

Kinetics and Mechanism of Addition of Benzylamines to Benzylidene-1,3-indandiones in Acetonitrile

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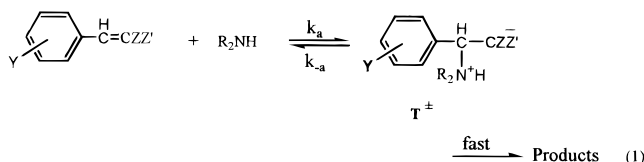
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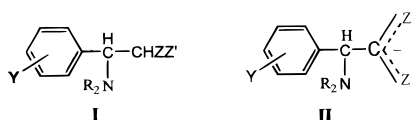
Nucleophilic addition reactions of benzylamines (BA; $\text{XC}_6\text{H}_4\text{CH}_2\text{NH}_2$) to benzylidene-1,3-indandiones (BID; $\text{YC}_6\text{H}_4\text{CH}=\text{C}(\text{C}=\text{O})_2\text{C}_6\text{H}_4$) have been studied in acetonitrile at 25.0 °C. The rate is first-order with respect to BA and BID, and no base catalysis is observed. The structure–reactivity behaviors (k_2 , ρ_X , β_X , and β_Y) are intermediate between the two series of addition reactions of BA to β -nitrostyrene (NS) and benzylidenemalononitrile (BMN) in acetonitrile. The normal kinetic isotope effects, $k_{\text{H}}/k_{\text{D}} > 1.0$, involving deuterated BAs ($\text{XC}_6\text{H}_4\text{CH}_2\text{ND}_2$) are smaller than those for the reactions of NS and BMN suggesting a somewhat looser bond formation in the transition state. The reaction is predicted to proceed in a single step with concurrent $\text{C}_\alpha\text{--N}$ bond formation and proton transfer to C_β . A hydrogen-bonded, four-center type cyclic transition state is proposed.

Introduction

Studies of substituent effects on the reactions of amine nucleophiles with olefins which are activated by electron-acceptors, Z and Z' in eq 1, have shown important



differences in the mechanism between the reactions in aqueous solution and in acetonitrile. In aqueous solution, the reactions were found to proceed through a zwitterionic intermediate, T^\pm , with imbalanced transition states (TSs) in which the development of resonance into the ZZ' group lags behind charge transfer or bond formation.¹ The lag in resonance development has been expressed

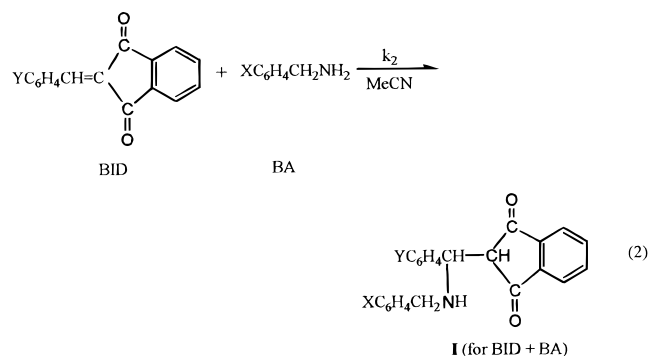


by a larger α_{nuc} , obtained by varying substituent Y (eq 1), than β_{nuc} , a Brønsted type coefficient based on a variation of an amine nucleophile.¹ The imbalance, $I_m = \alpha_{\text{nuc}} - \beta_{\text{nuc}}$, was found to increase with increasing resonance stabilization of the carbanionic product, **II**, in aqueous solution, e. g., in the order $\text{CN}, \text{CN} < \text{H}, \text{NO}_2$.¹

