

Fig. 2.—Scheme of Metzler, Ikawa and Snell for pyridoxal catalyzed decarboxylation.

some of the studies is almost certainly attributable to non-enzymatic CO₂-H₂O¹⁸ exchange and to substrate enrichment enzymatically catalyzed by processes independent of the decarboxylation mechanism, as discussed above. It is concluded that in all of the enzymatic reactions studied and in the

metal-catalyzed decarboxylation of oxalacetic acid as well, the carboxyl group is released intact by simple cleavage of a carbon-carbon bond. Water does not appear to play a role in the CO₂-release mechanism nor does the CO₂ equilibrate with water in the course of the reaction except at the rate anticipated for non-enzymatic CO₂-H₂O¹⁸ exchange.

On the basis of these studies it is possible to rule out any of the mechanisms described above which would result in enrichment of the CO₂. The results are compatible with the mechanism recently proposed by Metzler, Ikawa and Snell on the basis of their studies of pyridoxal phosphate catalyzed reactions.⁴⁰ These workers propose that the formation of an amino acid-pyridoxal complex as shown in Fig. 2, with the carboxyl group involved only electrostatically can weaken the carboxyl carbon- α -carbon bond by electromeric displacement of electrons to the heterocyclic nitrogen. The enzyme or an enzyme-metal complex⁴¹ is presumed to be equivalent to the simple metal ion used in the non-enzymatic model experiments. The present results show that splitting of this carbon-carbon bond does not involve water and that the carboxyl group is released intact.

(40) D. E. Metzler, M. Ikawa and E. E. Snell, *THIS JOURNAL*, **76**, 648 (1954).

(41) B. M. Guirard and E. E. Snell, *ibid.*, **76**, 4745 (1954).
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The Role of Neighboring Groups in Replacement Reactions. XXII. Competition between *o*-MeO-5 and Ar₁-3 Participation in Solvolysis of *o*-Methoxyneophyl Toluenesulfonate^{1,2}

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Solvolysis of *o*-methoxyneophyl *p*-toluenesulfonate involves two competing anchimerically assisted ionization processes. One of the ionization modes is the Ar₁-3-assisted one; the other involves *o*-MeO-5 participation. From Ar₁-3-assisted ionization, rearranged substitution and elimination products are obtained. From *o*-MeO-5-assisted ionization is obtained mainly 3,3-dimethyl-4,5-benzodihydrofuran. From the composition of the isolated products it is possible to dissect the first-order rate constants of acetolysis and formolysis into component k_{Δ}^{Ar} and k_{Δ}^{OMe} values corresponding to each of the anchimerically-assisted ionizations. The ratio, $k_{\Delta}^{\text{OMe}}/k_{\Delta}^{\text{Ar}}$, is quite sensitive to the nature of the solvent, being much smaller in formic than in acetic acid. Ar₁-3-assisted ionization of *o*-methoxyneophyl toluenesulfonate is unusually slow in comparison with the *p*-isomer, while *o*-MeO-5-assisted ionization is approximately as fast as that of δ -methoxybutyl toluenesulfonate.

In solvolysis of 2-*o*-anisylethyl *p*-toluenesulfonate (I), there is no indication³ of substantial competition of *o*-methoxyl participation, in the sense of I \rightarrow II, with Ar₁-3⁴ participation to yield III. On the other hand, with *o*-methoxyneophyl toluenesulfonate (VII), *o*-MeO-5-assisted ionization competes very successfully with the Ar₁-3-assisted process. The results obtained in a study of this solvolysis are now reported and discussed.

(1) Research supported by the Office of Naval Research.

(2) Some of the material of this paper has been reported in summary by S. Winstein at the Symposium on Dynamic Stereochemistry of the Chemical Society, Manchester, England, March 31, 1954 [*Chemistry & Industry*, 562 (1954)].

(3) S. Winstein, C. R. Lindegren, H. Marshall and L. L. Ingraham, *THIS JOURNAL*, **75**, 147 (1953).

(4) (a) S. Winstein, R. Heck, S. Lapporte and R. Baird, *Experientia*, **12**, 138 (1956); (b) R. Heck and S. Winstein, *THIS JOURNAL*, **79**, 3105 (1957).

Results

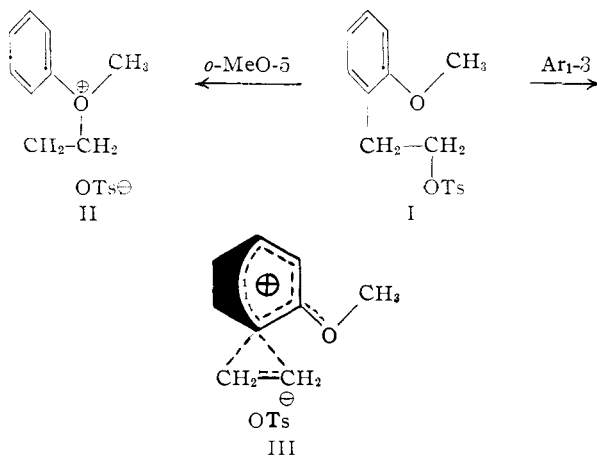
***o*-Methoxyneophyl *p*-Toluenesulfonate.**—The *o*-methoxyneophyl alcohol was obtained from the sequence of reactions previously employed for neophyl alcohol^{5,6} itself. This sequence involves formation of the neophyl chloride from methallyl chloride and anisole, followed by oxidation of the Grignard reagent of the chloride. Originally, the sequence of reactions was employed with the intention of preparing *p*-methoxyneophyl alcohol.⁷ However, alkylation of anisole with methallyl

(5) F. C. Whitmore, C. A. Weisgerber and A. C. Shabica, Jr., *ibid.*, **65**, 1469 (1943).

