the direct freezing of the bromine oxidation products, melted at 159.5–160.5°.

The filtrate was made more alkaline by adding 2 ml. of 10% sodium hydroxide and extracted ten times with ether. The ether solution, after drying, gave 0.37 g. of a mixture of yellowish thick liquid and a small amount of solid. Attempts to make an amide by the method of Mooradian and Cloke failed. Extraction of the filtrate with ether gave a negligible amount of viscous liquid which was not identified.

The alkaline aqueous solution was acidified with 20% sulfuric acid and extracted ten times with ether. From the ethereal solution was obtained 1.64 g. of a clear, mobile, yellowish liquid (81% based on the original liquid minus the recovered cyclic isomers). Distillation of the liquid gave, after a small forerun, γ-cyano-*n*-valeric acid, b.p. 119° (0.4 mm.), 0.85 g. (45%). The liquid solidified on cooling, m.p. 91–96°. The solid was allowed to dry on filter paper for two weeks, m.p. 96.5–97.5° (95–96°, prepared from γ-valerolactone and potassium cyanide).[13]

Anal. Calcd. for $C_6H_9O_2N$: C, 56.69; H, 7.09; N, 11.02. Found: C, 56.90; H, 7.34; N, 10.79.

In another experiment, 0.70 g. of the crude cyano-acid obtained from the oxidation of 1.38 g. of the liquid unsaturated dinitrile was hydrolyzed with 20 ml. of 50% sulfuric acid by refluxing at 180° for 1.5 hours. At the end of this time, the tea-colored acid solution was cooled and poured onto chopped ice. The resulting solution was extracted ten times with ether. The ether extract on being processed in the usual manner and decolorized with carbon gave 0.70 g. of yellowish liquid which solidified. The solid was purified by allowing a liquid contaminant to distil at 0.4 mm. at 80°. The liquid distillate, $n^{25}\text{D}$ 1.4422, was dried in ether solution. An attempt to prepare an anilide derivative from the residue was not successful. The residual solid, 0.25 g. (31%), m.p. 65–72°, was pressed dry on filter paper. The α-methylglutaric acid was dissolved in an ether–petroleum ether mixture and the solution was allowed to stand overnight in a Dry Ice box, to give a solid m.p. 77.0–78.0° (77.5°, prepared by oxidation of 1-methyl-3-isopropylidenecyclopentanone-2)[14] (77–78°)[15] (79°, prepared by oxidation of γ-methyl-δ-acetylvaleric acid).[16]

Anal. Calcd. for $C_6H_{10}O_4$: C, 49.32; H. 6.85; neut. equiv., 73.0. Found: C, 49.48; H, 6.60; neut. equiv., 74.2.

To further prove that the above hydrolysis product was α-methylglutaric acid, an authentic sample was prepared. The ethyl β-iodopropionate required in the synthesis was prepared according to Perkin.[17] From 20 g. (0.1 mole) of β-iodopropionic acid (Eastman Kodak, recrystallized from water, white solid, m.p. 84–85°), there was obtained 20.0 g. of the ester (87.7% yield), b.p. 53–56° (1.1–1.2 mm.), $n^{25}\text{D}$ 1.4961, d^{30}_4 1.6226 [136° (100 mm.), 94% yield].[17] Esterification at temperatures higher than room temperature was found to be unsuccessful. The condensation of the ethyl β-iodopropionate with ethyl methyl malonate was carried out according to the direction of Auwers.[15] From 17.57 g. (1.101 moles) of ethyl β-iodopropionate there was obtained 18.03 g. of the triester (64.9% yield), b.p. 120–124° (1.5 mm.), $n^{25}\text{D}$ 1.4328 [65%, 164.5° (15 mm.)].[15] An attempted condensation with free β-iodopropionic acid with twice the amount of sodium used for the ester was unsuccessful. To saponify and decarboxylate the triester to α-methylglutaric acid, 5.56 g. (0.02 mole) of the above triester was refluxed with 5 ml. of concentrated hydrochloric acid and 5 ml. of water (*ca.* 1 hour). The residue was distilled under vacuum to give, after a forerun, a product distilling at 116–118° (1.6–1.7 mm.), 2.24 g., 76.7% (81%, b.p. 220–227°, m.p. 77–78°).[16] After the product was chilled in the Dry Ice box, a white precipitate separated and was removed by filtration. The solid, after removal of traces of liquid in vacuum, had a melting point of 77.5–78.0°. A mixed m.p. with the α-methylglutaric acid (77.0–78.0°) obtained from the permanganate oxidation melted at 77.5–78.0°.

