Table II. Metastable Decompositions of $C_4H_8O_2^{+\cdot}$ and $C_3H_5O_2^+$ [a]

Compd	Ion	$-CH_3$	$-C_2H_4$	$-H_2O$
$CH_3CH_2CH_2CO_2H$	**1**	2.4×10^{-2}	1.2×10^{-2}	
$(CH_3CH_2)_2CHCO_2H$	**4**	9.6×10^{-3}	9.0×10^{-5}	
$CH_3CH_2CH_2CO_2H$	**5**			4.5×10^{-3}
$(CH_3CH_2)_2CHCO_2H$	**5**			2.0×10^{-3}

[a] Values are the intensities of the peaks representing the metastable transitions divided by the intensities of the peaks in the normal spectra representing the precursor ions. The intensities of the peaks representing metastable transitions were determined by metastable defocussing achieved by lowering the electrostatic analyzer potential at constant accelerating potential.

noic acid. The average of the ratios of the intensities of the ions produced by γ cleavage to those produced by γ-hydrogen rearrangement-β cleavage is ~0.3 in the mass spectra[7] of acids, esters, and aldehydes with *n*-propyl and *n*-butyl moieties attached to their carbonyl groups. Therefore, five-membered-ring hydrogen rearrangements occur up to $\frac{1}{3}$ as frequently as competing six-membered-ring hydrogen rearrangements.

Hydrogen rearrangements via six-, seven-, and eight-membered rings followed by further rearrangement to ions analogous to **5** also lead to γ cleavage.[5,8] HDO was lost in 44% of the metastable decompositions of the $C_3H_3D_2O_2^+$ ions formed from hexanoic acid-*3,3-d*$_2$. The first step leading to the formation of the ions that lost Hdo must have been five-membered-ring hydrogen transfer to an oxygen. Since the γ-cleavage product $C_3H_3D_2O_2^+$ was 45% as abundant as $C_2H_4O_2^+$ formed by γ-hydrogen rearrangement-β cleavage in the spectrum of hexanoic acid-*3,3-d*$_2$, five-membered-ring hydrogen rearrangements probably generally accompany six-membered-ring rearrangements.

Acknowledgment. We wish to thank the Robert A. Welch Foundation Grant H-609 for financial support.

References and Notes

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(3) H. Budzikiewicz, C. Djerassi, and D. H. Williams, "Mass Spectrometry of Organic Compounds", Holden-Day, San Francisco, Calif., 1967, pp 138, 155–162.
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(5) G. Eadon, *J. Am. Chem. Soc.*, **94**, 8938–8939 (1972).
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Degenerate Rearrangements in Solvolytic Studies with *cis*- and *trans*-2-Phenyl-1,2-di-*p*-tolylvinyl-*2*-^{13}C Bromides

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Abstract: Acetolysis in the presence of AgOAc of either *cis*- or *trans*-2-phenyl-1,2-di-*p*-tolylvinyl-*2*-^{13}C bromide (*cis*- or *trans*-**1**-Br-2-^{13}C) gave a 1:1 mixture of cis and trans products. After conversion of this product mixture to 2-phenyl-1,2-di-*p*-tolylethanol-*x*-^{13}C (**2**-x-^{13}C) and upon analysis of its ^{13}C NMR spectrum, about the same extent (1.5–2.0%) of scrambling of the ^{13}C label from C-2 to C-1 was found for either the cis or trans reactant. Nearly the same rate was also observed for the acetolysis, in the presence of NaOAc, with either *cis*- or *trans*-**1**-Br as substrate. Similarly, trifluoroacetolysis in the presence of CF_3COOAg of either *cis*- or *trans*-**1**-Br-2-^{13}C also gave about the same extent of ^{13}C scrambling (34–35%). All of these results point to the formation, without phenyl participation, of a free 2-phenyl-1,2-di-*p*-tolylvinyl cation which could then undergo competitively degenerate rearrangement by 1,2-phenyl shift and solvent capture to give product, the less nucleophilic the solvent, the greater the extent of isotopic scrambling. A solvent isotope effect, k_H/k_D, of 3.4–3.9 was observed for the reaction of *cis*- and *trans*-**1**-Br in CF_3COOH or CF_3COOD, without the presence of any Ag salt. This finding indicated that, in the reaction with CF_3COOH in the absence of Ag salt, an electrophilic addition–elimination process must have played an important role. Reaction of *cis*- and *trans*-**1**-Br-2-^{13}C with CF_3COOH, without any CF_3COOAg, gave 45 and 48–49% scrambling after ~2.5 and 6 half-lives. It is suggested that these latter results may be chiefly attributable to a subsequent ionization, in the reaction medium, of the addition–elimination product, followed by degenerate 1,2-phenyl shifts and recombination with solvent.

Degenerate rearrangements from 1,2-aryl shifts across the double bond in a number of labeled triarylvinyl cations, with various combinations of phenyl and/or *p*-anisyl as the aryl groups, have been studied in this laboratory,[1] and by Rappoport and coworkers.[2] 1,2-Phenyl and 1,2-anisyl shifts in triphenylvinyl and trianisylvinyl cationic systems have been investigated using the ^{14}C label as tracer,[1a,b,e] and using ^{13}C labeling coupled with analysis by ^{13}C NMR,[1b,c] while the ^{13}C NMR technique has also been applied in a study on the possible 1,2-phenyl shift in the reaction of *cis*- and *trans*-1,2-dianisyl-2-phenylvinyl-*2*-^{13}C bromide with HOAc–AgOAc.[1d] Rappoport et al. have utilized a D-labeled phenyl group and ^1H NMR as well as mass spectrometry in investigating degenerate 1,2-anisyl shifts during the solvolysis of *cis*- and *trans*-2-anisyl-1,2-diphenylvinyl bromides.[2a] Degenerate rearrangements in the trianisylvinyl and the *cis*- and *trans*-1,2-dianisyl-2-phenylvinyl systems have also been studied by Rappoport et al. in a number of solvolytic reactions with a $CD_3OC_6H_4$ group as label and again with analyses by ^1H NMR and mass spectrometry.[2b] Very recently, we have in-

