tic picture of olefin metathesis are difficult to access. While it is established that cyclobutanes can be formed in high yield in carefully constructed structural situations under metathesis conditions, our results in no way implicate cyclobutane containing intermediates for all olefin metathesis reactions. Clearly, the sum of data which are currently available would implicate a variety of different mechanistic paths.

We are continuing to investigate the mechanism of these useful olefin disproportionation reactions.

**Acknowledgment.** We are indebted to the National Science Foundation for a grant which supported this investigation.

## References and Notes


(1) Paper XLVI on "The Chemistry of Bent Bonds". For the previous paper in this series see P. G. Gassman and J. J. Valcho, *J. Am. Chem. Soc.*, **97**, 4768 (1975).

(2) For recent reviews, see R. J. Haines and G. J. Leigh, *Chem. Soc. Rev.*, **4**, 155 (1975), and ref 12–24 therein, especially N. Calderon, *Acc. Chem. Res.*, **5**, 127 (1972), and G. C. Bailey, *Catal. Rev.*, **3**, 37 (1969).

(3) F. D. Mango and J. H. Schachtschneider, *J. Am. Chem. Soc.*, **89**, 2484 (1967); "Transition Metals in Homogeneous Catalysis", G. N. Schrauzer, Ed., Marcel Dekker, New York, N.Y., 1971, p 223; *J. Am. Chem. Soc.*, **93**, 1123 (1971); C. P. Bradshaw, A. J. Howman, and L. Turner, *J. Catal.*, 7, 269 (1967); E. A. Zuech, *Chem. Commun.*, 1182 (1968); C. T. Adams and S. G. Brandenburger, *J. Catal.*, **13**, 360 (1969); W. B. Hughes, *Chem. Commun.*, 431 (1969); R. Pettit, H. Sugahara, J. Wristers, and W. Merk, *Diss. Faraday Soc.*, **47**, 71 (1969); G. S. Lewandos and R. Pettit, *Tetrahedron Lett.*, 789 (1971); G. S. Lewandos and R. Pettit, *J. Am. Chem. Soc.*, **93**, 7087 (1971).

(4) R. H. Grubbs and T. K. Brunck, *J. Am. Chem. Soc.*, **94**, 2538 (1972); C. G. Biefeld, H. A. Eick, and R. H. Grubbs, *Inorg. Chem.*, **12**, 2166 (1973). See also A. R. Fraser, P. H. Bird, S. A. Bezman, J. R. Shapley, R. White, and J. A. Osborn, *J. Am. Chem. Soc.*, **95**, 597 (1973); J. X. McDermott and G. M. Whitesides, *ibid.*, **98**, 947 (1974).

(5) D. J. Cardin, M. J. Doyle, and M. F. Lappert, *J. Chem. Soc., Chem. Commun.*, 927 (1972); T. J. Katz and J. McGinnis, *J. Am. Chem. Soc.*, **97**, 1592 (1975); R. H. Grubbs, P. L. Burk, and D. D. Carr, *ibid.*, **97**, 3265 (1975). See also C. P. Casey and T. J. Burkhardt, *ibid.*, **96**, 7808 (1974); J. L. Herrisson and Y. Chauvin, *Makromol. Chem.*, **141**, 161 (1970); J. P. Soufflet, D. Commereuc, and Y. Chauvin, *C.R. Acad. Sci., Ser. C.*, **276**, 1969 (1973).

(6) Ample precedent exists for this portion of our findings. See H. Hogeveen and H. C. Volger, *J. Am. Chem. Soc.*, **89**, 2486 (1967); P. G. Gassman, D. H. Aue, and D. S. Patton, *ibid.*, **90**, 7271 (1968); L. Cassar and J. Halpern, *Chem. Commun.*, 1082 (1970).

(7) P. G. Gassman, S. R. Korn, and R. P. Thummel, *J. Am. Chem. Soc.*, **96**, 6948 (1974).

(8) W. Grahlert, K. Milowski, and V. Langbein, *Z. Chem.*, **14**, 287 (1974).

