

Available online at www.sciencedirect.com





Chemical Physics Letters 454 (2008) 415-418

www.elsevier.com/locate/cplett

Halogen abstraction reaction between aminoalkyl radicals and alkyl halides: Unusual high rate constants

J. Lalevée*, X. Allonas, J.P. Fouassier

Department of Photochemistry, UMR CNRS 7525, University of Haute Alsace, ENSCMu, 3 rue Alfred Werner, 68093 Mulhouse Cedex, France

Received 29 January 2008; in final form 14 February 2008 Available online 20 February 2008

Abstract

The very high reactivity of aminoalkyl radicals toward the halogen abstraction reaction is reported for the first time. Reaction rate constants with CCl_4 and CBr_4 are close to the diffusion limit: they are about 4–5 orders of magnitude higher than those previously determined for typical alkyl radicals. A better understanding of this unusual behavior is obtained using molecular orbitals (MO) calculations. The participation of polar effects is directly evidenced. This approach can be useful for the design of new reducing agents. © 2008 Elsevier B.V. All rights reserved.

1. Introduction

The halogen abstraction reaction is particularly important in the reduction processes used in synthetic organic chemistry. The reaction scheme allows a change from R-X (where X is often a halogen atom) to R-H and consists in a halogen abstraction step (1) followed by a hydrogen transfer reaction (2) [1–3].

 $\mathbf{R'} + \mathbf{R} - \mathbf{X} \to \mathbf{R'} - \mathbf{X} + \mathbf{R}^{\star}$ (1)

$$\mathbf{R'} + \mathbf{R'}\mathbf{H} \to \mathbf{R} - \mathbf{H} + \mathbf{R'}.$$
 (2)

Many efforts have been done for the design of new reducing agents. Actually, tris(trimethylsilyl)silane appears as a very powerful agent [1,3]. The driving force for the reaction (1) is the bond dissociation energy (BDE) of the R–X and R'–X bonds [1–4]. For carbon centered alkyl radicals, the halogen abstraction from alkyl halides RX exhibits a very low exothermicity (as both the cleavage and the formation of a C–X bond are involved) and is a rather slow reaction (rate constant $k < 10^5 \text{ M}^{-1} \text{ s}^{-1}$): [5–7] as a consequence, the alkyl radicals are not encountered in the reduction reactions. Due to their high reactivity, Sn centered radicals were largely used but the associated toxicity of

E-mail address: j.lalevee@uha.fr (J. Lalevée).

0009-2614/\$ - see front matter $\textcircled{}{}^{\odot}$ 2008 Elsevier B.V. All rights reserved. doi:10.1016/j.cplett.2008.02.052

tin derivatives has led to the search for other radicals, e.g. the Si centered radical based reduction reactions [1–3]. Both the Si–Cl and Sn–Cl BDEs render the process exothermic [4].

During our previous works on the aminoalkyl radicals (A) reactivity, we found that the stabilization and the nucleophilic character of A' induce specific properties such as (i) a very high reactivity for the addition to alkenes bearing withdrawing substituents and (ii) a low reactivity toward phenolic derivatives in the hydrogen transfer process [8,9]. These A' species might be interesting for the reduction reactions. The reaction rate constants and the halogen atom abstraction properties are, however, by now unknown. A better understanding of the key factors governing the (1) and (2) reactions is basically interesting for the development of new radical systems. In this Letter, we will be interested in reaction (1) and we will use laser flash photolysis (LFP) to directly observe the generation of two selected A[.] radicals (Scheme 1) and to evaluate their interaction rate constants with alkyl halides. DFT calculations will help to provide a coherent picture of the process.

2. Results and discussions

The aminoalkyl radicals are easily observed by LFP using a procedure (described elsewhere in detail [8,9])

^{*} Corresponding author. Fax: +33 3 89 33 68 95.



which briefly consists in a hydrogen abstraction by the *t*butoxyl radical (generated through the direct cleavage of di-*tert*-butylperoxide upon light excitation) from the corresponding amine [10]. The absorption spectra of **I** and **II** are known [8]. The observation of the radical decay traces at different RX concentrations gives a direct access to the halogen abstraction rate constant (Fig. 1). The results are gathered in Table 1 and compared to those found for both Et₃Si[•] and the classical alkyl radicals (*n*-butyl, cyclopentyl, *tert*-butyl) [1a,6b].