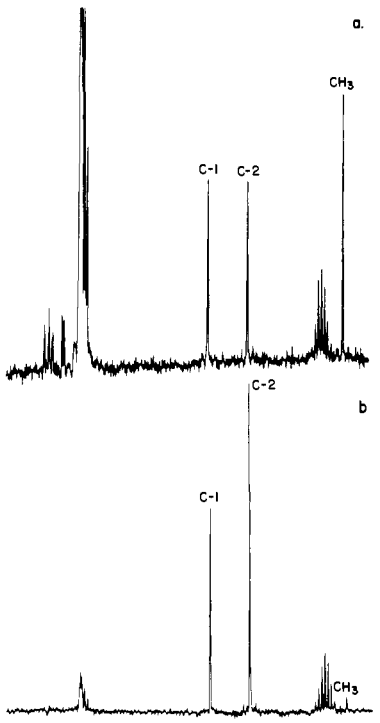
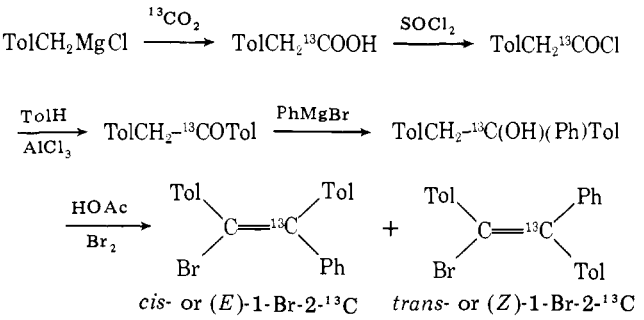


Figure 1. ^{1}H decoupled NMR spectra: (a) unenriched 2-phenyl-1,2-di-*p*-tolylethanol (**2**); (b) **2**-x-^{13}C derived from the CF_3COOAg-catalyzed trifluoroacetolysis of 45% ^{13}C-enriched *cis*-2-phenyl-1,2-di-*p*-tolylvinyl-2-^{13}*C* bromide (*cis*-**1**-Br-2-^{13}C).

Scheme I



vestigated the degenerate rearrangements in solvolytic reactions with tri-*p*-tolylvinyl-2-^{13}*C* bromide.[3] In the present work, some acetolysis and trifluoroacetolysis reactions with *cis*- and *trans*-2-phenyl-1,2-di-*p*-tolylvinyl-2-^{13}*C* bromides (*cis*- and *trans*-**1**-Br-2-^{13}C) were carried out in order to obtain further mechanistic information on degenerate 1,2-aryl shifts in triarylvinyl cationic systems.

Results

Analogous to the preparation of *cis*- and *trans*-1,2-dianisyl-2-phenylvinyl-2-^{13}*C* bromides,[1d] *cis*- and *trans*-**1**-Br-2-^{13}C were prepared by the series of reactions shown in Scheme I.

In preliminary trials using unlabeled materials, acetolysis of *cis*- or *trans*-**1**-Br in the presence of AgOAc gave an essentially 1:1 mixture of *cis*- and *trans*-**1**-OAc. Conversion[1c,d] of this mixture of acetates to 2-phenyl-1,2-di-*p*-tolylethanol (**2**), the compound to be used for the ^{13}C NMR analysis, gave a mixture of the erythro and threo diastereomers, and the ^{1}H NMR spectrum of **2** (Table I) indicated that the relative composition of this diastereomeric mixture was ~54:46.[4] The ^{1}H-decoupled ^{13}C NMR spectrum of **2** (diastereomeric mixture), however, showed that the three carbon absorptions of interest, C-1, C-2, and CH_3, all appeared as singlets (Figure 1a and Table II).

cis- and *trans*-**1**-Br-2-^{13}C were solvolyzed in HOAc in the presence of 1.1 equiv of AgOAc, or in CF_3COOH with or without the presence of 1.1 equiv of CF_3COOAg. The ester products were converted to **2**-x-^{13}C, the ^{13}C NMR spectra of which were used for the determination of the extents of isotopic scrambling from C-2 to C-1. An example of such a spectrum is shown in Figure 1b. The method, based on measurements of the relative intensities of the C-1 and C-2 absorptions, using the CH_3 absorption containing ^{13}C in its natural abundance as an internal reference standard, is the same as described previously in the study with trianisylvinyl-2-^{13}*C* bromide in which the CH_3O absorption served as the internal reference standard.[1c] The results obtained are summarized in Table III. (A sample calculation is given in the Experimental Section.)

To provide kinetic data for consideration together with the scrambling results, the rates of some reactions with *cis*- or *trans*-**1**-Br were determined by potentiometric titration of the liberated bromide ion.[5] The results are given in Table IV. It may be noted that no kinetic measurements were made for the acetolysis or trifluoroacetolysis in the presence of AgOAc or CF_3COOAg. Under the conditions employed in the present work, the Ag salts did not completely dissolve in the HOAc or CF_3COOH and, because of this heterogeneity, the rates were not determined. However, qualitatively, the presence of the Ag salt greatly enhanced the solvolysis rate. For example, in an attempt to follow the rate of trifluoroacetolysis in the presence of 1.1 equiv of CF_3COOAg at 0 °C by potentiometric titration, the reaction was apparently complete in <3 min, which was the minimum amount of time involved in the manipulations.