In contrast, however, the amine additions to olefins in acetonitrile were found to occur by a concerted formation of the $\text{C}_\alpha\text{--N}$ and $\text{C}_\beta\text{--H}$ bonds in a single-step process

leading to a neutral product, **I**.² The rates of amine additions in acetonitrile are, in general, extremely slower than in aqueous solution ($k_{\text{a}}(\text{aq}) \cong 10^4 \cdot k_{\text{a}}(\text{MeCN})$), but the relative order remains the same, $k_{\text{a}}(\text{CN}, \text{CN}) \gg k_{\text{a}}(\text{H}, \text{NO}_2)$.^{1,2} An unexpected trend was observed in acetonitrile, however, that the α -carbon becomes more positive ($\rho_Y < 0$) in the TS than in the reactant for Z, Z' = CN, CN (benzylidenemalononitrile, BMN)^{2b} in contrast to the negatively charged C_α ($\rho_Y > 0$) for Z, Z' = H, NO_2 (β -nitrostyrene, NS).^{2a} The sign of ρ_Y is invariably positive in aqueous solution¹ as expected from an imbalanced TS in which a greater degree of negative charge builds up C_α than that expected from a delocalized TS.

In view of this interesting trend, we conducted a similar amine addition reaction with benzylidene-1,3-indandione (BID)^{3c} in acetonitrile, eq 2.



The purpose of the present paper is to further explore the different mechanisms of the amine addition to olefin between the reactions in aqueous solution and in aceto-

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(1) (a) Bernasconi, C. F. *Acc. Chem. Res.* **1987**, *20*, 301. (b) Bernasconi, C. F. *Tetrahedron* **1989**, *45*, 4017.

(2) (a) Oh, H. K.; Yang, J. H.; Sung, D. D.; Lee, I. *J. Chem. Soc. Perkin Trans 2* **2000**, 101. (b) Oh, H. K.; Yang, J. H.; Lee, H. W.; Lee, I. *J. Org. Chem.* **2000**, *65*, 2188.

(3) (a) Bernasconi, C. F.; Renfrow, R. A.; Tia, P. R. *J. Am. Chem. Soc.* **1986**, *54*, 4541. (b) Brenasconi, C. F.; Killion, R. B., Jr. *J. Org. Chem.* **1989**, *54*, 2878. (c) Bernasconi, C. F.; Stronach, M. W. *J. Am. Chem. Soc.* **1991**, *113*, 2222. (d) Bernasconi, C. F.; Panda, M. *J. Org. Chem.* **1987**, *52*, 3042.

nitrile by examining the structure–reactivity behavior of olefins activated by keto groups, eq 2. The resonance stabilization of the carbanion product in aqueous solution has been reported to be in the order NS > BID > BMN^{1,3} so that an intermediate type of structure–reactivity behavior may be expected.

Another interest in this work is to examine the sign and magnitude of the cross-interaction constant,⁴ ρ_{XY} in eqs 3 where X and Y are substituents in the

$$\log(k_{XY}/k_{HH}) = \rho_X\sigma_X + \rho_Y\sigma_Y + \rho_{XY}\sigma_X\sigma_Y \quad (3a)$$

$$\rho_{XY} = \partial\rho_X/\partial\sigma_Y = \partial\rho_Y/\partial\sigma_X \quad (3b)$$

the amine (BA) and in the substrate (BID), respectively, in eq 2. The ρ_{XY} has been shown to have a negative sign in addition processes, e. g., bond formation in the S_N2 reactions and in the addition of amines to an olefin with ca. -0.6 to -0.8 .⁴

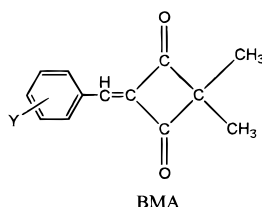
Results and Discussion

All the reactions studied in this work followed a simple kinetic law given by eqs 4 and 5 where k_2 is the rate constant for the amine (BA) addition to the substrate (BID).

