$$c_1 \cong 0$$
$$c_2|Z_2| = c_3|Z_3|$$

and hence (2) can be written as

$$d(\omega_1) = \frac{|Z_1|}{|Z_2| + |Z_3|}\left[\frac{|Z_2|\lambda_2^0}{|Z_2|\lambda_1^0 + |Z_1|\lambda_2^0}\right] + \frac{Z_3|\lambda_3^0}{|Z_3|\lambda_1^0 + |Z_1|\lambda_3^0}\Big] \qquad (3)$$

If we take $\lambda^0_{\mathrm{Cl}^-} = 76.36$, $\lambda^0_{\mathrm{Ca}^{++}} = 59.4$, and using the relationship $\sum_i c_i Z_i^2 = 6c$ where c is the salt concentration in formular weight of $CaCl_2$ per liter of solution, we obtain by combining (1) and (3)

$$D_{\mathrm{Ca}^{++}} \times 10^5 = 0.791 - 0.808\sqrt{c} \qquad (4)$$

and

$$D_{\mathrm{Cl}^-} \times 10^5 = 2.033 - 1.729\sqrt{c} \qquad (5)$$

for the self-diffusion of Ca^{++} and Cl^-, respectively, in dilute calcium chloride solutions.

Values of $D_{\mathrm{Ca}^{++}} \times 10^5$ and $D_{\mathrm{Cl}^-} \times 10^5$ are plotted *vs.* $\sqrt{c}$ in Fig. 1. The two straight lines in the dilute concentration range represent equations (4) and (5), respectively.

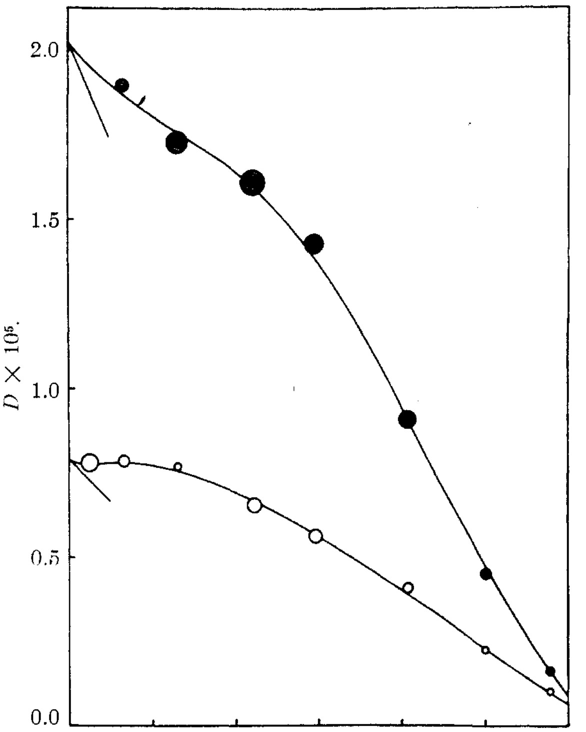

Fig. 1.—Self-diffusion coefficient of Ca^{++} and Cl^- in $CaCl_2$ (aq.) at 25°: ●, self-diffusion of Cl^-; ○, self-diffusion of Ca^{++}.

It can be noticed from Fig. 1 that as the concentration of calcium chloride solution decreases continuously to zero the self-diffusion coefficients of both Ca^{++} and Cl^- appear to approach the Nernst's limiting values from above the two straight lines representing Onsager's equations (4) and (5). This tendency of approaching the limiting value from above Onsager's equation appears to be especially apparent in the self-diffusion of calcium ion. It is interesting to recall that an analogous behavior exists in the transference number data of calcium ion in dilute aqueous calcium chloride solutions.[8]

The general shapes of the curves in Fig. 1 are in apparent agreement with the general qualitative interpretation suggested in the three preceding papers of this series.[1] Thus because of the larger mean radius of the hydrated calcium ion and the fact that calcium chloride is a 2–1 electrolyte, all the previously mentioned "distortion-effect" on the structure of solvent water, "effect of sharing of hydration," etc., should become important at lower formular concentration of the salt for calcium chloride than for sodium or potassium chloride solutions.

It may also be noticed from the values listed in Table I that the ratio of the self-diffusion coefficient at infinite dilution to that in 5.36 formular wt. per liter calcium chloride solution is approximately 13 for Cl^- and 8 for Ca^{++}. The ratio of viscosity of 5.36 formular wt. per liter calcium chloride solution to that of pure water at 25° is about 11.

