Solvolysis of the Sulfonate Esters of 1-(4,6-Dimethyl-*s*-triazin-2-yl)-2-propanol and 4-(4,6-Dimethyl-*s*-triazin-2-yl)-2-butanol Involving a Special Salt Effect and Anchimeric Assistance

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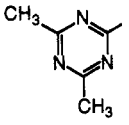
The sulfonate esters of 1-(4,6-dimethyl-*s*-triazin-2-yl)-2-propanol (**2a**) and of 4-(4,6-dimethyl-*s*-triazin-2-yl)-2-butanol (**3a**) have been synthesized and solvolyzed in formic acid and acetic acid to determine their products and rates. The solvolysis of the esters of **2a** gave predominantly alkene, and the results of formolysis are consistent with an E2 mechanism. However, in buffered acetic acid the 20-fold increase in rate relative to the unbuffered acetic acid requires the postulation of an E1cB-like mechanism involving ion pairs and a special salt effect by acetate ion. In contrast, the solvolysis of the sulfonate ester of **3a** gave a product (**11**) which resulted from anchimeric assistance by the triazine ring. Qualitative and quantitative evidence of **11** was obtained from the hydrolysis of **11** and subsequent derivatization of the 4-aminopentanoic acid.

In a previous paper we reported[1] the substituent constants for the 4,6-dimethyl-*s*-triazinyl substituent **1** which had been determined from the ionization constants of the



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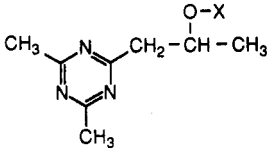
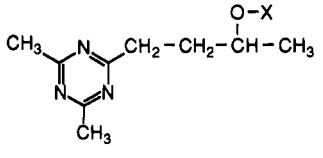
m- and *p*-(4,6-dimethyl-*s*-triazin-2-yl) benzoic acids as well as the ^{19}F NMR chemical shifts of the corresponding meta- and para-substituted fluorobenzenes. These substituent constants of σ_I, +0.15, and σ_R^p, +0.24, gave evidence of the triazinyl substituent's ability to withdraw electrons via a field effect and especially via a conjugative or resonance mechanism relative to other substituents.[2] Therefore, it was of interest to determine how this electron-withdrawing ability of the triazinyl substituent would influence solvolysis reactions. The systems selected were the substituted benzenesulfonate esters of 1-(4,6-dimethyl-*s*-triazin-2-yl)-2-propanol (**2a**) and 4-(4,6-dimethyl-*s*-triazin-2-yl)-2-butanol (**3a**).

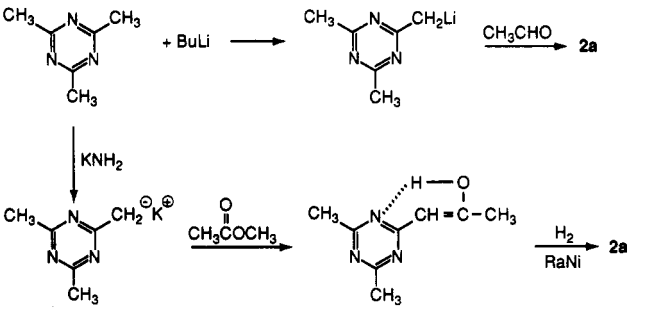


2a (X = H)
2b (X = $O_2SC_6H_4CH_3$-*p*)
2c (X = $O_2SC_6H_4Br$-*p*)



3a (X = H)
3b (X = $O_2SC_6H_4CH_3$)

Scheme I



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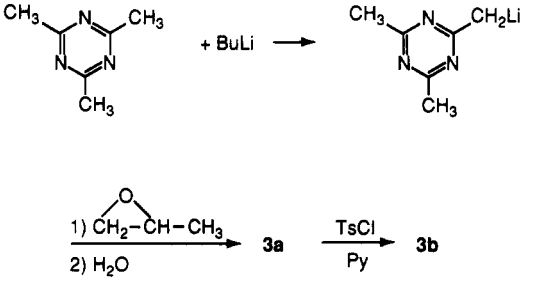
Scheme II



Results and Discussion

The alcohol **2a** from which the sulfonate esters **2b** and **2c** were synthesized was prepared by the two routes shown in Scheme I. The second route using potassium amide has been reported[3] to yield a keto–enol mixture derived from **4**. In our laboratory the potassium amide route gave an initial product which contained some keto form of **4**, but upon repeated sublimation, the pure enol **4** was obtained. The enol structure was confirmed by IR, NMR, and UV spectra[4] and crystallographic studies. Both the tosylate **2b** and the brosylate **2c** of alcohol **2a** were synthesized for the purpose of determining the element effect and comparing their solvolytic rates to analogous com-

(1) Nyquist, H. L.; Wolfe, B. *J. Org. Chem.* **1974**, *39*, 2591.
(2) (a) McDaniel, D. H.; Brown, H. C. *J. Org. Chem.* **1958**, *23*, 420. (b) Taft, R. W.; Price, E.; Fox, I. R.; Lewis, I. C.; Anderson, K. K.; Davis, G. T. *J. Am. Chem. Soc.* **1963**, *85*, 709.
(3) Osborne, D.; Wieder, W.; Levine, R. *J. Heterocycl. Chem.* **1964**, *1*, 145.
(4) (a) Silverstein, R. M.; Bassler, G. C.; Morrill, T. C. *Spectrometric Identification of Organic Compounds*, 4th ed.; Wiley: New York, 1981; p 118. (b) Branch, R. F. *Nature* **1956**, *177*, 671.

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Table I. Kinetic Data for the Solvolyses of the Sulfonate Esters of 2a and 3a

ester	solvent	conc × 10^3 (M)	temp (°C)	$k \times 10^4$ s^{-1}	no. of runs
2c	HCOOH	40	25.00 ± 0.04	2.75 ± 0.28[a]	2
2c	AcOH	1.13	50.00 ± 0.01	5.57 ± 0.17[b,c]	9
2b	HCOOH	10.0	25.00 ± 0.02	0.884 ± 0.06[b,d]	9
2b	HCOOH	5.10	25.00 ± 0.04	0.713 ± 0.03[b,d]	7
	HCOONa	5.52			
2b-d_8	HCOOH	10.0	25.00 ± 0.04	0.153 ± 0.01[b,d,e]	3
2b	AcOH	0.351	50.00 ± 0.01	2.02 ± 0.28[b,f]	1
2b	AcOH	1.37	50.00 ± 0.01	3.66 ± 0.21[b,c]	9
2b	AcOH	1.34	50.00 ± 0.01	71.7 ± 5.1[b,c]	9
	AcONa	1.50			
2b-d_8	AcOH	1.38	50.00 ± 0.01	1.87 ± 0.24[b,c,g]	7
2b-d_8	AcOD	1.80	50.00 ± 0.01	0.777 ± 0.01[b,c,h]	5
3b	HCOOH	10.0	25.00 ± 0.02	0.463 ± 0.06[b]	3
3b	AcOH	0.351	25.00 ± 0.01	0.461 ± 0.02[b]	3
3b	AcOH	0.351	50.00 ± 0.01	9.93 ± 0.20[b,i]	4

[a] Potentiometric method. Isopropyl brosylate as a control gave $k = (5.73 \pm 0.06) \times 10^{-5}$ s^{-1} (lit[5a] 6.20×10^{-5} s^{-1}). [b] Conductometric method. Correlation coefficients for pseudo-first-order kinetics were greater than 0.998. [c] No correlation diagram used. 1-*p*-Anisyl-2-propyl tosylate as a control (AcOH, 50.00 °C) gave $k = (1.46 \pm 0.01) \times 10^{-5}$ s^{-1} (lit.[5d] titrimetric, $k = (1.17 \pm 0.01) \times 10^{-5}$ s^{-1}). [d] No correlation diagram used. 1-*p*-Anisyl-2-propyl tosylate as a control (HCOOH, 25.00 °C) gave $k = (5.01 \pm 0.09) \times 10^{-4}$ s^{-1} (lit.[5e] $k = (5.1 \pm 0.5) \times 10^{-4}$ s^{-1}). [e] Experimental rate constant of $(4.31 \pm 0.24) \times 10^{-5}$ s^{-1} for 62 atom % deuterium in **2b** corrected to 100 atom %. [f] Correlation diagram used. 1-*p*-Anisyl-2-propyl tosylate as a control (AcOH, 50.00 °C) gave $k = (1.20 \pm 0.03) \times 10^{-5}$ s^{-1} with a correlation diagram (lit.[5d] $k = (1.17 \pm 0.01) \times 10^{-5}$ s^{-1}). [g] Experimental rate constant of $(2.55 \pm 0.15) \times 10^{-4}$ s^{-1} for 62 atom % deuterium in **2b** corrected to 100 atom %. [h] 100 atom % in **2b**. [i] No correlation diagram used. 1-*p*-Anisyl-2-propyl tosylate as a control (AcOH, 50.00 °C) gave $k = (1.52 \pm 0.01) \times 10^{-5}$ s^{-1}.

pounds in the literature.[5] Alcohol **3a** and its toluenesulfonate ester **3b** were synthesized according to Scheme II.

