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Cyanide Abstractions from Benzyl Isocyanides by Phenyl and Tri-*n*-Butyltin Radicals: New Examples of S_H2 Reactions[†]

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An isonitrile[2] can be considered as a hybrid of resonance structures of **1** and **2** with the former being responsible for the radical reactions. Various radicals[3] add to the terminal carbon atom to produce imidoyl radicals.[4] The presence of imidoyl radicals was, however, detected only at quite low temperatures i.e. −60 °C. The

$$\underset{\mathbf{1}}{R-\ddot{N}=C:} \leftrightarrow \underset{\mathbf{2}}{R-\overset{+}{N}\equiv\overset{-}{C}:}$$

reactions of benzyl isocyanides[5] with phenyl radical at 100 °C take place in a concerted manner.[6] Tri-*n*-butyltin (at 120−130 °C)[3b] and phenyl (at 100 °C)[5] radicals attack benzyl isocyanides to give corresponding cyanides and benzyl radicals via eq 1. The benzyl radicals were then

$$YC_6H_4CH_2NC + R\cdot \rightarrow YC_6H_4CH_2\cdot + RCN \quad (1)$$
$$R\cdot\text{: n-}Bu_3Sn\cdot \text{ and } C_6H_5\cdot$$

trapped by tri-*n*-butyltin hydride and carbon tetrachloride to yield toluenes[3b] and benzyl chlorides,[5] respectively. In our own hand,[7] the material balance was excellent (over 98%) between consumption of benzyl isocyanides and formation of toluenes. These outcomes[6,7] could imply that the homolytic α-additions via imidoyl radicals are unimportant at the temperatures. Reaction 1 is therefore the major sink for the radical reactions of benzyl isocyanides. The reactivities of phenyl and tri-*n*-butyltin radicals toward benzyl isocyanides are now to be comparatively discussed.

Table 1. Relative Rates, Hammett Correlations, and Secondary α-Deuterium Kinetic Isotope Effect for Cyanide Abstractions from Benzyl Isocyanides by Phenyl Radical at 100 °C

relative rates	Y					
	p-CH$_3$	H	*m*-OCH$_3$	*p*-Cl	*m*-CN	*p*-CN
k_{YH}/k_{Cl}[a]	4.02	4.76	5.16	5.24	6.11	6.64
k_{YD}/k_{Cl}[a]		4.24				

$\rho = 0.24^b$ ($r = 0.982$);[c] $k_{YH}/k_{YD}{}^d = 1.075$

[a] Error limits are less than 2% with average deviations of more than four runs. [b] The values of σ were taken from Ritchie, C. D.; Sager, W. F. *Prog. Phys. Org. Chem.* **1964**, *2*, 334. [c] Correlation coefficient. [d] $k_{YH}/k_{YD} = k_{YH}/k_{Cl} \times k_{Cl}/k_{YD}$.

Scheme 1

$$BP \longrightarrow \longrightarrow C_6H_5\cdot + CO_2 \quad (2)$$

$$YC_6H_4CH_2(D_2)NC + C_6H_5\cdot \xrightarrow{k_{YH(YD)}} YC_6H_4CH_2(D_2)\cdot + C_6H_5CN \quad (3)$$

$$CCl_4 + C_6H_5\cdot \xrightarrow{k_{Cl}} CCl_3\cdot + C_6H_5Cl \quad (4)$$

(Y: ***p***-CH$_3$, H, ***m***-OCH$_3$, ***p***-Cl, ***m***-CN and ***p***-CN)

Results

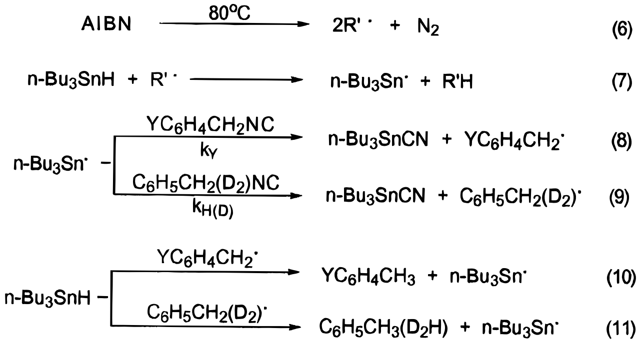
Reactions at 100 °C of the ampoules containing $YC_6H_4CH_2NC$ (0.5−1.0 M), CCl_4 (1.5−2.0 M), C_6H_5Br (3mM, internal standard), benzoyl peroxide (BP, 5 mM), and C_6H_6 (sovlent) gave C_6H_5CN and C_6H_5Cl as the principal products according to eqs 2−4 in Scheme 1. The molar ratios of $[YC_6H_4CH_2NC + CCl_4]/[BP] \geq 400$ could realize pseudo-first-order kinetics, whereby eq 5 has been derived from reactions 2−4. The relative rates (k_{YH}/k_{Cl} and k_{YD}/k_{Cl}) were then determined using eq 5. A Hammett correlation was obtained

