A facile photoinduced iodoperfluoroalkylation of dienes, diynes, and enynes with perfluoroalkyl iodides via selective radical cyclization

Kaname Tsuchii,[a] Yukihiro Ueta,[b] Nagisa Kamada,[a] Yoshiyuki Einaga,[a]
Akihiro Nomoto[b] and Akiya Ogawa[b],*

[a]Department of Chemistry, Faculty of Science, Nara Women's University, Kitauoyanishi-machi, Nara 630-8506, Japan
[b]Department of Applied Chemistry, Faculty of Engineering, Osaka Prefecture University, 1-1 Gakuen-cho, Sakai,
Osaka 599-8531, Japan

Abstract—Perfluoroalkyl iodides serve as excellent mediators for the radical cyclization of dienes, diynes, and enynes upon irradiation with near-UV light, providing the corresponding iodoperfluoroalkylated cyclic compounds in moderate to good yields.
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Recently, the utility of fluorinated compounds in medicinal chemistry, agricultural chemistry, material science, and organic synthesis is growing, and therefore, the development of new methodologies for selective introduction of fluorinated functions into organic molecules is of great importance.[1] Among the fluorinated functions, perfluoroalkyl groups (R_F) are useful fluorous tags in organic synthesis,[2] and, to introduce these R_F groups to organic molecules, perfluoroalkyl iodides (R_F–I) are employed as representative perfluoroalkylating reagents.[3] Recently, we have revealed that the near-UV irradiation technique makes it possible to attain the selective iodoperfluoroalkylation of a wide range of unsaturated compounds with R_F–I.[4] This letter describes a useful application of this photoirradiation technique to the radical cyclization reactions of dienes, diynes, and enynes, because the fast 5-*exo* radical cyclization processes are expected to assist strongly the efficient introduction of fluorous groups into unsaturated compounds.[5,12]

At first, the radical cyclization reaction was conducted by the use of $^nC_{10}F_{21}I$ and diallyl ether under photoirradiation conditions. In a Pyrex glass tube under a N_2 atmosphere, a mixture of diallyl ether (**1a**) and $^nC_{10}F_{21}I$ in BTF (i.e., $PhCF_3$)[13] was irradiated with a xenon lamp (500 W) at room temperature for 10 h. After

the reaction was completed, the corresponding iodoperfluoroalkylated cyclization product (**2a**) was obtained in 58% yield, along with small amounts of acyclic adduct (**3a**) as a byproduct (Eq. 1). This photoirradiation procedure is also applicable for the radical cyclization of 1,6-heptadiene (**1b**) as a simple diene.[14]


(1)
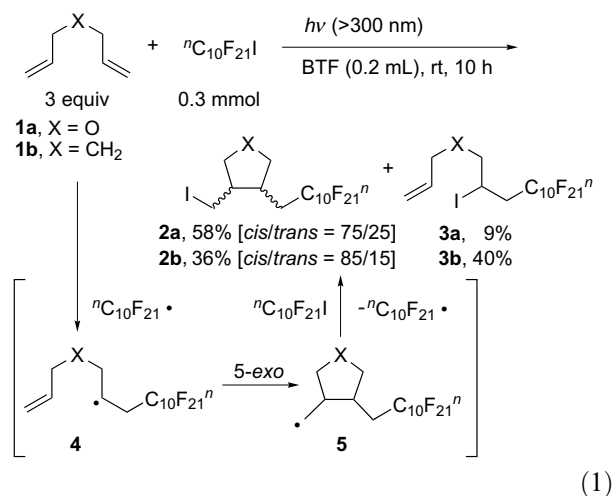
A possible mechanistic pathway may include the following: (i) upon irradiation with the light of wavelength of over 300 nm, $^nC_{10}F_{21}I$ undergoes homolytic dissociation to generate $^nC_{10}F_{21}$·,[15] (ii) $^nC_{10}F_{21}$· adds to diene (**1**), forming the secondary alkyl radical (**4**), (iii) **4** cyclizes

* Corresponding author. Tel./fax: +81 72 254 9290; e-mail: ogawa@
chem.osakafu-u.ac.jp

in a 5-*exo* manner to give cyclic radical intermediate (**5**), which undergoes S_H2 reaction with $^nC_{10}F_{21}I$ to provide the corresponding cyclic product (**2**).

