JOC The Journal of Organic Chemistry
Article
pubs.acs.org/joc

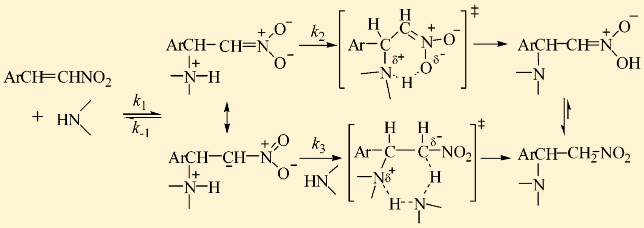
Kinetic Study on Michael-Type Reactions of β-Nitrostyrenes with Cyclic Secondary Amines in Acetonitrile: Transition-State Structures and Reaction Mechanism Deduced from Negative Enthalpy of Activation and Analyses of LFERs

Ik-Hwan Um,*[,†] Ji-Sun Kang,[†] and Jong-Yoon Park[‡]

[†]Department of Chemistry and Division of Nano Sciences and [‡]Department of Science Education, Ewha Womans University, Seoul 120-750, Korea

Ⓢ *Supporting Information*

ABSTRACT: A kinetic study is reported for the Michael-type reactions of X-substituted β-nitrostyrenes (**1a–j**) with a series of cyclic secondary amines in MeCN. The plots of pseudo-first-order rate constant k_{obsd} vs [amine] curve upward, indicating that the reactions proceed through catalyzed and uncatalyzed routes. The dissection of k_{obsd} into Kk_2 and Kk_3 (i.e., the rate constants for the uncatalyzed and catalyzed routes, respectively) revealed that Kk_3 is much larger than Kk_2, implying that the reactions proceed mainly through the catalyzed route when [amine] > 0.01 M. Strikingly, the reactivity of β-nitrostyrene (**1g**) toward piperidine decreases as the reaction temperature increases. Consequently, a negative enthalpy of activation is obtained, indicating that the reaction proceeds through a relatively stable intermediate. The Brønsted-type plots for the reactions of **1g** are linear with β_{nuc} = 0.51 and 0.61, and the Hammett plots for the reactions of **1a–j** are also linear with ρ_X = 0.84 and 2.10 for the uncatalyzed and catalyzed routes, respectively. The reactions are concluded to proceed through six-membered cyclic transition states for both the catalyzed and uncatalyzed routes. The effects of the substituent X on reactivity and factors influencing β_{nuc} and ρ_X obtained in this study are discussed.

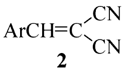


INTRODUCTION

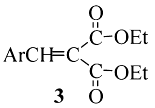
Michael-type reactions of olefins activated by strong electron-withdrawing groups (e.g., **1–4**) are an important type of reaction not only for synthetic chemists but also for mechanistic investigators. Accordingly, numerous synthetic and mechanistic studies have been carried out.[1−8] The Michael-type reactions of activated olefins with anionic nucleophiles have generally been reported to proceed through a stepwise mechanism in which nucleophilic attack is the rate-determining step (RDS).[1,4,5] The reactions of activated olefins with amine nucleophiles have also been reported to proceed through a zwitterionic intermediate ($T^{\pm}$) with imbalanced transition states (TSs) in aqueous solution, in which the delocalization of the negative charge into the activating group lags behind the C−N bond formation (i.e., the principle of nonperfect synchronization).[4,5]

$ArCH{=}CH{-}NO_2$

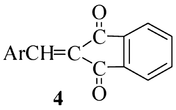
1



2



3



4

However, the mechanism for the Michael-type reactions of activated olefins with amines in aprotic solvents has been much less studied, although most organic syntheses are carried out in aprotic solvents. Accordingly, the reaction mechanism is not well understood but remains controversial, i.e., a stepwise mechanism versus a concerted pathway.[6−8]

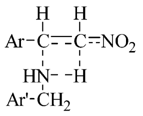
The Michael-type reaction of β-nitrostyrene (**1**, Ar = Ph) with anilines in MeCN has been reported to proceed through a stepwise mechanism in which formation of $T^{\pm}$ is the RDS.[6a] In contrast, Jalani et al. reported that the reactions of β-nitrostyrene with a series of benzylamines in MeCN proceed through a stepwise mechanism, in which formation of $T^{\pm}$ occurs in the preequilibrium, and the decomposition of $T^{\pm}$ to the reaction product via proton transfer occurs through uncatalyzed and catalyzed routes.[6b] A similar conclusion was drawn by Popov et al. for the Michael-type reactions of E-(2-furyl)nitroethene with primary and secondary amines in MeCN.[7]

Oh et al. also reported that the Michael-type reactions of β-nitrostyrene with benzylamines in MeCN follow two mechanistic routes (i.e., the uncatalyzed and catalyzed routes)[8a] as reported previously by Jalani et al.[6b] However, Oh et al. concluded that the reactions proceed through a concerted mechanism with the TS structures TS_I and TS_{II} for the uncatalyzed and catalyzed routes, respectively.[8a] Besides, the reactions of **2–4** with benzylamines in MeCN have also been concluded to proceed through a concerted mechanism with a

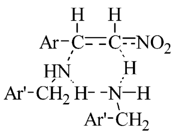
Received: April 9, 2013
Published: May 8, 2013

dx.doi.org/10.1021/jo4007442 | J. Org. Chem. 2013, 78, 5604−5610

four-membered cyclic TS (e.g., similar to TS_I).[8b−d] Clearly, the concerted mechanism suggested by Oh et al.[8a] for the reaction of β-nitrostyrene with benzylamines in MeCN contrasts with the stepwise mechanism proposed by Jalani et el.[6b] for the same reaction, indicating that more systematic studies are necessary to clarify the reaction mechanism.



