[CONTRIBUTION NO. 1146 FROM THE STERLING CHEMISTRY LABORATORY OF YALE UNIVERSITY]

# Bolaform Electrolytes. III.[1] Conductance of Bisquaternary Salts of Dicarboxylic Acid Bis-β-tertiaryaminoalkyl Amides in Methanol

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The conductances in methanol at 25° of the following salts have been measured: N,N′-bis-(β-dimethylaminoethyl)-oxalamide bis-methiodide, N,N′-bis-(β-dimethylaminoethyl)-succinamide bis-methiodide, N,N′-bis-(β-dimethylaminoethyl)-adipamide bis-methiodide and N,N′-bis-(β-dimethylaminoethyl)-suberamide bis-methiodide. These salts are bolaform electrolytes with, respectively, 8, 10, 12 and 14 atoms joining their two quaternary nitrogens. The last three salts show markedly higher association of the first anion than corresponds to an extended chain of atoms between the terminal cationic nitrogens. From the identity of the association constants for the oxalamide and suberamide derivatives, formation in the chain of a ring stabilized by intramolecular hydrogen bonds between the two amide groups is inferred.

Phillips[3] has recently synthesized a series of bolaform electrolytes[4] in which the cation has the general structure

$$Me_3N^+(CH_2)_2NHCO(CH_2)_nCONH(CH_2)_2N^+Me_3 \quad \text{I-}n$$

Unlike the corresponding esters, these salts showed no curare-like activity; instead, they prolong the duration of the block of neuromuscular transmission produced by certain bis-esters.[3] Correlation between chain length and physiological activity has been proposed for the bis-quaternary salts; our results suggest that the amides and esters differ in configuration, and that charge separation rather than maximum chain length is the significant variable.

The amides are also of especial interest in our program of correlating ionic interaction with molecular structure, because the chain connecting their cationic sites contains two groups which might interact in such a way that the intercationic distances would be different from those in which the cationic sites were connected by a polymethylene or ester chain. We have measured the conductance of four of these salts in methanol at 25° ($n$ = 0, 2, 4 and 6; *i.e.*, derivatives of oxalic, succinic, adipic and suberic acids) and analyzed the conductance data by previously described[4] methods in order to obtain the reciprocal association constant $k_2$ which describes the interaction of a bolaform cation and an anion.

$$^+B\ldots\ldots B^+ + A' \rightleftharpoons A'B^+\ldots B^+ \quad (1)$$

$$k_2 = [A'][B_2^{++}]/[AB_2^+] \quad (2)$$

The bracketed quantities in (2) represent the activities of the corrresponding species. We find that $k_2$ is practically the same for the oxalic and the suberic derivatives and is somewhat larger for these compounds than for the succinic and adipic derivatives. This observation suggests that an intramolecular ring structure, stabilized by hydrogen bonds between the amide groups is formed, which shortens the effective charge–charge distance. The association is markedly greater than for a bolaform cation with the same number of chain atoms where shortening of the chain by intramolecular forces would not be expected to occur; this contrast demonstrates the usefulness of conductance measurements as a tool in the study of molecular configuration.

## Experimental

**Materials.**—Four salts of structure I-$n$ were investigated: **N,N′-bis-(β-dimethylaminoethyl)-oxalamide bis-methiodide** ($n$ = 0); **N,N′-bis-(β-dimethylaminoethyl)-succinamide bis-methiodide** ($n$ = 2); **N,N′-bis-β-dimethylaminoethyl)-adipamide bis-methiodide** ($n$ = 4) **and N,N′-bis-(β-dimethylaminoethyl)-suberamide bis-methiodide** ($n$ = 6). These compounds were given to us by Dr. A. P. Phillips[2] of the Wellcome Research Laboratories. The first three were used as received; the suberamide derivative was recrystallized from boiling isoamyl alcohol (*ca.* 1% solution); after washing with petroleum ether and drying under reduced pressure, the salt melted at 168–169°.