$$-d[\text{BID}]/dt = k_{\text{obs}}[\text{BID}] \quad (4)$$

$$k_{\text{obs}} = k_2[\text{BA}] \quad (5)$$

No catalysis by a second benzylamine molecule was detected, which is similar to the benzylamine additions to BMN^{2b} but in contrast with the benzylamine catalysis found in the additions to NS.^{2a} Plots of k_{obs} vs [BA] were linear for 8-fold increase in [BA] from 1.0×10^{-3} M as shown in Table 1 for X = *p*-Me. The k_2 values obtained from the slopes of these plots are summarized in Table 2. Comparison of k_2 values for benzylamine additions to NS, BMN and BID with X = Y = H shows that the BID has an intermediate value of $1.48 \text{ M}^{-1} \text{ s}^{-1}$ at 25 °C (2.63×10^{-2} and $9.84 \text{ M}^{-1} \text{ s}^{-1}$ at 25 °C⁵ for NS and BMN, respectively). The ratios of rates at 25 °C are thus 1.0 (BMN): 1.5×10^{-1} (BID): 2.7×10^{-3} (NS), which is very close to those of intrinsic rates, k_0 , which is the rate (with piperidine) at $k_a = k_{-a}$ (eq 1) in 50% DMSO: 50% H₂O solution at 20 °C; 1.0(BMN): 1.6×10^{-1} (BMA): 4.0×10^{-3} (NS). In this comparison the k_0 value for benzylidene Meldrum's acid^{1,3d} (BMA) is used due to lack of the



corresponding data for BID in aqueous solution.⁶ These rate ratios suggest that rates of amine additions in

Table 1. The k_{obs} and k_2 Values for the Reactions of Y-Benzylidene-1,3-indandiones with Varying Concentration of *p*-CH₃-Benzylamine in Acetonitriles at 25 °C

Y	[<i>p</i> -CH ₃ -BA]/M	$k_{\text{obs}}/10^{-3} \text{ s}^{-1}$	$k_2/\text{M}^{-1} \text{ s}^{-1}$	correl coeff
<i>p</i> -OMe	0.001	0.307	1.65 ± 0.03	0.999
	0.002	1.69		
	0.003	3.21		
	0.004	4.82		
	0.005	6.79		
	0.006	8.21		
	0.007	9.92		
	0.008	11.8		
	<i>p</i> -Me	0.001		
0.002		2.81		
0.003		4.03		
0.004		7.17		
0.005		8.61		
0.006		9.80		
0.007		12.1		
0.008		14.2		
H		0.001	2.25	2.18 ± 0.07
	0.002	5.13		
	0.003	7.83		
	0.004	9.45		
	0.005	12.0		
	0.006	14.2		
	0.007	15.6		
	0.008	17.8		
	<i>p</i> -Cl	0.001	2.09	
0.002		5.79		
0.003		8.16		
0.004		11.9		
0.005		13.5		
0.006		16.4		
0.007		19.3		
0.008		21.8		
<i>p</i> -Br		0.001	2.32	2.97 ± 0.08
	0.002	5.93		
	0.003	9.24		
	0.004	12.0		
	0.005	15.5		
	0.006	18.3		
	0.007	20.4		
	0.008	23.3		

acetonitrile as well as in aqueous solution are dependent on the positive charge on the α -carbon (C_α) due to electron-withdrawing groups, Z, Z', in the substrate; Swain–Lupton's field parameter (F) and inductive substituent constant σ_1^7 are F : $\sigma_1 = 1.02:1.02$, $0.78:0.72$, and $0.65:0.65$ for Z, Z' = (CN, CN), (C₆H₄(CO)₂), and (H, NO₂), respectively, assuming additive effects. The Hammett coefficients for variation of substituents in the nucleophile, ρ_X , and in the substrate, ρ_Y , are compared in Table 3. The ρ_Y value for the reactions of BID is positive but is considerably smaller than that for NS, indicating that negative charge development on C_α at the TS is much weaker in the BID than in the NS series. This is reasonable since the charge imbalance in the TS, i.e., build-up of negative charge at C_β in the TS, is much greater for the NS than that for the BID.^{1,3} The negative ρ_Y , value, i.e., more positive C_α in the TS, for BMN may result partially from the strong electron-withdrawing effect of the two activating groups, CN, CN. Partially, this could result from a more extensive bond formation, i.e., a larger negative ρ_X and/or a larger positive β_X value in Table 3, since the positive charge developed on the nitrogen atom of the benzylamine in the TS should be nearer to C_α than those for the reactions of NS and BID for which the extent of bond formation is smaller with smaller magnitudes of ρ_X and β_X . The smallest magnitude of ρ_X for BID in Table 3 suggests that the degree of C_α –N

(4) (a) Lee, I. *Adv. Phys. Org. Chem.* **1992**, 27, 57. (b) Lee, I. *Chem. Soc. Rev.* **1990**, 19, 317. (c) Isaacs, N. S. *Physical Organic Chemistry*, 2nd ed; Longman: Harlow, 1995; Chapter 4.

