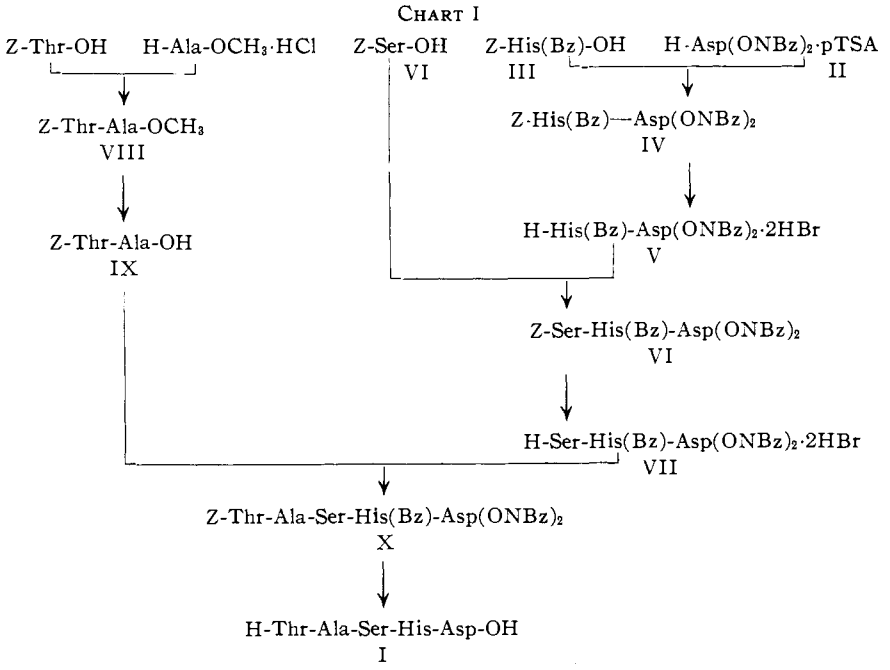
CHART I



C, 59.29; H, 4.94; N, 11.53. Found: C, 59.21; H, 4.93; N, 11.89). Hydrogen bromide in trifluoroacetic acid was used to cleave the carbobenzyloxy group of VI, affording bis-*p*-nitrobenzyl-L-seryl-*im*-benzyl-L-histidyl-L-aspartate dihydrobromide (VIII), m.p. 93–103° dec., $[\alpha]^{21}D$ −4.1° (*c* 2.2, dimethylformamide) (*Anal.* Calcd. for $C_{34}H_{37}N_7O_{11}Br_2$: C, 46.43; H, 4.24; N, 11.15; Br, 20.01. Found: C, 45.95; H, 4.27; N, 10.59; Br, 19.50).

Condensation of carbobenzyloxy-L-threonine and methyl-L-alaninate hydrochloride in methylene chloride containing 1 equiv. of triethylamine afforded the dipeptide ester methyl carbobenzyloxy-L-threonyl-L-alaninate (VIII), m.p. 132.5–134°, $[\alpha]^{25}D$ −34.1° (*c* 2.0, CH_3OH) (*Anal.* Calcd. for $C_{16}H_{22}N_2O_6$: C, 56.8; H, 6.55; N, 8.28. Found: C, 56.6; H, 6.51; N, 8.19). Saponification of VIII with barium hydroxide afforded carbobenzyloxy-L-threonyl-L-alanine (IX), m.p. 129–130.5°, $[\alpha]^{25}D$ −18.5° (*c* 2.0, CH_3OH) (*Anal.* Calcd. for $C_{15}H_{20}N_2O_6$: C, 55.5; H, 6.22; N, 8.64. Found: C, 55.3; H, 6.32; N, 8.48). Condensation of IX and VII was effected in methylene chloride containing 2 equiv. of triethylamine. The pentapeptide bis-*p*-nitrobenzyl carbobenzyloxy-L-threonyl-L-alanyl-L-seryl-*im*-benzyl-L-histidyl-L-aspartate (X), m.p. 145° dec., $[\alpha]^{21}D$ −24.3° (*c* 1.9, CH_3OH) (*Anal.* Calcd. for $C_{49}H_{53}N_9O_{16}$: C, 57.47; H, 5.22; N, 12.37. Found: C, 57.24, 57.34; H, 5.54, 5.18; N, 12.42), was purified by chromatography over silica gel using a 9:1 chloroform–methanol eluent.

