J. Am. Chem. Soc. 1992, 114, 6575–6576


(a) (b)

Figure 1. Plots of $-\nabla^2\rho$ in the E–M–L plane of the assumed transition states in the $Ta(CO)_6$ + CO (a) and $W(CO)_6$ + CO (b) carbonyl exchange reactions. ρ is the valence-electron density.

and similar preexponential factors.

In Figure 1, we plot the Laplacian of the valence-electron density, i.e., $-\nabla^2\rho$,[11] on the yz plane (i.e., E–M–L plane) from the ab initio calculations on these assumed transition states (**1**). In these plots solid lines show regions of local electron concentrations, while dotted lines show regions of local electron depletions. A significant difference in the valence-electron $-\nabla^2\rho$ plots is seen clearly in Figure 1. Two concentrations in the $+y$ and $-y$ directions, 180° apart, are observed for the 19-electron system ($Ta(CO)_7$, Figure 1a), while the 20-electron system ($W(CO)_7$, Figure 1b) gives four concentrations with an angle of about 109.5° between the two concentrations in the $+z$ direction (toward the entering/leaving ligands).

Although this difference seems large, its qualitative origin is easily understood through a simple scheme, where for a C_{2v} ML_7 (**1**) complex we consider the orbital interaction between a square-pyramidal ML_5 fragment and the two entering/leaving ligand σ orbitals in the yz plane. The d_{yz} orbital of the "t_{2g}" set of the ML_5 fragment is antibonding and the $d_{x^2-y^2}$ orbital is slightly antibonding. The electron density contributed by the d_{yz} and $d_{x^2-y^2}$ orbitals is of primary importance in comparing the two systems ($Ta(CO)_7$ and $W(CO)_7$) since for a 19-electron ML_7 system the d_{yz} orbital is singly occupied (Scheme Ia), while for a 20-electron ML_7 system it is doubly occupied (Scheme Ib). Scheme I illustrates how the single electron difference leads to a significant difference in the electron density between 19-electron and 20-electron systems.

In summary, the significant difference in the substitution reaction rates of 17-electron and 18-electron transition-metal carbonyl complexes is reflected in the significant difference in the valence-electron distributions of their transition states. This large difference was unanticipated through traditional valence-bond or molecular orbital concepts. In the substitution reaction of an 18-electron metal carbonyl complex, where the transition state corresponds to a 20-electron system, the valence-electron charge concentrations are located along the directions of metal–entering/leaving ligand bonds in the transition state. For a 19-electron system, the two maxima in the charge concentration are not directed toward the entering/leaving ligands. Therefore, a more stable transition state is observed for the substitution reaction of a 17-electron transition-metal complex.

Acknowledgment. We thank the National Science Foundation (Grant No. CHE 91-13634) and the Robert A. Welch Foundation (Grant No. A-648) for financial support and M. F. Guest for providing the GAMESS package of programs. This research was conducted in part with use of the Cornell National Supercomputer Facility, a resource for the Center for Theory and Simulation in Science and Engineering at Cornell University, which is funded in part by the National Science Foundation, New York State, and the IBM Corporation.

---

(11) (a) Bader, R. F. W.; MacDougall, P. J.; Lau, C. D. H. *J. Am. Chem. Soc.* **1984**, *106*, 1594. (b) Bader, R. F. W. *Acc. Chem. Res.* **1985**, *18*, 9. (c) MacDougall, P. J.; Bader, R. F. W. *Can. J. Chem.* **1986**, *64*, 1496.

Can Acyl Transfer Occur via a Concerted Mechanism? Direct Evidence from Heavy-Atom Isotope Effects

Alvan Hengge

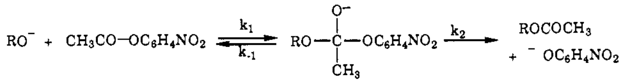
Institute for Enzyme Research
University of Wisconsin
Madison, Wisconsin 53705

Received March 27, 1992

Nucleophilic acyl-transfer reactions most often occur by way of a two-step mechanism with a tetrahedral intermediate, described in the IUPAC system[1] as $A_N + D_N$. Acyl halides can react through an acylium ion intermediate by an S_N1 ($D_N + A_N$) mechanism.[2] There has been interest in the question of whether ester acyl transfers can proceed by a concerted S_N2 (A_ND_N) pathway.[3] On the basis of structure–reactivity studies, Williams et al. proposed that the reaction of phenoxide anions with p-nitrophenyl acetate proceeds by such a concerted pathway,[4a] and they proposed a theory predicting when ester acyl transfers will be concerted and when they will go by the limiting stepwise mechanisms.[5] These conclusions have been challenged.[6] Recently, theoretical arguments have been presented in support of a concerted mechanism in reactions of aryl acetates with phenoxide anions.[7]