**Methanol** (J. T. Baker absolute) was usually distilled immediately before use from aluminum amalgam,[5] using about one gram of mercuric chloride per liter. This procedure gave methanol of specific conductance $\kappa_0$ less than $0.05 \times 10^{-6}$; distillation from magnesium methoxide[6,7] (5 g. of magnesium per liter) never gave better than $0.10 \times 10^{-6}$ and this method was therefore abandoned. The variable take-off shown in Fig. 1 avoided a stopcock in the still-head. By rotation of the conical joint at the base of the reflux condenser, the reflux ratio can be set reproducibly to any desired value; the plug of glass cotton in the delivery arm is, of course, essential to minimize the spilling of vapor over the saddle point. Solutions were made up by weighing solution from a weight buret into a known weight of solvent in the cell or by weighing solid salt into the cell from a narrow weighing bottle with a 6-inch handle which permitted the bottle to be inserted through the long neck of the conductance cell. The density of methanol at 25° (0.7866) was used to compute volume concentrations $c$ in equivalents per liter.

The conductance cells were the Erlenmeyer type described by Kraus and Fuoss.[8] The electrodes were unplatinized; even so, some difficulties due to adsorption were encountered at the lower concentrations. These were eliminated by repeatedly rocking the cell to replace the solution between the electrodes, and using the final constant value. Calculation showed that the error in concentration due to loss of electrolyte by adsorption was negligible in our working range of concentration. Cell constants (0.04148 and 0.05299) were determined by comparison with a cell ($k$ = 2.5367) which was calibrated by measuring the resistance of solutions of potassium chloride and calculating conductances from the known concentrations by means of the equation[9]

$$(\Lambda + 59.79c^{1/2})/(1 - 0.2274c^{1/2}) = 149.86 + 141.9c + 29.24c \log c - 180.6c^2$$

Polarization errors were eliminated by extrapolating[10] to infinite frequency ($R$ *vs.* $f^{-1/2}$). All measurements were made at 25.00 ± 0.01°.

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[1] Office of Naval Research, Project NR 054-002, Paper No. 35.

[2] On leave of absence from the Weizmann Institute of Science; Postdoctoral Research Fellow, Yale University, 1952–1953.

[3] A. P. Phillips, *Science*, **112**, 536 (1950); THIS JOURNAL, **73**, 5822 (1951).

[4] (a) R. M. Fuoss and D. Edelson, *ibid.*, **73**, 269 (1951); (b) R. M. Fuoss and V. F. H. Chu, *ibid.*, **73**, 949 (1951).

[5] H. Hartley and H. R. Raikes, *J. Chem. Soc.*, **127**, 524 (1925).

[6] H. Lund and J. Bjerrum, *Ber.*, **64**, 210 (1931).

[7] N. Bjerrum and L. Zechmeister, *ibid.*, **56**, 894 (1923).

[8] C. A. Kraus and R. M. Fuoss, THIS JOURNAL, **55**, 21 (1933).

[9] T. Shedlovsky, A. S. Brown and D. A. MacInnes, *Trans. Electrochem. Soc.*, **66**, 165 (1934).

[10] G. Jones and S. M. Christian, THIS JOURNAL, **57**, 272 (1935).

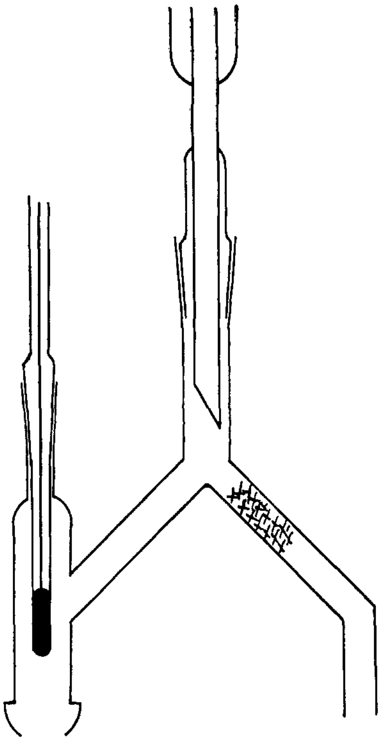

Fig. 1.—Variable take-off head.

