-5 : 6-*dimethoxyindole*-2-*carboxylic acid.* Ethyl 5 : 6-dimethoxyindole-2-carboxylate (5·5 g.), zinc cyanide (5·5 g.), dry ether (100 ml.), and dry chloroform (100 ml.) were treated, with stirring at 0°, with dry hydrogen chloride for 3 hr., then for 2 hr. at room temperature. The supernatant fluid was decanted, and the yellow aldimine washed with dry ether and boiled with water. The yellow crystals were warmed in ethanol with dilute aqueous sodium hydroxide (1·5 mol.) on the water-bath for 0·25 hr. and treated with aniline (1·5 mols., redistilled). After clarification with charcoal, the alcohol was removed *in vacuo*, and the solution acidified with dilute sulphuric acid (litmus). The yellow needles of the *anil*, recrystallised from ethanol and from dioxan (3·75 g., 29·0%), had m. p. 257° (Found : C, 65·3; H, 4·9; N, 18·8. $C_{18}H_{16}N_2O_4$ requires C, 66·6; H, 4·9; N, 8·6%). Treating this with dilute sulphuric acid and then with phenylhydrazine hydrochloride and sodium acetate gave the *phenylhydrazone* as yellow needles (from ethanol), m. p. 220° (Found : C, 63·7; H, 5·0. $C_{18}H_{17}O_4N_3$ requires C, 63·8; H, 4·8%).

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[*Received, April 4th,* 1955.]