



Short communication

Indium-mediated radical addition of perfluoroalkyl iodide in water

Toshiyuki Takagi*, Toshiyuki Kanamori

Research Center of Stem Cell Engineering (RCSC), National Institute of Advanced Industrial Science and Technology (AIST), AIST Tsukuba Central 5, 1-1-1 Higashi, Tsukuba, Ibaraki 305-8565, Japan

ARTICLE INFO

Article history:

Received 9 December 2010

Received in revised form 7 March 2011

Accepted 7 March 2011

Available online 1 April 2011

Keywords:

Indium

Perfluoroalkyl iodide

Water

Radical addition

Carbon–carbon unsaturated compound

ABSTRACT

Reaction of perfluoroalkyl groups with carbon–carbon unsaturated compounds using indium in water proceeded smoothly to provide the addition products in high yields.

© 2011 Elsevier B.V. All rights reserved.

1. Introduction

Many fluorinated compounds exhibit unique properties such as thermal and chemical stability, and noteworthy hydrophobicity and lipophilicity, and new methods for their synthesis are being widely investigated [1–6]. We have already reported the synthesis of fluorinated fatty acids or double chained phosphatidylcholines and their interfacial properties [7–11]. Surface pressure–area isotherms of their monolayers at the air/water interface were measured to consider the effect of fluorine substituents on their interfacial stability, and as a result, the introduction of fluorine atoms was found to improve the interfacial stability of monolayers.

Many studies on synthesis with perfluoroalkyl iodides using several metals as initiators for the radical reactions have already been carried out [12,13]. The intermolecular carbon–carbon bond formation reactions are initiated by copper [14], iron [15], Raney nickel [16], etc. and are achieved in organic solvents or organic–water mixture solvents. While intermolecular radical perfluoroalkylation reactions in water have attracted attention in the field of fluorine chemistry, reports of the addition reaction in water are rare. Blancou and co-workers reported that the reaction of perfluoroalkyl iodide with 2-methyl-3-buten-2-ol produced an addition product in the presence of zinc in water [17]. However, severe conditions (110 °C, 17 h) are needed to obtain the compound, and their approach has not been widely employed for reductively initiated addition reactions in water. Recently,

Vallejo and Postigo reported the intermolecular radical perfluoroalkylation reaction in water [18]. This reaction required 1,1'-azobis(cyclohexanecarbonitrile) or dioxygen as the radical initiator, and tris(trimethylsilyl)silane as the reducing agent.

In this paper, we report the introduction of perfluoroalkyl groups into carbon–carbon unsaturated compounds using indium metal in water without employing organic solvents. This reaction proceeds under mild conditions and provides the addition products with high yields.

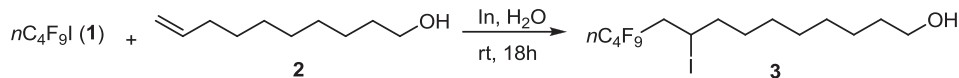
2. Results and discussion

Indium has been demonstrated to be an efficient and promising metal for mediating organic reactions in aqueous media [19–23]. Indium-mediated carbon–carbon bond-forming reactions in aqueous media have been of great importance both economically and environmentally. Recently, Naito and co-workers reported the addition of an indium-mediated alkyl radical to an electron-deficient C=N bond or C=C bond [23]. However, the addition of an indium-mediated perfluoroalkyl radical to C=C bonds has yet to be studied. Thus, our goal was to develop the reaction of perfluoroalkyl iodides with carbon–carbon unsaturated compounds in aqueous media in the presence of indium.

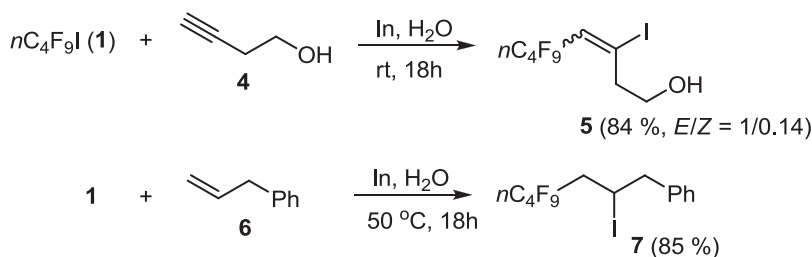
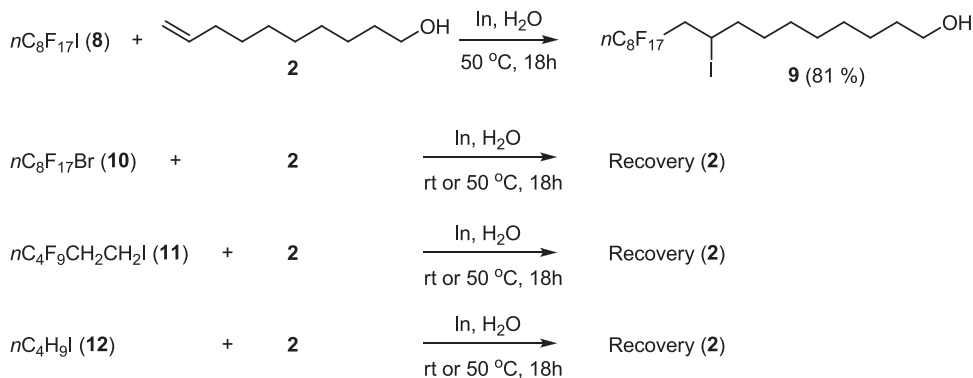
We found that when indium powder was added to a heterogeneous aqueous mixture of perfluorobutyl iodide (**1**) and 9-decen-1-ol (**2**), the addition product **3** was obtained. Thus, we studied a way to optimize the reaction conditions as shown in Table 1. An examination of the mole ratio perfluorobutyl iodide (**1**):9-decen-1-ol (**2**):indium at room temperature revealed the highest yield of **3** when the **2**:**1**:In ratio was 1:2:0.5 (run 4 in Table

