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The α-Effect in Reactions of sp-Hybridized Carbon Atom: Michael-Type Reactions of 1-Aryl-2-propyn-1-ones with Primary Amines

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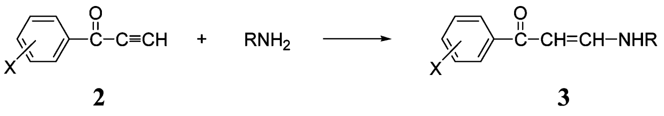

X = 4-MeO (**2a**), 4-Me (**2b**), H (**2c**), 4-Cl (**2d**), 4-CN (**2e**), 3-NO$_2$ (**2f**).

Second-order rate constants (k_N) have been measured for the Michael-type reaction of 1-(X-substituted phenyl)-2-propyn-1-ones (**2a**−**f**) with a series of primary amines in H_2O at 25.0 ± 0.1 °C. A linear Brønsted-type plot with a small β_{nuc} value ($\beta_{nuc} = 0.30$) has been obtained for the reactions of 1-phenyl-2-propyn-1-one (**2c**) with non-α-nucleophile amines. Hydrazine is more reactive than other primary amines of similar basicity (e.g., glycylglycine and glycine ethyl ester) and results in a positive deviation from the linear Brønsted-type plot. The reactions of **2a**−**f** with hydrazine exhibit a linear Hammett plot, while those with non-α-nucleophile amines give linear Yukawa−Tsuno plots, indicating that the electronic nature of the substituent X does not affect the reaction mechanism. The α-effect increases as the substituent X in the phenyl ring of **2a**−**f** becomes a stronger electron-donating group. However, the magnitude of the α-effect for the reactions of **2a**−**f** is small (e.g., $k_N^{hydrazine}/k_N^{glycylglycine} = 4.6-13$) regardless of the electronic nature of the substituent X. The small β_{nuc} has been suggested to be responsible for the small α-effect. A solvent kinetic isotope effect (e.g., $k_N^{H_2O}/k_N^{D_2O} = 1.86$) was observed for the reaction with hydrazine but absent for the reactions with non-α-nucleophile amines. The reactions with hydrazine and other primary amines have been suggested to proceed through a five-membered intramolecular H-bonding structure VI and a six-membered intermolecular H-bonding structure VII, respectively. The transition state modeled on VI can account for the substituent dependent α-effect and the difference in the solvent kinetic isotope effect exhibited by the reactions with hydrazine and other primary amines. It has been proposed that the β_{nuc} value is more important than the hybridization type of the reaction site to determine the magnitude of the α-effect.

Introduction

The term α-effect was given to the abnormally enhanced nucleophilicity exhibited by nucleophiles possessing one or more nonbonding electron pairs at the position adjacent to the nucleophilic site.[1] Numerous studies have been performed to account for the cause of the α-effect.[2] Some theories suggested as the cause of the α-effect include destabilization of the ground-state through electron repulsion between the nonbonding electron pairs,[3] stabilization of the transition state,[4,5] enhanced thermodynamic stability of the reaction product,[6−9] and differential solvation effect.[2a,10−14] Many factors have been reported to influence the magnitude of the α-effect, e.g., solvent,[2a,10−14] β_{nuc},[4−6,9] basicity of nucleophiles,[11] and hybridization type of the electrophilic center.[4,15,16]

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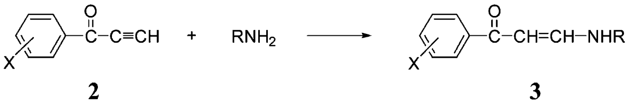
The role of solvent on the α-effect has been reported to be significant.[2a,10–14] DePuy et al. have found that HOO^- exhibits no enhanced reactivity compared with OH^- in the gas-phase reactions with methyl formate,[10a] while Wolfe et al. have calculated that HOO^- and FO^- do not exhibit the α-effect.[10b] Similarly, we have recently shown that the α-effect is strongly dependent on the solvent composition for the nucleophilic substitution reaction of 4-nitrophenyl acetate and related esters.[2a,12,13]

