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Kinetics and Mechanism of the Aminolysis of Aryl *N*-Allyl Thiocarbamates in Acetonitrile

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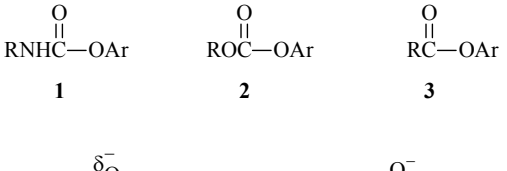
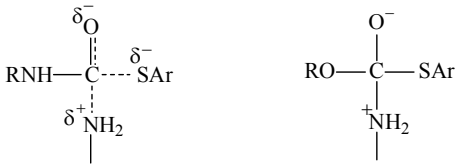
The aminolysis mechanism of aryl carbamates, **1**, is quite similar to that of aryl carbonates, **2**, and aryl esters, **3**.[1-3] A change in the mechanism of the aminolysis with benzylamines in acetonitrile has been observed from stepwise through a tetrahedral intermediate, $T^{\pm}$, to concerted for the carbamates[1] (**1** with R = Ph) as well as for the carbonates[2] (**2** with R = Et) when leaving group is changed from phenoxides (**a** : $^{-}$OAr) to thiophenoxides (**b** : $^{-}$SAr). This suggests that the strength of push provided to expel the leaving group from $T^{\pm}$ by PhNH is similar to that by EtO, and the destabilization of $T^{\pm}$ due to this push is strong enough for $^{-}$SAr but is too weak for $^{-}$OAr to lead the aminolysis to a concerted process.

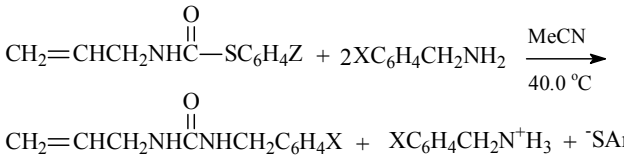


1 **2** **3**



TS : for **1b** $T^{\pm}$: intermediate for **2b**

In this work, we carried out kinetic studies on the aminolysis of aryl *N*-allyl thiocarbamates (**1b : AATC**) with benzylamines in acetonitrile at 40.0 °C, eq 1. The first purpose of the present work is to establish the aminolysis reaction mechanism for eq. 1 and to see whether the mechanistic change from a stepwise to a concerted by the change **2a** → **2b** is also carried on to the change **1a** → **1b** or not. In this work, we varied substituents in the nucleophile (X) and leaving group (Z) and the rate constants, k_2, are subjected to a multiple regression analysis to determine the cross-interaction constant,[4] ρ_{XZ} in eqs 2. For a concerted mechanism the sign of ρ_{XZ} was found to be negative[4] and the reactivity-selectivity principle (RSP) failed.[5]



(1)

$$\log(k_{XZ}/k_{HH}) = \rho_X\sigma_X + \rho_Z\sigma_Z + \rho_{XZ}\sigma_X\sigma_Z \quad (2a)$$

$$\rho_{XZ} = \partial\rho_Z/\partial\sigma_X = \partial\rho_Y/\partial\sigma_Z \quad (2b)$$

Results and Discussion

The reactions of aryl *N*-allyl thiocarbamates (AATC : CH_2=$CHCH_2HNC(=O)SC_6H_4Z$) with X-benzylamines (BA) in acetonitrile follow a clear second-order kinetics, eqs. 3. Unlike in the aminolysis of aryl *N*-phenylcarbamates[1] (APC : $PhNHC(=O)OC_6H_4Z$) we found no base catalysis by the amine. The rate constants, k_2, determined are summarized in Table 1 together with selectivity parameters ρ_X, β_X, ρ_Z, and β_Z. The β_X (β_{nuc}) values are obtained by using the pK_a values of benzylamines in water. This procedure was found to be reliable since the pK_a values in acetonitrile and in water vary in parallel, although the absolute values are different.[6] For the β_Z (β_{lg}) values, a factor of 0.62 was multiplied to all the β_Z values determined using the pK_a (H_2O) values.[7]

$$\text{rate} = k_{obs}[\text{AATC}] \quad (3a)$$

$$k_{obs} = k_2[\text{BA}] \quad (3b)$$

Since strong destabilization of $T^{\pm}$ should be provided by a stronger push to expel the leaving group by the amino nonleaving group, R = NH_2 in **1b**, the aminolysis of AATC (**1b** with R = CH_2=$CHCH_2$-) with benzylamines in acetonitrile is proposed to proceed by a concerted mechanism. The β_Z values in Table 1 are within the range of values that are expected for a concerted mechanism.[8] Further supports for the concerted mechanism is provided by a negative ρ_{XZ} (−0.43) values, and failure of the reactivity-selectivity principle (RSP).[9] The selectivities (ρ and β values in Table 1) are greater for the faster reactions. This type of anti-RSP is considered another criterion for the concerted aminolysis.[5]