Table I. ^{1}H NMR Data for the Diastereomeric Mixture of *p*-$CH_3Ph(Ph)CHCH(OH)PhCH_3$-*p* (**2**)

Proton	δ (acetone-d_6), ppm from TMS (*J*, Hz)
CH_3, 3 singlets	2.08,[a] 2.13,[b] 2.19[a]
C-2 H, 2 doublets[c]	3.98 (*J* = 4.4), 4.00 (*J* = 4.3)
OH, 2 singlets	4.31, 4.16
C-1 H, 2 doublets[c]	5.47 (*J* = 4.4), 5.32 (*J* = 4.1)
Arom multiplet	6.6–7.6

[a] Integrated intensity ratio of ~54:46. [b] Overlapping peak of a CH_3 from each diastereomer. [c] Decoupling showed that the doublet centered at δ 3.98 coupled to 5.47, and δ 4.00 coupled to 5.32.

Table II. ^{13}C NMR Data for the Diastereomeric Mixture of *p*-$CH_3Ph(Ph)CHCH(OH)PhCH_3$-*p* (**2**)

Carbon	δ (acetone-d_6), ppm from TMS
CH_3	20.5
C-2	59.8
C-1	76.1
Arom	126.0, 127.3, 128.1
	128.5, 128.9, 129.3
Quat arom	135.3, 136.2, 141.6
	142.2, 143.1, 145.9

Discussion

Acetolysis. The acetolysis, in the presence of AgOAc, of *cis*- or *trans*-**1**-Br-2-^{13}C gave 1.5–2.0% scrambling of the label from C-2 to C-1 (Table III). This value did not change when the reaction time was increased from 3 to 20 h, indicating that, under the conditions employed, the reaction product did not undergo further scrambling in the reaction mixture. The formation of a 1:1 mixture of cis and trans products from *cis*- or *trans*-**1**-Br, the similarity in the extents of ^{13}C scrambling

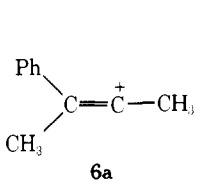
Table III. Scrambling Data from the ^{13}C NMR Spectra of 2-Phenyl-1,2-di-*p*-tolylethanol-*x*-^{13}C (**2**-x-^{13}C) Derived from Solvolyses of *cis*- and *trans*-2-Phenyl-1,2-di-*p*-tolylvinyl-2-^{13}C Bromides (*cis*- and *trans*-**1**-Br-2-^{13}C)

Reactant[a]	Solvent and added salt	Reaction time, min	Reaction temp, °C	Relative intensities[b] I_1/I_s	Relative intensities[b] I_2/I_s	Calcd ^{13}C enrichment, %	^{13}C scrambling from C-2 to C-1, %
Unenriched **2**				0.625[c]	0.625[c]		
				0.667	0.667		
cis	HOAc–AgOAc	180	Reflux	1.13[c]	25.7[c]	45.0[d]	2.0
trans	HOAc–AgOAc	180	Reflux	0.825[c]	15.3[c]	26.3	1.5
cis–trans	HOAc–AgOAc	1200	Reflux	0.950	18.5	29.4	1.5
cis	CF_3COOH–CF_3COOAg	20	Room temp	9.63[c]	17.0[c]	44.6[d]	35
trans	CF_3COOH–CF_3COOAg	20	Room temp	5.47[c]	10.2[c]	25.3	34
cis–trans	CF_3COOH–CF_3COOAg	180	Room temp	9.40	16.6	40.7	35
cis–trans	CF_3COOH	105[e]	100	6.22	7.44	20.4	45
cis–trans	CF_3COOH	260[f]	100	5.67	6.00	17.3	49
cis–trans	CF_3COOH	260[f]	100	6.22	6.71	19.1	48

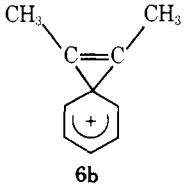
[a] The reactants were pure *cis*-**1**-Br-2-^{13}C, pure *trans*-**1**-Br-2-^{13}C or an ~3:2 mixture of the cis and trans isomers. [b] I_1, I_2, and I_s are the integrated intensities of the absorption for C-1, C-2, and the CH_3 internal standard, respectively. [c] Data were obtained using a Bruker WP-60 spectrometer, the other data being derived from a Varian XL-100 spectrometer. [d] The expected enrichment is 45% from the commercial designation of the ^{13}C content of the starting material, $Ba^{13}CO_3$. The other samples were further diluted with ordinary carriers. [e] About 2.5 half-lives. [f] About 6 half-lives.

(Table III), and in the acetolysis rates (Table IV) for either the cis or trans reactant all point to a reaction via the open, classical 2-phenyl-1,2-di-*p*-tolylvinyl cation without anchimeric assistance or phenyl participation for the acetolysis of *cis*- or *trans*-**1**-Br. Similar conclusions regarding the intermediacy of such free, linear triarylvinyl cations in other triarylvinyl systems have also been arrived at previously by Rappoport and co-workers.[6] With the present work, scrambling data arising from 1,2-phenyl shifts in a series of related triarylvinyl systems are now available. Thus degenerate rearrangements in the AgOAc-catalyzed acetolysis of triphenylvinyl-2-^{13}C, *cis*- and *trans*-2-phenyl-1,2-di-*p*-tolylvinyl-2-^{13}C and *cis*- and *trans*-1,2-dianisyl-2-phenylvinyl-2-^{13}C bromides (**3**-Br-2-^{13}C, *cis*- and *trans*-**1**-Br-2-^{13}C, and *cis*- and *trans*-**4**-Br-2-^{13}C, respectively) have all been investigated. For comparison, the scrambling results, together with the data of Stang and Dueber[7] from the solvolysis of *cis*- and *trans*-1,2-dimethyl-2-phenylvinyl triflate (*cis*- and *trans*-**5**-OTf), are summarized in Table V.

