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# Reactions of *tert*-butyl isocyanide with distonic radical cations

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## Abstract

The reactivity of *tert*-butyl isocyanide was examined toward representative distonic radical cations. Two distinct types of reactivity were found, that characteristic of the electrophilic and/or acidic nature of the charge site of the ion, and that characteristic of the unpaired spin at the free radical moiety. *Tert*-butyl isocyanide reacts with charged groups via transfer of a cyanide ion and/or abstraction of a proton, while a cyano radical is transferred to the radical site. These two types of reactivity are usually mutually exclusive due to great differences in reaction rates. *Tert*-Butyl isocyanide reacts preferentially at the distonic radical cation's charge site. Reaction occurs at the radical site only if the charge site is inert, for example, by virtue of low acidity and coordinative saturation. The applicability of *tert*-butyl isocyanide to the study of distonic radical cations is demonstrated and insight into the structures of selected charged phenyl radicals is provided. (Int J Mass Spectrom 185/186/187 (1999) 91–96) © 1999 Elsevier Science B.V.

**Keywords:** Distonic ions, isocyanides, ion-molecule reactions

## 1. Introduction

Distonic ions [1] (i.e. ionized biradicals, zwitterions, and ylides) are a class of radical ions that has been the focus of numerous recent gas-phase and computational studies. Such radical ions occur commonly as mass spectral fragments [2]. Furthermore, much data has been mounting over the last decade suggesting that many conventional radical cations spontaneously isomerize to distonic ion structures [2,3]. Many more ions can be converted to their more stable distonic forms through the intermediacy of ion–molecule interactions [4]. Yet other distonic ions have been purposely designed and generated via MS<sup>n</sup>

procedures to address important chemical questions [5].

By their very nature, distonic ions often have spatially separated centers of charge and odd spin density. Because of this separation, their reactions can usually be cleanly divided into ionic reactions occurring at the charge site and radical reactions occurring at the radical site [2,5]. Taking advantage of this dichotomy of reactions, several reagents have emerged whose radical-type reactivity toward distonic ions is qualitatively different from their reactivity toward conventional radical cations. For example, dimethyl disulfide and dimethyl diselenide react with most distonic ions by thiomethyl and selenomethyl transfer, respectively, while conventional radical cations either are neutralized by electron transfer or no reaction takes place [6].

Dimethyl disulfide and dimethyl diselenide share a

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Dedicated to Professor Michael T. Bowers on the occasion of his 60th birthday.

common origin as radical traps [7]. Another radical trap with potential application for the characterization of distonic ions is *tert*-butyl isocyanide [8]. Isocyanides are carbenoids that react with neutral radicals in the gas-phase and in solution to produce a cyanide and the *tert*-butyl radical via an imidoyl intermediate [9]. Some distonic radical anions have been observed to react with *tert*-butyl isocyanide by cyano-radical abstraction [10]. We report here a study on the reactions of *tert*-butyl isocyanide with several well-known distonic radical cations. These preliminary experiments show that radical-type reactivity is indeed observed, but that reactions at the radical site are unable to compete effectively with reactions at the charge site. The observation of cyano-radical abstraction therefore implies that the charge site is unreactive. Thus, the reactions of *tert*-butyl isocyanide are complementary to those of dimethyl disulfide and dimethyl diselenide and can be used to identify the subcategory of distonic ions with inert charge sites.

## 2. Experimental

All experiments were carried out using an Extrel FTMS Model 2001 Fourier-transform ion cyclotron resonance (FT-ICR) mass spectrometer. This instrument contains a differentially pumped dual cell which is placed within the magnetic field produced by a 3.0 T superconducting magnet. The nominal base pressure is less than  $10^{-9}$  Torr, as maintained by two Balzers turbomolecular pumps ( $330 \text{ L s}^{-1}$ ), each backed with an Alcatel mechanical pump. The pressure is measured with two ionization gauges located on either side of the dual cell. The two cells are separated by a common wall (the conductance limit) which contains a 2 mm hole in the center. Ions were transferred from one cell into the other by grounding the conductance limit for approximately  $100 \mu\text{s}$ . After transfer, the ions were kinetically and internally cooled by multiple collisions with argon that was introduced into the cell via a pulse valve assembly.

