Elimination Reactions of Aryl Furylacetates Promoted by R_2NH in MeCN: Effects of Base Solvent and β-Aryl Group on the Ketene-forming Transition State

Sang Yong Pyun,[†,*] Kyu Cheol Paik,[‡] Man So Han,[‡] Byung Tae Kim,[§] and Bong Rae Cho[¶,*]

[†]*Department of Chemistry, Pukyong National University, Pusan 608-737, Korea.*
**E-mail: sypyun@pknu.ac.kr*
[‡]*Department of Chemistry, Daejin University, Gyeonggi-do 11159, Korea*
[§]*Division of Energy and Environmental Engineering, Daejin University, Gyeonggi-do 11159, Korea*
[¶]*Department of Chemistry, Korea University, Seoul 136-713, Korea. *E-mail: chobr@korea.ac.kr*
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Ketene-forming elimination from $C_4H_3(O)CH_2C(O)OC_6H_3$-2-X-4-NO_2 (**1**) promoted by R_2NH in MeCN has been studied. The reactions produced elimination products and exhibited second-order kinetics with Brönsted $\beta = 0.51$, and $|\beta_{lg}| = 0.47–0.53$, indicating that the reaction proceeds by the E2 mechanism via an E2-central transition state. Comparison of β, $|\beta_{lg}|$, $\Delta H^{\neq}$, and $\Delta S^{\neq}$ values for R_2NH-promoted eliminations from $ArCH_2C(O)OC_6H_3$-2-X-4-NO_2 reveals that the transition-state structures for Ar = furyl and thienyl are similar and more symmetrical than that for Ar = Ph. This outcome has been attributed to the greater double bond stabilizing ability of the former than that of the latter.

Keywords: Elimination, Ketene, E2 mechanism, Base solvent, β-Aryl group

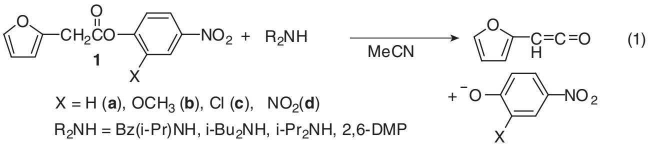
Introduction

Base-promoted eliminations from 2-alkyl halides produce 1-alkene, *cis*- and *trans*-2-alkenes. The C=C bond produced by this reaction is an important conjugation bridge in organic materials including organic light-emitting diode, organic semiconductors, and nonlinear optical materials.[1] Due to the lack of selectivity, however, Wittig reaction rather than the elimination reaction is usually employed to introduce the C=C bonds. Understanding the detailed mechanism of the elimination reactions might lead to a new synthetic method for the C=C bond formation. More importantly, the E2 transition state involving two partially broken bonds and two partially formed bonds is one of the most complex transition states in organic reactions. Understanding the E2 transition state would thus enhance our insight into the mechanistic organic chemistry. In fact, the three-dimensional reaction coordinate diagram,[2] which is useful to explain the structure–reactivity relationship of elimination, substitution, and carbonyl addition reactions relevant to bio-organic chemistry, has been evolved from the study of the E2 reaction.

There was a long standing controversy on the borderline mechanism between E2 and E1cb in the elimination reactions. Earlier, Jencks proposed that the change in the mechanism from E2 to E1cb occurs by the "merging of the transition states."[3] He argued that the E1cb-like and E1cb transition states are so closely located in the reaction coordinate diagram that they cannot coexist, *i.e.*, the concurrent E2 and E1cb mechanisms are not possible. The proposal was invalidated by the experimental results demonstrating that the E2 mechanism changes to a competing E2 and E1cb and then to E1cb by the change in the reactant structure in the reactions of $ArCH_2C(O)OC_6H_3$-2-X-4-NO_2 (Ar = aryl, **3**) with $R_2NH/R_2NH_2^+$ in 70 mol% MeCN(aq).[4] Additional examples of such mechanistic changes were reported for eliminations from aryl thienylacetates (Ar = thienyl, **2**) and aryl furylacetates (Ar = furyl, **1**) under the same condition.[5,6]

When R_2NH in MeCN was used as the base solvent system; however, the reactions of **2** and **3** proceeded by the E2 mechanism via the E2-central transition state.[4a,7,8] This outcome has been ascribed to the poorly anion solvating MeCN. Since MeCN cannot stabilize the partial negative charge at the β-carbon as effectively as 70 mol % MeCN(aq), the charge should be distributed as much as possible throughout the transition state. This can be achieved by forming a symmetrical transition state with increased partial double bond. The observation of more symmetrical transition state for **2** than **3** underlined the importance of the partial double bond character under this condition.

