Kinetic and Mechanistic Studies of the Rearrangement of Benzaldoxime to Benzamide Catalysed by Nickel Acetate

A. K. JOHNSON and J. D. MILLER

Department of Chemistry, The University of Aston in Birmingham, Birmingham B4 7ET, U.K.
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When solutions of benzaldoxime in digol are heated with nickel acetate, the solute undergoes the Beckmann rearrangement yielding benzamide as the major product. Kinetic studies of this reaction show that the reaction proceeds via two distinct slow steps. The data are interpreted in terms of an initial attack of solvent on benzaldoxime, co-ordinated to nickel in the anti-isomeric form. This reaction yields a benzimidate which subsequently reacts to yield either benzamide or a side product. Numerical data are cited, together with information on the effect of other complexes as catalysts, and on the requirements imposed by different solvents.

Introduction

Recently we have become interested in ligand reactivity, especially in complexes where the central metal ion is exhibiting a normal oxidation state. Here we report the results of experiments aimed at elucidating the role of simple nickel compounds in the conversion of benzaldoxime to benzamide. The Beckmann rearrangement of oximes to amides[1] can be effected by a variety of reagents, including some metals and metal salts, *e.g.* cuprous chloride[2]. The first detailed study of such reactions under homogeneous conditions was that of Field *et al.*[3], who studied the effect of nickel acetate tetrahydrate on solutions of oximes in xylene. Although the synthetic possibilities of metal salts as catalysts for this rearrangement are documented, the mechanistic aspects of such isomerizations have, as yet, remained a matter for speculation[4].

The ability of oximes to act as monodentate ligands is documented. Normally, aldoximes co-ordinate to metals in the β- or *anti*-form using the nitrogen atom as donor[5-8]. Occasionally co-ordination can be achieved using oxygen as the donor atom[6-8].

Results

The more stable isomeric form of benzaldoxime, the α- or *syn*-form, is used throughout as the form of reagent

initially added in our kinetic experiments. We have not been able to identify, unequivocally, the form of the oxime which is actually involved in reaction. We believe it to be the *anti*-isomer. Some ^{1}H n.m.r. studies cast light on the feasibility of this postulate. The spectra of the *syn*- and *anti*-isomers are sufficiently distinct for their relative concentrations in a mixture to be determined by n.m.r. We find that solutions of either in digol (diethyleneglycol) show a pure *syn*-spectrum after being heated for five minutes at 100°C. However solutions containing 0.3 M oxime, in either form initially, and 0.3 M zinc chloride show a *syn* : *anti* ratio of approximately 10 : 1 after being heated to 100°C for eighty minutes. We therefore infer that metal ions are capable of isomerizing one form of benzaldoxime to the other, and of stabilizing the *anti*-form to some extent.

When solutions of benzaldoxime in hydrocarbon solvents are refluxed in the presence of nickel acetate tetrahydrate, benzamide is produced. The yield decreases as the boiling point of the solvent increases. Xylene (b.p. = 140°C) yields circa 85% benzamide after several hours, whereas higher boiling solvents such as tetrahydronaphthalene (b.p. = 207°C) yield less product (40%), but more rapidly. Clearly a side reaction of high activation energy is involved. In these solvents nickel formate, nickel chloride and stable nickel complexes do not behave as catalysts, while the amide produced precipitates from solution on cooling. Zinc acetate is effective as a catalyst whereas manganese and cobalt acetates are ineffective. The most convenient experimental system for kinetic studies under homogeneous conditions uses digol as solvent, and the benzamide production is monitored in the infra-red region. The band at 1675 cm^{-1} is suitable, and solutions obey Beer's law. Any benzaldehyde produced could also be detected in the region, at 1700 cm^{-1}. Calibration shows that 10% production of benzaldehyde would be readily detected. We never observed evidence of benzaldehyde production, which therefore represents a minor factor, at most, in the overall disappearance of benzaldoxime[9].

Plots of benzamide concentration against time for individual runs with added nickel acetate are reproducible, and show the characteristic profile for a consecutive

reaction sequence. The data were successfully fitted, using an iterative least squares computer programme, to equation (1), which occurs when two consecutive pseudo-first order reactions lead to the formation of benzamide.

$$[\text{amide}] = [\text{amide}]_x \left\{ 1 - \frac{k_b}{k_b - k_a} \exp(-k_a t) + \frac{k_a}{k_b - k_a} \right.$$

$$\left. \exp(-k_b t) \right\} \quad (1)$$

The values of the constants k_a and k_b are presented in Table I, together with data for the fractional conversion, F, to benzamide. In Table II, we present data for the analogous reaction using deuterated benzaldoxime, C_6H_5CDNOH, as reagent. The sample of this material prepared by us contained 60% of the deuterated form and 40% of the undeuterated oxime. The data for the pure deuterated reagent were determined from a comparison of otherwise identical reactions using the mixed reagent and undeuterated reagent. The C–D absorption of the reagent is found at 2205 cm^{-1}, a region clear of solvent absorption, and so the rate of disappearance of the reagent can be monitored when a higher oxime concentration $(2M)$ is used. The diminution of the peak at 2205 cm^{-1} obeys first order kinetics, and the observed rate constant is also quoted in Table II.