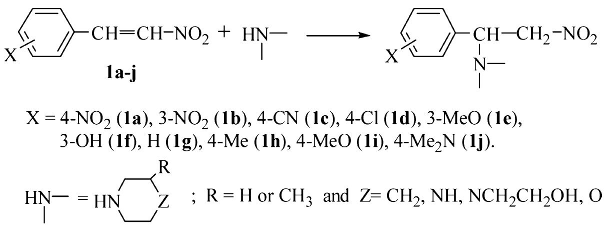
TS_I



TS_{II}

To shed more light on the reaction mechanism, we have carried out a systematic study on the Michael-type reactions of X-substituted β-nitrostyrenes (**1a−j**) with a series of cyclic secondary amines in MeCN as shown in Scheme 1. The kinetic results have been analyzed through linear free energy relationships (e.g., the Brønsted-type and Hammett correlations) together with the activation parameters (e.g., $\Delta H^\ddagger$ and $\Delta S^\ddagger$). A Brønsted-type analysis is possible now because the pK_a values of the cyclic secondary amines used in this study in MeCN have only recently become available.[9] We wish to report that the reactions of **1a−j** with the amines in MeCN proceed through a stepwise mechanism, in which the formation of an intermediate occurs in the preequilibrium state, and the decomposition of the intermediate into the reaction product follows two mechanistic routes, viz. uncatalyzed and catalyzed ones.

Scheme 1



X = 4-NO_2 (**1a**), 3-NO_2 (**1b**), 4-CN (**1c**), 4-Cl (**1d**), 3-MeO (**1e**), 3-OH (**1f**), H (**1g**), 4-Me (**1h**), 4-MeO (**1i**), 4-Me_2N (**1j**).

; R = H or CH_3 and Z= CH_2, NH, NCH_2CH_2OH, O

RESULTS AND DISCUSSION

The kinetic study was performed spectrophotometrically by monitoring the disappearance of the substrate under pseudo-first-order conditions (e.g., the concentration of the amines was kept in excess over that of the substrates). All of the reactions obeyed first-order kinetics, and the pseudo-first-order rate constants (k_{obsd}) were calculated from the equation, $\ln A_t = -k_{obsd}t + C$. The plots of $\ln A_t$ vs t were linear over 90% of the total reaction. The correlation coefficient for the linear regression was always over 0.9998. The uncertainty in the k_{obsd} values was estimated to be less than ±3% from duplicate runs. As shown in Figure 1A, the plot of k_{obsd} against the amine concentration [NH] for the reaction of β-nitrostyrene (**1g**) with piperidine curves upward as a function of the amine concentration. Similarly curved plots are shown in Figures S1A −S13A in the Supporting Information for the other reactions studied in this work. The k_{obsd} values together with detailed kinetic conditions are summarized in Tables S1−S18 in the Supporting Information.

Dissection of k_{obsd} into Kk_2 and Kk_3. The upward curvature shown in Figure 1A (and in Figures S1A−S13A in the Supporting Information) is typical of reactions in which a second amine molecule behaves as a general acid/base catalyst. Thus, one can suggest that the reactions in question proceed through a stepwise mechanism as illustrated in Scheme 2, in which the resonance structures I and II are the intermediate while TS_{III} (or TS_{IV}) and TS_V represent the TS structures for the uncatalyzed and catalyzed routes, respectively.

One can express k_{obsd} as eq 1 on the basis of the kinetic results and the mechanism proposed in Scheme 2, in which [NH] represents the concentration of the amines studied. Equation 1 can be simplified as eq 2 under the assumption, $k_{-1} \gg k_2 + k_3[NH]$. Thus, one would expect the plot of k_{obsd}/[NH] vs [NH] to be linear if the above assumption is valid.

$$k_{obsd} = (k_1k_2[NH] + k_1k_3[NH]^2)/(k_{-1} + k_2 + k_3[NH]) \tag{1}$$

$$k_{obsd}/[NH] = Kk_2 + Kk_3[NH], \text{ where } K = k_1/k_{-1} \tag{2}$$

In fact, as shown in Figure 1B, the plot of k_{obsd}/[NH] vs [NH] is linear for the reaction of **1g** with piperidine. The corresponding plots for the reactions of **1g** with the other amines are also linear

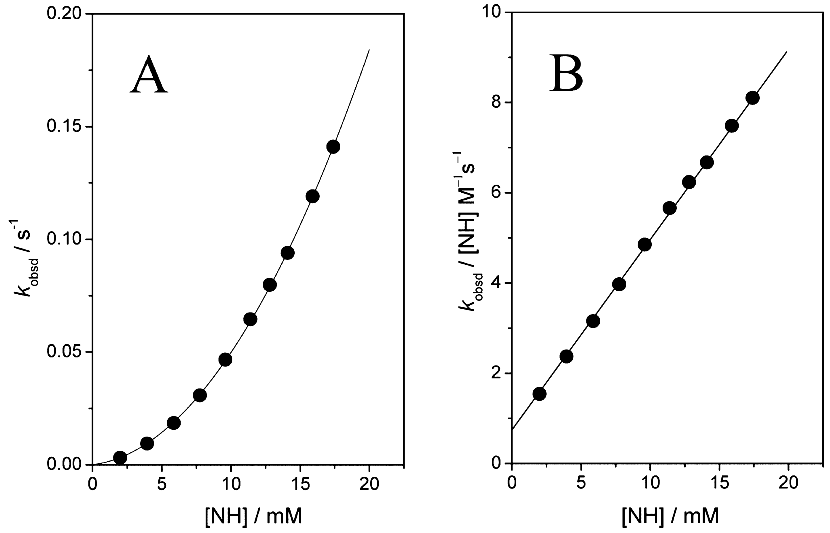
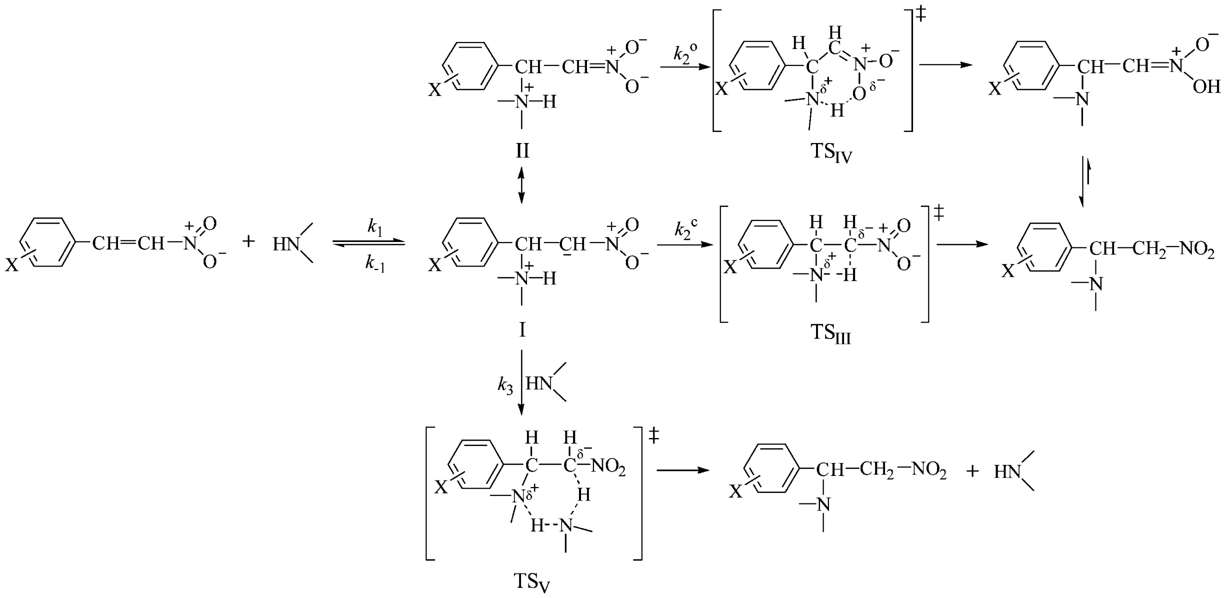


