and 2.19 (acetates), 2.28 and 2.32 (dimethylamino), and 3.05 (methanesulfonate)).

When megalomicin A was treated with 0.6 *N* hydrogen chloride in methanol, erythralosamine,[4,5a,b,7] 1-*O*-methyl L-mycaroside,[8] and a new amino sugar, 1-*O*-methyl D-rhodosaminide,[1] were formed. The β-glycosidic attachment of the desosamine was evident from the nmr spectra of megalomicin A (**1**), megalalosamine (**3**), and erythralosamine, which showed doublets (J = 7 Hz) for the anomeric proton at δ 4.33, 4.42, and 4.26, respectively. Reduction of **1** with sodium borohydride followed by mild acid hydrolysis of the product gave 5-*O*-D-desosaminyl-9-dihydroerythronolide (**7**).[5a,b,9,10] The formation of erythralosamine and **7** from megalomicin A demonstrated the location of the desosamine moiety at C_5 and indicated that the aglycone of megalomicin A was identical with that of erythromycin A. When megalalosamine (**3**) was reduced with sodium borohydride, 5-*O*-D-desosaminyl-11-*O*-D-rhodosaminyl-9-dihydroerythronolide (**8**, $C_{37}H_{70}N_2O_{12}$; M^+ 734; mp 118–128°; $[\alpha]_D$ −31.5° (MeOH); pK_a = 8.9; ν_{max} ($CHCl_3$) 3440, 2790, 1725, 1170 cm^{-1}; δ 2.28 and 2.33 (dimethylamino) and 4.50 (d, J = 7 Hz, H_1 of desosamine)) was obtained. The application of Klyne's rule[11] to the molecular rotations[12] of **7**, **8**, and 9-dihydroerythronolide (**9**)[9] indicated that both the D-desosamine and the D-rhodosamine moieties were β-glycosidically attached to the aglycone in megalomicin A (**1**). The mass spectra of megalomicin A (**1**) and its derivatives indicated that the D-rhodosamine moiety was located in the C_9–C_{13} portion of the molecule,[14] while the formation of a triacetate from megalalosamine, under reaction conditions which would be expected to acetylate all of the secondary hydroxyl groups in the molecule, and not a tetraacetate, indicated that the D-rhodosamine was glycosidically attached to the secondary hydroxyl group at C_{11}.

The mycarose moiety was shown to be located at C_3 by the following series of reactions. Methanolysis of the mesylate **6** derived from megalomicin A gave 2′-acetyl-3-mesylerythralosamine ($C_{32}H_{53}NO_{11}S$; M^+ − CH_3SO_3H 563; mp 100–104°; $[\alpha]_D$ +33.5°; pK_a = 7.1; ν_{max} 2780, 1740, 1235, 1175 cm^{-1}; δ 1.78 (J = 1.5 Hz) (-(CH_3)C=CH-), 2.07 (acetate), 2.30 (dimethylamino), 3.20 (methanesulfonate), 5.48 (J = 1.5 Hz) (vinylic proton)). Methanolysis of 4′,2″-diacetylerythromycin A[4] gave 2′-acetylerythralosamine ($C_{31}H_{51}NO_9$; mp 140–150° (dec); $[\alpha]_D$ +30.8°; ν_{max} 3430, 2780, 1740, 1235 cm^{-1}; δ 1.81 (J = 1.5 Hz) (-(CH_3)C=CH-), 2.07 (acetate), 2.29 (dimethylamino), 5.51 (J = 1.5 Hz) (vinylic proton)), which on treatment with mesyl chloride gave 2′-acetyl-3-mesylerythralosamine, which was identical with that prepared from megalomicin A above.

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Participation by Neighboring Aryl Groups. V. Determination of Assisted and Nonassisted Rates in Primary Systems. Rate–Product Correlations

Sir:

Recently we applied three purely kinetic analytical methods[1] to the dissection of the titrimetric solvolysis rates (k_t) for a series of secondary β-arylalkyl substrates

Table I. Titrimetric Acetolysis Rate Constants (k_t) for a Series of β-Arylethyl Tosylates, $XC_6H_4CH_2CH_2OTs$ (I)