$$k_{YH(YD)}/k_{Cl} = [C_6H_5CN]/[C_6H_5Cl] \times [CCl_4]_o/[YC_6H_4CH_2NC]_o \quad (5)$$

from the plot of k_{YH}/k_{Cl} against σ. A secondary α-deuterium kinetic isotope effect has been also obtained as follows, $k_{YH}/k_{YD} = k_{YH}/k_{Cl} \times k_{Cl}/k_{YD}$. These are shown in Table 1.

Reactions at 80 °C of the ampoules containing $YC_6H_4CH_2NC$ (1 M), $C_6H_5CH_2NC$ (1 M), n-Bu_3SnH (2.5 M), naphthalene (3 mM, internal standard), azoisobutyronitrile (AIBN, 3 mM), and C_6H_6 (solvent) gave rise to formations of $YC_6H_4CH_3$ and $C_6H_5CH_3$ through reactions 6−11 (Scheme 2). The disappearance of benzyl isocya-

Scheme 2



[†] Dedicated to Professor Lawrence A. Singer on the occasion of his 60th birthday.

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[6] A control experiment strongly excludes the occurrence of the α-addition. *tert*-Butyl isocyanide (25 mmol), *tert*-butyl chloride (50 mmol), and AIBN (2.5 mmol) were dissolved in 5 mL of benzene. The mixture was flushed with nitrogen and heated at 75 °C for 22 h. The NMR spectrum of the resulting mixture showed only the formation of pivalonitrile and absence of the α-addition product, $(CH_3)_3CN{=}C(Cl)C(CH_3)_3$. The present concerted mechanism could be compared to the two-bond homolysis of the peresters (Bartlett, P. D.; Simons, D. M. *J. Am. Chem. Soc.* **1960**, *82*, 1753 and Bartlett, P. D.; Rüchart, C. *J. Am. Chem. Soc.* **1960**, *82*, 1756). The benzyl radical possesses sufficient stability to cause the thermolysis of *tert*-butyl phenylperacetates to take place with synchronous cleavage of an O−O and a C−C bond producing carbon dioxide and the benzyl and *tert*-butoxy radicals: $C_6H_5CH_2C(O)O_2C(CH_3)_3 \rightarrow C_6H_5CH_2\bullet + CO_2 + \bullet OC(CH_3)_3$.

[7] Benzyl isocyanides were reacted with tri-*n*-butyltin hydride at 80 °C using AIBN as the initiator (refer to the Experimental Section). The excellent material balance indicates that reaction 1 must be the sole pathway for the reactions of benzyl isocyanides.

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Table 2. Relative Rates, Hammett Correlations, and Secondary α-Deuterium Kinetic Isotope Effect for the Cyanide Abstractions from Benzyl Isocyanides by Tri-*n*-butyltin Radical at 80 °C

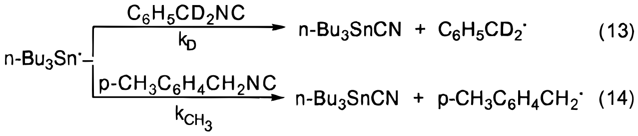
relative rates	Y				
	p-OCH$_3$	*p*-CH$_3$	H	*p*-Cl	*p*-CN
k_Y/k_H^{a}	0.63	0.80	1	2.04	3.12
$\rho = 0.77^b$ ($r = 0.979$);^{c} $k_H/k_D{}^d = 1.112$					

^{a} Error limits are less than 3% with average deviations of more than three runs. ^{b} The values of σ were taken from Ritchie, C. D.; Sager, W. F. *Prog. Phys. Org. Chem.* **1964**, *2*, 334. ^{c} Correlation coefficient. ^{d} $k_H/k_D = k_H/k_{p-CH_3} \times k_{p-CH_3}/k_D = 0.89/0.80 = 1.112$.

