energy of activation for N-fluoro-N-methylformamide is in harmony with this conclusion.[7]

The dependence of the rotational barrier on the nature of the aromatic substituent can be contrasted with the analogous relationship for the inversion process in amines. Electron-releasing substituents also increase the barrier to inversion in arylaziridines, but $\Delta G^{\ddagger}$ is more strongly influenced by the substituent (slope $(\Delta G^{\ddagger}$ $vs.$ $\sigma^-) = -2.8$ at $-60°$).[8]

The data of Table I also reveal that the values of $\Delta G^{\ddagger}$ do not vary significantly with the size of the N-alkyl group. The same result has been reported for N,N-dialkylformamides.[9] Therefore, if the activation energies do parallel the free energies of activation and if an increase in size of the alkyl group does indeed result in a greater destabilization of the ground state, this barrier-lowering steric effect must be compensated for by a barrier-increasing electronic effect.

Acknowledgment. The authors are indebted to the Camille and Henry Dreyfus Foundation for partial support of this work.

(7) J. Cantacuzene, J. Leroy, R. Jantzen, and F. Dudragne, *J. Amer. Chem. Soc.*, **94**, 7924 (1972).
(8) J. D. Andose, J.-M. Lehn, K. Mislow, and J. Wagner, *J. Amer. Chem. Soc.*, **92**, 4050 (1970).
(9) T. H. Siddall, III, W. E. Stewart, and F. D. Knight, *J. Phys. Chem.*, **74**, 3580 (1970).

Claude H. Yoder,* James A. Sandberg, William S. Moore
Department of Chemistry, Franklin and Marshall College
Lancaster, Pennsylvania 17604

A Proposed Mechanism for the Base Catalyzed Protonation of the e_{aq}^- Adduct to Acrylate

Sir:

A recent letter[1] has reported data on the e_{aq}^- adduct to acrylate which the authors interpret as showing a *base catalyzed protonation* on carbon of the dianion radical to give the radical $CH_3\dot{C}HCO_2^-$. No mechanism for this unusual catalysis was proposed. In the course of esr studies of the anion radicals derived from the reaction of e_{aq}^- with fumarate, it was found[2] that the fully dissociated form $[^-O_2CCH=CHCO_2^-]^{\cdot -}$ reacted slowly with water (millisecond time scale) to give a radical protonated on carbon ($^-O_2CCH_2\dot{C}HCO_2^-$) while the form $[^-O_2CCH=CHCO_2H]^{\cdot -}$ reacted at a significantly slower rate. A greater reactivity of the more highly charged species should carry over to the acrylate system, and consequently we would like to suggest an alternative interpretation of that data[1] as well as a mechanism for the base catalysis.

We propose that the equilibrium for the second dissociation

$$OH^- + [CH_2=CHCO_2H]^{\cdot -} \rightleftharpoons [CH_2=CHCO_2^-]^{\cdot -} + H_2O \quad (1)$$

corresponds to a pK_a of above 11 and that the value of 7.0 determined for this system corresponds to the first dissociation

$$CH_2=CH\dot{C}(OH)_2 \rightleftharpoons [CH_2=CHCO_2H]^{\cdot -} + H^+ \quad (2)$$
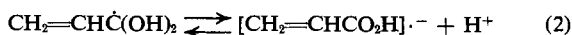
(1) E. Hayon, N. N. Lichtin, and V. Madhavan, *J. Amer. Chem. Soc.*, **95**, 4762 (1973).
(2) O. P. Chawla and R. W. Fessenden, *J. Phys. Chem.*, to be submitted for publication.

rather than the second as stated.[1] The immediate appearance of $CH_3\dot{C}HCO_2^-$ at pH 12 ($k > 7 \times 10^6$ sec^{-1})[3] means that, in this scheme, the dianion radical $[CH_2=CHCO_2^-]^{\cdot -}$ must protonate on carbon at this rate. The rate at lower pH values is reduced because of the shift of equilibrium 1 to the left and the fact that the form $[CH_2=CHCO_2H]^{\cdot -}$ protonates on carbon more slowly ($k = 7.7 \times 10^4$ sec^{-1}).[1] It is the protonation of this latter form which is catalyzed by OH^- by a shift of equilibrium 1.

The state of dissociation of the e_{aq}^- adduct to acrylate can readily be checked by pulse conductivity measurements as was done for the adducts to fumarate and maleate.[4] If the e_{aq}^- adduct remains fully dissociated at pH 8-11 as originally suggested,[1] then the net conductivity change will involve conversion of $CH_2=CHCO_2^-$ to $[CH_2=CHCO_2^-]^{\cdot -}$ and the removal of a corresponding amount of OH^- by the H^+ produced by the pulse.[5] Because the equivalent conductance of OH^- (192)[6] is considerably higher than that associated with organic ions (40–70), a decrease in equivalent conductance (per equivalent of e_{aq}^- produced) of 120–150 units will occur. If the radical reacts with water to give a protonated form (either $[CH_2=CHCO_2H]^{\cdot -}$ or $CH_3\dot{C}H$-CO_2^-) then the OH^- is regenerated and the conductance will return to a value near that before the irradiation.