The bridge was designed according to Shedlovsky's recommendations[11] around a Campbell–Shackelton ratio box; several changes have been made since we last described[12] our circuit. The present circuit is shown in the block diagram, Fig. 2. Either a General Radio Type 913 B or a Hewlett–Packard Model 200 C oscillator may be used without hazard of pick-up. This was demonstrated by observing no dependence of bridge balance on input voltage or on the position of the oscillator. For detector-amplifier, we now use a General Radio Type 1231 A Null Detector. The filter (two 0.1 $\mu f$ in series, two 26 × $10^3$ ohms in series; center shunt 0.2 $\mu f$ in series with 13 × $10^3$ ohms) ise ssential to eliminate 60 cycle noise. The phase shifter is made up of two 0.01 $\mu f$ condensers and two 0.1-megohm resistors; the resistors are ganged and have an additional 0.01 megohm in series for fine adjustment. Coupling between the phase shifter and the oscilloscope is through a Stancor A 4205 shielded transformer. The most important precaution in assembling the bridge is to use *only* very low loss insulation on *all* cables; until we replaced our previous rubber insulated cables by polythene insulated lines, the bridge balance for a pure resistance circuit showed an appreciable frequency dependence. Now, with 100,000 ohms as unknown, the bridge resistor changes by less than 5 ohms on going from 500 cycles to 10 kilocycles; at 10,000 ohms, the change is less than 0.1 ohm.

## Results

The experimental results are summarized in Table I; the salts are identified by giving the value of $n$ in Formula I-$n$. At least two runs were made on each salt; absolute values are probably good to 0.1% and relative values were reproducible to better than 0.05%.

## Discussion

The conductance curves for the four salts are shown in Fig. 3, where $\Lambda$ is plotted against $c^{1/2}$. It will be noted that all the curves may be approximated by straight lines *over our working range of concentration.* These linear segments may, however, not be used for extrapolation[13] to $\Lambda_0$ (although in these examples they happen by coincidence to extrapolate to almost the correct values). The conductance data were analyzed by using the extrapolation function of Fuoss and Chu.[4] We used $\lambda^0{}_1 = 61.0$ as the conductance of the iodide ion in methanol[14,15] at 25° in order to compute $F\ (c, \Lambda_0)$:

$$F = \left(\frac{1}{1 + \lambda^0{}_2/2\Lambda_0}\right)\left(\frac{1}{1 - \delta_{12}\ \Gamma^{1/2}} + \frac{\lambda^0{}_2}{2\Lambda}\right) \quad (3)$$

The Onsager mobility term for 2 − 1 salts is

$$\delta_{12} = 3.94 \times 10^6 Q(DT)^{-3/2} + 3(28.98)/\eta\Lambda_0(DT)^{1/2} \quad (4)$$

where $Q = q/(1 + q^{1/2})$ and $q = 2/3\ (1 + \lambda^0{}_1/\Lambda_0)$. In methanol at 25°, $\delta_{12} = 4.329\ Q + 164.2/\Lambda_0$. For the ionic strength $\Gamma$, we used the approximation $\Gamma \approx c\ (-1 + 4\ \Lambda/\Lambda_0)$. For $\Lambda_0$ in zeroth ap-

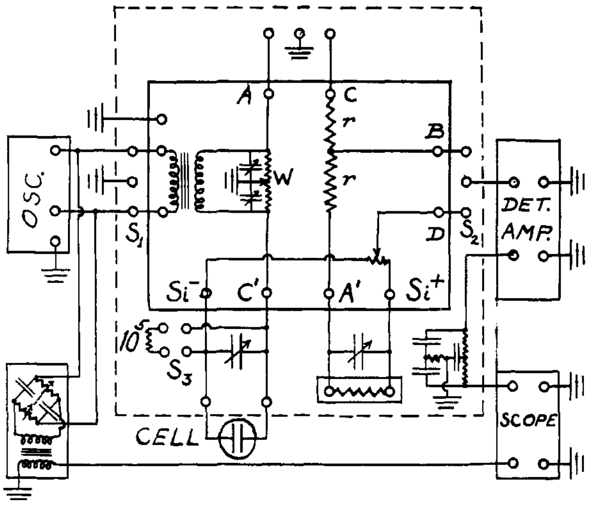

Fig. 2.—Schematic bridge circuit: W, Wagner ground; r, r, ratio arms. (A and A′ are internally connected; likewise C and C′.)