Reference to Table 1 reveals that the β_X values are 1.42 ~ 1.60 which are rather greater than the values normally expected for the concerted aminolysis processes, β_X = 0.4 ~ 0.7[9] However, β_X values smaller than 0.4[10]as well as those larger than 0.7[11] have also been observed for the concerted reactions. Especially in solvents less polar than water, larger β_X (1.3 ~ 1.6)[12] are often obtained for the concerted processes. Thus the

Table 1. The Second Order Rate Constants, k_2 (10^2 dm^3 mol^{-1} s^{-1}) for the Reactions of *Z*-Aryl *N*-Allyl Thiocarbamates with X-Benzylamines in Acetonitrile at 40.0 °C

X	Z				ρ_Z[a]	β_Z[b]
	p-Me	H	*p*-Cl	*p*-Br		
p-OMe	1.14 0.764[c] 0.519[d]	2.74	9.55	10.7 7.28[c] 5.02[d]	2.39 ± 0.02	−0.99 ± 0.05
p-Me	0.757	1.79	6.30	6.98	2.37 ± 0.02	−0.98 ± 0.04
H	0.440	0.988	3.32	3.76	2.29 ± 0.03	−0.94 ± 0.04
p-Cl	0.225 0.153[c] 0.103[d]	0.501	1.56	1.67 1.10[c] 0.737[d]	2.15 ± 0.01	−0.90 ± 0.04
m-Cl	0.135	0.285	0.893	1.00	2.13 ± 0.03	−0.88 ± 0.03
ρ_X[a]	−1.41 ± 0.04	−1.49 ± 0.02	−1.58 ± 0.02	−1.59 ± 0.01	ρ_{XZ}[e] = −0.43 ± 0.13	
β_X[f]	1.42 ± 0.03	1.50 ± 0.03	1.59 ± 0.03	1.60 ± 0.02		

[a]The σ values were taken from Hansch, C.; Leo, A.; Taft, R. W. *Chem. Rev*. **1991**, *91*, 166. Correlation coefficients were better than 0.998 in all cases. [b]The pK_a values were taken from Albert, A.; Serjeant, E. P. *The Determination of Ionization Constants*; 3rd ed., Chapman and Hall: London, p145. Correlation coefficients were better than 0.997 in all cases. [c]At 30 °C. [d]At 20 °C. [e]Calculated by a multiple regression analysis using eq 2a. r = 0.999, n = 20 and F_{calc} = 1410 (F_{tab} = 10.66 at the 99.9% confidence level). [f]The pK_a values were taken from Fischer, A.; Galloway, W. J.; Vaughan, J. *J. Chem. Soc*. **1964**, 3588. Correlation coefficients were better than 0.997 in all cases. For X = *p*-CH_3O an extrapolated value of pK_a = 9.64 was used.

Table 2. The Kinetic Isotope Effects for the Reactions of Z-Phenyl *N*-Allyl Thiocarbamates with X-Benzylamines in Acetonitrile at 40.0 °C

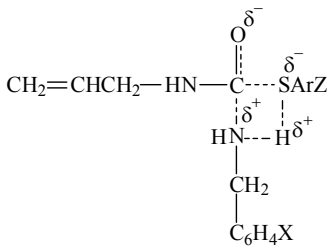
X	Z	k_H (×10^2 M^{-1}s^{-1})	k_D (×10^2 M^{-1}s^{-1})	k_H/k_D
p-OMe	*p*-Me	1.14 (±0.02)	0.844 (±0.008)	1.35 ± 0.02[a]
p-OMe	H	2.74 (±0.04)	1.94 (±0.03)	1.41 ± 0.02
p-OMe	*p*-Cl	9.55 (±0.08)	6.49 (±0.06)	1.47 ± 0.03
p-OMe	*p*-Br	10.7 (±0.10)	6.90 (±0.07)	1.55 ± 0.03
p-Cl	*p*-Me	0.225 (±0.002)	0.163 (±0.001)	1.38 ± 0.03
p-Cl	H	0.501 (±0.003)	0.343 (±0.003)	1.46 ± 0.02
p-Cl	*p*-Cl	1.56 (±0.01)	1.01 (±0.01)	1.53 ± 0.02
p-Cl	*p*-Br	1.67 (±0.02)	1.03 (±0.01)	1.61 ± 0.03

[a]Standard deviations.

large β_X values in the present work may be due to the less polar solvent used, acetonitrile. The relatively large β_X values may reflect rather tight bond formation in the TS.

