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# Ambident Reactivity of the Cyanate Anion

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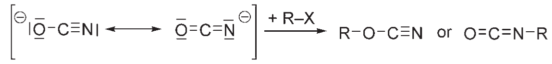
*Dedicated to Professor Heinrich Nöth on the occasion of his 80th birthday*

The cyanate anion is an ambident nucleophile, which may react with electrophiles either at the oxygen terminus to yield alkyl cyanates or at the nitrogen terminus to yield isocyanates (Scheme 1).[1]



Scheme 1. Ambident reactions of the cyanate anion.

Because the charge density is higher at the more electronegative oxygen center while the larger HOMO coefficient is at nitrogen,[2] the concept of charge and orbital control[3] predicts hard electrophiles to attack at the oxygen side and soft electrophiles to attack at the nitrogen. It was, therefore, expected that alkyl cyanates should be formed in nucleophilic substitution reactions with $S_N1$ character while alkyl isocyanates should be formed in nucleophilic substitution reactions with $S_N2$ character.[4]

In line with early work of Wurtz on the alkylation of potassium cyanate with diethyl sulfate,[5] Slotta and Lorenz reported that the reaction of dialkyl sulfates with alkali metal cyanates is the best method for synthesizing alkyl isocyanates [Eq. (1)].[6]

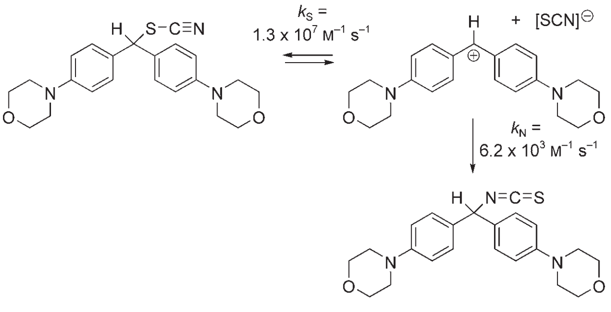
$$\mathrm{KOCN} + (\mathrm{RO})_2\mathrm{SO}_2 \rightarrow \mathrm{R\text{-}NCO} + \mathrm{ROSO_3K} \qquad (1)$$

It cannot be excluded, however, that the selective formation of alkyl isocyanates under these conditions is due to a cyanate ion catalyzed isomerization of an initially formed alkyl cyanate into its thermodynamically more stable isomer [Eq. (2)].[7]

$$\mathrm{R\text{-}OCN} + \mathrm{NCO}^- \rightarrow \mathrm{R\text{-}NCO} + \mathrm{NCO}^- \qquad (2)$$

Subsequent isomerization of the initial products may also be responsible for the selective formation of alkyl isocyanates by the reaction of silver cyanate with primary alkyl halides and trityl chloride. On the other hand, almost equal amounts of alkyl cyanates and isocyanates were obtained when secondary iodoalkanes were treated with silver cyanate, and the formation of *tert*-butyl isocyanate together with 2-methylpropene and cyanic acid was also considered as an indication for concomitant O- and N-attack.[4]

In previous work,[8] kinetic investigations were employed to demonstrate the change of regioselectivity in reactions of the thiocyanate ion with benzhydrylium ions of variable electrophilicity. A biexponential decay of the benzhydrylium absorbances, a fast reversible attack at the sulfur terminus and the slow irreversible attack at nitrogen side was observed when morpholino-substituted benzhydrylium ions were photolytically generated in the presence of $SCN^-$ ions (Scheme 2).



Scheme 2. Ambident reactivity of the thiocyanate anion (20 °C, acetonitrile).

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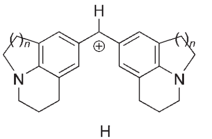
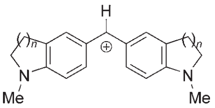
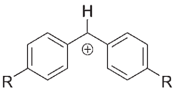
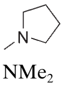
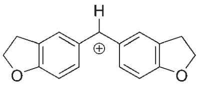
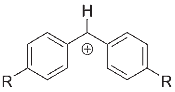
In reactions with more electrophilic carbocations, the $k_S/k_N$ ratio decreased because both reactions approach diffusion control.