An ac conductivity method is necessary because the starting material is an electrolyte. Experiments were carried out using the 10-MHz conductivity apparatus previously described,[4] and the transient signal on the oscilloscope was photographed.[7] Radiolysis was with 2.8 MeV electrons and the dose was monitored with a secondary emission chamber. Sensitivity of the conductivity detector was calibrated by use of a slightly acid (pH $\sim$5) solution of saturated CH_3Cl containing 0.1 M *tert*-butyl alcohol.[8] The initial experiment used 0.5×10^{-3} M acrylic acid (Eastman Chemical Co.) neutralized to pH 9.3 with KOH and containing 0.1 M *tert*-butyl alcohol to scavenge OH. An experimental trace with this solution is shown in Figure 1a. The initial decrease in conductance (3 mm) measured at 3 μsec after the pulse[9] corresponds to a value of about 15–20 units with no fast decay evident. This value is much less than that expected if the e_{aq}^- adduct were to exist as $[CH=CH$-$CO_2^-]^{\cdot -}$. The data presented by Hayon, *et al.*,[1] for the rate of protonation on carbon give a first-order rate

(3) Based on the stated time resolution of 0.1 μsec, the half-life for protonation to form $CH_3\dot{C}HCO_2^-$ must be >0.1 μsec for a first-order rate of >7 × 10^6 sec^{-1}.
(4) J. Lilie and R. W. Fessenden, *J. Phys. Chem.*, **77**, 674 (1973).
(5) Reaction of OH with *tert*-butyl alcohol does not produce any conducting species and therefore only the fate of e_{aq}^- and H$^+$ must be considered.
(6) Values of equivalent conductance given here are in units of Ω^{-1} cm equiv^{-1} and pertain to 25° as given in "Handbook of Chemistry and Physics," 45th ed, Chemical Rubber Publishing Co., Cleveland, Ohio, 1966, p D89.
(7) Previously the transient signal was digitized at a number of times, and the data were processed by computer. This approach has been abandoned *temporarily* because of equipment changes and the need to rewrite the program.
(8) For this solution, the conductivity change corresponds to production of H$^+$ + Cl$^-$ with an equivalent conductance of 426. The e_{aq}^- yield for a saturated CH_3Cl solution was taken as 3.12 as a result of corrections for spur scavenging. Other yields were also corrected for this effect: T. I. Balkas, J. H. Fendler, and R. H. Schuler, *J. Phys. Chem.*, **74**, 4497 (1970).
(9) Currently, the conductivity detection is gated off during the pulse, and for about 2 μsec after, to prevent recovery problems. The output of the detector becomes valid at about 3–3.5 μsec after the end of the pulse.
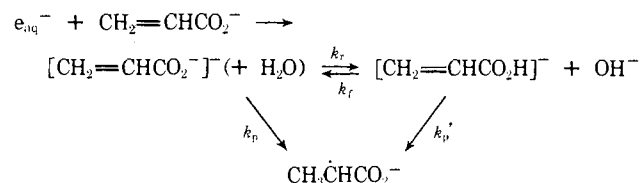
constant at pH 10 of 1.5×10^5 sec^{-1} or a half-life of 5 μsec. Below this pH the half-life increases to a maximum of 10 μsec. Thus at the time of the first valid data (3 μsec after the pulse) more than half of the initial conductance change should still be present. Similar curves were obtained at pH 9.9 and 10.9 with 1 mM acrylic acid.

The validity of the conductivity data can be demonstrated by an experiment on acrylamide. Hayon, et al.,[10] report the pK for

$$[CH_2=CH\dot{C}(OH)NH_2] \rightleftharpoons CH_2=CH\dot{C}(O^-)NH_2 + H^+$$
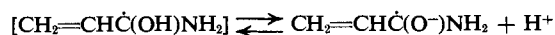
to be 7.9 and the rate constant for protonation on carbon of $CH_2CH\dot{C}(O^-)NH_2$ to be 1.5×10^5 sec^{-1} (half-life of 4.6 μsec). Again, because the e_{aq}^- adduct is dissociated above pH 9, there should be a large initial decrease in conductivity followed by a decay back to little or no overall change as the species $CH_3\dot{C}HCONH_2$ is produced. The experimental result shown in Figure 1b is in complete agreement with this expectation. The value at 3 μsec after the pulse corresponds to a conductance change of -60 units. A first-order plot of the points gave a reasonable straight line and allowed extrapolation to the end of the pulse. Average data for five curves gave an initial conductance change of -130 units and a half-life of 4.2 μsec ($k = 1.6 \times 10^5$ sec^{-1}). In this case the e_{aq}^- adduct is obviously dissociated and the rate of protonation agrees with previous data.[10]

The conductivity results on the acrylate system together with the qualitatively different behavior of acrylamide show clearly that the e_{aq}^- adduct in the former case initially takes up a proton to form $[CH_2=CHCO_2H]^-$. The complete reaction scheme for pH >8 can be written as

$$e_{aq}^- + CH_2=CHCO_2^- \longrightarrow$$

$$[CH_2=CHCO_2^-]^- (+ H_2O) \underset{k_f}{\overset{k_r}{\rightleftharpoons}} [CH_2=CHCO_2H]^- + OH^-$$

$$CH_3\dot{C}HCO_2^-$$

(with k_p and k_p' arrows)