Acknowledgment.—This work was supported by contract AT(30-1)-1375 between the U. S. Atomic Energy Commission and Yale University. When preparing the present manuscript, the author benefited through discussion with Professor H. S. Harned.

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Local Anesthetics. III. Modifications of β'-4-Methylphenoxyethyl β-N-Methylbenzylaminoethyl Ether

BY HOWARD B. WRIGHT AND M. B. MOORE

RECEIVED DECEMBER 5, 1952

In papers I and II we have reported that the salts of aryl alkamine ethers $ArOR'NR_2$[1a] and aryloxyalkyl alkamine ethers $ArOR'OR''NR_2$[1b] in which Ar is an aryl, R' and R'' are alkylene and R is an alkyl or aralkyl group, have been tested as local anesthetics. As a continuation of this work, we have now prepared a number of compounds related to β-4-methylphenoxyethyl β'-N-methylbenzylaminoethyl ether which was reported in paper II[1b] to produce good corneal anesthesia.

Table I lists the compounds synthesized, with pertinent physical and analytical data. Solutions of hydrochlorides or other salts of these ethers were tested for local anesthetic activity by Dr. R. K. Richards and his staff to whom we are indebted. All these ethers displayed corneal and wheal anesthesia but the activity was accompanied by some irritation.

Experimental

The *o*-diphenoxyethoxyethyl chloride was prepared in 47.5% yield by a method Bruson[2] developed for analogous compounds. The boiling point of an analytical sample was 162° (1.0 mm.), n^{26}D 1.5792.

Anal. Calcd. for $C_{16}H_{27}ClO_2$: C, 69.43; H, 6.19; Cl, 12.81. Found: C, 69.51; H, 6.29; Cl, 12.81.

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[1] (a) H. B. Wright and M. B. Moore, THIS JOURNAL, **73**, 2281 (1951); (b) **73**, 5525 (1951).

[2] H. A. Bruson, U. S. Patent 2,115,250, April 26, 1938.

TABLE I

ALKAMINE ETHERS, $ArO(CH_2)_2O(CH_2)_2NR_2$

	Compound Structural formula		Time,		Yield,	B.p.			Carbon, %		Hydrogen, %	
No.	Ar	NR_2	hr.	Method	%	°C.	Mm.	Formula	Calcd.	Found	Calcd.	Found
1	$2\text{-}C_6H_5C_6H_4$	$N(CH_3)CH_2C_6H_5$	4.5	B	[e]	218–220	1.0	$C_{24}H_{27}NO_2$	79.74	79.69	7.53	7.25
2	$2\text{-}C_6H_5C_6H_4$	$N(C_2H_5)CH_2C_6H_5$	24	A	[e]	210–211	0.45	$C_{25}H_{29}NO_2$	79.97	79.86	7.78	7.59
3	$4\text{-}CH_3C_6H_4$	$C_5H_{10}N$[a]	24	A	30	171	2.6	$C_{16}H_{25}NO_2$	72.97	72.77	9.57	9.48
4	$4\text{-}CH_3C_6H_4$	$C_6H_{12}N$[b]	24	A	39	180–181	3.1	$C_{17}H_{27}NO_2$	73.60	73.85	9.81	9.79
5	$4\text{-}CH_3C_6H_4$	$C_6H_{12}NS$[c]	24	A	57.5	190–191	1.1	$C_{17}H_{27}NO_2S$	65.98	66.17	8.79	8.67
6	$4\text{-}CH_3C_6H_4$	$N(C_4H_9)_2$	24	A	[e]	191–192	4.4	$C_{19}H_{33}NO_2$	74.22	74.36	10.82	10.56
7	$4\text{-}CH_3C_6H_4$	$NHCH_2CH(CH_3)_2$	24	A	14	156–158	2.4	$C_{15}H_{25}NO_2$	71.67	71.91	10.03	9.81
8	$4\text{-}CH_3C_6H_4$	$NH(CH_2)_4CH_3$	24	A	20	175	2.9	$C_{16}H_{27}NO_2$	72.41	73.03[d]	10.25	10.13[d]
9	$4\text{-}CH_3OC_6H_4$	$N(CH_3)CH_2C_6H_5$	3.5	B	[e]	204–205	1.4	$C_{19}H_{25}NO_3$	72.35	72.68[d]	7.99	8.05[d]

[a] 1-Piperidyl radical. [b] 2-Methyl-1-piperidyl radical. [c] 2,6-Dimethyl-4-thiomorpholinyl radical. [d] Average of two analyses. [e] Obtained in low yield.