nides quantitatively (over 98%) accounts for the production of corresponding toluenes. Application of steady state approximation to the radical concentrations for $YC_6H_4CH_2\bullet$ and $C_6H_5CH_2\bullet$ could lead to eq 12. The

$$k_Y/k_H = [YC_6H_4CH_3]/[C_6H_5CH_3] \times [C_6H_5CH_2NC]_o/[YC_6H_4CH_2NC]_o \quad (12)$$

relative rates (k_Y/k_H) and Hammett correlations have been accordingly calculated (refer to Table 2). Tri-*n*-butyltin radical could react with $C_6H_5CD_2NC$ and *p*-$CH_3C_6H_4CH_2NC$ with rate constants k_D and k_{CH_3}, respectively. The relative rates (k_H/k_{CH_3} and k_D/k_{CH_3}) were



$$n\text{-}Bu_3Sn^{\cdot} \xrightarrow[k_D]{C_6H_5CD_2NC} n\text{-}Bu_3SnCN + C_6H_5CD_2^{\cdot} \quad (13)$$

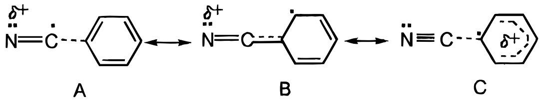
$$n\text{-}Bu_3Sn^{\cdot} \xrightarrow[k_{CH_3}]{p\text{-}CH_3C_6H_4CH_2NC} n\text{-}Bu_3SnCN + p\text{-}CH_3C_6H_4CH_2^{\cdot} \quad (14)$$

similarly obtained by the competition method using *p*-$CH_3C_6H_4CH_2NC$ as the standard. The secondary α-deuterium kinetic isotope effect has been thus available from $k_H/k_D = k_H/k_{CH_3} \times k_{CH_3}/k_D$ and is shown in Table 2.

Discussion

When phenyl radical was derived from thermolysis of benzoyl peroxide, weakly nucleophilic character had been disclosed for hydrogen atom abstractions from toluenes ($\rho = 0.18$)[8] and for bromine atom abstractions from benzyl bromides ($\rho = 0.13$).[9] Our $\rho = 0.24$ of Table 1 is thus consistent with those observations[8,9] and suggests the polar transition state (TS) structure: $[YC_6H_4C^{\delta-}H_2\cdots N{=}C\cdots C_6{}^{\delta+}H_5]$, **3**. The small ρ value could be associated with modest degree of the polarization. In case of electrophilic radicals,[10,11] the hydrogen abstraction reactions usually exhibit $\rho^+-\sigma^+$ Hammett correlations with $\rho^+ < 0$. The negative sign of ρ^+ tells that the polarity of the TS is opposite to that of **3**. $\rho^+-\sigma^+$ relations also testify to the conjugation of the positive charge on the benzylic carbon atom with the adjacent phenyl ring.

The deprotonations of nitroalkanes (CH_3NO_2, $MeCH_2NO_2$, Me_2CHNO_2) by the bases[12] could yield corresponding carbanions which experience dispersion of the negative charge into nitro group. However, such delocalization could not occur and the charge localizes instead on the carbon atom for the corresponding TS. The fractional benzylic anion moiety of TS **3** could behave similarly so that the negative charge may not conjugate with the phenyl ring. The validity of $\rho-\sigma$ correlation in Table 1 could be thus soley derived from the inductive effects caused by the substituents (Y). On the other hand, the structure of cationic portion of **3** could be equivalent to a resonance hybrid of A, B, and C. In particular, C could significantly reduce the free energy of activation for **3**.



The cyanide abstractions by tri-*n*-butyltin radical show a relatively large Hammett constant ($\rho = 0.77$) which indicate also the similar polarization to that of **3**, that is $[YC_6H_4C^{\delta-}H_2\cdots N{=}C\cdots Sn^{\delta+}(n\text{-}Bu)_3]$, **4**. TS **4** could draw more charge separations than **3**. Here again the negative charge stays on the benzylic carbon atom. The cationic part of **4** resembles tri-*n*-butyltin cation. The bond dissociation energy of n-Bu_3Sn-H is 74 kcal.[13] The ionization potential of n-$Bu_3Sn\bullet$ could be roughly 143 kcal which is actually the oxidation potential of $Me_3Sn\bullet$.[14] The bond strength of C_6H_5−H is 112 kcal[15] and ionization potential of $C_6H_5\bullet$ is 212 kcal.[16,17] Tri-*n*-butyltin cation, n-Bu_3Sn^+, could be thereby 107 kcal below the phenyl cation, $C_6H_5{}^+$, in terms of the heat content. The vigorous stabilization of tri-*n*-butyltin cation could provoke decent $N{=}C\cdots Sn^{\delta+}(n\text{-}Bu)_3$ bond formation for **4**, which may be then translated into the equivalent $YC_6H_4C^{\delta-}H_2\cdots N{=}C$ bond breaking. Accordingly, **4** could involve more bond cleavage than **3**. This is eminently consistent with the larger figures of Hammett constant and secondary α-deuterium kinetic isotope effect for the tin radical ($\rho = 0.77$; $k_H/k_D = 1.112$) than for the phenyl radical ($\rho = 0.24$; $k_{YH}/k_{YD} = 1.075$).