(9) The catalyst system was prepared from 0.66 g of aluminum trichloride and 1.86 g of phenyltungsten trichloride in 100 ml of carefully deoxygenated chlorobenzene. The formation of the catalyst system was carried out in Schlenk apparatus under an argon atmosphere. After 15 min of reaction time, the catalyst preparation was centrifuged and the clear supernatent liquid was used as the active catalyst-containing solution.

(10) On exposure to air the activity of the cayalyst system is destroyed immediately. A flocculent precipitate was formed when a solution of the active catalyst was exposed to air. This precipitate was removed by filtration prior to VPC analysis of the reaction mixture.

(11) The activity of the catalyst system deteriorated with time. In our hands, the phenyltungsten trichloride–aluminum trichloride catalyst system retained its activity for approximately 36 h.

(12) Control reactions established that neither phenyltungsten trichloride nor aluminum trichloride alone promoted the conversion of **1** into **2**.


**Paul G. Gassman,* Thomas H. Johnson**

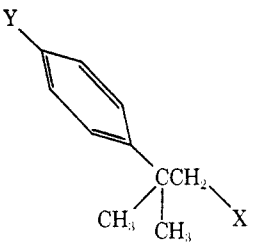
*Department of Chemistry, University of Minnesota*
*Minneapolis, Minnesota 55455*

*Received October 3, 1975*

## Influence of Neighboring Phenyl Participation on the α-Deuterium Isotope Effect on Solvolysis Rates. Neophyl Esters

*Sir:*

Winstein and co-workers[1-3] originally suggested that the rearranging solvolyses of neophyl esters (I) are accelerated by nucleophilic participation of neighboring phenyl in the displacement of the leaving group leading to a phenyl-bridged cationic intermediate. For example, despite the expected electron withdrawing and rate retarding inductive effect of the phenyl ring, neophyl *p*-toluenesulfonate (I, Y = H; X = OTs) at 50 °C acetolyzes 460 times faster than neopentyl *p*-toluenesulfonate.[1] Further, substituents in the phenyl ring have marked effects on the solvolysis rate, e.g., the acceleration of acetolysis at 50 °C with *p*-methoxy relative to the unsubstituted compound is a factor of 122.[2] Because these and other results conclusively demonstrate that for these compounds solvolysis proceeds via participation in the rate determining ionization, we have measured α-deuterium (α-d) effects on the rates of solvolysis of some substituted neophyl esters in order to establish unambiguously what influence participation has on the α-d rate effect and to probe the variation of transition state structure with changes in substituent, solvent, and leaving group.




I

Table I. Solvolysis Rates and α-d Rate Effects for Neophyl Esters, 25 °C[a]

| Ring substituent | Leaving group[b] | $k_H$, $10^{-5}$ s$^{-1}$ | | | $k_H/k_{\alpha\text{-D}}$ per D[c] | | |
|---|---|---|---|---|---|---|---|
| | | 97T | 70T | 48E | 97T | 70T | 48E |
| *p*-MeO | OMs | 34.46 | 29.15 | 10.67 | 1.113 | 1.117 | 1.119 |
| *p*-Me | OMs | | 4.451 | | | 1.120 | |
| None | OMs | | 0.3965 | | | 1.128 | |
| None | OTr | 45.16 | 40.90 | 7.548 | 1.128 | 1.134 | 1.134 |
| *m*-$CF_3$ | OTr | | 0.2346 | | | 1.099 | |

[a] Rates were measured conductometrically;[13] standard error is 0.1% in the isotope effect. [b] OMs is methanesulfonate, OTr is 2,2,2-trifluoroethanesulfonate. 97T is 97 wt % 2,2,2-trifluoroethanol–3 wt % water, 70T is 70 wt % 2,2,2-trifluoroethanol–30 wt % water, 48E is 48 vol % ethanol–52 vol % water. [c] Isotope effect per α-d atom; the square root of the ratio of the rate constant for solvolysis of the undeuterated compound divided by the rate constant for the α-d analogue prepared via $LiAlD_4$ reduction of the corresponding carboxylic acid.

In order to measure the isotope effects as accurately as possible with the conductometric method, we have used principally aqueous ethanolic and trifluoroethanolic solvent mixtures at 25 °C with both methanesulfonate and trifluoroethanesulfonate leaving groups to obtain convenient reactivity and to assess the effect of leaving group change in the reaction. These results are shown in Table I.

