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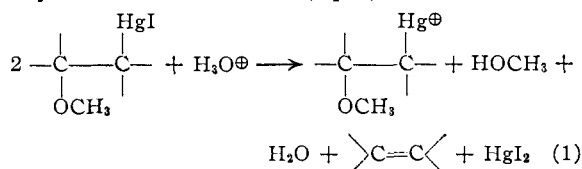
The Effect of Solvent on Rates of Acid-induced Deoxymercuration<sup>1</sup>

BY MAURICE M. KREEVOY, JOHN W. GILJE AND RICHARD A. KRETCHMER

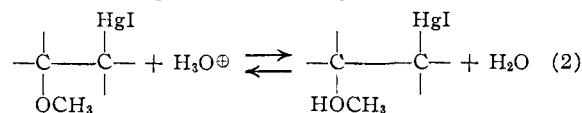
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Rates of deoxymercuration by non-halogen acid have been obtained for four methoxy mercurials in ethanol-water mixtures and dioxane-water mixtures. All of the rates exhibit a minimum in intermediate solvent compositions, but otherwise the rates are quite different functions of solvent composition. Previously suggested measures of solvent acidity fail to correlate the rate constants quantitatively.

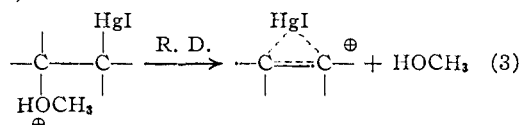
In previous papers<sup>2,3</sup> the mechanism of the deoxymercuration reaction (eq. 1) has been shown to



involve a rapid, reversible, proton transfer (eq. 2)



followed by a rate-determining step not requiring the intimate participation of a nucleophilic reagent (eq. 3).



Several proposals have been offered for the correlation of such reaction rates with solvent composition in mixed solvents.<sup>4-7</sup> The deoxymercuration reaction presents a good opportunity to test such ideas because a substantial number of substrates are available with a wide variety of structures and rates, and those rates are readily measured with reasonable precision.<sup>2,3</sup> The present paper reports and discusses the rates of deoxymercuration of 2-methoxyethylmercuric iodide (I), *trans*-2-methoxycyclopentylmercuric iodide (II), *cis*-2-methoxycyclopentylmercuric iodide (III) and 1-*exo*iodomercuri-2-*exomethoxy*[2.2.1]bicycloheptane (IV) in ethanol-water mixtures and dioxane-water mixtures.

## Results

The progress of the reactions was followed by observing the buildup of the mercuric iodide peak at 2800 Å.<sup>2</sup> All of the reactions gave linear plots of  $\log \{(D_{\infty} - D_0)/(D_{\infty} - D_t)\}$  vs. time ( $t$ ) ( $D$  is optical density at 2800 Å.). Pseudo first-order

rate constants ( $k_1$ ) were obtained graphically and were reproducible with an average deviation from the mean of 5%. The hydronium ion was provided by perchloric acid in all experiments except those with II in water and the two most aqueous dioxane-water mixtures. In the latter cases acetic acid-acetate buffers were used. In all experiments the acid concentrations were chosen so that it would not change by more than 5% during the course of the reaction. (The reaction is not truly acid-catalyzed—it consumes acid.)

For all four substrates rates were measured in dioxane-water mixtures and in ethanol-water mixtures ranging up to 80-90% by weight of the organic component. With III and IV it was generally not convenient to measure rates at acid concentrations below 0.1 *M*. For these compounds rates were measured at a series of acid concentrations between 0.1 and 1.0 *M*. As expected, the apparent second-order rate constants ( $k_2$ , obtained by dividing  $k_1$  by the hydronium ion concentration) were dependent on the acid concentration. Plots of  $\log k_2$  vs. the perchloric acid concentration were linear, however, and these plots were extrapolated to infinite dilution to get the dilute solution values,  $k_2^{\circ}$ . Figure 1 shows typical examples of these plots and their slopes are given in Table I. The percentage composition indicated was determined by weight and pertains to solvent mixtures containing neither substrate nor acids.

