sults, when considered in conjunction with our other published[1,12] and unpublished observations in several different plant species and involving completely different indole alkaloid families, suggest that there probably exists a biointermediate with structural features resembling secodine which plays a central role in the later stages of many indole alkaloid biosynthetic pathways. Obviously some of the results already suggest that a secodine derivative possessing a higher oxidation level in the piperideine unit, for example VII or its isomers, may be a better representation of the biointermediate. However, the high instability associated with dihydropyridine derivatives will provide considerable difficulty in isolation and utilization of such systems for biosynthetic studies. Additional support for the above postulates will be published shortly.

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Cation–Anion Combination Reactions. VI. Trapping of Solvolysis Reaction Intermediates with Azide Ion

Sir:

In the previous papers of this series[1] and in further work under way, we have found that the selectivities of a wide range of cations toward nucleophiles are independent of the nature of the cation (*i.e.*, aryldiazonium, triarylmethyl, and tropylium ions show the same selectivities toward a series of nucleophiles). This finding appeared to be in conflict with the results of many studies involving the trapping of intermediates in solvolysis reactions,[2] in which the selectivities toward nucleophiles vary considerably among various reactants. For example, Swain[3] found that the intermediate in the solvolysis of trityl compounds shows greater reactivity with azide than with hydroxide ions, while the reverse is true for benzhydryl compounds. More recently, both Sneen[4] and Schleyer[5] have shown that there exists a reactivity–selectivity relationship in the trapping of solvolysis intermediates by azide ion and solvent.

I wish to report the results of a preliminary study of the solvolysis and azide trapping in the methanolysis of *p,p′*-dimethoxybenzhydryl mesitoate which resolves the conflict of the earlier studies and provides a simple and rational explanation of the selectivity–reactivity relationships explored by Sneen and Schleyer.

The syntheses of ester, tritium-labeled ester, and other compounds used are summarized in Scheme I.

Scheme I

$$\mathrm{Ar_2C{=}O} \xrightarrow[\text{reflux 5 days}]{(\mathrm{CF_3CO})_2\mathrm{O},\ \mathrm{T_2O}} \mathrm{Ar_2C{=}O}\ \text{(ring tritiated)}$$

$$\mathrm{Ar_2C{=}O} \xrightarrow[n\text{-PrOH, reflux 2 hr}]{\text{excess LiBH}_4\ 90\%\ \text{yield}} \mathrm{Ar_2CHOH}$$

(mp 67–68°, from MeOH)

$$\mathrm{Ar_2CHOH} \xrightarrow[\text{reflux 0.5 hr, 83\% yield}]{\mathrm{CH_3COCl},\ \text{benzene}} \mathrm{Ar_2CHCl}$$

(mp 80–81°, from hexane)

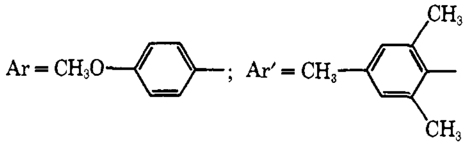
$$\mathrm{Ar'COOH} \xrightarrow[\mathrm{AgNO_3}]{\mathrm{NH_4OH}} \mathrm{Ar'COOAg}$$

$$\mathrm{Ar_2CHCl} + \mathrm{Ar'CO_2Ag} \xrightarrow[\text{20 hr, 85\% yield}]{\text{benzene, reflux}} \mathrm{Ar_2CHO_2CAr'}$$

(mp 76–77°, from petroleum ether)

$$\mathrm{Ar_2CHCl} \xrightarrow[\text{aq acetone}]{\mathrm{NaN_3}} \mathrm{Ar_2CHN_3}\ \text{(mp 46–47°, from MeOH)}$$

$$\mathrm{Ar_2CHCl} \xrightarrow{\mathrm{MeOH}} \mathrm{Ar_2CHOMe}\ \text{(mp 33.5–34°, from petroleum ether)}$$



The solvolysis reaction in methanol could be followed by observing the change in absorbance in the ultraviolet spectrum of the methanol solution of the ester. Using this direct method, high precision (*i.e.*, precision was about ±5% in rate constant) of rate measurement was not possible because the changes in absorbance were not great. Much better precision was obtained using added *p*-nitrophenoxide ion as an indicator. Since the p*K*'s of mesitoic acid (p*K* = 8.69) and *p*-nitrophenol (p*K* = 11.15) in methanol are quite different, the use of a slight excess of *p*-nitrophenoxide ensures virtually complete reaction of the mesitoic acid to form *p*-nitrophenol. The results of the kinetic studies are summarized in Table I.

