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. phyzik. 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).

the correlation were water, hydroxide and thiosulfate. Similar data from the same source gave *s* values of 1.00 and 1.03 for methyl chloride and methyl bromide, respectively. This lends reasonable assurance that methyl iodide is properly placed on the Swain and Scott scale.

TABLE I

THE REACTION OF METHYL IODIDE WITH CYANIDE AND HYDROXIDE IONS IN 50% AQUEOUS DIOXANE AT 25.5°

Concn., mole/l.	Nucleophile	Concn., mole/l.	k_2,[a] l./mole min.
0.1268	CN^-	0.168	3.72×10^{-1}
.0708	CN^-	.224	5.05×10^{-1}
.1868	CN^-	.0890	4.07×10^{-1}
.1110	OH^-	.1475	1.55×10^{-2}
.0786	OH^-	.1840	1.76×10^{-2}

[a] Mean $k_{CN} = 4.4 \times 10^{-1}$ l./mole min. Mean $k_{OH} = 1.6 \times 10^{-2}$ l./mole min.

The data for log k/k_0 for iodoacetate[3,6] are plotted against the *n* values of various nucleophiles in Fig. 1 and those for methyl iodide are presented similarly in Fig. 2. The iodoacetate data give a value of 5.1 for the *n* value of cyanide. The cyanide rate is included in Fig. 2 using this figure. The agreement may be considered to be ideal since the cyanide rate is faster than predicted from the plot by almost the same amount as the increase in the hydroxide rate in the mixed solvent as compared with water solution.

It is instructive to consider the lack of correlation of the electrode potential for the couple

$$2CN^- \rightleftarrows (CN)_2 + 2e^- \qquad (4)$$

with the *n* value of the cyanide ion. While there is some variation in the literature values for the standard free energy of cyanogen, the value of ±0.19 for the electrode potential which is listed by Latimer[7] is based upon the value for the heat of combustion of 70.8 kcal. per mole which is close to the highly accurate value recently reported.[8] From consideration of the *n* value of 5.1 for cyanide and the Edwards equation one would estimate a value of 107 kcal. if the value of 39.6 kcal. per mole is accepted for the standard free energy of aqueous cyanide ion.[8] While the quantitative significance of this discrepancy is questionable there is a strong indication that cyanogen is stabilized by some factor which is not operative in the transition states for the nucleophilic displacement reactions. This is reasonable in view of the fact that cyanogen is a highly conjugated system and therefore may possess an uncommonly high resonance energy. This is borne out by the observation that the C–C bond distance is reported to be 1.37 ± 0.02 Å. which is close to the aromatic C–C distance.[9] If this explanation of the deviant behavior of cyanide in displacement reactions is accepted it also implies that π-bonding contributes a substantial amount to the stability of metal cyanide complexes since they show deviations in the opposite sense.

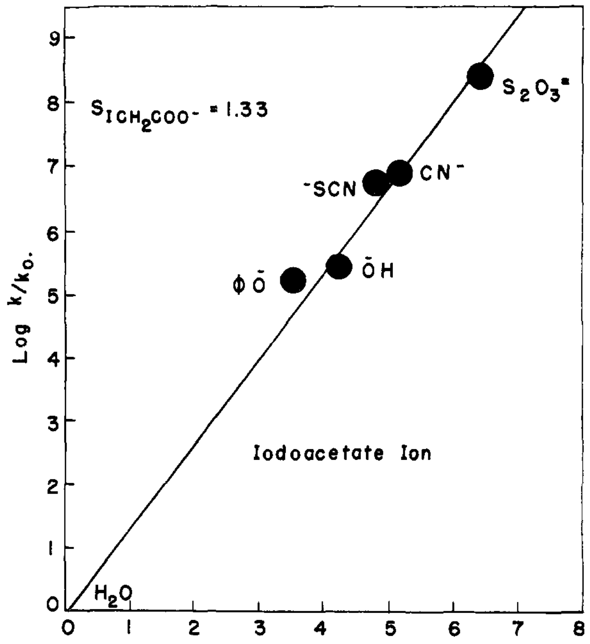

Fig. 1.

