TABLE I

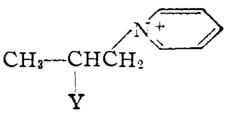
HALF-WAVE POTENTIALS IN VOLTS *vs.* S.C.E. OF SUBSTITUTED PROPYLPYRIDONIUM SALTS

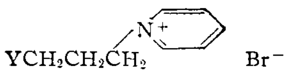
Salt	Aq. *p*H 7	Aq. *p*H 8	Aq. 0.05 *M* KOH	Aq. 0.05 *M* KNO_3	0.05 *M* LiCl in ethanol	0.02 *M* TEAB[a] in 90.5% dioxane
n-Propyl bromide	−1.38	−1.36	−1.37	−1.37, −1.43[b]	−1.29	−1.15
Isopropyl bromide		−1.40	−1.38	−1.37, −1.43[b]		−1.20
β-OH bromide	−1.36	−1.36	−1.37	−1.42		−1.23
β-Cl bromide	−1.22	−1.24	−1.23	−1.24, −1.40,[b] −1.72[c]		−1.10
β-Br bromide	−1.34	−1.33	−1.33	−1.33, −1.43,[b] −1.66[c]		−1.15
β-I bromide		−1.40	−1.39	−1.42	−0.19,[c] −1.35	
γ-OH bromide	−1.28	−1.28	−1.30	−1.28, −1.42[b]		−1.16
γ-Cl chloride	−1.12	−1.12	−1.13	−1.13		−1.03
γ-Br bromide	−1.18	−1.17	−1.18	−1.18, −1.38,[b] −1.70[c]		−1.10
γ-I iodide	−1.20	−1.19	−1.20	−1.23, −1.60[c]		−0.96

[a] Tetraethylammonium bromide. [b] Catalytic waves. [c] These waves are assumed to be halogen reduction waves.

are obtained with quaternary nitrogen salts such as methylpyridonium salts and trigonelline.

In the present investigation, the polarographic properties of a series of beta (I) and gamma (II)


I


II

substituted propylpyridonium halides were studied in relationship to structural variation. Recently reported[7] dissociation constants for these same isomeric pyridonium salts bear consideration in correlating structure and electron distribution within the propylpyridonium ion–molecule.

Experimental

The polarographic equipment, materials and characteristics were the same as described in previous reports from this Laboratory.[8,9] All measurements were at a drop-time equal to 3.00 sec. and at 25.00 ± 0.05°. The "*m*" value for the capillary was 2.00 mg. per second.

$m^{2/3}t^{1/6} = 1.907$ mg.$^{2/3}$ sec.$^{-1/2}$ (open circuit) at $h = 64$ cm.

Preparation of the various pyridonium salts was described recently.[7] The aqueous buffer solutions containing 0.05 *M* potassium dihydrogen phosphate with different concentrations of sodium hydroxide were made according to directions given by Britton.[10] Gelatin was found to be an excellent maximum suppressor in the aqueous solutions. It was employed at concentrations 0.01–0.05%. The use of a maximum suppressor generally made it possible to ascertain the catalytic hydrogen waves with greater certainty. Methyl cellulose was used as a suppressor at concentrations 0.1 to 0.2% in the alcohol solutions. Minimum quantities of suppressor were employed so that diffusion currents were not materially altered. A satisfactory maximum suppressor was not found for the polarographic waves in dioxane. Maxima obtained in these cases did not prevent accurate evaluation of the half-wave potentials. Dioxane used was purified by distillation from sodium.

Results and Discussion

The $E_{1/2}$ values (Table I) obtained for all of the pyridonium salts were unaffected, within experimental error, by the nature of the buffered or unbuffered aqueous solutions employed. Diffusion current was found to be directly proportional to concentration, and half-wave potential values were found to be unaffected by concentration change over the range investigated, 5×10^{-4} to 5×10^{-3} *M*, for the various pyridonium salts tested in both aqueous and non-aqueous solutions.