The benzalethylimine prepared by the method of Cromwell[3,4] was obtained in 75% yield. The imine, boiling point 84–88° (10 mm.), $n^{26}D$ 1.5365, was hydrogenated at 1025 p.s.i. (80°) with Raney nickel for 1.5 hours in the absence of a solvent by G. R. Stone and Morris Freifelder. The N-ethylbenzylamine, b.p. 195–200° (747 mm.), n_D^{25} 1.5090, was obtained in 75% yield.[5]

Anal. Calcd. for $C_9H_{13}N$: C, 79.95; H, 9.69. Found: C, 80.22; H, 9.54.

All of the ethers in Table I were prepared by Method A or B described in paper II.[1b]

Acknowledgment.—We are indebted to E. F. Shelberg, Chief Microanalyst, and his staff for the analytical data.

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[3] N. H. Cromwell, THIS JOURNAL, **65**, 313 (1943).

[4] H. Zaunschirm, *Ann.*, **245**, 279 (1888).

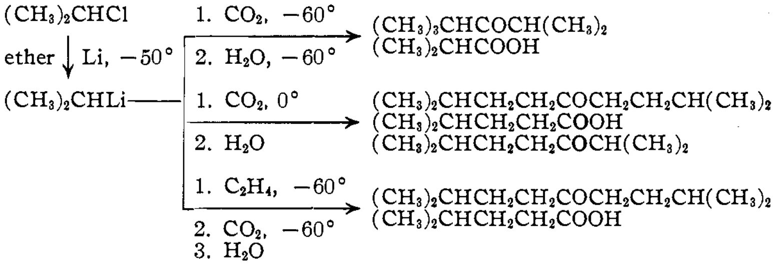
[5] (a) A. Mailke, *Bull. soc. chim.*, [4] **25**, 322 (1919); (b) O. Wallach, *Ann.*, **343**, 73 (1905); (c) F. Kraft, *Ber.*, **23**, 278 (1890).

COMMUNICATIONS TO THE EDITOR

THE REACTION OF ISOPROPYLLITHIUM AND *t*-BUTYLLITHIUM WITH SIMPLE OLEFINS

Sir:

Isopropyllithium[1] and *t*-butyllithium[2] are advantageously manipulated in ether, being much more readily prepared in this solvent than in hydrocarbons. However, they show in enhanced degree the well known tendency of organolithium compounds to decompose ether.[3,4,5,6,7,8] When isopropyllithium is prepared and carbonated in ether at temperatures below −50°, hydrolysis of the resulting solution yields the normal products, diisopropyl ketone and some isobutyric acid. When however, a solution of isopropyllithium from one mole of isopropyl chloride was allowed to warm to room temperature, a reaction was observed which caused the ether to boil, and subsequent carbonation yielded only *diisoamyl ketone* (0.25 mole, b.p. 87° (8 mm.); calcd. for $C_{11}H_{22}O$: C, 77.78, H, 13.01; found: C, 77.80, H, 13.13) and 0.05 mole of isocaproic acid. Since these products could be formed only by the addition of isopropyllithium to ethylene (resulting from decomposition of ether), an experiment was performed in which ethylene was bubbled at −60° through a solution of isopropyllithium prepared at −50°. The ethylene was readily absorbed. This solution was carbonated without allowing the temperature to rise. Hydrolysis yielded diisoamyl ketone in addition to a smaller acid fraction and residue. The diisoamyl ketone (2,4-dinitrophenylhydrazone, m.p. 53.5–54°) was identified by Beckmann degradation to isoamylamine (phenylthiourea, m.p. 105–105.5°; no depression on mixture with an authentic specimen, m.p. 104–105°)[9] and isocaproic acid (anilide, m.p. 110.5–111°; *p*-phenylphenacyl ester, m.p. 70°), and by synthesis from isoamyl chloride by carbonation of the lithium derivative.



It is clear from these experiments that iso-

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[4] A. Luttringhaus and G. von Saaf, *Angew. Chem.*, **51**, 915 (1938); *Ann.*, **557**, 25 (1947).

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[9] The melting point is given as 101–102° by M. L. Willard and M. Z. Jones, *ibid.*, **62**, 2876 (1940).