Kinetics and mechanism of the base–catalyzed cleavage of 2-diazo-1,3-indandione and the acid– catalyzed decomposition of its hydrolysis product, 2-(diazoacetyl)benzoic acid

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Abstract

Rates of hydroxide–ion induced cleavage of 2-diazo-1,3-indandione were measured in aqueous (H_2O) sodium hydroxide solutions over the concentration range [NaOH] = 0.0004–0.1 M. The reaction was found to be first-order in hydroxide ion up to [NaOH] $\cong$ 0.01 M, but a second order term had to be added to account for the data in the region [NaOH] = 0.01–0.1 M. A mechanism is proposed involving hydroxide ion addition to one of the substrate carbonyl groups, and hydroxide–ion induced ionization of the O–H bond of this adduct in the more concentrated solutions, followed by C–C bond cleavage.

Rates of acid–catalyzed transformation of the product of this cleavage, 2-(diazoacetyl)benzoic acid, to 1,4-isochromandione were measured in aqueous (H_2O and D_2O) perchloric acid solutions over the concentration range [$LClO_4$] = 0.0001–0.1 M and in formic acid and acetic acid buffers. The isotope effects that these data provide suggest that the reaction occurs by rate–determining proton transfer from hydronium ion to the substrate diazo carbon in the more acidic region of the range examined, but that in the less acidic region the reaction mechanism switches to intramolecular general acid catalysis by the substrate's carboxylic acid group.

Keywords: 2-Diazo-1,3-indandione, hydroxide–ion induced ionization, 1,4-isochromandione, intramolecular acid catalysis, 2-(diazoacetyl)benzoic acid

Introduction

Some years ago Holt and Wall reported that dissolution of 2-diazo-1,3-indanedione **1** in dilute aqueous sodium hydroxide followed by acidification of the resulting solution, produced 1,4-

isochromandione **3**.[1] They then advanced the hypothesis that this transformation occurred by hydroxide ion induced cleavage of the diazoindanedione followed by acid–catalyzed de– diazotization and cyclization of the 2-(diazoacetyl)benzoic acid cleavage product **2** (eq 1). We have now substantiated this hypothesis by examining the kinetics of these transformations. Our work has also provided some insight into the mechanisms of the reactions involved.

(1)
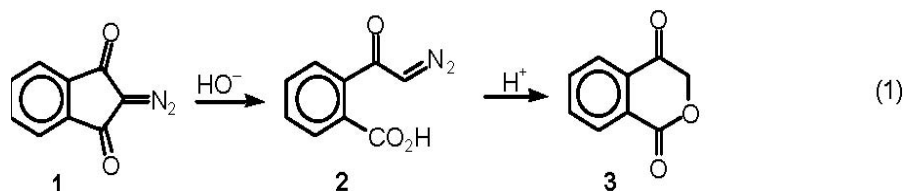
Experimental Section

Materials. 2-Diazo-1,3-indandione was prepared by diazo transfer from tosyl azide to 1,3-indanedione,[2] and 1,4-isochromandione was prepared from this diazo compound by treatment first with sodium hydroxide and then with sulfuric acid.[1] All other materials were best available commercial grades.

Kinetics. Rates of cleavage of 2-diazo-1,3-indanedione were measured spectrophotometrically by monitoring the decay of the absorbance of this substance at λ= 250 nm. The measurements were made using both conventional (Cary 2200) and stopped-flow (Hi-Tech Scientific SF–S1) spectrometers, and the temperature of all reacting solutions was controlled at 25.0 ± 0.05 °C. Substrate concentrations in the reacting solutions were of the order of 2 x 10^{-5} M. The data so obtained conformed to the first-order rate law well and observed first–order rate constants were determined by least squares fitting of an exponential function.

Rates of decomposition of 2-(diazoacetyl)benzoic acid were also measured spectrophotometrically using the Cary spectrometer operating at 25.0 ± 0.05 °C. A stock solution of this substrate was prepared by mixing equal volumes of 0.05 M 2-diazo-1,3-indanedione in acetonitrile and 0.06 M aqueous sodium hydroxide and then allowing the resulting mixture to stand at room temperature for a few minutes. Kinetic runs were initiated by adding 1 µL portions of this stock solution to 1.00 mL of acid or buffer contained in spectrometer cuvettes that had been allowed to reach temperature equilibrium with the spectrometer cell compartment. The kinetic data once again obeyed the first–order rate law well, and observed first–order rate constants were again determined by least squares fitting of an exponential function.

