Trapping Chlorine Radicals via Substituting Nitro Radicals in the Gas Phase

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Trapping Chlorine Radicals via Substituting Nitro Radicals in the Gas Phase

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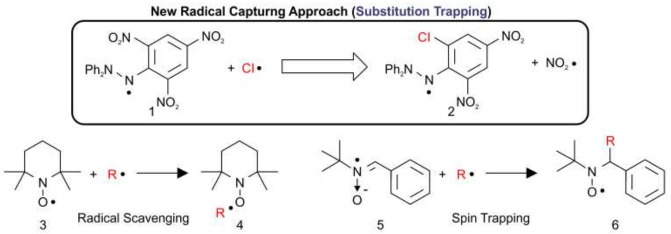
Although chlorine radicals are strong atmospheric oxidants, their direct spectroscopic detection in the environment (gas phase) with conventional analytical technique has not been reported. Herein, chlorine radicals (Cl•), generated by the YAG laser photolysis (λ = 355 nm) of Cl_2 in the gas phase, were captured by 2,2-diphenyl-1-picrylhydrazyl (DPPH•). The product was identified as DPPH, wherein NO_2 was substituted by Cl• at the *ortho*-carbon on the picryl aromatic ring, and was characterized using ion attachment ionization-quadrupole mass spectrometry. This reaction mechanism is a rare example of the detection and characterization of radical species, where radical spin densities on trapping reagents and frontier orbital interactions play important roles.

Introduction

Reactive organic radicals play important roles in the field of organic chemistry and environmental chemistry as key intermediates or transition-state species. If these reactive radicals can be trapped and characterized efficiently, essential clues and novel insights into reaction mechanisms may be obtained. For example, short-lived reactive radicals such as •OH, •OOH, and Cl• are said to be toxic to humans and can induce chain reactions of volatile components in the atmosphere, leading to environmental concerns such as ozone depletion[1] or methane degradation caused by Cl•. However, there are few reports that show concrete experimental results about radical trapping and the identification of reactive hetero radicals using conventional analytical equipment. We have used the results of computational studies[2] to design experiments to capture these radicals by chemical methods using functional organic compounds.[3] Radical scavenging[4] and spin trapping[5] constitute examples of conventional techniques (Scheme 1).



Scheme 1. Experiments for capturing short-lived reactive radicals.

However, these radical scavenging and spin trapping methods are only suitable for carbon-centred radicals, and will not be suitable for hetero radicals such as •OH, •OOH, and Cl• because the radical-trapped products are often not stable enough[6] (the mean bond enthalpy of the O-Cl bond is 203 kJ mol^{-1}) to be identified. In addition, although methods to detect HO_2• and RO_2• in the atmosphere are known,[7] direct spectroscopic detection of Cl• in the environment with standard equipment has rarely been reported, with the exception of tandem mist chamber experiments combined with photochemical model calculations.[8] Sophisticated resonance fluorescent methods[9] are suitably sensitive to detect Cl•; however, such techniques cannot be considered generally applicable because of the strict experimental conditions requisite for vacuum ultraviolet spectroscopy. Indirect analyses based only on the reaction products from radical reactions are liable to lead to uncertain conclusions with regard to essential

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† Electronic Supplementary Information (ESI) available: General remarks in experimental section; Preparation of DPPH-Cl paramagnetic adduct([DPPH+Cl-NO_2]•)and its reduced diamagnetic DPPHH-Cl adduct([DPPHH+Cl-NO_2]•) via an organic reaction in the liquid phase; Spectral characterization data of DPPH adducts (High-resolution Mass spectrometry, ESR,IR, ^{1}H- , ^{13}C-NMR, 2D-HMQC, 2D-HMBC spectra of the reduced DPPHH-Cl.; Procedure for Cl• capture by DPPH• in the gas-phase and characterization of [DPPH+Cl-NO_2]•using IA-QMS;. See DOI: 10.1039/b000000x/