The Solvolysis of 2b,c. The rate of formolysis of **2c** was carried out potentiometrically to correspond to that reported[5a] for the parent isopropyl brosylate, but the subsequent rates of **2b** in both acetic acid and formic acid were determined conductometrically. The conductometric data were evaluated via a linear regression computer program which determined the infinity value based upon achieving a minimum deviation in the slope of the plot of $-\ln (C_\infty - C_t)$ versus time obtained between approximately 15 and 85% completion of the solvolyses. One of the consequences of the conductometric method is that the rate constants in some solvents are frequently higher (16–25%) in value than the corresponding titrimetric values if correlation diagrams are not used.[6] In acetic acid a correlation diagram was necessary to achieve agreement with the titrimetric value for our control compound, 1-anisyl-2-propyl tosylate. In formic acid correlation diagrams were not necessary to achieve agreement within 2%. However, due to the experimental complexities of constructing correlation diagrams in acetolysis, only the control and one run for the acetolysis of **2b** were determined via correlation diagrams. The remaining rate constants for purposes of comparison within the triazinyl systems were determined without the use of correlation diagrams. The kinetic results are reported in Table I. The deuterium analogue of **2b** was synthesized by two methods, one yielding **2b**-d_8 with approximately 62% atom % and the other yielding essentially 100 atom % deuterium at the β-carbon as determined by NMR. The isotope effect and the extent of deuterium exchange in formolysis were determined by solvolyzing **2b**-d_8 (62 atom %) in protium formic acid at 25 °C. The isotope effect, when corrected for the percent protium, gave a value of $k_H/k_D = 5.8$. The isolated product after formolysis for 48 h (1 half-life: 2.2 h) at 25 °C showed no significant increase in protium within experimental error (<5%) at the initially deuterated β-carbon relative to the terminal methyl group. The acetolysis of **2b**-d_8 (100 atom %) was carried out in acetic acid-d_1 to exclude possible protium exchange, and an isotope effect of $k_H/k_D = 4.7$ was obtained. It is assumed that any differences between protium acetic acid and acetic acid-d_1 would be negligible.[7] The absence of deuterium exchange in acetolysis was determined by isolating the products from the acetolysis of protium tosylate **2b** in acetic acid-d_1 after 24 h (1 half-life: 0.53 h) at 50.0 °C. Within experimental error (5–8%) no deuterium was detected at the β-carbon. Likewise, solvolyzing protium tosylate **2b** in acetic-d_3 acid-d_1 in an NMR tube at 28 °C gave no evidence of exchange after approximately 10 h.

The products from both the acetolysis and the formolysis of **2b** were identified and determined quantitatively by ^1H NMR and GLC and found to be primarily the conjugated alkene, namely 90 ± 5% from acetolysis and 85 ± 5% from formolysis. The other product was the ester. Control experiments carried out in both acetolysis and formolysis indicated that the alkene and the corresponding esters underwent some thermodynamic equilibration at the solvolysis temperatures. In both solvolyses the thermodynamic equilibration compositions (acetolysis: 79% alkene, 21% acetate) were somewhat lower in alkene than that obtained in the solvolyses. This would indicate that in both cases, in the absence of any thermodynamic equilibration, kinetic control of the products would have given even a higher yield of alkene than that isolated from the solvolyses.

The dimethyl-*s*-triazinyl substituent **1** was shown to be stable in both acetic acid and formic acid under solvolytic conditions by the quantitative recovery of 2,4,6-trimethyl-*s*-triazine from the solvents and by the quantitative isolation of the products in which the triazine ring was shown to be intact by spectroscopic methods.

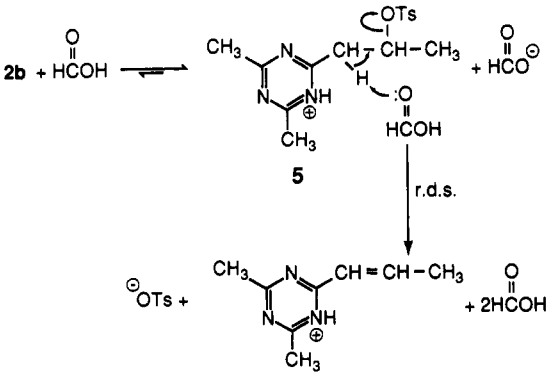
The resistance of a control solution of 2,4,6-trimethyl-*s*-triazine and *p*-toluenesulfonic acid in formic acid at 25 °C was shown to be stable within 2 Ω throughout 90% of the reaction time for **2b** after which there was a downward drift in the resistance. One interesting observation was

(5) (a) Winstein, S.; Marshall, H. *J. Am. Chem. Soc.* **1952**, *74*, 1120. (b) Lancelot, C. J.; Harper, J. J.; Schleyer, P. v. R. *J. Am. Chem. Soc.* **1969**, *91*, 4294. (c) Lancelot, C. J.; Schleyer, P. v. R. *J. Am. Chem. Soc.* **1969**, *91*, 4291. (d) Winstein, S.; Klinedinst, P. E., Jr.; Robinson, G. C. *J. Am. Chem. Soc.* **1961**, *83*, 885. (e) Winstein, S.; Brown, M.; Schreiber, K. C.; Schlesinger, A. H. *J. Am. Chem. Soc.* **1952**, *74*, 1140.

(6) (a) McDonald, R. N.; Davis, G. E. *J. Org. Chem.* **1973**, *38*, 138. (b) Bentley, T. W.; Schleyer, P. v. R. *J. Am. Chem. Soc.* **1976**, *98*, 7658.

(7) Lowry, T.; Richardson, K. S. *Mechanism and Theory in Organic Chemistry*, 3rd ed.; Harper & Row: New York, 1987; pp 241–247.

Scheme III



that as the formolysis of **2b** progressed, the resistance of the solution increased. In contrast, in the acetolysis of **2b** and the formolysis of the control compound, 3-anisyl-2-butyl tosylate, the resistance decreased as one would anticipate from the generation of the toluenesulfonate anion and the conjugate acid of the solvent and/or products. Thus, the formolysis of **2b** appears to be anomolous. It may be postulated that the initial conductance of the formolysis solution is attributable in part to the conjugate acids of **2b** and of formic acid, and the formate anion. As the elimination reaction proceeded the formate anion was neutralized and replaced by the bulkier toluenesulfonate anion which would give decreased conductance. This trend was confirmed experimentally by a comparison of the resistances of comparable concentrations of sodium formate and sodium benzenesulfonate in formic acid in which the latter showed lower conductivity.

The basicity of the *s*-triazine ring should be less than that of the 3,5,6-trimethyl-1,2,4-triazine (7×10^{-12})[8] due to the symmetry of the three nitrogens[9] and is probably comparable to the basicity of the chloroacetate anion. Therefore, it is reasonable that acetic acid would not convert **2b** into its conjugate acid to a significant amount whereas formic acid would. In addition, the acidity of formic acid as a pure solvent is much greater relative to pure acetic acid than that shown by their relative acidities in water.[10] This difference is indicated by the pK's of the self-ionization constants for formic acid (6.17[11]) and acetic acid (14.45[12]) and, for example, that urea is a weak base in acetic acid,[13] but a strong or moderately strong base in formic acid.[10] Therefore, in formolysis the significantly larger self-ionization constant and the anomolous increase in resistance as the formolysis progressed would support the existence of the conjugate acid **5** of tosylate **2b** as the major reacting species as shown in Scheme III. Both the isotope effect of 5.8 and the element effect of 3.1 would support species **5** undergoing a traditional E2 reaction as illustrated in Scheme III. The decrease in the pseudo-first order rate constant by 20% by the presence of sodium formate would be due to the common ion effect in reversing the initial equilibrium and decreasing the concentration of **5**. The high polarity of the formic acid would not favor the existence of intimate ion pairs between species **5** and the formate ion but would rather favor solvent-separated ions.[14]