Figure 1. Plots of k_{obsd} vs [NH] (A) and k_{obsd}/[NH] vs [NH] (B) for the reaction of β-nitrostyrene (**1g**) with piperidine in MeCN at 25.0 ± 0.1 °C.

Scheme 2



as shown in Figures S1B−S4B in the Supporting Information, indicating that the above assumption is valid under the experimental conditions. Thus, the Kk_2 and Kk_3 values were calculated from the intercept and the slope of the linear plots of k_{obsd}/[NH] vs [NH], respectively. The Kk_2 and Kk_3 values calculated in this way are summarized in Table 1 for the reactions of **1g** with all the amines studied.

Table 1. Summary of Kinetic Data for the Reactions of *β*-Nitrostyrene (1g) with Cyclic Secondary Amines in MeCN at 25.0 ± 0.1 °C

	amine	pK_a[a]	Kk_2/M^{-1}s^{-1}	Kk_3/M^{-2}s^{-1}
1	piperidine	18.8	0.685	428
2	3-methylpiperidine	18.6	0.642	307
3	piperazine	18.5	0.695	720
4	1-(2-hydroxyethyl)piperazine	17.6	0.180	71.3
5	morpholine	16.6	0.0546	19.0

[a] The pK_a data for the conjugate acid of the amine in MeCN were taken from ref 9.

As shown in Table 1, the Kk_2 and Kk_3 values for the reactions of **1g** decrease as the amine basicity decreases, except those for the reaction with piperazine. However, this is not an unexpected result, since piperazine has two basic sites. It is also noted that the rate constant for the catalyzed route (Kk_3) is much larger than that for the uncatalyzed process (Kk_2) in all cases, indicating that the current reactions proceed mainly through the catalyzed process when the amine concentration is high (e.g., [amine] > 0.01 M).

Brønsted-Type Analysis: Effect of Amine Basicity on k_2 and k_3. To obtain more information on the TS structures, Brønsted-type plots have been constructed for the reactions of **1g** with the cyclic secondary amines. As shown in Figure 2, the Brønsted-type plots exhibit excellent linear correlations with β_{nuc} = 0.51 for Kk_2 and β_{nuc} = 0.61 for Kk_3, when the rate constants and pK_a values are corrected statistically by p and q (i.e., $p = 2$ while $q = 1$ except $q = 2$ for piperazine).[10] The β_{nuc} value found for the current reactions is roughly β_{nuc} = 0.5−0.6, which is typical of aminolysis of esters reported previously to proceed through a concerted mechanism, but is much smaller than the value of 0.9 ± 0.1 reported for the reactions proceeding through a stepwise mechanism.[11−15] Thus, one might suggest that the current reactions proceed through a concerted mechanism with TS structures similar to TS$_{III}$ and TS$_V$ for the uncatalyzed and catalyzed routes, respectively, as proposed previously by Oh et al. for the reactions of **1g** with a series of benzylamines in MeCN.[8a]

However, we propose that the current reactions proceed through a stepwise mechanism as illustrated in Scheme 2 for the following reasons, although the β_{nuc} value of 0.51 or 0.61 obtained in this study is much smaller than that reported for the aminolysis of esters which proceeds through a stepwise mechanism. It has been reported that the k_2 and k_3 values for aminolysis of esters are independent of the amine basicity.[11−13,16,17] Gresser and Jencks concluded that amine basicity does not affect k_2 in the aminolysis of diaryl carbonates, since there is little or no electron donation from the aminium moiety of the zwitterionic tetrahedral intermediate $T^{\pm}$ to push out the nucleofuge.[11a] A similar conclusion was drawn by Castro et al. for the aminolysis of ethyl phenyl thionocarbonate,[16a] methyl 4-nitrophenyl thionocarbonate,[16b] 4-methylphenyl 4-nitrophenyl thionocarbonate,[16c] and 3-methoxyphenyl 4-nitrophenyl thionocarbonate.[16d] It is also well-known that k_3 is independent of the amine basicity, since a more basic amine would deprotonate more rapidly from the aminium moiety of $T^{\pm}$, while the aminium ion would tend to hold the proton more strongly as the amine becomes more basic.[17] In contrast, the k_2 and k_3 values in the current reactions would be highly dependent on the amine basicity. This is because the rate constants for the proton transfer processes (i.e., k_2 for the uncatalyzed route through TS$_{III}$ or TS$_{IV}$, and k_3 for the catalyzed route via TS$_V$) should decrease as the amine basicity increases or vice versa. This accounts for the fact that the β_{nuc} value obtained in this study is much smaller than that reported for aminolysis of esters, which proceeds through a stepwise mechanism.