TABLE I

CONDUCTANCE OF I′[$Me_3N^+(CH_2)_2NHCO(CH_2)_nCONH(CH_2)_2N^+Me_3$]I′ IN METHANOL AT 25°

| $10^4 c$ | $\Lambda$ | $10^4 c$ | $\Lambda$ |
|---|---|---|---|
| $n = 0$ | | $n = 4$ | |
| 3.336 | 111.42 | 2.664 | 106.46 |
| 4.873 | 108.06 | 3.506 | 104.21 |
| 7.389 | 103.65 | 4.082 | 102.74 |
| 10.464 | 99.74 | 6.031 | 98.84 |
| 15.051 | 94.80 | 6.243 | 98.49 |
| | | 9.619 | 93.30 |
| $n = 2$ | | 13.644 | 88.97 |
| 1.755 | 113.28 | 18.436 | 84.88 |
| 2.792 | 109.85 | $n = 6$ | |
| 4.591 | 105.64 | 2.260 | 104.40 |
| 5.317 | 103.76 | 2.952 | 102.61 |
| 9.225 | 97.64 | 4.380 | 99.53 |
| 9.839 | 96.45 | 5.113 | 98.32 |
| 18.059 | 88.49 | 7.006 | 95.06 |
| | | 8.537 | 92.99 |
| | | 11.955 | 89.10 |

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[11] T. Shedlovsky, THIS JOURNAL, **52**, 1793 (1930).

[12] D. Edelson and R. M. Fuoss, *J. Chem. Education*, **27**, 610 (1950).

[13] F. M. Sacks and R. M. Fuoss, *J. Electrochem. Soc.*, **99**, 483 (1952).

[14] A. Unmack, E. Bullock, D. M. Murray-Rust and H. Hartley, *Proc. Roy. Soc.* (*London*), **A132**, 427 (1931).

[15] J. E. Frazer and H. Hartley, *ibid.*, **109**, 351 (1925).