The structure of polar TS i.e. **3** and **4** must not be a resonance hybrid of the reactants and the products of eq 1. The polar TS is thereby displaced from the "intermediate configuration". The phenomenon of such displacement has been rationalized as the Perpendicular Effect.[18] Due to the Perpendicular Effect,[18] the polarity of **3** and **4** may not be adequately correlated with the entities inherent in the corresponding reactants and products. The Marcus theory[19] also maintains that the intrinsic barrier is independent of the free energy of reaction.

When a σ bond is located at position β to a phenyl ring and involved with the atom transfer reactions, the TS could take a polar structure. The direction of the polarization could be critically influenced by the character

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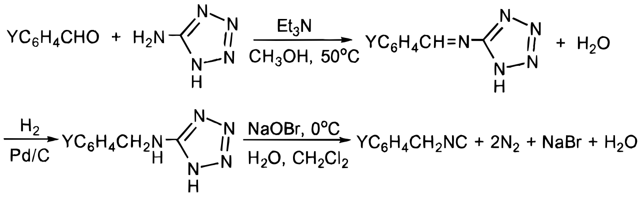
of the attacking radicals. Since the cyanide group is univalent and the reactions are concerted, the cyanide abstractions can be classified as the S_H2 reactions.

Experimental Section

Materials. The reagents are commercially available from major suppliers. Liquids were distilled with center-cut collection, and solids recrystallized according to standard procedures.[20]

Benzyl isocyanides ($YC_6H_4CH_2NC$; Y = *p*-OCH_3, *p*-CH_3, H, *m*-OCH_3, *p*-Cl, *m*-CN, and *p*-CN) were prepared according to a known method[21] and characterized by NMR and IR data.



Deuterated benzyl isocyanide ($C_6H_5CD_2NC$)[22] was obtained via dehydrations of $C_6H_5CD_2NDCHO$, which could be derived from reactions of $C_6H_5CD_2ND_2$ with HCO_2H. Reductions of C_6H_5CN with $LiAlD_4$ gave $C_6H_5CD_2ND_2$.[23] The percent of deuteration of the isonitrile was 98%, according to the NMR spectrum.

$$C_6H_5C{\equiv}N + LiAlD_4 \xrightarrow[\text{gentle reflux}]{\text{ether}} C_6H_5CD_2ND_2$$

$$C_6H_5CD_2ND_2 + HCO_2H \longrightarrow C_6H_5CD_2NDCHO + H_2O$$

$$2C_6H_5CD_2NDCHO + POCl_3 + 4C_5H_5N \longrightarrow 2C_6H_5CD_2N{\equiv}C + 3C_5H_5N\cdot HCl + C_5H_5N\cdot HPO_3$$

Kinetic Procedure and Gas Chromatographic Analyses. A reaction mixture consisted of $YC_6H_4CH_2NC$ (0.5−1.0 M), CCl_4 (1.5−2.0 M), C_6H_5Br (3 mM, internal standard), benzoyl peroxide (BP, 5 mM), and C_6H_6 (solvent). This was placed and degassed in Pyrex ampoules by the freeze-pump-thaw method. The mixture was then heated at 100 °C for 3.5 h. The products were analyzed on DB-1 capillary column (30 m) with Varian 3300 gas chromatography equipped with FID. The resolutions were optimum with temperature programming from 80−230 °C.

A reaction mixture consisted of $YC_6H_4CH_2NC$ (1 M), $C_6H_5CH_2NC$ (1 M), n-Bu_3SnH (2.5 M), naphthalene (3 mM, internal standard), AIBN (3 mM), and C_6H_6 (solvent). This was placed and degassed in Pyrex ampoules by freeze-pump-thaw method for the thermal reactions at 80 °C for 1 h. The reaction time was adjusted to consume 10−15% of starting benzyl isocyanides. The products were analysed on carbowax 20M capillary column (70 m) with a Varian 3300 gas chromatograph equipped with FID. The resolutions were optimum with temperature programming from 50−180 °C. A reaction mixture was of $C_6H_5CH_2NC$ (0.5 M) or $C_6H_5CD_2NC$ (0.5 M), *p*-$CH_3C_6H_4CH_2NC$ (0.5 M), n-Bu_3SnH (0.5 M), naphthalene (3 mM, internal standard), AIBN (3 mM), and C_6H_6 (solvent). This was similarly treated as above for the thermolyses and analyses when otherwise stated. DB-1 capillary column (30 m) was instead employed.

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