Similarly, the photoinduced reaction of dienes with $^nC_4F_9I$ was also examined. In this case, $^nC_4F_9I$ is easily miscible with the dienes even in the absence of BTF, and therefore, the reactions were conducted in the absence of solvent. Upon irradiation with near-UV light ($hv > 300$ nm), the reaction of diallyl ether (**1a**) proceeded efficiently as in the case of $^nC_{10}F_{21}I$ (Eq. 2). 1,6-Heptadien-4-ol (**1c**) also provided the desired cyclization product preferentially (Eq. 3).[17] On the other hand, diallyl sulfide (**1d**, $(CH_2=CHCH_2)_2S$) did not undergo the desired cyclization reactions effectively.[16] In the case of allyl methacrylate (**1e**, $CH_2=CHCH_2OC(O)C(CH_3)=CH_2$), polymerization reaction proceeded exclusively.


(2)

(3)
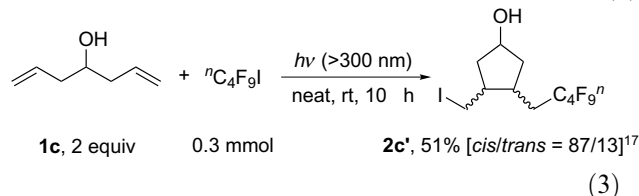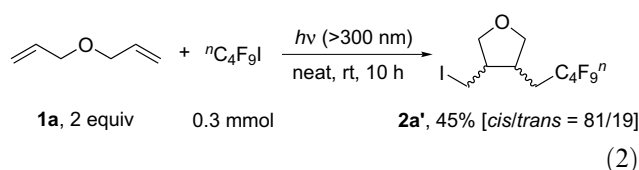
Next, we examined the radical cyclization of diynes with R_F–I. Upon irradiation with a xenon lamp through Pyrex, dipropargyl ether (**6a**) successfully reacts with $^nC_{10}F_{21}I$ to give the corresponding cyclic iodoperfluoroalkylated product (**7a**) in 65% yield (Eq. 4). Moreover, in the cases of bis(propargyl)malonic acid diethyl ester (**6b**), the desired cyclic products (**7b**) were obtained with high stereoselectivity.[18,19]


(4)
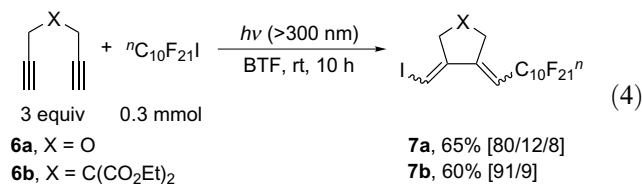
We next examined the radical cyclization reactions of enynes. In the case of enynes, two types of cyclizations may take place, that is, cyclization by the attack of β-perfluoroalkyl-substituted vinyl radical to the carbon–carbon double bond and that by the attack of β-perfluoroalkyl-substituted alkyl radical to the carbon–carbon triple bond. Presuming the related reports on the radical addition of iodoperfluoroalkanes to 1-octyne and 1-octene,[20] perfluoroalkyl radical can attack both the double bond and triple bond. Indeed, the photoinduced reaction of diethyl allylpropargylmalonate (**8a**) with $^nC_{10}F_{21}I$ was completed in a short time (1 h), and the corresponding two types of five-membered cycli-

zation products (**9a** and **10a**) were obtained in almost quantitative yields (Eq. 5). In general, radical cyclization of enynes mediated by tin hydrides, thiols, or diselenides proceeds selectively by the attack of these heteroatom-centered radicals to carbon–carbon triple bonds. Interestingly, in this reaction, perfluoroalkyl radical generated by photoirradiation attacks the carbon–carbon double bond of **8a** preferentially, and the subsequent 5-*exo* cyclization followed by the S_H2 reaction with R_F–I provides the cyclization product (**9a**) as the major product.[20] The driving force of this iodoperfluoroalkylated cyclization conceivably depends, partly, on the stability of the product iodides (vinyl iodide (**9a**) vs alkyl iodide (**10a**)).[21]