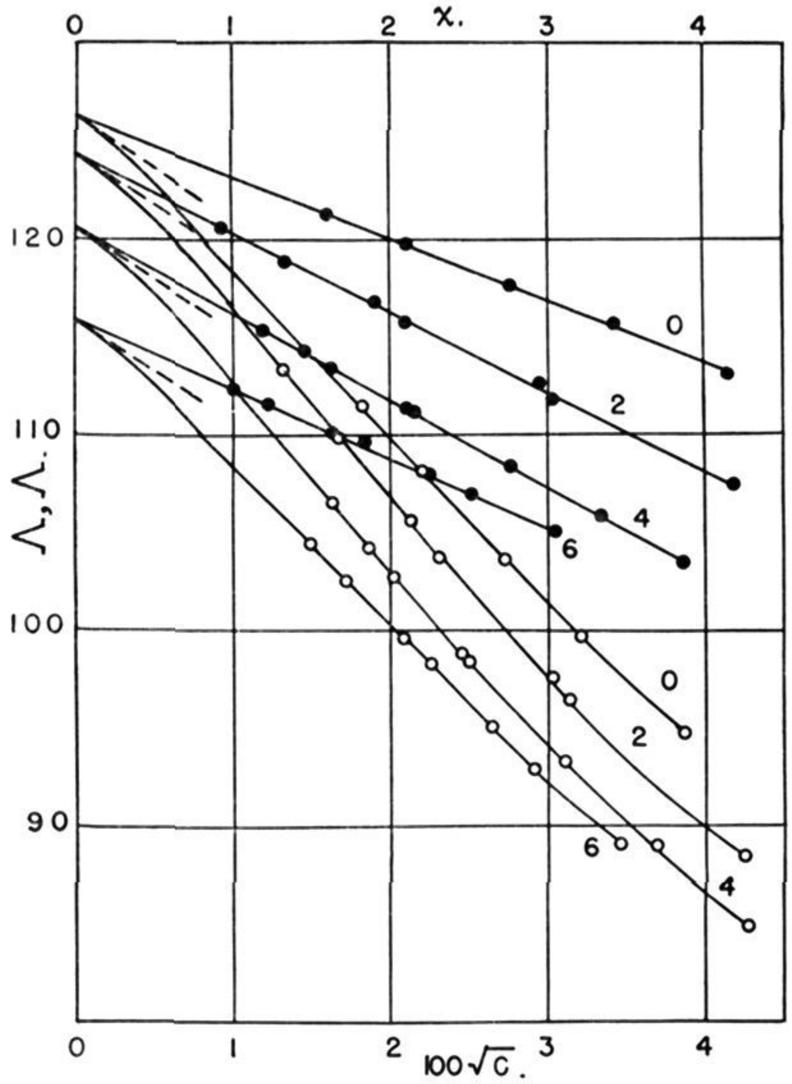

Fig. 3.—Conductance curves (open circles) and extrapolation plots (solid circles). Onsager tangents, dotted lines.

proximation to start the calculation, we extrapolated the linear segments of the $\Lambda - c^{1/2}$ curves of Fig. 3 to $c = 0$. Then $\Lambda' = F\Lambda$ was plotted against $x$, where

$$x = cf_B\Lambda'(\Lambda' - \Lambda_0/2) \qquad (5)$$

The results are shown as solid circles in Fig. 3. Data for all four salts gave excellent straight lines, which were extrapolated to $x = 0$ to give the $\Lambda_0$ values summarized in Table II. The slopes of the $\Lambda'$ *vs.* $x$ plots give $k_2$, the constant which describes the association of the first anion to one end of the bolaform cation.

TABLE II

PROPERTIES OF I-*n* IODIDES IN METHANOL AT 25°

| $n$ | $\Lambda_0$ | $\lambda^0_2$ | $10^3 k_2$ | $R$ (calcd). |
|---|---|---|---|---|
| 0 | 126.3 | 65.3 | 2.55 | 10.2 |
| 2 | 124.4 | 63.4 | 2.00 | 9.0 |
| 4 | 120.6 | 59.6 | 1.90 | 8.7 |
| 6 | 115.9 | 54.9 | 2.47 | 10.0 |

The cationic conductances (obtained by subtracting 61.0 from $\Lambda_0$) decrease as $n$ increases, as might be expected from the increasing bulk of the cation. No similar pattern of regularity appears in the $k_2$ values; instead, the constant for the oxalate is about the same as that for the suberate, and that for the succinate is about the same as that for the adipate. This pairwise equality is clearly visible in Fig. 3; roughly speaking, salts with the same association constants have parallel inflection slopes on $\Lambda$ *vs.* $c^{1/2}$ plots.

Let us consider the oxalamide derivative first. Hydrogen bonds would probably stabilize the cation into the *trans* configuration as shown in Fig. 4; according to the model, the distance between quaternary nitrogens is 11.5 Å. Bjerrum's treatment[16] of doubly charged ions may be applied to our results. Suppose each of the cationic sites of the bolaform cation is characterized by an intrinsic association constant $1/K$. Then our second association constant $1/k_2$ is given by