Acknowledgment.—We are grateful to Dr. F. M. Rugg of the Bakelite Corporation and Dr. Stephen M. Nagy of the Massachusetts Institute of Technology for the interpretation of infrared spectra reported here. We are also grateful to the Plastics Laboratory of Princeton University for the use of their equipment in the determination of the dipole moments.

Brooklyn, New York

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[13] W. Wislicenus, *Ann.*, **233**, 101 (1886).

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[15] K. Auwers, *Ann.*, **292**, 209 (1896).

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[Contribution from the W. H. Chandler Chemistry Laboratory, Lehigh University]

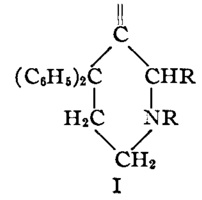
Synthesis of Some Substituted 3-Piperidones[1]

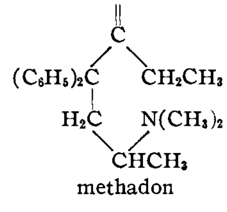
By Nelson R. Easton, Lester R. Bartron,[2] Francis L. Meinhofer and Velmer B. Fish

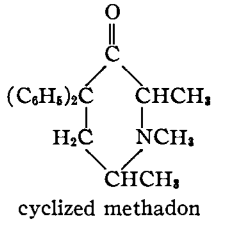
Received September 2, 1952

The synthesis of a series of substituted piperidones which possess the general structure I was accomplished in the following manner: Diphenylacetonitrile was converted into γ-bromo-α,α-diphenylbutyronitrile and this substance was allowed to react with the appropriate secondary amine. The amino nitriles were then converted into the desired ketones by use of the proper Grignard reagent. Bromination of the hydrobromides of the ketones yielded the monobrominated products. Neutralization of these compounds with sodium bicarbonate was followed by a rapid cyclization to the quaternary salt of the desired piperidone. Pyrolyses of these salts gave the expected piperidones in varying yields.

In light of the interest in methadon as an analgesic, we were interested in preparing a series of 3-piperidones (I) which would correspond structurally to a cyclized methadon (II). Since experimental


I


methadon


cyclized methadon

II

Ia, R = CH_3, R′ = H; Ib, R = CH_3, R′ = CH_3; Ic, R = CH_3CH_2, R′ = H; Id, R = CH_3CH_2, R′ = CH_3

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[1] The synthesis of some of these compounds was reported by F. F. Blicke and John Krapcho at the Spring Meeting of the American Chemical Society, April, 1948. Recently they have been described by these authors in This Journal, **74**, 4001 (1952).

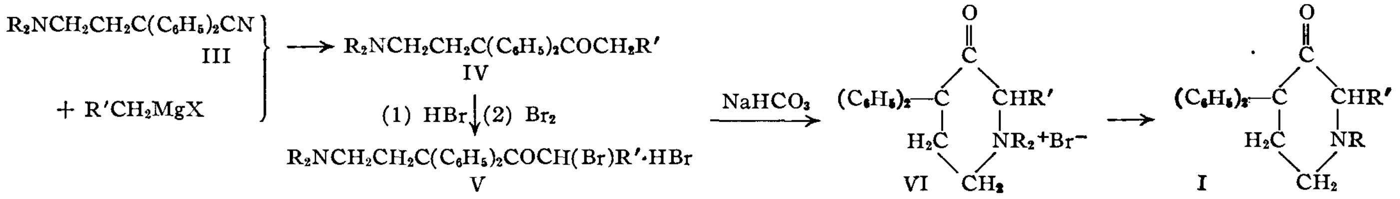
[2] Abstracted in part from the Thesis submitted in partial fulfillment of the requirements for the degree of Doctor of Philosophy.