TABLE I  
SLOPES OF LOG  $k_2$  vs. (HClO<sub>4</sub>) IN VARIOUS SOLVENT MIXTURES

Substrate	Percentage (org. component) <sup>a</sup>	Slope	Substrate	Percentage (org. component) <sup>a</sup>	Slope
	0.0	0.256	IV	34.0 (E)	0.605
IV	42.0 (D)	.725	IV	52.7 (E)	.836
	49.6 (D)	.864	III	65.6 (E)	.616
IV	61.3 (D)	1.023	IV	73.3 (E)	1.007
III	70.4 (D)	1.363	III	76.8 (E)	0.727
III	80.2 (D)	1.709	IV	84.0 (E)	1.254
IV	80.7 (D)	1.846	III	92.1 (E)	0.686
IV	90.4 (D)	3.320			

<sup>a</sup> Dioxane is indicated by (D) following the percentage, ethanol by (E). <sup>b</sup> Derived from indicator measurements of  $H_0$  tabulated in ref. 9. <sup>c</sup> Average of a number of values, principally based on acetal and ketal hydrolysis rates, reported by M. M. Kreevoy, *J. Am. Chem. Soc.*, **78**, 4236 (1956).

For substrate II the acid concentration in 0%, 10% and 20% dioxane was maintained by using acetic acid-acetate buffers. The calculation of hydronium ion concentrations in such solutions is straightforward and has been previously de-

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(2) M. M. Kreevoy, *J. Am. Chem. Soc.*, **81**, 1099 (1959).

(3) M. M. Kreevoy and F. R. Kowitz, *ibid.*, **82**, 739 (1960).

(4) E. A. Braude and E. S. Stern, *J. Chem. Soc.*, 1982 (1948).

(5) F. A. Long and M. A. Paul, *Chem. Revs.*, **57**, 935 (1957); this review article contains many references to earlier work.

(6) B. Gutbezahl and E. Grunwald, *J. Am. Chem. Soc.*, **75**, 567 (1953).

(7) H. P. Marshall and E. Grunwald, *ibid.*, **76**, 2000 (1954).

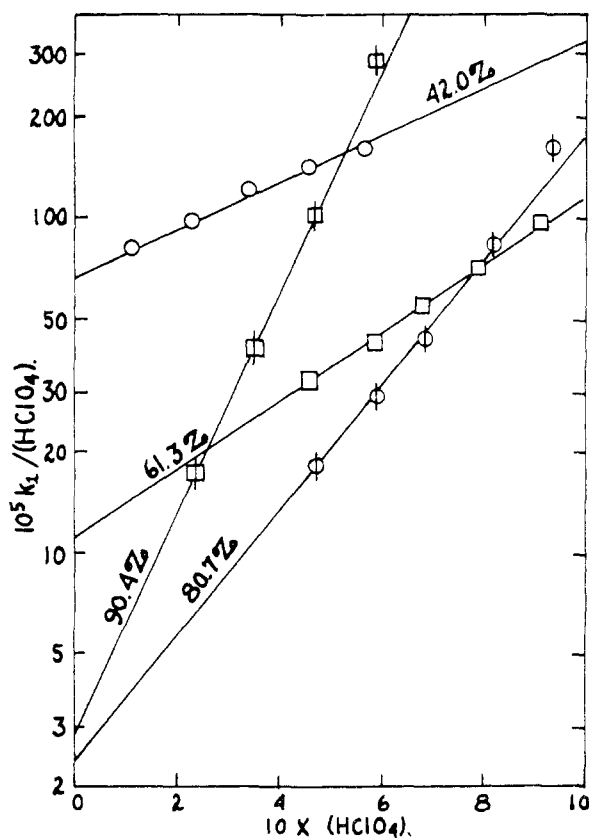


Fig. 1.—Plots of  $\log \{10^5 k_1 / (\text{HClO}_4)\}$  vs.  $(\text{HClO}_4)$  for IV in dioxane-water mixtures. The weight percentages of dioxane are shown on each line.

scribed.<sup>2,8</sup> For ethanol-water mixtures and the remaining dioxane-water mixtures the hydronium ion concentration was provided by perchloric acid in the  $10^{-2}$ – $10^{-4}$  *M* concentration range. In both these types  $k_2$  is obtained directly by dividing  $k_1$  by the hydronium ion concentration.