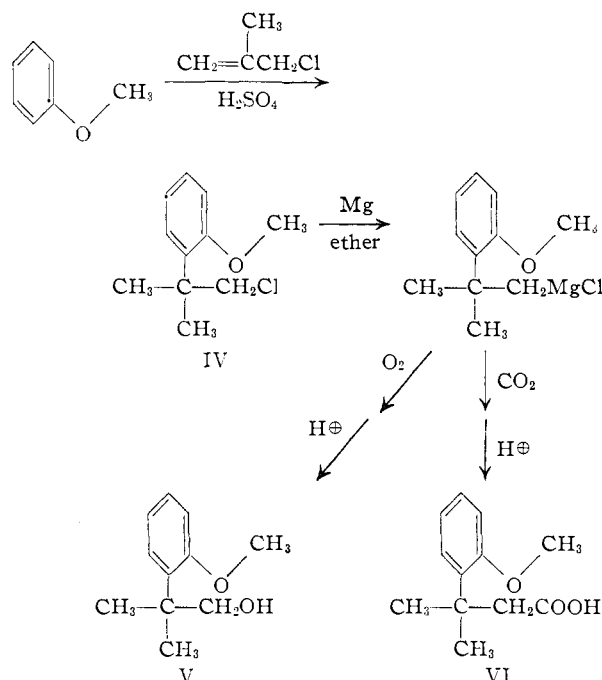
(6) S. Winstein, B. K. Morse, E. Grunwald, K. C. Schreiber and J. Corse, *ibid.*, **74**, 1113 (1952).

(7) S. Winstein and R. Heck, *ibid.*, **78**, 4801 (1956).

chloride and sulfuric acid yields a chloride mixture containing as much *ortho* isomer IV as *para*.



Carbocation of the Grignard reagent of the chloride mixture gave an acid mixture from which approximately equal quantities of β -*p*-anisylisovaleric and β -*o*-anisylisovaleric (VI) acids were isolated.



Oxidation of the Grignard reagent gave rise to a mixture of methoxyneophyl alcohols which led to an inseparable mixture of *p*-nitrobenzoates. Fortunately, the *p*-toluenesulfonate of *o*-methoxyneophyl alcohol (V) is considerably higher melting and less soluble than the *p*-isomer,⁷ so that it was possible to obtain a *ca.* 50% yield of pure *o*-methoxyneophyl *p*-toluenesulfonate (VII) from the methoxyneophyl alcohol mixture.

Kinetics of Solvolysis.—The *o*-methoxyneophyl *p*-toluenesulfonate exhibited good first-order behavior in ethanolysis and formolysis, the pertinent rate constants being summarized in Table I. As indicated in Table I, nearly theoretical infinity titers were observed in ethanol and formic acid solvents.

TABLE I
SOLVOLYSIS RATES OF *o*-METHOXYNEOPHYL *p*-TOLUENESULFONATE

Solvent	Added salt	Temp., °C.	[RO-Ts], 10 ³ M	% ∞	<i>k</i> , sec. ⁻¹
EtOH		75.00	3.60	98.2	(1.43 ± 0.03) × 10 ⁻⁴
HOAc		48.90	0.83	56.0	(2.63 ± .08) × 10 ⁻⁴
HOAc		74.81	1.44	63.2	(4.26 ± .05) × 10 ⁻⁴
HOAc		75.00	2.87	63.4	(4.21 ± .10) × 10 ⁻⁴
HOAc	0.0310M NaOAc	75.00	2.74	96.4	(4.88 ± .04) × 10 ⁻⁴
HCOOH		25.00	2.94	99.3	(1.33 ± .01) × 10 ⁻⁴
HCOOH	0.0317M NaOCHO	25.00	2.63	98.4	(1.37 ± .01) × 10 ⁻⁴

^a Δ*H*† = 23.2 kcal./mole; Δ*S*† = -7.5 e.u.

In acetic acid solvent, the solvolysis of *o*-methoxyneophyl toluenesulfonate (VII) appeared to stop at 63% completion at 75° and at a smaller figure at 49°. The data for a typical acetolysis which gave a low infinity titer are given in Table II. In these cases of acetolysis, good first-order rate constants were obtained when these were calculated on the basis of the experimental infinity titers employing equation 1. This point is illustrated in Table II.

$$2.303 \log \left[\frac{(\text{HOTs})_{\infty} - (\text{HOTs})_0}{(\text{HOTs})_{\infty} - (\text{HOTs})} \right] = kt \quad (1)$$

TABLE II
ACETOLYSIS OF 0.0287 *M* *o*-METHOXYNEOPHYL *p*-TOLUENESULFONATE AT 75.00°

Time, sec.	NaOAc soln., ml. ^a	10 ⁴ <i>k</i> , sec. ⁻¹
0	0.510	
180	.694	4.22
480	.972	4.19
840	1.290	4.38
1440	1.675	4.27
3060	2.300	3.99
5160	2.680	(3.73)
∞	3.050	
∞ calcd.	4.808	

Mean 4.21 ± 0.10

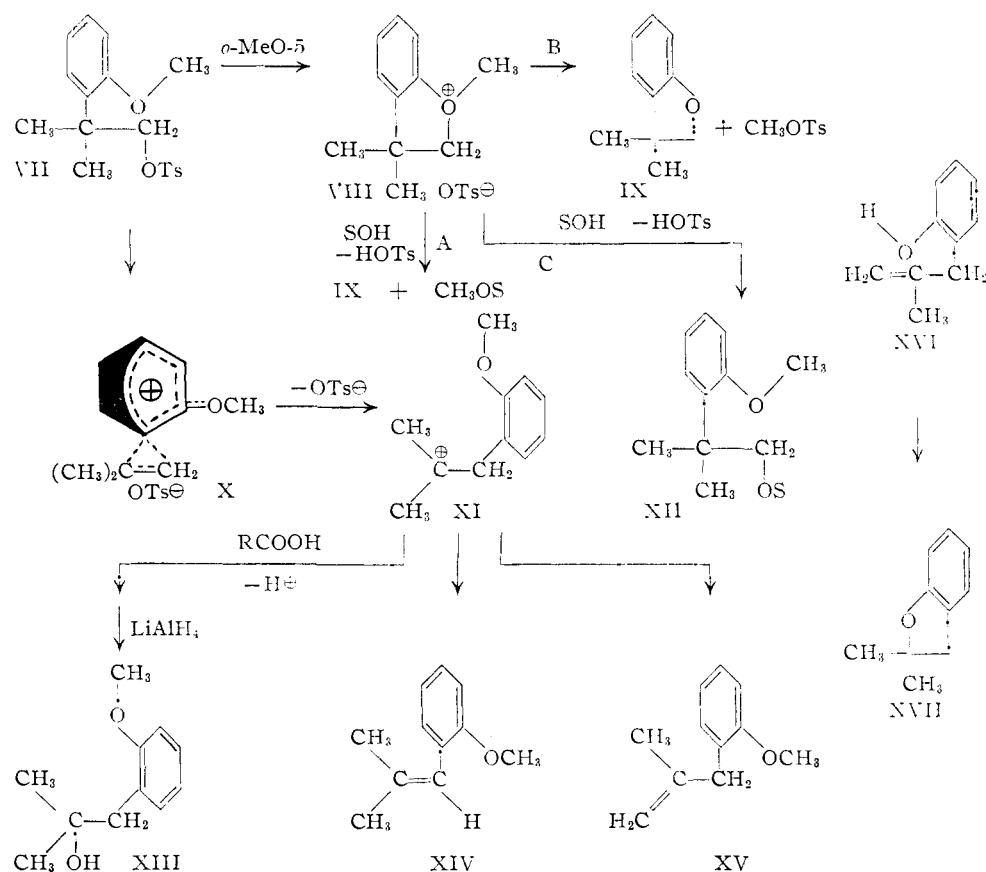
^a Per 5-ml. aliquot.

