The Nature of the Transition State in Amides Pyrolysis. The Rates of Pyrolysis of N-benzoyl and N-acetylpropanamide, N-benzoyl and N-acetyl-2methylpropanamide, and N-thioacetylpropanamide

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Abstract

The rates of gas-phase elimination reactions of N-benzoyl and N-acetyl-propanamide and N-benzoyl and N-acetyl-2-methylpropanamide are measured and discussed. They undergo unimolecular first-order elimination reactions. The reactivities of N-benzoylamides have been compared with each other and with those of N-acetylamides. The kinetic data together with the product analysis reveals that, the statistical factor of the availability of β -hydrogen atoms for elimination as well as steric factor are obscured by polar factor in gas-phase elimination reactions of N-benzoylamides while the statistical factor rather than electronic effect operates in each of N-acetylamides. © 1995 John Wiley & Sons, Inc.

Introduction

Amides which possess a β -alkyl group were found [1] to undergo the six centered elimination reaction characteristic of esters (1) with β -hydrogens and also of acid anhydrides and other related compounds. Considerable progress has been made in understanding the mechanism of these six-centered process by considering the relative rates of thermolysis of analogous groups of compounds. Some notable features: (i) the reaction pathway is semiconcerted process involving 6 atoms in a cyclic array; (ii) the



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reaction is aided by electron supply at C_{α} so that the order of reactivity of alkyl ester is $3^0 > 2^0 > 1^0$; (iii) the reaction is aided by electron withdrawal by R. Reactivity series are therefore (a) Formates > acetates > propanoates (R = H, CH₃, C₂H₅) and (b) carbonates > carbamate > acetates (R = R⁻O, R⁻NH, CH₃); and (iv) the reactivity is aided by increased electronegativity of X. A reactivity series is therefore, acetates > thioacetates > amides.

The statistically corrected rate ratio at 600 K between acetic anhydride and diacetamide was 9 [2], while that between N-tert-butylacetate and N-tert-butyl-acetamide was 68710 [2] and that between tert-butylthioacetate and tert-butylacetate is 83 [3]. The explanation was likely to be that in the transition state for esters, breaking the C_{α} —X bond is the most important factor, for others nucleophilic attack of the carbonyl group upon β -hydrogen atom predominates.

In this article we describe the pyrolysis of N-benzoyl and N-acetylamides which decompose via a transition state analogous to that which applies to esters.

Experimental

Synthesis

N-benzoylpropanamide: Refluxing of benzamide with propanoylchloride in a ratio of 1:1 in the presence of pyridine for 2h [4] gave after normal work-up *N*-benzoylpropanamide in 70% yield (mp 103.5–104.5°C) from water: ¹H NMR (CDCl₃, 80 MHz), δ 1.3(t, 3H), 3.1(q, 2H), 7.5–7.9 (m, 5H), and 8.9(bs, 1H). Anal. calcd. for C₁₀H₁₁NO₂: C, 67.79; H, 6.21; and N, 7.91. Found: C, 67.96; H, 6.09; and N, 8.02.

N-Benzoyl-2-methylpropanamide: Refluxing of benzamide with 2-methyl-propanoylchloride in a ratio of 1:1 in the presence of pyridine for 2 h gave after normal workup *N*-benzoyl-2-methylpropanamide in 66% yield (mp 152–154°C) from petroleum ether 60–80: ¹H NMR (CDCl₃, 80 MHz), δ 1.2(d, 6H), 3.7(m, 1H), 7.5–7.9(m, 5H), and 9.2(bs, 1H). Anal. calcd. for C₁₁H₁₃NO₂: C, 69.11; H, 6.81; and N, 7.33. Found: C, 69.12; H, 6.86; and N, 7.41.

N-acetylpropanamide: Refluxing of acetamide with propanamide in a ratio of 1:1 in the presence of pyridine for 1 h gave after normal work-up *N*-acetylpropanamide in 72% yield (mp 77.5–78.5°C) from petroleum ether 80–100: ¹H NMR (CDCl₃, 80 MHz), δ 1.2(t, 3H), 2.3(s, 3H), 2.6(q, 2H), and 9.2(bs, 1H). Anal. calcd. for C₅H₉NO₂: C, 52.17; H, 7.83; and N, 12.17. Found: C, 52.06; H, 7.91; and N, 12.26.