Ando and co-workers[4] have measured α-$^{14}$C, β-$^{14}$C, and phenyl-*1*-$^{14}$*C* effects for acetolysis and trifluoroacetolysis of neophyl *p*-bromobenzenesulfonate and have concluded that the results are consistent with participation. In particular, modest phenyl-*1*-$^{14}$*C* effects (2.34% in HOAc) and medium-sized α-$^{14}$C (9.31% in HOAc) indicate an involvement of the two atoms similar to that expected in an SN2 reaction.[5]

First, the α-d effects are all below 1.135 and thus significantly less than the value of 1.15–1.16 shown by 3,3-dimethyl-2-butyl sulfonates in a wide variety of solvents and which we associate with rate determining unassisted ionization.[6] Therefore phenyl participation, as expected, lowers the α-d effect because bonding of the phenyl ring to the α-carbon partially compensates for the reduction in α-CH bending force caused by ionization of the leaving group.

In order to show that the α-d effects in the neophyl ester

Table II. Solvolysis Rates and α-d Isotope Effects in 98% Trifluoroacetic Acid–2% Water, 25 °C

| Compound[a] | $k$, $10^{-5}$ $s^{-1}$ [b] | $k_H/k_{\alpha\text{-D}}$ per D |
|---|---|---|
| $PhC(CH_3)_2CH_2OBs$ | 172 ± 1 | |
| $PhC(CH_3)_2CD_2OBs$ | 135 ± 1 | 1.129 ± 0.008 |
| $PhCH_2\underset{\underset{OTs}{\vert}}{C}HCH_3$ | 48.2 ± 0.1 | |
| $PhCH_2\underset{\underset{OTs}{\vert}}{C}DCH_3$ | 42.5 ± 0.3 | 1.134 ± 0.01 |

[a] OBs is *p*-bromobenzenesulfonate; OTs is *p*-toluenesulfonate; Ph is phenyl. [b] Rates were determined spectrophotometrically; uncertainties are differences between duplicate rate measurements.

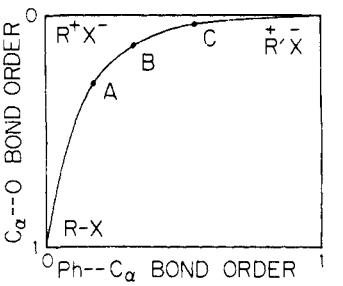



**Figure 1.** Schematic representation of bond order changes during ionization with phenyl participation. (R is neophyl; R′⁺ is the phenonium ion.)

solvolyses are lower than those for the 3,3-dimethyl-2-butyl ester solvolyses because of phenyl participation and not because the α-d effects are somehow smaller for primary than for secondary compounds, we have determined the α-d effects in trifluoroacetolysis for 1-phenyl-2-propyl tosylate (II) and for neophyl brosylate shown in Table II; the effects, 1.134 and 1.129, respectively, are comparable and both are below the value (1.15)[7] for the 3,3-dimethyl-2-butyl ester. Nordlander and Kelly[8] have shown that the trifluoroacetolysis of II is accelerated relative to 2-propyl *p*-toluenesulfonate by a factor of 17.1 despite the electron withdrawing inductive effect of the phenyl group and, to further strengthen the case for phenyl participation, they showed that the trifluoroacetate ester product had fully retained configuration.

The substituted neophyl compounds show a spread of α-d values which can be correlated with transition state structure and reactivity. As will be apparent later in the discussion, because of the fact that two transition state partial bonds, $C_\alpha$···O and Ph···$C_\alpha$, are subject to the influence of substituents, the simple Hammond postulate[9] does not adequately correlate the isotope effect results. For example, both the faster reacting *p*-MeO derivative and the slower reacting *m*-$CF_3$ derivative show α-d effects *smaller* than those of the corresponding parent esters.