Stang and Dueber[7] have demonstrated that *trans*-**5**-OTf solvolyzes predominantly, if not exclusively, with phenyl participation via the phenyl-bridged ion **6b**, since, in 60% EtOH, *trans*-**5**-OTf reacted faster than the cis isomer and gave almost 50% scrambling of the CD_3 label (Table V), while, in trifluoroethanol (TFE), it gave almost exclusively the trans product. With *cis*-**5**-OTf, solvolysis in TFE also gave predominantly the trans product, and thus it was suggested that solvolysis of *cis*-**5**-OTf initially gave an ion pair with the cationic partner as the open, classical vinyl cation **6a**, which could capture solvent to give product or convert to **6b** before giving rise to the isotopically scrambled product.[7]



6a



6b

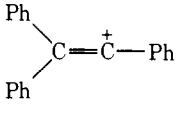
From the present work with *cis*- and *trans*-**1**-Br and in the previous studies with *cis*- and *trans*-**4**-Br,[1d,2b,8] the formation of an essentially 1:1 mixture of cis and trans products, starting from either the cis or trans reactant, suggests that "free" triarylvinyl cations[2,5] were produced in the solvolysis with either of these systems. If ion pairs were involved, analogous to the predominant formation of the trans product from *cis*-**5**-OTf,[7] and similar to the extra inversion observed in the solvolysis of other vinylic systems which proceeded through ion pairs,[9] one would expect some shielding by the leaving counterion which would not give rise to a 1:1 mixture of cis and trans products.[10]

Table IV. Kinetic Data for the Acetolysis and Trifluoroacetolysis of *cis*- and *trans*-2-Phenyl-1,2-di-*p*-tolylvinyl Bromides (*cis*- and *trans*-**1**-Br)

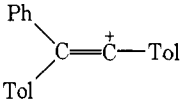
Reactant	Solvent	Temp, °C	k, s^{-1}	k_H/k_D
cis-**1**-Br	HOAc[a]	118[b]	5.4×10^{-8}	
trans-**1**-Br	HOAc[a]	118[b]	5.7×10^{-8}	
cis-**1**-Br	HOAc	150	9.6×10^{-7}	
cis-**1**-Br	DOAc	150	1.0×10^{-6}	0.96
cis-**1**-Br	CF_3COOH	100	2.2×10^{-4}	
cis-**1**-Br	CF_3COOD	100	6.5×10^{-5}	3.4
1:1 *cis*- and *trans*-**1**-Br	CF_3COOH	100	2.7×10^{-4}	
1:1 *cis*- and *trans*-**1**-Br	CF_3COOD	100	6.9×10^{-5}	3.9

[a] Containing 2.0 equiv of NaOAc. [b] Reaction followed under reflux; the other reactions were carried out in sealed ampules.

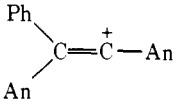
From the data in Table V, it is seen that there appears to be a gradation of changes in the involvement of bridged ion to free ion, and a progressive decrease in the extents of degenerate rearrangement in going from the 1,2-dimethyl-2-phenylvinyl to the triphenylvinyl, 2-phenyl-1,2-di-*p*-tolylvinyl, and 1,2-dianisyl-2-phenylvinyl systems. Since the migrating group in all of these systems is the same, it has been suggested[1d] that the effect of the α substituent on the stability of the vinyl cation may play an important role. For the triarylvinyl systems, the bridged structures **7b, 8b,** and **9b** may be regarded as models



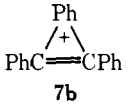
7a



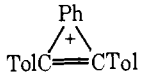
8a



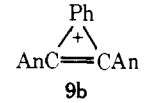
9a



7b



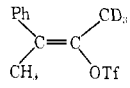
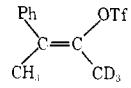
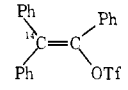
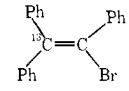
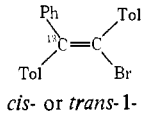
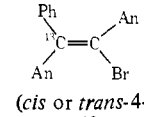
8b



9b

of the transition states for the 1,2-phenyl shifts in cations **7a, 8a,** and **9a.** The different extents of scrambling as summarized in Table V indicate that, for the scrambling process, the activation energies in going from vinyl cation to bridged transition

Table V. Isotopic Scramblings in Solvolytic Reactions with Labeled Vinylic Systems

Reactant	 *trans*-5-OTf	 *cis*-5-OTf	 3-OTf-2-^{14}C	 3-Br-2-^{13}C	 *cis*- or *trans*-1-Br-2-^{13}C	 (*cis* or *trans*-4-Br-2-^{13}C)
Solvent and base or salt	60% EtOH–pyridine	60% EtOH–pyridine	HOAc[a]	HOAc–AgOAc	HOAc–AgOAc	HOAc–AgOAc
% scrambling	47.6 ± 0.3[b]	34.5 ± 0.4[b]	6.5–7.0	6.8 ± 0.9	1.5–2.0	0
Ref	7	7	1a	1b	Present work	1d

[a] With or without added NaOAc. [b] Similar results were obtained with the CD_3 label at C-β.