X	Temp, °C	k_t, sec^{-1}	$\Delta H^{\pm}$, kcal/mol	$\Delta S^{\pm}$, eu
p-CH_3O	75.1	$(8.66 \pm 0.05) \times 10^{-6}$	25.1	−10
	100.5	$(1.09 \pm 0.01) \times 10^{-4}$		
	90[a]	3.98×10^{-5}		
	115[a]	4.00×10^{-4}		
p-CH_3	90[b]	4.08×10^{-6}	25.6	−13
	115[b]	4.30×10^{-5}		
H	90[b]	1.31×10^{-6}	24.8	−18
	115[b]	1.27×10^{-5}		
p-Cl	100.7	$(2.38 \pm 0.01) \times 10^{-6}$	24.6	−19
	124.8	$(1.90 \pm 0.01) \times 10^{-5}$		
	90[a]	8.80×10^{-7}		
	115[a]	8.45×10^{-6}		
m-F	100.2	$(2.10 \pm 0.01) \times 10^{-6}$	24.2	−20
	124.5	$(1.64 \pm 0.01) \times 10^{-5}$		
	90[a]	8.24×10^{-7}		
	115[a]	7.61×10^{-6}		
m-Cl	100.2	$(2.03 \pm 0.01) \times 10^{-6}$	23.9	−21
	124.5	$(1.59 \pm 0.01) \times 10^{-5}$		
	150.0	$(9.89 \pm 0.05) \times 10^{-5}$		
	90[a]	8.07×10^{-7}		
	115[a]	7.28×10^{-6}		
m-CF_3	100.3	$(2.01 \pm 0.01) \times 10^{-6}$	23.4	−22
	124.8	$(1.49 \pm 0.01) \times 10^{-5}$		
	90[a]	8.00×10^{-7}		
	115[a]	6.89×10^{-6}		
p-CF_3	100.3	$(1.92 \pm 0.02) \times 10^{-6}$	24.6	−19
	124.8	$(1.57 \pm 0.01) \times 10^{-5}$		
	90[a]	7.30×10^{-7}		
	115[a]	6.99×10^{-6}		
p-NO_2	100.6	$(1.87 \pm 0.01) \times 10^{-6}$	23.7	−22
	124.9	$(1.40 \pm 0.03) \times 10^{-5}$		
	90[a]	7.15×10^{-7}		
	115[a]	6.35×10^{-6}		
3,5-$(CF_3)_2$	100.3	$(1.67 \pm 0.01) \times 10^{-6}$	23.8	−22
	124.8	$(1.28 \pm 0.01) \times 10^{-5}$		
	90[a]	6.54×10^{-7}		
	115[a]	5.84×10^{-6}		

[a] Calculated from data at other temperatures. [b] Calculated from a combination of literature data at other temperatures: S. Winstein, C. R. Lindegren, H. Marshall, and L. L. Ingraham, *J. Am. Chem. Soc.*, **75**, 147 (1953), and ref 5.

(1) (a) C. J. Lancelot and P. von R. Schleyer, *J. Am. Chem. Soc.*, **91**, 4291 (1969); (b) *ibid.*, **91**, 4296 (1969); (c) C. J. Lancelot, J. J. Harper, and P. von R. Schleyer, *ibid.*, **91**, 4294 (1969); (d) P. von R. Schleyer and C. J. Lancelot, *ibid.*, **91**, 4297 (1969).

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(8) P. P. Regna, F. A. Hochstein, R. L. Wagner, Jr., and R. B. Woodward, *ibid.*, **75**, 4625 (1953).
(9) M. V. Sigal, Jr., P. F. Wiley, K. Gerzon, E. H. Flynn, U. C. Quarck, and O. Weaver, *ibid.*, **78**, 388 (1956).
(10) P. V. Demarco, *Tetrahedron Lett.*, 383 (1969).
(11) (a) W. Klyne, The Royal Institute of Chemistry Lecture Series, Vol. IV, London, 1962, p 13; (b) T. Reichstein and E. Weiss, *Advan. Carbohydr. Chem.*, **17**, 99 (1962).
(12) $[M]_D$ of **9**[9] +39.9°; $[M]_D$ of 7 from megalomicin A −7.5° ($\Delta[M] = [M]_{D_7} - [M]_{D_9} = -47.4°$) and from erythromycin A[9] −11.5° ($\Delta[M]_D = [M]_{D_7} - [M]_{D_9} = -51.4°$); $[M]_D$ of 1-*O*-*n*-butyl α-D-desosaminide[13] +323° and of the β anomer −11.5°; $[M]_D$ of **8** −231° ($\Delta[M]_D = [M]_{D_8} - [M]_{D_9} = -223.5°$); $[M]_D$ of 1-*O*-methyl α-D-rhodosaminide[1] +225.1° and of the β anomer −111.1°.
(13) W. D. Celmer in "Biogenesis of Antibiotic Substances," Z. Vanek and Z. Hostalek, Ed., Academic Press, New York, N. Y., 1965, p 118.
(14) A. K. Mallams and R. S. Jaret, unpublished observations.