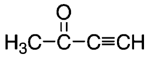
The β_{nuc} value[4–6,9] and the basicity of nucleophiles[11,17] have also been reported to be important to determine the magnitude of the α-effect. The α-effect has been shown to be small or absent for reactions in which the β_{nuc} value is small[4–6,9] or for reactions with highly basic α-nucleophiles.[11,17] However, the type of hybridization of the electrophilic center has been suggested to dominate the magnitude of the α-effect. A small or even no α-effect was observed for reactions at sp^3-hybridized carbon atoms, while the α-effect for reactions at sp^2-hybridized carbon atoms was generally reported to be ca. 10^2.[4,15] Buncel et al. showed that HOO^- and hydrazine are 5.7–11 and 3.0–5.2 times more reactive than the corresponding normal nucleophiles HO^- and glycylglycine, respectively, in the methyl group transfer reactions with methyl sulfates.[4] Fountain et al. found a similar result for the reaction at sp^3-hybridized carbon atoms with benzohydroxamate anions and hydroxylamine.[15] On the other hand, the largest α-effect was observed in the reaction at an sp-hybridized carbon atom. For example, HOO^- was reported to be 20000–60000 times more reactive than OH^- toward the sp-hybridized carbon of benzonitriles in 50% aqueous acetone or in H_2O.[16]

SCHEME 1



X = 4-MeO (**2a**), 4-Me (**2b**), H (**2c**), 4-Cl (**2d**), 4-CN (**2e**), 3-NO_2 (**2f**).

We have recently found an unexpectedly small α-effect for the reactions at an sp-hybridized carbon atom of 3-butyn-2-one (**1**).[18] Hydrazine and methoxylamine exhibited positive deviations from the Brønsted-type plot. However, the degree of deviation from the linear Brønsted-type plot was not significant; i.e., hydrazine and methoxylamine were found to be only 11 and 8.4 times more reactive than the corresponding normal nucleophiles glycylglycine and trifluoroethylamine, respectively.[18] Such a small α-effect was considered to be quite surprising for the reactions at an sp-hybridized carbon atom.



$H_3C-\overset{O}{\overset{\|}{C}}-C\equiv CH$

1

Thus, for a more systematic investigation, we have extended our study to the reactions of 1-(X-substituted phenyl)-2-propyn-1-ones (**2a**–**f**) with a series of primary amines in H_2O, as shown in Scheme 1. In the present paper, we report the effect of substituent X on the α-effect together with a plausible cause of the small α-effect found in the reactions at the sp-hybridized carbon atoms of **1** and **2a**–**f**.

Results and Discussion

The enaminones (**3**) formed from the reactions of **2a**–**f** with non-α-nucleophile amines were stable under the kinetic conditions, while those from the reactions with hydrazine reacted further to yield 3-(X-substituted phenyl)pyrazoles. All of the reactions obeyed pseudo-first-order kinetics. Pseudo-first-order rate constants (k_{obsd}) were calculated from the slope of the linear plots of ln($A_\infty - A_t$) vs time. The plots of k_{obsd} vs amine concentration were linear passing through the origin. Generally, five different concentrations of amines were used to determine second-order rate constants (k_N) from the slope of the linear plots of k_{obsd} vs amine concentration. Correlation coefficients of the plots were usually higher than 0.9995. It is estimated from replicate runs that the uncertainty in the rate constants is less than ±3%. The second-order rate constants determined in this way are summarized in Tables 1 and 2.

α-Effect in Reaction at sp-Hybridized Carbon Atom. As shown in Table 1, the reactivity of amines toward **2c** increases as the amine basicity increases. The

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TABLE 1. Summary of Second-Order Rate Constants for the Michael-Type Reactions of 1-Phenyl-2-propyn-1-one (2c) with Primary Amines in H_2O at 25.0 ± 0.1 °C

no.	amines	pK_a[a]	$k_N/M^{-1}s^{-1}$
1	ethylamine	10.63	1.33
2	glycine	9.76	1.13
3	ethanolamine	9.50	0.703
4	benzylamine	9.34	1.22
5	glycylglycine	8.25	0.595
6	hydrazine	8.10	4.41
7	glycine ethyl ester	7.75	0.466
8	trifluoroethylamine	5.70	0.0407

[a] pK_a taken from: Jencks, W. P.; Regenstein, J. In *Handbook of Biochemistry*, 2nd ed.; Sober, H. A., Ed.; Chemical Rubber Publishing Co.: Cleveland, OH, 1970; p J-203. Gilchrist, M.; Jencks, W. P. *J. Am. Chem. Soc.* **1968**, *90*, 2622−2237.