The kinetic studies show that: (1) the addition of *p*-nitrophenoxide indicator does not change the rate of methanolysis; (2) the addition of sodium azide does not change the rate of methanolysis; (3) the reaction, as expected, shows a small positive salt effect; and (4) there is a small mass law effect on the rate of reaction.

Under the conditions used to establish that added azide did not influence the rate of reaction, the observed loss of *p*-nitrophenoxide absorption showed that approximately 90% of the product was the benzhydryl azide. The fact that no further changes in absorption occurred over a period of 24 hr shows that the products are stable under reaction conditions.

The product distributions resulting from methanolyses of the ester in the presence of azide ion were determined by isotope dilution techniques. A carefully measured volume of a solution of the tritiated ester in heptane was added to a buffered methanolic solution of sodium azide. The reaction was allowed to proceed at ambient temperature for ten half-lives of the methanolysis reaction. A carefully weighed quantity of *p,p′*-dimethoxybenzhydryl azide or methyl ether was then dissolved in the reaction solution and reisolated by dilution with water and extraction into pentane. The isolated

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(1) C. D. Ritchie and P. O. I. Virtanen, *J. Amer. Chem. Soc.*, in press.

(2) L. C. Bateman, E. D. Hughes, and C. K. Ingold, *J. Chem. Soc.*, 974, 979 (1940).

(3) C. G. Swain, C. B. Scott, and K. H. Lohmann, *J. Amer. Chem. Soc.*, 75, 136 (1953).

(4) R. A. Sneen, J. V. Carter, and P. S. Kay, *ibid.*, **88**, 2594 (1966).

(5) D. J. Raber, J. M. Harris, R. E. Hall, and P. v. R. Schleyer, *ibid.*, **93**, 4821, 4829 (1971). I thank Professor Schleyer for allowing me to read this work prior to publication.

Table I. Methanolysis of *p,p'*-Dimethoxybenzhydryl Mesitoate at 26 ± 1°

No.	Ester concn, *M*	Added salts (Concn, *M*)	Method[a]	k, sec^{-1}
1	5×10^{-5}	None	Uv	$6.0\,(\pm 0.3) \times 10^{-4}$
2	5×10^{-5}	$NaClO_4$ (5.0×10^{-4})	Uv	$6.1\,(\pm 0.3) \times 10^{-4}$
3	5×10^{-5}	NaN_3 (5.0×10^{-4})	Uv[e]	$6.0\,(\pm 0.3) \times 10^{-4}$
4	8×10^{-5}	NaN_3 (2.0×10^{-3}) *p*-NO_2PhOK (1.2×10^{-4})	Vis[e]	$6.0\,(\pm 0.3) \times 10^{-4}$
5	7.7×10^{-5}	*p*-NO_2PhOK (1.2×10^{-4})	Vis[b]	$6.41\,(\pm 0.05) \times 10^{-4}$
6	7.7×10^{-5}	$NaClO_4$ (1.1×10^{-2}) *p*-NO_2PhOK (1.2×10^{-4})	Vis[b]	$6.8\,(\pm 0.1) \times 10^{-4}$
7	7.7×10^{-5}	NaMes[c] (1.0×10^{-2}) *p*-NO_2PhOK (1.2×10^{-4})	Vis[b,d]	$5.25\,(\pm 0.1) \times 10^{-4}$

[a] Uv, runs followed at 244–255 nm; vis, runs followed at 390 nm. [b] These runs utilized a thermostated cell holder which gave temperature control of better than ±0.1°. [c] Sodium mesitoate. [d] In this run, the conversion of *p*-nitrophenoxide is not quantitative. The rate constant was calculated from the observed concentration of phenoxide and the known p*K*'s of mesitoic acid and of *p*-nitrophenol in methanol. [e] The spectrum of the product solution showed no changes for 24 hr, clearly indicating the stability of the azide product in the solution.