We have shown that in displacement reactions where p-nitrophenol is the leaving group the degree of transition-state bond cleavage is reflected in a measurable ^{15}N isotope effect.[8] The isotope effect arises from bonding changes that occur in the nitro group as a result of the delocalization of charge arising from partial cleavage of the bond to p-nitrophenol in the transition state. Because the ^{15}N isotope effect is a secondary one and reaction coordinate motion does not make a contribution, it is a better measurement of transition-state bond cleavage than the primary phenolic oxygen isotope effect. The utility of this method for examining transition-state structure was demonstrated in a study of the hydrolysis reactions of phosphate esters of p-nitrophenol.[8]

This technique offers a direct means for distinguishing a concerted mechanism from a tetrahedral one for acyl-transfer reactions with p-nitrophenyl acetate. In the tetrahedral mechanism shown here, where the pK_a of the nucleophile is higher than that of the leaving group, nucleophilic attack will be rate-limiting and the intermediate will partition completely forward to products. Only the first step of this process can show isotope effects since it is rate-limiting, and no ^{15}N isotope effect is expected in this step since the bond to the leaving group is scarcely affected. Therefore, this mechanism predicts no significant ^{15}N isotope effect. A concerted mechanism on the other hand will exhibit an isotope effect corresponding to the degree of transition-state cleavage of the bond to the p-nitrophenol leaving group.



$$RO^- + CH_3CO{-}OC_6H_4NO_2 \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} RO{-}\underset{CH_3}{\overset{O^-}{C}}{-}OC_6H_4NO_2 \xrightarrow{k_2} \begin{matrix} ROCOCH_3 \\ + {}^-OC_6H_4NO_2 \end{matrix}$$

---

(1) Guthrie, R. D.; Jencks, W. P. *Acc. Chem. Res.* **1991**, *22*, 343–349. Guthrie, R. D. *Pure Appl. Chem.* **1989**, *61*, 23–56.

(2) Williams, A.; Douglas, K. T. *Chem. Rev.* **1975**, *75*, 627. Jencks, W. P. *Chem. Soc. Rev.* **1981**, *10*, 345. Song, B. D.; Jencks, W. P. *J. Am. Chem. Soc.* **1987**, *109*, 3160. Song, B. D.; Jencks, W. P. *J. Am. Chem. Soc.* **1989**, *111*, 8470–8479.

(3) Curran, T. C.; Farrar, C. R.; Niazy, O.; Williams, A. *J. Am. Chem. Soc.* **1980**, *102*, 6828–6837. Luthra, A. K.; Ba-Saif, S.; Chyrstiuk, E.; Williams, A. *Bull. Soc. Chim. Fr.* **1988**, 391. Jencks, W. P.; Gilchrist, M. *J. Am. Chem. Soc.* **1968**, *90*, 2622–2637. Fersht, A. R.; Jencks, W. P. *J. Am. Chem. Soc.* **1970**, *92*, 5442. Hupe, D. J.; Jencks, W. P. *J. Am. Chem. Soc.* **1977**, *99*, 451–464.

(4) (a) Ba-Saif, S.; Luthra, A. K.; Williams, A. *J. Am. Chem. Soc.* **1987**, *109*, 6362–6368. (b) Ba-Saif, S.; Colthurst, M.; Waring, M. A.; Williams, A. *J. Chem. Soc., Perkin Trans. 2* **1991**, 1901–1908.

(5) Ba-Saif, S.; Luthra, A. K.; Williams, A. *J. Am. Chem. Soc.* **1989**, *111*, 2647–2652.

(6) Buncel, E.; Um, I. H.; Hoz, S. *J. Am. Chem. Soc.* **1989**, *111*, 971–975. Suh, J.; Heo, J. S. *J. Org. Chem.* **1990**, *55*, 5531–5532. Kwon, D. S.; Lee, G. J.; Um, I. H. *Bull. Korean Chem. Soc.* **1990**, *11*, 262.

(7) Guthrie, J. P. *J. Am. Chem. Soc.* **1991**, *113*, 3941–3949.