In acetolysis, the weaker acetic acid and the normal decrease in resistance as the acetolysis progressed would support the neutral tosylate **2b**, rather than **5**, as the reactive species. The isotope effect of 4.7 and the element effect of 1.5 could be supported by a simple E2 mechanism, but the first-order kinetics obtained in the 20-fold rate increase due to the presence of acetate ion during the acetolysis of **2b** requires a different mechanistic scheme. The kinetics were first order with correlation coefficients greater than 0.998, and the data would not fit second-order kinetics. Three possible solutions present themselves. First, the acetate ion could shift the position of equilibrium so as to convert any existing charged species **5** to the neutral **2b**, but then the rate of proton removal and carbanion formation should be decreased as in formolysis. Secondly, the acetate ion could increase the ionic strength of the acetolysis solution to account for the observed 20-fold increase in rate. However, the normal salt effect as approximated by the equation $k = k^\circ\,[1 + b(\mathrm{NaOAc})]$[15] would increase the rate less than 1%. A third possible effect which the acetate ion could have is shown within Scheme IV. This scheme postulates an E1cB-like mechanism[16] which yields a zwitterion **7** as a result of an acetic acid molecule serving to donate a proton (or a deuteron) to the nitrogen while simultaneously abstracting a β-hydrogen. The association of the proton or deuteron of the acetic acid with the nitrogen in a loose six-membered ring would minimize deuterium exchange as found experimentally. In a possible slow step[17] the *p*-toluenesulfonate moiety of **7** would ionize to give the solvent-separated ion pair **8**. In the absence of sodium acetate, the ion pair **8** would be partitioned between **7** via k_{-2} route and the route k_4 yielding *p*-toluenesulfonate ions and ultimately alkene **9**. The rate of formation of the *p*-toluenesulfonate ions in the absence of sodium acetate is given by the following kinetic expression (supplementary material, eq 6).

$$\frac{\mathrm{d[OTs^-]}}{\mathrm{d}t} = \frac{k_1 k_2 [\mathbf{2b}]}{\dfrac{k_{-1}k_{-2}}{k_4} + k_{-1} + k_2}$$

In the presence of sodium acetate, species **8** would undergo exchange of the *p*-toluenesulfonate anion for the acetate ion in a special salt effect[5d,18] so that it would be diverted faster to alkene **9** and *p*-toluenesulfonate anion via k_3 to give the 20-fold increase in rate. The rate of formation of the *p*-toluenesulfonate anion in the presence of sodium acetate is given by the following expression (supplementary material, eq 11).

$$\frac{\mathrm{d[OTs^-]}}{\mathrm{d}t} = \frac{k_1 k_2 [\mathbf{2b}]}{\dfrac{k_{-1}k_{-2}}{k_3[\mathrm{OAc^-}]} + k_{-1} + k_2}$$

The acetate ion has been reported to display a special salt

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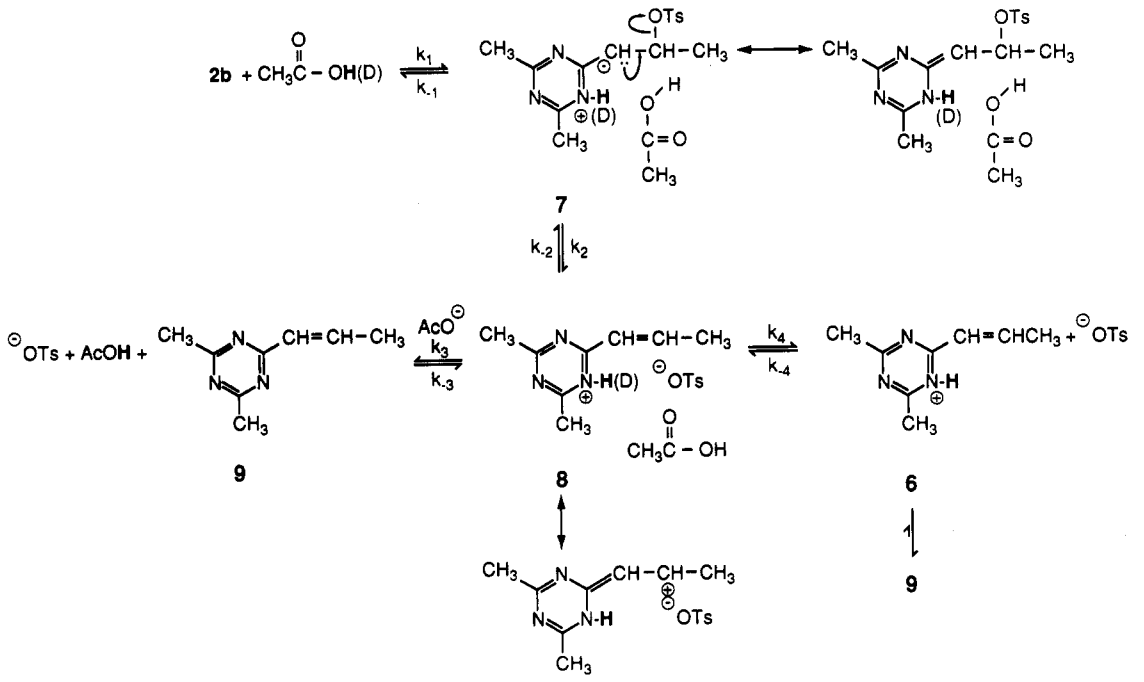
(9) Albert, A.; Goldacre, R.; Phillips, J. *J. Chem. Soc.* **1948**, 2240.
(10) Hammett, L. P.; Dietz, N., Jr. *J. Am. Chem. Soc.* **1930**, *52*, 4795.
(11) Hammett, L. P.; Deyrup, A. J. *J. Am. Chem. soc.* **1932**, *54*, 4239.
(12) Bruckenstein, S.; Kolthoff, I. M. *J. Am. Chem. Soc.* **1956**, *78*, 2974.
(13) Hall, N. F.; Conant, J. B. *J. Am. Chem. Soc.* **1927**, *49*, 3047.
(14) (a) Parker, A. J. *Chem. Rev.* **1969**, *69*, 1. (b) See ref 7, p 178. (c) Fainberg, A. H.; Winstein, S. *J. Am. Chem. Soc.* **1956**, *78*, 2770. (d) Winstein, S.; Schreiber, K. C. *J. Am. Chem. Soc.* **1952**, *74*, 2165.
(15) (a) Fainberg, A. H.; Robinson, G. C.; Winstein, S. *J. Am. Chem. Soc.* **1956**, *78*, 2777. (b) Fainberg, A. H.; Winstein, S. *J. Am. Chem. Soc.* **1956**, *78*, 2780. (c) Fainberg, A. H.; Winstein, S. *J. Am. Chem. Soc.* **1956**, *78*, 2763.
(16) (a) Bordwell, F. G. *Acc. Chem. Res.* **1972**, *5*, 374. (b) Saunders, W. H., Jr. *Acc. Chem. Res.* **1976**, *9*, 19.
(17) (a) Laidler, K. J. *Chemical Kinetics*, 3rd ed.; Harper & Row: New York, 1987; pp 283–285. (b) Murdock, J. R. *J. Chem. Educ.* **1981**, *58*, 32.
(18) (a) Fainberg, A. H.; Winstein, S. *J. Am. Chem. Soc.* **1956**, *78*, 2767. (b) Winstein, S.; Clippinger, E. *J. Am. Chem. Soc.* **1956**, *78*, 2784. (c) Crampton, M. R.; Grunwald, E. *J. Am. Chem. Soc.* **1971**, *93*, 2990. (d) Simon, J. D.; Peters, K. S. *J. Am. Chem. Soc.* **1982**, *104*, 6142.

Scheme IV



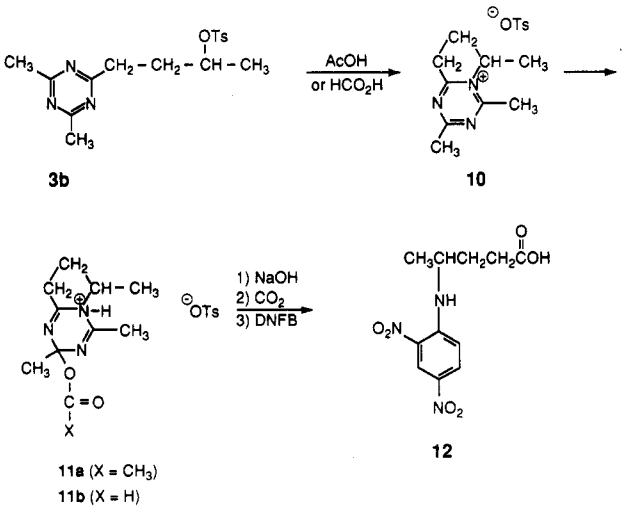
effect in a limited number of cases, such as in the acetolysis of *p*-anisylethyl tosylate,[18a] cholesteryl tosylate,[18b] 2-(2,4-dimethoxyphenyl)ethyl brosylate,[18b] in which the special salt effects are small (2.5 ± 0.4), and the *syn*-7-chlorobenzonorbornadiene.[19] Thus, this study presents an example of a rather large special salt effect by the acetate anion.