Results

2-Diazo-1,3-indandione. Rates of cleavage of 2-diazo-1,3-indandione were measured in aq. sodium hydroxide solution over the concentration range of [NaOH] = 0.0004 – 0.1 M. The ionic

strength of these solutions was maintained at 0.10 M through the addition of sodium perchlorate as required. The data so obtained are displayed in Figure 1.

Observed first–order cleavage rate constants were accurately proportional to sodium hydroxide concentration up to [NaOH] $\cong$ 0.01 M. At higher concentrations, however, observed rate constants increased somewhat more strongly than in direct proportion to the first power of [NaOH]. This is illustrated in Figure 1, whose broken line represents the relationship obtained by least squares fitting of a linear rate law using data only up to and including [NaOH] = 0.10 M: observed rate constants at the highest sodium hydroxide concentrations used clearly deviate from this expression.
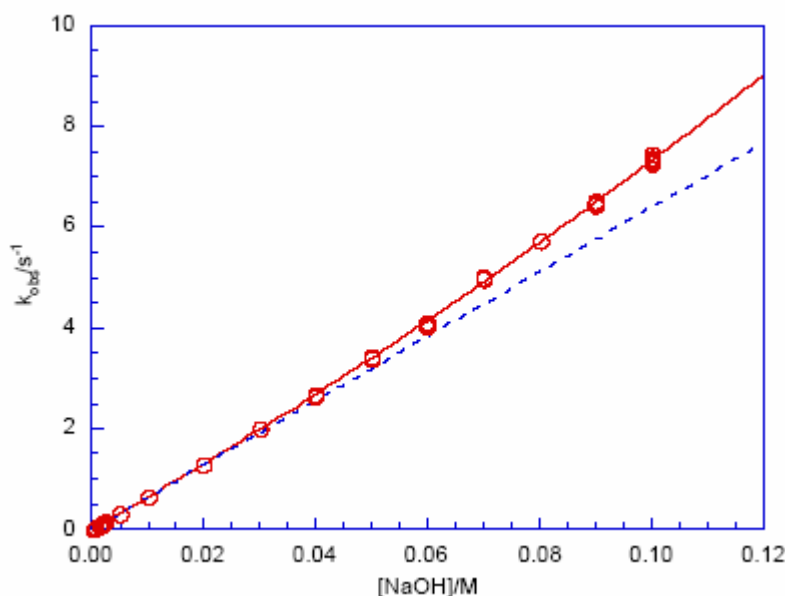

Figure 1 Rates of hydrolysis of 2-diazo-1,3-indandione in aqueous sodium hydroxide solution at 25 °C. The broken line is an extension of the relationship obtained by least squares fitting of a linear expression using data up to and including [NaOH] = 0.01 M.

Adding a term in sodium hydroxide concentration squared to this linear rate law, however, produced an expression, eq 2, that accounted for all of the data nicely. Least squares fitting gave the parameters, $k_o = -(9.67\pm6.85) \times 10^{-3}$ s^{-1}, $k_1 = (6.30\pm0.04) \times 10^{1}$ Ms^{-1}, and $k_2 = (1.04\pm0.05) \times 10^{2}$ M^{-2} s^{-1}, which were used to draw the solid line of Figure 1. It may be seen that the data conform to this rate law with good precision.

$$k_{obs} = k_o + k_1[NaOH] + k_2[NaOH]^2 \qquad (2)$$

2-(Diazoacetyl)benzoic Acid. Rates of hydrolysis of 2-(diazoacetyl)benzoic acid were measured in aqueous (H$_2$O) perchloric acid solutions over the concentration range [HClO$_4$] = 0.001 – 0.1 M and also in formic acid and acetic acid buffers. In addition, some measurements were also made in D$_2$O solutions of perchloric acid ([DclO$_4$] = 0.0001 – 0.1 M) and in D$_2$O solutions of

acetic acid buffers. The ionic strength of all of these solutions was maintained at 0.10 M by adding sodium perchlorate as required.