* Corresponding author. Tel.: +81 29 861 6392; fax: +81 29 861 4651.

E-mail address: t.takagi@aist.go.jp (T. Takagi).

Table 1Reaction of perfluorobutyl iodide (**1**) with 9-decen-1-ol (**2**) in the presence of indium

Run	Molar ratio 2 : 1 :In	Product 3 (%)	Recovery 2 (%)
1	1:1:1	33 ^a	18 ^a
2	1:2:1	54	–
3	1:3:1	57	–
4	1:2:0.5	78	–
5	1:2:0.2	29 ^a	64 ^a

^a Yields were estimated by ¹H NMR.**Scheme 1.** Reaction of perfluorobutyl iodide (**1**) with carbon–carbon unsaturated compounds in the presence of indium.**Scheme 2.** Reaction of 9-decen-1-ol (**2**) with alkyl halides (**8**, **10–12**) under indium in water.

1). In the course of the purification of this reaction, the compound **3** can be easily separated with column chromatography.

As an extension of this reaction, we chose 3-butyne-1-ol (**4**) as a compound containing a carbon–carbon triple bond and allylbenzene (**6**) as an aromatic compound. The reaction of **4** was examined using the same reaction conditions as those used for **2** and gave the corresponding product **5** [24] in a similar way. The *E/Z* ratio of **5** was estimated to be 1/0.14 based on ¹H NMR. Next, the reaction of **6** was carried out at room temperature using a similar molar ratio, but the starting material **6** was recovered. Thus, the temperature was raised to 50 °C to provide the corresponding product **7** [25] in a high yield (Scheme 1).

Further, we examined the reaction of perfluorooctyl iodide (**8**), perfluorooctyl bromide (**10**), 1-iodo-1H,1H,2H,2H-nonafluorohexane (**11**) and 1-iodobutane (**12**) with 9-decen-1-ol (**2**). Although the reaction of **2** with **8** as the perfluorobutyl iodide in the presence of indium in water proceeded as shown in Scheme 2 and produced the corresponding addition product **9** [8] in a high yield, the starting material **2** was recovered for the reagents bearing hydrogen atoms as **11** and **12**, or the perfluoroalkyl reagent bearing bromine instead of iodine as **10**. Thus, we found that the indium-mediated reaction proceeded smoothly using a perfluor-

oalkyl reagent with iodine to produce the addition product in water.

In conclusion, we succeeded in introducing perfluoroalkyl moieties into carbon–carbon unsaturated compounds using indium in water. Our method provides a new route using indium metal for the synthesis of fluorinated compounds in water.

3. Experimental

3.1. Instruments

¹H and ¹⁹F NMR spectra were measured on a JEOL JNM-LA 600 FT-NMR system (600 MHz) using TMS and CCl₃ as internal standards, respectively. Mass spectra (ESI-MS) were measured on a JEOL JMS-700T Tandem MStation. Column chromatography purifications were carried out using silica gel 60 (Merck 7734).

3.2. Materials

Perfluorobutyl iodide, perfluorooctyl iodide and 1-iodo-1H,1H,2H,2H-nonafluorohexane were purchased from Daikin Finechemical Laboratory (Japan). Perfluorooctyl bromide and 1-

iodobutane were purchased from Tokyo Chemical Industry Co., Ltd. (Japan). Indium powder was purchased from Lancaster and its purity was over 99%.