The reasons for the absence of detectable deuterium exchange may be due to one or all of the following: (1) the deuterium of the solvent associates with the nitrogen as shown in Scheme IV, (2) the exchange within a methylene group is slower than that within a methyl group on the triazine ring,[20] and (3) within an $(E1cB)_I$ reaction the initially formed carbanions are tightly hydrogen bonded in protic solvents so that internal return is extensive and that tests for preequilibrium carbanion formation such as deuterium exchange are negative when a good leaving group, such as a tosylate, is present.[16]

The Solvolysis of 3b. A comparison of the rate constants in Table I for **3b** in acetic acid with the titrimetric rate constant of 2.60×10^{-5} s^{-1} at 65 °C[21] for the parent compound, 2-butyl tosylate, would indicate that the triazinyl ring is responsible for accelerating the rate by a significant amount. The activation energy for the acetolysis is calculated as 23.8 kcal/mol which is lower than the activation energy of 26.8–27.2 kcal/mol[21] for the parent tosylate and comparable to the activation energy of 24.1 kcal/mol reported[5e] for the 1-*p*-anisyl-2-propyl tosylate which undergoes anchimeric assistance by the anisyl group.

Isolation of the acetolysis products from **3b** in the normal manner in which the extract was dried over potassium carbonate gave a residue which was neither the anticipated ester nor the alkene. Spectral data indicated the absence of the triazine ring. Therefore, the treatment of the extract with potassium carbonate was omitted and the amorphous solid resulting from the removal of the acetic acid was triturated repeatedly with ether until a hydroscopic powder was obtained. This powder could not be satisfactorily crystallized, and it gave an infrared spectrum, which, in addition to absorption bands characteristic of an ester, gave a broad absorption band from 2800 to 2200 cm^{-1} characteristic of an amine salt.[22] The elemental analysis of the powder gave results consistent with the original formula for **3b** into which a molecule of acetic acid had been incorporated. As a result of these and subsequent experimental results, the solvolyses of **3b** was postulated as shown in Scheme V to proceed via anchimeric assistance to give compound **11a** via intermediate **10**. The structure of compound **11a** was able to account for the elemental analysis and the infrared spectrum of the powder. The ^{1}H NMR spectrum gave evidence of the methine group and the attached methyl group, but the signals for the four remaining methyl groups were overlapped and superimposed upon the underlying signals for the methylene groups. However, no methyl signals were

Scheme V



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(20) Cram, D. J. *Fundamentals of Carbanion of Carbanion Chemistry*; Academic Press: New York, 1965; p 21.
(21) Pritzkow, W.; Schoeppler, K. H. *Chem. Ber.* **1962**, *95*, 834.
(22) (a) Silverstein, R. M.; Bassler, G. C.; Morrill, T. C. *Spectrometric Identification of Organic Compounds*, 4th ed.; Wiley: New York, 1981; p 128. (b) Brand, J. C. D.; Eglinton, G. *Applications of Spectroscopy to Organic Chemistry*; Oldbourne Press: London, 1965; p 111.

present at δ 2.5 where the ring methyl groups of **3** absorbed, but were shifted upfield as a result of the interruption of the aromaticity of the triazine ring in **11a**. When tosylate **3b** was solvolyzed in acetic acid-d_1 the ^1H NMR signals for the methyl and the methylene groups adjacent to the triazine ring essentially disappeared after 20 h. In contrast, a control experiment with 2,4,6-trimethyl-*s*-triazine in acetic-d_3 acid-d_1 and an equal amount of trifluoroacetic acid-d_1 gave only a 33% exchange after approximately 24 h. These results would be consistent with the formation of product **11a** in which the positive charge on the ring would enhance the acidity, and hence the exchange of the hydrogens on the adjacent carbons. Likewise, ^{13}C NMR, although unable to account for all of the carbons, gave evidence of significant changes in the triazinyl substituent. All attempts to isolate the free base from salt **11a** failed. The methods attempted were displacement by ammonia, elution from a basic resin (–N(CH_3)$_2$), and treatment with anhydrous potassium carbonate.

To substantiate the formation of **11** as the principal product from the acetolyses and the formolysis, the semiquantitative formation and derivatization of the 4-aminopentanoic acid obtained from the basic hydrolysis of **11** were undertaken. The pH was adjusted to 9 with carbon dioxide, and the resulting 4-aminopentanoic acid was derivatized with 2,4-dinitrofluorobenzene. Upon isolation, the crude derivative was purified by removal of the 2,4-dinitrophenol via sublimation. The purified derivative **12** was obtained in 36% and 18% overall yields from acetolysis and formolysis, respectively. A control experiment in which 5-methyl-2-pyrrolidone was treated in a similar manner gave an overall yield of the purified derivative **12** of 38%. This quantitative data would indicate that anchimeric assistance is the principal route for the acetolysis reaction and a major route for the formolysis reaction. It is significant to note that anchimeric assistance would have to occur via the neutral reactant, and that the latter is the predominant species in acetic acid but probably a minor species in formic acid as indicated by the change in the conductance within the formolysis of **2b**. The conjugate acid of **3b**, in the case of formolysis, could be responsible for giving rise to other products in addition to **11b** and hence account for the lower yield of the 2,4-DNP derivative **12** from formolysis.

As shown in Scheme V, immediately after anchimeric assistance by the triazine ring, it acquires a positive charge in the formation of the intermediate **10**. This positive charge may be delocalized throughout the ring on the attacking nitrogen and the three carbons. Thus, it is conceivable that the acetic acid, or the formic acid, molecule could attack at any one of the three carbon atoms. However, examination of models of the ester products resulting from the attack by the acid molecule at the three possible positions would indicate a preference for the position shown in **11** because it enables the carbonyl oxygen to hydrogen bond with the acidic hydrogen of the tertiary amine salt. It is on this basis that the positional assignment is made.

Numerous examples exist in which nitrogen atoms in acyclic compounds display neighboring group participation to form cyclic products, as well as nitrogen atoms within heterocyclic compounds which influence reactions intramolecularly without the resulting formation of a new ring.[23] However, a number of examples have been reported in which nitrogen atoms within heterocyclic compounds have been involved in neighboring-group participation which leads to the formation of a new ring. The dibromo derivative of 1-allylpyrazole has been thermally quaternized to give N-5 cyclization followed by dehydrobromination to give diazapentalene.[24] Likewise, 2-(3-buten-1-yl)-pyridine, upon iodination in chloroform, has been converted to 2-(iodomethyl)-1,5-pyridopyrrolidinium iodide.[25] Transannular cyclizations also represent examples of heterocyclic nitrogen atoms which participate in the formation of bicycloproducts.[26] Heterocyclic nitrogen atoms have also been postulated as being involved in the formation of 1-*tert*-butyl-1-azabicyclobutonium ion intermediates through anchimerically assisted ionization of 1-*tert*-butyl-3-chloroazetidine and its corresponding toluenesulfonate ester.[27]

Experimental Section

Melting points are corrected, but boiling points are uncorrected. ^1H NMR and ^{13}C NMR spectra were determined at 60 and 80 MHz, respectively. Mass spectra were obtained with a Finnigan 3000 gas chromatograph/mass spectrometer. Gas–liquid chromatographic analyses were carried out on an Antek Model 400 GC equipped with a 6-ft 5% SE 30 Chrom P column and a Shimadzu data processor. Elemental analyses were performed by Schwarzkopf Microanalytical Laboratory, Woodside, NY. Unless stated otherwise, acetolysis and formolysis rates were determined conductometrically similar to the method used by McDonald and Davis.[6] The conductivity cells used for acetolysis and formolysis were made by Industrial Instruments, Inc., Model 3L005 (k = 0.05 cm^{-1}) and Model 3L025 (k = 0.25 cm^{-1}), respectively. The cells were connected to a conductivity instrument whose construction was based upon the design of Eisenberg and Fuoss.[28] The stability of the instrument during a rate determination was checked periodically by replacing the conductivity cell with resistors of known values.