state would be in the order of **9a** → **9b** > **8a** → **8b** > **7a** → **7b.** The stabilization by the α-aryl group in the vinyl cation would render the stability of **9a** > **8a** > **7a.** Similarly, the stabilization of the bridged transition state by the nonmigrating aryl substituents at C-α and C-β would also be in the order of **9b** > **8b** > **7b.** Apparently the stabilizing effect of the α-aryl group on the vinyl cation is of greater importance than the stabilization of the bridged transition state by the nonmigrating aryl groups. Hence the energy is lowered to a greater extent in **9a, 8a,** and **7a** than in **9b, 8b,** and **7b,** giving rise to the observed order of activiation energy, namely, **9a** → **9b** > **8a** → **8b** > **7a** → **7b.**

With the 1,2-dimethyl-2-phenylvinyl system, it is not surprising that the phenyl-bridged ion **6b** is more stable than the open ion **6a,** the latter being stabilized only with an α-CH_3 group. Hence **6b** can be formed from **6a** or directly from a trans substrate as observed by Stang and Dueber.[7]

Another factor which also fits the observed scrambling results and thus cannot be excluded from consideration is the electrophilic character of the migration terminus. As suggested by Bonner et al.[11] in their discussion on the migratory aptitudes of the phenyl and anisyl groups in the saturated 1,2,2-triarylethyl cations, the greater the ability of an α-aryl group in delocalizing the + charge, the lesser will be the electrophilic character of the migration terminus, and lesser will be the extent of 1,2-aryl shift. From this point of view, the expected extent of 1,2-phenyl shift in the triarylvinyl cations would be **9a** < **8a** < **7a,** as was observed.

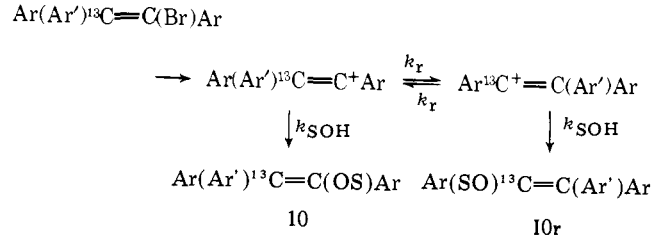
Another approach to the treatment of data such as the present results can be made from consideration of the mechanism given in Scheme II for solvolyses, in the presence of Ag salt, of triarylvinyl systems. Using the steady-state treatment and a method analogous to that employed by Bonner and Collins,[12] it can be shown[2b] that, after complete reaction, the relationship shown in eq 1 holds.

$$[\mathbf{10}]/[\mathbf{10r}] = 1 + (k_{SOH}/k_r) \qquad (1)$$

For reactions in HOAc–AgOAc, *cis*- or *trans*-**1**-Br-2-^{13}C (Ar′ = Ph; Ar = Tol) and tri-*p*-tolylvinyl-2-^{13}C bromide (**11**-Br-2-^{13}C, Ar′ = Ar = Tol) gave, respectively, ^{13}C scramblings from C-2 to C-1 of 1.5–2.0% (Table III) and 13–14%.[3] Using the precision limits of the observed results, k_{SOH}/k_r calculated for *cis*- or *trans*-**1**-Br-2-^{13}C (1.5–2.0% scrambling) is 48–65 and k_{SOH}/k_r calculated for **11**-Br-2-^{13}C (13–14% scrambling) is 5.1–5.7. Assuming k_{SOH} to be equal for the two reactions, $k_{r\text{-Tol}}/k_{r\text{-Ph}}$ should be within the range of 48/5.7 to 65/5.1, or 8.4–13. This is a measure of relative migratory aptitudes for *p*-tolyl/phenyl in the triarylvinyl cations derived from *cis*- or *trans*-**1**-Br-2-^{13}C and **11**-Br-2-^{13}C, which differ only in the migrating group and have the same aryl substituent at the migration origin and migration terminus. Moreover, the value of 8.4–13 is quite a reasonable one in comparison with the well-known migratory aptitude of 15.7 for *p*-tolyl/phenyl reported many years ago by Bachmann[13] for the pinacol-type rearrangements.

Trifluoroacetolysis. As can be seen from Table III, more scrambling was observed (34–35%) in the trifluoroacetolysis in the presence of CF_3COOAg of *cis*- or *trans*-**1**-Br-2-^{13}C than in the acetolysis in the presence of AgOAc. An increase in the reaction time, at room temperature, also did not change the extent of scrambling. Moreover, the similar amount of degenerate rearrangement found for either the cis or trans isomer further supports the conclusion that the solvolysis proceeded via the free vinyl cation, **8a.** In previous studies with the triphenylvinyl and trianisylvinyl systems, more extensive scramblings were also observed for trifluoroacetolysis than for acetolysis.[1a,c] Analogously, solvolysis in trifluoroethanol gave more degenerate rearrangements than reactions in more nucleophilic solvents such as HOAc or aqueous ethanol.[2a,b] It is generally agreed that the different extents of rearrangement in different solvents reflect the competition between solvent capture and 1,2-aryl shifts in the triarylvinyl cations,[1a,c,2a,b] and the greater amount of scrambling found in the trifluoroacetolysis in the present work is to be expected.

Scheme II



Applying eq 1, for scramblings of 34–35%, k_{SOH}/k_r for the trifluoroacetolysis of *cis*- or *trans*-**1**-Br-2-^{13}C, in the presence of CF_3COOAg, is calculated to be 0.86–0.94. In the reaction of **11**-Br-2-^{13}C with CF_3COOH–CF_3COOAg, the ^{13}C scrambling was 46–47%,[3] which corresponds to k_{SOH}/k_r of 0.13–0.17. Again, if k_{SOH} were assumed to be equal for the two reactions, $k_{r\text{-Tol}}/k_{r\text{-Ph}}$ for the trifluoroacetolysis would be 0.86/0.17 to 0.94/0.13, or 5.1–7.2. Such a measure of the relative migratory aptitudes of tolyl/phenyl is certainly more realistic than a simple comparison of the overall extents of scrambling, such as 47/35 = 1.3.

