Communication to the Editor

Photo-Induced Atom-Transfer Radical Reactions Using Charge-Transfer Complex between Iodine and Tertiary Amine

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Received October 17, 2016; accepted October 24, 2016

In the presence of charge–transfer complexes between iodine and tertiary amines, the aqueous-medium atom-transfer radical reactions proceeded under visible light irradiation without the typical photocatalysts.

Key words radical; iodine; photochemistry; perfluoroalkyl; charge–transfer complex; aqueous media

The charge–transfer complex (CT complex) is formed by weak association of electron-donor and electron-acceptor. Particularly, the CT complexes between metal atoms and ligands are widely studied in inorganic chemistry.1–2) In recent years, the metal-to-ligand charge transfer in transition metal photocatalysts has been applied to the synthetic organic chemistry.3–5) Although the physical properties of organic CT complexes are investigated,6–10) less is known about the utility of organic CT complexes in synthetic reactions.11–15) In our laboratory is interested in developing a new method which doesn’t require the external photocatalysts. In this communication, we report the experiments to prove the utility of organic CT complexes between iodine (I2) and tertiary amines in the aqueous-medium carbon–carbon bond-forming radical reactions.

Iodine is known to interact with amines to form the CT complexes, which have the two broader absorption bands at ca. 230–280 and 410–430 nm.20,21) (Chart 1). Therefore, we expected that the visible light irradiation of CT complex A in the ground state gives the excited state B, which may promote the single electron transfer (SET) from the donor amine to the acceptor iodine giving the iodine radical.22–24)

At first, we studied the effect of CT complexes derived from I2 and several amines on the iodine atom-transfer radical reaction of alkene 1 with i-C3F7I (Table 1). In the presence of I2 (0.1 eq) and trimethylamine (1.1 eq), the biphasic solution of 1 and i-C3F7I (5 eq) in H2O was stirred for 1 h with white LED light (400–700 nm, 1000 lm) irradiation under Ar atmosphere (entry 1). In this reaction, 1.1 eq of trimethylamine were employed, because 1.0 eq of amine also acts as an electron-donor leading to C. As expected, the desired product 2 was obtained in 89% yield. In marked contrast, the reaction did not occur when MeCN was employed as solvent (entry 2). The use of (i-Pr)2NEt as a tertiary amine led to enhancement in chemical yield (entry 3), although pyridine did not promote the reaction probably due to its low reactivity as an electron-donor (entry 4). The chemical yield of 2 dramatically decreased by using secondary amine such as (i-Pr)2NH, owing to the oxidation of secondary amine by I2 (entry 5).25–27) Interestingly, in the absence of iodine, this transformation took place slowly by using (i-Pr)2NEt (entry 6). Even in the absence of I2, CT complex between (i-Pr)2NEt and I2 would be formed, because i-C3F7I is gradually decomposed to give I2. However, in the absence of amine, the reaction using only iodine did not occur and the solubility of iodine also decreased without the association with amine (entry 7). Therefore, this CT complex-promoted reaction is differentiated from the reported iodine-mediated radical reactions.28,29) Theoretical and computational studies

![Chart 1. Charge–Transfer Complex between Amine and Iodine](Image)

Table 1. Iodine-Atom Transfer Reaction Using Charge–Transfer Complexes

| Entry | Amine   | Solvent | Yield (%) |
|-------|---------|---------|-----------|
| 1     | Me3N    | H2O     | 89        |
| 2     | Me3N    | MeCN    | ND        |
| 3     | (i-Pr)2NEt | H2O     | 98        |
| 4     | Pyridine| H2O     | ND        |
| 5     | (i-Pr)2NH | H2O     | 3         |
| 6     | (i-Pr)2NEt | H2O     | 56        |
| 7     | None    | H2O     | ND        |

a) Reactions of 1 (1 eq) with i-C3F7I (5 eq) were carried out in the presence of I2 (0.1 eq) and amine (1.1 eq) under the LED light irradiation. The calculation studies were performed on density functional B3LYP 6–311+G** by using Spartan’10 (WAVEFUNCTION, INC.). b) Isolated yields. c) Reaction was carried out in the absence of I2 for 4 h. d) The formation of product 2 was not detected.