A value for $k_p > 7 \times 10^6$ sec^{-1} can be derived from the immediate appearance of $CH_3\dot{C}HCO_2^-$ at pH 12;[1,3] the rate constant k_p' is given as 7.7×10^4 sec^{-1} by Hayon, et al.[1] The rate constant k_r for protonation on the carboxyl group must be larger than k_p because $[CH_2=CHCO_2H]^-$ is mainly produced at lower pH. Thus we can take $k_r > 7 \times 10^7$ sec^{-1} (i.e., ten times k_p). The rate constant k_f can reasonably be taken to be[11] 5×10^9 M^{-1} sec^{-1} so that, using k_f and k_r, the pK_a for dissociation of $[CH_2=CHCO_2H]^-$ can be estimated to be >12.1. A comparable value can be obtained by considering the linearity of the overall protonation rate with [OH$^-$] as given in Figure 1 of ref 1. With rate constants as given here, the dynamics of equilibrium 1 are such that the reaction corresponding to k_f will not be rate determining at any pH studied (pH <11.3[1]) and the equilibrium will be maintained. A pK near 12 makes the ion $[CH_2=CHCO_2H]^-$ rather similar to $[C_6H_5CO_2H]^-$ which has a pK of 12.0.[12] Parallel
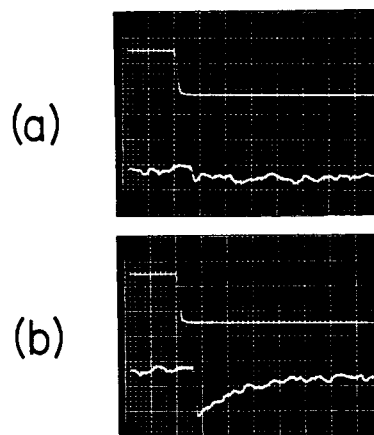

Figure 1. Oscilloscope traces showing the conductivity change following pulse irradiation of (a) 0.5 mM acrylic acid at pH 9.3 and (b) 1 mM acrylamide at pH 9.7. The step in the upper trace of each photograph gives the dose as monitored by a secondary emission chamber; the lower trace in each shows the conductivity change. The dose corresponds to about 1×10^{-5} M of total radicals. All traces have the same sweep rate, 5 μsec per large (cm) division, and start at the same time. The conductivity and dose curves have the same vertical sensitivities in both photographs. The conductivity curve becomes valid at about 3 μsec after the end of the pulse (i.e., at 2.8 cm).[9]

behavior for derivatives of ethylene and benzene is seen also in the pK values of $CH_2=CH\dot{C}(OH)NH_2$ (7.9)[10] and $C_6H_5\dot{C}(OH)NH_2$ (7.7).[13]

While the conductivity results suggest a simple mechanism for the catalysis of protonation by OH$^-$, the fact that equilibrium 1 is maintained during reaction rules out any similar mechanism for catalysis by other bases as was reported.[1] Although a shift of equilibrium 1 by high ionic strength would influence the protonation rate, some other process must probably be invoked to explain the increased rate in the presence of the various buffer species.

(13) E. Hayon, T. Ibata, N. N. Lichtin, and M. Simic, J. Phys. Chem., 76, 2072 (1972).

Richard W. Fessenden,* **Om P. Chawla**
Radiation Research Laboratories, Center for Special Studies and Department of Chemistry
Mellon Institute of Science, Carnegie-Mellon University
Pittsburgh, Pennsylvania 15213
Received December 7, 1973

Biosynthetic Incorporation of [1-^{13}C]Glucosamine and [6-^{13}C]Glucose into Neomycin[1,2]

Sir:

The biosynthesis of the commercially important antibiotic neomycin (B = 1, C = 2) has been studied for

(10) E. Hayon, N. N. Lichtin and V. Madhavan, Radiat. Res., 55, 989 (1973). Abstracts of 21st Annual Meeting of the Radiation Research Society, St. Louis, Mo., April 29, 1973.
(11) Values for some typical reaction rates of OH$^-$ with acids can be seen in M. Eigen, Angew. Chem., Int. Ed. Engl., 3, 1 (1964).
(12) M. Simic and M. P. Hoffman, J. Phys. Chem., 76, 1398 (1972).

(1) Presented in part at the 166th National Meeting of the American Chemical Society, Chicago, Ill., Aug 27–31, 1973; Abstract MEDI 069.
(2) Paper IV in the series "Carbon-13 as a Biosynthetic Tool" (Paper III: R. D. Johnson, A. Haber, B. I. Milavetz, and K. L. Rinehart, Jr., submitted for publication) and Paper XVIII in the series "Chemistry and Biochemistry of the Neomycins" (Paper XVII: W. T. Shier, S. Ogawa, M. Hichens, and K. L. Rinehart, Jr., J. Antibiot., 26, 551 (1973)).