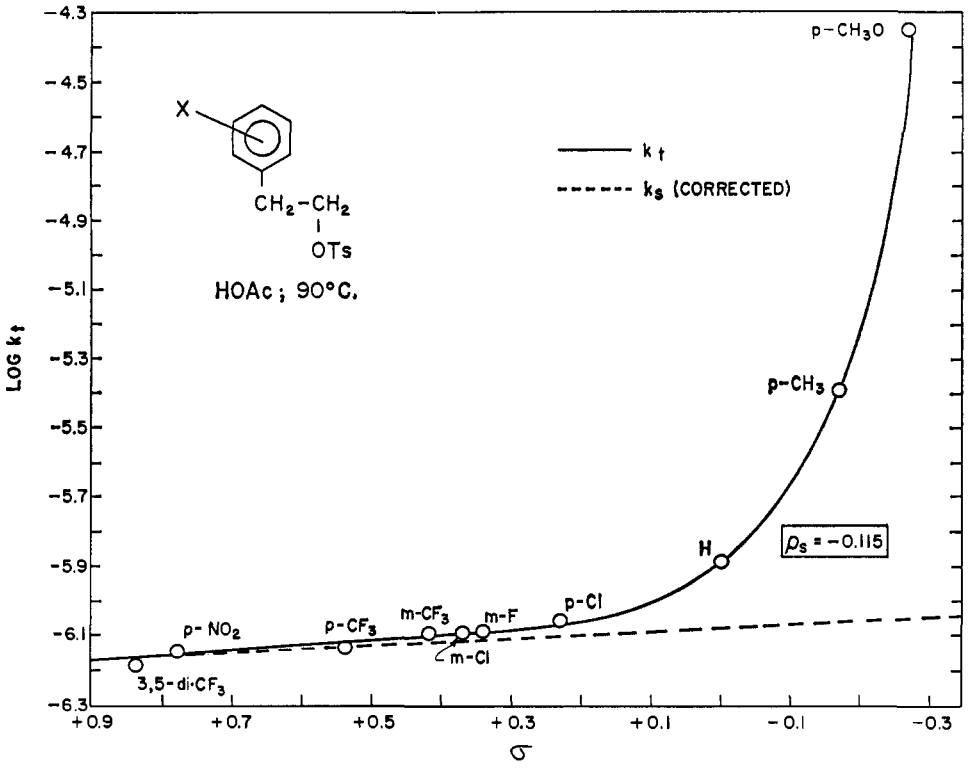

Figure 1. Log k_t *vs.* σ; β-arylethyl tosylate acetolysis.

into their constituent anchimerically assisted (Fk_Δ) and solvent-assisted (k_s)[2] pathways according to the equation $k_t = k_s + Fk_\Delta$.[3] The discreteness of these two pathways was established by means of a rate–product correlation.[1d] We now apply one of these kinetic methods, based on the Hammett equation,[1a] to the parent primary β-arylethyl system (I).

In the past, the dissection of k_t into k_s and Fk_Δ components for primary β-arylalkyl systems has required the use of a combination of rate data and product data;[4,5] we have now accomplished for the first time this dissection using rate data alone. This enables an independent comparison of rate-derived with product-derived data to be made in order to test the assumption that Fk_Δ and k_s are discrete pathways.[4-6]

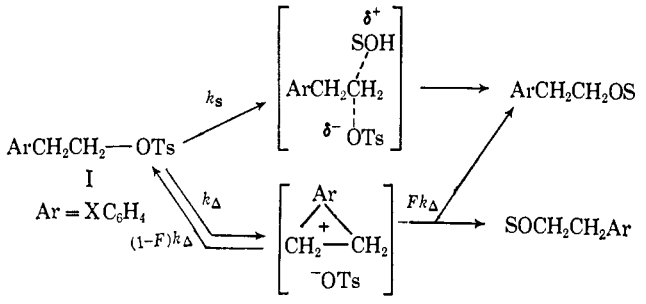

Table I lists the acetolysis data obtained for a series of β-arylethyl tosylates (I), from which were constructed Hammett plots (*e.g.*, Figure 1) of the type previously reported.[1a] Following a suggestion of Winstein[7] we have refined our previous treatment of such plots.[1a] Formerly, the assumption was made that $k_s = k_t$ for the deactivated compounds. In other words, the k_s line was drawn through the k_t points for the deactivated compounds, *e.g.*, those with *p*-NO_2, *m*-CF_3, etc., substituents. It is clear, however, that even these deactivated compounds have a small Fk_Δ component. Thus, the true k_s line should fall slightly below all of the k_t points. We have used a computer program[8] to dissect k_t into the k_s and Fk_Δ components; the corrected k_s line plotted in Figure 1 and the data in Table II are the results of this analysis.