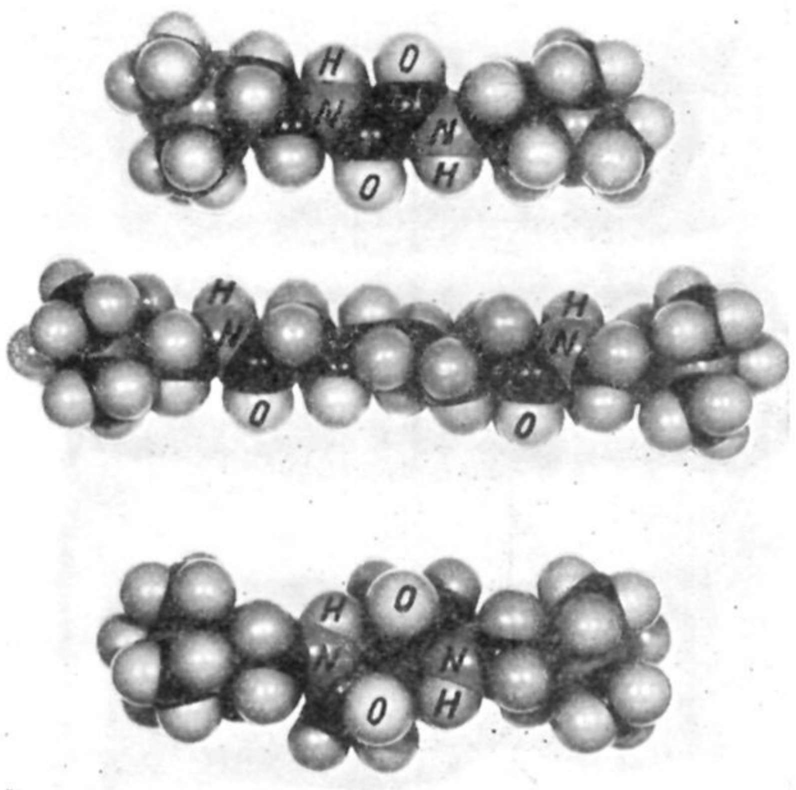

Fig. 4.—Models of salts: top, I-0; center, I-6 extended; bottom, I-6 with central ring formed.

$$k_2 = (1/2)K \exp(-\epsilon^2/DkTR) \qquad (6)$$

where $R$ is the average intercharge distance in the cation. The factor of (1/2) is the statistical factor which allows for the fact that the dissociation of an anion $A'$ from the cluster $(BA)^+$ has only half the probability of the inverse process of association of an anion to the doubly charged structure $B^{++}$, on which there are two possible sites to locate the approaching anion.[17] We can obtain a reliable estimate of $K$ from conductance data on tetramethylammonium iodide in methanol,[18] because short range interaction between $Me_4N^+$ and an iodide ion should be practically the same as that between one end of the $Me_3N^+(....)N^+Me_3$ ion and an iodide ion. Extrapolation[19] gives $K = 29 \times 10^{-3}$. If we substitute this value for $K$ in eq. (6) and use $D = 31.5$ (the bulk dielectric constant), the value of $k_2$ given in Table II for $n = 0$ leads to $R = 10.2$ Å. This value is in reasonably good agreement with the value obtained from the model (Fig. 4) with a hydrogen bonded ring.

If we calculate $k_2$ in a similar fashion by eq. (6) for the suberamide derivative, using the value $R =$ 19 Å. from the extended model, we obtain $k_2 = 11.2 \times 10^{-3}$, which is much larger than the ob-

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(16) N. Bjerrum, *Z. physik. Chem.*, **106**, 219 (1923).

(17) The ratio $k_1/k_2$ is four; Fuoss and Chu (ref. 4b) erroneously stated that the ratio $K/k_2$ should approach four as the value of $R$ increases. The constant $k_1$ measures the association of the second anion to $(AB)^+$ to give the neutral cluster $A_2B$.

(18) T. H. Mead, O. L. Hughes and H. Hartley, *J. Chem. Soc.*, 1207 (1933).

(19) R. M. Fuoss and T. Shedlovsky, THIS JOURNAL, **71**, 1496 (1949).

served value of $2.47 \times 10^{-3}$. We therefore conconclude that the charges are much closer in Salt I-6 than in the extended configuration, and hence present a more powerful attractive field to an anion. In fact, the identity of the $k_2$'s for Salts I-0 and I-6 suggests that they have the *same* value of $R$. A configuration is readily obtained in which this identity appears: as shown in Fig. 4, the suberamide can contract to form a compact central ring structure stabilized by hydrogen bonds between the two amide groups. (The hexamethylene chain joining the latter is curled up behind the central ring.) In Salts I-2 and I-4, ring formation is also possible, according to the models, although a little strain and steric hindrance interfere somewhat. Since $k_2$ is somewhat smaller (*i.e.*, more association) for I-2 and I-4 than for I-0 and I-6, the former probably exist partly as bent configurations in which the externally positive NH dipoles also contribute to the electrostatic binding of an associated anion. Further data on salts of related structure are needed to clarify these speculations: we feel reasonably certain, however, that the cation of Salt I-6 must be intramolecularly bonded to a compact structure, in view of the identity of its $k_2$ with that of Salt I-0.