Since the aromatic resonance energy of furan (16 kcal/mol) is smaller than those of thiophene (29 kcal/mol) and benzene (36 kcal/mol),[9] the furyl group is expected to stabilize the developing double bond character more than thienyl and phenyl groups. In order to understand the effect of aromaticity on the ketene-forming transition state, we have now studied the elimination reactions of aryl furylacetates promoted by R_2NH in MeCN (Eq. (1)). By comparing with the existing data for elimination reactions from **1–3** promoted by $R_2NH/R_2NH_2^+$ in 70 mol % MeCN(aq)[4–6] and from **2** and **3** promoted by R_2NH in MeCN,[4a,7,8] the effects of base solvent and β-aryl groups are assessed.



Results

Aryl furylacetates **1a–1d** were available in our laboratory.[6] The products of the reaction of **1a–1d** with R_2NH in MeCN were characterized as before.[4–8] The yields of aryloxides for the reactions of **1a–1d** with R_2NH in MeCN were determined as reported.[4–8] The yields were in the range of 95–98%. These results established that the reactions produce elimination products only.

The kinetic experiments were performed under pseudo-first-order condition.[4–8] The kinetic plots showed straight lines with excellent correlations up to three half-lives. The observed rate constants (k_{obs}) are summarized in Tables S1–S4, Supporting Information. The plots of k_{obs} vs. base concentration were straight lines passing through the origin. This outcome indicates that the reactions proceed by the second-order kinetics, first order to the substrate and first order to the base (Figures S1–S4). The second-order rate constants (k_2) were calculated from the slopes of these plots. The only exception is the reaction between **1d** with 2,6-DMP, for which the rate was measured at a single base concentration because the rate was too fast to follow at a higher base concentration. The k_2 value for this reaction was calculated by dividing the k_{obs} by the base concentration. The k_2 values are summarized in Table 1.

Table 1. Rate constants for ketene-forming elimination from $C_4H_3(O)CH_2C(O)OC_6H_3$-2-X-4-NO_2[a] promoted by R_2NH in MeCN at 25.0 °C.

R_2NH[b]	pK_a[c]	k_2, M^{-1} s^{-1}[d,e]			
		X = H	X = OMe	X = Cl	X = NO_2
Bz(*i*-Pr)NH	16.8	0.0176	0.00798	0.258	2.67
i-Bu_2NH	18.2	0.045	0.0405	1.03	10.6
i-Pr_2NH	18.5	0.139	0.123	3.46	21.4
2,6-DMP[f]	18.9	0.279	0.207	8.12	31.6

[a] [Substrate] = 5.0×10^{-5} M.
[b] $[R_2NH] = 2.0 \times 10^{-3}$ to 5.0×10^{-2} M.
[c] Ref. 10.
[d] Average of three or more rate constants.
[e] Estimated uncertainty, ±3%.
[f] *cis*-2,6-Dimethylpiperidine.

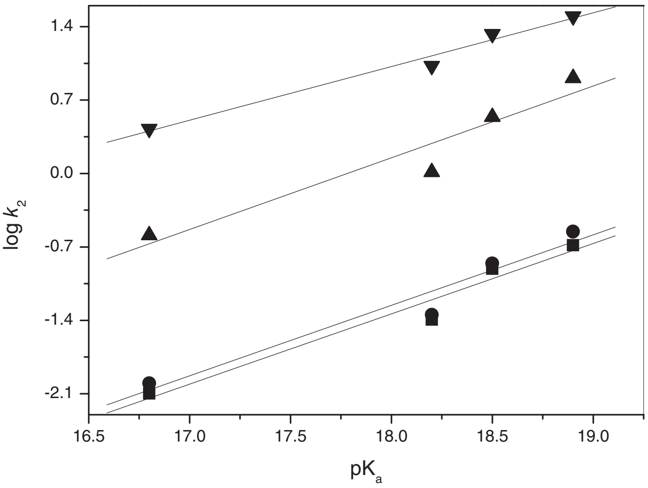


Figure 1. Brönsted plots for the elimination from $C_4H_3(O)CH_2C(O)OC_6H_3$-2-X-4-NO_2 promoted by R_2NH in MeCN at 25.0 °C [X = H (**1a**, ●), OMe (**1b**, ■), Cl (**1c**, ▲), NO_2 (**1d**, ▼)].

Table 2. Brönsted β values for elimination from $C_4H_3(O)CH_2C(O)OC_6H_3$-2-X-4-NO_2 promoted by R_2NH in MeCN at 25.0 °C.

	X = *p*-OMe	X = H	X = Cl	X = NO_2
pK_{lg}[a]	21.6	20.7	18.1	16.0
β	0.67 ± 0.09	0.67 ± 0.11	0.68 ± 0.14	0.51 ± 0.05

[a] Ref. 11.

