6 and 7. The reduction in the proportion of radioactivity found in the cellulose from these cultures shows that impurities must have been present in experiments 1 to 4, and accounts for the higher value recorded.

As may be seen, the greater proportion of the C^{14} in each culture can be accounted for in the CO_2 evolved. The liquid culture products, exclusive of the CO_2 and cellulose, were radioactive and accounted for the remainder of the activity.

These observations indicate that, while both the ethanol and acetate are extensively metabolized by *A. xylinum*, neither of these 2-carbon compounds, nor any fragments thereof, appeared in the final cellulose product. It is interesting to note in this same respect the report[1] that this microorganism cannot synthesize cellulose from glycol, another 2-carbon compound. This information suggests that the use of any 2-carbon metabolic intermediate may be similarly restricted, and further investigation of the mechanism of cellulose synthesis by *A. xylinum* may well deal with this possibility.

The results of the present experiments indicate conclusively that even in the presence of D-glucose, neither ethanol nor acetate contribute carbon to the cellulose synthesis. The enhanced yields of cellulose are therefore caused in some other way.

Acknowledgment.—We wish to express our gratitude to the United States Atomic Energy Commission for the grant which supported this research. We are also indebted to Dr. B. M. Tolbert of the University of California for making available samples of ethanol-1-C^{14} and sodium acetate-2-C^{14} for some of these experiments, and to Dr. H. S. Isbell and his associates at the National Bureau of Standards for the vibrating reed measurements.

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Regularities in the Basicity of Some Tertiary Ethylenediamines, Trimethylenediamines and 2-Hydroxytrimethylenediamines

BY ALEXANDER GERO

Pharmacological studies on certain tertiary amines called for an investigation of their basicities in aqueous solution. The amines were *sym*-disubstituted ethanes X-CH$_2$-CH$_2$-X (I), propanes X-CH$_2$-CH$_2$-CH$_2$-X (II), and 2-propanols X-CH$_2$-CHOH-CH$_2$-X (III), the substituents X being diethylamino (A), pyrrolidino (B), piperidino (C) or morpholino (D) groups linked to the ends of the carbon chain by their nitrogen atoms. These number and letter symbols will be used throughout the present paper; thus IIID is 1,3-dimorpholino-2-hydroxypropane
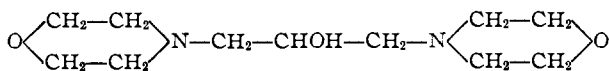
IA is tetraethylethylenediamine (C$_2$H$_5$)$_2$N-CH$_2$-CH$_2$-N(C$_2$H$_5$)$_2$, etc.

IA,[1] IIA,[2] IIIA,[3] IC,[4] IIC[5] and IIIC[6] are known compounds, the others are first described here. All are colorless or pale yellow oils of characteristic basic odor, with the exception of ID which is a solid, melting at 64°. Their corrected boiling points, determined at 760 ± 5 mm. pressure, are shown in Table I.

TABLE I
BOILING POINTS

	A	B	C	D
I	194	236	273	285
II	214	256	292	317
III	243	286	328	352

Table II shows the measured thermodynamic ionization constants as pK_A values; each column shows both the first and second ionization constants of the respective bases, and the difference Δ between the two ionization constants.

TABLE II
IONIZATION CONSTANTS

	A		B		C		D	
I	9.55	6.18	9.47	6.30	9.47	6.25	6.65	3.63
	($\Delta = 3.37$)		($\Delta = 3.17$)		($\Delta = 3.22$)		($\Delta = 3.02$)	
II	10.18	8.20	10.04	8.03	9.95	7.90	7.25	6.25
	($\Delta = 1.98$)		($\Delta = 2.01$)		($\Delta = 2.05$)		($\Delta = 2.00$)	
III	9.80	7.74	9.73	7.75	9.48	7.47	6.98	5.00
	($\Delta = 2.06$)		($\Delta = 1.98$)		($\Delta = 2.01$)		($\Delta = 1.98$)	