Negative Enthalpy of Activation: Evidence for Presence of a Stable Intermediate. To obtain further information on the reaction mechanism, the activation parameters ($\Delta H^{\ddagger}$ and $\Delta S^{\ddagger}$) for the reaction of **1g** with piperidine have been calculated from the rate constants measured at five different temperatures.

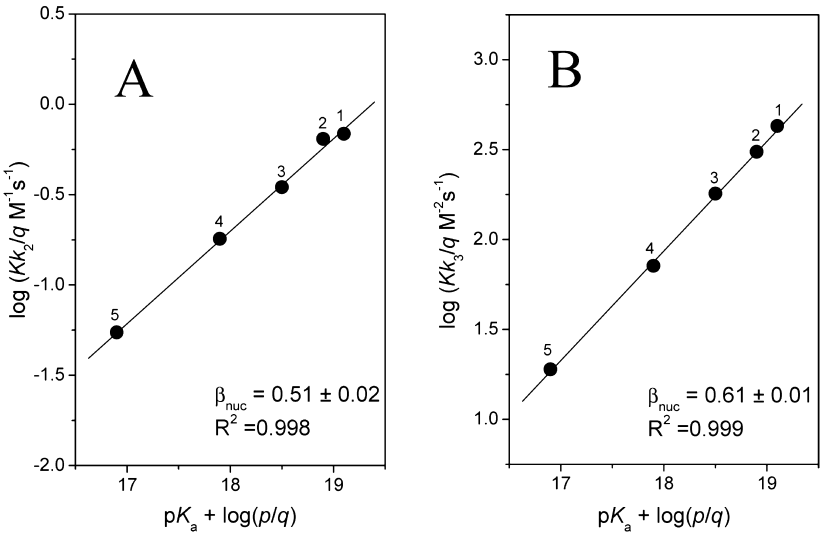


Figure 2. Brønsted-type plots for the reactions of *β*-nitrostyrene (**1g**) with cyclic secondary amines in MeCN at 25.0 ± 0.1 °C. log Kk_2 vs pK_a (A); log Kk_3 vs pK_a (B). The identity of the points is given in Table 1.

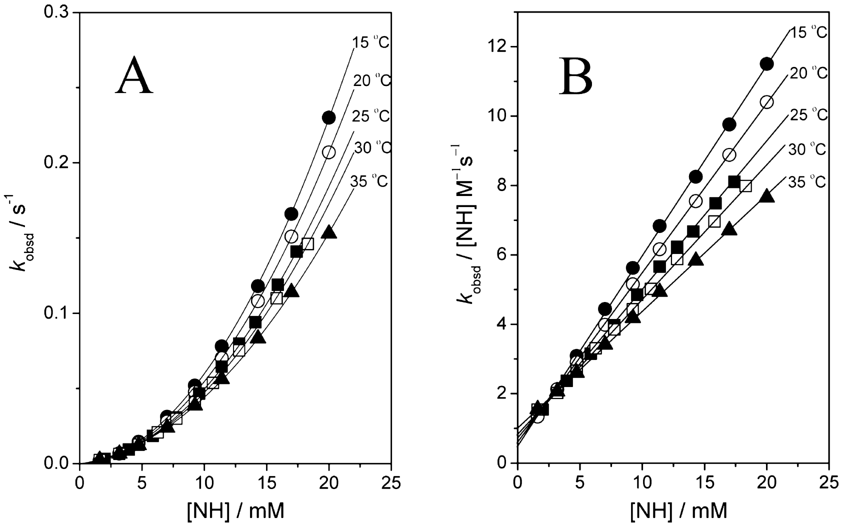


Figure 3. Plots of k_{obsd} vs [NH] (A) and k_{obsd}/[NH] vs [NH] (B) for the Michael-type reaction of *β*-nitrostyrene (**1g**) with piperidine in MeCN at 15.0 (●), 20.0 (○), 25.0 (■), 30.0 (□), 35.0 (▲) ± 0.1 °C.

Table 2. Summary of Kinetic Results for the Reactions of *β*-Nitrostyrene (1g) with Piperidine in MeCN at Five Different Temperatures

	15.0 °C	20.0 °C	25.0 °C	30.0 °C	35.0 °C	$\Delta H^\ddagger$ (kcal mol^{-1})	$\Delta S^\ddagger$ (eu)
Kk_2 (M^{-1} s^{-1})	0.483	0.568	0.685	0.848	1.04	6.22 ± 0.28	−38.3 ± 1.0
Kk_3 (M^{-2} s^{-1})	550	490	428	389	334	−4.92 ± 0.18	−63.0 ± 0.6

As shown in Figure 3, the plots of k_{obsd} vs [NH] curve upward (A), while those of k_{obsd}/[NH] vs [NH] are linear with positive intercept (B). *Strikingly, the k_{obsd} value decreases as the reaction temperature increases.* It is also noted that the slope of the linear plots in Figure 3B decreases as the reaction temperature increases, while the intercept of the linear plots increases with increasing reaction temperature.

The Kk_2 and Kk_3 values for the reactions of **1g** with piperidine calculated from the intercept and slope of the linear plots are summarized in Table 2 and are illustrated graphically as a function of 1/T in Figure 4. The Arrhenius plots exhibit excellent linear correlations for both the uncatalyzed and catalyzed reactions, indicating that the $\Delta H^\ddagger$ and $\Delta S^\ddagger$ values calculated in this way are highly reliable.