The inclusion of 0.03 *M* sodium acetate in the glacial acetic acid solvent brought the infinity titer nearly to the theoretical value, the first-order rate constant being slightly increased (Table I).

The low infinity titers observed in acetolysis appear to be connected with the formation of methyl toluenesulfonate. This substance solvolyzes⁸ at a rate one-five-hundredth of that of the *o*-methoxyneophyl ester, explaining why the low infinity titer in acetolysis was relatively constant over many solvolytic half-lives of the *o*-methoxyneophyl toluenesulfonate. A rough determination of the rate constant of acetolysis of the slow material remaining after the first infinity titer was reached gave a value approximately equal to the previously⁸ reported value for methyl toluenesulfonate.

It is clear that no significant amount of methyl *p*-toluenesulfonate is being formed in ethanolysis because the rate constant for *o*-methoxyneophyl *p*-toluenesulfonate is twice that for methyl *p*-toluenesulfonate.⁸ A drifting rate constant would have been observed if methyl *p*-toluenesulfonate were formed. Also, there can be no formation of

(8) S. Winstein and H. Marshall, *THIS JOURNAL*, **74**, 1120 (1952).



methyl *p*-toluenesulfonate in formolysis, because *o*-methoxyneophyl *p*-toluenesulfonate solvolyzes 10^3 times as rapidly as the methyl ester,⁸ yet high infinity titers are observed after only 10 half-lives of the neophyl ester.

In order to ascertain the reason for the high infinity value observed in acetolysis of *o*-methoxyneophyl toluenesulfonate in the presence of added sodium acetate, the second-order rate constant for reaction of methyl *p*-toluenesulfonate with sodium acetate was measured. An acetolysis run on 0.0313 *M* methyl *p*-toluenesulfonate in acetic acid, 0.0310 *M* in sodium acetate, at 75° is summarized in Table III. Because of the importance of second-order substitution of methyl toluenesulfonate by sodium acetate, a downward trend is observed both in the integrated first-order constants or the instantaneous first-order constants, k_1 , obtained from the slopes of a plot of $\ln [(R\text{OTs})_0/(R\text{OTs})]$ vs. time. Second-order rate constants, k_2 , were evaluated with the aid of equation 2, using for k_1 the previously⁸ reported first-order constant for acetol-

$$k_1 = k_1 + k_2 (\text{NaOAc}) \quad (2)$$

ysis of methyl toluenesulfonate at 75°. The relatively constant value for k_2 is listed in the last column of Table III, the mean value being 6.8×10^{-5} l. mole⁻¹ sec.⁻¹.

The reaction of methyl toluenesulfonate with sodium acetate turns out to be too slow to account for the high infinity titers observed in acetolysis of *o*-methoxyneophyl toluenesulfonate on the basis of reaction of methyl toluenesulfonate subsequent

to its formation. Therefore, the role of the sodium acetate is one of preventing formation of methyl toluenesulfonate, rather than destroying it after it is formed.

TABLE III
ACETOLYSIS OF 0.0313 *M* METHYL *p*-TOLUENESULFONATE
WITH 0.0310 *M* SODIUM ACETATE AT 75.00°

Time, 10 ⁻³ sec.	HClO ₄ soln., ml. ^a	[NaOAc], 10 ² <i>M</i>	Integ. 10 ³ <i>k</i>	10 ³ <i>k</i> ₁	10 ⁵ $\frac{(k_1 - k_1)}{[\text{NaOAc}]}$
0	4.310	3.029		3.17	7.8
0.907	3.340	2.347	2.84	2.40	6.6
1.669	2.950	2.073	2.30	2.10	6.0
3.293	2.160	1.518	2.13	1.74	5.9
5.021	1.570	1.131	1.99	1.58	6.5
6.375	1.290	0.935	1.88	1.47	6.6
10.283	0.790	0.555	1.69	1.31	8.3
∞	0.040				

Mean 6.8 ± 0.6

^a Per 5.14-ml. aliquot.

Products of Solvolysis.—The products from acetolysis and formolysis of *o*-methoxyneophyl *p*-toluenesulfonate in solvent containing excess sodium acetate or formate, respectively, were treated with lithium aluminum hydride to reduce any esters to alcohols. By chromatography, each product was separated into an easily-eluted fraction and a more difficultly-eluted alcohol fraction.

The easily-eluted material in each case gave rise to two fractions on vacuum distillation. The lower-boiling material was inert to potassium permanganate in acetone, and its C, H and methoxyl

TABLE IV
 PRODUCTS OF SOLVOLYSIS OF *o*-METHOXYNEOPHYL *p*-TOLUENESULFONATE

Solvent	Temp., °C.	[ROT _D], 10 ² M	Added base	Reacn. time, hours	Total yield, %	% of product Alcohol			
						Olefin	Tert.	Prim.	Furan
EtOH	78	3.97	CaCO ₃	5					46
AcOH	75	2.89	0.0310 M NaOAc	4	96	8	15	4	73
HCOOH	50	4.84	0.0515 M NaOCHO	2	92	32	42	..	26

analyses and ultraviolet absorption spectrum were proper for a dimethyl-4,5-benzodihydrofuran. The higher-boiling material gave a slow test for unsaturation with potassium permanganate in acetone and had the correct C, H analysis for 1-*o*-anisyl-2-methyl-1-propene (XIV) or its unconjugated isomer XV.