Unless otherwise noted, materials were obtained from commercial suppliers and used without further purification. Either Mallinckrodt anhydrous ether was used or the ether was distilled from sodium/benzophenone prior to use. Anhydrous acetic acid was prepared by refluxing glacial acetic acid (99.8%) with 1% acetic anhydride for several hours followed by distillation. Anhydrous formic acid was prepared by the procedure of Schlesinger and Martin.[29] 2,4,6-Trimethyl-*s*-triazine was prepared by the method of Schaefer and Peters.[30]

1-(4,6-Dimethyl-*s*-triazin-2-yl)-2-propanol (2a). *n*-Butyllithium (105 mL, 0.168 mol) in hexane (1.6 M) was added via a syringe to a solution of 2,4,6-trimethyl-*s*-triazine (20.0 g, 0.162 mol) in 200 mL of anhydrous ether under an argon atmosphere at 0 °C. The reaction mixture was cooled (–78 °C), and freshly prepared acetaldehyde (7.44 g, 0.168 mol), dissolved in anhydrous ether (100 mL), was added rapidly. The bath was removed, the reaction mixture was warmed to room temperature, and water (25 mL) was added. The ether solution was decanted, the slurry was washed with ether, and the combined ether phases were dried ($MgSO_4$). The ether was evaporated to yield a yellow liquid residue which was distilled to afford 12.7 g (47%) of product: bp 95–110 °C (3 Torr); mp 31.5–33.5 °C; IR (neat) 3400, 2980, 1550, 1430, 1100, 950 cm^{-1}; ^1H NMR (CCl_3) δ 1.28 (d, 3 H, J = 6 Hz), 2.56 (s, 6 H), 2.91 (d, 2 H, J = 6 Hz), 4.1–4.6 (m, 2 H). Anal. Calcd for $C_8H_{13}N_3O$: C, 57.47; H, 7.84; N, 25.13. Found: C, 57.19; H, 8.01; N, 24.88.

1-(4,6-Dimethyl-d_6-*s*-triazin-2-yl)-1,1-d_2-propan-2-ol-d_1 (2a-d_9). Alcohol **2a** (2.33g, 0.0140 mol) was dissolved in D_2O (3.5

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mL), and a small stream of ND_3 was bubbled through the solution briefly. After 7 days the solvent was removed under vacuum at 25 °C to give a viscous liquid. The above procedure was repeated twice to give a liquid residue (95 atom % D) which was extracted with ether and dried (Na_2SO_4). After removal of the solvent, the liquid residue was distilled to afford 0.450 g of product: bp 81–83 °C (0.65 Torr).

1-(4,6-Dimethyl-*s*-triazin-2-yl)prop-1-en-2-ol (4) and (2a). Compound 4 was prepared by the method reported by Levine[3] for the synthesis of the corresponding keto compound. After repeated sublimations of the crude product, the yellow compound 4 was obtained (23%): mp 67.0–68.0 °C; IR ($CHCl_3$) 3005, 1640, 1540, 1430, 1320, 1040(w), 910 cm^{-1}; (neat) 3200–2200, 1720(w), 1630, 1530, 1420, 1300, 890 cm^{-1}; UV_{max} (C_6H_{12}) 296 nm; ^1H NMR ($CDCl_3$) δ 2.10 (s, 3 H), 2.55 (s, 6 H), 5.42 (s, 1 H), 14.0 (broad s, 1 H). Anal. Calcd for $C_8H_{11}N_3O$: C, 58.17; H, 6.71; N, 25.44. Found: C, 58.00; H, 6.73; N, 25.74. Continued sublimation of the residue after removal of 4 gave a white solid, mp 180–183.5 °C, which was identified as 4-acetamido-2,6-dimethylpyrimidine by mmp (183–185 °C) with an authentic sample, mp 185–187 °C (lit.[3] mp 186–187 °C).

Compound 4 (0.75 g, 0.0045 mol) was hydrogenated (50 psi) in cyclohexane (60 mL) with freshly prepared Raney nickel (0.75 g). The hydrogenation reaction was followed by the change in λ_{max} (296 to 265 nm), and when completed, the mixture was filtered, and the solvent was removed under vacuum to afford 0.605 g (80%) of solid: mp 34.0–35.5 °C. Spectral data were identical to that obtained for **2a** prepared above.

1-(4,6-Dimethyl-*s*-triazin-2-yl)-2-propyl *p*-Toluenesulfonate (2b). This compound was prepared by the method of Fieser and Fieser[31] to afford impure tosylate (66%) which was recrystallized from ether/pentane: mp 51.5–52.5 °C; IR (neat) 3010, 2980, 1610, 1550, 1450, 1380, 1180, 930 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.48 (d, 3 H, J = 6 Hz), 2.43 (s) and 2.49 (s) (combined 9 H), 2.9–3.3 (m, 2 H), 5.1–5.5 (m, 1 H), 7.23 (d, J = 8 Hz) and 7.65 (d, J = 8 Hz) (combined 4 H). Pure **2b** decomposed within hours at room temperature.

1-(4,6-Dimethyl-d_6-*s*-triazin-2-yl)-2-propyl-1,1-d_2 *p*-Toluenesulfonate (2b-d_8). This compound was prepared by two methods. It was prepared as 99+ atom % D from alcohol **2a**-d_9, 95 atom % D, by the above method, and also by a manner analogous to the synthesis of compounds **2a** and **2b** except that acetonitrile-d_3 (99 atom % D) was substituted for acetonitrile in the synthesis of 2,4,6-trimethyl-*s*-triazine. The purified tosylate was found to be 62% deuterium on the basis of NMR data: mp 51.5–52.5 °C; ^1H NMR ($CDCl_3$) δ 1.48 (d, 3 H, J = 6 Hz), 2.43 (s) and 2.49 (s) (combined 5.2 H), 2.8–3.2 (m, 0.75 H), 5.0–5.4 (m, 1 H), 7.23 (d) and 7.65 (d) (combined 4 H). The compound decomposed within hours at room temperature.

1-(4,6-Dimethyl-*s*-triazin-2-yl)-2-propyl *p*-Bromobenzenesulfonate (2c). This compound was prepared by the method of Tipson[32] to afford crude product (72%) which was dissolved in pentane, treated with charcoal, filtered, and cooled (−80 °C) to yield a white powder. The powder was recrystallized several times from pentane to give a white powder: mp 64.0–64.5 °C; IR (neat) 3120, 3005, 2970, 1540, 1435, 1370, 1190, 915, 760 cm^{-1}. The compound decomposed within hours at room temperature. Anal. Calcd for $C_{14}H_{16}N_3O_3SBr$: C, 43.53; H, 4.18; N, 10.88; Br, 20.69. Found: C, 43.47; H, 4.50; N, 10.66; Br, 20.09.

Preparation of Buffered Solutions. Sodium formate (0.190 g, 99.0% pure, dried under vacuum for 2 months) was dissolved in 500 mL of anhydrous formic acid to give a 0.005 52 M solution. The buffer solution was stored in stoppered flasks at 5 °C.

Sodium carbonate (0.0319 g, 99.84% pure, 0.300 mmol, dried 150 °C/3 h) was dissolved in 400 mL of anhydrous acetic acid. Acetic anhydride (31 μL, 0.330 mmol) was added, and the solution was refluxed for six days and stored in a stoppered flask.

Formolysis Rate of 2c. Potentiometric Method. The potentiometric determination of the rate constant was carried out according to the method of Winstein and Marshall[5a] using an I. L. Deltamatic Model 245 pH meter with standard glass and calomel electrodes. A control to determine the effectiveness of the quench with time was carried out, and each aliquot was appropriately corrected for a slight drift. The formolysis rate of isopropyl brosylate was carried out as a control.

Acetolysis Rate of 1-*p*-Anisyl-2-propyl Toluenesulfonate: Conductometric Method with a Correlation Diagram. *p*-Toluenesulfonic acid monohydrate (3.80 g, 0.0200 mol), acetic anhydride (2.17 g, 0.0213 mol) and 1 mL of a 3.5×10^{-2} M solution of estragole in anhydrous acetic acid were diluted to 100 mL. Aliquots of this solution (3.5×10^{-4} M in estragole, 0.200 M in toluenesulfonic acid) were added to an acetic acid solution of estragole (3.5×10^{-4} M), and the resistances were measured to obtain a correlation diagram. 1-*p*-Anisyl-2-propyl tosylate (0.180 g, 5.62×10^{-4} mol) was dissolved in and diluted to 10 mL with anhydrous acetic acid (time zero). A 1.0-mL aliquot was diluted to 100 mL, the solution was transferred to the conductivity cell, the latter was immersed in a 50.0 ± 0.01 °C bath, and the resistances were measured with time. The rate constant was determined by the utilization of the correlation diagram and a least-squares analysis of the equation $-\ln (C_\infty - C_t) = kt - \ln (C_\infty - C_0)$.