(5) This value at 25.0 °C is extrapolated using Eyring equation with activation parameters in ref 2b.

(6) The structure–reactivity behaviors of the two, BID and BMA, are reported to be similar.^{1,3c,d}

Table 2. The Second Order Rate Constants, k_2 ($M^{-1} s^{-1}$) for the Addition Reactions of Y-Benzylidene-1,3-indandiones with X-Benzylamines in Acetonitrile at 25.0 °C

X	Y					ρ_Y^a
	<i>p</i> -OMe	<i>p</i> -Me	H	<i>p</i> -Cl	<i>p</i> -Br	
	2.08	2.33	2.83	3.49	3.76	0.48 ± 0.03
<i>p</i> -OMe	1.40^b				2.55	
	0.929^c				1.69	
<i>p</i> -Me	1.65	1.85	2.18	2.76	2.97	0.48 ± 0.03
H	1.14	1.25	1.48	1.76	1.87	0.41 ± 0.02
	0.659	0.692	0.797	0.926	0.969	0.33 ± 0.02
<i>p</i> -Cl	0.436				0.639	
	0.287				0.415	
ρ_X^d	-1.01	-1.06	-1.10	-1.17	-1.20	$\rho_{XY}^e = -0.33$
	(± 0.02)	(± 0.02)	(± 0.03)	(± 0.02)	(± 0.03)	
β_X^f	1.00	1.07	1.09	1.18	1.21	
	(± 0.04)	(± 0.01)	(± 0.02)	(± 0.02)	(± 0.02)	

^a The σ values were taken from Hansch, C.; Leo, A.; Taft, R. W. *Chem. Rev.* **1991**, 91, 165. Correlation coefficients were better than 0.995 in all cases. ^b At 15.0 °C. ^c At 5.0 °C. ^d Correlation coefficients were better than 0.999 in all cases. ^e Correlation coefficient was 0.999. ^f The pK_a values were taken from Fischer, A.; Galloway, W. J. *Chem. Soc.* **1964**, 3588. Correlation coefficients were better than 0.999 in all cases. $pK_a = 9.67$ was used for X=*p*-CH₃O (Oh, H. K.; Lee, J. Y.; Lee, I. *Bull. Korean Chem. Soc.* **1998**, 19, 1198).

Table 3. Comparison of ρ_X (β_X) and ρ_Y Values for the Reactions of Benzylamines (XC₆H₄CH₂NH₂) with NS, BMN, and BID in Acetonitrile at 25.0 °C

	ρ_X (β_X)	ρ_Y
NS	-1.22 (1.36)	1.73
BMN ^a	-1.62 (1.54)	-0.55
BID	-1.10 (1.09)	1.41

^a At 15.0 °C.

bond formation is the least in the TS for BID among the three systems compared. Again this is consistent with the magnitude of normalized β_{nuc} values in aqueous solution; the β_{nuc} values are 0.30, 0.15, and 0.25 for the reactions of BMN, BMA (but not BID),⁶ and NS, respectively, with piperidine and morpholine in aqueous solution.^{1,3}

The cross-interaction constants, ρ_{XY} in eqs 3, are all negative for the three series of BMN ($\rho_{XY} = -0.31$), BID ($\rho_{XY} = -0.33$), and NS ($\rho_{XY} = -0.41$). This shows that the cross-interaction constant, ρ_{XY} , in the bond formation process is always negative irrespective of whether the reaction center, C_α, becomes more negative or positive in the TS, in agreement with the negative ρ_{XY} values observed in the associative ($\rho_Y > 0$) as well as in the dissociative ($\rho_Y < 0$) S_N2 processes.^{4a,b,8} The size of ρ_{XY} for BID has again an intermediate value, but is well within the range of the ρ_{XY} values found for S_N2 processes ($\rho_{XY} = -0.6$ to -0.8) provided the falloff factor of ca. 2.2⁹ for an intervening CH₂ group in the benzylamine is accounted for $\rho_{XY} \cong -7.3$.