Table II. Selectivities in Azide Trapping in the Methanolysis of *p,p'*-Dimethoxybenzhydryl Mesitoate[a]

Series[b] no.	$[NaN_3]$, *M*	Compd[c] analyzed	Buffer[d] concn, *M*	$\%\ RN_3/(\%\ ROCH_3 \cdot [NaN_3])$[e]
1	1.0×10^{-4}	Both	9.0×10^{-3}	1350
1	2.5×10^{-4}	Both	9.0×10^{-3}	1230
1	5.0×10^{-4}	Both	9.0×10^{-3}	1090
2	6.0×10^{-5}	RN_3	9.0×10^{-3}	1350
2	1.2×10^{-4}	RN_3	9.0×10^{-3}	1240
2	1.0×10^{-3}	$ROCH_3$	9.0×10^{-3}	1020
2	5.0×10^{-3}	$ROCH_3$	9.0×10^{-3}	990
3	9.7×10^{-6}	RN_3	9.0×10^{-3}	1850
3	2.4×10^{-5}	RN_3	9.0×10^{-3}	1400
3	4.8×10^{-5}	RN_3	9.0×10^{-3}	1340
3	9.7×10^{-5}	RN_3	9.0×10^{-3}	1330
4	1.0×10^{-3}	$ROCH_3$	9.0×10^{-3}	950
4	1.0×10^{-3}	$ROCH_3$	4.5×10^{-3}	1020
4	1.0×10^{-3}	$ROCH_3$	2.3×10^{-3}	1040
4	1.0×10^{-3}	$ROCH_3$	9.0×10^{-4}	1120

[a] Initial ester concentration, 1.0×10^{-4} *M*; ionic strength = 9.0×10^{-3} *M*. [b] The runs within each series were performed simultaneously. Since solutions were not thermostated and ambient temperature varies wildly in Buffalo summers, slight discrepancies between series may be attributed to temperature variation. [c] In series 1, duplicate runs were made at each azide ion concentration, and both products were determined by isotope dilution. The isolated materials accounted for 95 ± 1% of the total activity added to the solutions. This figure for the purity of the tritiated ester was used for those runs in which only one of the products was actually isolated. [d] The solutions were buffered with triethylamine–triethylammonium mesitoate in a 1:1 ratio. Thus the buffer concentration is equal to the concentration of triethylammonium mesitoate. In the runs of series 4, ionic strength was maintained by addition of sodium perchlorate. [e] Units of M^{-1}.

material was recrystallized from pentane at −20°, using Craig Tube technique, until constant activity was obtained.

The results of these experiments are shown in Table II and Figure 1.

The variation of the quantity $(\%\ RN_3)/([\%\ ROCH_3] \cdot [NaN_3])$ with concentration of NaN_3 shows clearly that at least two intermediates with different selectivities are being trapped by azide ion.

The data are consistent with Winstein's solvolysis scheme[6] involving an ion pair and a free carbonium ion, both of which may react with either methanol or azide ion. The quantitative evaluation of the selectivities of the two intermediates from the present data depends on details of the kinetic scheme assumed, but it is clear that the ion pair is considerably less selective than is the carbonium ion.

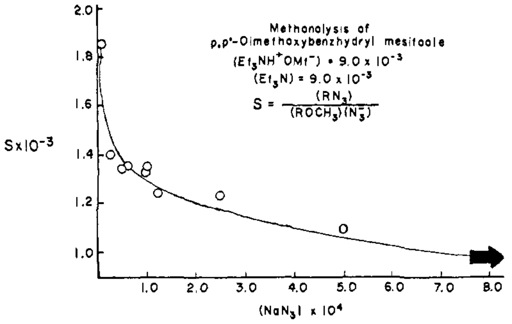

Figure 1. Plot of the quantity $S\ (M^{-1}) = (\%\ RN_3)/(\%\ ROCH_3 \cdot [NaN_3])$ *vs.* $[NaN_3]\,(M)$.

It seems quite likely that a major factor influencing the reactivity–selectivity relationship for "SN1" solvolyses is a variation in the proportion of product arising from free ions and ion pairs from various reactants. It is also clear, however, that the interpretation of selectivities determined from runs at only one azide concentration could be misleading.

Our studies of the trapping of SN1 intermediates are continuing.

Acknowledgment. I wish to express my appreciation to Dr. Dupont Durst of this department for many helpful suggestions and discussions concerning the isotope labeling and counting techniques used in the present study.

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[6] S. Winstein, P. E. Klinsdinst, Jr., and G. C. Robinson, *J. Amer. Chem. Soc.*, **83**, 885 (1961), and earlier papers cited therein.

The Directed Mixed Ester Condensation of Two Acids Bound to a Common Polymer Backbone

Sir:

In previous reports from this laboratory, it has been demonstrated that a cross-linked polymer exerts a strong immobilizing effect on molecules covalently bound to it. The effect was illustrated by the directed