(8) Hengge, A. C.; Cleland, W. W. *J. Am. Chem. Soc.* **1990**, *112*, 7421–7422.

0002-7863/92/1514-6575$03.00/0

Table I. Isotope Effect Results

reaction	$^{14}k/^{15}k$
acyl transfer to hydroxide[a]	1.0002 ± 0.0001[c]
acyl transfer to phenolate[b]	1.0010 ± 0.0002

[a] 2 mM *p*-nitrophenyl acetate, 100 mM CHES buffer (pH 9.0), 23 °C; $t_{1/2} \approx 2.5$ h. The rate of reaction was independent of buffer concentration, and this pH is well within the range where solvolysis is known to be solely catalyzed by hydroxide.[11] [b] 1.5 mM *p*-nitrophenyl acetate, 15 mM phenol, 50 mM CHES buffer (pH 9.5), 5 °C; $t_{1/2} \approx 8$ min. This reaction was approximately 25-fold faster than that with hydroxide at the same pH and temperature, and the rate varied in a linear fashion with added phenol. [c] Errors reported are the standard errors.

Prior experimental evidence in favor of the concerted process comes from reactions of aryl esters with phenoxide nucleophiles.[4] Recent theoretical arguments concur and also conclude that the reaction of hydroxide with aryl acetates should have no intermediate of significant lifetime.[7] The ^{15}N isotope effects have been measured for the acyl-transfer reactions of *p*-nitrophenyl acetate with hydroxide and with phenolate under the conditions given in Table I. The pK_a values of both these nucleophiles satisfy the requirement that nucleophilic attack, coupled or not with leaving group displacement, occurs at the rate-limiting step.

The small and possibly insignificant isotope effect on the hydroxide reaction is consistent with a tetrahedral mechanism, but it cannot rule out a concerted process where bond cleavage to the leaving group is only slightly advanced in the transition state. Due to the small magnitude of the ^{15}N isotope effects, this method is not sensitive enough to measure changes in bond order smaller than about 15%.

The isotope effect for the phenolate reaction indicates that the bond to the leaving group cleaves in the rate-limiting step, which is not consistent with a tetrahedral mechanism and favors the contention that this reaction follows a concerted A_ND_N displacement. This isotope effect is within the range of those found for the phosphoryl-transfer reactions of phosphate diesters and triesters of *p*-nitrophenol,[8] reactions known to occur by concerted nucleophilic displacement at phosphorus. Using the value of 1.0028 to represent a fully broken bond,[8] the acyl-transfer reaction with phenolate has a transition state with about 35% bond cleavage to the leaving group.

Comparison of the present data with those from studies of phosphoryl-transfer reactions indicates that, in terms of leaving group departure at the transition state, the reaction of *p*-nitrophenyl acetate with phenoxide most resembles phosphoryl-transfer reactions with neutral phosphate esters of *p*-nitrophenol. For these substrates (a triester or a protonated diester), transition-state bond cleavage was about 25-32%, whereas for anionic phosphodiesters of *p*-nitrophenol, transition-state bond cleavage was higher, about 55%.[8,9]

Further isotope effect studies are under way to better characterize the present reactions, particularly that with hydroxide, and to examine the nature of this acyl-transfer reaction with different nucleophiles. It will be of interest to determine whether the apparent concertedness of acyl-transfer reactions between phenoxides arises from their pK_a values or is due to some other characteristic specific to phenoxides.

Determination of Isotope Effects. Aqueous solutions of *p*-nitrophenyl acetate were made by prolonged stirring. The isotope effect reactions were run on 100-μmol samples of *p*-nitrophenyl acetate and allowed to run to about 50% completion. The *p*-nitrophenol product was separated from the residual starting material, and each was assayed to determine the exact fraction of reaction. The nitrogen from both was separately converted to N_2, and the isotopic composition was determined by an isotope ratio mass spectrometer, as previously described.[9] The isotopic composition of unreacted starting material was separately determined. Isotope effects were calculated from the isotope ratios of the unreacted starting material and the residual starting material after partial reaction and, independently, from those of the unreacted starting material and product.[10] Six separate isotope effect experiments were run, giving 12 independent measurements of each isotope effect.

Acknowledgment. This research was supported by a grant from the National Institutes of Health to W. W. Cleland (GM 18938).

---

(9) Hengge, A. C.; Cleland, W. W. *J. Am. Chem. Soc.* **1991**, *113*, 5835-5841.