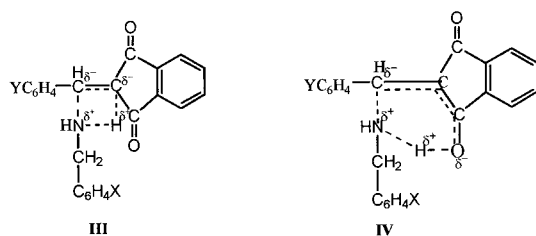
The kinetic isotope effects, k_H/k_D (Table 4), involving deuterated benzylamine nucleophiles (XC₆H₄CH₂ND₂) are greater than unity, $k_H/k_D \cong 1.25$ – 1.81 , suggesting a possibility of forming hydrogen-bonded four-center type

Table 4. Kinetic Isotope Effects on the Second-order Rate Constants (k_2) for the Reactions of Y-Benzylidene-1,3-indandiones with Deuterated X-Benzylamines in Acetonitrile at 25.0 °C

X	Y	$k_H/M^{-1} s^{-1}$	$k_D/M^{-1} s^{-1}$	k_H/k_D
<i>p</i> -OMe	<i>p</i> -OMe	2.08 ± 0.02	1.28 ± 0.01	1.63 ± 0.02^a
<i>p</i> -OMe	<i>p</i> -Me	2.33 ± 0.03	1.66 ± 0.02	1.40 ± 0.03
<i>p</i> -OMe	H	2.83 ± 0.04	2.06 ± 0.02	1.37 ± 0.02
<i>p</i> -OMe	<i>p</i> -Cl	3.49 ± 0.05	2.75 ± 0.04	1.27 ± 0.03
<i>p</i> -OMe	<i>p</i> -Br	3.76 ± 0.05	3.02 ± 0.05	1.25 ± 0.03
<i>p</i> -Cl	<i>p</i> -OMe	0.659 ± 0.006	0.364 ± 0.005	1.81 ± 0.03
<i>p</i> -Cl	<i>p</i> -Me	0.692 ± 0.005	0.424 ± 0.005	1.63 ± 0.02
<i>p</i> -Cl	H	0.797 ± 0.008	0.592 ± 0.006	1.35 ± 0.02
<i>p</i> -Cl	<i>p</i> -Cl	0.926 ± 0.010	0.715 ± 0.008	1.30 ± 0.02
<i>p</i> -Cl	<i>p</i> -Br	0.969 ± 0.010	0.756 ± 0.010	1.28 ± 0.02

^a Standard deviations.

TS, **III**, as has often been proposed for similar reactions.^{2,8b} The hydrogen bonding of N–H proton toward a carbonyl oxygen (**IV**) may be a possibility, but involves a too long



hydrogen-bond since the lone pair on N (n_N) of benzylamine approaches almost vertically from above (or below) the molecular plane of BID to the C_α–C_β π-bond. The relatively smaller values of k_H/k_D (1.25–1.81) than those corresponding values for the reactions of NS ($k_H/k_D \cong 2.30$ – 3.08)^{2a} and of BMN ($k_H/k_D \cong 2.25$ – 2.71)^{2b} could be due to the lower degree of bond formation (smaller magnitude of ρ_X and β_X) in the TS for BID. Another interesting result is that the k_H/k_D value for BID increases with an electron-acceptor X ($\delta\sigma_X > 0$) and with an electron-donor Y ($\delta\sigma_Y < 0$), which is exactly opposite to the trends found for NS and BMN, for which the k_H/k_D value decreases with an electron-acceptor X and an electron-donor Y.² This opposite trend may also be due to the looser TS with a lower degree of bond-making. In such a case, the greater negative charge on C_β (with an electron-donor Y) and the greater acidity of NH proton (with an electron-acceptor X) are important for the hydrogen bond bridge formation. This is in contrast to the tightly formed C_α–N bond for the NS and BMN for which the k_H/k_D depends on the extent of bond-making, i.e., a greater degree of bond-making by an electron-donor X and an electron-acceptor Y leads to a stronger hydrogen bond (larger k_H/k_D) which varies more sensitively with substituents X and Y.