Strong destabilization incurred by powerful nucleofugality of benzylamines from $T^{\pm}$ is known to cause the aminolysis to proceed by a concerted mechanism.[13] The order of the increasing rate of expulsion of amines from $T^{\pm}$ is reported as [5] pyridines < anilines < secondary alicyclic amines < quinuclidines < benzylamines. Moreover, it has been shown that carbonyl (C=O) has a greater proclivity for the concerted mechanism than thiocarbonyl (C=S) group[14] due to a narrower energy gap between π* and σ* levels, $\Delta\varepsilon = \varepsilon(\pi^*_{C=O}) - \varepsilon(\sigma^*_{C-S}) < \Delta\varepsilon = \varepsilon(\pi^*_{C=S}) - \varepsilon(\sigma^*_{C-S})$, enabling efficient mixing of the two antibonding orbitals.[15] Thus, concerted mechanisms are found for the aminolyses of *S*-(2,4-dinitrophenyl)[14] and *S*-(2,4,6-trinitrophenyl)[3b] *O*-ethyl thiocarbonates in contrast to the stepwise mechanisms for the corresponding dithiocarbonates.[16] Less polar solvents are also conductive to a concerted mechanism as observed for the aminolysis of carbonates from stepwise in water to concerted in acetonitrile.[17] For example, the aminolysis of 2,4,6-trinitrophenyl *O*-ethyl dithiocarbonates is stepwise[18] (biphasic Brönsted plot) in water, but is concerted (β_X = 0.53) in a less polar solvent (44 wt % aqueous EtOH).[19] The change of solvent from water to a less polar solvent such as MeCN destabilizes the zwitterionic intermediate by enhancing the rate of expulsion of the amine from $T^{\pm}$, and renders the intermediate, $T^{\pm}$, more unstable kinetically so that a concerted mechanism is enforced.[19]

The kinetic isotope effects, k_H/k_D, involving deuterated benzylamines ($XC_6H_4CH_2ND_2$)[20] in Table 2 are larger than unity (1.35 ~ 1.61) indicating that a proton transfer is involved in the TS, which in turn suggests that a hydrogen bonded cyclic TS. The relatively low $\Delta H^{\neq}$ with large negative $\Delta S^{\neq}$ values in



TS

Table 3 are consistent with this proposed TS structure. The $\Delta H^{\neq}$ values are small due to a large energy gain in C-N bond formation relative to energy loss in C-S bond cleavage in the TS and also the assistance in the C-S bond cleavage by the hydrogen bonding, and the $\Delta S^{\neq}$ values are large negative due to the strained cyclic four-membered TS structure.

In summary, we propose a concerted mechanism with a hydrogen bonded cyclic transition state for the aminolysis of aryl *N*-allyl thiocarbamates with benzylamines in acetonitrile based on the negative cross-interaction constant, failure of RSP,

Table 3. Activation Parameters[a] for the Reactions of Z-Phenyl *N*-Allyl Thiocarbamates with X-Benzylamines in Acetonitrile

X	Z	$\Delta H^{\neq}$/kcal mol^{-1}	$-\Delta S^{\neq}$/cal mol^{-1} K^{-1}
p-OMe	*p*-Me	6.6	46
p-OMe	*p*-Br	6.2	43
p-Cl	*p*-Me	6.4	50
p-Cl	*p*-Br	6.6	46

[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 ±1.0 kcal mol^{-1} and ±4 e.u. for $\Delta H^{\neq}$ and $\Delta S^{\neq}$, respectively.

the kinetic isotope effects greater than unity and relatively low $\Delta H^{\neq}$ with large negative $\Delta S^{\neq}$ values.

Experimental Section

Materials. GR grade acetonitrile was used after three distillations. GR grade benzylamine nucleophiles were used after recrystallization.

Substrates.

Phenyl *N*-allyl thiocarbamate. A solution of thiophenol (0.01 mol) in dry toluene (10 mL) was added to a solution of allyl isocyanate (0.01 mol). A catalytic quantity (0.5 mL) of pyridine was added and the solution refluxed for 2 h. On evaporation of the solvent *in vacuo*, the thiocarbamate precipitated and was recrystallized from chloroform-pentane. The other substituted phenyl *N*-allyl thiocarbamates were prepared in an analogous manner and recrystallized from chloroform-pentane. The substrates synthesized were confirmed by spectral and elemental analysis as follows.