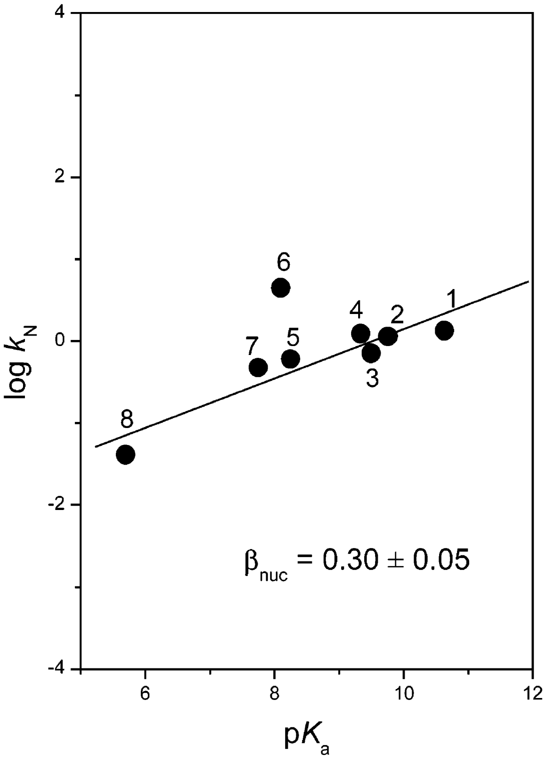

FIGURE 1. Brønsted-type plot for the Michael-type reactions of 1-phenyl-2-propyn-1-one (**2c**) with primary amines in H_2O at 25.0 ± 0.1 °C. The identity of the points is given in Table 1.

effect of amine basicity on reactivity is illustrated in Figure 1. As shown, the second-order rate constant k_N increases linearly with increasing the pK_a of the conjugate acid of all the amines studied except hydrazine, which exhibits a positive deviation from the linear Brønsted-type plot. One can estimate from Figure 1 that hydrazine behaves like a primary amine with a pK_a value of 11.8 rather than its actual pK_a value of 8.10. The positive deviation exhibited by hydrazine is diagnostic for an α-effect. However, the α-effect in the present system (e.g., $k_N^{hydrazine}/k_N^{glycylglycine}$) is only ca. 7.4, which is quite small for the reaction at an sp-hybridized carbon atom, since the α-effect has often been reported to be about 10, 10^2, and 10^3−10^4 for reactions at the sp^3, sp^2, and sp-hybridized carbon atom, respectively.[4,15,16]

In the addition reactions of primary amines to activated C═C bonds (e.g., benzylidene Meldrum's acid, β-methoxy-α-nitrostilbene, and benzylidenemalonodialdehyde), Bernasconi et al. have found that the α-nucleophiles such as hydrazine, methoxylamine, and semicarbazide exhibit no α-effect for the nucleophilic attack process.[9] In all cases, the k_1 values for these α-nucleophiles show good linear Brønsted-type correlations with those for the other primary amines with a β_{nuc} value of ca. 0.2.[9] On the other hand, the rate constants for the reverse process (k_{-1}) are markedly depressed for the reaction with these α-nucleophiles. As a result, these α-nucleophiles exhibit positive deviations from the linear plots of log k_1/k_{-1} vs amine basicity. Bernasconi et al. have suggested that the small β_{nuc} value is responsible for the absence of the α-effect for the k_1 process.[9] Dixon and Bruice have found a similar result for the addition reactions of primary amines including hydrazine and methoxylamine to malachite green, i.e., the reaction with a small β_{nuc} value exhibits a small α-effect and vice versa.[6a,b] Clearly, these studies suggest that the β_{nuc} value is an important factor to determine the magnitude of the α-effect.