As shown in Table 2, the $\Delta H^\ddagger$ values are 6.22 and −4.92 kcal mol^{-1} for the uncatalyzed and catalyzed reactions, respectively. The negative $\Delta H^\ddagger$ value found for the catalyzed route is quite surprising. However, it results from the fact that the reactivity of **1g** decreases as the reaction temperature increases. A negative $\Delta H^\ddagger$ value is definitive evidence for reactions which proceed through a relatively stable intermediate.[18] Thus, one can suggest that the zwitterionic intermediate I (or II) as illustrated in Scheme 2 is stable even in the aprotic solvent.

It is well-known that MeCN is a good cation solvator, due to the presence of nonbonding electrons.[19] It is noted that the

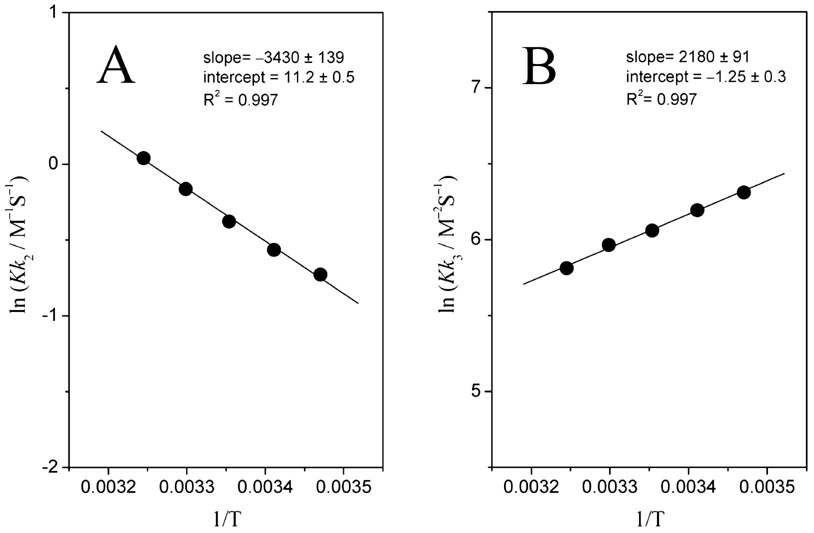


Figure 4. Arrhenius plots for the reactions of *β*-nitrostyrene (**1g**) with piperidine in MeCN. Kk_2 (A) and Kk_3 (B).

positive charge in the zwitterionic intermediate I (or II) is localized on the NH^+ moiety, while the negative charge is delocalized through the *β*-carbon and the NO_2 group. Accordingly, I (or II), which might behave as a cation, could be strongly solvated in MeCN through ion-dipole interactions. This idea is consistent with the large negative $\Delta S^{\ddagger}$ values shown in Table 2 (i.e., −38.3 and −63.0 eu for the uncatalyzed and catalyzed processes, respectively).

Effect of Substituent X on Reactivity and Reaction Mechanism. To obtain more conclusive information on the TS structures, the reactions of X-substituted-*β*-nitrostyrenes (**1a**−**j**) with piperidine have been carried out. As shown in Figures S5A-S13A in the Supporting Information, the plots of k_{obsd} vs [NH] curve upward in all cases. On the other hand, the plots of k_{obsd}/[NH] vs [NH] shown in Figures S5B−S13B in the Supporting Information are linear with a positive intercept, implying that $k_{-1} \gg k_2 + k_3[NH]$. Thus, the Kk_2 and Kk_3 values were calculated from the intercept and slope of the linear plots of k_{obsd}/[NH] vs [NH], respectively. The Kk_2 and Kk_3 values calculated in this way are summarized together with the σ_X values of the substituent X in Table 3.

As shown in Table 3, the rate constant for the uncatalyzed reactions (i.e., Kk_2) decreases as the substituent X changes from a strong electron-withdrawing group (EWG) to a strong electron-donating group (EDG), e.g., it decreases from 5.08 M^{-1} s^{-1} to 0.685 and 0.210 M^{-1} s^{-1} as the substituent X changes from 4-NO_2 to H and 4-NMe_2, in turn. A similar result is observed for the catalyzed reactions, although Kk_3 is much larger than Kk_2 for a given substituent X.

Table 3. Summary of kinetic Data for the Reactions of X-Substituted *β*-Nitrostyrenes (1a−j) with Piperidine in MeCN at 25.0 ± 0.1 °C

entry	X	σ_X[a]	Kk_2 (M^{-1} s^{-1})	Kk_3 (M^{-2} s^{-1})
1a	4-NO_2	0.78	5.08	11800
1b	3-NO_2	0.71	3.21	10700
1c	4-CN	0.66	2.93	7520
1d	4-Cl	0.23	1.11	1190
1e	3-MeO	0.12	0.685	499
1f	3-OH	0.12	0.761	375
1g	H	0	0.685	428
1h	4-Me	−0.17	0.569	165
1i	4-MeO	−0.27	0.463	66.5
1j	4-NMe_2	−0.83	0.210	5.63

[a] The σ_X values were taken from ref 20.

The effects of the substituent X on Kk_2 and Kk_3 are illustrated in Figure 5A and B, respectively. The Hammett plots are linear with $\rho_X = 0.84$ for Kk_2 and $\rho_X = 2.10$ for Kk_3, indicating that the rate constant for the catalyzed route (i.e., Kk_3) is significantly more sensitive to the electronic nature of the substituent X than that for the uncatalyzed route (i.e., Kk_2).

Many factors have been reported to influence the magnitude of ρ_X (e.g., the charge type and basicity of nucleophile, the nature of the reaction medium, the distance from the reaction site to the substituent and the nature of the reaction mechanism).[14b,21,22] Generally, a large ρ_X value has been reported for reactions with an anionic nucleophile (or with a strongly basic nucleophile)[21] and for reactions in aprotic solvents,[21] while a small ρ_X value has been obtained for reactions of substrates possessing one $-CH_2-$ or $-CH{=}CH-$ group[14b,21] and for reactions reported to proceed through an S_N2 mechanism.[22] The nucleophile, substrates and reaction medium in this study are common for the catalyzed and uncatalyzed routes. Thus, the above factors cannot be responsible for the large difference in the ρ_X values found in this study (i.e., $\rho_X = 0.84$ and 2.10 for Kk_2 and Kk_3, respectively).