In solvolytic studies with vinylic systems, under acidic conditions, there is the possibility of an electrophilic addition followed by elimination to give the same product as that derived from an S_N1 reaction.[14] For reactions of vinylic substrates with CF_3COOH (TFA), the addition-elimination alternative is a distinct possibility, and TFE rather than TFA may be a preferred choice as a solvent of low nucleophilicity. However, in our present and previous work,[1a,c] TFA has been employed since the reaction products could be converted to 1,2,2-triarylethanols for ^{13}C NMR analysis or for further degradation in the case when ^{14}C was used as tracer.[1a]

It has been pointed out[14c,d] that a solvent kinetic isotope effect is a good diagnostic test for electrophilic addition-elimination. From Table IV, it is seen that reaction of *cis*- and *trans*-**1**-Br with CF_3COOH or CF_3COOD, without the presence of any silver salt, gave a solvent isotope effect of 3.4–3.9, indicating an important role for electrophilic addi-

tion–elimination under these conditions. In the presence of CF_3COOAg, the reaction is very much faster (too fast for measurement at 0 °C by potentiometric titration), any addition–elimination component would be too slow to contribute, and it is likely that the CF_3COOAg-catalyzed trifluoroacetolysis is an S_N1 process via vinyl cation **8a.**

An electrophilic addition–elimination, as depicted by eq 2, should not give any scrambling.

$$\mathrm{Ar(Ar')^{13}C{=}C(Br)Ar} \xrightarrow[\text{slow}]{\mathrm{HOS}} \mathrm{Ar(Ar')^{13}CH{-}C(OS)(Br)Ar} \xrightarrow{-\mathrm{HBr}} \mathrm{Ar(Ar')^{13}C{=}C(OS)Ar} \quad (2)$$

However, it is seen from Table III that reaction of *cis*- and *trans*-**1**-Br-2-^{13}C with CF_3COOH at 100 °C gave 45 and 48–49% scrambling, respectively, after 105 and 260 min (~2.5 and 6 half-lives). Apparently, the scrambling increases with an increase in reaction time. It may also be noted that these reactions gave extensive decomposition, the yields of **2**-x-^{13}C being only ~10–20%, in contrast to ~50% yields of **2**-x-^{13}C for the experiments in CF_3COOH–CF_3COOAg. In an attempt to scramble completely the ^{13}C label over C-2 and C-1, *cis* and *trans*-**1**-Br-2-^{13}C was heated with CF_3COOH at 100 °C for 16 h, but only a gummy decomposition product resulted.

In the study with tri-*p*-tolylvinyl-2-^{13}C bromide (**11**-Br-2-^{13}C),[3] while trifluoroacetolysis in the presence of CF_3COOAg gave 46–47% scrambling, reaction with CF_3COOH alone at 100 °C for 25 and 60 min (~2 and 5 half-lives) and for 3 h gave, respectively, 43, 47, and 50% scrambling. A solvent isotope effect, $k_{CF_3COOH}/k_{CF_3COOD}$, of 2.6 was also observed. Thus the results from the trifluoroacetolysis, without Ag salt, obtained from **11**-Br-2-^{13}C are quite similar to those found in the present work with *cis*- and *trans*-**1**-Br-2-^{13}C. Since the extent of scrambling increases with increasing reaction time, and as was concluded previously,[3] the ^{13}C scrambling observed in the surviving product from reactions with CF_3COOH, without Ag salt, is likely chiefly due to a subsequent ionization in the reaction medium of the addition–elimination product. This may be followed by degenerate 1,2-aryl shifts and then recombination with solvent to give the observed results.

Experimental Section

Deoxy-*p*-toluoin-*carbonyl*-^{13}C. $TolCH_2{}^{13}COOH$ was prepared from reaction of $TolCH_2MgCl$ with $^{13}CO_2$ generated from 45% enriched $Ba^{13}CO_3$, using the procedure previously described for the synthesis of *p*-anisylacetic acid.[1d,15] The labeled acid was converted to the acid chloride,[1d] which in turn was used to acylate toluene[1d] to give an overall 74% yield, based on the labeled acid, of $TolCH_2{}^{13}COTol$: mp 101–102 °C (lit.[16] mp 102.5–103.5 °C); ^1H NMR δ ($CDCl_3$) 2.28, 2.35 (CH_3, 2 s), 4.17 (CH_2, t, $J_{^{13}CCH_2}$ = 6.4 Hz), and 7.1–7.4, 7.8–8.1 (arom, m).

Anal. Calcd for $C_{16}H_{16}O$, 45% ^{13}C enrichment for one carbon: C, 85.70; H, 7.18. Found: C, 85.63; H, 7.22.