N-acetyl-2-methylpropanamide: Refluxing of acetamide with 2-methyl-propanoylchloride in a ratio of 1:1 in the presence of pyridine for 1 h gave after normal workup *N*-acetyl-2-methylpropanamide in 72% yield (mp 66–67°C) from petroleum ether 60–80: ¹H NMR (CDCl₃, 80 MHz), δ 1.2(d, 6H), 2.4(m, 1H), and 9.2(bs, 1H). Anal. calcd. for C₆H₁₁NO₂: C, 55.81; H, 8.53; and N, 10.85. Found: C, 55.67; H, 8.64; and N, 10.68.

N-thioacetylpropanamide: By following the same procedures using thioacetamide instead of acetamide *N*-thioacetylpropanamide produced in 70% yield (mp 66.5-67.5°C) from petroleum ether 60-80; lit mp 67.5°C [5]: ¹H NMR (CDCl₃, 80 MHZ), δ 1.3(t, 3H), 2.5(q, 2H), 3.0(s, 1H), and 9.7(bs, 1H). Anal. calcd. for C₅H₉NOS: C, 45.80; H, 6.87; and N, 10.69. Found: C, 46.00; H, 6.89; and N, 10.71.

Kinetic Studies

The flow system used for measuring reaction rates consists of two main parts: CDS custom made pyrolysis unit where the reaction takes place, coupled to a Varian 3300 gas chromatograph, where the products of the reaction and the residual reactants are analyzed. The pyrolysis unit consists of an insulated aluminum block, a glass reactor vessel, a platinum resistance thermometer and a thermocouple connected to a comark micro-processor thermometer. The internal surface of the reaction vessel has been deactiviated by injecting 4–5 portions of 50 μ of allylbromide at 450°C in the absence of air, this process has coated the internal surface of the tube by homogeneous carbon film [6]. The residence time of the sample vapor in the glass reactor is 40–43 s. 15% SE-30 packed column on chromosorb W., AW., mesh size 80–100 of 2 m length and 1/8 OD with flow rate of nitrogen carrier gas of 25–30 ml/min has been used in the analysis.

Product Analysis

Solutions of substrates in chlorobenzene were passed down a reactor column (of 1m length) packed with helices [6]. The column was heated to temperature comparable to those used in kinetic investigations. The product of pyrolysis were swept out using a stream of nitrogen gas, and the effluents were firstly passed through a trap in the form of a glass coil surrounded by a jacket of dry ice; and the effluent was passed into sodium hydroxide solution.

The material collected on the walls of trap was analyzed using G.L.C., N.M.R., and I.R. spectrophotometry, all of which confirms the presence of benzamide in case of N-benzoylamides, alkylamides in case of N-acetylamides, and the thioacetamide in case of N-thioacetylpropanamide. The aqueous sodium hydroxide solution was acidified, extracted, and then analyzed by G.L.C., N.M.R., and I.R. spectroscopy. The products obtained from the pyrolysis of N-benzoylpropanamide and N-benzoyl-2-methylpropanamide were propanoic and isobutanoic acid, respectively. The only organic component revealed in the extract of N-acetylamides was acetic acid produced by the hydrolysis of ketene, while that obtained from N-thioacetylpropanamide was propanoic acid [2] [7].

Results and Discussion

In our analytical flow apparatus, the amides were each well behaved kinetically and gave excellent and reproducible first-order rate coefficients with a linearity of 95% reaction and with no deviation in the Arrhenius plots. Since six fold change in the amount of substrate use per kinetic run gave no significant change in rate coefficient, these reactions were deemed to be first-order process.