The electronic nature of the substituent X would affect not only the microscopic rate constants (i.e., $K = k_1/k_{-1}$, k_2 and k_3) but also the contribution of the resonance structures I and II illustrated in Scheme 2. The resonance structure I would be expected to become the major contributor when the substituent X is a strong EWG or vice versa. Besides, the equilibrium constant K and the acidity of the NH^+ moiety of the zwitterionic intermediate should increase as the substituent X changes from an EDG to an EWG. It is apparent that the enhanced acidity would accelerate the proton transfer, if it occurs from the NH^+ moiety to the negatively charged *β*-carbon. Thus, the Hammett plots for both the Kk_2 and Kk_3 terms would result in a large ρ_X if the reactions proceed through TS_{III} for the uncatalyzed routes and via TS_V for the catalyzed reactions.

On the contrary, if the proton transfer occurs from the NH^+ moiety to the negatively charged oxygen atom of the NO_2 group (i.e., through TS_{IV} for the uncatalyzed route), the rate of proton transfer would not increase significantly although the substituent

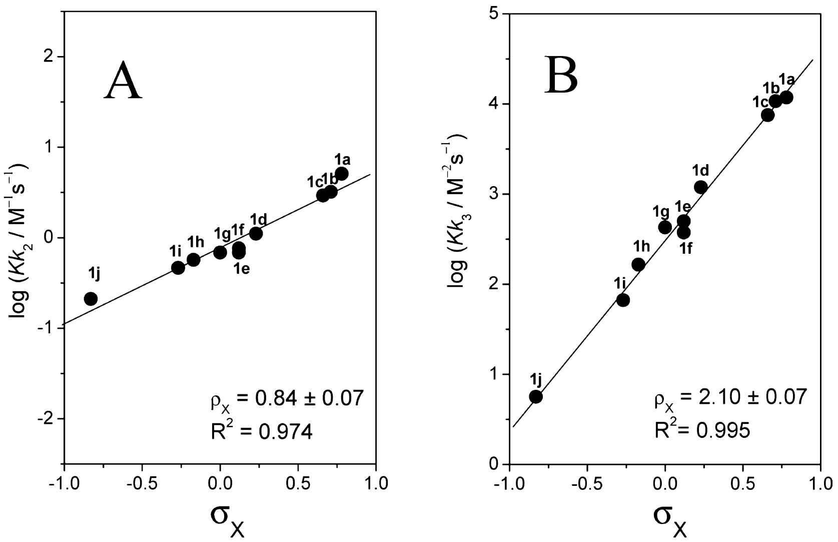


Figure 5. Hammett plots for the reactions of X-substituted β-nitrostyrenes (**1a**−**j**) with piperidine in MeCN at 25.0 ± 0.1 °C. log Kk_2 vs σ_X (A); log Kk_3 vs σ_X (B). The identity of points is given in Table 3.

X becomes a strong EWG. This is because the resonance structure II, from which TS_{IV} is formed, would be the minor contributor when the substituent X becomes a strong EWG. Accordingly, a small ρ_X value would be expected if the uncatalyzed reactions proceed through TS_{IV}. In fact, Figure 5 shows that the ρ_X value for the uncatalyzed reaction is much smaller than that for the catalyzed reaction. Thus, one can conclude that the uncatalyzed reactions proceed through TS_{IV}, but not via TS_{III}. This is consistent with the idea that the four-membered cyclic TS (i.e., TS_{III}) would be much less stable than the six-membered one (i.e., TS_{IV}).

■ CONCLUSIONS

The current study has allowed us to conclude the following: (1) The curved plots of k_{obsd} vs [NH] suggest that the reactions proceed through catalyzed and uncatalyzed routes. The dissection of k_{obsd} into Kk_2 and Kk_3 has revealed that the reactions proceed mainly through the catalyzed route when [amine] > 0.01M. (2) The Brønsted-type plots for the reactions of **1g** with the amines are linear with β_{nuc} = 0.51 and 0.61 for the uncatalyzed and catalyzed reactions, respectively. The decrease in the rate of proton transfer from the NH^+ moiety as the amine basicity increases is responsible for the small β_{nuc} values. (3) The negative $\Delta H^{\ddagger}$ value found in this study is definitive evidence for the presence of a relatively stable intermediate. (4) The electronic nature of the substituent X affects the contribution of the resonance structures I and II, i.e., the former becomes the major contributor when X is a strong EWG and vice versa. (5) The Hammett plots for the reactions of **1a**−**j** with piperidine are linear with ρ_X = 0.84 and 2.10 for Kk_2 and Kk_3, respectively. The small ρ_X value for the uncatalyzed reactions supports the hypothesis that the reactions proceed through TS_{IV} rather than through TS_{III}.

■ EXPERIMENTAL SECTION

Materials. X-Substituted β-nitrostyrenes (**1a**−**j**) were readily synthesized by the literature methods.[8a,23] The crude products were purified by column chromatography (silica gel and 20% ethyl acetate/80% *n*-hexane), and their purity was checked by their melting points and ^{1}H NMR spectra. The amines studied were of the highest quality available. MeCN was distilled over P_2O_5 and stored under nitrogen.