This reversal of the trend in variation of k_H/k_D with substituents in the substrate, Y and nucleophile, X, can be rationalized as follows: In the incipient bond formation, interaction of frontier molecular orbitals (FMO), i.e., between the highest occupied MO (HOMO) of the nucleophile, n_N , and the lowest unoccupied MO (LUMO) of the substrate (in this case, the π^* MO of the C_α=C_β double bond, π_S^*) is important, eq 6.¹⁰

$$\Delta E = -\frac{2(c_N c_S \beta_{NS})^2}{\epsilon(\pi_S^*) - \epsilon(n_N)} \quad (6)$$

(7) Taken from Hansch, C.; Leo, A.; Taft, R. W. *Chem. Rev.* **1991**, 91, 165.

(8) (a) Lee, I.; Koh, H. J.; Lee, B.-S.; Sohn, D. S.; Lee, B. C. *J. Chem. Soc. Perkin Trans. 2* **1991**, 1741. (b) Lee, I. *Chem. Soc. Rev.* **1995**, 24, 223.

(9) Hansch, C.; Hoekman, D.; Gao, H. *Chem. Rev.* **1996**, 96, 1045.

(10) (a) Klumpp, G. W. *Reactivity in Organic Chemistry*; Wiley: New York, 1982; Chapter 3. (b) Fleming, I. *Frontier Orbitals and Organic Chemical Reactions*; Wiley: London, 1976; Chapter 3.

Thus an electron acceptor Y in the substrate (lowers π_S^*) and/or an electron donor X in the nucleophile (elevates n_N) stabilizes the TS and also enhances the extent of bond making by increasing interaction (ΔE) since interfrontier energy gap, $\Delta\epsilon = \epsilon(\pi_S^*) - \epsilon(n_N)$, decreases and the coefficient c_N and c_S increases,¹¹ i.e., overlap of the FMOs increases. This is then the normal case in which the extent of bond making (and hence the k_H/k_D value) increases with a stronger electron acceptor Y ($\delta\sigma_Y > 0$) and a stronger donor X ($\delta\sigma_X < 0$) as has been observed in the reactions of benzylamines with NS and BMN. The proton transfer from the nucleophile, N, to the substrate, S, has an effect of further increasing the interaction by elevating the n_N and depressing the π_S^* levels since partial deprotonation of N and partial protonation of S play the role of an electron donation in N and withdrawing substituent in S.¹² If the $\Delta\epsilon = \epsilon(\pi_S^*) - \epsilon(n_N)$ value is too large due to high π_S^* level, the frontier orbital interaction, and hence orbital overlap, becomes small. In such case, the interaction of n_N and π_S^* can be facilitated by a proton transfer initiated by the high acidity of the donor nucleophile, i.e., a more facile N–H proton transfer with a stronger electron-withdrawing X substituent, $\delta\sigma_X > 0$, can reduce the interfrontier energy gap, $\Delta\epsilon$, to reduce the incipient exclusion repulsion in bond formation energy. Thus the degree of proton transfer (and hence k_H/k_D) is greater with an electron acceptor X ($\delta\sigma_X > 0$) coupled with an electron donor Y ($\delta\sigma_Y < 0$). A typical example is the aminolysis of $\text{EtOC(=S)SC}_6\text{H}_4\text{Z}^{13}$ (EtO group is a resonance electron donor with $R = -0.50^9$ so that the LUMO level of $\pi^*_{\text{C=S}}$ should be high leading to a large interfrontier energy gap, $\Delta\epsilon$ in eq 6.) for which k_H/k_D increases with a stronger donor Z ($\delta\sigma_Z < 0$) and a stronger acceptor X ($\delta\sigma_X > 0$), as we found (k_H/k_D increases) in the present work for the addition of benzylamine, $\text{XC}_6\text{H}_4\text{CH}_2\text{ND}_2$ ($\delta\sigma_X > 0$) to BID, $\text{YC}_6\text{H}_4\text{CH}=\text{C(CO)}_2\text{C}_6\text{H}_4$ ($\delta\sigma_Y < 0$). Our experimental results of the trends of change of increasing k_H/k_D for the benzylamine additions to NS and BMN with $\delta\sigma_X < 0$ and $\delta\sigma_Y > 0$ and the opposite trend for those to BID with $\delta\sigma_X > 0$ and $\delta\sigma_Y < 0$ suggest that the activating groups in NS (Z, Z' = H, NO_2) and in BMN (Z, Z' = CN, CN) are stronger resonance electron acceptors than that in BID (Z, Z' = $\text{C}_6\text{H}_4(\text{CO})_2$) since stronger acceptors lower the π_S^* level leading to a narrower interfrontier energy gap, $\Delta\epsilon$ in eq 6. In fact, the additive resonance parameters for the groups are 0.13, 0.30, and 0.05 for (Z, Z') of (H, NO_2), $(\text{CN})_2$, and $(\text{C}_6\text{H}_4(\text{CO})_2)$, respectively,⁹ so that the activating groups in the BID are the weakest electron acceptors.