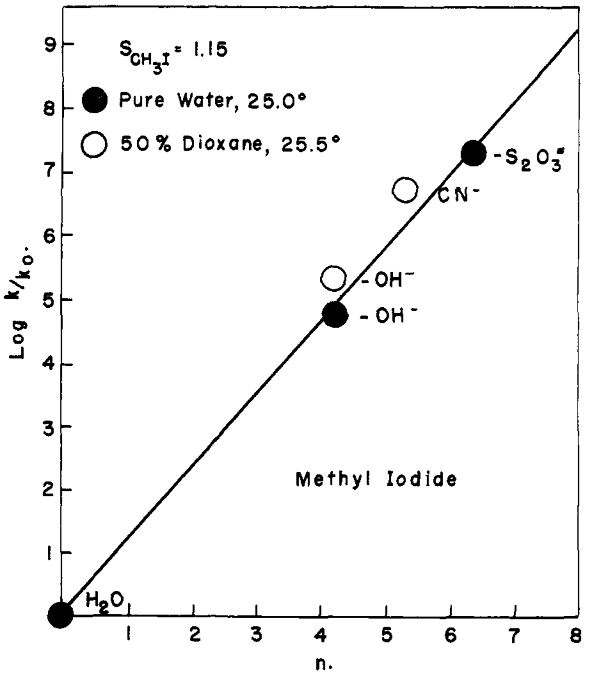

Fig. 2.

Experimental

Dioxane was purified by the usual acid treatment followed by eventual distillation from sodium.

The methyl iodide was Eastman White Label grade and was used without further purification. The potassium cyanide was reagent grade (98%) as was the potassium hydroxide.

Kinetic Procedure.—All kinetics were measured at 25.5 ± 0.05°. The reaction vessels were 125-ml. glass-stoppered erlenmeyer flasks from which 5-ml. aliquots were removed at intervals.

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(6) H. J. Backer and W. H. Van Mels, *Rec. trav. chim.*, **49**, 177, 363, 457 (1930).

(7) W. Latimer, "Oxidation Potentials," 2nd Ed., Prentice–Hall, Inc., New York, N. Y., 1952.

(8) J. W. Knowlton and E. J. Prosen, *J. Research Natl. Bur. Standards*, **46**, No. 6, 489 (1951).

(9) G. W. Wheland, "The Theory of Resonance and Its Application to Organic Chemistry," John Wiley and Sons, Inc., New York, N. Y., 1944.

Stock solutions (*ca.* 0.3 *M*) were prepared in dioxane diluted to twice its original volume with distilled water. A methyl iodide solution was similarly prepared and its concentration was determined from infinity titers. At zero time the proper volumes of the reactant solutions were mixed rapidly and the time was recorded. Zero time titers were determined by dilution of the stock hydroxide or cyanide solutions with water in the same manner as in the runs. Infinity titers were determined after at least ten half-lives and gave reproducible results.

The hydroxide ion runs were monitored titrimetrically using 0.145 *M* hydrochloric acid and brom thymol blue indicator. The runs using cyanide ion were followed by the argentimetric titration of cyanide ion in the presence of added ammonium hydroxide and potassium iodide, using an 0.0200 *N* silver nitrate solution.[10] Since cyanide ion is only slightly hydrolyzed in water at the concentrations employed the equilibrium

$$CN^- + H_2O \rightleftharpoons HCN + OH^- \qquad (5)$$

was considered for practical purposes to lie completely on the left.

All rate data were treated graphically by a plot of log $(a - x)/(b - x)$ against time and the results are shown in Table I. In each case the reaction was followed to at least 80% reaction and a smooth linear relationship obtained.

Acknowledgment.—The authors wish to thank the Rohm and Haas Co., Redstone Arsenal Research Division, and the Ordnance Corps of the United States Army for the financial support of this work.

[10] I. M. Kolthoff and E. B. Sandell, "Textbook of Quantitative Inorganic Analysis," The Macmillan Co., New York, N. Y., 1948, p. 574.