CH_2=CHCH_2-NHC(=O)SC_6H_4-*p*-CH_3: mp 80 - 82 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.31 (3H, s, CH_3), 3.78 (2H, t, CH_2), 5.01 (2H, t, =CH_2), 5.70 (1H, m, =CH). 6.22 (1H, s, NH), 7.20-7.52 (4H, m, C_6H_4); ^{13}C NMR (100.4 MHz, $CDCl_3$) δ 166.5, 140.1, 135.0, 130.3, 124.8, 133.4, 116.5, 43.6, 21.3; ν_{max} (KBr), 3307 (NH), 2834 (CH, aromatic), 1651 (C=O), 598 (C-S); MS *m*/z 207 (M^+). Anal. Calcd for $C_{11}H_{13}NOS$: C, 63.7; H, 6.31. Found; C, 63.9; H, 6.32.

CH_2=CHCH_2-NHC(=O)SC_6H_5: mp 65 - 67 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.71 (2H. t, CH_2), 4.91 (2H, t, =CH_2), 5.61 (1H, m, =CH). 6.25 (1H, s, NH), 7.29-7.65 (4H, m, C_6H_4); ^{13}C NMR (100.4 MHz, $CDCl_3$) δ 165.8, 135.1, 133.2, 129.2, 129.0, 128.1, 116.2, 43.4; ν_{max} (KBr), 3306 (NH), 2835 (CH, aromatic), 1681 (C=O), 595 (C-S); MS *m*/z 193 (M^+). Anal. Calcd $C_{10}H_{11}NOS$: C, 62.1; H, 5.70. Found; C, 62.3; H, 5.72.

CH_2=CHCH_2-NHC(=O)SC_6H_4-*p*-Cl: mp 114 - 116 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.84 (2H. t, CH_2), 5.09 (2H, t, =CH_2), 5.74 (1H, m, =CH). 6.21 (1H, s, NH), 7.34-7.52 (4H, m, C_6H_4); ^{13}C NMR (100.4 MHz, $CDCl_3$) δ 165.1, 136.4, 135.8, 133.1, 129.4, 126.6, 116.9, 43.8; ν_{max} (KBr), 3304 (NH), 2832 (CH, aromatic), 1656 (C=O), 601 (C-S); MS *m*/z 227 (M^+). Anal. Calcd $C_{10}H_{10}ClNOS$: C, 52.7; H, 4.41. Found; C, 52.9; H, 4.42.

CH_2=CHCH_2-NHC(=O)SC_6H_4-*p*-Br: mp 120 - 122 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.86 (2H. t, CH_2), 5.05 (2H, t, =CH_2), 5.75 (1H, m, =CH). 6.28 (1H, s, NH), 7.38-7.59 (4H, m, C_6H_4); ^{13}C NMR (100.4 MHz, $CDCl_3$) δ 165.0, 136.7, 133.2, 132.4, 127.3, 124.2, 117.0, 43.9; ν_{max} (KBr), 3306 (NH), 2833 (CH, aromatic), 1657 (C=O), 595 (C-S); MS *m*/z 272 (M^+). Anal. Calcd $C_{10}H_{10}BrNOS$: C, 44.1; H, 3.70. Found; C,44.3; H, 3.71.

Kinetic measurement. Rates were measured conductometrically in acetonitrile. The conductivity bridge used in this work was a homemade computer-automatic A/D converter conductivity bridge. Pseudo-first-order rate constants, k_{obsd}, were determined by the Guggenheim method[21] with large excess of pyridine. Second order rate constants, k_2, were obtained from the slope of a plot of k_{obsd} *vs*. [BA] with more than five concentrations of benzylamine. The k_2 values in Table 1 are the averages of more than three runs and were reproducible to within ± 3%.

Product analysis. The substrate phenyl *N*-allyl thiocabamate (0.01 mol) was reacted with excess benzylamine (0.1 mol) with stirring for more than 15 half-lives at 40.0 °C in acetonitrile (*ca*. 200 mL) and the products were isolated by evaporating the solvent under reduced pressure. The product mixture was subjected to column chromatography (silica gel, 20% ethyl acetate-*n*-hexane). Analysis of the product gave the following results.

CH_2=CHCH_2-NHC(=O)NH$CH_2C_6H_5$: mp 89 - 91 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.52 (2H. t, CH_2), 4.05 (2H, d, CH_2), 4.90 (2H, m, =CH_2), 5.88 (1H, m, =CH). 6.19 (1H, s, NH), 7.05-7.35 (5H, m, C_6H_5); ^{13}C NMR (100.4 MHz, $CDCl_3$) δ 147.3, 127.9, 123.8, 116.8, 115.5, 115.3, 103.4, 32.4, 31.0; ν_{max} (KBr), 3322 (NH), 2837 (CH, aromatic), 1622 (C=O), 1247 (C-N); MS *m*/z 188 (M^+). Anal. Calcd for $C_{11}H_{12}N_2O$: C, 70.2; H, 6.41. Found; C, 70.4; H, 6.42.

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