3.2.1. 11,11,12,12,13,13,14,14,14-Nonafluoro-9-iodotetradecan-1-ol (3)

To a heterogeneous mixture of 9-decen-1-ol (**2**, 155 mg, 1.0 mmol) and perfluorobutyl iodide (**1**, 708 mg, 2.0 mmol) in water (1 ml) was added indium powder (57 mg, 0.5 mmol), and this mixture was stirred at room temperature for 18 h. The aqueous mixture was subjected to direct column chromatography on SiO₂ (ca. 80 g) with hexane/EtOAc (7/3) as an eluent to give **3** (387 mg, 78%).

3: Colorless liquid. ESI-MS *m/z*: 503 (M+H)⁺. HRMS (ESI) calcd. for C₁₄H₂₁OF₉I (M+H)⁺ 503.0493; Found: 503.0499. ¹H NMR (CDCl₃) δ: 1.37–1.46 (10H, m), 1.50–1.60 (3H, m), 1.73–1.83 (2H, m), 2.72–2.82 (1H, m), 2.87–2.97 (1H, m), 3.64 (2H, t, *J* = 6.59 Hz), 4.33 (1H, m). ¹⁹F NMR (CDCl₃) ppm: –81.55 (3F, t, *J* = 9.19 Hz), –112.48 (1F, dm, *J* = 268.41 Hz), –115.33 (1F, dm, *J* = 268.41 Hz), –125.06 (2F, m), –126.39 (2F, m).

3.2.2. 5,5,6,6,7,7,8,8,8-Nonafluoro-3-iodo-3-octen-1-ol (5)

To a heterogeneous mixture of 3-buyn-1-ol (**4**, 74 mg, 1.1 mmol) and perfluorobutyl iodide (**1**, 726 mg, 2.1 mmol) in water (1 ml) was added indium powder (58 mg, 0.5 mmol), and this mixture was stirred at room temperature for 18 h. The aqueous mixture was subjected to direct column chromatography on SiO₂ (ca. 80 g) with hexane/EtOAc (4/1) as an eluent to give **5** (367 mg, 84%) as *E/Z* mixture (*E:Z* = 1:0.14). Each configuration was determined from ¹H NMR and ¹⁹F NMR spectra [8,24].

5: Colorless liquid. ESI-MS *m/z*: 416 (M)⁺. HRMS (ESI) calcd. for C₈H₆OF₉I (M)⁺ 415.9320; Found: 415.9324. **E-5**: ¹H NMR (CDCl₃) δ: 1.51 (1H, t, *J* = 5.86 Hz), 2.94 (2H, m), 3.84 (2H, td, *J* = 6.23, 5.86 Hz), 6.49 (1H, t, *J* = 14.29 Hz). ¹⁹F NMR (CDCl₃) ppm: –81.50 (3F, t, *J* = 9.19 Hz), –105.74 (2F, m), –124.52 (2F, m), –126.24 (2F, m). **Z-5**: ¹H NMR (CDCl₃) δ: 1.50 (1H, t, *J* = 5.50 Hz), 2.92 (2H, m), 3.85 (2H, td, *J* = 5.86, 5.50 Hz), 6.41 (1H, t, *J* = 13.19 Hz). ¹⁹F NMR (CDCl₃) ppm: –81.50 (3F, t, *J* = 9.17 Hz), –109.55 (2F, m), –124.32 (2F, m), –126.26 (2F, m).

3.2.3. 4,4,5,5,6,6,7,7,7-Nonafluoro-2-iodoheptylbenzene (7)

To a heterogeneous mixture of allylbenzene (**6**, 123 mg, 1.0 mmol) and perfluorobutyl iodide (**1**, 720 mg, 2.1 mmol) in water (1 ml) was added indium powder (58 mg, 0.5 mmol), and this mixture was stirred at 50 °C for 18 h. The aqueous mixture was subjected to direct column chromatography on SiO₂ (ca. 80 g) with hexane/EtOAc (9/1) as an eluent to give **7** (438 mg, 85%).

7: Colorless liquid. ESI-MS *m/z*: 464 (M)⁺. HRMS (ESI) calcd. for C₁₃H₁₀F₉I (M)⁺ 463.9684; Found: 463.9691. ¹H NMR (CDCl₃) δ: 2.80–2.96 (2H, m), 3.19 (1H, dd, *J* = 14.65, 8.79 Hz), 3.29 (1H, dd, *J* = 14.65, 5.86 Hz), 4.46 (1H, m), 7.18–7.20 (2H, m), 7.28–7.35 (3H, m). ¹⁹F NMR (CDCl₃) ppm: –81.54 (3F, t, *J* = 9.19 Hz), –112.70 (1F,

dm, *J* = 268.41 Hz), –114.47 (1F, dm, *J* = 268.41 Hz), –125.03 (2F, m), –126.38 (2F, m).