The data summarised in Tables I and II represent the bulk of our experimental effort. But there are further results of relevance to the discussion. Under the conditions of our kinetic studies benzonitrile is not converted to benzamide. We have prepared imidates as their hydrochlorides from the reactions of benzonitrile with digol and with 2-methoxyethanol. These compounds yield benzamide on heating in digol. Table III contains data for catalysts, other than nickel acetate, in digol. Some of these compounds are ineffective in hydrocarbon solvents. We also observed qualitatively that zinc acetate dihydrate, zinc chloride and dichloro-bis(triphenylphosphine)platinum(II) show slight catalytic activity whereas the analogous palladium(II) complex does not.

Discussion

From an examination of the data of Tables I and II, the following results emerge. The first step in the reaction sequence is that described by k_a. This step shows a strong dependance on the nickel concentration, and involves the cleavage of the side chain C–H bond. Additionally, since the formation of benzamide is accurately described by two consecutive pseudo-first order rate constants, the concentration of the active nickel catalyst must remain essentially constant throughout the course of a reaction. Since the initial oxime concentration is much more than the total nickel concentration, it follows that any nickel oxime complex must be formed only at low concentrations. The experimental results

TABLE I. Computed Pseudo-first Order Rate Constants, k_a and k_b; and the Fraction of Oxime Converted to Amide, F; for the Rearrangement of Benzaldoxime to Benzamide in the Presence of Nickel Acetate Tetrahydrate in Digol.

Initial [oxime] /M	[Ni (OAc)₂] /M	Temp/ °C	$10^4 k_a/s^{-1}$	$10^4 k_b/s^{-1}$	F
0.1	0.012	184	3.93	6.59	0.535
0.2	0.012	184	3.83	6.34	0.569
0.3	0.012	184	4.24	6.76	0.553
0.2	0.004	184	1.57	6.99	0.580
0.2	0.008	184	2.65	6.52	0.573
0.2[a]	0.016	184	4.70	5.09	0.595
0.2	0.020	184	6.08	4.69	0.606
0.2	0.024	184	7.45	5.23	0.594
0.2	0.012	160.5	1.38	0.87	0.749
0.2[a]	0.012	168.5	2.20	2.07	0.685
0.2[a]	0.012	176.5	3.18	3.20	0.639
0.2	0.012	191.5	5.05	10.04	0.537
0.2	0.012	200.0	7.25	20.66	0.483

[a] Under conditions where the rate constants are very similar the accuracy of the individual values becomes suspect.

TABLE II. Computed Rate Data in Digol at 189.0° C in the Presence of 0.012M Nickel Acetate.

Initial Reagent Conc.	Peak Followed	$10^4 k_a/ s^{-1}$	$10^4 k_b/ s^{-1}$	F
0.2M C₆H₅CHNOH	Amide 1675 cm^{-1}	4.98	9.30	0.538
0.2M C₆H₅CDNOH	Amide 1675 cm^{-1}	3.15	8.95	0.525
2.0M C₆H₅CDNOH	C–D 2205 cm^{-1}	2.93	–	–

TABLE III. Pseudo-first Order Rate Constants for the Rearrangement of Benzaldoxime to Benzamide in Digol at 184° C. Initial concentrations being 0.2M oxime and 0.012M catalyst.
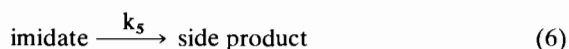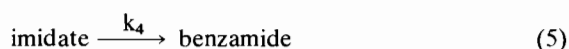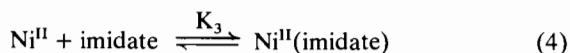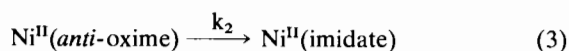
Catalyst	$10^4 k_a/s^{-1}$	$10^4 k_b/s^{-1}$	F
Ni(PPh₃)₂Cl₂	1.15	5.60	0.646
Ni(PPh₃)₂I₂	19.0	7.40	0.612
Ni(PhCHNOH)₄Cl₂	1.73	3.47	0.675[a]
Ni(PhCHNOH)₄I₂	9.88	6.74	0.670[a]
NiCl₂·6H₂O	2.57	3.52	0.587
Ni(OAc)₂·4H₂O	3.83	6.34	0.569

[a] These data take into account the additional quantity of oxime added as a ligand.