reactive species. Furthermore, the reactivity of radical-capturing reagents is insufficient to capture Cl•. Although there are a few reports[10] on Cl spin trapping, Cl-adducts often cannot be identified. For actual gas- (10^4–10^5 atom cm^{-3}) and liquid-phase environmental Cl•, a novel approach with enhanced sensitivity must be developed; moreover, reliable and rapid analytical methods are necessary for characterization. We have found a new method to enable to capture Cl• by using a popular stable radical reagent 2,2-diphenyl-1-picrylhydrazyl (DPPH•) through a substitution mechanism on the picryl aromatic ring with elimination NO_2•. In the present paper, we will show the experimental results for capturing Cl• by DPPH• through Substitution-Trapping and the details of characterizing the Cl• trapped product with ion attachment ionization-quadrupole mass spectrometry (IA-QMS) combined with general spectroscopic analyses such as NMR of the reduced Cl• trapped DPPH• product. In addition, we will study regioselectivity of Cl• substitution on the picryl aromatic ring and the reaction mechanism based on the DFT calculations (UB3LYP/6-31G* or B3LYP/6-31G*) of Cl• trapped DPPH• paramagnetic or diamagnetic compounds.

Results and discussion

How to capture Cl• by DPPH• (Substitution-Trapping)

We have found a new approach to meet the aforementioned analytical demands by taking advantage of functional paramagnetic organic molecules, wherein Cl• is captured by substituting a stable radical (NO_2•) on DPPH• 1 (substitution-trapping). Consequently, DPPH• functions as a "radical-substitution reagent", as opposed to taking part in simple radical addition reactions, which occur in conventional radical scavenging experiments. The nitro group is suitable for this radical-substitution reaction because NO_2• is very stable in ambient air, and is easily eliminated from the aromatic ring because of its lower bond enthalpy DH_{298}(Ar-NO_2) (303 kJ mol^{-1}).[11] Furthermore, because of the small energy difference between the SOMO/HOMO of DPPH• and the LUMO of Cl•, DPPH• (1.1 eV energy profit: refer to the section below describing frontier orbital interactions) undergoes facile nucleophilic substitution reactions with Cl• radicals to generate NO_2•. Nevertheless, the substitution of the NO_2 group in dia-magnetic substrates with Cl• at ambient temperature has seldom been reported.[12] Specifically, most chlorination experiments were carried out either at higher temperatures (250 °C)[13] or in the presence of light at room temperature,[14] resulting in a low yield[13] or requiring longer reaction times,[14] respectively. Notably, DPPH• has many sensitive atoms (as shown in Figure 1) with significant spin densities that can donate an electron to the LUMO of Cl•.

Although DPPH• has been used to assess the radical-scavenging properties of antioxidants in plants,[15] it has rarely been used as a radical-capturing reagent.[16] Notably, both the substitution and addition reactions of the Cl• radical are expected, although substitution is favoured over addition.

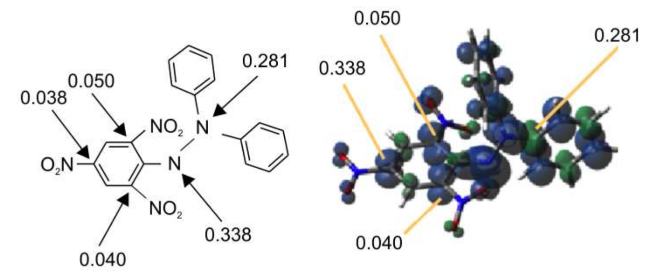
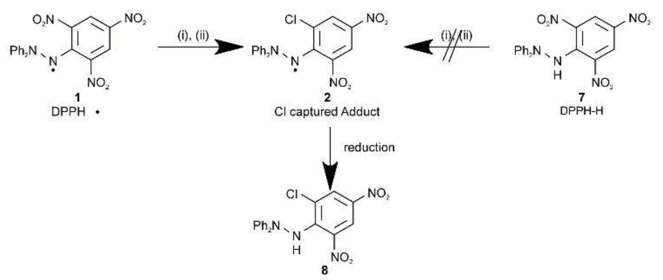


Fig. 1. Spin density map of DPPH• with UB3LYP/6-31G* calculation.