Kinetics. The kinetic study was carried out using a UV−vis spectrophotometer for slow reactions ($t_{1/2}$ > 10 s) or a stopped-flow spectrophotometer for fast reactions ($t_{1/2} \leq$ 10 s) equipped with a constant temperature circulating bath. The reactions were followed by monitoring the disappearance of the substrate at a fixed wavelength corresponding to the maximum absorption (λ_{max}, e.g., 309 nm for β-nitrostyrene). ^{1}H NMR spectra for the reactions confirmed the reaction products as previously reported.[5,8a] Typically, the reaction was initiated by the injection of 5 μL of a 0.02 M β-nitrostyrene (**1g**) stock solution (MeCN) via a 10 μL syringe into a 10 mm UV cell containing 2.50 mL of the reaction medium and the amine. The amine stock solution (ca. 0.2 M) was prepared in a 25.0 mL volumetric flask under nitrogen. The transfer of the solutions was carried out by means of gastight syringes. All reactions were carried out under pseudo-first-order conditions in which the amine concentrations were at least 20 times greater than the substrate concentration.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

Figures S1−S13 for plots of k_{obsd} vs [NH] (A) and k_{obsd}/[NH] vs [NH] (B) for the reactions of β-nitrostyrenes with alicyclic secondary amines in MeCN at 25.0 ± 0.1 °C. Tables S1−S14 for kinetic conditions and data for the reactions of β-nitrostyrenes with alicyclic secondary amines in MeCN at 25.0 ± 0.1 °C. Tables S15−S18 for kinetic conditions and data for the reactions of β-nitrostyrene **1g** with piperidine in MeCN at 5 different temperatures. This material is available free of charge via the Internet at http://pubs.acs.org.

■ AUTHOR INFORMATION

Corresponding Author

*E-mail: ihum@ewha.ac.kr.

Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

This research was supported by Basic Science Research Program through the National Research Foundation of Korea (NRF) funded by the Ministry of Education, Science and Technology (2012-R1A1B-3001637). J.S.K. is also grateful for the BK 21 Scholarship.

■ REFERENCES

(1) (a) Smith, M. B.; March, J. *March's Advanced Organic Chemistry*, 5th ed.; Wiley-Interscience: New York, 2001; p 976. (b) Lowry, T. H.; Richardson, K. S. *Mechanism and Theory in Organic Chemistry*, 3rd ed.; Harper Collins Publishers: New York, 1987; p 622. (c) Carey, F. A.; Sundberg, R. J. *Advanced Organic Chemistry Part B: Reactions and Synthesis*, 3rd ed.; Plenum Press: New York, 1990; pp 39−46.

(2) (a) Mortezaei, S.; Catarineu, N. R.; Canary, J. W. *J. Am. Chem. Soc.* **2012**, *134*, 8054−8057. (b) Sharma, A. K.; Sunoj, R. B. *J. Org. Chem.* **2012**, *77*, 10516−10524. (c) Liu, Y. Z.; Cheng, R. L.; Xu, P. F. *J. Org. Chem.* **2011**, *76*, 2884−2887. (d) Anderson, J. C.; Stepney, G. J.; Mills, M. R.; Horsfall, L. R.; Blake, A. J.; Lewis, W. *J. Org. Chem.* **2011**, *76*, 1961−1971.

(3) (a) Trost, B. M.; Hirano, K. *Angew. Chem., Int. Ed.* **2012**, *51*, 6480−6483. (b) Tuchman-Shukron, L.; Miller, S. J.; Portnoy, M. *Chem.—Eur. J.* **2012**, *18*, 2290−2296. (c) Nugent, T. C.; Bibi, A.; Sadiq, A.; Shoaib, M.; Umar, M. N.; Tehrani, F. N. *Org. Biomol. Chem.* **2012**, *10*, 9287−9294. (d) Zhou, J.; Chang, Q.; Gan, L. H.; Peng, Y. G. *Org. Biomol. Chem.* **2012**, *10*, 6732−6739. (e) Puglisi, A.; Benaglia, M.; Raimondi, L.; Lay, L.; Poletti, L. *Org. Biomol. Chem.* **2011**, *9*, 3295−3302.

(4) Reviews: (a) Bernasconi, C. F. *Acc. Chem. Res.* **2011**, *44*, 1253−1254. (b) Bernasconi, C. F. *Adv. Phys. Org. Chem.* **2010**, *44*, 223−324. (c) Bernasconi, C. F.; Rappoport, Z. *Acc. Chem. Res.* **2009**, *42*, 993−1003. (d) Bernasconi, C. F. *Pure Appl. Chem.* **2009**, *81*, 649−665.

(5) (a) Bernasconi, C. F.; Paschalis, P. *J. Am. Chem. Soc.* **1989**, *111*, 5893−5902. (b) Bernasconi, C. F.; Renfrow, R. A.; Tia, P. R. *J. Am. Chem. Soc.* **1986**, *108*, 4541−4549. (c) Bernasconi, C. F.; Schuck, D. F. *J. Org. Chem.* **1992**, *57*, 2365−2373. (d) Bernasconi, C. F.; Zitomer, J. L.; Schuck, D. F. *J. Org. Chem.* **1992**, *57*, 1132−1139.

(6) (a) Varghese, B.; Kothari, S.; Banerji, K. K. *J. Chem. Res., Synop.* **1998**, 422−423. (b) Jalani, N.; Kothari, S.; Banerji, K. K. *Can. J. Chem.* **1996**, *74*, 625−629.

(7) Popov, A. F.; Perepichka, I. F.; Kostenko, L. I. *J. Chem. Soc., Perkin Trans. 2* **1989**, 395−400.

(8) (a) Oh, H. K.; Yang, J. H.; Sung, D. D.; Lee, I. *J. Chem. Soc., Perkin Trans. 2* **2000**, 101−105. (b) Oh, H. K.; Kim, I. K.; Lee, H. W.; Lee, I. *J. Org. Chem.* **2004**, *69*, 3806−3810. (c) Oh, H. K.; Yang, J. H.; Lee, H. W.; Lee, I. *J. Org. Chem.* **2000**, *65*, 5391−5395. (d) Oh, H. K.; Yang, J. H.; Lee, H. W.; Lee, I. *J. Org. Chem.* **2000**, *65*, 2188−2191.

(9) (a) Spillane, W. J; McGrath, P.; Brack, C.; O'Byrne, A. B. *J. Org. Chem.* **2001**, *66*, 6313−6316. (b) Um, I. H.; Bae, A. R. *J. Org. Chem.* **2011**, *76*, 7510−7515.

(10) Bell, R. P. *The Proton in Chemistry*; Methuen: London, 1959; p 159.