The results *can* be rationalized through the use of the energy contour diagrams of O'Ferrall[10] and Jencks.[11] These are analogues of the usual potential energy diagrams but allow two different bond changes to be represented on the two in-plane axes while energy is represented in the third dimension by contours. The diagram can be simplified by eliminating the contours and representing only the path of least energy, or reaction pathway, by a single line; the energy is assumed to increase at all points in either direction normal to the line.[12] Thus in the figure the Ph···$C_\alpha$ bond order is represented on the horizontal axis and the $C_\alpha$···O bond order on the vertical axis. The reactant is represented at the lower left-hand corner, the unrearranged carbonium ion pair at the upper left, the bridged ion pair at the upper right, and the highly unstable pentacoordinate species with $C_\alpha$ bonded to both O and phenyl at the lower right. A precisely concerted reaction pathway would be represented by a diagonal line connecting the lower left corner to the upper right corner; at all points along the diagonal the sum of $C_\alpha$···O and Ph···$C_\alpha$ is equal to one. Because of the tetracovalent nature of carbon it is assumed that Ph···$C_\alpha$ bond formation cannot run ahead of $C_\alpha$···O bond breaking and that the lower right-hand diagonal half of the diagram is inaccessibly high in energy. Thus participation reaction pathways must lie between the concerted diagonal and the stepwise route up the left-hand border and across the top. This requires that early in the reaction C-O bond breaking runs ahead of Ph-C bond formation and that later in the reaction Ph-C bond formation "catches up". Therefore an electron attracting group which acts to increase the energy of the bridged ion moves a moderately late transition state (e.g., point B) to a later point along the reaction coordinate (e.g., point C) and may increase Ph···$C_\alpha$ bond formation more than it increases $C_\alpha$···O bond breakage; the net effect is an increase in bond order around $C_\alpha$ relative to the transition state for the unsubstituted compound and a smaller isotope effect. Thus in 70T the *m*-$CF_3$ neophyl trifluoroethanesulfonate shows an α-d effect of 1.099, considerably smaller than the value for the unsubstituted compound, 1.134. On the other hand, electron releasing groups would move the transition state along the reaction pathway back toward starting material (e.g., point A). In this direction the slope increases so the $C_\alpha$···O bond order may increase more than Ph···$C_\alpha$ bond order decreases. Thus, in 70T the effect for *p*-methoxyneophyl mesylate (1.117) is smaller than that for the corresponding *p*-methyl ester (1.120) which in turn is smaller than the value for the unsubstituted methanesulfonate, 1.128. The effect of substituents in moving the transition state *perpendicular* to the reaction coordinate is expected to be much less since substituents have little influence on the stability of the unbridged cation or on the contour heights in the upper left-hand part of the diagram. However, a better *leaving group* would be expected to lower the energies of both unbridged *and* bridged ion pairs and move the reaction coordinate line toward the *top* of the diagram, increasing $C_\alpha$···O bond breakage more than it decreases Ph···$C_\alpha$ bond formation. Thus neophyl trifluoroethanesulfonate shows a larger isotope effect (1.134) than the methanesulfonate ester (1.128). We note that solvolysis rates increase in the order 48E, 70T, and 97T. We believe that in this order the ability to solvate the delocalized, bridged carbonium ion pair increases while the ability to solvate the localized ion pair decreases. (The Y values, based on *tert*-butyl chloride solvolysis rates, and reflective of solvating ability for a localized carbonium ion-counter-ion pair, are: 97T, 1.148; 70T, 1.659; 48E, 1.76.)[13] Thus in 97T the upper right-hand energy contours are lower than in 70T or 48E, the transition state is moved back as with a *p*-$CH_3$ substituent and the effect is lower; e.g., 1.128 (97T) vs. 1.134 (70T, 48E) for neophyl trifluoroethanesulfonate. A similar trend shows for the *p*-methoxyneophyl methanesulfonate isotope effects in 97T, 70T, and 48E.

Thus we have demonstrated that α-d effects are lower in these reactions where phenyl participation occurs than in reactions where we have concluded that participation is absent. Further, we have demonstrated a remarkable consistency in the ability of the O'Ferrall-Jencks contour diagrams to rationalize variations in transition state structure, as signaled by changes in the α-d rate effects, with substituent. This provides another demonstration of the power and sensitivity of isotope effects as probes of transition state structure.