Rate coefficients and Arrhenius parameters obtained in the pyrolysis of various amides are given in Table I, each rate coefficient represents an average of three kinetic runs in agreement to $\pm 2\%$ rate spread. The rate coefficients at 550 has been calculated from Arrhenius equation, we have chosen 550 K as a temperature most nearly experimentally accessible to all amides. The kinetic data together with the product of analysis reveals the following: (i) Gas-phase elimination reaction of *N*-benzoylamide involves a 6-membered transition state described in (2); (ii) The

G	R	х	T/K	$10^3 k/{ m s}^{-1}$	$\log A/s^{-1}$	$E_a~{ m KJ/mol}$
Ph	Et	0	532.7	1.2	14.1 ± 0.3	170.4 ± 3.8
			533.2	2.1		
			543.5	4.8		
			548.5	8.0		
			553.3	9.3		
			560.2	13.3		
Ph	iso-pro.	0	534.8	12.3	$13.6~\pm~0.7$	158.8 ± 7.6
	-		543.5	26.9		
			552.5	42.7		
			558.7	60.3		
			565.0	89.1		
Me	\mathbf{Et}	0	514.8	0.7	$12.4~\pm~0.6$	153.1 ± 5.7
			524.4	1.3		
			533.9	2.1		
			544.2	5.8		
			557.9	12.8		
			573.0	21.7		
			583.0	41.7		
Me	iso-pro.	0	540.5	3.5	12.6 ± 0.3	155.1 ± 3.8
	-		546.5	4.7		
			549.1	6.0		
			558.7	11.0		
			561.8	13.5		
			574.7	24.5		
			578.0	33.1		
			581.4	40.7		
			588.2	56.2		
Me	\mathbf{Et}	\mathbf{s}	455.5	1.8	$10.3~\pm~0.1$	114.9 ± 1.9
			488.4	14.3		
			498.0	23.5		
			505.1	35.5		
	_		507.6	39.8		

TABLE I. Rate coefficients for the pyrolysis of GCXNHCOR.





Figures 3 and 4.

rate coefficients calculated from Arrhenius equations at 550 K in Table II show that although $3-\beta$ -hydrogen atoms are available for elimination in N-benzoylethanamide (a) this compound eliminates at less rate than N-benzoyl-propanamide (b) of $2-\beta$ hydrogen atom and N-benzoyl-2-methylpropanamide (c) with one β -hydrogen eliminates at a faster rate than (a) and (b). This indicates that the statistical factor of the number of β -hydrogen atoms available for elimination is obscured by polar factor in gas-phase elimination reaction of N-benzoylamides, otherwise we would obtain the reverse order of reactivity as we go from (a) to (c); (iii) This order of reactivity obtained in N-benzoylamide series is due to the electronic effect of methyl groups in stabilizing the slightly electron deficient β -carbon atom in the transition state. Steric effect of the methyl groups in this N-benzoylamide series should also accelerate the reaction in the same order, but if the latter effect operates, one would expect much higher differences in rate of reaction. So the statistical as well as steric factors are obscured by polar factor in gas-phase elimination reaction of N-benzoylamides; (iv) Two possible mechanisms can be postulated for the elimination reaction of N-acetylamides (3) and (4). In product analysis, we have identified $R_1R_2CHCONH_2$ and not CH_3CONH_2 , and based on the absence of acetamide that should arise via transition state (4) in the product of the elimination reaction of N-acetylpropanamide and N-acetyl-2-methylpropanamide, we can rule out the mechanism which proceeds via transition state (4); (v) According to transition state (3), the number of β -hydrogen atoms available for elimination in N-acetylamides is constant and this explains the very slight differences in the elimination rate of

G Ph Ph Ph Me Me Me R Me \mathbf{Et} iso-pro Me Et iso-pro 2.5^{a} 8.3 32.27.27.5 $10^3 k(s)^{-1}$ 3.1^{b}

TABLE II. Rate coefficients for the pyrolysis of GCONHCOR at 550 K.

^{a,b} Literature value [7] and [2], respectively.

this series in Table II. In other words statistical factor of the availability of β -hydrogen atoms for elimination rather than electronic effect of the methyl groups operates in each of *N*-acetylamides; and (vi) We thought it would be of interest to see how long this statistical effect will survive, so *N*-thioacetylpropanamide has been prepared and its rate of reaction and Arrhenius parameter has been calculated, product analysis for the elimination reaction of this compound reveals the formation of thioacetamide, which suggest that the reaction takes place via transition state (5), so the statistical factor is obscured by polar factor in this compound and this is a result of the greater nucleophicity of C= S over C= O, which is reflected in the high rate coefficient of 246 $\times 10^{-3}$ calculated at 550 K relative to the *N*-acetyl and *N*-benzoylamides.



Figure 5.

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