Mechanism and Linear Free Energy Relationships in the Kinetics of Formation of Bicyclo[3.3.1]nonane Derivatives from 1,3,5-Trinitrobenzene, Phenyl-Substituted 1-Benzyl-1-(ethoxycarbonyl)-2propanones, and Triethylamine

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ABSTRACT: The kinetics and mechanism of cyclization of the anionic sigma complex obtained from the reaction of 1,3,5-trinitrobenzene (TNB) and 1-benzyl-1-(ethoxycarbonyl)-2-propanone (BEP) in the presence of triethylamine (NEt₃) have been studied in CH₃CN–CH₃OH (50% v/v). The order of the reaction has been found to be zero in TNB and BEP, unity in NEt₃, and negative and nonintegral in triethylammonium chloride. The rate has been observed to increase slightly

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with an increase in the concentration of the added salt (tetraethylammonium chloride). The rate constants for the formation of bicyclic adducts from phenyl-substituted BEP and TNB in the presence of triethylamine have been correlated with σ values. © 2011 Wiley Periodicals, Inc. Int J Chem Kinet 43: 467–473, 2011

INTRODUCTION

Various electron-deficient aromatic compounds have been reported to form amazingly stable crystalline metabridged bicyclic adducts containing bicyclo[3.3.1]nonane skeleton with the anions of acetylacetone, dicarbomethoxyacetone, ethylacetoacetate, cyclohexanone, dibenzylketone etc. [1–4]. Previous studies in our laboratories have proved that α -bromo and ω -bromo acetoacetanilides do not form stable bicyclic adducts with 1,3,5-trinitrobenzene (TNB) in the presence of NEt₃ due to the presence of the bulky bromine atom at the site of condensation [5]. The growing interest in examining the steric effects caused by the substituents during the cyclization of 1:1 sigma adduct prompted us to isolate a series of crystalline adducts containing the bicyclo[3.3.1]nonane skeleton from the carbanions of beta keto esters and TNB in our laboratories [6]. Although a number of carbon-bonded sigma complexes and bicyclic adducts have been isolated in the crystalline form and characterized [2–9], there are relatively few [3,10-15] comprehensive kinetic and thermodynamic studies of their formation because some carbon nucleophiles are difficult to generate under conditions suitable for studies. Structurereactivity correlation studies, which are effective tools in deducing the reaction mechanism in their formation and decomposition, are still more limited. A search of the literature indicates that only a few reports have so far appeared on the structure-reactivity correlations in the conversion of sigma complexes to bicyclo[3.3.1]nonane derivatives [3,10,13,14]. Attempts have now been made to expand the scope of correlation analysis in the formation of bicyclic adducts.

EXPERIMENTAL

CH₃CN (Merck, India) was dried over molecular sieves, type 4A, distilled, and used. Methanol was purified by the known procedure [16]. TNB was prepared from *p*-nitrotoluene [17] and was repeatedly recrystallized from ethanol (mp 396 K). Triethylamine (analar grade) was distilled from small quantities of phenyl isocyanate [18]. Triethylammonium chloride was recrystallized from absolute ethanol and dried under vacuum. Tetraethylammonium chloride (Fluka AG, Mumbai, India) was used as such. 1-(Ethoxycarbonyl)-

1-(X-benzyl)-2-propanones were prepared from corresponding substituted benzyl chlorides and the sodium salt of ethyl acetoacetate [19].

Kinetic Measurements

Stock solutions of TNB, NEt₃, 1-benzyl-1-(ethoxycarbonyl)-2-propanone (BEP), and the salts were prepared in CH₃CN-CH₃OH (50% v/v), and the required quantities for each run were pipetted into volumetric flasks and diluted to volume. TNB and BEP were taken in one flask, and NEt₃ and the salts were in another flask. After injection of the appropriate solutions into the reaction chamber of the spectrophotometer thermostated at 298 K, the decrease in the absorbance as a function of time was recorded at 570 nm. In all the experiments, pseudo-first-order conditions are maintained and good kinetic plots resulted. The results are reproducible within 5% error. Kinetic measurements were made employing a Carl-Zeiss Vsu2-P spectrophotometer.