Removal of all protective groups from X was accomplished by hydrogenolysis over 10% palladium on charcoal using 80% ethanol as solvent, affording I, m.p. dec. 177°, $[\alpha]^{24.6}D$ −17.4° (*c* 1.95, H_2O) (*Anal.* Calcd. for $C_{20}H_{31}N_7O_{10}\cdot 0.5H_2O$: C, 44.6; H, 5.99; N, 18.2. Found: C, 44.5; H, 6.39; N, 17.8). Quantitative amino acid analysis on acid hydrolysates of each peptide were carried out using a gas chromatographic technique which is to be published. The free pentapeptide I was homogeneous to paper chromatography and paper electrophoresis under a variety of conditions and was completely digested by the enzyme leucine aminopeptidase,[7] indicating that all amino acids were present in the natural configuration.

Studies on the catalytic activity and other chemistry of I and closely related derivatives are continuing.

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(7) K. Hofmann and H. Yajima, *J. Am. Chem. Soc.*, **83**, 2289 (1961).

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Nonclassical Bridged Ion in Acetolysis of *threo*-3-Anisyl-2-butyl *p*-Bromobenzenesulfonate[1]

Sir:

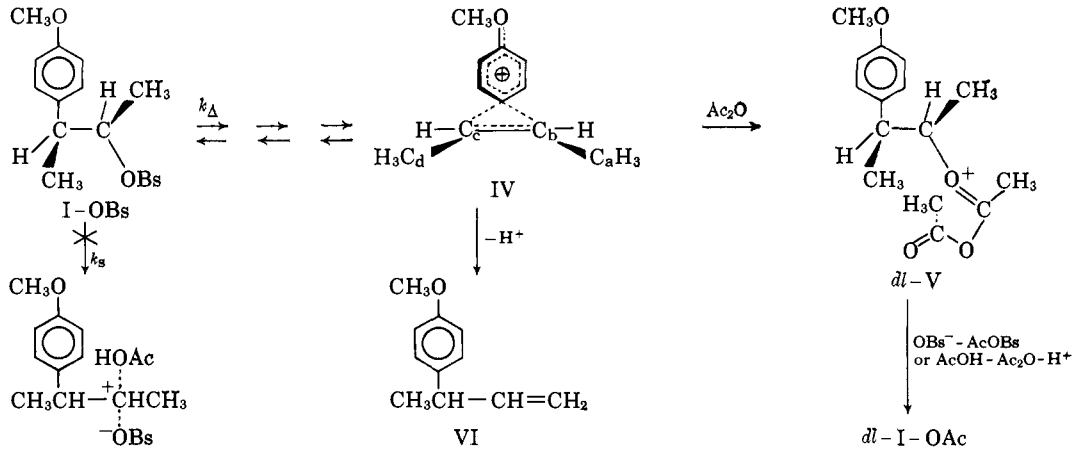
Some results of our further investigation of the acetolysis of *threo*-3-anisyl-2-butyl *p*-bromobenzenesulfonate[2] (I-OBs) are of special interest as regards the competition between bridged and classical ions and that between ion pairs and dissociated ions[2a,d] in solvolysis. In this communication we report on the bridged ion and in the following one we discuss ion pairs and dissociated carbonium ions from I-OBs.

Acetolysis of I-OBs has been studied in a series of acetic acid–acetic anhydride mixtures.[3] The major product is *threo* acetate in all the solvents, even in pure acetic anhydride, although some of the exact details of how I-OAc is produced in the latter solvent are not clear. Reproducible values of the titrimetric rate constant, k_t^0, followed by titration with standard sodium acetate in acetic acid, were obtained in pure acetic anhydride, the k_t^0 values in several different batches of solvent showing no variation due to changes in concentration of trace contaminants (*e.g.*, AcOH).

(1) Research sponsored by the National Science Foundation.

(2) S. Winstein, *et al.*: (a) *Chem. Ind.* (London), 664 (1954); (b) *J. Am. Chem. Soc.*, **74**, 1140 (1952); (c) *ibid.*, **76**, 2597 (1954); (d) *ibid.*, **78**, 328 (1956); (e) *ibid.*, **80**, 169 (1958); **83**, 885, 4986 (1961).

(3) S. Smith, A. H. Fainberg, and S. Winstein, *ibid.*, **83**, 618 (1961).



Therefore, it would appear that acetate formation is determined when acetic anhydride becomes covalently bound to the carbonium ion to yield a species like V, the latter reacting inevitably with, *e.g.*, AcOH or OBs^- to yield I-OAc along with Ac_2O or AcOBs. The latter substance titrates as HOBs in the titrimetric procedure.