The product of ethanolysis of *o*-methoxyneophyl *p*-toluenesulfonate was examined sufficiently to isolate the dimethyl-4,5-benzodihydrofuran fraction. All three dimethylbenzodihydrofuran fractions from formolysis, acetolysis and ethanolysis appeared to be the same. The infrared spectra of the materials from formolysis and ethanolysis were compared and found to be identical. It is clear that the dimethylbenzodihydrofuran product is not 2,2-dimethyl-4,5-benzodihydrofuran (XVII) which was prepared from *o*-methallylphenol (XVI).⁹

The differences in the infrared spectra of the synthetic and isolated materials, especially at 10.2 μ , where the synthetic material is relatively transparent, and at 11.3 and 14.4 μ , where the product has low absorption, indicate that the solvolysis product is not the synthetic one. For this reason, and from mechanistic considerations mentioned later, the structure of 3,3-dimethyl-4,5-benzodihydrofuran (IX) is assigned to the product.

The alcohol product from acetolysis of *o*-methoxyneophyl *p*-toluenesulfonate (VII) contained a large proportion of the rearranged tertiary alcohol, 1,1-dimethyl-2-*o*-anisylethanol (XIII), prepared from methyl *o*-methoxyphenylacetate and methylmagnesium iodide. The tertiary alcohol was conveniently characterized by means of its *p*-nitrobenzoate. The presence of ca. 20% of *o*-methoxyneophyl alcohol (V) in the solvolysis alcohol was demonstrated by treatment of a sample of the alcohol with *p*-toluenesulfonyl chloride in pyridine and acetolysis of the crude toluenesulfonate. The observed rate constant was that for *o*-methoxyneophyl toluenesulfonate (VII) and the observed infinity titer provided an estimate of the proportion of *o*-methoxyneophyl component in the solvolysis alcohol.

The alcohol product from formolysis of *o*-methoxyneophyl *p*-toluenesulfonate also gave rise to pure *p*-nitrobenzoate of 1,1-dimethyl 2-*o*-anisylethanol (XIII), the proportion of this material in the product apparently being very high.

In Table IV are summarized the results of the examination of the solvolysis products.

Discussion

Mechanism.—The absence of 2,2-dimethyl-4,5-benzodihydrofuran (XVII) in the solvolysis product indicates that cyclic ether does not arise from

cyclization of olefin XIV or XV or rearranged tertiary solvolysis product such as the acetate of alcohol XIII. The formation of cyclic ether IX and the other solvolysis products requires a mechanism involving two competing anchimerically-assisted ionization processes in the solvolysis of *o*-methoxyneophyl *p*-toluenesulfonate (VII). One of the ionization modes is the Ar₁-3-assisted one; the other involves *o*-MeO participation, leading to the intermediate oxonium toluenesulfonate ion pair VIII. A convenient designation for the *o*-MeO participation in this specific case is *o*-MeO-5, the number 5 designating the size of the ring created by the anchimerically-assisted ionization.

From Ar₁-3-assisted ionization, tertiary solvolysis product, e.g., acetate of alcohol XIII, and olefins XIV and XV are expected, just as in solvolysis of neophyl bromobenzenesulfonate.¹⁰ From *o*-MeO-5-assisted ionization, the benzodihydrofuran IX and unrearranged *o*-methoxyneophyl substitution product XII are presumed to arise, the former by nucleophilic attack on methyl, the latter by such attack on C α . The formation of methyl toluenesulfonate in the absence of sodium acetate, but not in its presence, is due to ion pair chemistry which has been studied¹¹ and discussed¹² further elsewhere. For present purposes, the *o*-MeO-5 reaction pathway will be subdivided into: A, leading to furan IX, but not methyl toluenesulfonate; B, leading to furan IX and methyl toluenesulfonate; and C, leading to *o*-methoxyneophyl substitution product XII.

Dissection of Solvolysis and Related Rate Constants.—The division of the solvolysis reactions into the Ar₁-3 and *o*-MeO-5 paths and the subdivision of *o*-MeO-5 into the A, B and C pathways may be carried out by reference to the composition of the reaction products summarized in Table IV. In Table V are summarized the resulting rough figures for percentage reaction along each reaction route.

 TABLE V
 ASSIGNMENT OF REACTION PATHS IN SOLVOLYSIS OF *o*-METHOXYNEOPHYL *p*-TOLUENESULFONATE

Solvent	Temp., °C.	Percentage reaction along path				
		Ar ₁ -3	Total	<i>o</i> -MeO-5		
				A	B	C
EtOH	78	<55	>45	45		
AcOH	75	25 ^a	75 ^a	31	40	4 ^a
AcOH	75	25	75	68	3	4
(0.031 M NaOAc)						
HCOOH	50	73	27	ca. 27 ^b	0	Small

^a Assumed the same as in presence of sodium acetate.
^b Neglecting any possible *o*-methoxyneophyl alcohol in the product; the latter must be relatively small, judging by the much greater importance of Ar₁-3-assisted ionization than in acetic acid.

(10) R. Heck and S. Winstein, *ibid.*, **79**, July (1957).

(11) R. Heck, unpublished work.

(12) (a) S. Winstein, *Experientia Supplementum II*, 153 (1955);

(b) S. Winstein, VIth Reaction Mechanisms Conference, Swarthmore, Pa., September 12, 1956.

(9) Q. R. Bartz, R. F. Miller and R. Adams, *THIS JOURNAL*, **67**, 371 (1935).

Having divided ionization of *o*-methoxyneophyl *p*-toluenesulfonate into Ar₁-3- and *o*-MeO-5-assisted portions, one may dissect the observed solvolysis rate constants into k_{Δ}^{Ar} and k_{Δ}^{OMe} , the rate constants corresponding to each one of the anchimerically-assisted ionizations. The estimated rate constants are summarized in Table VI, along with the ratios, $k_{\Delta}^{\text{OMe}}/k_{\Delta}^{\text{Ar}}$.