The β_{nuc} value determined is 0.30 for the reactions of **2c** with primary amines in this study. We have reported a similar β_{nuc} value (0.32) for the corresponding reactions of **1**, in which the α-effect found is 11.[18] Edwards et al. have also reported a small α-effect for the substitution reactions of ClCN (another sp-hybridized carbon atom) with primary amines including hydrazine.[19] The nucleophilic substitution reactions of ClCN with primary amines proceed by C−Cl bond scission. They have found that the α-effect $k_N^{hydrazine}/k_N^{glycine\ amide} = 18$, while $\beta_{nuc} = 0.36$ for the substitution reactions at the *sp*-hybridized carbon atom.[19] Thus, one might suggest that the small β_{nuc} value is mainly responsible for the small α-effect found in the present and the previous reactions of the sp-hybridized carbon atoms. This argument is consistent with the proposal by Bruice, Buncel, and Hoz that the α-effect should decrease as the β_{nuc} value decreases.[2b,4−6] In fact, Dixon and Bruice have experimentally shown that the α-effect ($k_N^{hydrazine}/k_N^{glycylglycine}$) decreases linearly with decreasing β_{nuc} value for nucleophilic substitution reactions of 17 different substrates with hydrazine and glycylglycine (or glycine amide).[6c] Dependence of the α-effect on the β_{nuc} value has also been found for the reactions of carbon-, sulfur-, and phosphorus-centered esters with anionic nucleophiles, e.g., butan-2,3-dione monoximate (Ox^-) and 4-chlorophenoxide ($ClPhO^-$) as an α- and a reference normal nucleophile, respectively.[12b] We have recently reported that the α-effects (k^{Ox-}/k^{ClPhO-}) are 300, 200, and 40 in the reaction of 4-nitrophenyl acetate (C═O), benzenesulfonate (SO_2), and diphenylphosphinate (P═O), respectively, while the β_{nuc} value decreases from 0.64 to 0.54 and 0.21 in accordance with decreasing the α-effect.[12b] Thus, one can suggest that the β_{nuc} value is a more important factor than the type of hybridization of the reaction site to determine the magnitude of the α-effect.

Effect of Substituent on Reaction Mechanism. To obtain further information about the effect of substituents on the α-effect, the study has been extended to the reactions of 1-(X-substituted phenyl)-2-propyn-1-ones

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TABLE 2. Summary of Second-order Rate Constants for the Michael-type Reactions of 1-(X-Substituted phenyl)-2-propyn-1-ones (2a−f) with Primary Amines in H_2O at 25.0 ± 0.1 °C

	$k_N/M^{-1}\ s^{-1}$				
X	hydrazine	ethylamine	glycylglycine	trifluoroethylamine	α-effect[a]
2a, *p*-OMe	3.43	0.615	0.267	0.0174	13
2b, *p*-Me	4.13	0.984	0.466	0.0280	8.9
2c, H	4.41 (2.42)[b]	1.33 (1.46)[b]	0.595 (0.660)[b]	0.0407 (0.0384)[b]	7.4
2d, *p*-Cl	5.54	1.83	0.855	0.0532	6.5
2e, *p*-CN	9.90	4.36	2.17	0.152	4.6
2f, *m*-NO2	9.66	4.28	2.11	0.138	4.6

[a] α-Effect = $k_N^{\text{hydrazine}}/k_N^{\text{glycylglycine}}$. [b] The data in parentheses are the second-order rate constants for the reactions run in D_2O.

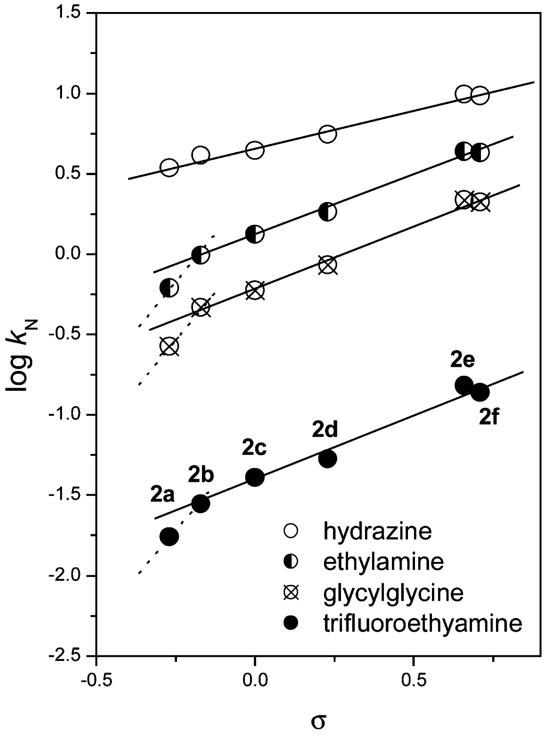
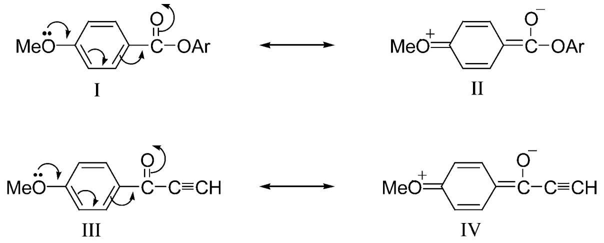


FIGURE 2. Hammett plots for the Michael-type reactions of 1-(X-substituted phenyl)-2-propyn-1-ones (**2a**−**f**) with primary amines in H_2O at 25.0 ± 0.1 °C. The identity of the points is given in Table 2.

