Perfluoroalkylation of α-Methylstyrene Using Titanium Oxide as a Photocatalyst

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A redox system for fluoroalkylation with perfluoroalkyl iodide using TiO_2 as a photocatalyst was developed. Photoirradiation of perfluoroalkyl iodide and α-methylstyrene in CH_3CN in the presence of TiO_2 and $NaBF_4$ gave α-fluoroalkylstyrene.

Perfluoroalkyl iodide is well known as a source of perfluoroalkyl radical. These radicals are produced from the iodide thermally, photochemically, or by the use of radical initiator.[1] A one-electron reduction of the iodide is an alternative way to produce perfluoroalkyl radical.[2] Free-radical chain iodoperfluoroalkylation of olefins using the iodide with the olefin is the most important method for the introduction of perfluoroalkyl group into organic molecules.[1] However, in the reaction with α-methylstyrene, the produced benzyl type radical is too stable to abstract the iodine from perfluoroalkyl iodide promoting the radical chain reaction (Scheme 1).[3]

We have been exploring the synthetic utility of the reaction of perfluoroalkyl iodide with α-methylstyrene. In the course of our work, we have discovered TiO_2-catalyzed perfuoroalkylation of α-methylstyrene with perfluoroalkyl iodide. The results are described in this communication (Scheme 2).

The photochemical decomposition of perfluoroalkyl iodide in the presence of TiO_2 was examined. Light of more than 350-nm wavelength was irradiated to the solution of $CF_3(CF_2)_5I$ (1.25 mmol) in 30-mL CH_3CN in the presence of TiO_2 (ST-01; Ishihara Sangyo Co., Ltd.) using a metal halide lamp under a N_2 atmosphere, and the decay of the iodide was monitored by HPLC. HPLC analysis was performed by a Shimadzu SPD-6A liquid chromatograph equipped with a Cosmosil 5C18 ($4.6 \times 250\,mm^2$, Nacalai Tesque reverse phase column) with $MeOH/H_2O$ (80/20 in volume) as eluent. The photochemical decomposition of perfluoroalkyl iodide did not proceed smoothly even in the presence of TiO_2; for 9 h irradiation, 82% of the iodide was left unchanged, as determined by HPLC
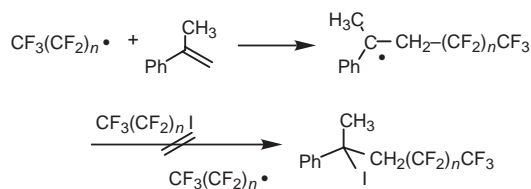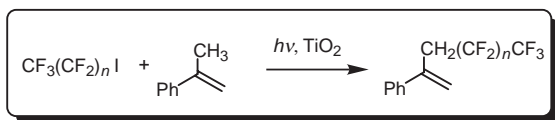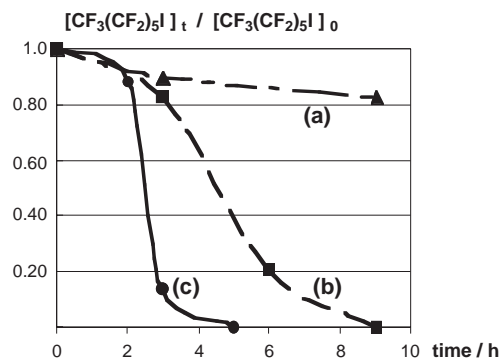

Figure 1. Photochenical decomposition of $CF_3(CF_2)_5I$. Conditions: (a) $CF_3(CF_2)_5I$ (1.25 mmol), TiO_2 (40 mg) in CH_3CN (30 mL); (b) $CF_3(CF_2)_5I$ (1.25 mmol), TiO_2 (40 mg) in CH_3CN (25 mL) and MeOH (5 mL); (c) $CF_3(CF_2)_5I$ (1.25 mmol), TiO_2 (40 mg), $NaBF_4$ (0.5 mmol) in CH_3CN (25 mL) and MeOH (5 mL).

(Figure 1a). Interestingly, in the presence of 5 mL of MeOH, a smooth decomposition began to proceed after an induction period (Figure 1b). Photoirradiation of TiO_2 excites the electrons from the valence band to the conduction band, leaving holes in the valence band. However, these electrons did not achieve the reduction of the iodide, since the recombination between the electrons and the holes was probably much faster (Scheme 3, eq 1). In the presence of MeOH, the holes should react with MeOH before recombination (Scheme 3, eq 2), and the electrons therefore acted to reduce the iodide to give perfluoroalkyl radicals (Scheme 3, eq 3). The decomposition of the iodide was further accelerated by the addition of $NaBF_4$ (Figure 1c). The enhancement of the efficiency of $CF_3(CF_2)_5I$ decomposition may be explained by the suppression of back electron transfer to the radical cation.[4]