The ratios, $k_{\Delta}^{\text{OMe}}/k_{\Delta}^{\text{Ar}}$, in Table VI point out most clearly the large solvent dependence of the competition between the Ar₁-3 and *o*-MeO-5 reaction paths.

TABLE VI

ASSIGNMENT OF RATE CONSTANTS IN ACETOLYSIS AND FORMOLYSIS OF *o*-METHOXYNEOPHYL TOLUENESULFONATE

Solvent	Temp., °C.	k_{Δ}^{OMe} , sec. ⁻¹	k_{Δ}^{Ar} , sec. ⁻¹	$k_{\Delta}^{\text{OMe}}/k_{\Delta}^{\text{Ar}}$
HCOOH ^a	25	2.6×10^{-5}	7.5×10^{-5}	0.35
AcOH	75	3.7×10^{-4}	1.1×10^{-4}	3.4

^a Assuming products the same at 25° as those observed at 50°.

The ratio of *o*-MeO-5 to Ar₁-3 drops from 3.4 in acetic acid to 0.35 in formic acid. While we have not explored how much of this change can be due to change in temperature, most of the change is due to much smaller sensitivity to solvent ionizing power¹³ in the case of *o*-MeO-5-assisted ionization than for the Ar₁-3 variety.

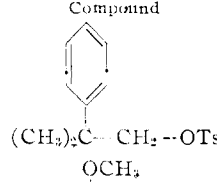
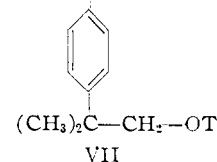
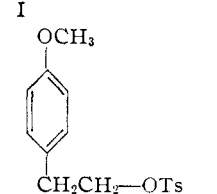
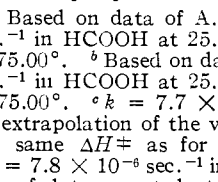
It is worthwhile to consider the competition between Ar₁-3 and *o*-MeO-5-assisted ionizations of *o*-methoxyneophyl *p*-toluenesulfonate (VII) in terms of the individual k_{Δ}^{Ar} and k_{Δ}^{OMe} values and their relation to similar rate constants for other systems. Taking the k_{Δ}^{Ar} values for *o*-methoxyneophyl *p*-toluenesulfonate and contrasting them with the values for the neophyl,⁶ *p*-methoxyneophyl⁷ and *o*- and *p*-anisylethyl³ systems, one obtains the comparison summarized in Table VII.

From Table VII, it is clear that k_{Δ}^{Ar} for *o*-methoxyneophyl is slower than for *p*-methoxyneophyl by factors of 15 in acetic acid and 11 in formic acid. The *gem*-dimethyl grouping increases k_{Δ}^{Ar} from the level observed with the anisylethyl systems by factors of only 9.7 in formic acid and 5.7 in acetic acid, when the anisyl group is *ortho*, but by factors of 107 and 77 when the anisyl group is *para*. It would seem that there is steric retardation of k_{Δ}^{Ar} in *o*-methoxyneophyl relative to *p*-methoxyneophyl, due to the accumulation of both the *o*-methoxyl and the *gem*-dimethyl groupings. Steric interferences not present in the *p*-methoxyneophyl case make it more difficult to reach the Ar₁-3 transition state. The steric retardation of Ar₁-3-assisted ionization serves to increase the $k_{\Delta}^{\text{OMe}}/k_{\Delta}^{\text{Ar}}$ ratio observed with the *o*-methoxyneophyl system.

While the structure of *o*-methoxyneophyl *p*-toluenesulfonate (VII) is relatively unfavorable for Ar₁-3 participation, it is very suitable for *o*-MeO-5-assisted ionization. The k_{Δ}^{OMe} in this

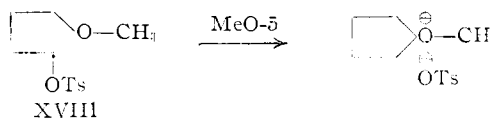
(13) (a) E. Grunwald and S. Winstein, *THIS JOURNAL*, **70**, 846 (1948); (b) S. Winstein, E. Grunwald and H. W. Jones, *ibid.*, **73**, 2700 (1951); (c) A. H. Fainberg and S. Winstein, *ibid.*, **78**, 2770 (1955).

TABLE VII
SOME RELATIVE RATES INVOLVING ANISYL PARTICIPATION

Compound	Rel. k_{Δ} values	
	HCOOH 25.00°	AcOH 75.00°
	1.00 ^a	1.00 ^a
	72 ^b	88 ^b
	6.47 0.66 ^c	5.5 0.99 ^c
	0.67 ^d	1.3 ^f

^a Based on data of A. H. Fainberg; $k = 1.16 \times 10^{-5}$ sec.⁻¹ in HCOOH at 25.00°, 2.00×10^{-5} sec.⁻¹ in AcOH at 75.00°. ^b Based on data⁷ of R. Heck; $k = 8.31 \times 10^{-4}$ sec.⁻¹ in HCOOH at 25.00°, 1.77×10^{-3} sec.⁻¹ in AcOH at 75.00°. ^c $k = 7.7 \times 10^{-6}$ sec.⁻¹ in HCOOH at 25.00° by extrapolation of the value reported at 75.01°, assuming the same ΔH^{\ddagger} as for *p*-anisylethyl *p*-toluenesulfonate.³ ^d $k = 7.8 \times 10^{-6}$ sec.⁻¹ in HCOOH at 25.00° by extrapolation of data reported at higher temperatures.³ ^e $k_{\text{ext.}}^{\circ} = 1.98 \times 10^{-5}$ sec.⁻¹ in AcOH at 75.00°, reported by A. Fainberg.¹⁴ ^f $k_{\text{ext.}}^{\circ} = 2.6 \times 10^{-5}$ sec.⁻¹ in AcOH at 75.00°, reported by A. Fainberg.¹⁴

case is *ca.* 20 times as large as the whole solvolysis rate constant (at least mainly k_{Δ}^{Ar}) observed for the *o*-anisylethyl ester in acetic acid. A typical substance which is well-disposed toward MeO-5-assisted ionization is δ -methoxybutyl^{12,15} tolu-



enesulfonate (XVIII), the acetolysis rate constant of this material exceeding that of the *n*-butyl analog by 3 powers of ten.¹⁵ However, k_{Δ}^{OMe} for *o*-methoxyneophyl *p*-toluenesulfonate (VII) in acetic acid is approximately equal to that for the δ -methoxybutyl derivative XVIII, even though the *o*-methoxyl group is rendered less nucleophilic by resonance interaction with a benzene ring.