We now set out to examine whether reactions with benzhydrylium ions (Table 1) can also be employed to elucidate the ambident reactivity of cyanate ions.

Table 1. Second-order rate constants of the reactions of cyanate ions with the benzhydrylium ions **1** (20 °C, acetonitrile).

| Benzhydrylium ions | | | | $E^{[a]}$ | $k_2$ [$\mathrm{M}^{-1}\,\mathrm{s}^{-1}$] |
|---|---|---|---|---|---|
|  | $n=1$ | | **1a** | −10.04 | $1.11\times10^3$ |
| | $n=2$ | | **1b** | −9.45 | $2.53\times10^3$ |
|  | $n=1$ | | **1c** | −8.76 | $1.33\times10^4$ |
| | $n=2$ | | **1d** | −8.22 | $3.47\times10^4$ |
|  | R= |  | **1e** | −7.69 | $1.09\times10^5$ |
| | R= | $NMe_2$ | **1f** | −7.02 | $3.21\times10^5$ |
| | R= | NMePh | **1g** | −5.89 | $2.88\times10^6$ |
| | R= | $N(Ph)_2$ | **1h** | −4.72 | $3.48\times10^7$ |
| | R= | $NMe(CH_2CF_3)$ | **1i** | −3.85 | $1.60\times10^8$ |
|  | | | **1j** | −1.36 | $1.06\times10^{10}$ |
|  | R= | OMe | **1k** | 0.00 | –[b] |
| | R= | Me | **1l** | 3.63 | $2.47\times10^{10}$ |
| | R= | Cl | **1m** | 6.02 | –[b] |

[a] Electrophilicity parameters as defined previously.[9,10] [b] Only used for product studies.

Exclusive formation of benzhydrylium isocyanates was observed when benzhydrylium tetrafluoroborate **1h**-$BF_4$ or chloro-bis(4-methoxyphenyl)methane **1k**-Cl was treated with tetraethylammonium cyanate in acetonitrile (for product identification see Supporting Information). As in the examples quoted above, it was not clear whether the isolated products resulted from kinetic or thermodynamic control.

The kinetics of the reactions of the less electrophilic benzhydrylium ions were followed photometrically by combining acetonitrile solutions of (**1a**–**f**)-$BF_4$ with solutions of $Et_4N^+OCN^-$ in a stopped-flow instrument and monitoring the decay of the absorbance at the absorption maxima[8,11] in the visible as described previously.[9] The experiments were carried out with an excess of $Et_4N^+OCN^-$ under first-order conditions, resulting in an exponential decay of the absorbances of the benzhydrylium ions, from which the first-order rate constants $k_{obs}$ were derived.

The reactions of the carbocations **1g**–**j** and **1l** were too fast to be determined in this way. Therefore, the corresponding diarylisocyanatomethanes, which were obtained by mixing the benzhydrylium tetrafluoroborates (**1g**–**i**)-$BF_4$ or the chlorodiarylmethanes (**1j**,**l**)-Cl with an excess of $Et_4N^+OCN^-$, were irradiated by laser pulses (<1 ps, approx. 1 μJ, center wavelengths between 265 and 300 nm matched to the absorption maxima) to yield the benzhydrylium ions **1g**–**j** and **1l** as described previously.[12,13] The generated benzhydrylium ions then reacted with the cyanate anion, and the change of absorbance due to the reaction of the benzhydrylium ions with the cyanate anions was monitored at appropriate timescales. As in the stopped-flow experiments, these reactions were also performed under first-order conditions.

As depicted in the Supporting Information, plots of the first-order rate constants $k_{obs}$ vs $[OCN^-]$ were linear, and the resulting slopes gave the second-order rate constants $k_2$ listed in Table 1.