For substrate I and also for substrates III and IV in the more aqueous mixtures it was possible to determine  $k_1$  in the  $10^{-1}$ – $10^{-2}$  *M* acid range. The apparent  $k_2$  values obtained were corrected to infinite dilution by assuming a linear dependence of  $\log k_2$  on the perchloric acid concentration and estimating the necessary slope. The slopes were estimated by drawing smooth curves through the measured slope values and interpolating, and then averaging where two values were available.

Table II gives  $k_2^\infty$  for each of the substrates in water. These were subtracted from  $k_2^\infty$  values in the various solvents to give  $\Delta \log k_2^\infty$ , which is shown in Figs. 2 and 3 as a function of solvent parameters.

It is hard to estimate the uncertainties inherent in obtaining  $k_2^\infty$  by the extrapolation procedures. In water  $\log k_1$  for deoxymercuration rates has been shown to depend on the Hammett acidity function,  $H_0$ , in a linear fashion.<sup>3</sup> Simple algebraic considerations then require that the quantity  $-\{H_0 + \log(\text{HClO}_4)\}$  be a linear function of the perchloric acid concentration with intercept zero.

(8) M. M. Kreevoy and R. W. Taft, Jr., *J. Am. Chem. Soc.*, **77**, 5590 (1955).

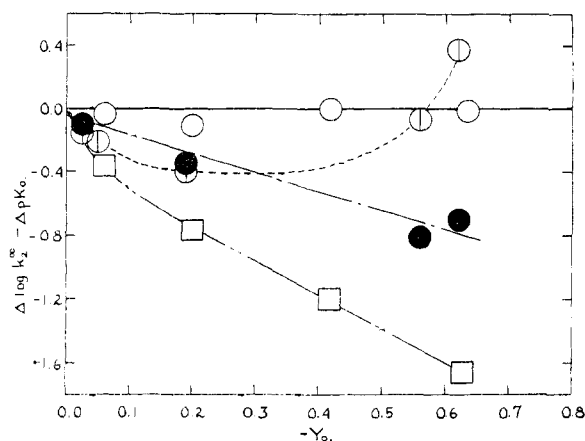


Fig. 2.—Plots of  $(\Delta \log k_2^\infty - \Delta pK_0)$  vs.  $-Y_0$  for dioxane-water mixtures: substrate I,  $\circ-\circ$ ; substrate II,  $\odot-\odot$ ; substrate III,  $\bullet-\bullet$ ; substrate IV,  $\square-\square$ . The origin is a point on each of the curves.

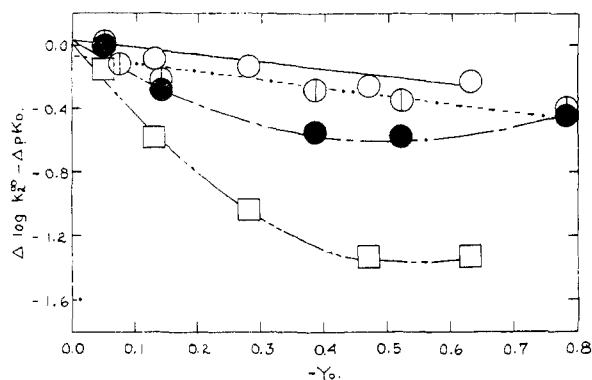


Fig. 3.—Plots of  $(\Delta \log k_2^\infty - \Delta pK_0)$  vs.  $Y_0$  ethanol-water mixtures: substrate I,  $\circ-\circ$ ; substrate II,  $\odot-\odot$ ; substrate III,  $\bullet-\bullet$ ; substrate IV,  $\square-\square$ . The origin is a point on each of the curves.