3.2.4. 11,11,12,12,13,13,14,14,15,15,16,16,17,17,18,18,18-Heptafluoro-9-iodooctadecan-1-ol (9)

To a heterogeneous mixture of 9-decen-1-ol (**2**, 157 mg, 1.0 mmol) and perfluorooctyl iodide (**8**, 1.095 g, 2.0 mmol) in water (1 ml) was added indium powder (57 mg, 0.5 mmol), and this mixture was stirred at 50 °C for 18 h. The aqueous mixture was subjected to direct column chromatography on SiO₂ (ca. 80 g) with hexane/EtOAc (7/3) as an eluent to give **9** (573 mg, 81%) [8]. NMR shifts of **9** were congruent with the shifts of the compound in ref. [8].

9: Colorless waxy solid. ¹H NMR (CDCl₃) δ: 1.26–1.46 (10H, m), 1.50–1.61 (3H, m), 1.80 (2H, m), 2.78 (1H, m), 2.92 (1H, m), 3.64 (2H, td, *J* = 6.59 Hz), 4.33 (1H, tt, *J* = 8.61, 4.33 Hz). ¹⁹F NMR (CDCl₃) ppm: –81.29 (3F, t, *J* = 9.19 Hz), –112.23 (1F, dm, *J* = 272.08 Hz), –115.07 (1F, dm, *J* = 272.08 Hz), –122.03 (2F, bs), –122.38 (4F, bs), –123.19 (2F, bs), –124.07 (2F, bs), –126.60 (2F, m).

Acknowledgement

We thank Drs. Masanori Tamura and Masao Shimizu of AIST for fruitful discussions.

References

- [1] R.A. Guethner, M.L. Vietor, Ind. Eng. Chem. Prod. Res. Dev. 1 (1962) 165–167.
- [2] J.R. Riess, F. Frezard, J. Greiner, M.P. Krafft, C. Santaella, P. Vierling, L. Zarif, in: Y. Barenholz, D.D. Lasic (Eds.), Handbook of Nonmedical Applications of Liposomes, vol. III, CRC Press, Boca Raton, 1996, pp. 97–141.
- [3] M. Sagisaka, A. Ito, Y. Kondo, N. Yoshino, K.O. Kwon, H. Sakai, M. Abe, Colloids Surf. A 183–185 (2001) 749–755.
- [4] E. Kissa, Fluorinated Surfactants and Repellents, 2nd Ed., Marcel Dekker, New York, 2001.
- [5] J.G. Riess, Tetrahedron 58 (2002) 4113–4131.
- [6] K. Matsuoka, Y. Moroi, Curr. Opin. Colloid Interface Sci. 8 (2003) 227–235.
- [7] T. Takagi, K. Takai, T. Baba, T. Kanamori, J. Synth. Org. Chem. Jpn. 68 (2010) 206–216.
- [8] K. Takai, T. Takagi, T. Baba, T. Kanamori, J. Fluorine Chem. 125 (2004) 1959–1964.
- [9] K. Takai, T. Takagi, T. Baba, T. Kanamori, J. Fluorine Chem. 128 (2007) 120–126.
- [10] T. Takagi, K. Takai, T. Baba, T. Kanamori, J. Fluorine Chem. 128 (2007) 133–138.
- [11] K. Takai, T. Takagi, T. Baba, T. Kanamori, J. Fluorine Chem. 129 (2008) 686–690.
- [12] W.R. Dolbier Jr., Chem. Rev. 96 (1996) 1557–1584.
- [13] N.O. Brace, J. Fluorine Chem. 108 (2001) 147–175.
- [14] P.L. Coe, N.E. Milner, J. Organomet. Chem. 39 (1972) 395–402.
- [15] Q.-Y. Chen, Y.-B. He, Z.-Y. Yang, J. Fluorine Chem. 34 (1986) 255–258.
- [16] Q.-Y. Chen, Z.-Y. Yang, J. Chem. Soc., Chem. Commun. (1986) 498–499.
- [17] B. Abou-Ghazaleh, Ph. Laurent, H. Blancou, A. Commeyers, J. Fluorine Chem. 68 (1994) 21–24.
- [18] S.B. Vallejo, A. Postigo, J. Org. Chem. 75 (2010) 6141–6148.
- [19] C.J. Li, T.H. Chan, Tetrahedron 55 (1999) 11149–11176.
- [20] J. Podlech, T.C. Maier, Synthesis 5 (2003) 633–655.
- [21] V. Nair, S. Ros, C.N. Jayan, B.S. Pillai, Tetrahedron 60 (2004) 1959–1982.
- [22] J. Auge, N.L. Germain, J. Uziel, Synthesis 12 (2007) 1739–1764.
- [23] H. Miyabe, M. Ueda, A. Nishimura, T. Naito, Org. Lett. 4 (2002) 131–134.
- [24] N.O. Brace, J. Fluorine Chem. 20 (1982) 313–327.
- [25] M. Kuroboshi, T. Ishihara, J. Fluorine Chem. 39 (1988) 299–303.