The physiological behavior of the amide derivatives also appears to support the conclusion that they are not extended chains in solution. In the series $Me_3N^+(CH_2)_mN^+Me_3$, curarimimetic activity reaches a peak when approximately ten atoms are between the quaternary nitrogen atoms.[20] In the amide series, a chain of ten atoms appears in Salt I-2. Nevertheless, it shows no curare activity (at least in the conventional dose levels); instead, it and its homologs prolong the neuromuscular block induced by diacetylcholine. Phillips[3] emphasized that "this latter activity persisted in all members of the group above oxalic regardless of chain length." If, therefore, we are to assume any correlation between configuration and activity, we must conclude that the Salts I-2, I-4 and I-6 have essentially the same configuration, and this is precisely the conclusion reached on the basis of the conductance measurements. In effect, the formation of a hydrogen bonded central ring wastes the chain atoms between the amide nitrogens in Salts I-*n;* lengthening the external methylene chains joining the quaternary nitrogen to the amide nitrogen should then produce curare activity (unless the amide groups *per se* are anticurare). Also, the malonamide should behave differently from the other members of the series, because the presence of a single methylene between amides makes ring closure by hydrogen bonds sterically impossible.

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[20] "Curare and Anti-curare Agents," *Ann. N. Y. Acad. Sci.*, **54**, 297 (1951).

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[CONTRIBUTION FROM THE FRICK CHEMICAL LABORATORY, PRINCETON UNIVERSITY]

# A Magnetic Study of Polymerization Retardation

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In the retardation of vinyl polymerization by quinones and aromatic nitro compounds, the primary step is considered to be the formation of a resonance-stabilized radical too inactive to continue the chain. The experimental confirmation of this idea was the purpose of the present investigation. The diamagnetic susceptibility of a polymerizing methyl methacrylate mixture initiated by benzoyl peroxide and retarded by a quinone was found to be initially lower than the same mixture without retarder present. As the polymerization proceeded, the difference in susceptibilities decreased. The same polymerizing mixture retarded by aromatic nitro compounds, aromatic amines, or hydroquinone showed no initial susceptibility difference between the retarded and non-retarded systems. Conclusions drawn from the experimental results give evidence for: (a) the formation of stabilized radicals in quinone-retarded polymerizations in concentrations much above that of the chain carriers; (b) the formation of these radicals before the polymer chain has grown to a length of more than five monomer units; (c) the absence of appreciable concentration of stabilized radicals formed by direct interaction of quinone molecules and initiator fragments; (d) the operation of a different retarding mechanism in systems containing an amine, nitro compound, or hydroquinone.

It has long been known that the addition of certain classes of organic molecules to vinyl monomers may retard or even inhibit their polymerization to long-chain products.[2,3] These substances include quinones, aromatic nitro compounds, aromatic, primary and secondary amines, and some polyhydric phenols. Only very small quantities are necessary to bring about a decrease in polymerization rate and often a marked change in the character of the final polymer. With quinones and nitro compounds the primary step in the retardation process is usually considered to be the addition of the neutral molecule to a growing radical chain resulting in the formation of a new resonance-stabilized radical which is not sufficiently reactive to propagate the chain further without difficulty, if at all.[4-6] The locus of attack upon the retarder

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[1] This article is based upon a thesis submitted by Judson L. Ihrig in partial fulfillment of the requirements for the degree of Ph.D. at Princeton University. Now at University of Hawaii, Honolulu, Hawaii.

[2] K. K. Jeu and H. N. Alyea, THIS JOURNAL, **55**, 575 (1933).

[3] F. A. Bovey and I. M. Kolthoff, *Chem. Revs.*, **42**, 491 (1948).

[4] P. D. Bartlett, G. S. Hammond and H. Kwart, *Discussions of the Faraday Soc.*, **2**, 342 (1947).

[5] S. G. Cohen, THIS JOURNAL, **69**, 1057 (1947).

[6] H. W. Melville and W. F. Watson, *Trans. Faraday Soc.*, **44**, 886 (1948).