(11) (a) Gresser, M. J.; Jencks, W. P. *J. Am. Chem. Soc.* **1977**, *99*, 6970−6980. (b) Jencks, W. P. *Chem. Rev.* **1985**, *85*, 511−527. (c) Jencks, W. P. *Chem. Soc. Rev.* **1981**, *10*, 345−375. (d) Jencks, W. P. *Acc. Chem. Res.* **1980**, *13*, 161−169.

(12) (a) Castro, E. A. *Chem. Rev.* **1999**, *99*, 3505−3524. (b) Castro, E. A.; Ugarte, D.; Rojas, M. F.; Pavez, P.; Santos, J. G. *Int. J. Chem. Kinet.* **2011**, *43*, 708−714. (c) Castro, E. A.; Aliaga, M.; Campodonico, P. R.; Cepeda, M.; Contreras, R.; Santos, J. G. *J. Org. Chem.* **2009**, *74*, 9173−9179. (d) Castro, E. A.; Ramos, M.; Santos, J. G. *J. Org. Chem.* **2009**, *74*, 6374−6377. (e) Castro, E. A. *Pure Appl. Chem.* **2009**, *81*, 685−696. (f) Castro, E. A.; Aliaga, M.; Santos, J. G. *J. Org. Chem.* **2005**, *70*, 2679−2685. (g) Castro, E. A.; Gazitua, M.; Santos, J. G. *J. Org. Chem.* **2005**, *70*, 8088−8092.

(13) (a) Sung, D. D.; Koo, I. S.; Yang, K.; Lee, I. *Chem. Phys. Lett.* **2006**, *432*, 426−430. (b) Sung, D. D.; Koo, I. S.; Yang, K.; Lee, I. *Chem. Phys. Lett.* **2006**, *426*, 280−284. (c) Oh, H. K.; Oh, J. Y.; Sung, D. D.; Lee, I. *J. Org. Chem.* **2005**, *70*, 5624−5629. (d) Oh, H. K.; Jin, Y. C.; Sung, D. D.; Lee, I. *Org. Biomol. Chem.* **2005**, *3*, 1240−1244. (e) Lee, I.; Sung, D. D. *Curr. Org. Chem.* **2004**, *8*, 557−567.

(14) (a) Um, I. H.; Bae, A. R. *J. Org. Chem.* **2012**, *77*, 5781−5787. (b) Um, I. H.; Lee, J. Y.; Ko, S. H.; Bae, S. K. *J. Org. Chem.* **2006**, *71*, 5800−5803. (c) Um, I. H.; Chun, S. M.; Chae, O. M.; Fujio, M.; Tsuno, Y. *J. Org. Chem.* **2004**, *69*, 3166−3172. (d) Um, I. H.; Kim, K. H.; Park, H. R.; Fujio, M.; Tsuno, Y. *J. Org. Chem.* **2004**, *69*, 3937−3942.

(15) (a) Um, I. H.; Akhtar, K.; Shin, Y. H.; Han, J. Y. *J. Org. Chem.* **2007**, *72*, 3823−3829. (b) Um, I. H.; Shin, Y. H.; Han, J. Y.; Mishima, M. *J. Org. Chem.* **2006**, *71*, 7715−7720. (c) Um, I. H.; Han, J. Y.; Shin, Y. H. *J. Org. Chem.* **2009**, *74*, 3073−3078.

(16) (a) Castro, E. A.; Cubillos, M.; Santos, J. G. *J. Org. Chem.* **1996**, *61*, 3501−3505. (b) Castro, E. A.; Saavedra, C.; Santos, J. G.; Umana, M. I. *J. Org. Chem.* **1999**, *64*, 5401−5407. (c) Castro, E. A.; Garcia, P.; Leandro, L.; Quesieh, N.; Rebolledo, A.; Santos, J. G. *J. Org. Chem.* **2000**, *65*, 9047−9053. (d) Castro, E. A.; Leandro, L.; Quesieh, N.; Santos, J. G. *J. Org. Chem.* **2001**, *66*, 6130−6135.

(17) (a) Um, I. H.; Lee, S. E.; Kwon, H. J. *J. Org. Chem.* **2002**, *67*, 8999−9005. (b) Um, I. H.; Seok, J. A.; Kim, H. T.; Bae, S. K. *J. Org. Chem.* **2003**, *68*, 7742−7746. (c) Um, I. H.; Hwang, S. J.; Yoon, S.; Jeon, S. E.; Bae, S. K. *J. Org. Chem.* **2008**, *73*, 7671−7677.

(18) Atkins, P.; de Paula, J. *Atkins' Physical Chemistry*, 9th ed.; Oxford University Press: Oxford, 2010; p 811.

(19) Reichardt, C. *Solvents and Solvent Effects in Organic Chemistry*, 2nd ed.; VCH Publishers Ltd.: Cambridge, 1988; p 69.

(20) Jones, R. A. Y. *Physical and Mechanistic Organic Chemistry*, 2nd ed.; Cambridge University Press: Cambridge, 1984; p 65.

(21) (a) Carroll, F. A. *Perspectives on Structures and Mechanism in Organic Chemistry*; Brooks/Cole: New York, 1998; pp 371−380. (b) Jencks, W. P. *Catalysis in Chemistry and Enzymology*; McGraw-Hill: New York, 1969; pp 480−483. (c) Jaffe, H. H. *Chem. Rev.* **1953**, *53*, 191−261. (d) More O'Ferrall, R.; Miller, S. I. *J. Am. Chem. Soc.* **1963**, *85*, 2440−2444. (e) Hansch, C.; Leo, A.; Taft, R. W. *Chem. Rev.* **1991**, *91*, 165−195.

(22) (a) Um, I. H.; Park, Y. M.; Fujio, M.; Mishima, M.; Tsuno, Y. *J. Org. Chem.* **2007**, *72*, 4816−4821. (b) Um, I. H.; Lee, J. Y.; Fujio, M.; Tsuno, Y. *Org. Biomol. Chem.* **2006**, *4*, 2979−2985.

(23) Worrall, D. E. *Organic Synthesis*; Gilman, H., Blatt, A., Eds.; Wiley: New York, 1941; Collect. Vol. *1*; p 413.