The Brönsted plots for the reactions of **1a–1d** were linear with excellent correlations (Figure 1). The β values are in the range of 0.51–0.68 and almost the same within experimental error (Table 2). Similarly, the log k_2 values showed reasonable correlation with the pK_{lg} values of the leaving groups (Figure 2). The $|\beta_{lg}|$ values are in the range of 0.47–0.53. Here again, the values are very similar (Table 3).

Rates of the reactions of $ArCH_2C(O)OC_6H_4$-4-NO_2 (**1a**, **2**, **3**) with Bz(*i*-Pr)NH in MeCN and those of **1a** with Bz(*i*-Pr)

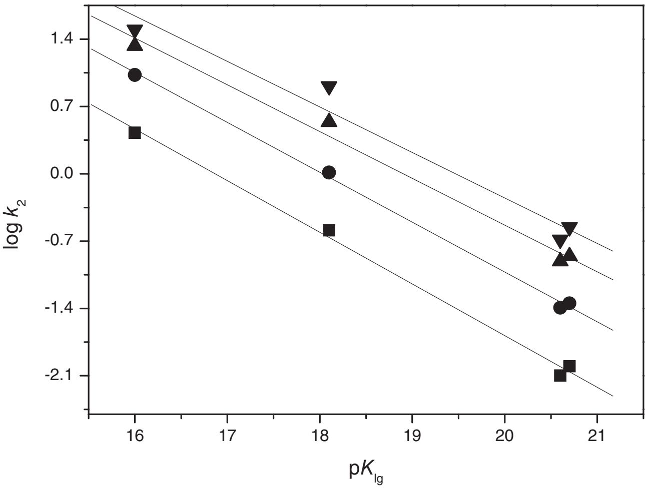


Figure 2. Plots log k_2 vs. pK_{lg} values of the leaving group for the elimination from $C_4H_3(O)CH_2C(O)OC_6H_3$-2-X-4-NO_2 (**1a–1d**) promoted by R_2NH in MeCN at 25.0 °C [R_2NH = Bz(*i*-Pr)NH (■), i-Bu_2NH (▲), i-Pr_2NH (●), 2,6-DMP (▼)].

Table 3. Brönsted β_{lg} values for elimination from $C_4H_3(O)CH_2C(O)OC_6H_3$-2-X-4-NO_2 promoted by R_2NH in MeCN at 25.0 °C.

R_2NH	Bz(*i*-Pr)NH	*i*-Bu_2NH	*i*-Pr_2NH	2,6-DMP[a]
pK_a[b]	16.8	18.2	18.5	18.9
β_{lg}	−0.53 ± 0.03	−0.52 ± 0.02	−0.49 ± 0.03	−0.47 ± 0.06

[a] *cis*-2,6-Dimethylpiperidine.

[b] Ref. 10.

NH/Bz(*i*-Pr)NH_2^+ in 70 mol% MeCN(aq) were measured at 25.0, 35.0, and 45.0 °C, respectively (Table S5). Arrhenius plots were linear with excellent correlations (Figure S5). The enthalpies and entropies of activation were calculated from the Arrhenius plots. The values are summarized in Table 4.

Discussion

Mechanism of Eliminations from 1. The reactions of **1a–1d** with R_2NH in MeCN produced only elimination products. Neither aminolysis nor S_NAr product was obtained presumably because of the high acidity of the C_β—H bond and the steric hindrance of the secondary amines, which would have facilitated the elimination reaction while retarding the aminolysis and S_NAr reactions. All of the reactions exhibited second-order kinetics, indicating that the reactions proceed either by the E2 or E1cb mechanism.[2] The E1cb mechanism is negated by the substantial values of Brönsted β and $|\beta_{lg}|$, for which either Brönsted β values near unity or negligible $|\beta_{lg}|$ values are expected.[2,12] Hence, the most reasonable mechanism for these reactions is E2. This conclusion is supported by the interaction coefficients. The decrease in the Brönsted β_{lg} value decreases with a stronger base corresponds to a positive p_{xy} interaction coefficient, $p_{xy} = \partial\beta_{lg}/\partial pK_{BH}$ (Table 3). The positive p_{xy} interaction coefficient is in agreement with the concerted E2 mechanism, but not with an E1cb mechanism for which $p_{xy} = 0$ is expected.[12]

Effects of Base Solvent and β-Aryl Group on the Ketene-forming Transition State. The rate of elimination from **1a** promoted by Bz(i-Pr)NH increased by eightfold faster as the base solvent system was changed from $R_2NH/R_2NH_2^+$–70 mol% MeCN(aq) to R_2NH–MeCN (Table 4). However, the β, $|\beta_{lg}|$, $\Delta H^{\neq}$, and $\Delta S^{\neq}$ values remained nearly the same by the same change in the base solvent, indicating that the ketene-forming transition state is insensitive to the base solvent variation. Similar results were reported for the ketene-forming eliminations from **2** and **3**.[4a,7,8] The combined results indicate that the ketene-forming transition states are relatively insensitive to the base solvent variation regardless of the β-aryl group. This outcome could be explained, if the developing negative charge at the β-carbon is more stabilized by the combined effects of β-aryl group, carbonyl group, and leaving group than by the solvation.