***cis*- and *trans*-2-Phenyl-1,2-di-*p*-tolylvinyl-2-^{13}C Bromides (*cis*- and *trans*-1-Br-2-^{13}C).** The procedures were analogous to those used in the preparation of *cis*- and *trans*-1,2-dianisyl-2-phenylvinyl-2-^{13}C bromides (*cis*- and *trans*-**4**-Br-^{13}C).[1d] Deoxy-*p*-toluoin-*carbonyl*-^{13}C (45% enriched) was treated with PhMgBr in THF to give 1-phenyl-1,2-di-*p*-tolylethanol-1-^{13}C. This alcohol, recovered as an oil (^1H NMR δ ($CDCl_3$) 2.17, 2.23 (CH_3, 2 s), 2.83 (OH, s), 3.57 (CH_2, t, $J_{^{13}CCH_2}$ = 4.4 Hz), and 6.8–7.8 (arom, m)) was used directly without further purification. It was dissolved in HOAc, heated under reflux for 2 h, cooled, and then treated with Br_2 as described previously[1d] to give a mixture of *cis*- and *trans*-**1**-Br-2-^{13}C.[17] Separation of the mixture into pure isomers was effected by fractional crystallization in CH_3OH, the trans isomer being less soluble. The overall yield of recrystallized products, based on the deoxy-*p*-toluoin, was ~50%. The assignment of the cis or trans structure was made by analogy with *cis*- and *trans*-**4**-Br[1d,8] on the basis of differences in melting points and ^1H NMR spectra. Pure *cis*-**1**-Br-2-^{13}C melted at 119–120 °C: ^1H NMR δ ($CDCl_3$) 2.18, 2.25 (CH_3, 2 s) and 6.8–7.4 (arom, m). The trans isomer melted at 147–149 °C: ^1H NMR δ ($CDCl_3$) 2.25, 2.35 (CH_3, 2 s) and 6.9–7.3 (arom, m).

Anal. Calcd for $C_{22}H_{19}Br$, 45% ^{13}C enrichment for one carbon: C, 72.77; H, 5.26. Found for the cis isomer: C, 72.52; H, 5.13. Found for the trans isomer: C, 72.73; H, 5.27.

Solvolysis Reactions. The acetolysis of *cis*- or *trans*-**1**-Br-2-^{13}C was carried out by heating the substrate under reflux and with stirring for 3 h in HOAc–Ac_2O containing 1.1 equiv of AgOAc. The trifluoroacetolysis was effected by stirring a mixture of the substrate and 1.1 equiv of CF_3COOAg in CF_3COOH–$(CF_3CO)_2O$ for 20 min at room temperature. For the reaction of the *cis*- and *trans*-**1**-Br-2-^{13}C mixture with CF_3COOH without an Ag salt, the solution of the reactant in CF_3COOH was heated at 100 °C for 105 or 260 min. A typical experiment is described below.

A mixture of 1.1 g (3.0 mmol) of *cis*-**1**-Br-2-^{13}C and 0.55 g (3.3 mmol) of AgOAc in 20 mL of HOAc containing 2.0 mL of Ac_2O was heated under reflux and with stirring for 3 h. The AgBr and excess AgOAc were then removed by filtration and washed with 20 mL of warm HOAc. The combined filtrate was evaporated under reduced pressure (3–5 Torr) to give a residual product of *cis*- and *trans*-**1**-OAc-x-^{13}C which was used directly for conversion to 2-phenyl-1,2-di-p-tolylethanol-*x*-^{13}C (**2**-x-^{13}C). The overall yield of **2**-x-^{13}C from the acetolysis was ~60%. In preliminary trials with unlabeled bromides, the crude mixed acetates were redissolved in ether, washed with 10% $NaHCO_3$, and dried over $MgSO_4$. After removal of the ether, the residual acetates were examined by ^1H NMR: δ ($CDCl_3$) 1.93, 1.97 (AcO, 2 s), 2.25, 2.33 (CH_3, 2 s), and 6.9–7.3 (arom, m). Integration of the acetate absorptions showed that the cis–trans composition was essentially 1:1 (50 ± 2%).

The mixed esters from each experiment with *cis*- or *trans*-**1**-Br-2-^{13}C were converted to **2**-x-^{13}C (diastereomeric mixture) by two successive treatments with $LiAlH_4$ in THF.[1c,d] From the ^{13}C NMR spectrum of **2**-x-^{13}C, the extent of scrambling of the label from C-2 to C-1 was determined. An illustration of the calculations, using the data given in Table III, is as follows.

Let $I_1{}^0$ and $I_1{}^*$, respectively, be the integrated intensities of the ^{13}C absorption due to the naturally abundant ^{13}C at C-1 and to the ^{13}C enrichment at C-1.

From the unenriched **2**, $I_1{}^0/I_s = 0.625$

From the **2**-x-^{13}C derived from the reaction of *cis*-**1**-Br-2-^{13}C with CF_3COOH–CF_3COOAg $I_1/I_s = (I_1{}^0 + I_1{}^*)/I_s = 9.63$. Hence $(I_1{}^0 + I_1{}^*)/I_1{}^0 = 9.63/0.625 = 15.4$. Converting the intensities to % ^{13}C $(1.1 + I_1{}^*)/1.1 = 15.4$ and $I_1{}^* = 15.8\%$. Similarly, $I_2{}^0/I_s = 0.625$ and $I_2/I_s = (I_2{}^0 + I_2{}^*)/I_s = 17.0$. Hence $(I_2{}^0 + I_2{}^*)/I_2{}^0 = 17.0/0.625 = 27.2$, $(1.1 + I_2{}^*)/1.1 = 27.2$, and $I_2{}^* = 28.8\%$. Therefore, the calculated ^{13}C enrichment = 15.4 + 28.8 = 44.6% and the scrambling from C-2 to C-1 = (15.8/44.6) × 100 = 35%.