TABLE I

4,4-DIPHENYL-3-PIPERIDONES AND INTERMEDIATE COMPOUNDS

Compound	Formula	R	R'	Yield, %	Deriv.	Crystn. solvent	M.p., °C.[a]	Nitrogen, %		Halogen, %		Carbon, %		Hydrogen, %	
								Calcd.	Found	Calcd.	Found	Calcd.	Found	Calcd.	Found
IVa	$C_{19}H_{23}NO$	CH_3	H		(B.p. 137–147° (1.0 mm.)[b])										
	$C_{19}H_{24}NOBr$				HBr	Ethanol	172–173[c]	3.87	4.06, 3.93	22.06	22.20				
IVb	$C_{20}H_{25}NO$	CH_3	CH_3		(B.p. 141–156° (2.0 mm.)[b])										
	$C_{20}H_{26}NOBr$				HBr	Ethanol	142.5–143.5[d]	3.72	3.71, 3.69	21.24	20.95				
IVc	$C_{21}H_{27}NO$	CH_2CH_3	H		(B.p. 145–149° (1.0 mm.)[b])										
	$C_{21}H_{28}NOBr$				HBr	Ethyl acetate	140–142	3.58	3.64, 3.62	20.47	20.95				
IVd	$C_{22}H_{29}NO$	CH_2CH_3	CH_3		(B.p. 159–161° (1.0 mm.)[b])										
	$C_{22}H_{30}NOBr$				HBr	Ethanol–isopropyl ether	119–120	3.46	3.50	19.76	20.20				
Va	$C_{19}H_{23}NOBr_2$	CH_3	H	75.6	HBr	Ethyl acetate	158–160 d.[e]	3.17	3.13, 3.24	36.22	36.45				
Vb	$C_{20}H_{25}NOBr_2$	CH_3	CH_3	95	HBr	Ethanol–isopropyl ether	174–176 d.[f]	3.08	3.08, 3.08	35.11	35.20				
Vc	$C_{21}H_{27}NOBr_2$	CH_2CH_3	H	66.9	HBr	Ethyl acetate	140–141 d.			34.07	34.00				
Vd	$C_{22}H_{29}NOBr_2$	CH_2CH_3	CH_3	78.0	HBr	Ethanol	167–168.5 d.	2.90	2.96	33.07	33.40				
VIa	$C_{19}H_{22}NOBr \cdot 1H_2O$	CH_3	H	93		Ethanol	197.5–198.0 d.[g]	3.70	3.72	21.13	21.20	60.32	60.00	6.39	6.49
VIb	$C_{20}H_{24}NOBr \cdot 2H_2O$	CH_3	CH_3	95		Ethanol	200.0–202.0 d.[h]	3.41	3.54	19.48	20.00, 19.90	58.53	58.60	6.88	7.07
VIc	$C_{21}H_{26}NOBr \cdot 1H_2O$	CH_2CH_3	H	90.1		Ethanol	218.0–219.5 d.	3.45	3.45	19.67	19.85	62.07	62.30	6.94	6.80
VId	$C_{22}H_{28}NOBr \cdot 1H_2O$	CH_2CH_3	CH_3	92.0		Ethanol	209.5–210.0 d.	3.33	3.42, 3.45			62.85	62.75	7.19	7.35
Ia	$C_{18}H_{19}NO$	CH_3	H	57.0		Ethanol	97–100	5.28	5.25, 5.25						
	$C_{18}H_{20}NOCl$				HCl	Ethanol	218–220 d.[i]			11.75	11.70				
	$C_{19}H_{22}NOI$				CH_3I	Ethanol	201.5–202.5 d.	3.44	3.42, 3.40	31.16	31.35				
Ib	$C_{19}H_{21}NO$	CH_3	CH_3	78.7		Ethanol	103–107[j]								
	$C_{19}H_{22}NOCl$				HCl	Ethanol	191–193 d.[k]			11.22	11.32				
	$C_{20}H_{24}NOI$				CH_3I	Ethanol	199.5–200.5 d.	3.32	3.34, 3.33	30.12	30.10				
Ic	$C_{19}H_{22}NOCl$	CH_2CH_3	H	15.9	HCl	Ethanol	199–201			11.22	11.18				
	$C_{20}H_{24}NOI$				CH_3I	Ethanol	227–229.0 d.[m]	3.32	3.33	30.12	29.75				
Id	$C_{20}H_{24}NOCl$	CH_2CH_3	CH_3	81.9	HCl	Ethanol	201.5–202.5 d.			10.75	10.70				
	$C_{21}H_{26}NOI$				CH_3I	Ethanol	191.5–192.0[l]	3.22	3.22, 3.14	29.15	28.70				

