

Grunwald E & Winstein S. The correlation of solvolysis rates.

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For substrates that solvolyze by a rate-determining ionization, log-log plots of first-order rate constants in various solvents are linear. This permits the prediction of solvent effects on rate constants for such reactions and provides a test for the reaction mechanism. Reactions that fail to give linear plots are likely to proceed by other mechanisms, and the pattern of the deviations may be diagnostic. [The SCI® indicates that this paper has been cited in over 600 publications since 1955.]

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"My PhD problem, under the direction of Saul Winstein at the University of California, Los Angeles, was to measure driving forces due to participation by *neighboring groups* ( $\beta$ -substituents with unshared electron pairs, such as -Br-, -O-, or -(CH<sub>3</sub>)S-) in solvolytic displacement reactions. In addition to doing the experimental work, which involved synthesis, purification, and kinetic measurements and never seemed to progress fast enough, I regularly spent time in the chemistry library browsing through the then-recent literature of the period between the two World Wars for related facts. I say 'browsing,' because physical organic chemistry was then a young science, and the kind of quantitative kinetic data we sought were mostly published and indexed under titles not containing our keywords. Being a refugee from Nazi Germany helped me to make an unusually effective search of the central and eastern European literature, which was largely in German. The browsing paid off because I found good data for substrates of key interest, but alas, the rate mea-

surements were spread over many different solvents and would not be useful to us unless there was a way to predict changes of rate constant with the solvent.

"Winstein and I were both admirers of Louis P. Hammett's 1940 monograph, *Physical Organic Chemistry*,<sup>1</sup> which includes pathmaking chapters on the quantitative prediction of reactivity by means of linear log-log plots of rate and/or equilibrium constants for a series of related reactions. Extending this approach to solvolysis reactions, I hoped that solvent effects on rate constants might similarly be predictable for reaction series with a common reaction mechanism. For our substrates with neighboring groups, this reaction mechanism would be the *unimolecular* or *SN1* mechanism proposed by Hughes and Ingold,<sup>2,3</sup> whose scope and characterization were then hot topics for research.

"The hoped-for 'correlation of solvolysis rates' succeeded euphoriantly well. Although I would have been satisfied to predict reactivity within a factor of two, it soon became evident that solvent effects on rate constants for unimolecular solvolysis can be predicted to within 20-30 percent. Our paper reports a formal method for quantitative prediction that encompasses several dozen solvents and is based on rate constants for several dozen substrates. As a result, I was able to express the reactivity data discovered in my literature search on a uniform basis and thus to substantiate a general theory of reactivity in the presence of neighboring groups.<sup>4</sup> But beyond that, Winstein and I were able in our paper to propose a convenient test for the reaction mechanism: successful correlation by our method indicates the unimolecular mechanism, while failure of correlation indicates some other mechanism with high probability. This test became popular, and its application, and the discovery of limitations,<sup>5,6</sup> may well account for the majority of citations."

1. Hammett L P. *Physical organic chemistry: reaction rates, equilibria, and mechanisms*. New York: McGraw-Hill, 1940. p. 157-228, 251-90.
2. Hughes E D. Substitution at a saturated carbon atom. *Trans. Faraday Soc.* 37:603-32, 1941.
3. Dostrovsky I, Hughes E D & Ingold C K. Mechanism of substitution at a saturated carbon atom. *J. Chem. Soc.* 1946:173-94.
4. Winstein S & Grunwald E. General theory of neighboring groups and reactivity. *J. Amer. Chem. Soc.* 70:828-37, 1948. (Cited 125 times since 1955.)
5. Winstein S, Fahnberg A & Grunwald E. Solvolysis of benzhydryl chloride and bromide. *J. Amer. Chem. Soc.* 79:4146-55, 1957. (Cited 115 times since 1957.)
6. Schadt F L, Bentley T W & Schleyer P V R. Quantitative treatments of nucleophilic solvent assistance. *J. Amer. Chem. Soc.* 98:7667-74, 1976. (Cited 140 times.)