The activation parameters, ΔH^\ddagger and ΔS^\ddagger in Table 5, are quite similar to those for the reactions of benzylamines with BMN^{2b} with low ΔH^\ddagger and large negative ΔS^\ddagger values. These are consistent with the concurrent addition of nucleophile and proton transfer, **III**. Since exclusion repulsion energy in the bond formation is partially offset by the bond energy of the forming bond and also by the proton transfer from N to C_β , barrier to bond formation is normally low showing little variation with substituent

(11) A conjugative group, YC_6H_4 , attached to C_α depresses the LUMO $p\pi$ orbital of S, and an electron donor X elevates the HOMO and increases the size of the HOMO lobe (n_N).^{10b}

(12) Deprotonation leaves an excess electron (electron-donation) on N, which raises the HOMO, while protonation has an electron-withdrawing effect on S, which depresses the LUMO.^{10b}

(13) Oh, H. K.; Lee, J. Y.; Yun, J. H.; Park, Y. S.; Lee, I. *Int. J. Chem Kinet.* **1998**, *30*, 419.

Table 5. Activation Parameters for the Reactions of Y-Benzylidene-1,3-indandiones with X-Benzylamines in Acetonitrile

X	Y	$\Delta H^\ddagger/\text{kcal mol}^{-1}$	$-\Delta S^\ddagger/\text{cal mol}^{-1} \text{K}^{-1}$
<i>p</i> -OMe	<i>p</i> -OMe	6.1	37
<i>p</i> -OMe	<i>p</i> -Br	6.3	38
<i>p</i> -Cl	<i>p</i> -OMe	6.0	36
<i>p</i> -Cl	<i>p</i> -Br	6.4	37

^a Calculated by the Eyring equation. The maximum errors calculated (by the method of Wiberg, K. B. *Physical Organic Chemistry*; Wiley, New York, 1964; p 378) are $\pm 0.5 \text{ kcal mol}^{-1}$ and $\pm 2 \text{ e.u.}$ for ΔH^\ddagger and ΔS^\ddagger , respectively.