If k_s and Fk_Δ represent truly discrete pathways, then the magnitude of aryl assistance calculated from either rate or product data should be the same.[1d] The β-arylethyl system I is particularly easily treated in this regard, since the only product of acetolysis is the β-arylethyl acetate.[9-11]

(2) As indicated previously,[1d] we take "k_s" to denote the solvent-assisted (N) solvolytic mechanism.[3]

(3) S. Winstein, E. Allred, R. Heck, and R. Glick, *Tetrahedron*, **3**, 1 (1958), and references cited therein.

(4) E. F. Jenny and S. Winstein, *Helv. Chim. Acta*, **41**, 807 (1958); A. Diaz, I. Lazdins, and S. Winstein, *J. Am. Chem. Soc.*, **90**, 6546 (1968).

(5) J. L. Coke, E. L. MacFarlane, M. C. Mourning, and M. G. Jones, *ibid.*, **91**, 1154 (1969); M. G. Jones and J. L. Coke, *ibid.*, **91**, 4284 (1969).

(6) (a) L. Eberson, J. P. Petrovich, R. Baird, D. Dyckes, and S. Winstein, *ibid.*, **87**, 3504 (1965); S. Winstein and R. Baker, *ibid.*, **86**, 2071 (1964); (b) D. J. Cram and J. A. Thompson, *ibid.*, **89**, 6766 (1967); **91**, 1778 (1969).

(7) A. Diaz and S. Winstein, *ibid.*, **91**, 4300 (1969).

(8) The program calculates a first set of approximate Fk_Δ values as deviations ($Fk_\Delta = k_t - k_s$) from the "crude" k_s correlation line defined by k_t for the deactivated substrates.[1a] From these approximate Fk_Δ values, a log Fk_Δ *vs.* σ^+ Hammett plot is constructed and extended through the σ^+ constants for the deactivated substrates. This extrapolation yields for these deactivated substrates Fk_Δ values of small magnitude. These are then deducted from their k_t values to give refined k_s points, from which a new k_s correlation is constructed. A second improved set of approximate Fk_Δ values is thus obtained from the deviations from the new k_s line. The cycle is repeated until the Fk_Δ corrections approach zero and ρ_s becomes constant. We thank Mr. Wallace F. Sliwinski for the development of this program.

(9) Y. Yukawa, T. Ando, K. Token, M. Kawada, and S.-G. Kim, *Tetrahedron Letters*, 2367 (1969).

(10) R. J. Jablonski and E. I. Snyder, *J. Am. Chem. Soc.*, **91**, 4445 (1969); *Tetrahedron Letters*, 1103 (1968).

(11) J. E. Nordlander and W. G. Deadman, *J. Am. Chem. Soc.*, **90**, 1590 (1968).

Table II. Partitioning of Rate Constants for β-Arylethyl Tosylates at 115°

		Substrate: X =			
		p-Cl	H	*p*-CH_3	*p*-CH_3O
$k_s \times 10^7$, sec^{-1}	This work[a]	70	73	76	78
	Coke, Jones[b]	64 ± 0.1[d]	79 ± 11	78 ± 44	282[e] ± 250
$Fk_\Delta \times 10^7$, sec^{-1}	This work[a]	15	54	354	3922
	Coke, Jones[b]	6.1 ± 0.08	48 ± 11	352 ± 43	4807[e] ± 419
$\Delta S^{\pm}$ (k_s), eu	This work[a]	−22	−22	−22	−22
	Coke, Jones[b]	−25 ± 1	−21 ± 2	−24 ± 8	
$\Delta S^{\pm}(Fk_\Delta)$, eu	This work[a]	−8	−15	−12	−10
	Coke, Jones[b]	−26 ± 8	−12 ± 1	−12 ± 1	−9 ± 1
$(Fk_\Delta/k_t) \times 100$	This work[a]	18	42	82	98
	Coke, Jones[b]	8.7 ± 0.1	38 ± 8.5; 32[c]	82 ± 10	95
k_t/k_s	This work[a]	1.21	1.73	5.63	51.1

[a] Hammett treatment. [b] ^{14}C scrambling combined with kinetic data.[5] [c] Per cent retention of configuration in *threo*-1,2-dideuterio derivative.[10] [d] Since Coke and Jones's[5] treatment consists of two data sets with somewhat differing results, we have followed their approach of listing the average value together with the error spread from either data set. Our treatment consists of a single data set in which the intrinsic error in the successive approximations[8] is difficult to assess quantitatively. An estimate of ±7% can be made from the scatter in the Fk_Δ *vs.* σ^+ plot. [e] Calculated from data at other temperatures.