Acetolysis Rate of 2b: Conductometric Method with a Correlation Diagram. Tosylate **2b** (0.113 g, 0.351 mmol) was dissolved in anhydrous acetic acid to a volume of 10.0 mL. A 1.0-mL aliquot was diluted with anhydrous acetic acid to 100.0 mL (3.51×10^{-4} M). The solution (50.0 mL) was pipetted into the conductivity cell and the latter was immersed in a bath (50.00 ± 0.01 °C). Resistances were measured at appropriate intervals for approximately 2 half-lives, and t_∞ was determined after 8 half-lives. A usable correlation diagram to relate the resistance to the log of the concentration of toluenesulfonic acid was constructed by utilizing both 2,4,6-trimethyl-*s*-triazine and the acetolysis residue. The latter two triazine-containing components were combined in different ratios so that the molar sum of the triazine compounds remained at 3.5×10^{-4} M, but the concentration of the triazine component from the acetolysis residue was varied and was matched by an equal concentration of the toluenesulfonic acid. The concentration of triazine compound in the acetolysis residue was shown to be representative of the alkene by titration to an inflection point with *p*-toluenesulfonic acid.

Acetolysis Rate of 2b: Conductometric Method without a Correlation Diagram. The conductivity cell was rinsed (3 × 5 mL) with anhydrous acetic acid and immersed in a bath at 50.00 ± 0.01 °C. Tosylate **2b** (0.0222 g, 0.0691 mmol) was dissolved in and diluted to 50.0 mL with anhydrous acetic acid (52–53 °C) to give a solution 0.001 29 M in **2b**. The solution was transferred to the conductivity cell and resistances were measured at appropriate intervals for approximately 3 half-lives. The data were evaluated via a linear regression computer program which determined the infinity value based upon achieving minimum deviation in the slope of the plot of $-\ln (C_\infty - C_t)$ vs time.

Acetolysis Rate of 2b-d_8 without a Correlation Diagram. The procedure was identical to that for tosylate **2b** above.

Buffered Acetolysis Rate of 2b without a Correlation Diagram. The conductivity cell was rinsed (3 × 5 mL) with the buffered anhydrous acetic acid solution (0.001 50 M in NaOAc), flushed with Ar, and immersed in a bath at 50.00 ± 0.01 °C. Tosylate **2b** (0.0201 g, 0.0625 mmol) was dissolved in and diluted to 50 mL with the buffered anhydrous acetic acid solution (50–55 °C) to give a solution 0.001 25 M in **2b**. The solution was transferred to the conductivity cell, and resistances were measured as rapidly as possible until essentially no further change in resistance occurred.

Formolysis Rate of 2b: Conductometric Method. Tosylate **2b** (0.160 g, 0.499 mmol) was dissolved in and diluted to 50.0 mL with anhydrous formic acid to give a solution 0.0100 M in **2b**. The conductivity cell was rinsed, and the remaining solution was transferred to the conductivity cell immersed in a bath at 25.00 ± 0.02 °C. Resistances were measured at appropriate intervals for several half-lives. The data were evaluated as in acetolysis.

Buffered Formolysis Rate of 2b: Conductometric Method. The conductivity cell was rinsed (3 × 5 mL) with the buffered anhydrous formic acid solution (0.005 52 M in NaOOCH), flushed with Ar, and immersed in a bath at 25.00 ± 0.04 °C. The tosylate **2b** (0.0398 g, 0.124 mmol) was dissolved in and diluted to 25.0 mL with the buffered anhydrous formic acid solution to give a solution 0.004 95 M in tosylate **2b**. The solution was transferred

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to the conductivity cell, and resistances were measured at appropriate intervals for approximately 3 half-lives. The data were evaluated as in acetolysis.

Conductance of Benzenesulfonate and Formate Anions in Formic Acid. A solution (25 mL, 0.0251 M) of dried sodium benzenesulfonate (113 mg) in anhydrous formic acid was added in 5 mL aliquots to anhydrous formic acid (25 mL) contained in the conductivity cell at 25.0 °C. After equilibrating for 15 min after each addition, the resistance was measured. In a similar manner a solution (25 mL, 0.0269 M) of dried sodium formate (45.8 mg) in anhydrous formic acid was added in 5.0-mL aliquots to anhydrous formic acid (25 mL) contained in the conductivity cell, and the resistances were measured.

Preparation of the Acetate of 2a. Alcohol **2a** (0.726 g, 4.34 mmol) was dissolved in pyridine (4.0 mL, Karl Fischer grade), the solution was cooled to 0 °C, acetic anhydride (0.5 mL, 5.3 mmol) was added with stirring, and the solution was allowed to stand at 5 °C (5 days). The solvent was removed under vacuum (<40 °C), ether (5 mL) was added, and the solution was extracted with water (3 × 7 mL). The aqueous phases were extracted with dichloromethane (10 mL), and the organic extracts were combined, dried ($MgSO_4$), and distilled to yield a forerun of alkene followed by the acetate: bp 91 °C (1.8 Torr); IR (neat) 2990, 1740, 1545, 1440, 1240 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.3 (d, 3 H, CH_3), 1.9 (s, 3 H, $COCH_3$), 2.5 (s, 6 H), 2.9 (d, 2 H), 5.3 (m, 1 H). Anal. Calcd for $C_{10}H_{15}N_3O_2$: C, 57.40; H, 7.23; N, 20.08. Found: C, 57.42; H, 7.41; N, 20.17.

Preparation of 1-(4,6-Dimethyl-*s*-triazin-2-yl)-1-propene (9). Alcohol **2a** (3.061 g, 0.0183 mol) was dissolved in dry benzene (225 mL), and P_2O_5 (6 g) was added portionwise during 24 h as the mixture was refluxed with stirring for 48 h. The mixture was filtered, and the solvent was evaporated under vacuum to yield a liquid residue which was distilled: bp 69 °C (3.4 Torr); IR (neat) 3025, 2980, 1660, 1540, 1440, 970 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.98 (dd, 3 H, J = 7, 2 Hz), 2.59 (s, 6 H), 6.30 (dq, 1 H, J = 15, 2 Hz, —CH=), 7.30 (dq, 1 H, J = 15, 7 Hz, =$CHCH_3$). Anal. Calcd for $C_8H_{11}N_3$: C, 64.40; H, 7.43; N, 28.17. Found: C, 64.46; H, 7.71; N, 28.03.

Product Analysis from Acetolysis of 2b. Tosylate **2b** (0.907 g, 2.84 mmol) was dissolved in anhydrous acetic acid (25 mL) and maintained at 50.00 °C for 3 h. The mixture was cooled, and the solvent was distilled (30–37 °C (24 Torr)) to yield a liquid residue which was dissolved in dichloromethane (30 mL) and permitted to stand 24 h over anhydrous K_2CO_3 and $MgSO_4$. The solvent was removed (25 °C) to afford 0.410 g of liquid residue (97% if totally alkene). Spectral and GLC data were used to determine the relative yield of alkene (90 ± 5%) and acetate within the residue.

Equilibration in Acetic Acid of the Acetate of 2a and Alkene 9. Alkene **9** (0.453 g) was dissolved in acetic acid (0.491 g) contained in a stoppered 1-mL volumetric flask, and the latter was flushed with Ar and placed in a bath (50.00 ± 0.01 °C). Samples were withdrawn and analyzed via GLC: 5 h, 82% alkene, 18% acetate; 21 h, 79% alkene, 21% acetate.

Similarly, the acetate of **2a** (0.0168 g) was dissolved in acetic acid (0.168 g) and analyzed: 5 h, 77% alkene, 23% acetate; 21 h, 79% alkene, 21% acetate.

Product Analysis from Formolysis of 2b. Tosylate **2b** (0.501 g, 1.56 mmol) was dissolved in anhydrous formic acid (25 mL) and permitted to stand at 25 °C for 24 h. The formic acid was removed (25 °C) under reduced pressure, the residue was dissolved in dichloromethane, and the resulting solution was treated with anhydrous K_2CO_3 (12 h). The solution was filtered, and the solvent was removed to afford 0.214 g of liquid (92% if totally alkene). Spectral and GLC data were used to determine the relative yield of alkene (85 ± 5%) and formate ester within the residue.