RESULTS AND DISCUSSION

Addition of NEt₃ to a solution of BEP and TNB in CH₃CN–CH₃OH (50% v/v) gives rise immediately upon mixing to a visible spectrum with two maxima at 450 and 570 nm characteristic of 1:1 Meisenheimer adduct, and this rapidly changes to give a peak at 500 nm owing to the formation of the bicyclic adduct. As reported earlier [10,14], in the present study, the slow disappearance of 1:1 adduct during the formation of a bicyclic adduct has been followed by observing the decrease in optical density at 570 nm.

Effect of the TNB Concentration

The slope of a log–log plot of k_{obs} versus the concentration of TNB (Fig. 1, line A) is ~ -0.08 , which indicates that TNB has no significant effect on the rate of the cyclization reaction (see Table I).

Effect of BEP and NEt₃ Concentrations

Log-log plots of k_{obs} versus BEP concentration have slopes very close to zero (Fig. 2, lines A–D). This implies that BEP is not involved in the rate-determining



Figure 1 Effect of TNB, N Et4, and H N Et3 concentrations of the rate of cyclization: (A) 1–5, (B) 26–29, and (C) 22–25.

Table I Effect of the TNB Concentration on Cyclization in CH ₃ CN/CH ₃ O	H (50% v/v) at 298 K
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Run	[TNB] (× 10^4 mol dm ⁻³)	$[BEP] (\times 10^1 \text{ mol dm}^{-3})$	$[NEt_3] \\ (\times 10^1 \text{ mol } dm^{-3})$	$[H \stackrel{+}{N} Et_3 C \stackrel{-}{1}]$ (× 10 ⁴ mol dm ⁻³)	$[\stackrel{+}{N}$ Et ₄ C $\overline{1}]$ (×10 ² mol dm ⁻³)	$k_{\rm obs} (\times 10^3 \\ {\rm min}^{-1})$
1	2.50	4.56	4.03	8.54	5.22	4.20
2	5.00	4.56	4.03	8.54	5.22	4.06
3	7.50	4.56	4.03	8.54	5.22	3.84
4	10.00	4.56	4.03	8.54	5.22	3.70
5	15.00	4.56	4.03	8.54	5.22	3.62

step. A log–log plot of k_{obs} versus NEt₃ concentrations has slope close to unity (Fig. 2, line E), indicating that the cyclization is catalyzed by NEt₃ (see Table II).

Effect of Salt Concentrations

A log-log plot of k_{obs} versus H $\stackrel{+}{N}$ Et₃C1 concentration is nonlinear with an approximate slope of -0.4 in the high-concentration region (Fig. 1, curve C). When the concentration of N Et₄C1 is varied, little effect on the rate is seen (Fig. 1, line B; see Table III). This is expected for a reaction where charge is neither created nor destroyed.

The kinetic results lead to the establishment of the mechanism outlined in Scheme 1. The rate of formation of 3 can be given as

$$-\frac{\mathrm{d}[\mathbf{1}]}{\mathrm{d}t} = +\frac{\mathrm{d}[\mathbf{3}]}{\mathrm{d}t} = k_2[\mathbf{2}]$$

For the sequence of reactions under stage II outlined in Scheme 1, two rate-limiting expressions can be derived. On the basis of steady-state treatment,

$$-\frac{d[1]}{dt} = +\frac{d[3]}{dt} = \frac{k_1 k_2 [1] [\text{NEt}_3]}{k_{-1} [\text{H N Et}_3] + k_2}$$

On the basis of preequilibrium treatment,

$$-\frac{\mathbf{d}[\mathbf{1}]}{\mathbf{d}t} = +\frac{\mathbf{d}[\mathbf{3}]}{\mathbf{d}t} = \frac{K_1 k_2 [\mathbf{1}] [\text{NEt}_3]}{[\text{H N Et}_3]}$$