Ions **1–5** were produced by electron ionization of various organic precursors. Ions **6–10** were generated by a multiple-step gas-phase synthesis which has been

described previously [5a]. Ions **3–5** are fragment ions of 1,4-dioxane [1], 3-pentanone [11], and diethyl-ether, respectively. Ions **1** and **2** are the radical cations of methyl formate [3] and cyclobutanone [11]. These ions have been shown to spontaneously isomerize to distonic ion structures. All chemicals were used as received from the commercial supplier and were tested mass spectrometrically for purity.

In each experiment, the reactant ion was isolated by ejecting all other ions from the cell with several stored-waveform inverse Fourier-transform (SWIFT) excitation pulses. The reactant ion was then allowed to react with *tert*-butyl isocyanide ( $4.0 \times 10^{-8}$ – $1.2 \times 10^{-7}$  Torr) for varied time periods (ranging from  $<100$  ms to several seconds). Because ion–molecule reactions under the above conditions are governed by pseudo-first order kinetics, the second order reaction rate constant ( $k_{\text{exp}}$ ) was determined for each reaction from the pressure of *tert*-butyl isocyanide and the slope of the semilogarithmic plot of relative reactant ion abundance versus time. The reaction rate was compared to the theoretically predicted collision rate ( $k_{\text{coll}}$ ) obtained from parameterized trajectory theory [12]. The relative reaction efficiencies ( $k_{\text{exp}}/k_{\text{coll}}$ ) are presented in Table 1 [13]. The reaction efficiencies were corrected for the sensitivity of the ion gauge to *tert*-butyl isocyanide [14] and for the pressure gradient between the cell and ion gauge by comparison with a reference reaction that was assumed to proceed at the collision rate. The product branching ratios were determined at short reaction times where secondary reactions had not taken place.

## 3. Results and discussion

The reactions of *tert*-butyl isocyanide with distonic radical cations can be divided into two categories, depending on whether the reaction occurs at the charge site or the radical site of the ion. Reactions at the radical site proceed by cyano-radical transfer, just as is expected for neutral free radicals. Reactions at the charge site, in contrast, often involve cyanide-ion transfer, a reaction previously observed for a wide variety of organic cations [15]. These two types of

Table 1  
Product branching ratios (%) and efficiencies<sup>a</sup> of reactions of *tert*-butyl isocyanide with ions 1–10

Ion	Product(s)	Branching ratios	Efficiency <sup>a</sup>
1	Proton abstraction Cyanide transfer	50% 50%	118%
2	Cyanide transfer HCN transfer	90% 10%	95%
3	Cyanide transfer	100%	94%
4	Cyanide transfer	100%	77%
5	Cyanide transfer	100%	67%
6	Cyano-radical transfer	100%	28%
7	Cyano-radical transfer	100%	21%
8	Cyano-radical transfer	100%	15%
9	Addition accompanied by loss of a methyl radical Cyano-radical transfer	70% 30%	<sup>b</sup>
10	No reaction	<sup>b</sup>	<sup>b</sup>

<sup>a</sup> Efficiency =  $k_{\text{rxn}}/k_{\text{collision}}$ .

<sup>b</sup> Reaction does not follow pseudo-first order kinetics.

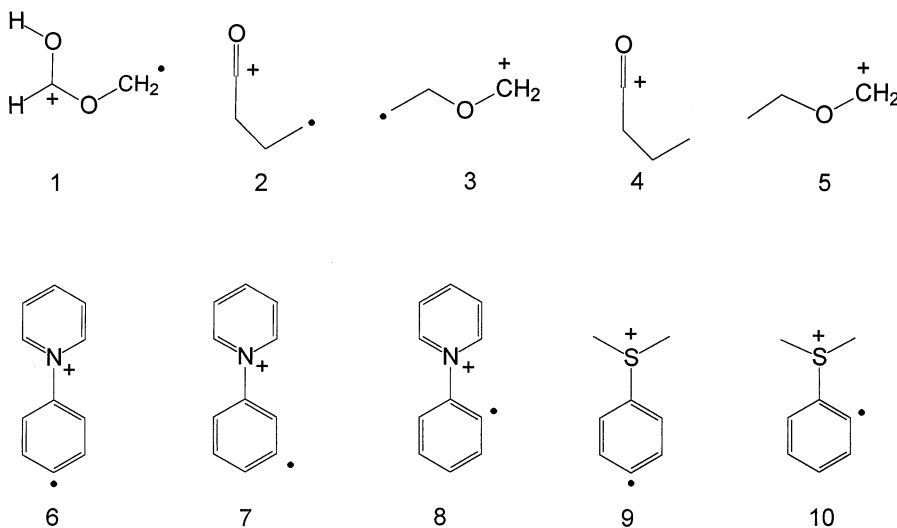
reactions are competitive, and only one type occurs for most distonic radical cations.