Fig. 1. Decay traces of I monitored at 340 nm; (a) $[CH_2Br_2] = 0$ M and (b) $[CH_2Br_2] = 0.23$ M. Insert: the Stern–Volmer treatment (plot of the reciprocal value of the radical lifetime vs. $[CH_2Br_2]$).

Table 1 Rate constants for halogen abstraction reaction in di-*tert*-butylperoxide (in $10^7 \text{ M}^{-1} \text{ s}^{-1}$)

Radical	CBr ₄	CH_2Br_2	C ₆ H ₁₃ Br	CCl ₄	CHCl ₃	CH ₂ Cl ₂
I	290	0.52	< 0.01	150	0.13 (1.1) ^a	<0.01 (<0.01) ^a
II Et ₃ Si ^{•b} <i>t</i> -Bu ^{•c}	67	<0.01	< 0.005	0.085 460 0.003	<0.01 25	<0.005 7.1

^a Solvent di-tert-butylperoxide/acetonitrile (30%/70% w/w).

^b From [1a].

^c From [6b]; for primary (*n*-butyl) and secondary (cyclopentyl) carbon centered radicals, low hydrogen abstraction rate constants (CCl₄) were found with values of 5.8×10^4 and 5.0×10^3 M⁻¹ s⁻¹, respectively.

Surprisingly, radicals I and II exhibit a high reactivity for the halogen abstraction from CCl₄ close to that of Et₃Si[.]. In the presence of CHX₃ and CH₂X₂, Et₃Si[.] is found more reactive, albeit noticeable values that are observed for the I and II species. The outstanding result concerns the rate constants which are 4-5 orders of magnitude higher than those previously measured for typical alkyl radicals (see for example in Table 1) [6b]. The most efficient carbon centered structures for the abstraction reaction from CCl₄ reported so far are the phenyl or the adamantyl radicals (rate constants of 7.8×10^6 and 4.4×10^7 M⁻¹ s⁻¹, respectively) [7a,6c]. The values presented here for the I/alkyl halide interaction remain two orders of magnitude higher. Lastly, I appears as more reactive than II, thereby demonstrating that the aminoalkyl structure also strongly affects the process.

The rate constants decrease with the number of halogen atom in the series $CX_4 > CHX_3 > CH_2X_2$. It is also worth noting that the halogen atom has a dramatic effect on the reactivity trend: Br > Cl. As generally stated, both trends are ascribed to an increase of the C–X bond strength in the series (i.e. $BDE(CX_4) < BDE(CHX_3) < BDE(CH_2X_2)$; BDE(R-Br) < BDE (R–Cl)) rendering the process more exothermic [1,4]. Similar general behaviors were already observed for the Si or Sn centered radicals [1a].

For a better understanding of the I and II reactivity, MO calculations were carried out in selected radical/RX couples [10–12]. The DFT procedure selected has been already applied for the addition of aminoalkyl radicals to a large range of alkenes [10,13,14]. This approach is assumed as accurate enough to compare aminoalkyl/alkyl radicals reactivity. Table 2 gathers the reaction enthalpies $\Delta H_{\rm R}$, the barriers, the C–Cl bond lengths d(C–Cl) and the amounts of charge transfer $\delta^{\rm TS}$ in the TS for various carbon centered radicals and alkyl chlorides RX. $\Delta H_{\rm R}$

Table 2

Thermodynamical data and transition state properties for the different radical/alkyl chloride systems

System	$\Delta H_{\rm R}^{\ a}$ (kJ/mol)	δ^{TSa}	d(C–Cl) ^a Å	Barrier ^b (kJ/mol)
I/CCl ₄	-73.4	+0.38	2.658	3.7
I/CHCl ₃	-46.6	+0.355	2.453	5.2
I/CH ₂ Cl ₂	-20.4	+0.34	2.357	21.2
I/CH ₃ Cl	8.8	+0.3	2.283	45.5
II/CCl ₄	-52.8	+0.29	2.392	7.1
CH ₃ C [·] HCH ₃ /CCl ₄	-73.8	+0.19	2.32	15.8
CH ₃ C·HCH ₃ /CH ₃ Cl	8.4	+0.11	2.142	69.2
(CH ₃) ₃ C [•] /CCl ₄	-64.9	+0.22	2.335	15.4
(CH ₃) ₃ C [•] /CH ₃ Cl	17.3	+0.14	2.153	71.7

See text [10].

^a UB3LYP/6-31G^{*} and ZPE corrected at 6-31G^{*} level.