concerning reactions in solvents other than digol, and the non-conversion of benzonitrile to benzamide imply that the overall constant k_a describes a series of reactions involving the attack of solvent on co-ordinated

oxime yielding an imidate. The variation of the fractional conversion to benzamide with temperature shows the existence of a high activation energy side reaction. The linear plot of $\log(F/(1-F))$ against $1/T$ enables the difference in activation energies of main to side reactions to be evaluated as -11.7 ± 0.6 kcal mol^{-1}. Within experimental error an Arrhenius plot k_a is linear, giving an overall activation energy of 15.8 ± 0.8 kcal mol^{-1}. The side reaction cannot therefore arise before the formation of imidate since, in that case, the numerical values would result in curvature of the Arrhenius plot. Further support for this conclusion comes from Table II. While k_a shows a strong isotope effect, F does not vary significantly. The constant k_b shows a small but real variation with the nickel concentration. The rate constant decreases slightly as the catalyst concentration increases.

Our observations lead us to deduce reactions (2) to (6) as representing the overall reaction sequence

$$Ni^{II} + syn\text{-oxime} \xrightleftharpoons{K_1} Ni^{II}(anti\text{-oxime}) \qquad (2)$$

$$Ni^{II}(anti\text{-oxime}) \xrightarrow{k_2} Ni^{II}(\text{imidate}) \qquad (3)$$

$$Ni^{II} + \text{imidate} \xrightleftharpoons{K_3} Ni^{II}(\text{imidate}) \qquad (4)$$

$$\text{imidate} \xrightarrow{k_4} \text{benzamide} \qquad (5)$$

$$\text{imidate} \xrightarrow{k_5} \text{side product} \qquad (6)$$
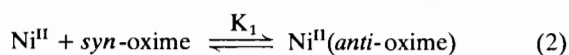
If the concentration of free nickel species, denoted by Ni^{II}, is approximately equal to the total nickel concentration, [Ni], then

$$k_a = K_1 k_2 [\text{Ni}] \qquad (7)$$

$$k_b = (k_4 + k_5)/(1 + K_3[\text{Ni}]) \qquad (8)$$

$$F = k_4/(k_4 + k_5) \qquad (9)$$

The calculated entropy of activation for the constant k_a is

$$\Delta S^{\ddagger}_a = \Delta S^{\circ}_1 + \Delta S^{\ddagger}_2 = Ca. -34 \text{ cal deg}^{-1} \text{ mol}^{-1}$$

An examination of known[10] entropy changes for equilibria comparable to reaction (2) suggests that $\Delta S^{\ddagger}_2$ must be large and negative. We feel that this supports the idea of reaction (3) being a bimolecular process involving attack by solvent. However we note that a reaction believed[11] to proceed by a similar mechanism shows a different value.

The second composite rate constant, k_b, varies little with [Ni]. This means that individual activation energies can be assigned to k_4 and k_5; 27.7 ± 1.3 kcal mol^{-1} and 39.1 ± 2.2 kcal mol^{-1} respectively. Unfortunately K_3 cannot be determined accurately : a value of $19M^{-1}$ at $184°$ C appears to be a reasonable estimate.

The aim of this work was to determine the role of metal salts in activating aldoximes towards rearrange-ment. The values of k_a in both Tables I and III show that the nickel salts are involved in the conversion to the intermediate imidate, but not directly beyond that stage. The variation of k_a with added catalyst appears to be one in which k_a increases as the availability of co-ordination sites on the nickel ion increases. Since the normal mode[6–8] of co-ordination of oximes is through N-bonding with the less stable [12] *syn*-form; this mode should mean that only small fractions of the total nickel are co-ordinated to oxime, as we find. Therefore we postulate the role of the nickel(II) species to be that of a Lewis acid, which co-ordinates to the nitrogen atom of *anti*-benzaldoxime, stabilizing this form and causing polarization within it. Attack of nucleophilic solvent molecules, or acetate in xylene, on the side chain carbon atom is thus made easier. Since the intermediate imidate is a poor ligand, the equilibrium between free and co-ordinated imidate, reaction (4), is very much in favour of the free ligand. Imidates are known[13] to undergo thermal rearrangement to amides. These reactions are not generally quantitative, as shown in our reactions (5) and (6). Since we were unable to isolate and characterize a pure specimen of the side product, we cannot comment in more detail on reaction (6). Other workers have studied such side products[6,13]. In accord with the scheme outlined by us, values of k_b vary little from one catalyst to another. Only when the catalyst contains chloride does k_b change significantly from the value with nickel acetate. This observation may reflect a change in K_3, or be related to the Pinner fission reaction between chloride ions and protonated imidates[14].