Equilibration of the Formate of 2a and Alkene 9. Alkene **9** (0.36 g) was dissolved in anhydrous formic acid (50 mL) and maintained at 25.0 °C for 48 h. The formic acid was removed under vacuum, dichloromethane (50 mL) was added, and the solution was treated with anhydrous K_2CO_3. The solvent was removed to afford 0.31 g (85%) of liquid residue; IR (neat) the 1750 cm^{-1} band (C=O) was stronger than the 1680 cm^{-1} band (C=C); IR (neat) of formolysis product, the 1750 cm^{-1} band (C=O) was weaker than the 1680 cm^{-1} band (C=C).

Product Analysis from Buffered Acetolysis of 2b. Tosylate **2b** (0.0816 g, 0.254 mmol) was weighed into a dried flask and dissolved in buffered anhydrous acetic acid solution (2.6 mL, 0.0987 M in NaOAc) to give a solution 0.0976 M in **2b**. The flask was flushed with Ar, stoppered, and immersed in a bath (50.00 ± 0.01 °C). After approximately 10 half-lives, the flask was cooled and the solvent was removed under vacuum (<22 °C) to yield a residue which was dissolved in dichloromethane and treated with anhydrous K_2CO_3. The solvent was evaporated to afford a liquid residue (0.0819 g). Chromatographic analysis showed 63% alkene and 37% acetate.

Alkene 9 with Anhydrous Toluenesulfonic Acid in Acetic-d_3 Acid-d_1. Alkene **9** (0.0773 g, 0.518 mmol) was dissolved in acetic-d_3 acid-d_1 within a NMR tube. After the initial spectrum had been taken, the tube was immersed in a 50 °C bath. Subsequent spectra showed no change in the magnitude of the signals from the alkenyl protons relative to the terminal methyl group, although the magnitude of the signal due to the proton of the acid increased. Anhydrous toluenesulfonic acid[33] (0.0901 g, 0.523 mmol) was added to the NMR tube, and after 4 h (50 °C), the relative magnitude of the signals from the alkenyl protons to that of the terminal methyl protons remained unchanged.

Stability of 2,4,6-Trimethyl-*s*-triazine in Acetic Acid and Formic Acid. 2,4,6-Trimethyl-*s*-triazine (0.510 g, 4.14 mmol) was dissolved in anhydrous acetic acid (25 mL) and maintained at 50 °C for 16 h. The solvent was removed under vacuum (<60 °C) to give a liquid residue which was dissolved in ether and dried (K_2CO_3). Removal of the ether afforded 0.486 g (95%) of solid: mp 31–46 °C (lit.[34] mp 59–60 °C).

2,4,6-Trimethyl-*s*-triazine (0.628 g, 5.10 mmol) was dissolved in anhydrous formic acid (25 mL) and maintained at ca. 24 °C for 21 h. The solvent was removed under vacuum (<25 °C) to give a liquid residue which was dissolved in ether and dried (K_2CO_3). Removal of the ether afforded 0.538 g (86%) of solid: mp 57–60 °C (lit.[34] mp 59–60 °C).

4-(4,6-Dimethyl-*s*-triazin-2-yl)-2-butanol (3a). *n*-Butyllithium (105 mL, 0.168 mol) in hexane (1.6 M) was added via a syringe to a solution of 2,4,6-trimethyl-*s*-triazine (19.6 g, 0.160 mol) in 500 mL of anhydrous ether under an argon atmosphere at 0 °C. The flask was cooled (−78 °C), and distilled propylene oxide (10.3 g, 0.198 mol), dissolved in anhydrous ether (100 mL), was added rapidly. The reaction mixture was stirred for 1 h, the bath was removed, the stirring was continued for 24 h, and water (50 mL) was added. The ether phase was decanted, the slurry was washed with ether (2 × 50 mL), and the combined ether extracts were dried ($MgSO_4$). The ether solution was evaporated under reduced pressure to give a crude yellow product which was purified by repeated (2×) chromatography on silica gel (3.5 cm × 10 cm) with ether (400 mL) as the eluant. This procedure afforded 3.00 g (10.3%) of compound **3a**: bp 114–116 °C (0.3 Torr); IR (neat) 3400, 2980, 2940, 2880, 1550, 1450, 1410, 1140, 1090, 1050, 980, 950 cm^{-1}; ^1H NMR (CCl_4) δ 1.14 (d, 3 H), 1.84 (m, 2 H), 2.45 (s, 6 H), 2.75 (t, 2 H), 3.75 (m, 1 H), 4.22 (s, 1 H). Anal. Calcd for $C_9H_{15}N_3O$: C, 59.64; H, 8.34; N, 23.20. Found: C, 60.09; H, 8.62; N, 22.93.

4-(4,6-Dimethyl-*s*-triazin-2-yl)-2-butyl *p*-Toluenesulfonate (3b). This compound was prepared in a 57% yield by a method similar to **2b** above: mp 89.0–89.5 °C; IR ($CHCl_3$) 3040, 2950, 1530, 1430, 1375, 1220, 1120 cm^{-1}; ^1H NMR (CCl_4) δ 1.36 (d, 3 H), 2.00 (m, 2 H), 2.48 (s, 3 H), 2.50 (s, 6 H), 2.71 (t, 2 H), 4.73 (m, 1 H), 7.52 (m, 4 H). Anal. Calcd for $C_{16}H_{21}N_3O_3S$: C, 57.29; H, 6.31; N, 12.53; S, 9.56. Found: C, 57.42; H, 6.36; N, 12.70; S, 9.83.

Acetolysis Rate of 3b. Tosylate **3b** (0.118 g, 0.351 mmol) was dissolved in anhydrous acetic acid (50 °C) to a volume of 10 mL (time zero). A 1.00-mL aliquot of this solution was diluted to 100 mL with acetic acid (3.51×10^{-4} M). The conductivity cell was rinsed twice with the acetolysis solution, 50.0 mL of the solution was placed in the cell, and the cell was immersed in a bath at 50.00 ± 0.01 °C. Resistances were measured at appropriate intervals for approximately 2–3 half-lives. Stability existed to approxi-

(33) Barton, D. M. Ger. Patent 1 160 433, 1964; *Chem. Abstr.* **1964**, *60*, 13189.

(34) Cairns, T. L.; Larchar, A. W.; McKusick, B. C. *J. Am. Chem. Soc.* **1952**, *74*, 5633.

mately 13 half-lives after which the resistance began to drift upward. The acetolysis rates of 1-*p*-anisyl-2-propyl tosylate at 50 °C and of **3b** at 25.00 ± 0.01 °C were carried out in a comparable manner.

Formolysis Rate of 3b. Tosylate **3b** (0.168 g, 0.500 mmol) was dissolved in anhydrous formic acid and diluted to 50.0 mL (0.0100 M, time zero). The conductivity cell was rinsed twice with the formolysis solution, 25 mL was placed in the cell, and the latter was immersed in a bath at 25.00 ± 0.01 °C. Resistances were measured at appropriate intervals for approximately 7 half-lives.

Product Analysis of the Acetolysis of 3b To Afford 11a. Tosylate **3b** (0.432 g, 1.29 mmol) was dissolved in anhydrous acetic acid (50 mL, 0.0258 M), flushed with argon, and placed in a 50.0 °C bath for 2.75 h (14 half-lives). The acetic acid was removed under reduced pressure (<45 °C, Ar bleed) to give a thick viscous orange residue (0.556 g). This residue was kept in an evacuated (0.05 Torr) desiccator (KOH) until a constant weight of residue was obtained (0.502 g). Repeated trituration of the residue with ether under inert atmosphere gave a hygroscopic light-orange powder: mp 60–80 °C; IR (KBr) 3420, 3200, 2950–2900, 2900–2200, 1710, 1615, 1450, 1210, 1160, 1110, 1015, 990 cm^{-1}; ^1H NMR (CD_2Cl_2) gave a broad signal (s) from δ 1.1 to 3.3 from which additional signals protruded at δ 1.3 (d, CH_3CH), 2.0 (s, CH_3CO), 2.3 ($CH_3C_6H_4$), and 3.0 (m), 4.3 (broad), 7.4 (C_6H_4). No signal was visible near δ 2.5 (CH_3-triazinyl). Anal. Calcd for $C_{18}H_{25}N_3O_5S$: C, 54.67; H, 6.37; N, 10.63; S, 8.11. Found: C, 54.52; H, 6.61; N, 10.85; S, 8.48.