For eliminations from $ArCH_2C(O)OC_6H_3$-2-X-4-NO_2 [Ar = furyl (**1a**), thienyl (**2**), Ph (**3**)] promoted by R_2NH in MeCN, the rate was similar for **1a** and **2** and slightly slower for **3**. Moreover, the β, $|\beta_{lg}|$, $\Delta H^{\neq}$, and $\Delta S^{\neq}$ values are similar for **1a** and **2**, indicating similar transition-state structures. This outcome indicates that the change of the β-aryl group from furyl to thienyl does not appreciably influence the ketene-forming transition state. The smaller resonance energy of the furan than that of thiophene[9] is not reflected in the transition-state structure. The only noticeable difference is the increase in the β value from 0.62–0.67 to 0.82 and the decrease in the $|\beta_{lg}|$ value from 0.50 to 0.43 by the change in the β-aryl substituent from furyl and thienyl to phenyl. This indicates a skewed transition state toward more C_β—H bond cleavage and less C_α—OAr bond rupture by the change in the β-aryl group. This result is in good agreement with the greater double bond stabilizing ability of the heterocycles compared with that of the phenyl group. Since the developing double bond character can be more stabilized by resonance with the former, a greater amount of the negative charge would be shifted from the β-carbon to the C_β—C_α bond, thereby increasing the partial double bond character and the extent of the C_α—OAr bond rupture. This would predict a larger $|\beta_{lg}|$ value for **1a** and **2**, as observed.

Table 4. Transition-state parameters for nitrile-forming eliminations from $ArCH_2C(O)OC_6H_4$-4-NO_2 promoted by R_2NH in MeCN at 25.0 °C.

	Ar = furyl (**1a**)[a,b]	Ar = furyl (**1a**)[c]	Ar = thienyl (**2**)[d]	Ar = phenyl (**3**)[e]
Rel. rate[c]	1	8	10	1
β	0.54 ± 0.12	0.67 ± 0.11	0.62 ± 0.05	0.82 ± 0.01
β_{lg}[f]	−0.45	−0.53 ± 0.06	−0.53 ± 0.03	−0.43 ± 0.01
$\Delta H^{\neq}$[c] kcal/mol	10.6 ± 0.4	10.1 ± 0.2	9.60 ± 0.4	11.1 ± 0.6
$\Delta S^{\neq}$, eu[c]	−32.8 ± 0.7	−30.7 ± 0.5	−33.1 ± 0.9	−31.1 ± 1.2

[a] Ref. 6.

[b] Base solvent = $R_2NH/R_2NH_2^+$–70 mol % MeCN(aq).

[c] This study.

[d] Ref. 8.

[e] Ref. 4a.

[f] R_2NH = Bz(*i*-Pr)NH.

In conclusion, we have studied the R_2NH-promoted eliminations from aryl furylacetates in MeCN. The reaction proceeded through the E2 mechanism via an E2-central transition state. The change of the base solvent from $R_2NH/R_2NH_2^+$–70 mol% MeCN(aq) to R_2NH–MeCN increased the reaction rate by eightfold without appreciable change in the transition-state structure. For eliminations from $ArCH_2C(O)OC_6H_3$-2-X-4-NO_2 promoted by R_2NH in MeCN, the transition-state structures for **1a** and **2** were similar and more symmetrical than that for **3**. This outcome has been attributed to the greater double bond stabilizing ability of the former than that of the latter. Noteworthy was the relative insensitivity of the ketene-forming transition state to the variation of the β-aryl group from thienyl to furyl.

Experimental Section

Materials. Aryl furylacetates **1a–1d** were available from previous investigations.[6] Reagent grade MeCN and R_2NH were fractionally distilled from CaH_2. The base solvent solutions were prepared by dissolving the appropriate amines to MeCN.

Kinetic Studies. Reactions of **1a–1d** with R_2NH in MeCN were followed by monitoring the increase in the absorbance of aryloxides at 400–434 nm with a UV–Vis spectrophotometer as described.[4–8]

Product Studies. The products of the reaction between **1a–1d** and R_2NH in MeCN were identified as before.[4–8] The yields of aryloxides determined by comparing the UV absorptions of the infinity samples with those for the authentic aryloxides were in the range of 95–98%.

Control Experiments. The stabilities of **1a–1d** were determined as reported.[4–8] The solutions of **1** in MeCN were stable for at least 3 weeks when stored in the refrigerator.

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Support Information. Observed rate constants for elimination from **1a–1d** promoted by R_2NH in MeCN, plots of k_{obs} vs. base concentration, and Arrhenius plots are available in the online version of this article.

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