(10) The equations used for the isotope effect calculations can be found in the following: O'Leary, M. H. *Methods Enzymol.* **1980**, *64*, 83.

(11) Bruice, T. C.; Mayahi, M. F. *J. Am. Chem. Soc.* **1960**, *82*, 3067-3071.

Color Benzyloxyl, Cumyloxyl Orange, and 4-Methoxycumyloxyl Blue. Unexpected Discovery That Arylcarbinyloxyl Radicals Have Strong Absorptions in the Visible[1]

David V. Avila,[2] J. Lusztyk,* and K. U. Ingold

Steacie Institute for Molecular Sciences
National Research Council of Canada
Ottawa, Ontario, Canada K1A 0R6

Received March 27, 1992

The pioneering application of nanosecond laser flash photolysis (LFP) to "real time" studies of *tert*-butoxyl chemistry by Small and Scaiano[3] in 1978 opened an exciting new era in free radical kinetics. Because the *tert*-butoxyl radical had no absorption band in the visible and showed only a weak "tail-end" absorption in the near UV[4] (see Figure 1A), Small and Scaiano developed a competitive kinetic "probe" technique to monitor the evolution in time of the *tert*-butoxyl concentration as this radical reacted with different substrates following the laser flash.[3,5] The probe chosen was a compound that, on reaction with *tert*-butoxyl, yielded a radical with a strong and characteristic absorption in the visible, e.g., diphenylmethanol which yields $(C_6H_5)_2\dot{C}OH$, $\lambda_{max} = 545$ nm.[6,7] In subsequent LFP kinetic studies on other alkoxyls,[8-10] including benzyloxyl[9] and cumyloxyl,[10] it appears to have been implicitly assumed that these radicals have the same UV-visible spectral characteristics as *tert*-butoxyl. This assumption is incorrect. Benzyloxyl, cumyloxyl, and *p*-methoxycumyloxyl exhibit strong, broad absorptions in the visible with $\lambda_{max} = 460$, 485, and 590 nm, respectively (see Figure 1).

Cumyloxyl radicals were generated at room temperature by direct 308-nm and (where solvent permitted) 266-nm LFP of dicumyl peroxide[11] and by direct 266-nm LFP and xanthone triplet ($E_t = 74.1$ kcal/mol, $\lambda_{max} = 630$ nm) photosensitized 355-nm LFP of dicumyl hyponitrite.[11] The visible and UV absorptions were observed to grow-in "instantaneously" in CCl_4, CH_3CN, CH_3CO_2H, $(CH_3)_3COH$, c-C_6H_{12}, C_6H_6, and C_6H_5Cl, with no significant shift in the visible absorption maximum from 485 nm over this range of solvents. Of course, the rates of cumyloxyl radical decay do depend on the solvent. However, in all cases, the rates

---

(1) Issued as NRCC No. 33300.

(2) Summit Postdoctoral Fellow, 1990-1991.

(3) Small, R. D., Jr.; Scaiano, J. C. *J. Am. Chem. Soc.* **1978**, *100*, 296-298.

(4) Chatgilialoglu, C.; Ingold, K. U.; Scaiano, J. C.; Woynar, H. *J. Am. Chem. Soc.* **1981**, *103*, 3231-3232.

(5) Paul, H.; Small, R. D., Jr.; Scaiano, J. C. *J. Am. Chem. Soc.* **1978**, *100*, 4520-4527.

(6) Land, E. J. *Proc. R. Soc. London Ser. A* **1968**, *305*, 457-471.

(7) Das, P. K.; Encinas, M. V.; Steenken, S.; Scaiano, J. C. *J. Am. Chem. Soc.* **1981**, *103*, 4162-4166.

(8) Druliner, J. D.; Krusic, P. J.; Lehr, G. F.; Tolman, C. A. *J. Org. Chem.* **1985**, *50*, 5838-5845.

(9) Mendenhall, G. D.; Stewart, L. C.; Scaiano, J. C. *J. Am. Chem. Soc.* **1982**, *104*, 5109-5114. Note the precautionary statement in the experimental section.

(10) Baignée, A.; Howard, J. A.; Scaiano, J. C.; Stewart, L. C. *J. Am. Chem. Soc.* **1983**, *105*, 6120-6123.

(11) Purified by triple crystallizations from methanol.

0002-7863/92/1514-6576$03.00/0