[a] These m.ps. are uncorrected and started with the bath reading less than 100°. If a hot bath is used much higher values can be found in most cases where decomposition is indicated. [b] A mixture of the desired product and decyanated product. [c] Reported m.p. 171–173°.[1] [d] Reported m.p. 142–143°.[1] [e] Reported m.p. 158–159°.[1] [f] Reported m.p. 173–174°.[1] [g] Reported m.p. 231–233°[1] no water of hydration. [h] Reported m.p. 208–210°[1] no water of hydration. [i] Reported m.p. 235–236°.[1] [j] Calcd.: N, 5.00. Found: N, 4.45–4.34. [k] Reported m.p. 211–213°.[1] [l] Identical to the ethiodide of Ib. [m] Identical to the ethiodide of Ia.



difficulties were anticipated in the preparation of compounds which contained the three alkyl groups in a cyclized methadon we first synthesized piperidones which contained only two alkyl groups.

The syntheses have been achieved through the series of reactions below Table I.

Diphenylacetonitrile was converted into 4-bromo-2,2-diphenylbutanenitrile and thence into the desired aminonitrile (III) by the method of Dupre, *et al.*[3] Treatment of the nitrile with the appropriate Grignard reagent at elevated temperature led to the desired ketone (IV). After the reaction of the dimethylaminonitriles with the Grignard reagent the desired ketone was easily isolated as the hydrobromide although the expected dialkylaminodiphenylpropane[4] was also produced. However, in the case of the diethylaminonitriles the solubilities of the two products were such that the hydrobromide of the diethylaminodiphenylpropane was first isolated. The ketones could be obtained most readily by first converting the mixture to the hydrochlorides and, after purification, converting these to the desired hydrobromides.

Although bromination of the basic ketone led to mixtures of products, bromination of the hydrobromide salts in acetic acid at 50° gave the desired monobrominated products (V). When the bromination of the hydrobromide of the dimethylaminoethyl ketone (IV) was attempted at room temperature the bromine was absorbed immediately, and an orange product, apparently a perbromide, crystallized; this compound could be decomposed by heating it above its melting point to give the desired bromo compound. At room temperature it gradually decomposed with the evolution of hydrogen bromide.

The salts (V) were then dissolved in an ethanol-water solution and while the mixture was kept cool an equal volume of ether was added. When the mixture was neutralized with a solution of sodium bicarbonate, cyclization took place so rapidly in the case of the dimethylamino compounds that the products (VI) were isolated from both the ether and the water layers. In the case of the diethylamino compounds the products were largely in the ether layer. These quaternary bromides retain water even after prolonged drying at 56°. The 1,1,2-trimethyl-4,4-diphenylpiperidonium bromide formed a dihydrate while the others were found as monohydrates. The pyrolyses of these compounds at reduced pressure gave the desired piperidones. In the case of the 1,1-diethyl-2-methyl-4,4-diphenyl-3-piperidonium bromide a by-product, which was isolated from the mother liquors as the hydrochloride, gave the correct analysis for the product produced by the cleavage of the ring, and probably has the structure (VII) or (VIII)

$$(C_2H_5)_2NCH(CH_3)COC(C_6H_5)_2CH{=}CH_2\cdot HCl$$

VII

$$(C_2H_5)_2NCH_2CH_2C(C_6H_5)_2COCH{=}CH_2\cdot HCl$$

VIII

These 3-piperidones were quite unstable, presumably decomposing through oxidation, and were characterized as the hydrochloride salts, which also turn pink on standing in the light, and as the methiodides. The compounds prepared are given in Table I.