Cl• capture experiments in the liquid phase

By generating Cl• via X-ray irradiation,[17] (Scheme 2) we first carried out Cl• capture experiments using DPPH• in the liquid phase. LCMS(**L**iquid **C**hromatography **M**ass **S**pectrometry) and ESR(**E**lectron **S**pin **R**esonance) of the crude reaction mixture suggested the formation of a paramagnetic product via the reaction between Cl• with DPPH• through a substitution-trapping mechanism. After irradiating a $CHCl_3$ solution containing NCS (*N*-chlorosuccinimide) and DPPH• for 11 h, compound **2** ([DPPH–NO_2+Cl]•, where the *ortho*-NO_2 group was substituted by Cl) was isolated and characterized, following the reduction of the crude reaction products with ascorbic acid. Compound **8**, obtained from the reduction of **2**, was analysed by ^{1}H-NMR (**N**uclear **M**agnetic **R**esonance), ^{13}C-NMR, HMBC (^{1}**H**-detected **M**ulti-**B**ond heteronuclear multiple quantum **C**oherence), HMQC (^{1}**H**-detected **M**ultiple **Q**uantum **C**oherence), IR (**I**nfra**R**ed), and high-resolution MS. The unisochronous ^{1}H-NMR chemical shifts of the *meta*-protons and the unisochronous nature of the two *ortho*-carbons seen in the ^{13}C-NMR in reduced adduct **8** confirmed the *ortho*-substitution of the NO_2 group (see the Supporting Information). Notably, NO_2• substitution by Cl• did not proceed at the *ortho*-position on the picryl ring upon reaction with relevant diamagnetic compounds such as DPPH-H (compound **7**) or 2,4,6-trinitrochlorobenzene with Cl•.



Scheme 2. Cl• trapping reactions using DPPH• and related compounds in the liquid and gas phases. *Experimental conditions*: (i), NCS, $CHCl_3$, RT 11h, X-ray irradiation (liquid); (ii), Cl_2, YAG laser irradiation (λ = 355 nm, 3.2 mJ $shot^{-1}$) in the gas phase.

The major by-products of this reaction were diamagnetic or paramagnetic compounds with the DPPH• framework, produced by the attack of the released NO_2• on the phenyl ring. Other radical-capturing reagents such as α-phenyl-*N*-*tert*-butylnitrone (PBN), *tert*-butyl(10-phenyl-9-anthryl)nitroxide

(BPAN), 2-phenyl-4,4,5,5-tetramethylimidazoline-3-oxide-1-oxyl (PTIO), and 4-oxo-2,2,6,6-tetramethylpiperidine-1-oxyl (4-oxo-TEMPO) were tested under the same conditions as those used to capture Cl•. Cl• captured adducts were not identified via LCMS.

Cl• capture experiments in the gas phase and efficient identification of the Cl• captured DPPH• product by ion attachment ionization-quadrupole mass spectrometry (IA-QMS)