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on halogen bonding interactions have been a subject of current interest.30,31) To understand the above results, we calculated the optimized structures of iodine complexes. The calculation shows that the noncovalent interaction between trimethylamine and I2 is strong to form the stable CT complex, while pyridine weakly interacts with I2. Additionally, we presume that the negligible interaction of MeCN solvent with I2 may suppress the formation of CT complex.

We next explored the iodine atom-transfer radical reaction of various alkenes 3–8 with i-C3F7I under the optimized reaction conditions (Table 2). Except for styrene 8, alkenes 3–7 reacted with excellent chemical efficiencies and regioselectivities. It is important to note that the reactions of alkene 6 having bromine atom and alkene 7 having hydroxy group proceeded without any problems.

To study the viability of the present method, n-C3F7I, ICH2CN and CCl3Br were next employed as carbon radical precursors (Chart 2). The reaction of 1 with n-C3F7I proceeded to give the product 14 in 81% yield. Although the reaction in MeCN did not occur (entry 2 in Table 1), ICH2CN having cyano group worked as a radical precursor to give the adduct 15 in 43% yield. Moreover, the bromine atom-transfer radical reaction using CCl3Br took place with moderate chemical efficiency.

We finally investigated the radical addition-cyclization-trapping reaction of symmetrical substrates 17, 19 and 21 in aqueous media (Chart 3). When i-C3F7I was employed, the reaction of 17 was completed within 1 h to give the products cis-18a and trans-18a in 81% combined yield. Other radical precursors n-C3F7I and c-C6F11I worked well. Similarly, the reaction of 19 with i-C3F7I gave the products cis-20 and trans-20 in 82% combined yield. The reaction of 21 also proceeded effectively to give the product 22 in 98% yield with excellent cis-diastereoselectivity.

The possible reaction pathway for the generation of i-C3F7 radical is shown in Chart 4. The reaction is initiated by the visible light irradiation of CT complex A in the ground state to produce the excited state B. We presume the generation of an iodine radical via the single electron transfer from the donor amine to the acceptor iodine in the excited state B, which is evident from observation of the transient species.

### Table 2. Reaction of 3–8 with i-C3F7I

| Entry | Substrate | Product (% Yield) |
|-------|-----------|------------------|
| 1     | MeO-       | 9 (98%)          |
| 2     | Br-        | 6 (98%)          |
| 3     | H-         | ND               |
| 4     | HO-        | 7 (98%)          |

*a) Reactions of 3–8 (1 eq) with i-C3F7I (5 eq) were carried out in H2O in the presence of I2 (0.1 eq) and (i-Pr)2NEt (1.1 eq) for 1 h under the LED light irradiation. b) Isolated yields. c) The formation of product was not detected.*
generated in the photoexcitation of quinuclidine–I₂ and triethylendiamine–I₂ complexes by means of transient absorption spectroscopy, although it cannot be excluded that the excited state B acts as a reducing agent toward i-C₃F₇I. Finally, an iodine radical reacts with i-C₃F₇I to give i-C₃F₇ radical and the regenerated iodine.

In summary, we have demonstrated that CT complexes between iodine and tertiary amines have the potential to induce the atom-transfer radical reactions in aqueous media. In addition to typical photocatalysts, the CT complexes disclosed a broader utility of photo-induced radical reactions.

Acknowledgment  This work was supported by JSPS KAKENHI Grant-in-Aid for Scientific Research (C) Grant Number 16K08188 (to H.M.).

Conflict of Interest  The authors declare no conflict of interest.

References
1) Akimov A. V., Neukirch A. J., Prezhdo O. V., Chem. Rev., 113, 4496–4565 (2013).
2) Rondi A., Rodriguez Y., Feurer T., Cannizzo A., Acc. Chem. Res., 48, 1432–1440 (2015).
3) Tucker J. W., Stephenson C. R. J., J. Org. Chem., 77, 1617–1622 (2012).
4) Ischay M. A., Yoon T. P., Eur. J. Org. Chem., 2012, 3359–3372 (2012).
5) Shi L., Xia W., Chem. Soc. Rev., 41, 7687–7697 (2012).
6) Onda K., Yamochi H., Koshihara S., J. Org. Chem., 80, 520–524 (1958).
7) Wang C., Xu Q.-W., Zhang W.-N., Peng Q., Zhao C.-H., J. Org. Chem., 73, 3848–3853 (2008).
8) Tsuzuki S., Wakisaka A., Ono T., Sonoda T., Chem. Eur. J., 18, 951–960 (2012).