In all the aqueous solutions investigated slope analyses data (values 0.059 ± 0.002) indicated that all pyridonium salts are reduced at the dropping mercury cathode by a one electron reversible reaction. Slope values equal to 0.10 and greater showed that these pyridonium salts are irreversiby reduced in dioxane solutions. Lower half-wave potentials were observed in dioxane.

It is seen (Table I) that a particular substituent group has a more pronounced influence in lowering the half-wave potential when in the gamma position as compared to when it is in the beta position. This greater enhancement in the ease of polarographic reduction by the gamma substituted salts is apparently related to the smaller dissociation constants found for these pyridonium salts.[7] It thus seems that polarographic properties as well as dissociation constant data[7] both indicate the probability that field effects rather than static inductive or direct resonance effects cause the unique influence noted with the gamma substituted salts. A previous communication[7] from this Laboratory indicates the possible nature of the field effect in these cases.

Acknowledgment.—The support of this investigation by the Research Corporation is acknowledged with appreciation.

DEPARTMENT OF CHEMISTRY
UNIVERSITY OF PORTLAND
PORTLAND 3, OREGON

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[8] E. L. Colichman, *ibid.*, **74**, 722 (1952).

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[10] H. T. S. Britton, "Hydrogen Ions," Vol. I, D. Van Nostrand Co., New York, N. Y., 1943, p. 306.

Reactions of Long-chain Amines. I. Preparation of 4-Alkylmorpholines and 4,4-Dialkylmorpholinium Chlorides[1]

BY JOHN G. ERICKSON AND JOAN S. KEPS

RECEIVED JANUARY 25, 1954

Long-chain 4-alkylmorpholines (I) have previously been prepared by alkylation of morpholine[2] or by catalytic dehydration of N,N-bis-(2-hydroxyethyl)-alkylamines.[3] We have found that they may also be prepared by the reactions of the corre-

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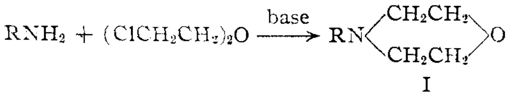
TABLE I

SUBSTITUTED MORPHOLINES

Substituents and positions	Yield, %	B.p. °C.	B.p. Mm.	Formula	Carbon, % Calcd.	Carbon, % Found	Hydrogen, % Calcd.	Hydrogen, % Found	Neut. equiv. Calcd.	Neut. equiv. Found
4-Dodecyl[a]	90	110–122	0.45–0.50	$C_{16}H_{33}NO$	75.35	75.42	13.05	12.76	255.4	260.5
4-Octadecyl[b]	88	160–175	.3	$C_{22}H_{45}NO$	77.81	78.39	13.36	13.54		
2,6-Dimethyl-4-dodecyl[c]	63	118–122	.4	$C_{18}H_{37}NO$	76.26	76.19	13.15	12.95	283.5	286
2,6-Dimethyl-4-octadecyl[d]	80	141–144	.03	$C_{24}H_{49}NO$	78.42	78.20	13.43	13.38	367.6	369

[a] A picrate could not be prepared. Styphnate, m.p. 112–113.5°. *Anal.* (calcd. and found): C, 52.79, 53.22; H, 7.25 7.30; N, 11.19, 10.63. [b] % N: Calcd., 4.12; found, 4.15. Picrate, m.p. 70–71°. *Anal.* (calcd. and found): C, 59.1, 59.2; H, 8.45, 8.67; N, 9.86, 9.49. [c] *p*-Toluenesulfonate m.p. 127–128°; N: calcd. 3.07, found 3.29. [d] M.p. 15–17°, n^{30}D 1.4602. *p*-Toluenesulfonate, m.p. 123–124.5°. *Anal.* (calcd. and found): C, 68.98, 68.83; H, 10.65, 10.57; N, 2.60, 2.74.

sponding primary amines with bis-(2-chloroethyl) ether. If bis-(1-chloro-2-propyl) ether is used, one obtains 4-alkyl-2,6-dimethylmorpholines. This