In a following paper, more cases of *o*-MeO-5 and related participations will be presented, and the connection between structure and rate of *o*-MeO-assisted ionization will be discussed further.

Experimental Part

o- and *p*-Methoxyneophyl Chloride Mixture.—To a cooled solution of 1226 ml. of concd. sulfuric acid and 77½ ml. of water, heated to 70°, 162 g. of anisole and 166 g. of methallyl chloride were added with stirring. The reaction mixture was kept at 70–80° for 2 hr. After the mixture was cooled, the products were extracted with two portions of low-boiling

(14) A. H. Fainberg and S. Winstein, *ibid.*, **78**, 2767 (1956).

(15) R. Glick, unpublished work.

petroleum ether. The extracts were washed with water and sodium bicarbonate solution. After the extract was dried, the solvent was removed and the residue was vacuum distilled. After a small forerun of anisole, the chloride mixture, b.p. 91–100° (2 mm.), n_D^{25} 1.5268, was collected. The nearly colorless product weighed 78 g. (26%). A redistilled sample, b.p. 111–112° (3 mm.), was analyzed.

Anal. Calcd. for $C_{11}H_{16}OCl$: C, 66.75; H, 7.61. Found: C, 67.21; H, 7.74.

o- and *p*-Methoxyneophyl Alcohol Mixture.—To 8.3 g. of magnesium covered by 700 cc. of ether, 76 g. of the above *o*- and *p*-methoxyneophyl chloride mixture was added. Several grams of methyl iodide was added and the mixture was refluxed and stirred for 6 hr. Then, while the mixture was stirred at room temperature, a slow stream of dry oxygen was passed in until no further heat of reaction was observed. The reaction mixture was worked up in the usual way to yield 29.5 g. (43%) of methoxyneophyl alcohols, b.p. 93–98° (2 mm.), n_D^{25} 1.5291. The residue remaining after the distillation crystallized on standing. Two recrystallizations from pentane gave 5–10 g. of what is probably a methoxyneophyl dimer, m.p. 83.5–84.5°.

Anal. Calcd. for $C_{22}H_{30}O_2$: C, 80.93; H, 9.26. Found: C, 80.65; H, 8.97.

The preparation of the *p*-nitrobenzoate from the alcohol mixture led to a mixture which could not be separated even after several crystallizations from methanol or ligroin.

o-Methoxyneophyl *p*-Toluenesulfonate.—Tosylation of 28 g. of the *o*-methoxyneophyl alcohol mixture by the usual method afforded 27 g. (49%) of pure *o*-methoxyneophyl *p*-toluenesulfonate, m.p. 67–69°. The substance formed large prisms when crystallized from a mixture of carbon tetrachloride and petroleum ether (b.p. 60–80°). It decomposes in a few days at room temperature but is stable for months at 0°.

Anal. Calcd. for $C_{18}H_{22}O_4S$: C, 64.64; H, 6.63. Found: C, 64.84; H, 6.76.

β -*o*-Anisylisovaleric Acid.—A Grignard reagent was prepared from 230 g. of the *o*- and *p*-methoxyneophyl chloride mixture and 24 g. of magnesium. Dry carbon dioxide was passed into the Grignard solution until the ether became cold. Cold dil. hydrochloric acid was added and the ether phase was separated. After the ether solution was washed with water, the acid product was extracted with aqueous sodium bicarbonate. Acidification of the extract produced an oil. This was isolated and crystallized, first from a small volume of pentane and then four times from petroleum ether (b.p. 60–80°). The product, m.p. 83–85°, mainly the *p*-isomer, weighed 12 g. Concentration of the mother liquors yielded a crop of crude *o*-acid in the form of large prisms. Another crystallization from petroleum ether (b.p. 60–80°) produced 14 g. of pure β -*o*-anisylisovaleric acid, m.p. 70.5–71°.

Anal. Calcd. for $C_{12}H_{16}O_3$: C, 69.21; H, 7.75. Found: C, 69.35; H, 7.94.

A mixed m.p. of the β -*o*-anisylisovaleric acid with the *p*-isomer described below was 55–67°.

β -*p*-Anisylisovaleric Acid.—Methyl β -(*p*-hydroxyphenyl)isovalerate, b.p. 153–155° (1.5 mm.), was prepared by esterification of the acid¹⁶ with methanol and hydrogen chloride.

Anal. Calcd. for $C_{12}H_{16}O_3$: C, 69.21; H, 7.75. Found: C, 69.3; H, 7.86.

A solution of 0.695 g. of methyl β -(*p*-hydroxyphenyl)isovalerate in 3.3 ml. of 1.03 *N* sodium methoxide in methanol was heated in a sealed tube for 5 hr. at 100–105° with 0.3 ml. of methyl iodide. The methanol was distilled, and the residue was treated with ether and water. The ether layer was separated, washed with two 4-ml. portions of 1 *N* sodium hydroxide solution, with water and then dried over magnesium sulfate. Saponification of the crude methyl β -*p*-anisylisovalerate was carried out by refluxing 0.424 g. with a solution of 0.25 g. of potassium hydroxide in 2 ml. of ethanol and 1 ml. of water for 4 hr. The acid was separated in the usual manner and recrystallized several times from ether–petroleum ether, m.p. 90–91°.

Anal. Calcd. for $C_{12}H_{16}O_3$: C, 69.21; H, 7.75. Found: C, 69.30; H, 7.87.

Methyl *o*-Methoxyphenylacetate.—To a mixture of 20 g. of *o*-methoxyphenylacetic acid¹⁷ and 100 cc. of ether was added an excess of diazomethane in ether. After 10 minutes the ether was evaporated and the residue was vacuum distilled. The ester, b.p. 94–98° (2 mm.), n_D^{25} 1.5160, weighed 16 g.

Anal. Calcd. for $C_{10}H_{12}O_3$: C, 66.65; H, 6.71. Found: C, 67.11; H, 6.64.