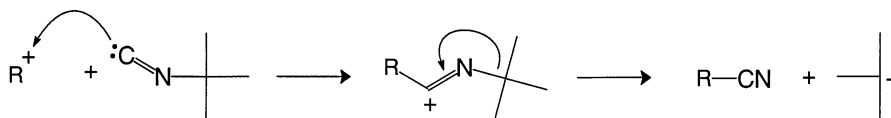
#### 4. Charge site reactions

*Tert*-butyl isocyanide reacts with most even-electron cations by cyanide-ion transfer, proton abstraction, or a mixture of both, depending on the acidity of the reactant ion [15]. The cyanide ion transfer is generally rapid. The driving force for this reaction is the barrierless formation of an intermediate adduct in

which the attacking cation is bonded to the isocyanide carbon (Scheme 1). This adduct dissipates its excess energy by heterolytically breaking the fragile bond between the *tert*-butyl and cyanide moieties to form the *tert*-butyl cation and a neutral cyanide. The *tert*-butyl cation reacts with neutral *tert*-butyl isocyanide by proton transfer, a result predicted by the high proton affinity *tert*-butyl isocyanide [16]. Protonated *tert*-butyl isocyanide reacts further to form a variety of tertiary and quaternary products.

The general description provided above for the





Scheme 1.

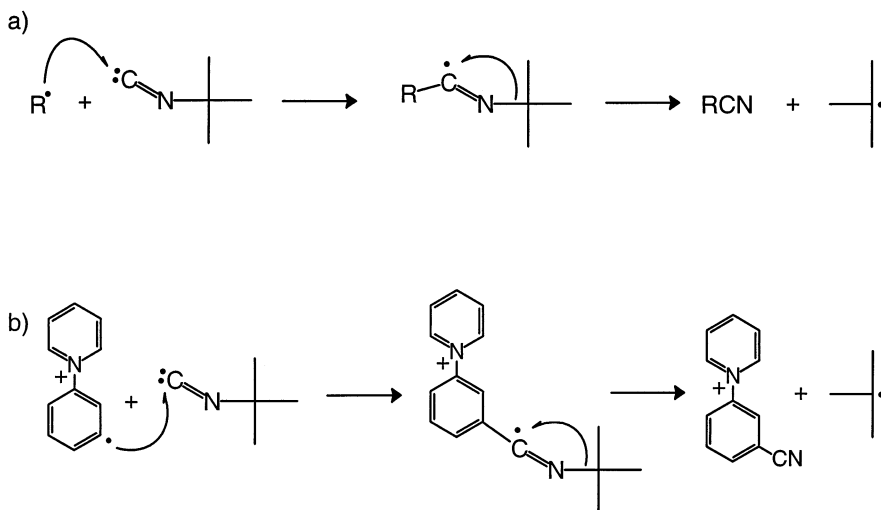
reactivity of *tert*-butyl isocyanide with even-electron cations also serves to characterize the reactions of distonic ions **1**–**3**. All these ions show cyanide ion abstraction (Table 1). Presumably, the rapid ionic reaction precludes reactions at the radical site. In support of this assumption, similar reactivity was observed for the even-electron analogs of the radical cations **2** and **3**, the ions **4** and **5**, respectively (Table 1). In addition to cyanide ion abstraction, the distonic methyl formate ion **1** readily transfers a proton to *tert*-butyl isocyanide. This can be understood based on the high acidity of the unsaturated charge site of this ion. Protonated methyl formate also rapidly protonates *tert*-butyl isocyanide.

Interestingly, the distonic ion **2** shows a minor reaction channel corresponding to net HCN-abstraction, a reaction that does not occur for its analog **4**. However, HCN abstraction was observed for some other cations. For example, a small amount of protonated cyanobenzene is produced upon reaction of

*tert*-butyl isocyanide with the phenylium ion (in addition to the major product *tert*-butyl cation). The protonated cyanobenzene is probably generated upon reaction between the initially produced *tert*-butyl cation and neutral cyanobenzene before they exit the collision complex. Similarly, HCN-abstraction has been reported for the reaction of some ionized singlet biradicals with *tert*-butyl isocyanide [5b,c].