Experimental

The rearrangement of benzaldoxime to benzamide is strongly exothermic, and is studied at a high temperature. The most satisfactory arrangement for kinetic studies requires the use of a heating bath of silicone oil as the heating medium. The reaction vessel is cylindrical with a flat base, to allow for magnetic stirring. A further cylinder of slightly smaller cross section is suspended within and connected to a reflux condenser. A liquid, whose boiling point is just below the working temperature, is placed in the inner compartment to act as a heat sink. The annular space containing the reaction solution is serviced via ground cones. Weighed amounts of finely divided catalyst are placed in a small glass cup, within which is sealed a small magnet. This container is held at the top of the vessel, and later dropped into the oxime solution to initiate reaction. In the case of nickel acetate dissolution of the solid was rapid, although some other added solids required longer times to dissolve. Samples of the reaction mixture were abstracted at known times using a syringe and quenched to room temperature. Since stainless steel can catalyse the reaction under study, the syringe needle was kept in

contact with the reaction solution for as short a time as possible, and also cleaned after each sampling. Benzamide concentrations were determined by infra-red spectroscopy using matched solution cells with silver chloride windows and a Perkin–Elmer 457 spectrometer. Essentially identical rate data were obtained from runs using unpurified and redistilled[15] solvent.

Syn- and *anti*-benzaldoxime were prepared by the method of Vogel[16] while the deuterated *syn*-benzaldoxime, C_6H_5CDNOH, was prepared from the ylide benzal–bispyridiniumbromide[17] and its hydrolysis[18] to benzaldehyde.

Benzimidate hydrochlorides were prepared from benzonitrile and digol or 2-methoxyethanol by the literature route[19], as were the various transition metal complexes; the tetrakis-benzaldoxime nickel(II) complexes[7,20], bisdimethylglyoxinatonickel(II)[21], and the dichlorobis(triphenylphosphine) complexes of nickel(II)[22], palladium(II)[23] and platinum(II)[23].

With the exception of the product derived from benzonitrile and digol, all reagents prepared gave melting or boiling point and analytical data in agreement with the expected values. The various attempts to prepare an imidate hydrochloride from digol, $HOCH_2CH_2OCH_2CH_2OH$, yielded products rich in chlorine. This probably indicates a significant degree of disubstitution on digol.

Microanalytical data were determined within this department, or commercially by Dr. F. B. Strauss of Oxford. Proton n.m.r. spectra were recorded on a Varian Associates HA 100D spectrometer.

Acknowledgments

References

1 L. G. Donaruma and W. Z. Heldt, *Organic Reactions*, 1960, *11*, 1.
2 W. J. Comstock, Amer. Chem. J., 1897, *19*, 485.
3 L. Field, P. B. Hughmark, S. H. Shumaker and W. S. Marshall, *J. Am. Chem. Soc.*, 1961, *83*, 1983.
4 M. E. Stone and K. E. Johnson, *Canad. J. Chem.*, 1973, *51*, 1260.
5 A. Bryson and F. P. Dwyer, *J. Proc. Roy. Soc. N. S. Wales*, 1940, *74*, 471.
6 *idem, ibid.*, p. 107.
7 W. Hieber and F. Leutart, *Chem. Ber.*, 1929, *62*, 1839.
8 A. Chakravorty, *Co-ord. Chem. Rev.*, 1974, *13*, 4.
9 R. Paul, *Compt. Rend.*, 1937, *204*, 363.
10 S. J. Ashcroft and C. T. Mortimer, "Thermochemistry of Transition Metal Complexes", Academic Press, London, 1970.
11 R. Breslow, R. Fairweather and J. Keana, *J. Am. Chem. Soc.*, 1967, *89*, 2135.
12 "Dictionary of Organic Compounds", Eyre and Spoltiswoode, London, 1965.
13 J. W. Schulenberg and S. Archer, *Organic Reactions*, 1965, *14*, 1.
14 S. M. McElvain and B. E. Tate, *J. Am. Chem. Soc.*, 1951, *73*, 2233.
15 W. H. Rinkerbach, *Ind. Eng. Chem.*, 1927, *19*, 474.
16 A. I. Vogel, "Practical Organic Chemistry", 2nd Ed., Longmans Green, London, 1951.
17 F. Krohnke and H. Leister, *Chem. Ber.*, 1958, *91*, 1295.
18 R. A. Olofson, D. M. Zimmerman, *J. Am. Chem. Soc.*, 1967, *89*, 5057.
19 G. D. Lander, *J. Chem. Soc.*, 1900, 736.
20 W. Hieber and F. Leutart, *Chem. Ber.*, 1927, *60*, 2296.
21 B. E. Dawson, "Practical Inorganic Chemistry", Methuen, London, 1963.
22 L. M. Venanzi, *J. Chem. Soc.*, 1958, 719.
23 L. Malatesta and C. Cariello, *J. Chem. Soc.*, 1958, 2323.