1,1-Dimethyl-2-*o*-anisylethanol.—To a Grignard reagent prepared from 16 g. of methyl iodide and 3 g. of magnesium in 100 ml. of ether, 10 g. of methyl *o*-methoxyphenylacetate was added slowly. After a further 30 minutes of stirring, a cold saturated solution of ammonium chloride was added. The ether phase was separated and washed with water and aqueous sodium bicarbonate. After the ether phase was dried, the ether was evaporated and the alcohol was distilled in vacuum. The tertiary alcohol, 9.7 g., b.p. 87–89° (2 mm.), n_D^{25} 1.5174, was a colorless, odorless liquid.

Anal. Calcd. for $C_{11}H_{16}O_2$: C, 73.30; H, 8.95. Found: C, 73.04; H, 8.67.

The alcohol formed a *p*-nitrobenzoate readily when it was treated with *p*-nitrobenzoyl chloride in pyridine for 24 hr. After two recrystallizations from a mixture of ether and pentane, the ester formed long pale yellow needles, m.p. 77.5–78.5°.

Anal. Calcd. for $C_{18}H_{19}O_5N$: C, 65.64; H, 5.81. Found: C, 65.61; H, 5.92.

2,2-Dimethylbenzofuran.—This material was prepared by the method of Bartz, Miller and Adams⁹ and fractionated. The pure material had b.p. 97–98° (25 mm.) and n_D^{25} 1.5161 [reported⁹ b.p. 62° (7 mm.), n_D^{25} 1.5190]. The ultraviolet spectrum in methanol showed λ_{max} 287 μ , ϵ 840; 278 μ , ϵ 1730; 271 μ , ϵ 1670; and 227 μ , ϵ 10,200.

Ethanolysis of *o*-Methoxyneophyl *p*-Toluenesulfonate.—A solution of 13.3 g. of *o*-methoxyneophyl *p*-toluenesulfonate in 1 l. of anhydrous ethanol was refluxed with 10 g. of calcium carbonate for 5 hr. The cooled solution was filtered, and most of the alcohol was distilled off through a fractionating column. The residue was again filtered and distilled rapidly. The distillate, 7.2 g., b.p. 90–130° (20 mm.), was fractionated through a 60-plate center-rod column using 10 ml. of purified diethyl phthalate as a pusher. Five fractions were collected. The first 3 fractions, combined weight 2.60 g., b.p. 89.5–100.5° (20 mm.), n_D^{25} 1.5161–1.5168, were mainly 3,3-dimethylbenzofuran. The infrared spectrum of a fraction of b.p. 91.2–92.5° (20 mm.) and n_D^{25} 1.5161 was essentially the same as the furan fraction obtained from the formolysis described below. Two higher boiling fractions were obtained from this fractionation, but they were not homogeneous and were not examined further.

Acetolysis of *o*-Methoxyneophyl *p*-Toluenesulfonate.—A solution of 12.0 g. of *o*-methoxyneophyl *p*-toluenesulfonate in 1200 cc. of 0.0310 *M* sodium acetate in dry acetic acid was heated at 75° for 4 hr. The cooled solution was then diluted with four liters of water and the products were extracted with several portions of pentane. The extracts were washed and concentrated, and then the residue was reduced with 1.5 g. of lithium aluminum hydride. The reduced product was chromatographed on 500 g. of activated alumina. The first fraction, eluted with 1.5 liters of pentane, gave two distinct fractions when it was distilled. The lower boiling fraction, b.p. 40–45° (2 mm.), n_D^{25} 1.5175, weighed 3.35 g. This material was inert to potassium permanganate in acetone.

Anal. Calcd. for $C_{10}H_{12}O$: C, 81.04; H, 8.16; MeO, 0.00. Found: C, 81.01; H, 8.25; MeO, 0.90.

The higher boiling fraction, b.p. 58–60° (2 mm.), n_D^{25} 1.5298, weighed 0.8 g., and it reacted slowly with potassium permanganate in acetone.

A second fraction was eluted from the alumina with one liter of ether. This material, b.p. 78–80° (2 mm.), n_D^{25} 1.5166, weighed 1.2 g.

Anal. Calcd. for $C_{11}H_{16}O_2$: C, 73.30; H, 8.95. Found: C, 73.06; H, 9.00.

A *p*-nitrobenzoate was prepared from 0.5 g. of the above alcohol fraction. The once crystallized product, 0.45 g., had m.p. 67–72.5°. A second crystallization from ether–

(16) J. Corse and E. Rohrmann, *THIS JOURNAL*, **70**, 370 (1948).

(17) F. Bergel, J. W. Haworth, A. L. Morrison and H. Rinderknecht, *J. Chem. Soc.*, 261 (1944).

pentane gave 0.2 g. of material, m.p. 74–76°, mixed m.p. with the *p*-nitrobenzoate of 1,1-dimethyl-2-*o*-anisylethanol, 74.5–76.5°.

In order to determine the amount of *o*-methoxyneophyl alcohol in the alcohol fraction, 0.40 g. of this material was treated with 1 g. of *p*-toluenesulfonyl chloride in dry pyridine at room temperature for 30 minutes. The sulfonate was isolated in the usual way and dissolved in 50 ml. of 0.0310 *M* sodium acetate in dry acetic acid. The acetolysis rate constant was $3.5 \pm 0.3 \times 10^{-4} \text{ sec.}^{-1}$ at 75°, the infinity titer being taken after 20 hr.

Formolysis of *o*-Methoxyneophyl *p*-Toluenesulfonate.—To a solution of 3.5 g. of sodium formate in 720 cc. of dry formic acid, heated to 50°, was added 12 g. of *o*-methoxyneophyl *p*-toluenesulfonate. After 2 hr. at 50°, the reaction mixture was cooled and worked up exactly as described for the acetolysis. The chromatography yielded 1.8 g. of benzofuran, b.p. 41–42° (2 mm.), n_D^{25} 1.5251, 1.2 g. of olefin, b.p. 60° (2 mm.), n_D^{25} 1.5458, and 2.5 g. of alcohol, b.p. 78–82° (2 mm.), n_D^{25} 1.5183.

The benzofuran fraction was redistilled to give material

with n_D^{25} 1.5178. The infrared spectrum of this material was essentially the same as that of the ethanolsis product mentioned above. In ultraviolet absorption in methanol, λ_{max} 285 m μ , ϵ 2170; 279 m μ , ϵ 2700; and 224 m μ , ϵ 4720.