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(4) A referee has suggested that there is the possibility of a tolyl migration in the vinyl cation leading to a *gem*-ditolyl compound and thus the mixture of cis and trans products may really contain a *gem*-ditolyl isomer and the mixture of erythro and threo alcohols **2** may really be structural isomers rather than diastereomers. These inferences of the referee are incorrect. The 2-phenyl-1,2-di-*p*-tolylvinyl cation does not undergo 1,2-tolyl shift to give the less stable 1-phenyl-2,2-di-*p*-tolylvinyl cation. Indeed, it has been known for a long time that the 1-phenyl-2,2-di-*p*-tolylvinyl cation could rearrange to the more stable 2-phenyl-1,2-di-*p*-tolylvinyl cation (W. M. Jones and F. W. Miller, *J. Am. Chem. Soc.*, **89**, 1960 (1967)). Moreover, the mass spectrum of the mixture of *erythro*- and *threo*-2-phenyl-1,2-di-*p*-tolylethanol (**2**) showed *m/e* 121 for $[CH_3C_6H_4CHOH]^+$ as the base peak and a prominant peak at *m/e* 181 (~80% of the base peak) corresponding to $[CH_3C_6H_4(C_6H_5)CH]^+$. These fragmentations agree with the structure for **2** and the absence of a peak at *m/e* 107 for $[C_6H_5CHOH]^+$, expected as

the base peak for 1-phenyl-2,2-di-*p*-tolylethanol, definitely excludes the presence of a *gem*-ditolyl isomer.
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Reaction of $^3O_2$ with Dihydroflavins. 1. $N^{3,5}$-Dimethyl-1,5-dihydrolumiflavin and 1,5-Dihydroisoalloxazines

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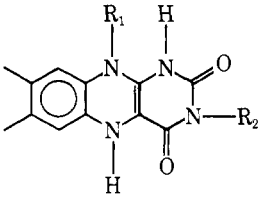
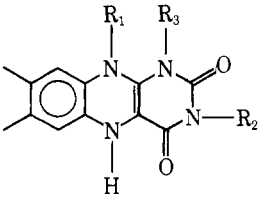
Abstract: The reactions of oxygen with $N^{3,5}$-dimethyl-1,5-dihydrolumiflavin ($FlHCH_3$) and a number of 1,5-dihydroisoalloxazines have been investigated and mechanisms suggested which are based on kinetic measurements, product ratios, and computed potentials. The rate constants for the pertinent reactions which must be considered in the oxidation of $FlHCH_3$ in methanol (30 °C) are provided in eq 11–18. These include the formation of a 4a-hydroperoxyflavin (4a-$FlCH_3$-OOH), its reaction with $FlHCH_3$ and $FlCH_3\cdot$, and ionization to the oxidized flavin ($Fl_{ox}{}^+CH_3$). The autocatalytic role of 4a-$FlCH_3$-OOH and the importance of each reaction in the overall $^3O_2$ oxidation of $FlHCH_3$ have been established. Previous proposals of mechanism have involved homolytic scission of the C_{4a}–OOH bond. No evidence for this process could be discerned. In place, the 4a-$FlCH_3$-OOH species is shown to undergo elimination of hydrogen peroxide to yield $Fl_{ox}{}^+CH_3$ (both in methanol and water solvents). The autoxidation of $FlHCH_3$ in water (30 °C) provides a complex dependence of both rate and products on pH. Arguments are presented which point to the operation of the reactions of eq 26, 27, and 30 above pH 8, the reactions of eq 26 and 27 between pH 7 and 8, and the reactions of eq 26–29 below pH 7 (Scheme V). Autocatalytic oxidation of 1,5-dihydroisoalloxazines (FlH_2) are discussed in terms of the reactions of Scheme VI. It is pointed out that the second-order rate constants for reaction of O_2 with FlH_2 and with $FlHCH_3$ are comparable (i.e., 250 vs. 220 M^{-1} s^{-1} at pH ~6.5) and that the greater lability of FlH_2 to O_2, when compared to $FlHCH_3$, is due to autocatalysis and in particular to the much greater rate of reaction of $Fl^{-}\cdot$ with O_2 when compared to $FlCH_3\cdot$. The time course for Fl_{ox} production has been shown to be reproducibly simulated when employing rate data from this and other studies. Lastly, feasibility of the intermediacy of the $[FlH_T\cdot O_2^{-}\cdot]$ intimate radical pair in the oxidation of singlet FlH_2 by triplet O_2 has been established by comparison of the standard free energy of formation of $FlH_T\cdot + O_2^{-}\cdot$ (standard states 1 M, $p_{[O_2]}$ = 1 atm, 30 °C, pH 7.0) to the value of $\Delta G^{\ddagger}$ for the second-order reaction of oxygen with 1,5-dihydroflavin.

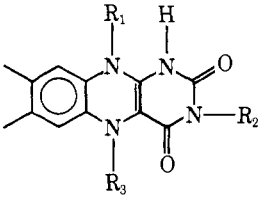
The not yet understood phenomenon of flavoenzyme mediated hydroxylation reactions[2] has prompted a number of investigations of the nonenzymic reduction of molecular oxygen by reduced flavins[3-11] and has inspired much speculation concerning the mechanisms of both enzymic and model reactions.[2,12-15] A large number of reduced flavins have been employed as models; these can be divided into three classes: (1) "normal" (FlH_2); (2) N^1-blocked; and (3) N^5-blocked. Of these, the first two have received the most attention.[3-8] Studies on the autoxidation of N^1-blocked reduced flavins by Mager and co-workers[6] have emphasized the ability of this system to hydroxylate phenylalanine (by HO· generated from $1e^-$ reduction of a flavin hydroperoxide intermediate and/or H_2O_2). Müller and co-workers,[7] on the other hand, have reported spectral evidence for the formation of a flavin hydroperoxide upon reaction of an N^1-blocked reduced flavin with oxygen in organic solvents.[16] The most detailed kinetic investigations have employed "normal" reduced flavins such as 1,5-dihydroflavin mononucleotide ($FMNH_2$) and 1,5-dihydrotetraacetylriboflavin ($TARFH_2$). Working solely with $FMNH_2$,



"normal" (FlH_2)



N^1-blocked



N^5-blocked (FlHR)