In fact, it is such a function with slope of 0.256 up to  $\sim 2$  *M* perchloric acid.<sup>9</sup> The intercept is 0.04, which would amount to an error of about 10% in making the extrapolation to 0.75 *M* (the lowest perchloric acid concentration at which  $H_0$  is available) to infinite dilution. The uncertainties in the

TABLE II  
VALUES OF  $k_2^\infty$  IN WATER<sup>a</sup>

Substrate	$k_2^\infty$
I	$3.74 \times 10^{-2}$
II	13.2
III	$1.92 \times 10^{-3}$
IV	$1.49 \times 10^{-2}$

<sup>a</sup> Solvent actually contained 1–2% ethanol or dioxane because the substrate was used as a stock solution in those solvents.

extrapolated rate constants may be of the same order of magnitude. Where an estimated slope was used it, of course, introduces an additional uncertainty but the extrapolations were shorter in those cases. The uncertainty in directly measured rate constants is about  $\pm 5\%$ .

(9) M. A. Paul and F. A. Long, *Chem. Revs.*, **57**, 1 (1957).

### Discussion

Braude has suggested the extension of the Hammett acidity function concept<sup>4</sup> to mixed solvents. If the activity coefficient ratio  $f_{\text{BH}}/f_{\text{B}}f_{\text{H}}$  (in which  $f_{\text{BH}}$  is the activity coefficient of a protonated indicator or transition state BH,  $f_{\text{B}}$  is the activity coefficient of a neutral indicator or substrate, and  $f_{\text{H}}$  is the activity coefficient of a proton; all referred to infinitely dilute aqueous solution) is assumed to be approximately independent of the structure of B it is readily shown that the second-order rate constants for "A-1" type reactions should be given by eq. 4. In eq. 4  $\Delta pK_0$  is the acid dissociation

$$\Delta \log k_2^\infty = \Delta pK_0 \quad (4)$$

constant of a protonated Hammett type, neutral indicator base in the appropriate solvent mixture less its  $pK$  in water. The same sort of considerations require that  $\Delta pK$  equal  $\Delta pK_0$  in all solvent mixtures if  $\Delta pK$  pertains to another Hammett type base.

Observing that  $\Delta pK$  values, in fact, were not equal, Gutbezahl and Grunwald made use of the activity postulate<sup>10</sup> to obtain eq. 5,<sup>11</sup> from which eq. 6 is readily deduced.<sup>6,12</sup> In all of the present work the anilinium ion has been used as the pro-

$$\Delta pK = \Delta pK_0 + (\Delta m) Y_0 \quad (5)$$

$$\Delta \log k_2^\infty = pK_0 + (\Delta m) Y_0 \quad (6)$$

tonated reference base. Once this choice has been made  $\Delta m$  becomes a constant characteristic of the base or substrate and  $Y_0$  is a parameter characteristic of the solvent mixture. Grunwald and co-workers have discussed  $Y_0$  and  $\Delta m$  at some length.<sup>6,11</sup>

If eq. 4 were to be obeyed by the present data, plots of  $\Delta \log k_2^\infty - \Delta pK_0$  vs.  $-Y_0$  should be linear and have zero slope. If eq. 6 is to be obeyed the plots can have varying slopes but must still be linear. The appropriate plots are shown in Fig. 2 for dioxane-water mixtures and Fig. 3 for ethanol-water mixtures. Of the eight plots only one (substrate I in dioxane-water mixtures) is linear with zero slope. Three others are linear with acceptable precision and non-zero slopes. Four of the plots show unmistakable curvature, all of them in the upward direction. Among these is the plot for substrate II in dioxane-water mixtures which is derived from  $k_2^\infty$  values requiring no extrapolation. On closer examination some of those plots which seem to be linear show signs of upward curvature.