In each of the lettered series (A–D) the trimethylenediamine is the strongest base, the ethylenediamine the weakest, with the 2-hydroxytrimethylenediamine in between. The difference between the first and second ionization constants is uniformly close to two pK_A units in all bases which have a three-carbon chain between the two N atoms, and more than three pK_A units in the ethylenediamines. Similar differences (2.01 and 3.07 pK_A units, respectively) were found for unsubstituted trimethylenediamine and ethylenediamine, and interpreted in terms of induction and hydrogen bonding.[7]

Within each numbered series (I, II, III) there is little difference between the A, B and C compounds, but the D compounds are definitely weaker bases. This may be attributed to the inductive effect of the oxygen atom which reduces the basicity of the amino group much as it increases the acidity of a carboxyl group under similar circumstances (*cf.* pK_A of propionic acid, 4.89, and of lactic acid, 3.15). The same effect may be called upon to explain why series III is less basic than series II.

Experimental

The bases were prepared from the appropriate secondary amines and, respectively, ethylene bromide, trimethylene bromide and epichlorohydrin

$$4R_2NH + BrCH_2CH_2Br =$$
$$2R_2NH \cdot HBr + R_2NCH_2CH_2NR_2 \quad (I)$$
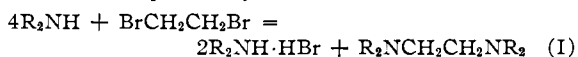
(1) A. W. Hofmann, "Jahresbericht ueber Forschritte der Chemie," 1861, p. 520.
(2) B. Flürscheim, *J. prakt. Chem.*, [2] **68**, 355 (1903).
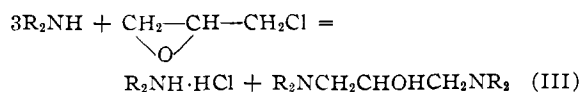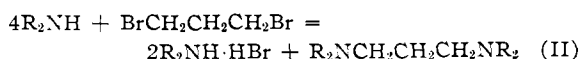(3) A. Reboul, *Bull. soc. chim.*, [2] **42**, 261 (1882).
(4) G. André, *Compt. rend.*, **126**, 1797 (1898).
(5) H. Hörlein and R. Kneisel, *Ber.*, **39**, 1434 (1906).
(6) L. Niemilowicz, *Monatsh.*, **15**, 129 (1894).
(7) A. Gero, THIS JOURNAL, **76**, 5158 (1954).

$4R_2NH + BrCH_2CH_2CH_2Br =$

$2R_2NH \cdot HBr + R_2NCH_2CH_2CH_2NR_2$ (II)

$3R_2NH + CH_2{-}CH{-}CH_2Cl =$
$\diagdown O \diagup$

$R_2NH \cdot HCl + R_2NCH_2CHOHCH_2NR_2$ (III)

As a representative example, the synthesis of 1,3-dimorpholinopropane (IID) is reported in detail: 8 g. of trimethylene bromide (Dow) and 14 g. (= 2% excess) of morpholine (Carbide & Carbon) were mixed with 20 ml. of dry benzene and placed in a flask fitted with reflux condenser. (Undiluted, morpholine and trimethylene bromide would react with explosive violence.) The mixture warmed up slightly and crystallization began soon. After standing overnight, the reaction mixture was refluxed for four hours on the water-bath, cooled, filtered from morpholinium bromide, the benzene removed and the residual oil distilled; yield 7.0 g. (77%).

TABLE III

NEW BASES

Compound	Formula	B.p., °C. at 760 ± 5 mm.	Nitrogen, % Calcd.	Found
IB	$C_{10}H_{20}N_2$	236	16.65	16.63
IIB	$C_{11}H_{22}N_2$	256	15.37	15.31
IIIB	$C_{11}H_{22}ON_2$	286	14.13	14.08
ID	$C_{10}H_{20}O_2N_2$	285	13.99	13.99
IID	$C_{11}H_{22}O_2N_2$	317	13.08	12.99
IIID	$C_{11}H_{22}O_3N_2$	352	12.17	12.14

The basicities were determined from the pH titration curves by means of the Henderson–Hasselbach equation. The pH titrations were carried out as described in detail for pyridine bases.[8]

(8) A. Gero and J. J. Markham, J. Org. Chem., 16, 1835 (1951).