In the pyrolyses of the quaternary bromides (VI) there was a possibility that compounds other than the desired piperidones could be formed. Proof of structure was accomplished in the case of the N-methyl compounds by the preparation of the 3-piperidone methiodides and comparison of these compounds with the quaternary iodides obtained from the quaternary bromides (VI) by treatment with sodium iodide. In the case of the N-ethyl compounds the methiodide derivatives were compared with the ethiodides obtained from the N-methyl compounds. The mixed melting points showed no depression in any case.

Experimental

4-Dimethyl-2,2-diphenylbutanenitrile.[3]—A mixture of 100 g. of 4-bromo-2,2-diphenylbutanenitrile,[3] 60 g. of dimethylamine and 400 ml. of ethanol was heated in a sealed container at 55° for 132 hours. The mixture was concentrated, extracted with ether, and the ether extract was washed with water and then extracted with 5% hydrochloric acid. The acidic extract was neutralized, the orange, oily precipitate was extracted with ether and the extract dried over anhydrous magnesium sulfate. The material (72.4 g., 82%) which boiled at 143–153° (1 mm.) was collected. The hydrobromide melted at 197.5–199° after recrystallization from methanol.

Anal. Calcd. for $C_{18}H_{21}N_2Br$: N, 8.11. Found: N, 8.12, 8.09.

4-Diethylamino-2,2-diphenylbutanenitrile.[3]—A mixture of 60 g. of 4-bromo-2,2-diphenylbutanenitrile, 58.5 g. of diethylamine and 180 ml. of 95% ethanol was refluxed for 12 hours. The solvent and excess diethylamine were distilled from the deep red mixture and the residue was made basic with sodium hydroxide and extracted with ether. The ether layer was extracted with a 5% solution of hydrochloric acid. Neutralization of the acid layer with sodium hydroxide gave an orange oil which was taken up in ether and dried over magnesium sulfate. The material which boiled at 142–152° (1 mm., 11.2 g.) was collected; 45 g. of unreacted bromo nitrile was recovered. The yield, based on unrecovered starting material, was 76.7%. The hydrobromide, after recrystallization from ethanol, melted at 129–130.5°. The methiodide, after recrystallization from ethanol, melted at 191–193°.

Anal. Calcd. for $C_{21}H_{27}N_2I$: N, 6.46. Found: N, 6.34.

Dialkylamino Ketones.—These compounds were prepared by modifying slightly the procedure of Bockmühl and Ehrhart.[5]

To the Grignard reagent there was added a solution of the dialkylamino nitrile in dry xylene. The reaction mixture was then refluxed for 3–5 hours and while still hot was poured into an acid solution. The oily layer was separated by decantation, neutralized with 5% sodium hydroxide, and extracted with ether. After drying over anhydrous magnesium sulfate the ether was removed under reduced pressure and the residual oil was distilled under 1.0 mm. pressure. This gave a mixture of the desired ketones and the decyanated products.

Dialkylamino Ketone Hydrobromides.—It was found that the hydrobromides could be prepared by dissolving the free base in absolute alcohol and adding a slight excess of 48% hydrobromic acid followed by sufficient isopropyl ether to produce turbidity.

In the case of the diethylamino compounds the first product isolated was usually 3-diethylamino-1,1-diphenylpropane hydrobromide. Concentration of the mother liquors yielded an oil which was neutralized and converted into the hydrochloride. The purified salt was then neutralized, extracted and reconverted to the hydrobromide.

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(3) D. J. Dupre, J. Elks, B. A. Herns, K. N. Speyer and R. M. Evans, *J. Chem. Soc.*, 500 (1949).

(4) J. H. Gardner, N. R. Easton and J. R. Stevens, THIS JOURNAL, **70**, 2906 (1948).