(**2a**−**f**) with hydrazine and three other primary amines. As shown in Table 2, the second-order rate constant increases as the substituent X changes from an electron-donating group (EDG) to an electron-withdrawing group (EWG) for all of the amines studied including hydrazine. The effect of substituent X on the reactivity is illustrated in Figure 2.

The Hammett plot for the reaction with hydrazine exhibits a good linearity. However, the corresponding Hammett plot for the reactions with the other primary amines shows poor correlation, i.e., the point for the substrate having a π-electron donor substituent (e.g., X = 4-MeO) exhibits a negative deviation from the linear Hammett plots. This result is similar to the nonlinear Hammett plots found for the aminolyses of aryl X-substituted benzoates[20] and benzenesulfonates[21] and alkaline hydrolyses of aryl X-substituted benzoates[22] and thionobenzoates.[23] In all cases, the points for π-electron-donating substituents (e.g., X = 4-MeO, 4-Me) exhibited negative deviations from the linear Hammett plots, and the degree of deviation was more significant for the stronger EDG. Traditionally, such a nonlinear Hammett plot has been interpreted as a change in the rate-determining step (RDS). However, we have attributed such a negative deviation to stabilization of the ground state through resonance interaction between the π-electron donating substituent and the carbonyl (or sulfonyl) group as shown in the resonance structures I and II.[20−23]



I

II

III

IV

Stabilization of the ground state through resonance interaction is also possible in the present system as illustrated by the resonance structures III and IV. This argument can be confirmed by the fact that the Yukawa−Tsuno plots shown in Figure 3 exhibit excellent linear correlation. Thus, one can suggest that the negative deviation shown by **2a** is not due to a change in the RDS or reaction mechanism but stabilization of the ground state by resonance is responsible for the nonlinear Hammett plots.

$$\log(k_X/k_H) = \rho\{\sigma^o + r(\sigma^+ - \sigma^o)\} \qquad (1)$$

The *r* value in the Yukawa−Tsuno equation (eq 1) represents the extent of resonance contribution.[24] Equation (1) becomes the Hammett equation when $r = 0$ or the Brown−Okamoto equation when $r = 1$. The *r* value determined is ca. 0.55 ± 0.1 for the reactions of **2a**−**f** with the non-α-nucleophile amines. This accounts for the result that the Yukawa−Tsuno plots exhibit much better linear correlation than the corresponding Hammett or Brown−Okamoto plots, in which σ or σ^+ constants alone

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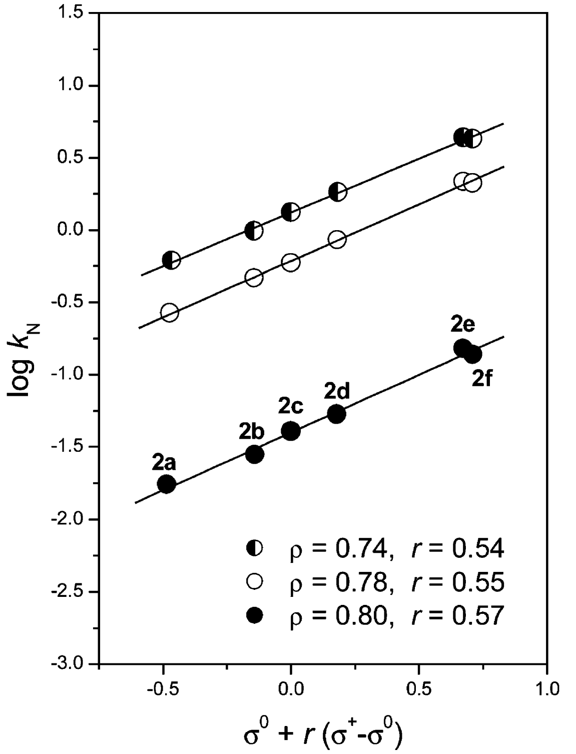


FIGURE 3. Yukawa–Tsuno plots for the Michael-type reactions of 1-(X-substituted phenyl)-2-propyn-1-ones (**2a**–**f**) with ethylamine (◐), glycylglycine (○), and trifluoroethylamine (●) in H_2O at 25.0 ± 0.1 °C. The identity of the points is given in Table 2.

are used. Thus, one can suggest that the electronic nature of the substituent X does not affect the reaction mechanism on the basis of the linear Yukawa–Tsuno plots.