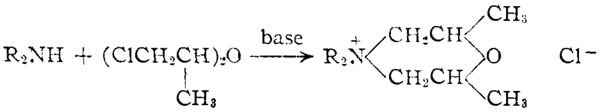


$$RNH_2 + (ClCH_2CH_2)_2O \xrightarrow{\text{base}} RN\begin{cases}CH_2CH_2\\CH_2CH_2\end{cases}O$$

I

type of cyclization has previously been employed with bis-(2-iodoethyl) ether and methylamine, ethylamine and benzylamine,[4] and with bis-(2-chloroethyl) ether and benzylamine,[5] ethylenediamine[6] and aromatic amines.[7–10] The reaction is conveniently carried out in refluxing butyl alcohol containing an alkali metal carbonate to neutralize the hydrogen chloride formed.

Secondary amines react with bis-(2-chloroethyl) ether and with bis-(1-chloro-2-propyl) ether to form cyclic quaternary ammonium chlorides. This may be illustrated with 4,4-dialkyl-2,6-dimethylmorpholinium chloride (II).



$$R_2NH + (ClCH_2\underset{\substack{|\\CH_3}}{CH})_2O \xrightarrow{\text{base}} R_2\overset{+}{N}\begin{cases}CH_2CH(CH_3)\\CH_2CH(CH_3)\end{cases}O \quad Cl^-$$

II

Such a result is unexpected in view of a report[11] that lower N-alkylanilines, heated with bis-(2-chloroethyl) ether, give only phenylmorpholine and alkyl chlorides. We have prepared these morpholinium chlorides in good yield by heating the reagents in butyl alcohol containing an alkali metal carbonate as acid acceptor. They can also be prepared by heating the chloroalkyl ether with at least a 100% excess of amine. Long-chain dialkylmorpholinium compounds have been previously prepared by the alkylation of alkylmorpholines with dialkyl sulfates.[2]

The morpholinium chlorides cling tenaciously to hydroxyl compounds. Traces of alcohols cannot be eliminated by recrystallization; only heating under reduced pressures will remove them. The glycol in an addition compound between two moles of didodecylmorpholinium chloride and one mole of ethylene glycol was removed only by azeotropy with xylene.

Acknowledgment.—Analyses were performed by James Kerns.

Experimental

Materials Used.—The dodecylamine was isolated from commercial coco amine by careful fractionation through a Podbielniak column. The octadecylamine was prepared by hydrogenation of octadecanenitrile which had been fractionated through a Podbielniak column; secondary amine was removed from the hydrogenation mixture by a second distillation. Neutral equivalents showed that both amines were over 99% pure.

Preparation of 4-Alkylmorpholines.—In each case a mixture of amine (0.50 mole), bis-(2-chloroethyl) ether or bis-(1-chloro-2-propyl) ether (0.55 mole), anhydrous sodium carbonate (0.50 mole) and butyl alcohol (300 ml.) was stirred and refluxed for a period indicated in Table I. It was poured into water and the upper layer was washed with dilute sodium hydroxide and water, then distilled. Boiling points of the products and melting points of their derivatives are also given in Table I.

4,4-Didodecylmorpholinium Chloride.—A mixture of didodecylamine (208.0 g., 0.59 mole) and bis-(2-chloroethyl) ether (127.0 g., 0.88 mole) was heated on the steam-bath for 70 hours. It was dissolved in one liter of hot 2-methoxyethanol. After cooling, didodecylamine hydrochloride separated and was filtered off. The filtrate was evaporated to half its volume, cooled and filtered, giving 56.8 g. of crude product, m.p. 50–110°. Some unreacted amine was still present; this was removed by dissolving the material in hot ethylene glycol, cooling and filtering. Removal of the glycol by vacuum distillation, followed by azeotropy with xylene gave 26.1 g. (10%) of didodecylmorpholinium chloride. This was crystallized from ethyl acetate to yield white crystals, m.p. 205–209° dec.