(5) M. Bockmühl and G. Ehrhart, *Ann.*, **561**, 52 (1948).

The ethyl ketone in the dimethylamino series was found to be polymorphic. The melting point depended largely on the solvent used for crystallization. When recrystallized from an ethanol–isopropyl ether solution it melted at 86–88°, and when dried in an Abderhalden at 56° it melted at 114–116°. When recrystallized from ethanol or ethanol-ether it melted at 142–142.5° after sintering at 86°.

Bromination of Dialkylamino Ketone Hydrobromides.—The hydrobromide salts were dissolved in glacial acetic acid in the ratio of 3 liters of acetic acid per mole of salt and the solution maintained at approximately 50°. Dropwise addition of a solution of the theoretical amount of bromine in glacial acetic acid in the ratio of 1500 ml. of acetic acid per mole of bromine was carried out over two hours. The solvent was removed by distillation under reduced pressure leaving an orange oily residue. Trituration with ethyl acetate yielded crystalline products.

1,1-Dialkyl-4,4-diphenyl-3-piperidonium Bromides and 1,1,2-Trialkyl-4,4-diphenyl-3-piperidonium Bromides.—The solid bromination products were dissolved in 50% ethanol and an equal volume of ether was added. The mixture was kept cool, neutralized with sodium bicarbonate solution, shaken and the ether layer was separated quickly. In the case of the dimethylamino compounds, it was found that the product which came out of the ether solution was much easier to purify.

Pyrolyses of the Quaternary Salts.—The quaternary salts were placed in a 10-ml. Claisen flask fitted with a 10-ml. receiver flask and the evacuated system heated with an oil-bath. The piperidones distilled and were dissolved in ether; the ether solutions were treated with hydrogen chloride to give the hydrochlorides. The methiodides were prepared in the usual manner and the ethiodides by refluxing with ethyl iodide in isopropyl ether.

1,1-Dimethyl-4,4-diphenyl-3-piperidonium Iodide.—A mixture of 5 ml. of absolute ethanol, 5 ml. of acetone, 0.75 g. of 1,1-dimethyl-4,4-diphenyl-3-piperidonium bromide and 0.5 g. of sodium iodide was heated to the boiling point and then filtered. The product, which separated from the cooled filtrate, melted at 201.5–202° after recrystallization from absolute ethanol; mixed m.p. with methiodide of Ia was 201.5–202.5°.

Anal. Calcd. for $C_{19}H_{22}NOI$: N, 3.44. Found: N, 3.36, 3.39.

1,1,2-Trimethyl-4,4-diphenyl-3-piperidonium Iodide.—A mixture of 5 ml. of absolute ethanol, 5 ml. of acetone, 0.6 g. of 1,1,2-trimethyl-4,4-diphenyl-3-piperidonium bromide and 0.4 g. of sodium iodide was heated to the boiling point and then filtered. The product, which separated from the cooled filtrate, melted at 199–200.5° after recrystallization from absolute ethanol; mixed m.p. with the methiodide of Ib was 199–200°.

Anal. Calcd. for $C_{20}H_{24}NOI$: N, 3.32. Found: N, 3.26, 3.23.

Isolation of VII or VIII.—The mother liquors obtained from the purification of the hydrochloride of 1-ethyl-2-methyl-4,4-diphenyl-3-piperidone were concentrated under reduced pressure. The residue was taken up in acetone and treated with decolorizing charcoal. After filtration isopropyl ether was added until turbidity was produced. Crystals separated from the cooled solution which, after recrystallization from acetone, sintered at 100° and melted at 150–151°.

Anal. Calcd. for $C_{21}H_{28}ONCl$: Cl, 9.91. Found: Cl, 9.69.

Bromination of 6-Dimethylamino-4,4-diphenyl-3-hexanone Hydrobromide at Room Temperature.—A solution of 18.5 g. of the hydrobromide in 75 ml. of glacial acetic acid was shaken and a solution of 7.8 g. of bromine in 10 ml. of glacial acetic acid was slowly added. The bromine was absorbed very rapidly. Yellow crystals which melted at 99–100° with decomposition and weighed 22.4 g. (85%) separated gradually. The melting point of the product was lower after recrystallization from acetic acid. It gave the best analysis after being dried under 2 mm. pressure.