HPLC analysis of spent reaction mixtures verified that the product of these reactions was 1,4-isochromandione, **3**, as reported by Holt and Wall.[1]

The rate measurements in buffers were made using series of solutions of constant buffer ratio, and therefore constant hydronium ion concentration, but varying total buffer concentration. Observed first–order rate constants increased linearly with increasing buffer concentration, and the data were therefore analyzed by least squares fitting of the buffer dilution rate law shown in eq 3. The zero–buffer–concentration intercepts, k_{int} obtained in this way were then combined with the rate constants obtained in perchloric acid solution to construct the rate profiles shown in Figure 2.

$$k_{obs} = k_{int} + k_{cat}[\text{buffer}] \qquad (3)$$

Hydronium ion concentrations of the buffer solutions needed for this purpose were obtained by calculation, using literature pK_a values of the buffer acids and activity coefficients recommended by Bates.[3]
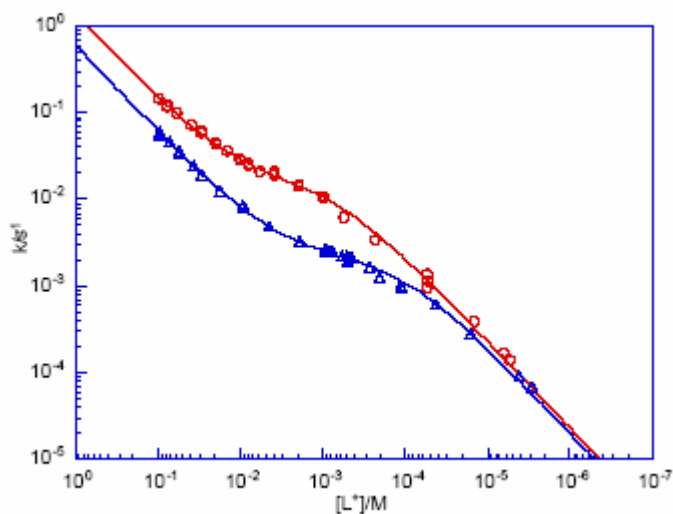

Figure 2 Rate profile for the hydrolysis of 2-(diazoacetyl)benzoic acid in H_2O (O) and D_2O (Δ) solutions at 25 °C.

These rate profiles show that observed first–order rate constants diminish steadily with decreasing solution acidity, indicating that the reaction under observation is an acid catalyzed process. The rate profiles, however, also show breaks near their centers. Such breaks are usually caused by the ionization of acidic or basic sites on the substrate, and the present substrate does have a carboxylic acid group, which would be expected to undergo ionization in the region of these breaks. A reaction scheme may consequently be formulated involving hydronium–ion–catalyzed reactions of the unionized and ionized forms of 2-(diazoacetyl)benzoic acid (eq 4).

The rate law that applies to this reaction scheme is shown in eq 5, whose rate and equilibrium constants are defined by eq 4. Analysis of the experimental data by least squares fitting of this expression gave, for H_2O solution: $k_H = (1.40 \pm 0.03)$ M^{-1} s^{-1}, $k'_H = (2.30 \pm 0.07)$ x 10^1 M^{-1} s^{-1}, and $(Q_a)_H = (7.44 \pm 0.40)$ x 10^{-4} M, $p(Q_a)_H = 3.13 \pm 0.02$,[5] and for D_2O solution: $k_D = (6.08 \pm 0.08)$ x 10^{-1} M^{-1} s, $k'_D = (1.97 \pm 0.08)$ x 10^1 M^{-1} s^{-1}, and $(Q_a)_D = (1.15 \pm 0.07)$ x 10^{-4} M, $p(Q_a)_D = 3.94 \pm 0.03$.[5] These parameters were used to draw the rate–profile lines shown in Figure 2. It may be seen that the data conform well to the reaction scheme (eq 4) and the rate law (eq 5).

$$(4)$$
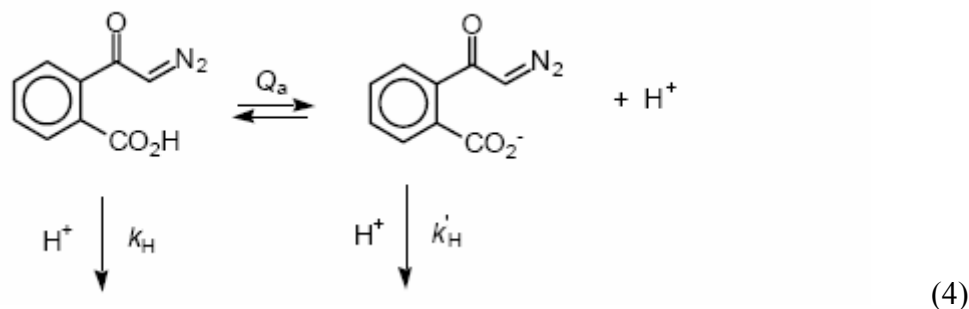
$$k_{obs} = (k_H[H^+]^2 + k'_H Q_a[H^+])/(Q_a + [H^+])$$

$$(5)$$

Discussion

2-Diazo-1,3-indandione. The alkaline acyl cleavage of 2-diazo-1,3-dicarbonyl compounds is a well known rection.[6] A reasonable mechanism for the process in aqueous solution involves addition of hydroxide ion to one of the carbonyl groups followed by cleavage of the bond between that group and the carbon atom bearing the diazo substituent; carbon-protonation of the acyl-diazo carbanion thus formed then completes the reaction (eq 6.)