^b At 6-31G^{*} level and ZPE corrected, as presented in detail in [14], by using an isodesmic reaction for the calculations of BDEs(C–Cl) (experimental BDE(C–Cl) for CCl₄ = 296.7 kJ/mol [4]), the C–Cl bond strengths are 369.9, 349.5, 370.3, 361.6 kJ/mol for the alkyl chlorides formed from I, II, CH₃C·HCH₃ and (CH₃)₃C^{*}, respectively.

corresponds to the difference between BDE(R–Cl) and BDE (R'–Cl). As presented in detail in [11], by using an isodesmic reaction for the calculations of BDEs(C–Cl) (experimental BDE(C–Cl) for $CCl_4 = 70.9 \text{ kcal/mol}$ [4]), the C–Cl bond strengths are 88.4, 83.5, 88.5, 86.4 kcal/ mol for the alkyl chlorides formed from I, II, CH₃C·HCH₃ and (CH₃)₃C[•], respectively (Table 2).

For I, it is observed that the barrier decreases with the number of chlorine atoms. This is in agreement with the experimental trend i.e. the rate constant decreasing in this series. This is ascribed to an increase of both the reaction exothermicity and δ^{TS} from CH₃Cl to CCl₄.

The reactivity of I which is a secondary radical can be advantageously compared to that of a classical secondary alkyl radical (CH₃C·HCH₃ – isopropyl radical). Similar reaction exothermicities (I vs. CH₃C·HCH₃) are calculated i.e. the enhanced reactivity of the aminoalkyl species cannot be ascribed to this factor. However, for both radicals, the barrier decreases with an increase of the exothermicity when going from CH₃Cl to CCl₄ which is in line with the increase of the rate constant. Changing the isopropyl radical for the *t*-butyl radical shows that the exothermicity slightly decreases in agreement with the lowest *t*-Bu–Cl BDE. The ΔH_R and δ^{TS} changes remain weak i.e. quite similar barriers are obtained (Table 2).

From the TS structures, the amounts of charge transfer δ^{TS} from the radical to the alkyl halide are found much higher for I and II than for alkyl radicals, the high nucleophilic character of the aminoalkyl species leading to high δ^{TS} values. The barrier is undoubtly related to δ^{TS} . An earlier TS is also found for I: d(C–Cl) is clearly elongated for similar ΔH_{R} (Table 2, Fig. 2). Therefore, the polar effects strongly affect the TS structure and likely appear as a key factor for the enhanced reactivity of the aminoalkyl radicals. A similar behavior was recently observed for the addition of I to alkenes bearing withdrawing substituents [13,14].

The ionization potentials IP and the electron affinity EA are calculated as 4.96, 5.85 and -0.35, 0.75 eV for I and II, respectively. From IP and EA, the absolute electronegativity χ is calculated according to Eq. (3) [13–16].

$$\chi = (IP + EA)/2 \tag{3}$$

The lower reactivity of **II** compared to **I** can be ascribed to:



Fig. 2. The Transition State structure TS for the halogen abstraction reaction in the I/CH_3Cl system (calculations at UB3LYP/6-31G^{*} level).

(i) its lower nucleophilic character evidenced by a higher electronegativity (2.31 and 3.3 eV for I and II, respectively). This is exemplified by the lower δ^{TS} found for II/CCl₄ system (0.29 compared to 0.38 for I/CCl₄).

(ii) The lower $\Delta H_{\rm R}$ for \mathbf{II}/\rm{CCl}_4 which leads to a higher barrier. This is ascribed to the lower BDE(R'-Cl) for \mathbf{II} (Table 2).

The solvent effects are also in agreement with the contribution of the strong polar effects in the aminoalkyl radical/ alkyl halide interaction. An increase of the solvent polarity – upon the addition of acetonitrile to di-*tert*-butylperoxide from 0% to 70% (w/w) – leads to a dramatic increase of the interaction rate constant, e.g. from 1.3×10^6 to 1.1×10^7 M⁻¹ s⁻¹ for the I/CHCl₃ system. The TS (that exhibits a charge transfer character) is stabilized in polar media which results in a lower barrier and a higher abstraction rate constant.

3. Conclusion

This Letter outlines the high reactivity of the aminoalkyl radicals toward the halogen abstraction reaction that is explained on the basis of strong polar effects. In addition to this never mentioned behavior, our approach should be useful for the design of new reducing agents.

Acknowledgement

The authors thank the CINES (Centre Informatique National de l'Enseignement Supérieur) for the generous allocation of time on the IBM SP supercomputer.