**Acknowledgment.** We are pleased to acknowledge the support of this work by the National Science Foundation Grant GP 32854.

## References and Notes


(1) S. Winstein, B. K. Morse, E. Grunwald, K. C. Schreiber, and J. Corse, *J. Am. Chem. Soc.*, **74**, 1113 (1952).
(2) S. Winstein and R. Heck, *J. Am. Chem. Soc.*, **78**, 4801 (1956).
(3) R. Heck and S. Winstein, *J. Am. Chem. Soc.*, **79**, 3432 (1957).
(4) H. Yamataka, S.-G. Kim, T. Ando, and Y. Yukawa, *Tetrahedron Lett.*, 4767 (1973).
(5) A. Fry in "Isotope Effects in Chemical Reactions", C. J. Collins and N. S. Bowman, Ed., Van Nostrand Reinhold, New York, N.Y., 1971, Chapter 6, pp 377–386.
(6) V. J. Shiner, Jr., R. D. Fisher, and W. Dowd, *J. Am. Chem. Soc.*, **91**, 7748 (1969).
(7) V. J. Shiner, Jr. and R. C. Seib, unpublished results.
(8) J. E. Nordlander and W. J. Kelly, *J. Am. Chem. Soc.*, **91**, 996 (1969).
(9) G. S. Hammond, *J. Am. Chem. Soc.*, **77**, 334 (1955).
(10) M. O'Ferrall, *J. Chem. Soc. B*, 274 (1970).
(11) W. P. Jencks, *Chem. Rev.*, **72**, 705 (1972).
(12) See, for example, D. A. Winey and E. R. Thornton, *J. Am. Chem. Soc.*, **97**, 3102 (1975).
(13) (a) V. J. Shiner, Jr., W. Dowd, R. D. Fisher, S. R. Hartshorn, M. A. Kessick, L. Milakovsky, and M. W. Rapp, *J. Am. Chem. Soc.*, **91**, 4838 (1969). (b) The Y value for 48E was interpolated from data in A. H. Fainberg and S. Winstein, *ibid.*, **78**, 2770 (1956).



**V. J. Shiner, Jr.,* R. C. Seib**

*Department of Chemistry, Indiana University*
*Bloomington, Indiana 47401*


*Received October 6, 1975*

## Preferred Base Sites of Actinomycin–Deoxyribonucleic Acid Bindings by Circular Dichroism

*Sir:*

Actinomycin D is a highly active chromopeptide antibiotic. Because of its antineoplastic properties it has aroused great interest leading to intensive studies during the past 30 years.[1] The drug forms a complex with DNA whereby its planar phenoxazinone moiety intercalates between two successive base pairs and its two cyclopentapeptides interact with adjacent nucleotides, inhibiting DNA dependent RNA synthesis and thus inhibiting protein synthesis. The DNA must be double-stranded, helical, and contain guanine residues, which are presumed to be directly adjacent to the intercalation site. The maximum ratio of bound actinomycin per nucleotide pair runs from 0 at 0% dG content to about 0.16 at 50% dG in poly(dGC:dGC) with relative constant stoichiometry of binding in the middle range (~25% dG) of base composition, suggesting the involvement of more than one base pair, one of which is G-C, at the intercalation site.[2]

While one of the base pairs adjacent to the chromophore must be a G-C pair there is uncertainty about the relative positions of the G-C pair and actinomycin as well as the preferred other neighboring base pair. Several studies have approached this problem by x-ray diffraction of an actinomycin-$dG_2$ complex,[5] by spectrophotometry of the complexes of actinomycin with several deoxydinucleotides (e.g., pGpC),[6] by $^1H$, $^{13}C$, and $^{31}P$ NMR of the complexes of actinomycin with several deoxynucleoside 5′-monophosphates,[7,8] and with several deoxydinucleotides[9,10] and by $^1H$ and $^{31}P$ NMR of the complex of actinomycin with the hexadeoxynucleotides d-ApTpGpCpApT and d-pGpC-pGpCpGpC.[11] The results seem to support an actinomycin–DNA model which was derived from the x-ray diffraction picture of the actinomycin-$dG_2$ complex.[5] In this model the planar phenoxazinone chromophore is intercalated between one GpC sequence on each side. While the supporting studies also allow for intercalation between other sequences GpN, the sequences CpN, specifically CpG, are not considered because of the restrictions imposed by the x-ray structure.