X and Y. This is because the higher barrier for a weaker nucleophile ($\delta\sigma_X > 0$) is partially offset by a stronger hydrogen bond formation. The large negative entropy of activation (-36 to -38 e.u.) is consistent with the four-membered type of constrained TS structure, **III**.²

In summary, the addition of benzylamine (BA) to benzylidene-1,3-indandione (BID) takes place in a single step in which the C_α –N bond formation and proton transfer to C_β of BID occur concurrently with a four-membered cyclic TS structure, **III**. The reaction center carbon, C_α , becomes more negative ($\rho_Y > 0$) on going from the reactant to TS, but the negative charge development is weaker than that for the reactions of NS. The structure–reactivity behaviors (k_2 , ρ_X , β_X , and ρ_Y) are intermediate between the two series of addition reactions of BA to NS and to BMN in acetonitrile. The sign and magnitude of the cross-interaction constant, ρ_{XY} , is comparable to those for the normal bond formation processes in the $\text{S}_\text{N}2$ and addition reactions. The normal kinetic isotope effects, k_H/k_D (> 1), involving deuterated benzylamine nucleophiles ($\text{XC}_6\text{H}_4\text{CH}_2\text{ND}_2$), are somewhat smaller than those corresponding values for the reactions of NS and BMN due to the smaller extent of bond formation in the TS. The relatively low ΔH^\ddagger and large negative ΔS^\ddagger values are also consistent with the mechanism proposed.

Experimental Section

Materials. Merck GR acetonitrile was used after three distillations. The benzylamine nucleophiles (Aldrich) were used after recrystallization. 1,3-Indandione and benzaldehydes were Aldrich reagents.

Preparations of Benzylidene-1,3-indandiones. The benzylidene-1,3-indandiones were prepared by the literature method of Behere and Nayak.¹⁴ A solution of 1,3-indandione (10 mmol) and benzaldehyde (10 mmol) in absolute ethanol was treated with a few drops of piperidine and refluxed for 1 h, during which a pale yellow solid separated. It was filtered off and purified by repeated recrystallizations from ethanol (yield $> 85\%$). Melting points, FT-IR, and ^1H and ^{13}C NMR (400 MHz) data were found to agree well with the literature values.¹⁵

Kinetic Measurement. The reaction was followed spectrophotometrically by monitoring the decrease in the concentration of benzylidene-1,3-indandione, [BID], at λ_{max} of the substrate to over 80% completion. The reaction was studied under pseudo-first-order condition, $[\text{BID}] = 8.0 \times 10^{-5} \text{ M}$ and $[\text{BA}] = (1.0\text{--}8.0) \times 10^{-3} \text{ M}$ at $25.0 \pm 0.1 \text{ }^\circ\text{C}$. The pseudo-first-order rate constant, k_{obs} , was determined from the slope of the plot ($r > 0.994$) of $\ln[\text{BID}]$ vs time and second-order rate constants, k_2 , were obtained from the slope of a plot ($r > 0.995$) of k_{obs} vs $[\text{BA}]$ with more than eight concentrations of benzyl-

(14) Behera, R. K.; Nayak, A. *Indian J. Chem.* **1976**, *14B*, 223.

(15) Pritchard, R. B.; Lough, C. E.; Currie, D. J.; Holmes, H. L. *Can. J. Chem.* **1968**, *46*, 775.

amine, carried out more than three runs, and were reproducible to within $\pm 3\%$. Typical example of k_{obs} vs [BA] data is shown in Table 1.

Product Analysis. Benzylidene-1,3-indandione (0.01 mol) and benzylamine (0.05 mole) were reacted in acetonitrile at 25.0 °C. After more than 15 half-lives, solvent was removed under reduced pressure, and product was separated by column chromatography (silica gel, 20% ethyl acetate-*n*-hexane). Analytical data of the product gave the following results: mp 207–209 °C, IR (KBr), 3345 (N–H, stretch), 3048 (C–H, alkene), 2915 (C–H, CH₃), 1720 (C=O), 1586 cm⁻¹ (C=C,

aromatic); ¹H NMR (400 MHz, CDCl₃), δ 2.35 (3 H, s, CH₃), 3.19 (2 H, s, benzyl), 3.53 (1 H, d, CO–CH, $J = 13.67$ Hz), 3.82 (1 H, d, NH–CH, $J = 13.67$ Hz), 6.60–7.44 (12 H, m, aromatic); ¹³C NMR (100.4 MHz, CDCl₃), δ 195.2, 137.5, 135.3, 134.2, 132.8, 129.5, 129.0, 128.7, 128.5, 128.0, 70.6, 51.1, 45.3, 20.5.

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