Anal. Calcd. for $C_{20}H_{26}ONBr_3$: C, 44.79; H, 4.89; N, 2.61; Br, 44.72. Found: C, 45.10; H, 4.88; N, 2.64; Br, 44.95.

3-Dimethylamino-1,1-diphenylpropane Hydrobromide.—To a solution of 14.6 g. (0.05 mole) of γ-diethylamino-α,α-diphenylbutyronitrile in 400 ml. of isopropyl alcohol there was added 40 g. (1.74 moles) of sodium. The mixture was allowed to reflux until most of the sodium had reacted. After refluxing for two hours the excess sodium was decomposed with a 50% solution of ethanol and water. The mixture was extracted with ether and the ether extract was dried over magnesium sulfate. The solution was filtered, the ether removed, and the residue was dissolved in 20 ml. of absolute ethanol and 48% hydrobromic acid was added until the mixture was acid to congo red paper. The solvent was removed under reduced pressure and the residue placed in an evaporating dish where crystallization occurred. After recrystallization from a mixture of absolute ethanol and isopropyl ether, the product melted at 136–137° and weighed 10.5 g.

Anal. Calcd. for $C_{19}H_{26}NBr$: N, 4.02; Br, 22.94. Found: N, 3.93; Br, 23.20.

A mixed melting point of this material with that obtained from the preparation of the diethylamino ketones showed no depression.

BETHLEHEM, PENNA.

[CONTRIBUTION FROM THE CHEMICAL LABORATORIES OF THE JOHNS HOPKINS UNIVERSITY]

Anomalous Displacements in the Pyrrole Series[1]

BY ALSOPH H. CORWIN AND GEORGE G. KLEINSPEHN[2,3]

RECEIVED DECEMBER 19, 1952

In an attempt to prove the structure of 2-bromo-3-methyl-4-carbethoxypyrrole, the Gattermann hydrogen cyanide-hydrogen chloride formylation was employed. The principal product isolated was 2-chloro-3-methyl-4-carbethoxy-5-formylpyrrole, along with 2-formyl-3-methyl-4-carbethoxy-5-chloropyrrole and 2-formyl-3-methyl-4-carbethoxypyrrole. Formylation using hydrogen bromide gave 2-bromo-3-methyl-4-carbethoxy-5-formylpyrrole and 2-formyl-3-methyl-4-carbethoxypyrrole. Differentiation between the 2-chloro- and the 2-bromoaldehyde by the method of mixed melting points failed. Possible mechanisms for the anomalous displacements are advanced. These anomalies constitute a definite limitation to the usefulness of the Gattermann aldehyde synthesis. Other displacement reactions are also presented.

Recently initiated investigations in this Laboratory of a proposed new synthetic route to chlorophyll-type porphyrins posed the problem of preparing 2-bromo-3-methyl-4-carbethoxypyrrole (II). It was decided to attempt preparation of this intermediate by means of a selective monobromination of 3-methyl-4-carbethoxypyrrole (I),[4a,5a] a substance which is best obtained from 2,4-dicarb-

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(1) Studies in the Pyrrole Series. XXIII. Paper XXII, K. W. Doak and A. H. Corwin, THIS JOURNAL, **71**, 159, 4165 (1949). A portion of this paper is taken from the doctoral dissertation of George G. Kleinspehn, The Johns Hopkins University, Baltimore, Md.

(2) du Pont Fellow in Chemistry, 1950–1951.

(3) Public Health Service Postdoctorate Research Fellow of the National Institutes of Health, 1951–1952.

(4) H. Fischer and O. Wiedemann, *Z. physiol. Chem.*, **155**, (a) 58, (b) 59 (1926).

(5) A. H. Corwin and P. Viohl, THIS JOURNAL, **66**, (a) 1145, (b) 1143 (1944).