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9(11)-Dehydrotestosterone and Esters

BY F. W. HEYL AND M. E. HERR

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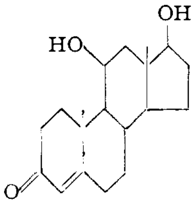
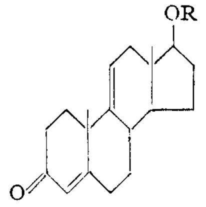
11β-Hydroxytestosterone (I) used for the work herein described was prepared from adrenosterone (V) by the method reported recently.[1] Dehydration of this compound (I) by *trans* elimination of the elements of water from carbon atoms 9 and 11 did not proceed smoothly according to published methods.[2] An efficient dehydration of this compound was effected, however, by using a two-phase system of benzene–ether and 18% hydrochloric acid; 9(11)-dehydrostestosterone (IIa) was obtained in 78% yield. This compound was esterified to form the propionate IIb, benzoate IIc and β-cyclopentylpropionate (IId).

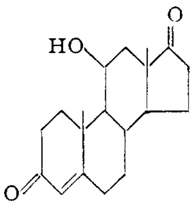
By a similar procedure, but using a higher concentration of acid, 11β-hydroxy-4-androstene-3,17-dione[1] (III) was dehydrated to 4,9(11)-androstadiene-3,17-dione (IV) in 87% yield.[3] This dienedione IV was prepared also by the chromic acid oxidation of 9(11)-dehydrotestosterone (IIa).



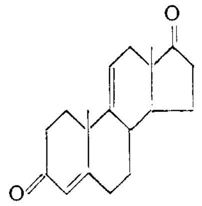
I



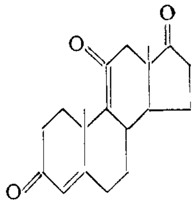
II a, R = H
b, R = COC_2H_5
c, R = COC_6H_5
d, R = $COC_2H_4CHC_4H_8$



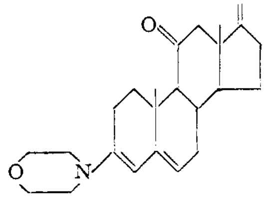
III



IV



V



VI

In studying the merits of the above two mentioned routes to IV it was determined that the method of dehydrating 11β-hydroxytestosterone (I) followed by chromic acid oxidation of IIa, although involving one more step from adrenosterone, was preferred over the procedure whereby III was dehydrated directly to IV. The reason for this becomes apparent when it is noted that the yield of hydroxy-dione III from adrenosterone was only 44% and involved a chromatographic purification.[1] On the other hand, the yield of I from adrenosterone was consistently better than 73% and the product was obtained by direct crystallization.[1] Moreover the total crude 11β-hydroxytestosterone (I) could be carried through the steps of dehydration and oxidation to give a better over-all yield of IV from adrenosterone (V). In the interest of brevity only the experiments conducted on the purified intermediates are described below.

During the course of this work we had occasion to study the reaction of morpholine with adrenosterone (V). It has been shown previously that the reaction of pyrrolidine in excess with V led to the facile isolation of the bis-enamine, 3,17-di-(N-pyrrolidyl)-3,5,16-androstatrien-11-one.[1] By comparison when morpholine was used, under the same conditions, the product isolated was 3-(N-morpholinyl)-3,5-androstadiene-11,17-dione (VI).

Experimental

9(11)-Dehydrotestosterone (IIa).—A two-phase mixture of 2.50 g. of 11β-hydroxytestosterone,[1] 250 ml. of benzene, 200 ml. of ether, 100 ml. of concentrated hydrochloric acid and 100 ml. of water was stirred vigorously and heated at gentle reflux for 18 hours. The aqueous acid layer was separated

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[1] M. E. Herr and F. W. Heyl, THIS JOURNAL, **75**, 5928 (1953). Alternative methods of preparation have been reported by O. Mancera, G. Rosenkranz and F. Sondheimer, *J. Chem. Soc.*, 2189 (1953); S. Bernstein, R. H. Lenhard and G. H. Williams, *J. Org. Chem.*, **18**, 1166 (1953).

[2] (a) C. W. Shoppee and T. Reichstein, *Helv. Chim. Acta*, **24**, 351 (1941); **26**, 1316 (1943); (b) H. Heymann and L. F. Fieser, THIS JOURNAL, **74**, 5939 (1952).

[3] S. Bernstein, R. H. Lenhard and J. H. Williams, *J. Org. Chem.*, **19**, 41 (1954), used 20% hydrochloric acid–glacial acetic acid to carry out this reaction according to the method of T. Reichstein, U. S. Patent 2,409,798; they report an inconsequential yield of IV by this procedure.