$$(6)$$
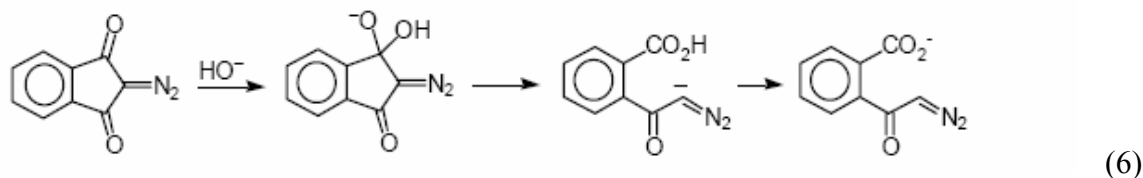
Such a reaction mechanism would give a rate law that is first–order in hydroxide ion, which is consistent with the fact that the rate constants determined here are proportional to the first power of hydroxide ion concentration up to $[HO^-] \cong 0.01$ M. However, our discovery that a term second order in hydroxide ion must be added to this rate law in order to account for data at $[HO^-] > 0.01$ M shows that there is also another parallel reaction which requires two hydroxide ions.

A plausible role for this second hydroxide ion is removal of the hydroxyl–group proton from

the first hydroxide ion adduct. This could occur in concert with carbon– carbon bond breaking, or it could occur in a prior step giving a full dianionic intermediate. Either way would increase the negative charge density adjacent to the carbon–carbon bond being cleaved, and that would raise the driving force for this reaction.

The present process is not unlike the Cannizzaro reaction, which also involves addition of hydroxide ion to a carbonyl group and in some cases requires a rate law that is second order in hydroxide ion.[7]

2–(Diazoacetyl)benzoic Acid. The acid-catalyzed decomposition of diazo compounds is a much–studied reaction known to occur by protonation of the substrate on its diazo carbon atom.[8] The present results indicate that this proton transfer is rate–determining for the reaction of 2-(diazoacetyl)benzoic acid in the high acidity region of the rate profile shown in Figure 2, which may be attributed to proton transfer from the hydronium ion to the unionized, carboxylic acid form of the substrate. This mechanistic assignment follows from the magnitude of the isotope effect on the reaction in this region: $k_H/k_D = 2.31 \pm 0.06$. Isotope effects on proton transfer from the hydronium ion contain a secondary component in the inverse direction ($k_H/k_D < 1$) that offsets the normal ($k_H/k_D > 1$) primary isotope effect component and reduces the magnitude of the overall effect.[9] The present determined value therefore, though of modest strength, nevertheless contains a substantial primary component,[10] suggesting that this proton transfer is the rate–determining step of the reaction. A mechanism may therefore be formulated in which rate–determining proton transfer is followed by rapid displacement of nitrogen from the diazonium ion thus formed to give the final 1,4-isochromandione product (eq 7.).

$$(7)$$
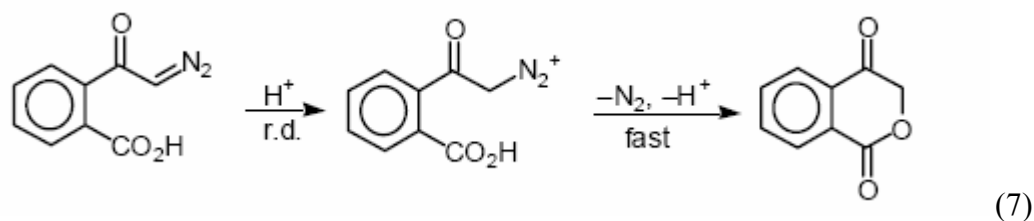
The rate profile of Figure 2 shows that the acid–catalyzed reaction of 2-(diazoacetyl)benzoic acid in the low acidity region of the range investigated, where the substrate is in its ionized carboxylate form, is faster than expected on the basis of a simple linear extension of the high acidity relationship. This rate acceleration could be caused by a stabilizing electrostatic interaction between the negatively charged carboxylate group and the positive charge being generated on the substrate in the transition state of a process that is essentially the same as that operating in the high acidity region of the rate profile. Alternatively, the acceleration could be due to incursion of a completely different reaction mechanism involving intramolecular general acid catalysis by the substrate's carboxylic acid group; intramolecular reactions are generally more favorable than their intermolecular counterparts.[11]

