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Cyanide Abstractions from Benzyl Isocyanides by Tri-n-Butyltin Radical: An Implication of Imbalanced Transition State and Entropy Control of Reactivities

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Abstract: The relative rates and Hammett constants (ρ= 0.70) are immune from the temperature effects thus violating reactivity/selectivity principle. The polar TS can be classified as the "imbalanced TS". The substituents control the extent of the bond fissions and the rates are governed by the entropy term.
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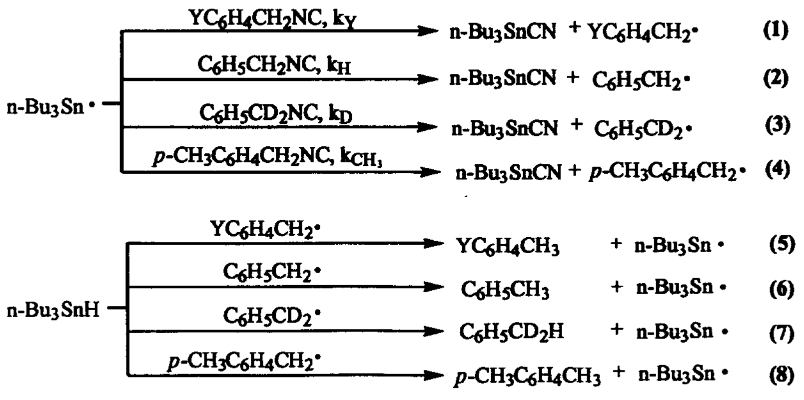
Benzyl isocyanide[1] reacts under homolytic condition with tri-n-butyltin hydride to produce toluene and tri-n-butyltin cyanide. Recently we[2] have reported the Hammett correlations for the same reactions with substituted-benzyl isocyanides. The reactions[1,2] can be explained with intervention of imidoyl radicals.[3]

$$YC_6H_4CH_2-\ddot{N}=C\!: + R_3Sn\cdot \xrightarrow{a} YC_6H_4CH_2-\ddot{N}=\dot{C}-SnR_3 \xrightarrow{b} YC_6H_4CH_2\cdot + R_3SnCN \text{ , (R : n-Bu)}$$

The substituent effects ($\rho = 0.77$) and the secondary α-deuterium kinetic isotope effects ($k_H/k_D = 1.11$) assign that *b* should be included in the rate-determining step.[4] The Hammett relations also suggest polarization of the transition state (TS) for *b*.

We wish to herein report novel temperature effects observed with the abstraction reactions. A substituted-benzyl isocyanide, benzyl isocyanide, tri-n-butyltin hydride, and naphthalene (internal standard) were dissolved in benzene. Tri-n-butyltin radical was generated in the benzene solutions either thermally with azoisobutyronitrile (AIBN) at 80 °C or photolytically with irradiations of 350 nm U.V. at the lower temperatures. Scheme 1 describes the reactions.[5]

Scheme 1



(Y : *p*-OCH_3, *p*-CH_3, H, and *p*-CN)

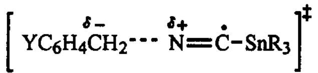
The disappearence of benzyl isocyanides excellently matches the formation of the toluenes (over 98%). The relative rates can be written down as with eq 9. The values of k_Y/k_H and ρ have been obtained at the temperatures. The relative rates (k_H/k_{CH_3} and k_D/k_{CH_3}) have been likewise obtained using the competition method. The secondary α-deuterium kinetic isotope effects were thereby calculated from $k_H/k_D = k_H/k_{CH_3} \times k_{CH_3}/k_D$. The differential activation parameters ($\Delta\Delta H^{\ddagger}_{Y\text{-}H}$ and $\Delta\Delta S^{\ddagger}_{Y\text{-}H}$) were calculated from the temperature studies with the Eyring equation.[6] These data are tabulated in Table 1.[5]

$$k_Y/k_H = [YC_6H_4CH_3]/[C_6H_5CH_3] \times [C_6H_5CH_2NC]_0/[YC_6H_4CH_2NC]_0 \qquad (9)$$

Table 1. Rate Data for the Cyanide Abstractions

temp. (℃)	$(k_Y/k_H)^{a,b}$				ρ (r)^c	$(k_H/k_D)^d$
	p-OCH$_3$	p-CH$_3$	H	p-CN		
0^e	0.68	0.84	1	3.26	0.70 (0.999)	1.110
25^e	0.69	0.83	1	3.24	0.70 (0.999)	1.110
40^e	0.66	0.84	1	3.19	0.70 (0.999)	1.110
80^f	0.63	0.80	1	3.12	0.71 (0.999)	1.110
$\Delta\Delta H^{\ddagger}_{Y\text{-}H}$^{g}, kcal/mol	-0.20	-0.11	0	-0.11		
$\Delta\Delta S^{\ddagger}_{Y\text{-}H}$^{h}, eu	-1.47	-0.74	0	1.96		
$T\Delta\Delta S^{\ddagger}_{Y\text{-}H}$ at 0℃	-0.40	-0.21	0	0.54		