Anal. Calcd. for $C_{28}H_{58}ClNO$: C, 73.06; H, 12.70; N, 3.04. Found: C, 73.02; H, 12.80; N, 3.13.

When the ethylene glycol was not completely removed by azeotropy with xylene, an addition compound of two moles of morpholinium chloride and one of glycol was isolated, m.p. 211–212° dec.

Anal. Calcd. for 2 $C_{28}H_{58}ClNO$: $C_2H_6O_2$: C, 70.91; H, 12.53; N, 2.85. Found: C, 70.67; H, 13.12; N, 3.24.

In an improved preparation, a mixture of didodecylamine (35.3 g., 0.10 mole), sodium carbonate (12.8 g., 0.12 mole), bis-(2-chloroethyl) ether (17.2 g., 0.12 mole) and *n*-butyl alcohol (300 ml.) was refluxed for 48 hours. It was filtered and stripped of volatiles under reduced pressure. The residue was dissolved in methanol (200 ml.), chilled at 5° and filtered, giving 38.0 g. (83%) of snow-white flakes, m.p., after drying *in vacuo*, 208–210°.

4,4-Dioctadecylmorpholinium Chloride.—A mixture of dioctadecylamine (122.5 g., 0.24 mole), bis-(2-chloroethyl) ether (42.9 g., 0.30 mole), sodium carbonate (31.8 g., 0.30 mole) and butyl alcohol (400 ml.) was stirred and refluxed for 18 hours. It was then filtered and stripped of volatile materials under reduced pressure. Two recrystallizations from ethyl acetate yielded 83.5 g. (55%) of white solid. It melts with decomposition at 198.5–202.5° when immersed in a rapidly heated bath at a temperature just below the m.p.

Anal. Calcd. for $C_{40}H_{82}ClNO$: C, 76.44; H, 13.16; Cl, 5.64; N, 2.23. Found: C, 76.05; H, 12.86; Cl, 5.28; N, 2.63.

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4,4-Didodecyl-2,6-dimethylmorpholinium Chloride.—A mixture of didodecylamine (35.3 g., 0.10 mole), bis-(1-chloro-2-propyl) ether (20.6 g., 0.12 mole), sodium carbonate (12.7 g., 0.12 mole) and butyl alcohol (200 ml.) was stirred and refluxed for 72 hours. It was cooled, filtered and evaporated under reduced pressure. The residue was dissolved in hot methanol (400 ml.); this solution was chilled in ice and filtered, giving 16.7 g. of unreacted amine. The filtrate was distilled and its residue was crystallized from ethyl acetate, giving 8.8 g. of waxy, white solid (34% yield, 18% conversion). This was recrystallized from ethyl acetate; m.p. (after drying *in vacuo*), 175–180°.

Anal. Calcd. for $C_{30}H_{62}ClNO$: C, 73.79; H, 12.80; Cl, 7.26. Found: C, 73.85; H, 13.03; Cl, 7.18.

2,6-Dimethyl-4,4-dioctadecylmorpholinium Chloride.—A mixture of dioctadecylamine (84.1 g., 0.16 mole), bis-(1-chloro-2-propyl) ether (33.0 g., 0.19 mole), sodium carbonate (20.5 g., 0.19 mole), and butyl alcohol (400 ml.) was stirred and refluxed for 20 hours. It was diluted to one liter with butyl alcohol and filtered while hot. The filtrate was chilled and filtered again, yielding 64.4 g. of unreacted amine. The filtrate was evaporated, leaving 27.0 g. of residue. This was dissolved in hot methanol (400 ml.), cooled, and filtered to remove a small amount of solid. The filtrate was evaporated to dryness. The residue was recrystallized from ethyl acetate, giving 16.3 g. (65.5% yield, 15.3% conversion) of white solid; m.p., after another recrystallization and drying *in vacuo*, 172–175°.

Anal. Calcd. for $C_{42}H_{86}ClNO$: Cl, 5.38; N, 2.13. Found: Cl, 5.31; N, 2.46.