The olefin fraction reacted slowly with potassium permanganate in acetone.

Anal. Calcd. for $\text{C}_{11}\text{H}_{14}\text{O}$: C, 81.44; H, 8.70. Found: C, 81.35; H, 8.71.

The alcohol fraction, 0.5 g., gave 0.2 g. of a *p*-nitrobenzoate of m.p. 76.5–77.5° after two crystallizations from ether-pentane. A mixed melting point with authentic material was 76.5–78°.

Kinetic Measurements.—Solvolysis rates were measured by the usual methods.^{6,7} An attempt was made to follow the acetolysis of *o*-methoxyneophyl toluenesulfonate after the first infinity value. The solvolysis solution became yellow and difficult to titrate, a rough rate constant of $ca. 6 \times 10^{-7} \text{ sec.}^{-1}$ being obtained at 75°. A value of $8.5 \times 10^{-7} \text{ sec.}^{-1}$ has been reported⁸ for methyl *p*-toluenesulfonate at 75°.

LOS ANGELES 24, CALIF.

COMMUNICATIONS TO THE EDITOR

EVIDENCE ON MECHANISMS OF HALOGEN AND TRITIUM RECOIL LABELLING REACTIONS

Sir:

Displacement reactions very different from ordinary atom and radical reactions have been observed between gaseous alkanes and iodine,^{1a,1b} bromine,^{1c} and chlorine^{1d,1e} activated by the (n, γ) process. Tritium activated by the $\text{Li}^6(n, \alpha)\text{H}^3$ process in the presence of liquid or solid organic compounds gives superficially similar reactions.² Tritium is of particular interest in this connection because of its chemical differences from the halogens and because a much larger fraction of its recoil kinetic energy is available for internal energy of the activated complex.

We have used the $\text{He}^3(n, p)\text{H}^3$ reaction to produce tritons in gaseous alkanes³ under conditions⁴

(1) (a) J. F. Hornig, G. Levey and J. E. Willard, *J. Chem. Phys.*, **20**, 1556 (1952); (b) G. Levey and J. E. Willard, *J. Chem. Phys.*, **25**, 904 (1956); (c) A. Gordus and J. E. Willard, *THIS JOURNAL*, in press; (d) J. C. W. Chien and J. E. Willard, *ibid.*, **75**, 6160 (1953); (e) J. E. Quinlan and J. E. Willard, unpublished.

(2) (a) R. Wolfgang, F. S. Rowland and C. N. Turton, *Science*, **121**, 715 (1955); (b) R. Wolfgang, J. Eigner and F. S. Rowland, *J. Phys. Chem.*, **60**, 1137 (1956); (c) F. S. Rowland, C. N. Turton and R. Wolfgang, *THIS JOURNAL*, **78**, 2354 (1956); (d) F. S. Rowland and R. Wolfgang, *Nucleonics*, **14**, 58 (1956).

(3) While this work was in progress, we received word from R. Wolfgang that he had observed the production of CH_3T and higher hydrocarbons from the $\text{He}^3(n, p)\text{H}^3$ reaction in CH_4 .

(4) A typical run consisted of irradiating a 5-ml., thin-walled, quartz bulb containing 6 mm. He^3 , 6 mm. H_2 , and 1 atm. of alkane in the isotope tube of the CP 5 reactor of the Argonne National Laboratory for one hour. The neutron flux⁵ was $3 \times 10^{12} \text{ n cm.}^{-2} \text{ sec.}^{-1}$. The bulb was broken in a stream of methane at the inlet of a 12 ft. long, 4 mm. i.d. spiral Pyrex column containing 30–80 mesh silica gel. The general technique was the same as reported earlier,⁶ the main difference being that a flow proportional counter⁷ was used to detect the radioactive components. The fraction of the activity

similar to those for which the halogen reactions have been studied. With a given target compound a multiplicity of tritium containing compounds is formed which cannot be explained by "conventional" reaction steps. In the absence of scavengers about 45% of the tritium appears as HT, 30% in the alkane target species and the remainder in four to ten other products. Halogen scavengers decrease or eliminate the yield of tritiated products with more carbons than the target but have relatively little effect on the HT, or the tritiated target compound or fragments thereof.

The only reaction steps which seem capable of explaining the extensive chain-lengthening are ion-molecule reactions⁸ (such as, for example, $\text{T}^+ + \text{CH}_4 \rightarrow \text{CH}_2\text{T}^+ + \text{H}_2$ and $\text{CH}_2\text{T}^+ + \text{CH}_4 \rightarrow \text{C}_2\text{H}_4\text{T}^+ + \text{H}_2$, followed by similar steps leading to further chain lengthening). Ion-molecule steps

in each component was estimated from the peak area; the identification of the minor components is tentative.

(5) The accompanying gamma flux was about $5 \times 10^5 \text{ r./hr.}$. That the gamma radiation was not the cause of the chain lengthening or the large fraction of tritium in the target compound seems evident from the three $\text{CH}_4\text{-He}^3\text{-H}_2$ samples which received about $7 \times 10^5 \text{ r.}$ from a Co^{60} source after the usual pile irradiation. This did not change the percentage of CH_3T much, but raised the percentage of HT slightly and lowered the percentages of the higher hydrocarbons somewhat.

(6) J. B. Evans and J. E. Willard, *THIS JOURNAL*, **78**, 2908 (1956).

(7) A. Gordus, Ph.D. thesis, University of Wisconsin, 1956, available from University Microfilms, Inc., Ann Arbor, Michigan.

(8) (a) V. L. Tal'roze and A. K. Lyubimova, *Doklady Akad. Nauk S.S.S.R.*, **86**, 909 (1952) (*Chem. Abs.*, **47**, 2590 (1953)); (b) D. O. Schlissler and D. P. Stevenson, *J. Chem. Phys.*, **24**, 926 (1956); (c) D. P. Stevenson and D. O. Schlissler, *ibid.*, **23**, 1353 (1955); (d) C. G. Meisels, W. H. Hamill and R. R. Willams, Jr., *ibid.*, **25**, 790 (1957); (e) F. H. Field, J. L. Franklin and P. W. Lampe, *THIS JOURNAL*, **79**, 2419 (1957).