These plots lead to the following conclusions: (1) Variations in  $k_2^\infty$  with solvent composition in mixed solvents are much more dependent on substrate structure than variations in  $k_2$  with strong acid concentration. (Deoxymercuration rates follow the Hammett acidity function,<sup>3</sup> which is based

on essentially the same approximation as eq. 4, except applied to moderately concentrated aqueous mineral acids.) (2) To achieve a quantitative correlation of  $k_2^\infty$  with solvent composition for a wide range of substrate structures the interactions of these structures with the solvent will have to be taken specifically into account. This sort of structural limitation in the types of bases to which eq. 5 can be applied had been previously recognized by Gutbezahl and Grunwald<sup>11</sup> and its extension to eq. 6 seems very reasonable.

Qualitatively all eight plots of  $k_2^\infty$  vs. solvent composition show the minima described by Braude<sup>4,5</sup> except for substrate IV in ethanol-water mixtures. Even in that case the appearance of the data suggests a minimum at higher ethanol concentrations. In most cases the rise in the largely organic mixtures is not so sharp and does not occur so soon as that described by Braude. The difference is due, in part, to the fact that Braude was considering apparent equilibrium constants at 0.1 *M* acid and the slope of the plots shown in Fig. 1 increases sharply as the mixtures become richer in the organic component. In part, it is also due to the general failure of eq. 4 to correlate the data quantitatively.

### Experimental

Methods for measuring rates have been previously described,<sup>2</sup> as have methods for making up standard acid solutions.<sup>2</sup>

**Solvents.**—Dioxane was purified by the method (a) described by Fieser.<sup>13</sup> The constant boiling ethanol-water azeotrope was prepared from commercial U.S.P. grade 95% alcohol by distillation. It contains 95.58% ethanol by weight. Solutions for kinetic experiments were made up by pipetting a known weight of the organic solvent into a volumetric flask and making up to the mark with water. The required substrate had been previously dissolved in the organic solvent and the acid in the water. The pipets were recalibrated for the organic solvents by weighing. The percentage of water was determined by weighing a volumetric flask before and after the water (with no acid present) had been delivered. All percentage compositions reported above are by weight.

**Substrates.**—The preparation of substrate I has been previously reported.<sup>14</sup>

Substrate II was prepared in these laboratories by Miss Frances Kowitt (who also made preliminary rate measurements in aqueous solution) by the methods of Brook, Donovan and Wright.<sup>15</sup>

Substrate III was prepared from *trans*-2-methoxycyclopentylmercuric chloride using the method described by Kreevoy and Kowitt.<sup>3</sup> The required *trans*-2-methoxycyclopentylmercuric chloride was prepared by the method of Brook, Donovan and Wright.<sup>15</sup>

Substrate IV was a gift of Dr. T. G. Traylor who has described the preparation and characterization of the corresponding chloride.<sup>16</sup>

The m.p.'s of all four substrates were in agreement with those previously reported.

**Acknowledgment.**—We are grateful to Dr. Traylor for the gift of substrate IV and to Dr. Grunwald for a discussion of this work.

(10) E. Grunwald and S. Winstein, *J. Am. Chem. Soc.*, **70**, 846 (1948).

(11) B. Gutbezahl and E. Grunwald, *ibid.*, **75**, 539 (1953).

(12) Gutbezahl and Grunwald prefer to replace  $\Delta pK_0$  with  $f_{\text{H}}$ , a sort of averaged  $\Delta pK$  which has the form of a degenerate activity coefficient for the proton. The present authors prefer to retain  $\Delta pK_0$  which means the comparisons are being made with a definite substance, the anilinium ion.

(13) L. F. Fieser, "Experiments in Organic Chemistry," 2nd ed., D. C. Heath and Co., Boston, Mass., 1955, p. 284.

(14) M. M. Kreevoy and L. T. Ditsch, *J. Org. Chem.*, **25**, 134 (1960).

(15) A. G. Brook, R. Donovan and G. F. Wright, *Can. J. Chem.*, **31**, 536 (1953).

(16) T. G. Traylor and A. W. Baker, *Tetrahedron Letters*, No. 19, 14 (1959).