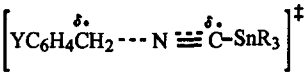
[a] The error limits are less than 5% for more than three runs. [b] Substituent constants are taken from reference 21. [c] Correlation coefficient. [d] Secondary α-deuterium kinetic isotope effects, Standard deviations: ±0.010. [e] Tri-n-butyltin radical was derived from the photolysis with 350 nm. [f] The tin radical was thermally produced using AIBN. [g] $\Delta\Delta H^{\ddagger}_{Y\text{-}H} = \Delta H^{\ddagger}_Y - \Delta H^{\ddagger}_H$ where $\Delta H^{\ddagger}_Y$ and $\Delta H^{\ddagger}_H$ are the activation enthalpies for substituted and unsubstituted benzyl isocyanides, respectively. [h] $\Delta\Delta S^{\ddagger}_{Y\text{-}H} = \Delta S^{\ddagger}_Y - \Delta S^{\ddagger}_H$ where $\Delta S^{\ddagger}_Y$ and $\Delta S^{\ddagger}_H$ are similarly related as with the enthalpy terms.



$$\left[YC_6H_4\overset{\delta-}{C}H_2 \cdots \overset{\delta+}{N}{=}\dot{C}{-}SnR_3 \right]^{\ddagger}$$

1

and



$$\left[YC_6H_4\overset{\delta\bullet}{C}H_2 \cdots N \equiv \overset{\delta\bullet}{C}{-}SnR_3 \right]^{\ddagger}$$

2

, R = n-Bu

The correlation coefficients are close to unity (r=0.999) and strongly validate the ρ-σ relation. Accordingly the negative charge in 1 may stay on the benzylic carbon without undergoing the conjugations. A similar localization of negative charge has been also proposed for the TS of deprotonations of nitroalkanes[7], which formulate the concept of "imbalanced TS". The Hammett constants (ρ = 0.70: a selectivity index) remain invariable against temperature gradient. The fragmentations of benzyl methyl substituted-benzyl carbinyloxy radicals (ρ^+ = -0.90) and the oxidations of 1-aryl-2,3-diphenylpropan-2-ols by cerium(IV) (ρ^+= -2.20) also show[8] an absence of the temperature effects. This has been rationalized[9] in terms of the entropic dominance using $Q = \Delta\Delta S^{\ddagger}_{Y\text{-}H}/R - \Delta\Delta H^{\ddagger}_{Y\text{-}H}/RT$ where $Q = \ln k_Y/k_H$ is defined as a measure of the selectivity. The contribution of differential entropy of activation ($\Delta\Delta S^{\ddagger}_{Y\text{-}H}$) becomes important when the radical reactions[8,10] traverse polar TS. The polar TS can be termed "imbalanced TS", a concept introduced by Jencks,[11] and justified with the perpendicular effect.[12,13] 2 is a resonance hybrid of $[YC_6H_4CH_2\text{-}N{=}\dot{C}\text{-}SnR_3] \longleftrightarrow [YC_6H_4CH_2{}^{\bullet} + N{\equiv}C\text{-}SnR_3]$, R=n-Bu, and retains an intermediate configuration between the two structures. Accordingly 1 deviates from 2 and assumes the "imbalanced structure".

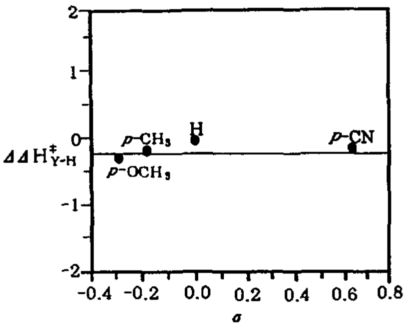


Figure 1. Plot of $\Delta\Delta H^{\ddagger}_{Y\text{-}H}$ vs σ for the cyanide abstractions

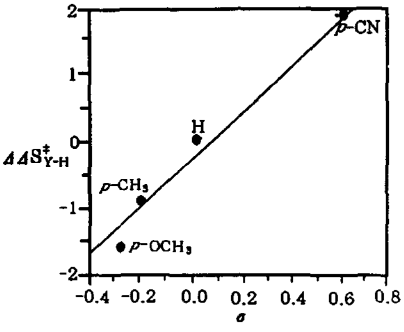


Figure 2. Plot of $\Delta\Delta S^{\ddagger}_{Y\text{-}H}$ vs σ for the cyanide abstractions

The differential activation parameters ($\Delta\Delta H^{\ddagger}_{Y\text{-}H}$ and $\Delta\Delta S^{\ddagger}_{Y\text{-}H}$) of Table 1 could be derived from the disturbances of the activation parameters ($\Delta H^{\ddagger}_{Y}$ and $\Delta S^{\ddagger}_{Y}$) stimulated by the substituents (Y). An electron-withdrawing substituent stabilizes the anionic moiety of $YC_6H_4\overset{\delta-}{C}H_2$ in 1 and thereby increases the extent of the bond cleavage i.e. $YC_6H_4\overset{\delta-}{C}H_2 \cdots NC$. The stabilizations may tend to lower enthalpy of activation($\Delta H^{\ddagger}_{Y}$) and the increase in the bond-breaking, on the other hand, heighten it. Such opposing interactions thus give rise to a nearly horizontal slope of Figure 1. Other radical reactions[8,10] involving polar TS also exhibit similar phenomena. If 2 were the effective TS, the substituent could monotonously either increase or decrease the enthalpy of activation ($\Delta H^{\ddagger}_{Y}$) and the differentials ($\Delta\Delta H^{\ddagger}_{Y\text{-}H}$) could assume variable magnitudes with different substituents (Y).