Table II compares the values for k_s, Fk_Δ, $\Delta S^{\pm}(k_s)$, and $\Delta S^{\pm}(Fk_\Delta)$ estimated in the present study with those derived from Coke and Jones's combination of ^{14}C scrambling and kinetic data.[5] Rate and product data also may be conveniently compared *via* the percentage of aryl participation, $(Fk_\Delta/k_t) \times 100$. These values are included in Table II. For all substrates, the agreement between the two methods is remarkably good. In addition, good agreement is obtained with the purely product-derived result of Snyder and Jablonski for *threo*-1,2-dideuterio-2-arylethyl tosylate.[10]

The close agreement between rate and product data provides the first direct experimental evidence that the assumption[4,5] of discreteness between the solvent-assisted (k_s) and aryl-assisted (Fk_Δ) pathways is valid for such primary systems. The solvent-assisted reaction is essentially an SN2 process; the magnitude of ρ_s (−0.10 at 115°) is very low,[12,13] indicating that virtually no positive charge is generated on carbon in the transition state. $\Delta S^{\pm}(k_s)$ is remarkably constant, −22 eu, and about 10 eu more negative than $\Delta S^{\pm}(Fk_\Delta)$.[14] This difference is almost certainly due to ordering of the solvent in the SN2-like transition state.[15]

In the aryl-assisted pathway (Fk_Δ), the high degree of charge delocalization into the participating aryl nucleus is revealed by the value of ρ^+, −2.4 at 115°.[16,17] Although the rate enhancements, as measured by k_t/k_s (Table II), are often of relatively small magnitude, this should not be taken to indicate that bridging is weak in the transition state.[18] Rather, as we have noted previously,[1] aryl assistance, in order to be seen at all, must be greater than the already efficient solvent assistance against which it is competing.

(12) Typical ρ_s values for secondary and tertiary aryl-unassisted processes are −0.7[13a] and −1.0,[13] respectively.
(13) H. C. Brown and C. J. Kim, *J. Am. Chem. Soc.*, **90**, 2082 (1968); M. Tessler and C. A. VanderWerf, *J. Org. Chem.* **30**, 405 (1965).
(14) S. Winstein and R. Heck, *J. Am. Chem. Soc.*, **78**, 4801 (1956); D. J. Cram and L. A. Singer, *ibid.*, **85**, 1075 (1963).
(15) See ref 5 for a summary of pertinent references.
(16) *Cf.* ρ^+ (Fk_Δ) = −2.96 for the neophyl system at 75° (R. Heck and S. Winstein, *J. Am. Chem. Soc.*, **79**, 3432 (1957)).
(17) Since F is nearly constant for all participating substrates,[5] plots of either log k_Δ or of log Fk_Δ *vs.* σ^+ will give essentially the same ρ^+ value.
(18) H. C. Brown, R. Bernheimer, C. J. Kim, and S. E. Scheppele, *J. Am. Chem. Soc.*, **89**, 370 (1967).

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Ionic Reactions of Carbon Tetrachloride. Survey of Reactions with Ketones, Alcohols, and Sulfones

Sir:

We have found that CCl_4 reacts rapidly with ketones, alcohols, and sulfones in the presence of KOH, leading to a variety of products often in high yields. Some of the products are derived from dichlorocarbene generated in the reactions. This communication surveys the types of reactions we have investigated (Table I).[1] Kinetic, mechanistic, and experimental details will be presented in subsequent reports.

Ketones. Ketones with α but no α′ hydrogens (class I) are readily poly-α-chlorinated and may subsequently be cleaved into carboxylic acids (*cf.* the haloform reaction). Ketones with α and α′ hydrogens (class II) are transformed *in situ* into the carboxylic

(1) General reaction conditions per gram of substrate: 3–6 g of powdered KOH, 1–10 ml of *t*-BuOH, 1 ml of H_2O, 10 ml of CCl_4, 25–80°, 10–60 min, vigorous stirring. In some cases additional H_2O replaced the *t*-BuOH.