Appendix A. Supplementary data

Description of the computational procedure and Z-Matrix corresponding to the reactants, products and TS structures. Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.cplett.2008.02.052.

References

- [1] (a) C. Chatgilialoglu, Organosilanes in Radical Chemistry, Wiley, Chichester, 2004;
 - (b) J. Fossey, D. Lefort, J. Sorba, Free Radicals in Organic Chemistry, Wiley&Sons, New York, 1995;
 - (c) S.Z. Zard, Radical reactions in Organic Synthesis, Oxford University Press, Oxford, UK, 2003;
 - (d) P. Renaud, M.P. Sibi (Eds.), Radicals in Organic Synthesis, Wiley-VCH, Weinheim, Germany, 2001.
- [2] M. Ballestri, C. Chatgilialoglu, K.B. Clark, D. Griller, B. Giese, B. Kopping, J. Org. Chem. 56 (1991) 678.
- [3] (a) C. Chatgilialoglu, A. Guerrini, M. Lucarini, J. Org. Chem. 57 (1992) 3405;
- (b) C. Chatgilialoglu, Chem. Eur. J. 2007, ASAP.
- [4] Y.R. Luo, Handbook of Bond Dissociation Energy in Organic Compounds, CRC Press, 2003.
- [5] B. Giese, J. Hartung, Chem. Ber. 125 (1992) 1777.

- [6] (a) D.A. Linsay, J. Lusztyk, K.U. Ingold, J. Am. Chem. Soc. 106 (1984) 7087;
 (b) J.A. Hawari, S. Davis, P.S. Engel, B.C. Gilbert, D. Griller, J. Am. Chem. Soc. 107 (1985) 4721;
 (c) F. Recupero, A. Bravo, H.R. Bjorsvik, F. Fontana, F. Minisci, M. Piredda, J. Chem. Soc. Perkin Trans. 2 (1997) 2399.
- [7] (a) J.C. Scaiano, L.C. Stewart, J. Am. Chem. Soc. 105 (1983) 3609;
 (b) T. Yu, M.C. Lin, J. Phys. Chem. 99 (1995) 8599.
- [8] J. Lalevée, X. Allonas, B. Graff, J.P. Fouassier, J. Phys. Chem. A 111 (2007) 6991.
- [9] J. Lalevée, X. Allonas, J.P. Fouassier, Chem. Phys. Lett. 415 (2005) 202.
- [10] Triethylamine (TEA), ethyldimethylaminobenzoate (EDB), di-*tert*butylperoxide and the different alkyl halides (CCl₄, CHCl₃, CH₂Cl₂, CBr₄, CH₂Br₂, C₆H₁₃Br) were obtained from Aldrich and used with the best available purity. Nanosecond laser flash photolysis (LFP) experiments were carried out using a Q-switched nanosecond Nd/ YAG laser ($\lambda_{exc} = 355$ nm, 9 ns pulses; energy reduced down to 10 mJ) from Powerlite 9010 Continuum and an analyzing system consisting of a pulsed xenon lamp, a monochromator, a fast

photomultiplier and a transient digitizer [11]. All the calculations were performed using the hybrid functional B3LYP from Gaussian 03 suite of program [12]. This procedure has been already applied for the addition of aminoalkyl radicals to a large range of alkenes [13,14]. Reactants, products and transition states (TS) were fully optimized at the B3LYP/6-31G^{*} level and frequency checked.

- [11] J. Lalevée, X. Allonas, J.P. Fouassier, J. Am. Chem. Soc. 124 (2002) 9613.
- [12] M.J. Frisch et al., GAUSSIAN 03, Revision B.2, Gaussian Inc., Pittsburgh, PA, 2003;
 (b) J.B. Foresman, A. Frisch, in: Exploring Chemistry with Electronic Structure Methods, second edn., Gaussian Inc., 1996.
- [13] J. Lalevée, X. Allonas, J.P. Fouassier, J. Org. Chem. 70 (2005) 814.
- [14] (a) J. Lalevée, X. Allonas, J.P. Fouassier, J. Am. Chem. Soc. 125 (2003) 9377;
 (b) J. Lalevée, X. Allonas, J.P. Fouassier, J. Phys. Chem. A 108 (2004)
- 4326.
- [15] R.G. Parr, R.G. Pearson, J. Am. Chem. Soc. 105 (1983) 7512.
- [16] R.G. Pearson, J. Am. Chem. Soc. 107 (1985) 6801.