A choice between these two alternative explanations may be made on the basis of the solvent isotope effect determined in the low acidity region. This isotope effect, $k'_H/k'_D = 1.17 \pm 0.06$, is

weak, much weaker than that, $k_H/k_D = 2.31$, determined in the high acidity region. This isotope effect difference seems to be too great to be produced by what is a rather modest rate difference: $k'_H/k_H = 16.4$, between two reactions with similar transition states, and it consequently tends to discredit the electrostatic explanation. A much stronger argument, however, may be made on the basis of the change in direction of the isotope effect that this acceleration makes.

Kinetic isotope effects on proton transfer reactions are known to vary in magnitude with transition state structure in a parabolic fashion.[10,12] They reach maximum values for reactions with symmetrical transition states in which the proton is moving between bases of equal strength, and for which the free energy of reaction is zero, and they fall off to either side of this maximum as the strengths of the bases become unequal, and the reaction becomes either endo– or exoergic. Whether an isotope effect on a reaction with an unsymmetrical transition state becomes weaker or stronger with increasing reactivity consequently depends upon whether that reaction is endo– or exoergic: for endoergic reactions, an increase in reactivity will make the isotope effect stronger, and for exoergic reactions, an increase in reactivity will make the isotope effect weaker.

Diazonium ions are unstable substances. They are, for example, formed in appreciable amounts by the carbon protonation of diazo compounds only in super acids at low temperatures.[13] Carbon protonation of 2-(diazoacetyl)benzoic acid is therefore an endoergic process, and the rate acceleration effected in going from the high acidity to the low acidity regions of the rate profile of Figure 2 should strengthen the isotope effect if the acceleration is caused by electrostatic transition state stabilization. Since the isotope effect becomes weaker rather than stronger, this explanation cannot be correct and must consequently be discarded.

The remaining explanation for the rate acceleration, intramolecular general acid catalysis, on the other hand, is entirely consistent with the experimental facts. In the low acidity region of the rate profile where the acceleration occurs, the substrate exists in its ionized carboxylate form. In order for intramolecular general acid to occur, this form must first be protonated in a rapid equilibrium step, which is then followed by the rate– determining intramolecular proton transfer, as shown in eq 8. Rapid nucleophilic displacement of nitrogen by the carboxylate group then completes the reaction, forming the 1,4-isochromandione final product.

(8)
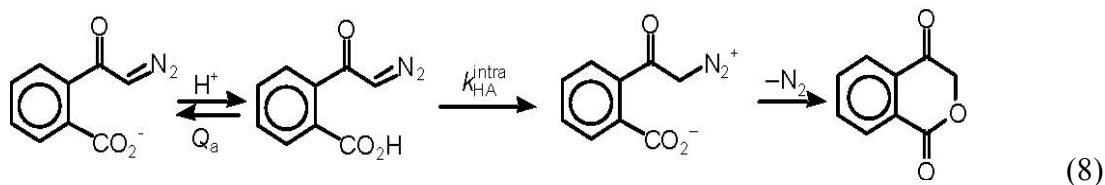
The rate constant for this intramolecular reaction path, k^{intra}_{HA} / Q_a, is equal to k'_H of the phenomenological reaction scheme of eq 4: $k'_H = k^{intra}_{HA}/ Q_a$, and k^{intra}_{HA} may consequently be calculated from the values of k'_H and Q_a obtained by least squares fitting of eq 5. The result is $k^{intra}_{HA} = (1.71 \pm 0.10) \times 10^{-2}$ s^{-1}, and combination of that with the value for D$_2$O solution gives the isotope effect $k^{intra}_{HA} / k^{intra}_{DA} = 7.58 \pm 0.70$. This is a purely primary isotope effect with no secondary component. Its magnitude is about half of the maximum value expected for breaking

an oxygen–hydrogen bond,[14] which is consistent with the fact that the isotope effect on the rate constant for the reaction of 2-(diazoacetyl)benzoic acid in the high acidity region of its rate profile $k_H/k_D = 2.31$, is about half of the maximum value expected for that kind of isotope effect as well.[10]

Acknowledgements

References and Notes

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