Effect of Substituent on the α-Effect. As shown in Table 2, the α-effect for the reactions of **2a**–**f** increases as the substituent X changes from a strong EWG to a strong EDG. The effect of the substituent on the α-effect is illustrated in Figure 4. One can see that the α-effect exhibits a linear correlation with the electronic nature of the substituent X. However, the magnitude of the α-effect for the reactions at the sp-hybridized carbon is small regardless of the electronic nature of the substituent X (e.g., the α-effect of only 4.6–13). To achieve an α-effect of 10^3–10^4, the largest α-effect suggested for the reaction of an sp-hybridized carbon atom,[16] the σ value should be at least ca. −6.7. However, such a σ value is practically impossible.

Dependence of the α-effect on the electronic nature of substituents has also been reported for the reactions of 4-nitrophenyl X-substituted benzoates with primary amines including hydrazine.[25] As shown in the inset of Figure 4, the α-effect of the benzoate system also increases as the substituent X changes from a strong EWG to a strong EDG. We have explained the increasing α-effect trend through the intramolecular general acid/base catalysis modeled on V, which is one of the first explanations to account for the α-effect exhibited by NH_2NH_2, $HONH_2$, HOO^-, etc.[2b–d,26] Such an intramolecular H-bonding interaction is possible only for the reactions

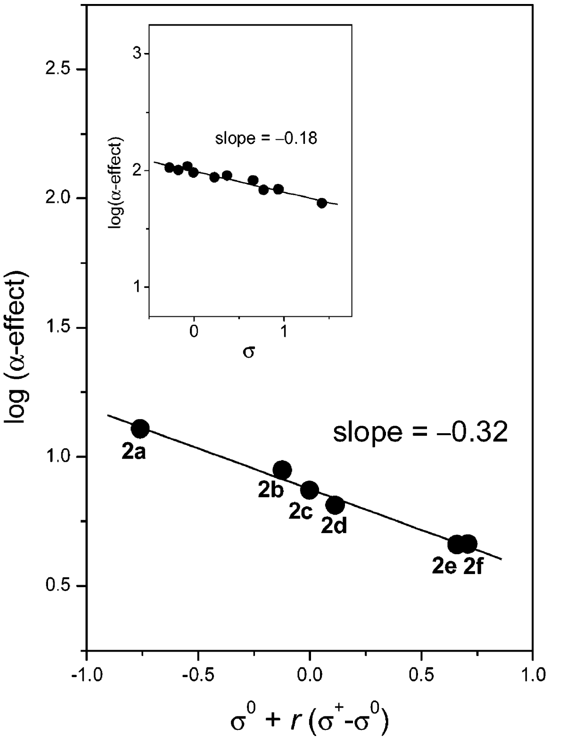
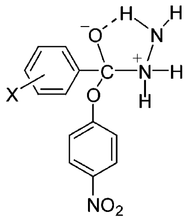
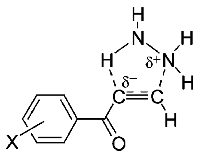


FIGURE 4. Plots showing dependence of the α-effect on the electronic nature of the substituent X for the reactions of 1-(X-substituted phenyl)-2-propyn-1-ones (**2a**–**f**) and 4-nitrophenyl X-substituted benzoates (inset) with hydrazine and glycylglycine in H_2O at 25.0 ± 0.1 °C. The identity of the points is given in Table 2. The data for the reactions of the benzoate system were taken from ref 25.

with hydrazine. As the substituent X in the benzoyl moiety changes from an EWG to an EDG, more negative charge would develop at the oxygen atom of the carbonyl bond, which enables a stronger H-bonding interaction (more stabilization of the transition state) and results in the increasing α-effect trend shown in the inset of Figure 4.