A portion of the above residue (0.115 g) was dissolved in a few mL of dichloromethane under inert atmosphere and placed on an Amberlyst A-21 column (12 mm × 65 mm) and eluted with dichloromethane to afford an amorphous solid (0.069 g) which rapidly darkened. Spectral data indicated decomposition.

Product Analysis of the Formolysis of 3b To Afford 11b. An experiment comparable to the above acetolysis analysis was carried out with **3b** (0.607 g, 1.81 mmol) in formic acid (56 mL) at 25.1 °C to ultimately give a pink amorphous residue (0.668 g) which would not powder or granulate upon trituration with ether under an inert atmosphere: IR (neat) 3600–2200, 1720, 1650, 1560, 1375, 1220, 1170, 1120, 1030, 1010 cm^{-1}; ^1H NMR ($CDCl_3$) gave a broad signal(s) from δ 0.6 to 3.5 from which additional signals protruded at δ 1.1 (d, CH_3CH), 1.9, 2.1 (s), 2.2 (s), and 3.05 (m), 4.1, 7.3 (m, $-C_6H_4-$).

^1H NMR Spectral Analysis of the Acetolysis of 3b. Tosylate **3b** (0.0445 g, 0.133 mmol) was dissolved in acetic-d_3 acid-*d* (0.4 mL) and placed in an NMR tube (34 °C): initial ^1H NMR (CD_3CO_2D) δ 1.30 (d, 3, CH_3CH), 2.10 (m, 2, CH_2), 2.40 (s, 3, $CH_3C_6H_4$), 2.60 (s, 6, triazinyl-CH_3), 2.85 (dd, 2, triazinyl-CH_2), 4.80 (m, CH), 7.55 (m, 4, C_6H_4); after 10 h, ^1H NMR (CD_3CO_2D) δ 1.60 (d, CH_3CH), 2.0 (m), 2.30 ($CH_3C_6H_4$), 2.55 (s), 2.8 (m), 5.35 (m), 7.45 (m, C_6H_4), 10.2 (s, CO_2H). The signal at δ 2.55 was very small and the signal at δ 10.2 was very large. A control with 2,4,6-trimethyl-*s*-triazine (0.0453 g, 0.318 mmol) dissolved in acetic-d_3 acid-*d* (0.4 mL) containing one drop of trifluoroacetic acid-*d* was placed in an NMR tube (34 °C): initial ^1H NMR (CD_3CO_2D) δ 2.8 (s, 9.0, triazinyl-CH_3), 11.8 (s, 0.26, CO_2H). After 7.5 h the NMR spectrum indicated 17.3% exchange and after 23.5 h 33.5% exchange.

^{13}C NMR Spectral Analysis of the Acetolysis of 3b. Tosylate **3b** (0.172 g, 0.513 mmol) was dissolved in a mixture (2 mL) of 20% acetic-d_3 acid-*d* in 80% acetic acid, transferred to an NMR tube and flushed with argon: initial ^{13}C NMR δ 20.67, 21.08, 23.74, 32.85, 33.35, 79.25, 127.92, 129.84, 134.39, 144.88, 167.07, 176.00. The NMR tube was placed in a 50 °C bath for 2 h (10 half-lives) and then cooled: final ^{13}C NMR δ 21.44, 26.04, 26.74, 31.50, 64.74, 141.11, 141.48, 167.26, 170.12, 176.03, 176.63, 177.70, 188.34. A control ^{13}C NMR of 2,4,6-trimethyl-*s*-triazine: ^{13}C (CH_3CO_2H) δ 21.34, 23.89, 167.10, 176.43.

Preparation of *N*-(2,4-Dinitrophenyl)-4-aminopentanoic Acid (12). 5-Methyl-2-pyrrolidone (0.181 g, 1.83 mmol) was refluxed for 6 h with 20% NaOH (2 mL). Carbon dioxide was bubbled through the solution until pH 9 was obtained, and then the reaction mixture was evaporated to dryness. The resulting solid was dissolved in water (4 mL), 2,4-dinitrofluorobenzene (1.03 g, 5.53 mmol) was added, and the mixture was stirred for 3.5 h. Saturated sodium chloride (2 mL) was added to the yellow reaction mixture (pH 8), and the latter was extracted with ether (2 × 20 mL). The ether extracts were in turn extracted with saturated sodium bicarbonate solution (3 mL) and water (4 mL), and these aqueous extracts were combined with the original aqueous phase. The aqueous phase was acidified to Congo Red with dilute hydrochloric acid and extracted with ether (3 × 25 mL). The combined ether extracts were dried ($MgSO_4$), filtered, and evaporated to afford 0.279 g of the crude 2,4-DNP derivative **12** (54%): mp 116–142 °C. A portion of the crude derivative was recrystallized twice from methanol: mp 154.5–156.0 °C. Anal. Calcd for $C_{11}H_{13}N_3O_6$: C, 46.65; H, 4.62; N, 14.84. Found: C, 46.35; H, 4.74; N, 14.90. A second portion (0.0327 g) of the crude derivative was sublimed (105–110 °C (0.10 Torr)) to give sublimate (0.0094 g, 28.7%), mp 99.5–107 °C (2,4-dinitrophenol) and residue (0.0233 g, 71.3%), mp 149–155 °C: mass spectrum, *m/e* (rel intensity) 283 (2), 210 (42), 164 (16), 134 (22), 118 (27), 91 (26), 63 (31), 55 (100). Total conversion of 5-methyl-2-pyrrolidone to the 2,4-DNP derivative **11**: 38%.

Preparation of *N*-(2,4-Dinitrophenyl)-4-aminopentanoic Acid (12) from the Acetolysis of 3b. Tosylate **3b** (0.603 g, 1.80 mmol) was dissolved in acetic acid (70 mL), and the solution was flushed with argon and maintained at 50.0 °C for 3 h. The acetic acid was removed as in the above acetolysis product analysis, except for the prolonged evacuation, to afford crude product (0.828 g). The crude product was treated with water (1 mL), 60% NaOH (1 mL) was added, and the solution was heated near reflux for 4.25 h. The mixture was cooled and treated with carbon dioxide and 2,4-dinitrofluorobenzene as in the above preparation of **12** from 5-methyl-2-pyrrolidone. After sublimation of the crude product to remove the 2,4-dinitrophenol, the pure derivative was obtained in an overall yield of 36% from the tosylate **3b**: mp 148–154 °C; mmp with authentic sample: 150.0–154.0 °C; mass spectrum, *m/e* (rel intensity) 283 (2), 210 (39), 164 (17), 134 (27), 118 (36), 91 (45), 63 (52), 55 (100).

Preparation of *N*-(2,4-Dinitrophenyl)-4-aminopentanoic Acid (12) from the Formolysis of 3b. Tosylate **3b** (0.607 g, 1.81 mmol) was dissolved in anhydrous formic acid (56 mL), and the solution was flushed with argon and maintained at 25.0 °C for 67 h. The formic acid was removed as in the corresponding acetolysis procedure to give a pink crude residue (0.668 g). This residue was treated successively with sodium hydroxide, carbon dioxide, and 2,4-dinitrofluorobenzene as in the acetolysis derivative preparation. After sublimation to remove the 2,4-dinitrophenol, the pure derivative was obtained in an overall yield of 18% from the tosylate **3b**: mp 146–153 °C, mmp with authentic sample 146–155 °C.

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Registry No. **2a**, 138606-42-5; **2a**-d_9, 138606-47-0; **2a** acetate, 138606-50-5; **2b**, 138606-43-6; **2b**-d_8, 138606-49-2; **2c**, 138606-44-7; **3a**, 138606-46-9; **3b**, 138606-45-8; **4**, 138606-48-1; **9**, 138606-51-6; **11a**, 138606-53-8; **11b**, 138606-55-0; **12**, 138606-56-1; 2,4,6-trimethyl-*s*-triazine, 823-94-9; acetaldehyde, 75-07-0; 4-acetamido-2,6-dimethylpyrimidine, 33721-00-5; 1-*p*-anisyl-2-propyl toluenesulfonate, 898-95-3; propylene oxide, 75-56-9; 5-methyl-2-pyrrolidone, 108-27-0; 2,4-dinitrofluorobenzene, 70-34-8.

Supplementary Material Available: Kinetics of Scheme IV (4 pages). Ordering information is given on any current masthead page.