#### 4.1. Distonic ions with inert charge sites

Like cations, radicals react with *tert*-butyl isocyanide via an addition–elimination mechanism (Scheme 2a). While the electrophilic addition of cations to the isocyanide carbon is a barrierless process, radical addition requires unpairing the lone pair of electrons on this carbon and thus involves a barrier. As a result, neutral radicals add relatively slowly to *tert*-butyl isocyanide in solution [17]. However, the charged nature of distonic radical cations is expected to lead to



Scheme 2.

a lower barrier since previous studies have demonstrated that the barrier to addition is subject to polar effects [18]. Nevertheless, the results shown in Table 1 demonstrate that whenever a distonic ion is presented with the choice between a barrierless reaction at the charge site and a reaction at the radical site, it will inevitably choose the former. Only when reaction at the charge site is not feasible, a distonic ion reacts with *tert*-butyl isocyanide by the cyano-radical abstraction characteristic of neutral radicals (Scheme 2b). Lack of reactivity at the charge site arises, for example, in cases of coordinative saturation and/or low acidity, as demonstrated by the reactivity observed for the distonic ions **6–8** (Table 1). These species react with *tert*-butyl isocyanide by exclusive cyano-radical abstraction.

#### 4.2. Structural characterization of distonic ions

The gas-phase synthesis of distonic ions that contain the phenyl radical moiety (e.g. ions **6–10**) was reported previously [5a]. Most of these charged phenyl radicals can be generated in a good yield. However, ions such as **8** and **10**, wherein the radical site is in the *ortho* position with respect to the charged substituent, do not react like other distonic ions with the reagents studied [5a]. Specifically, **10** was found to be unreactive toward dimethyl disulfide while its isomer **9** reacts in a typical radical fashion by thiomethyl abstraction. Likewise, only about half of the ion population of **8** reacts with allyl iodide by iodine atom abstraction (the reactivity observed for **6** and **7**), resulting in a marked deviation from the normal pseudo-first order kinetics. It was concluded from these results that at least part of the ion populations of **8** and **10** isomerize to nondistonic forms [5a]. It was unclear, however, whether this isomerization occurs during the multistep gas-phase synthesis of the distonic ions or whether it is catalyzed by ion–molecule collision complex formation with the various neutral reagents. Examination of the reactions of the *ortho*-distonic phenyl radicals **8** and **10** with *tert*-butyl isocyanide sheds additional light on the question of isomerization and provides new insight into each ion.

The dimethylsulfonium phenyl radical **10** was found to be entirely unreactive toward *tert*-butyl isocyanide, supporting the previous conclusion that this ion completely isomerizes to a nondistonic form while it is being synthesized. Additionally, since this ion also does not exhibit proton transfer or cyanide abstraction, its charge site must be neither acidic nor contain a carbon with an empty valence. These conditions are met by the *ortho*-methylthioanisole radical cation, the structure previously proposed [5a] as the unreactive isomerization product. The facile isomerization of **10** is understandable in light of the behavior of its *para* isomer **9**. In spite of the fact that the charge and radical sites of this species are too far apart to interact directly, the reactions of this ion suggest that isomerization is facile even in this case. Not only is a substantial fraction of the ion population unreactive toward *tert*-butyl isocyanide, but cyano-radical abstraction yields only a minor product. The major product corresponds to the loss of a methyl radical from the intermediate adduct. These results underline the relative instability of the dimethyl sulfonium charge site.

The pyridinium phenyl radical **8** is much less prone to isomerization, partially due to the aromatic nature of the charge-bearing substituent. Indeed, the previously reported reactions of this ion indicate some behavior characteristic of distonic ions, if only for part of the ion population [5a]. *Tert*-butyl isocyanide reacts with this ion by quantitative cyano-radical transfer. No other competing reactions were observed, and the ion population reacts to completion without the generation of unreactive isomers. These results suggest that **8** is produced intact as one homogenous ion population and that the reported partial isomerization must occur after ion formation, and is likely catalyzed by the formation of an ion–molecule complex with a neutral reagent molecule.

## 5. Conclusions

*Tert*-butyl isocyanide is a useful complement to the reagents already in use for the study of distonic radical cations. Reactions with *tert*-butyl isocyanide

occur preferentially at the charge site of the ion. Cyano-radical transfer is observed only if the charge site of the ion exhibits no reactivity. Rough criteria for radical-site reactivity include low acidity ( $PA < 200$  kcal/mol) and coordinative saturation of the charge site. These characteristics make *tert*-butyl isocyanide a good indicator for the chemical inertness of distonic ions' charge sites.

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