Based on the experimental results obtained using the liquid phase, we attempted to capture Cl• using DPPH• in the gas phase (Table 1, entry 1). The sample consisted of DPPH• and silica filter paper; 2.6 mg cm^{-2} DPPH• in CH_2Cl_2 was applied on a square of silica filter paper (3 mm edge length). The sample was placed in a reaction vessel with a Cl_2 vapour pressure of 1 Torr prior to UV irradiation by a YAG laser (λ = 355 nm, 3.2 mJ shot^{-1}) in 0.1 s intervals. Upon irradiation, the paramagnetic Cl-NO_2–exchanged product **2** was confirmed by preparative thin layer chromatography (TLC) and was identified as compound **8** after reduction by ascorbic acid. In addition, chemical species with m/z 46 (NO_2) and 30 (NO) were observed by EI-QMS, indicating that stable NO_2• was eliminated from DPPH• upon attack by Cl•. Without irradiation, the substitution product was not obtained, confirming that the Cl• radical was essential. Notably, the Cl•-substitution reaction was not observed with diamagnetic reagents such as 2,4,6-trinitrochlorobenzene or DPPH-H **7** as shown in Scheme 2. To improve the Cl• capture efficiency, the experimental conditions were explored (Table 1, entries 2-5). As the reaction in the gas phase was clean, only the reaction product, starting materials, and a small amount of uncharacterized compounds remained on the silica paper after the reaction. The yields, as judged by NMR and LCMS, were dependent on the reaction time (entries 3-5) and concentration of loaded DPPH• (entries 1-3), as shown in Table 1.

Table 1. Dependence of the yield of **2** on exposure time and loaded DPPH• in gas-phase experiments.

Entry	Exposure Time [min]	Loaded DPPH• concentration [mg/cm^2]	Yield of Cl-NO_2 Substituted Product **2** [%]$^{a)}$
1	60	2.6	2.3
2	60	1.3	4.5
3	60	0.65	7.9
4	20	0.65	4.4
5	120	0.65	11.4

a) The yields were judged by ^{1}H-NMR.

Yield of Cl-NO_2 substituted product **2** is presumed to be controled by the amount of DPPH• existing only in the top surface layer on the filter paper where DPPH• can react actually with Cl• in the gas phase. Redundant DPPH• remaining in the inner layer affect nothing to Cl• capturing reaction. That may be partly because why counter-intuitive experimental results (Table 1) were observed.

Although the reaction product could be identified by the NMR of the reduced form **8** of **2**, mass spectrometry (MS) using a soft-ionization method was adopted to improve the efficiency of the method. Among the available soft-ionization methods for MS analysis, ion attachment ionization-quadrupole mass spectrometry (IA-QMS)[18,19,20] is assumed to be superior owing to fragment-free ionization and high sensitivity. As such, intact samples for reactive radical-capturing experiments can be effectively analysed without separation or derivation prior to characterization and quantitative analysis. In IA-QMS, Li^+ ion produced by electrically heating the Li emitter attaches to the existing chemical species on the sample silica filter paper prior to ionization (see the supporting information). Therefore, the observed m/z numbers in Figure 2 denote the sum (M+Li) of the mass numbers of the chemical species (M) and lithium (i.e., 6.94). Because fragmentation and side reactions are negligible in ion attachment ionization, the approximate yield can be determined directly from the ratio of the ion currents of the product and starting material in the mass-chromatogram; thus, quantitative in situ sample analysis is possible. The yields of the Cl-substituted product determined by NMR and IA-QMS were very similar (IA QMS 4.3% vs NMR 4.5% in Table 1, entry 2).

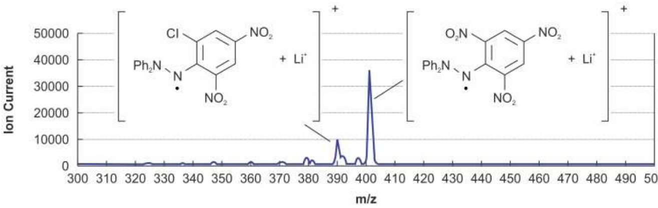


Fig.2. IA-QMS spectrum of reaction products formed between Cl• + DPPH• in the gas phase.

Theoretical consideration on Substitution-Trapping reaction based on the DFT-calculations.