We have approached the problem by studying the interaction of actinomycin with DNA by circular dichroism.

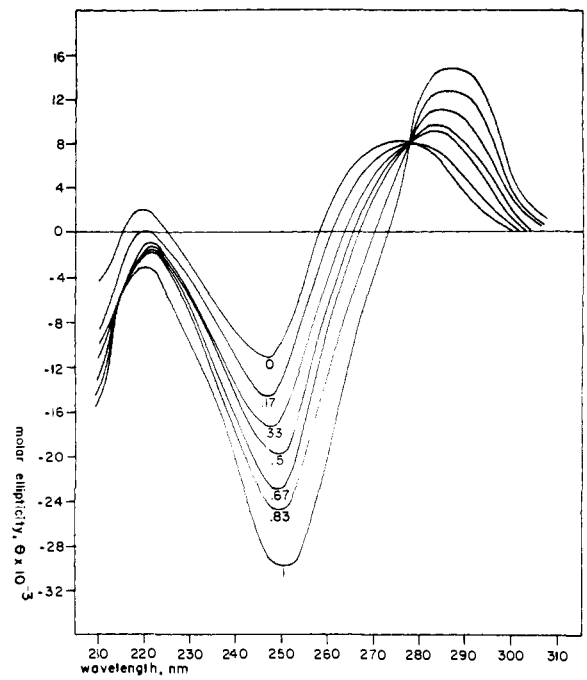



**Figure 1.** CD spectra of *E. aerogenes* DNA as a function of fraction actinomycin saturation.

Our method has the advantage that we employed the entire DNA molecule rather than mono-, di-, or hexadeoxynucleotides. We have applied a matrix analysis[12] to determine the contribution to the CD spectrum of a fully double stranded DNA from each of the first-neighbor units which comprise the polymer. There are eight independent first-neighbor units and, from the CD contributions of these, the effect on the CD spectrum of all 16 first-neighbor pairs can be determined. It is convenient to include two of the dependent first-neighbors with the set of eight independent units creating a set of ten semiindependent first-neighbors. A given spectral property for a DNA, $S_\lambda$, can then be represented as

$$S_\lambda = 2f_{AA}T_\lambda^{AA} + 2f_{AC}T_\lambda^{AC} + 2f_{AG}T_\lambda^{AG} + f_{TA}T_\lambda^{TA} + 2f_{TC}T_\lambda^{TC} + 2f_{TG}T_\lambda^{TG} + 2f_{CC}T_\lambda^{CC} + f_{GC}T_\lambda^{GC} + f_{AT}T_\lambda^{AT} + f_{CG}T_\lambda^{CG} \quad (1)$$

where the $f_{ij}$ are the mole fractions of the $I_pJ$ first neighbors when reading in the 3′ → 5′ direction and the $T_\lambda^{ij}$ are the contributions to the spectral property from the $I_pJ$ first-neighbor unit at wavelength λ. Note that the nonself complementary fractions are doubled thus accounting for the complementary first-neighbors which are dependent. By measuring $S_\lambda$ for at least eight DNA's one can solve the equations of the form of eq 1 which result for the $T_\lambda^{ij}$. This is most conveniently done with matrices and the result is the $T$ matrix which gives the contribution to the spectral property from each first-neighbor unit at the wavelengths of interest. In matrix form we have

$$S = TF \quad (2)$$

where $S$ is a matrix with the measured spectra as column vectors, $T$ is as described, and $F$ is a matrix of DNA first-neighbor frequency information.

The spectral property of interest in our work is the molar ellipticity. From this property and the above analysis we have been able to follow the binding of actinomycin D and to determine which first neighbors are favorable and unfavorable binding sites.

We have measured the CD spectra for 11 DNA's (calf thymus, *E. coli*, *E. aerogenes*, coliphage T4, *H. influenza*, poly[dAAC:dGTT], poly[dAAT:dATT], poly[dACT: