g. (88%) of the desired **tetrahydroisoquinoline I**, b.p. 137–139° at 0.5 mm., n^{25}_D 1.5283, λ^{EtOH}_{max} 285 mμ (log ε 3.59), λ^{EtOH}_{min} 254 mμ (log ε 2.75).

Anal. Calcd. for $C_{16}H_{25}NO_2$: C, 72.96; H, 9.57. Found: C, 72.75; H, 9.62.

The styphnate exhibited m.p. 212–214° after recrystallization from ethanol.

Anal. Calcd. for $C_{22}H_{28}N_4O_{10}$: C, 51.96; H, 5.55. Found: C, 52.23; H, 5.65.

The picrate melted at 185–187°.

Anal. Calcd. for $C_{22}H_{28}N_4O_9$: C, 53.65; H, 5.73. Found: C, 53.81; H, 6.07.

In another experiment, the base, prior to distillation, was chromatographed on alumina and the individual fractions (eluted with benzene) were converted to the picrate. In each instance the same picrate was obtained, an observation which was considered further evidence for the homogeneity of the Bischler–Napieralski cyclization product.

1-Isopropyl-2-methyl-6,7-dimethoxy-1,2,3,4-tetrahydroisoquinoline (II).—This substance was prepared exactly as the higher homolog and only the physical constants of the intermediates are listed:

N-isobutyl homoveratryl amide, m.p. 102.5–103.5°. *Anal.* Calcd. for $C_{14}H_{21}NO_3$: C, 66.90; H, 8.42. Found: C, 67.18; H, 8.74.

1-Isopropyl-6,7-dimethoxy-3,4-dihydroisoquinoline, b.p. 128–129° at 1.2 mm., n^{25}_D 1.5606. *Anal.* Calcd. for $C_{14}H_{19}NO_2$: C, 72.07; H, 8.21. Found: C, 72.14; H, 8.36.

The methiodide possessed nearly the same m.p. (200–202°) as the higher homolog described above. *Anal.* Calcd. for $C_{15}H_{22}NIO_2$: C, 48.01; H, 5.91. Found: C, 47.88; H, 6.17.

1-Isopropyl-2-methyl-6,7-dimethoxy-1,2,3,4-tetrahydroisoquinoline (II), b.p. 128–129° at 1.0 mm., n^{25}_D 1.5357, λ^{EtOH}_{max} 285 mμ (log ε 3.60), λ^{EtOH}_{min} 254 mμ (log ε 2.77). *Anal.* Calcd. for $C_{15}H_{23}NO_2$: C, 72.25; H, 9.30. Found: C, 72.17; H, 9.31.

The picrate was recrystallized from methanol, m.p. 155.5–157°. *Anal.* Calcd. for $C_{21}H_{26}N_4O_9$: C, 52.71; H, 5.48. Found: C, 52.65; H, 5.61.

Permanganate Oxidation of 1-Isobutyl-2-methyl-6,7-dimethoxy-1,2,3,4-tetrahydroisoquinoline (I).—A solution of 22.8 g. of the base I in 100 cc. of 10% sulfuric acid was made just alkaline with solid potassium hydroxide and then treated at room temperature in short intervals with a 15% solution of potassium permanganate. After 120 g. of permanganate had been added, the reaction mixture was heated on the steam-bath and an additional 34 g. of the oxidizing agent was added over a period of two hours; the oxidation was then permitted to continue at room temperature overnight. The excess permanganate was decomposed with sulfur dioxide, the clear solution was acidified with concentrated sulfuric acid and extracted continuously with ether for four days. During the extraction, a crystalline precipitate separated at the interface which was filtered and recrystallized from methanol to yield 1.3 g. of colorless needles of the **N-methyl imide of 3,4-dimethoxyphthalic acid** (*m*-**hemipinic acid**),[10] m.p. 269–270° (sublimation starting at *ca.* 225°).

Anal. Calcd. for $C_{11}H_{11}NO_4$: C, 59.72; H, 5.01. Found: C, 59.98; H, 5.19.

A 0.5-g. sample of the imide was cleaved by refluxing for one hour with 20% sodium hydroxide solution and furnished 0.4 g. of *m*-hemipinic acid, m.p. 201–202°; after solidification and remelting, m.p. 176–177° was observed.[11] Recrystallization from methanol–benzene changed the m.p. to 190–191° (m.p. 177° after resolidification); the variable melting points recorded[12] for *m*-hemipinic acid have been ascribed to solvation and/or rate of heating.

A more suitable derivative for characterization purposes is ***m*-hemipinic acid dimethyl ester** prepared in quantitative yield by diazomethane esterification of the acid; m.p. 88–89° (from ether), undepressed upon admixture with an authentic specimen.[7]

Anal. Calcd. for $C_{12}H_{14}O_6$: C, 56.69; H, 5.55. Found: C, 56.71; H, 5.84.

In another oxidation carried out as above but using only one-tenth the quantities listed, the residue from the ether extraction was steam distilled and the distillate, containing the volatile "stench acids," was again extracted continuously with ether. The resulting acid fraction was converted to the sodium salt and then by successive treatments with thionyl chloride and aniline into the anilide. Chromatography of the crude anilide fraction on 200 g. of neutral alumina (activity III) yielded four main fractions upon elution with hexane–benzene (1:1), benzene, ether and methanol. Recrystallization of the benzene fractions from hexane furnished 0.1 g. of **isobutyric acid anilide**, m.p. 101–102°, undepressed on admixture with authentic anilide (m.p. 101–102°) but depressed to 86–92° when mixed with isovaleric acid anilide. The ether and methanol eluates were rechromatographed and elution with benzene–ether mixtures gave 0.03 g. of **isovaleric acid anilide**, m.p. 106–107°. A mixture with authentic isovaleric acid anilide (m.p. 106.5–107.5°) showed the same melting point, while a 20° depression was observed on admixture with isobutyric acid anilide.

That the isobutyric acid was not formed to any appreciable extent by oxidation of isovaleric acid was demonstrated in appropriate blank experiments.

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(10) We are grateful to Prof. V. Deulofeu (Buenos Aires) and H. Schmid (Zürich) for samples of *m*-hemipinic acid.

(11) *m*-Hemipinic acid anhydride is reported to melt at 175° (Y. Hirshberg, D. Lavie and E. D. Bergmann, (*J. Chem. Soc.*, 1034 (1951)).

(12) M.p. 174–175° (G. Goldschmiedt, *Monatsh.*, **9**, 772 (1888)); m.p. 194–195° (A. W. Gilboy, W. H. Perkin and J. Yates, *J. Chem. Soc.*, 1405 (1901)): m.p. 203° (W. H. Perkin, Jr., G. A. Edwards and F. W. Stoyle, *ibid.*, 199 (1925)).

Reactions of Long-chain Amines. IV. Preparation of N-Alkylpyrrolidines, N,N-Dialkylpyrrolidinium Chlorides and N,N-Dialkylpiperidinium Chlorides[1]

BY JOHN G. ERICKSON AND JOAN S. KEPS

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von Braun[2] has described the preparation of methyl-, ethyl-, propyl- and amylpyrrolidines by heating 1,4-dibromobutane or 1,4-diiodobutane with the corresponding amines. In each case an excess of amine was used as acid acceptor. We have found that long-chain alkylpyrrolidines may be prepared conveniently by heating the amines with a slight excess of the commercially available 1,4-dichlorobutane. Sodium carbonate or other inorganic bases may be used as acid acceptors. Despite the comparative unreactivity of both the amines and the dichlorobutane, good yields of product are obtained.

The preparation of long-chain N-alkyl-piperidines by reactions of primary amines with 1,5-dibromopentane has been studied already.[3] von Braun[4] heated 1,5-dibromopentane with several secondary amines and thereby obtained piperidinium bromides. He used piperidine, diethylamine, diisoamylamine and methylaniline. Two moles of amine were heated with one of dibromopentane. We have prepared long-chain N,N-dialkylpyrrolidinium chlorides and N,N-dialkylpiperidinium chlorides in good yield by heating secondary amines with 1,4-dichlorobutane and 1,5-dichloropentane, respectively. An excess of dichloro compound was used

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(1) Paper No. 168, Journal Series, General Mills, Inc., Research Department.

(2) J. von Braun, *Ber.*, **44**, 1252 (1911); **49**, 966, 2629 (1916).

(3) J. A. Goodson, L. J. Goodwin, J. H. Gorvin, M. D. Goss, K. S. Kirby, J. A. Lock, R. A. Neal, T. M. Sharp and W. Solomon, *Brit. J. Pharmacol.*, **3**, 49 (1948); through *C. A.*, **43**, 3380 (1949).

(4) J. von Braun, *Ber.*, **41**, 2156 (1908).

TABLE I

N-ALKYLPYRROLIDINES, N,N-DIALKYLPYRROLIDINIUM CHLORIDES AND N,N-DIALKYLPIPERIDINIUM CHLORIDES

Compound	Time of heating, hr.	Yield, %	B.p. °C.	B.p. Mm.	M.p., °C.	Formula	Carbon, % Calcd.	Carbon, % Found	Hydrogen, % Calcd.	Hydrogen, % Found	Chlorine, % Calcd.	Chlorine, % Found	Nitrogen, % Calcd.	Nitrogen, % Found
N-Dodecylpyrrolidine	11.5	64	90–105	0.03–0.05	....	....	...	...	...	...	..	..	...	...
Picrate	..	..	.....	....	59–60.5	$C_{22}H_{36}N_4O_7$	56.40	56.94	7.75	7.67	..	..	11.96	12.02
N-Octadecylpyrrolidine	14	53	140–168	0.04–0.05	....	....	...	...	...	...	..	..	...	...
Picrate	..	..	.....	....	69–70	$C_{28}H_{48}N_4O_7$	60.86	61.59	8.75	8.81	..	..	10.14	10.30
Pyrrolidinium chlorides														
N,N-Didodecyl	17	68	.....	....	114–144^a	$C_{28}H_{58}ClN$	75.70	75.40	13.16	12.99	7.98	8.46	3.15	3.29
N,N-Dioctadecyl-	6.5	70	.....	....	159–161.5	$C_{40}H_{82}ClN$	78.42	78.91	13.49	13.45	5.79	4.93	2.29	2.26
Piperidinium chlorides														
N,N-Didodecyl	23.5	72	.....	....	179–180	$C_{29}H_{60}ClN$	76.00	75.38	13.20	13.24	7.74	7.43	3.06	2.81
N,N-Dioctadecyl-	26	94	.....	....	174.5–176.5	$C_{41}H_{84}ClN$	78.62	78.30	13.52	13.73	5.66	5.11	2.23	2.16

[a] Wax-like solid.

and in each case the acid acceptor was sodium carbonate. Long chain N,N-dialkylpiperidinium compounds have been prepared previously by alkylation of piperidine with alkyl bromides.[5]

The surface-active properties of these pyrrolidinium and piperidinium chlorides will be described elsewhere.

Acknowledgment.—Analyses were performed by James Kerns.

Experimental

Materials Used.—The dodecylamine was prepared by careful fractionation of commercial coco amine through a Podbielniak column. Octadecylamine was prepared by hydrogenation of stearonitrile which had been distilled through a Podbielniak column. Following the hydrogenation, the octadecylamine was distilled to remove secondary and tertiary amines. Didodecylamine and dioctadecylamine were prepared by hydrogenation of carefully fractionated nitriles. The secondary amines were purified by distillation and recrystallization from alcohol.

Procedure.—A mixture of the primary or secondary amine, dichloro compound (20% excess), sodium carbonate (120% excess) and butyl alcohol was stirred and refluxed for the time shown in Table I. The mixture was filtered and the butyl alcohol was distilled off. In the case of the pyrrolidines the product was then obtained by vacuum distillation of the residue. With the quaternary ammonium chlorides, the residue was recrystallized from ethyl acetate. Table I summarizes the properties and analytical values of the products. The pyrrolidines were analyzed as their picrates.

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(5) R. S. Shelton, M. G. Van Campen, C. H. Tilford, H. C. Lang, L. Nisonger, F. J. Bandelin and H. L. Rubenkoenig, THIS JOURNAL, **68**, 757 (1946).

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The Nucleophilicity of the Cyanide Ion

BY M. FREDERICK HAWTHORNE, GEORGE S. HAMMOND AND BRUCE M. GRAYBILL

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Edwards[1] has recently found that the nucleophilic constants, n, in the equation of Swain and Scott[2]

$$\log k/k_0 = ns \qquad (1)$$

are a linear function of the oxidation potentials of the various nucleophiles.

$$2N: \rightleftarrows N:N + 2e^- \qquad (2)$$

Furthermore, Edwards found that the rates of nucleophilic displacements on carbon were only one group of a wide variety of reactions of nucleophilic reagents which could be correlated on a common basis by equation 3.

$$\log k/k_0 = \alpha E_n + \beta H \qquad (3)$$

The constants α and β are characteristic of the substrates and E_n and H are parameters defined, respectively, in terms of the oxidation potentials and basicity constants of the nucleophiles. Since the values of β are rather small for carbon compounds which undergo nucleophilic displacements, equation 3 reduces approximately to equation 1 for such reactions. By means of the relationship between nucleophilic reactivity and oxidation potential it was possible to correlate the rates of displacements by a number of nucleophiles which were not included by Swain and Scott.

Since the agreement between calculated and observed rates was generally within an order of magnitude, it is significant that the reaction of cyanide with iodoacetate ion[3] was slower by two orders of magnitude than would be anticipated on the basis of the oxidation potential and basicity constant of the former. Since the values of the formation constants of cyanide complex ions are, on the other hand, larger than calculated, it appears that there is some genuine anomaly involved in the reactivity of cyanide. However, its reactivity in displacements has been measured in only one reaction involving a substrate which might be considered as atypical.[4] For this reason, and because of related interests, we have measured the rate of reaction of cyanide with methyl iodide, a classic substrate in displacement reactions.

The reaction was carried out in 50% aqueous dioxane at 25.5° and the rate of displacement by hydroxide on methyl iodide under the same conditions was measured as a control. The data are presented in Table I. The s value for methyl iodide in water at 25° was evaluated from data in the literature[5] as 1.15. The nucleophiles used in

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(1) J. O. Edwards, THIS JOURNAL, **76**, 1540 (1954).

(2) C. G. Swain and C. B. Scott, *ibid.*, **75**, 141 (1953).

(3) C. Wagner, *Z. physik. Chem.*, **A115**, 121 (1925).

(4) For example, it occurred to us that some of the other nucleophiles studied[3] might react, at least in part, by attack on iodine rather than carbon or that the charge type of the substrate may lead to deviations such as are observed with the mustard cation, a positively charged substrate.

(5) E. A. Moelwyn-Hughes, *Proc. Roy. Soc. (London)*, **A164**, 295 (1938); **A194**, 540 (1949).