According to the steady-state and preequilibrium treatment, the cyclization rate should be zero order in TNB, zero order in BEP, and first order in NEt₃. In the present investigation, a plot of log k_{obs} versus [H N Et₃] is nonlinear with slope ~ -0.4 and hence

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Figure 2 Effect of BEP and NEt₃ concentrations on the rate of cyclization. Line A: runs 6–9; line B: runs 10–13; C: runs 14–17; D: runs 18–21; E: runs 6,10,14, and 18.

Run	[TNB] (×10 ⁴ mol dm ⁻³)	$[BEP] (\times 10^1 \text{ mol dm}^{-3})$	[NEt ₃] (×10 ¹ mol dm ⁻³)	$[H \overset{+}{N} Et_3 C \overset{-}{1}] \\ (\times 10^4 \text{ mol } dm^{-3})$	$[\stackrel{+}{N}$ Et ₄ C $\overline{1}]$ (×10 ² mol dm ⁻³)	$(\times 10^3 \text{ min}^{-1})$
6	5.00	4.56	2.88	4.69	9.14	2.40
7	5.00	6.50	2.88	4.69	9.14	2.39
8	5.00	9.12	2.88	4.69	9.14	2.41
9	5.00	13.60	2.88	4.69	9.14	2.42
10	5.00	4.56	4.32	4.69	9.14	3.72
11	5.00	6.50	4.32	4.69	9.14	3.72
12	5.00	9.12	4.32	4.69	9.14	3.68
13	5.00	13.60	4.32	4.69	9.14	3.73
14	5.00	4.56	5.76	4.69	9.14	5.20
15	5.00	6.50	5.76	4.69	9.14	5.30
16	5.00	9.12	5.76	4.69	9.14	5.31
17	5.00	13.60	5.76	4.69	9.14	5.32
18	5.00	4.56	7.20	4.69	9.14	5.60
19	5.00	6.50	7.20	4.69	9.14	5.62
20	5.00	9.12	7.20	4.69	9.14	5.65
21	5.00	13.60	7.20	4.69	9.14	5.70

Table II Effect of the BEP and NEt₃ Concentration on Cyclization in CH₃CN/CH₃OH (50% v/v) at 298 K

steady-state treatment is applicable. A very slight increase in the rate with increasing concentration of $\stackrel{+}{N}$ Et₄ can be attributed to the stabilization of increasing charge in the transition state leading to di-

anionic intermediate. The mechanistic picture of the present work is comparable with that of Strauss et al. [10], who have worked with symmetrical ketone (dibenzylketone).

Run	[TNB] (×10 ⁴ mol dm ⁻³)	[BEP] (×10 ¹ mol dm ⁻³)	[NEt ₃] (×10 ¹ mol dm ⁻³)	$[H \overset{+}{N} Et_3 C \overset{-}{1}] \\ (\times 10^4 \text{ mol } dm^{-3})$	$[\stackrel{+}{N} Et_4C \ 1]$ (×10 ² mol dm ⁻³)	$(\times 10^3 \text{ min}^{-1})$
22	5.00	4.56	5.76	23.30	10.16	4.31
23	5.00	4.56	5.76	70.10	10.16	3.72
24	5.00	4.56	5.76	93.50	10.16	3.24
25	5.00	4.56	5.76	114.00	10.16	2.59
26	5.00	4.56	4.03	_	30.60	3.83
27	5.00	4.56	4.03	-	7.22	3.90
28	5.00	4.56	4.03	_	14.40	4.00
29	5.00	4.56	4.03	-	28.80	4.30

Table III Salt Effect on Cyclization in CH₃CN/CH₃OH (50% v/v) at 298 K



Figure 3 Substituent effect in cyclization process. Line A: $4 + \log k_{obs} \sigma$ at 308 K, line B: $3 + \log k_{obs} \sigma$ at 303 K, line C: $4 + \log k_{obs} \sigma$ at 298 K.