Figure 1 shows that the second-order rate constants $k_2$ for **1a**–**i** correlate linearly with the electrophilicity parameters $E$ of the benzhydrylium ions as required by Equation (3), where $E$ is the electrophilicity parameter, $N$ is the nucleophilicity parameter and $s$ is the nucleophile-specific slope parameter.

$$\log k_2 = s(N + E) \tag{3}$$

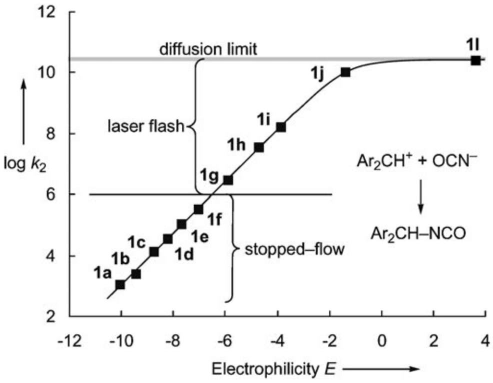
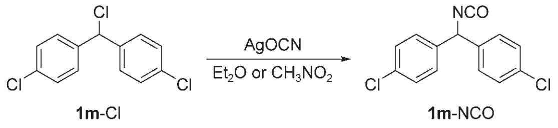


Figure 1. Plot of log $k_2$ for the reactions of the cyanate ion with benzhydrylium ions **1a**–**j**,**l** in acetonitrile at 20 °C versus their electrophilicity parameters $E$.

The flattening of the curve at log $k_2 > 10$ is due to diffusion control, which is in the same order of magnitude as for other reactions of benzhydrylium ions with anions in acetonitrile.[12,14] The fact that the rate constants determined by the stopped-flow and the Laser flash technique are on the same correlation line shows the internal consistency of our kinetic measurements, and from the linear part of this graph we can derive $N = 13.60$ and $s = 0.84$ for $OCN^-$ in acetonitrile.

Can all observed second-order rate constants be assigned to N-attack as suggested by the product studies? The smooth correlation line shown in Figure 1 indicates that the rate-determining step does not change throughout this reaction series. If N-attack would be accompanied by a fast and reversible O-attack, one should be able to observe a biexponential decay as in the previous studies with $SCN^-$.[8] From the fact that all kinetics investigated in this work show monoexponential decays, one can derive that the equilibrium constants for O-attack - if it occurs at all - must be so small that the low concentrations of the intermediate benzhydryl cyanates are kinetically irrelevant. This argument does not hold when N- and O-attack proceed with comparable rates, which may occur in the diffusion-controlled range. One can assume that highly electrophilic carbocations which do not meet a barrier when approaching OCN$^-$ from either side will give mixtures of R-NCO and R-OCN. However, when the benzhydryl chloride **1m**-Cl was treated with AgOCN in diethyl ether or nitromethane following a procedure reported by Holm and Wentrup,[4] the corresponding benzhydryl isocyanate **1m**-NCO was isolated exclusively (Scheme 3). We cannot specify whether the isocyanate **1m**-NCO is the result of kinetic or thermodynamic control because even primary alkyl cyanates have been reported to rearrange into alkyl isocyanates under mild conditions.[7]



Scheme 3.

The fact that NCO$^-$ reacts quantitatively even with **1a** and **1b**, that is, with carbocations of low Lewis acidity, while the ionization equilibrium is on the side of the ions for (**1a**–**f**)-NCS[8] indicates that NCO$^-$ is a much stronger Lewis base towards carbocations than NCS$^-$. A direct comparison of the N-nucleophilicities of NCO$^-$ and NCS$^-$ can be derived from their reactions with the benzhydrylium ions **1g** and **1i**: The nitrogen of NCO$^-$ is 500–1000 times more reactive than the nitrogen of NCS$^-$.

We finally want to come back to the question of orbital and charge control: Do $S_N1$ reactions of cyanates proceed with charge control to give alkyl cyanates? Figure 1 shows that carbocations with electrophilicity parameters $E > -1$, that is, carbocations which are less stabilized than the dianisylcarbenium ion **1k** or the tritylium ion undergo diffusion-controlled reactions with NCO$^-$. Those types of carbocations which are typically generated as intermediates of $S_N1$ reactions will therefore undergo barrier-less reactions with the cyanate anion without passing through a transition state, and reactivity concepts which are based on relative activation energies cannot be employed. Because similar situations have recently been reported for the reactions of carbocations with SCN$^-$,[8] CN$^-$,[15] and NO$_2^-$,[12] cyanate anions are the fourth example of prototype ambident anions, the behavior of which cannot be explained by the HSAB concept or the concept of charge and orbital control. Other cases can be expected to follow.

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**Keywords:** alkyl cyanates · carbocations · kinetics · linear free energy relationships

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