In order to clarify why substitution-trapping occurred on DPPH• resulting to the formation of Cl• captured product, DFT-calculations was carried out using Gaussin09 program. Notably, the regioselectivity of Cl• substitution at the *ortho*-carbon can be explained not only by thermodynamics, but also by frontier orbital considerations. Because the hydrazyl N• is sterically hindered,[21,22] simple Cl• attack on the hydrazyl N• (spin density: 0.338) is not thermodynamically favoured because the mean bond enthalpy ΔH^0 of the newly formed N-Cl bond is rather small (200 kJ mol^{-1})[23] and thus easily dissociative. From the bond dissociation energy data of the pertinent bonds associated with the DPPH• capture of Cl•, the thermodynamically favourable path involves the cleavage of an Ar-NO_2 bond (ΔH_0(Ar-NO_2):303 kJ mol^{-1}) and formation of an Ar-Cl bond (ΔH_0(Ar-Cl):406 kJ mol^{-1}).[11] With regard to the higher reactivity of paramagnetic DPPH• toward Cl• than that of diamagnetic substrates such as DPPH-H, B3LYP/6-31G* calculations revealed that an energetically favourable frontier orbital interaction between the electron-accepting LUMO of Cl• and electron-donating SOMO/HOMO of DPPH• was achieved at the *ortho*-position. As radicals are soft species, their reactions are driven by the coefficient (spin density) at that atom and the energy of the frontier orbitals. A schematic energy diagram illustrating the optimal frontier orbital interaction between Cl• and DPPH• is shown in Figure 3. The large frontier orbital spin density value at the *ortho*-carbon (0.050 in Figure 1) on the picryl ring supports the selective affinity toward Cl•; this *ortho*-attack was calculated to be the most energetically favourable as the net enthalpy gain was -91.9 kJ mol^{-1} without a significant activation barrier. In contrast, frontier orbital interactions between the HOMO of diamagnetic reagents and the LUMO of Cl• are not energetically feasible because additional energy is necessary to prevent the bonding between the pairing electrons in the HOMO.

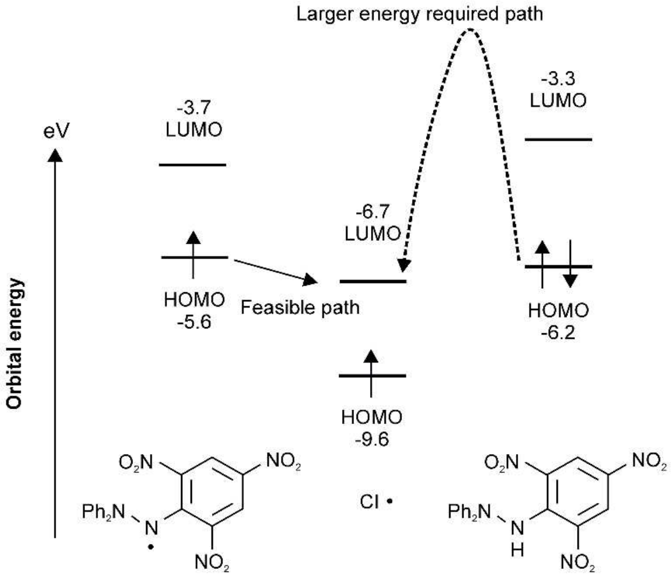


Fig. 3. Frontier orbital interaction between the LUMO of Cl• and SOMO/HOMO of DPPH• by B3LYP* or UB3LYP/6-31G* calculations.

Conclusions

We have developed a novel approach toward capturing Cl• using DPPH• in the gas and liquid phases at room temperature through substitution-trapping, which is thermodynamically reasonable and is controlled by frontier orbital interactions. This method is a rare example of the detection and characterization of Cl• species. In addition, IA-QMS is practical and sensitive enough to identify trapped radicals *in situ*. Further research is needed to clarify the selectivity of the substitution-trapping radical reaction and mechanism. Applications of this method in actual environmental gas-phase Cl• capture and theoretical investigations regarding the transition states are in progress to clarify the reaction mechanism.

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