V



VI

The importance of the structure V has been neglected because $MeONH_2$ cannot form such a transition state but it has often exhibited a large α-effect.[2b–d] Since the origin of the α-effect exhibited by NH_2NH_2 and $MeONH_2$ is not necessarily the same, we propose a transition state modeled on VI to account for the substituent dependent α-effect.[27] Hydrazine can stabilize the transition state through the five-membered intramolecular H-bonding

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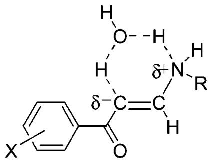
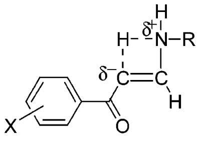
interaction. As the substituent X in the phenyl ring of **2a**−**f** changes from a strong EWG to a strong EDG, the developing negative charge would be more localized at the 2-carbon atom of **2a**−**f**. Then, the intramolecular H-bonding interaction would be stronger and the transition state VI can be more stabilized. On the contrary, as the substituent X becomes a strong EWG, the negative charge at the 2-carbon atom would be delocalized to the carbonyl group, which would result in a decrease in both the H-bonding interaction and the transition state stabilization. This argument can account for the substituent dependent α-effect shown in Figure 4.

The transition state VI can also explain the solvent kinetic isotope effect (KIE) determined in this study. As shown in Table 2, the second-order rate constant (k_N) for the reactions with non-α-nucleophile amines is almost the same in H_2O and in D_2O, i.e., $k_N^{H_2O}/k_N^{D_2O} = 1.0 \pm 0.1$, while the reactivity of hydrazine decreases significantly in D_2O, i.e., $k_N^{H_2O}/k_N^{D_2O} = 1.82$. The absence of solvent KIE suggests that the proton transfer occurs after the RDS for the reactions with the non-α-nucleophile amines, while the solvent KIE of 1.82 for the reaction with hydrazine indicates that the proton transfer occurs at the RDS. The difference in the solvent KIE is consistent with the proposal that the reactions of **2a**−**f** with hydrazine proceed through the transition state VI. In this model, the proton transfer can occur through the intramolecular H-bonding at the RDS. However, such an intramolecular H-bonding structure is not possible for the reactions with non-α-nucleophile amines. Instead, one might suggest a six-membered intermolecular H-bonding structure VII for the reactions with the non-α-nucleophile amines. This model would be better than a four-membered intramolecular H-bonding structure VIII. Thus, the proton transfer from the nitrogen atom to the 2-carbon atom of **2a**−**f** would occur after the RDS through the intermediate modeled on VII on the basis of the absence of solvent KIE for these reactions with non-α-nucleophiles.



VII



VIII

Origin of Small α-Effect. Nucleophilic reactivity is determined by the free energy gap between the ground state and the transition state of the reaction. One might suggest that α-nucleophiles exhibit enhanced reactivities (the α-effect) by destabilizing their ground state and/or by stabilizing their transition state. It has often been suggested that the ground state of α-nucleophiles is destabilized.[2] In fact, from a calorimetric study, we have recently shown that the α-nucleophile (butan-2,3-dione monoximate) is ca. 4 kcal/mol less solvated than its reference normal nucleophile (4-chlorophenoxide) in H_2O.[12d] Although the ground state of hydrazine might be destabilized by the electron repulsion between the adjacent nonbonding electrons or by other reasons, the difference in the ground-state energy between hydrazine and glycylglycine should be constant, since they were used as the α and the reference normal nucleophile for all the reactions of **2a**−**f** in this study. Thus, if the difference in the ground-state energy were responsible for the α-effect, the magnitude of the α-effect should have been about the same regardless of the electronic nature of the substituent X in the present system. However, our result shows that this is not the case. Accordingly, one can suggest that destabilization of the ground-state energy cannot be the cause of the substrate dependent α-effect shown in Figure 4. This argument is consistent with the conclusion drawn by Buncel and Hoz that ground state destabilization will contribute only slightly, if at all, to the manifestation of α-effects.[5b]

Stabilization of transition state through aromatic[28] or radicaloid[5] character, and/or intramolecular H-bonding interaction,[25,26] has been suggested as an origin of the α-effect. In the preceding section, we have suggested that the transition state for the reaction with hydrazine is stabilized through the intramolecular H-bonding structure VI. However, one can expect that the transition state stabilizing effect would be significant only for the system in which the β_{nuc} value is large. Since the β_{nuc} values are very small for the reactions of **1** and **2a**−**f**, the effect of transition state stabilization through the structure VI cannot be significant. This argument is consistent with the small α-effect found in this and previous reactions at the *sp*-hybridized carbon atoms (e.g., **1**, **2a**−**f**, and ClCN). Thus, one can suggest that stabilization of the transition state through the structure VI is responsible for the increasing α-effect trend shown in Figure 4, but the effect of transition state stabilization is not significant due to the small β_{nuc} value.