Table IV	Substituent Effect in the Cyclization Process

		$k_{\rm obs} (\times 10^3 \rm min^{-1})$		E_{a}	ΔH^{\neq} (kJ mol ⁻¹)	ΔS^{\neq} (kJ mol ⁻¹)	ΔG^{\neq} (kJ mol ⁻¹)		
Serial No.	Substituent	298 K	303 K	308 K	$(kJ mol^{-1})$	at 303 K	at 303 K	at 303 K	σ
1	4-OCH ₃	0.91	1.25	1.67	47.86	45.31	-151.08	91.12	-0.268
2	4-CH3	1.26	1.69	2.24	43.84	41.33	-161.75	90.37	-0.170
3	$4-C_2H_5$	1.29	1.74	2.35	46.48	43.93	-152.88	90.29	-0.150
4	Н	1.71	2.49	3.49	51.58	51.54	-124.85	89.41	0
5	4-Cl	4.31	5.01	5.76	22.09	19.53	-224.59	87.65	0.227
6	4-Br	4.67	5.28	5.90	17.53	15.02	-239.11	87.52	0.232
7	2-NO ₂	1.38	1.97	2.70	56.27	53.76	-119.49	89.99	-

 $[\text{TNB}] = 5 \times 10^{-4} \text{ mol dm}^{-3}, [\text{BEP}] = 4.56 \times 10^{-1} \text{ mol dm}^{-3}, [\text{NEt}_3] = 3.31 \times 10^{-1} \text{ mol dm}^{-3}, [\text{HN} \text{ Et}_3 \text{C1}] = 5.75 \times 10^{-4} \text{ mol dm}^{-3}, [\text{NEt}_4 \text{C1}] = 2.51 \times 10^{-2} \text{ mol dm}^{-3}, \text{ and solvent CH}_3 \text{CN/CH}_3 \text{OH} (50\% \text{ v/v}).$

Substituent Effect

The rate constants for the formation of bicyclic adducts from the 1:1 Meisenheimer adducts of TNB and vari-

ous phenyl-substituted BEP in the presence of NEt₃ in CH₃CN:CH₃OH (50% v/v) are presented in Table IV. It is evident from the magnitude of the rate constants that the reaction is susceptible to polar



Scheme 1 Mechanism of cyclization of anionic sigma complex.

effects. The rate data (Table IV) have been correlated with σ [20] (Fig. 3). The plot reflects good correlation (line A; r = 0.9999; s = 0.035; $\rho = 1.25$). As noticed in our previous work [12], the rate increases with an increase in the electron-withdrawing power of the substituent. The observed rates of the various selected substituents follow the following order: p-OCH₃ < p-CH₃ < p-C₂H₅ < P-H < P-Cl < p-Br. For these substituents, proton abstraction (k_1 ; Scheme 1) is rate determining. However, when a nitro group is introduced at the 2-position, the rate observed is much less than that of *p*-bromo compound. As the reaction site is one atom away from the ring-carrying substituent, the retardation in the rate observed could not be due to steric hindrance. The large I effect of the nitro group makes the proton abstraction (k_1 ; Scheme 1) faster and consequently cyclization (k_2 ; Scheme 1) becomes rate determining in this case. When ΔH^{\neq} values are plotted versus ΔS^{\neq} (Table IV; the isokinetic relationship), a straight line is obtained for all substituents including the *o*-NO₂ group, indicating the operation of same mechanism in all cases. As *p*-nitrobenzyl chloride is a serious contaminant of 1-(ethoxycarbonyl)-1-(*p*-nitrobenzyl)-2-propanone, kinetic studies could not be attempted with this substance. The entropy of activation is negative under all experimental conditions, indicating that the freedom of motion in the side chain of the sigma complex is hindered in the transition state due to the cyclization.

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