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Inductive Effect and Hydrogen Bonding as Factors in the Base Strength of Polymethylenediamines

BY ALEXANDER GERO

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The following factors may be expected to be important for the base strength of polymethylenediamines $NH_2(CH_2)_nNH_2$: (1) the inductive effect of the two nitrogen atoms on each other will mutually hinder their basic action, the more so the closer they are, i.e., the smaller n is in the formula. (2) If one of the amino groups coördinates with a proton, its inductive effect on the other, non-ionic, amino group will be greatly enhanced. In this case the electrostatic repulsion between the positive N^+ and a H_3O^+ ion approaching the uncharged N also must be taken into consideration; this repulsion, being inversely proportional to the square of the distance between the two positive charges, should fall off even more rapidly with increasing distance between the two nitrogens. (3) Considerable intramolecular hydrogen bonding may be expected between the two amino groups if one of them is ionized and the other is not. This hydrogen bond should be especially strong in trimethylenediamine where it forms a six-membered chelate ring

$\diagup CH_2 \diagdown$
$CH_2 \qquad CH_2$
$| \qquad\qquad |+$
$H{-}N \qquad N{-}H$
$\diagup \quad \cdot H \diagup \diagdown$
$H \qquad\qquad H$
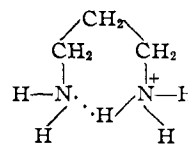
This chelate ring should stabilize the mono-cation of trimethylenediamine.

From the foregoing premises it may be concluded that ethylenediamine should be the weakest base among polymethylenediamines and that both ionization constants should increase with increasing length of the carbon chain, the second more than the first so that in long enough chains both ionization constants should become about equal. Besides, the first ionization constant (but not the second in which chelation cannot occur) of trimethylenediamine should be anomalously high.

A search of literature did not reveal any determinations of ionization constants of polymethylenediamines since those of Bredig[1] and Osaka[2] in the last century. Therefore this writer determined the thermodynamic ionization constants of the first four members of the polymethylenediamine series from their pH titration curves, by means of the Henderson–Hasselbach equation. The results (Fig. 1) bear out all predictions of the preceding paragraph, except that even in $n = 5$ the two ionization constants are not yet quite equal; but they are already so close as to make separate determination by pH titration barely possible.
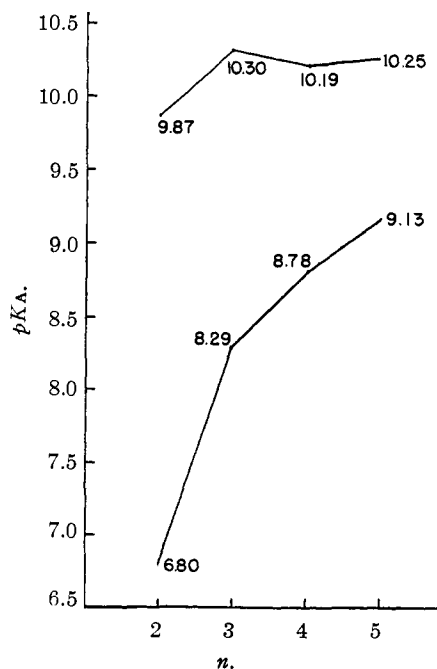

Fig. 1.

Experimental

Ethylenediamine was generously donated by Carbide & Carbon Chemicals Corp., trimethylenediamine by American Cyanamid Co. Putrescine and cadaverine were obtained from Bios Laboratories. All bases were purified by vacuum

(1) G. Bredig, Z. physik. Chem., 13, 289 (1894).

(2) Y. Osaka, ibid., 35, 661 (1900).