CHEMICAL LABORATORIES
GENERAL MILLS, INC.
MINNEAPOLIS 13, MINNESOTA

Vapor Phase Catalytic Isomerization of *m*-Xylene

BY E. R. BOEDEKER AND W. E. ERNER

RECEIVED MARCH 10, 1954

The production of certain of the synthetic fibers requires *p*-xylene as one of the starting materials. The separation of *p*-xylene from a xylene mixture by low temperature crystallization yields a high purity *p*-xylene fraction and a fraction containing a preponderance of *m*-xylene. Additional quantities of *p*-xylene are potentially available from the isomerization of the *m*-xylene-containing fraction to a xylene mixture, the composition of which approximates thermodynamic equilibrium. With this in mind, the vapor phase isomerization of a *m*-xylene-rich fraction over a synthetic silica–alumina cracking catalyst (Houdry Type S-45) was cursorily investigated.

The charge stock used in the present study contained 84% *m*-xylene, 9% *p*-xylene, 5% *o*-xylene and 2% ethylbenzene. The charge stock was obtained from a xylene fraction by freezing out a portion of the material.

The experimental conditions and results are summarized in Table I. The products were distilled to obtain a xylene and lighter overhead fraction; the bottoms from the distillation were C_9-aromatics. The overhead fraction from the distillation was analyzed by infrared absorption spectrometry. In all cases, liquid recoveries were in excess of 98% and were corrected to a no-loss basis.

The effect of operation at reduced pressure is very clearly shown. At atmospheric pressure, the isomerization of *m*-xylene proceeds simultaneously with a disproportionation reaction. In the disproportionation reaction, two molecules of xylene apparently are adsorbed on sites which are located sufficiently close to each other to allow a shift of a methyl group, thereby forming toluene and a C_9-aromatic. If, on the other hand, the operating pressure is reduced so that the catalyst surface is more sparsely covered, the isomerization reaction proceeds to the exclusion of the disproportionation reaction.

TABLE I

Conditions				
Temperature, °C.	515	515	515	
Pressure, mm., Abs.	~760	90	90	Charge
Vol. liq. feed/vol. cat./hr.	0.7	0.6	1.2	Stock
Product analyses, mole %				
Benzene	1.2	..	..	..
Toluene	13.0	1.1	1.0	..
m-Xylene	32.3	59.8	60.3	84.0
p-Xylene	18.9	18.1	20.6	9.0
o-Xylene	13.0	9.2	7.0	5.0
Ethylbenzene	5.1	11.5	11.1	2.0
C_9-Aromatics	16.5	0.3	..	..

Doubling the liquid hourly space velocity has no significant effect on the distribution of the xylene isomers.

Data have been published on the equilibrium composition of a xylene mixture.[1] Based on these data, the composition of an equilibrium mixture of xylenes at 515° is as follows: 47% *m*-xylene, 22.5% *o*-xylene, 21.5% *p*-xylene, and 9% ethylbenzene. Comparison of these figures with those obtained experimentally at 90 mm. pressure shows that the products contain approximately equilibrium amounts of *p*-xylene and ethylbenzene; the *m*-xylene content, however, is higher than and the *o*-xylene content lower than the calculated thermodynamic equilibrium.

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HOUDRY PROCESS CORPORATION
MARCUS HOOK, PENNA.

Thiosemicarbazones of Some Vanillin Derivatives

BY R. P. PERRY

RECEIVED MARCH 11, 1954

The purpose of the work described in this paper was to prepare a series of substituted vanillin thiosemicarbazones which might be useful as antifungal agents and provide some basis for determining the relation of structure to antimicrobic action. Since the introduction of Tibione (acetylaminobenzaldehyde thiosemicarbazone) by Domagk and his associates,[1-3] many changes have been effected in the structure of the molecule, particularly as regards the subordinate groups *para* to the thiosemicarbazone moiety and in only a few cases have thiosemicarbazones with poly-substituted benzenoid residues been studied.[4,5] Moreover, the thiosemicarbazones thus obtained have been screened generally only for their antitubercular activity.

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