The electron-withdrawing substituents increase the degree of bond cleavage and the translational motions[14] of 1 become more vigorous to increase the entropy of activation ($\Delta S^{\ddagger}_{Y}$). Therefore the differential entropy term ($\Delta\Delta S^{\ddagger}_{Y\text{-}H}$) could be the result of the bond-breaking for a substituted-benzyl isocyanide being less than for benzyl isocyanide itself. The plot of $\Delta\Delta S^{\ddagger}_{Y\text{-}H}$ vs σ (Figure 2) shows the differential substituent effects. The excellent linear relation tells that the substituents systematically control the bond rupture and the rates are governed through the entropic terms. Similar linearities have been observed also with our other radical reactions.[8,10] The reactions of tert-butyl radical[15] with substituted-toluenes show $\rho = 0.5$ at 80 °C. The positive ρ value implies that an electron-withdrawing substituent accelerates the rates. The same substituent[16] may also function to increase the bond dissociation energy of benzylic C-H bond being broken. Therefore the rate accelerations can be achieved only when the entropy contribution dominates over its enthalpic partner's. Hydrogen abstractions[17] from substituted-phenols by tert-butoxy radical exhibit Hammett correlations ($\rho^{+} = -0.90$ at 22°C). p-Methoxyphenol ($k = 1.6 \times 10^{9}\ M^{-1}s^{-1}$) reacts faster with tert-butoxy radical than phenol ($k = 3.3 \times 10^{8}\ M^{-1}s^{-1}$). However the former ($E_a$ = 4.0 kcal mol^{-1}) involves higher energy of activation than the latter (E_a = 2.8 kcal mol^{-1}). The entropy of activation ($\Delta S^{\ddagger}_{Y}$) must outweigh its enthalpic counterpart to render the faster rate. Recently entropic control of inductive effects[18] on hydrogen atom abstractions with o-tert-butylbenzophenone ($\Delta S^{\ddagger} = -9.23$ eu, $\Delta H^{\ddagger} = 2.06$ kcal/mol) and o-benzoyltrimethylanilinium ($\Delta S^{\ddagger} = -16.84$ eu and $\Delta H^{\ddagger} = 1.90$ kcal/mol) has been reported.

The present secondary α-deuterium kinetic isotope effects exhibit larger figure ($k_H/k_D = 1.11$) than that for the reactions of phenyl radical ($k_H/k_D = 1.075$).[2] b may experience relatively greater bond-breaking for 1. The temperature effects calculate the differential activation parameters as $\Delta\Delta H^{\ddagger}_{H\text{-}D}$ = 0 kcal/mol and $\Delta\Delta S^{\ddagger}_{H\text{-}D}$ = 0.21 eu with $\Delta\Delta H^{\ddagger}_{H\text{-}D} = \Delta H^{\ddagger}_{H} - \Delta H^{\ddagger}_{D}$ and $\Delta\Delta S^{\ddagger}_{H\text{-}D} = \Delta S^{\ddagger}_{H} - \Delta S^{\ddagger}_{D}$. Here again the entropic dominance is responsible for the isotopic accelerations ($k_H/k_D = 1.11$).

In conclusion, the entropy control of reactivities can be a general phenomenon when the radical reactions traverse polar TS. Regardless of the directions of the polarities whether $\rho^+ < 0$ or $\rho > 0$, the polar TS confines the utilizations of the Hammond postulate[19] and reactivity/selectivity principle[20].

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4. The imidoyl radicals[3] have been observed by esr at quite low temperatures, i.e. -20 ℃. The lifetime of the intermediate radicals at 80 ℃ could be short enough for the steps *a* and *b* to occur almost concurrently. However the lifetime could be lengthened at the lower temperatures and the stepwise reactions could emerge.
5. The preparations of various benzyl isocyanides and the procedures of the thermal reactions at 80 ℃ are described in the **Experimental Section** of reference 2. The reactions at 0, 25, and 40 ℃ maintained the concentrations: a substituted benzyl isocyanide (0.5 M), benzyl isocyanide (0.5 M), tri-n-butyltin hydride (0.5 M), naphtalene(internal standard: 0.15 mM) and benzene (solvent). The tin radical has been then derived from the photolysis of tri-n-butyltin hydride at 350 nm. The photolysis was stopped at 10~15% consumption of benzyl isocyanides. The analytical method is the same as that of the thermal reactions. The secondary α-deuterium kinetic isotope effects have been similarly obtained employing the competition method.
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