Products from I-OBs have been determined by vapor phase chromatographic analysis much more accurately than was possible in the former work[2e] in acetic acid. We find that acetate I-OAc is produced nearly exclusively both in AcOH (99.7%) and pure Ac_2O (99.4%). The I-OAc obtained is completely *dl-threo* (>99.9%), no *erythro* contaminant being visible, whereas 0.1% is easily detectable. Traces of olefin accompany the I-OAc in the solvolysis product, 0.3% being observed in AcOH and 0.6% in Ac_2O. Analysis of the olefin from Ac_2O at 50° with or without added potassium acetate showed it to be nearly entirely the terminal olefin VI (>97%). The nature of the products, as well as the high rate of solvolysis[2] compared to the 3-phenyl-2-butyl system, points to a very high ratio of anchimerically assisted ionization of I-OBs to a bridged ion (k_Δ) over anchimerically unassisted ionization to a classical ion (k_s). This ratio is understandably greater than in the case of the 3-phenyl-2-butyl system.[4] On the basis of classical carbonium ions, one cannot account for the high rate and the unique stereochemical result. Also, one could not understand the very small proportion of olefin and the tendency for the latter to be terminal rather than internal. General experience with carbonium ions suggests that a classical 3-anisyl-2-butyl cation would give considerable elimination, preferably leading to internal olefin. The bridged ion accounts not only for the high rate and stereospecificity, but also the difficulty in producing internal olefin and the preference for the terminal one. Elimination of a proton from the bridged ion to yield internal olefin can be expected to be stereoelectronically unfavorable because of the geometric position of the hydrogen atoms on C_b and C_c, but no such difficulty opposes removal of a proton from C_a or C_d to form terminal olefin.

One wonders whether H. C. Brown[5] would explain the present facts without recourse to a bridged carbonium ion.

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(4) D. J. Cram, *J. Am. Chem. Soc.*, **71**, 3863 (1949); **74**, 2129 (1952).

(5) H. C. Brown, paper at Transition State Symposium, Sheffield, Eng., April 3–4, 1962; Special Publication No. 16, The Chemical Society, London, 1962, pp. 140–157, 176–178. In our opinion this paper gives a poor perspective on the role of anchimerically assisted ionization and bridged or nonclassical ions in various solvolyses. Also, the paper suffers from important misquotations and omissions.

Dissociated Ions and Ion Pairs in Acetolysis of *threo*-3-Anisyl-2-butyl *p*-Bromobenzenesulfonate[1]

Sir:

Recent results of our further kinetic study of the acetolysis of *threo*-3-anisyl-2-butyl *p*-bromobenzenesulfonate[2] (I-OBs) are helpful in understanding the competition between ion pairs and dissociated carbonium ions[2a,d] in solvolysis.

Kinetic data for acetolysis of I-OBs in a series of acetic acid–acetic anhydride mixtures of decreasing ionization power and increasing dissociating ability[3] are illustrated in Table I for AcOH, 50% AcOH–Ac_2O, and pure Ac_2O. As acetic anhydride is added, to acetic acid solvent, the titrimetric rate constant, k_t^0, rises at first and passes through a maximum before dropping steeply as pure acetic anhydride is approached. On the other hand, the ionization rate constant, k_1^0, equal to the polarimetric value, k_α^0, drops as acetic anhydride is added. The maximum in k_t^0 is associated with a minimum in the over-all importance of ion-pair return as gauged by the ratio (k_α^0/k_t^0). The size of the special salt effect of added lithium perchlorate, a

TABLE I

KINETIC DATA FOR ACETOLYSIS OF I-OBs

	AcOH (25.0°)	50% AcOH–Ac_2O (25.0°)	Ac_2O (50.0°)
$10^7 k_\alpha^0$, sec.$^{-1}$ (polarimetric)	798	578	442
$10^7 k_t^0$, sec.$^{-1}$ (titrimetric)	196	318	107
k_α^0/k_t^0	4.1	1.8	4.1
k_{ext}^0/k_t^0	2.58	1.56	1.47
k_t^0/k_t^d	1.00	2.39	12.7
$10^4(Bu_4NOBs)_{0.5}$, *M*	...	3	0.8
k_3/k_s^{III}	*ca.* 0	3.87	35.7
% ROAc from III	*ca.* 100	21	3
% ROAc from IV	*ca.* 0	79	97

(1) Research sponsored by the National Science Foundation.

(2) S. Winstein, *et al.*: (a) *Chem. Ind.* (London), 664 (1954); (b) *J. Am. Chem. Soc.*, **74**, 1140 (1952); (c) *ibid.*, **76**, 2597 (1954); (d) *ibid.*, **78**, 328 (1956); (e) *ibid.*, **80**, 169 (1958); **83**, 885, 4986 (1961).

(3) S. Smith, A. H. Fainberg, and S. Winstein, *ibid.*, **83**, 618 (1961).