On the basis of these results, the introduction of perfluoroalkyl radicals thus produced into organic molecules was investigated. A solution of perfluoroalkyl iodide and α-methylstyrene in CH_3CN in the presence of TiO_2 was photoirradiated under similar conditions. Perfluoroalkylated olefins (**1** and **2**), the alcohol **3**, the methoxylated compound **4** (Chart 1) and other miscellaneous fluoroalkylated products were detected by GC-MS analysis. The distribution of the products was heavily influenced by the conditions.
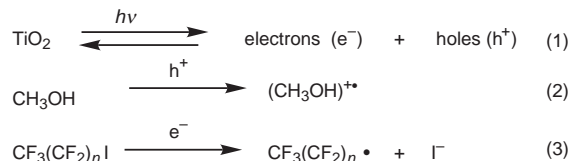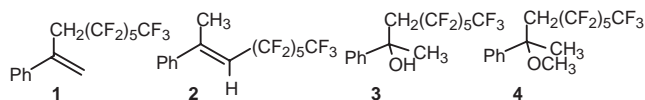

Scheme 1.

Scheme 2.

Scheme 3.

Chart 1.

Table 1. Preparation of fluoroalkylated olefin

Run	Solevnt system[a]	Ar /mmol	Time/h	Conversion of iodide/%	Yield/%[b]
1	30/0	Ph (1.25)	18	33	22 (66)
2	29/1	Ph (1.25)	18	56	48 (86)
3	27/3	Ph (1.25)	18	69	50 (72)
4	25/5	Ph (1.25)	18	71	43 (61)
5	25/3	Ph(1.25)	42	97	54[c]
6	27/3	Ph (2.50)	18	67	46 (71)
7	27/3	Ph (2.50)	42	100	67
8[d]	27/3	Ph (2.50)	18	72	54 (74)
9	27/3	4-MeC$_6$H$_5$ (2.50)	18	83	46 (56)
10	27/3	2-MeC$_6$H$_5$ (2.50)	18	76	54 (71)
11	27/3	4-ClC$_6$H$_5$ (2.50)	18	62	30 (47)
12[e]	27/3	Ph (2.50)	18	70	37 (53)

[a]The ratio of CH$_3$CN/MeOH is shown. [b]The characterization of **1** was performed by comparison with the spectral data for authentic samples.[3] Yield was determined by HPLC based on CF$_3$(CF$_2$)$_5$I using *m*-nitrotoluene as an internal standard. Yield based on consumed CF$_3$ (CF$_2$)$_5$I is shown in parentheses. [c]Produced **1** should undergo reaction with CF$_3$(CF$_2$)$_5$I to be converted into further fluoroalkylated products under these conditions. [d]LiBF$_4$ instead of NaBF$_4$ was used in this run. [e]Perfluorobutylation with CF$_3$(CF$_2$)$_3$I was investigated in this run.

Here, we focused our attention on the selective preparation of **1**. The results obtained under various conditions are summarized in Table 1.

MeOH was essential to make this reaction proceed smoothly (Table 1; Runs 1–4). This methodology was applied to various α-methylstyrenes possessing substituents on the aromatic ring (Table 1; Runs 9–11), or perfluorobutylation of α-methylstyrene using CF$_3$(CF$_2$)$_3$I (Table 1; Run 12). Unfortunately, an attempted run for trifluoromethylation with CF$_3$I was unsuccessful, and almost all of the CF$_3$I remained unchanged.

Recently, much attention has been given to TiO$_2$ as a photocatalyst.[5] However, application to organic synthesis, especially to carbon–carbon bond formation, has little been reported thus far. Now, we have developed a new redox system for perfluoroalkylation leading to carbon–carbon bond formation using
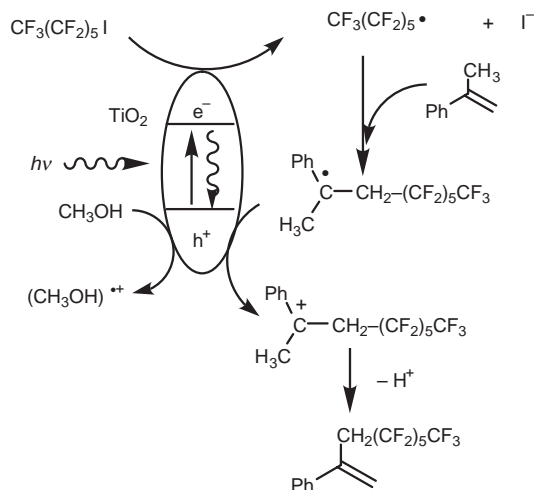
Scheme 4.

TiO$_2$ as a photocatalyst. A plausible reaction mechanism is shown in Scheme 4. Electrons and holes are produced on the surface of TiO$_2$. Owing to the electrons, perfluoroalkyl iodide is reduced to perfluoroalkyl radicals and iode anions. The produced radicals add to α-methylstyrene to give the corresponding benzyl type radical. This stable radical cannot abstract the iodine from perfluoroalkyl iodide, and is oxidized to the cation by the holes. Thus, this fluoroalkylation is achieved on the balance of the oxidation–reduction. MeOH and NaBF$_4$ may act as modulators to keep the balance successfully.

References and Notes
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