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Failure of the Principle of Hard and Soft Acids and Bases to Explain the Amount of Cyclization of Various Hex-5-enyl Derivatives during Acetolysis

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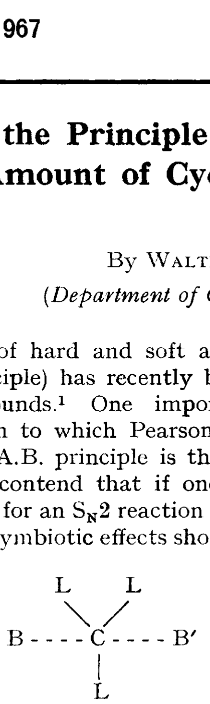
THE principle of hard and soft acids and bases (H.S.A.B. principle) has recently been applied to organic compounds.[1] One important type of organic reaction to which Pearson and Songstad apply the H.S.A.B. principle is the S_N2 reaction. These authors contend that if one considers the transition state for an S_N2 reaction as an acid–base complex, then symbiotic effects should operate and transition states with several soft or several hard ligands on the central carbon should be more stable than transition states with a mixture of soft and hard ligands. Thus, if B is an entering nucleophile and B′ the leaving group, faster rates are expected for S_N2 reactions when B and B′ are both soft or both hard.



Solvolysis of hex-5-enyl derivatives in acetic acid can be thought of as two competing substitution reactions: (a) nucleophilic attack by acetic acid which leads to hex-5-enyl acetate and (b) nucleophilic attack by the olefin which leads to the cyclic products, 1-methylcyclopentene, cyclohexene, and cyclohexyl acetate.[2] Since the olefin is clearly a soft base and acetic acid a hard base,[1] the H.S.A.B. principle predicts that hex-5-enyl iodide or bromide should lead to *more* cyclization than hex-5-enyl *p*-nitrobenzenesulphonate or toluene-*p*-sulphonate. The results in the Table are diametrically opposed to this prediction. Hex-5-enyl *p*-nitrobenzenesulphonate and toluene-*p*-sulphonate give 41% and 30% cyclic materials, respectively after complete reaction whereas hex-5-enyl iodide and bromide give 20% and 15% cyclic materials respectively after solvolysis of all but 16% of the halides. Even if all of the remaining halide were converted into cyclic materials, which is highly unlikely, the yields of cyclic materials from the halides would not greatly exceed the yields of cyclic materials from the arenesulphonates.

Less cyclization with hex-5-enyl iodide or bromide is easily rationalized on the basis of the suggestion by DePuy and Bishop[3] confirmed experimentally by Hoffmann.[4] Hoffmann found that the ratio of rate constants for substitution reactions of toluene-*p*-sulphonates and bromides can vary from 0·36 to 5000 depending on the particular reaction. If the nucleophile is powerful and the substrate does not tend to ionize, then $k_{\mathrm{OTs}}/k_{\mathrm{Br}}$ is small. Thus, less cyclization with hex-5-enyl iodide and bromide indicates that acetic acid is a stronger nucleophile than the olefin and therefore the transition state leading to direct displacement has less carbon-leaving group bond breaking than the transition state for cyclization.

Pearson and Songstad cited several collections of data to support the correlation of rates of S_N2

TABLE

Ratios of cyclic to open products from acetolysis of various hex-5-enyl derivatives at 100°[a]

Substrate	Reaction time (hr.)	Unchanged starting material, %[b]	% Cyclic products[b] / % Open product
Hex-5-enyl Iodide	48	75	0·20[c]
	672	16	0·40
Hex-5-enyl Bromide	96	48	0·19[c]
	396	15	0·26
Hex-5-enyl *p*-nitrobenzenesulphonate[d]	50	0	0·83
Hex-5-enyl toluene-*p*-sulphonate[e]	72	0	0·51

[a] See ref. 2 for experimental details. [RX] = 0·1 M, [urea] = 0·2 M. [b] Actual yields of starting material and products were determined by gas-liquid partition chromatography. Recovery was 85—90% for all runs. [c] The (% Cyclic/% Open) product ratios steadly increased with extent of reaction. [d] Average of four runs. [e] Average of three runs.

reactions by the H.S.A.B. principle.[1] Most of these data have been explained in other ways by the original workers and usually contain exceptions when interpreted by the H.S.A.B. principle. Indeed, Pearson and Songstad reinterpreted Hoffman's data by the H.S.A.B. principle which can readily be done since Hoffmann's better nucleophiles were also the softer ones.

In conclusion, none of the data cited by Pearson and Songstad[1] rigorously support the H.S.A.B. principle when applied to S_N2 reactions and failure of this principle to predict the present results clearly indicates its inadequacies and the need for more detailed considerations of S_N2 reactions.

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