Conclusions

The present study has allowed us to conclude the following: (1) The Brønsted-type plot for the reactions of **2c** with primary amines is linear with a β_{nuc} value of 0.30. Hydrazine exhibits a positive deviation from the linear Brønsted-type plot but the α-effect is very small (e.g., $k_N^{hydrazine}/k_N^{glycylglycine} = 7.4$). (2) The electronic nature of the substituent X does not influence the reaction mechanism for the reactions of **2a**−**f**, but the α-effect increases as the substituent X becomes a stronger EDG. (3) The reactions with hydrazine and other primary amines have been suggested to proceed through a five-membered intramolecular H-bonding structure VI and a six-membered intermolecular H-bonding structure VII, respectively. The transition state modeled on VI can account for the substituent dependent α-effect and the difference in the solvent KIE exhibited by the reactions with hydrazine and other primary amines. (4) The small β_{nuc} value has been suggested to be responsible for the small α-effect found in the reactions of **1** and **2a**−**f**. (5) We propose that the β_{nuc} value is a more important factor than the hybridization type of the reaction site to determine the magnitude of the α-effect.

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(27) A reviewer has suggested to note that "This transition state leads to the formation of a zwitterion. While ylides of second row elements are common, this one may be of a too high energy."

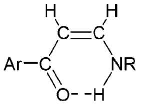
(28) Liebman, J. F.; Pollack, R. M. *J. Org. Chem.* **1973**, *38*, 3444−3445.

Experimental Section

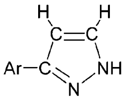
Materials. 1-(X-substituted phenyl)-2-propyn-1-ones (**2a**−**f**) were readily prepared from oxidation of the corresponding carbinols,[29] which were obtained from the reactions of X-substituted benzaldehydes with ethynylmagnesium bromide in dried diethyl ether as reported in the literature.[30] Their purity was checked by means of melting points and ^{1}H NMR spectra (Supporting Information). Doubly distilled water was further boiled and cooled under nitrogen just before use. Amines and other chemicals used were of the highest quality available.

Kinetics. The kinetic studies were performed with a UV−vis spectrophotometer equipped with a constant temperature circulating bath to keep the temperature of the reaction mixture at 25.0 ± 0.1 °C. The reactions were followed by monitoring the appearance of the enaminone (**3**) at a fixed wavelength corresponding to the maximum absorption (see Tables S2−S33 in the Supporting Information). All of the reactions were carried out under pseudo-first-order conditions in which the concentration of the amines was at least 20 times greater than that of **2a**−**f**. The amine stock solution of ca. 0.2 M was prepared in a 25.0 mL volumetric flask by adding 2 equiv of amine hydrochloride to 1 equiv of standardized NaOH solution (or by adding 2 equiv of free amine to 1 equiv of standardized HCl) in order to obtain a self-buffered solution under nitrogen just before use and transferred by gas-tight syringes. The detailed kinetic conditions and results are summarized in Tables S2−S33 in the Supporting Information.

Product Analysis. The enaminones (**3**) from the reactions with non-α-nucleophile amines were identified by means of their UV−vis and ^{1}H NMR spectra. ^{1}H NMR studies have shown that the enaminones exist as the *cis*-isomer exclusively in CD_3Cl but as 1:1 mixture of *cis*- and *trans*-isomers in CD_3OD. The measurement of ^{1}H NMR spectra in H_2O was not possible due to the low solubility of the reaction products. An intramolecular H-bonding structure IX has been suggested to be responsible for the *cis*-isomer in the aprotic solvent.[31] (See the ^{1}H NMR spectra in the Supporting Information.)



IX



4

The reactions of **2a**−**f** with hydrazine also produced the enaminones initially, but they reacted further to yield the ring closed products, 3-(X-substituted phenyl)pyrazoles (**4**), under the kinetic conditions as reported.[32]

Acknowledgment. We are grateful for the financial support from the Korea Science and Engineering Foundation (KOSEF-R01-2004-10279).

Supporting Information Available: Table S1 for melting points (determined in the present study and reported in the literatures) of **2a**−**f**. Tables S2−S33 for kinetic conditions and results. ^{1}H NMR spectra of 1-(4-cyanophenyl)-2-propyn-1-one (**2e**), 3-(benzylamino)-1-(4-methylphenyl)-prop-2-en-1-one (in $CDCl_3$ and CD_3OD), and 3-phenylpyrazole. This material is available free of charge via the Internet at http://pubs.acs.org.

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