(5)
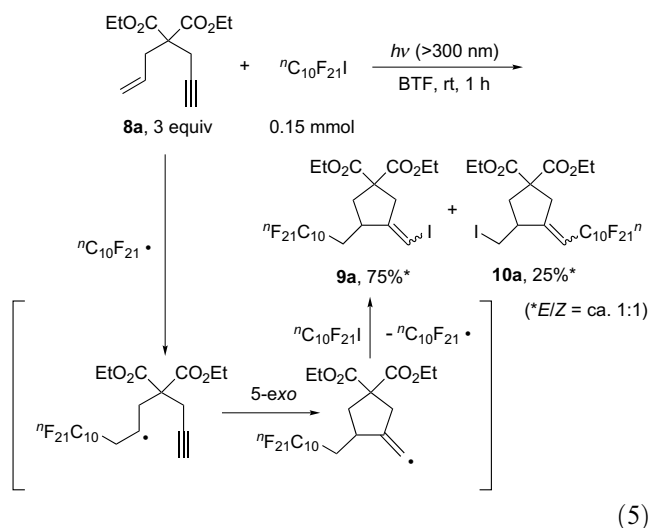
Similar conditions can be employed with allyl propargyl ether (**8b**) and again, cyclic vinyl iodide (**9b**) and alkyl iodide (**10b**) were obtained in 65% and 24% yields, respectively.

(6)
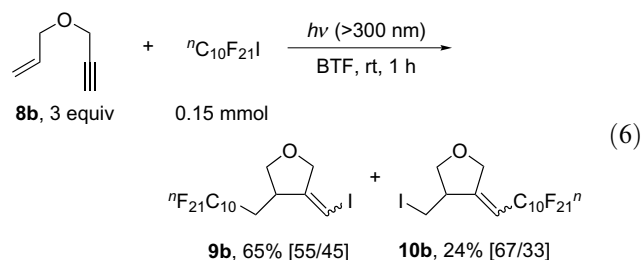
Although, in the case of allyldipropargylamine (**8c**), enyne cyclization and/or diyne cyclization are expected to take place, the major product was derived from enyne cyclization: **9c** was obtained in moderate yield, along with small amounts of its regioisomer and the diyne cyclization products.
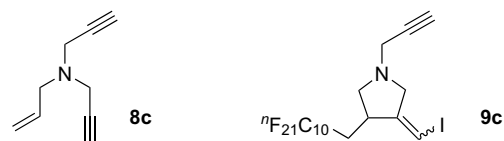
In summary, the radical cyclization of dienes, diynes, and enynes by using perfluoroalkyl iodides takes place successfully upon irradiation with a xenon lamp. In this reaction, the cyclization compounds bearing perfluoroalkyl groups are obtained under mild conditions with convenient procedure. Further study along these lines is now in progress.

Acknowledgments

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3. The iodoperfluoroalkylation of carbon–carbon unsaturated compounds such as alkenes and alkynes proceeds by a radical chain mechanism initiated by various radical initiators. However, the application of the photoinitiation to synthetic chemistry of organofluorous compounds has remained largely undeveloped, most probably due to the prejudice that the photoinitiation is an inefficient process. The photoinitiation, see for example: (a) Habibi, M. H.; Mallouk, T. E. *J. Fluorine Chem.* **1991**, *53*, 53; (b) Qiu, Z.-M.; Burton, D. J. *J. Org. Chem.* **1995**, *60*, 3465.

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5. Intramolecular radical cyclization of carbon–carbon unsaturated compounds has proven to be an efficient means for the synthesis of cyclic compounds. For this purpose, a variety of compounds bearing heteroatom–hydrogen or heteroatom–heteroatom bond have been employed as mediators, for example, tin hydrides,[6] silyl hydrides,[7] thiols,[8] selenols,[9] diselenides,[10] and S–Se mixed systems.[11]

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11. For thioselenation of alkynes with (PhS)₂ and (PhSe)₂, see for example: (a) Ogawa, A.; Obayashi, R.; Ine, H.; Tsuboi, Y.; Sonoda, N.; Hirao, T. *J. Org. Chem.* **1998**, *63*, 881; For selenosulfonation of various unsaturated compounds, see for example: (b) Back, T. G.; Collins, S. *J. Org. Chem.* **1981**, *46*, 3249; (c) Gancarz, R. A.; Kice, J. L. *J. Org. Chem.* **1981**, *46*, 4899.

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14. Products were purified by recycling preparative HPLC (Japan Analytical Industry, Model LC-908), equipped with JAIGEL-1H and -2H columns (GPC) with CHCl₃ as an eluent. The spectral and analytical data for the cyclization product (**2a**) is as follows: white solid; *cis*-**2a**/*trans*-**2a** = 75/25, The stereochemistry of **2a** was

determined by NOE experiments, in which, for *cis*-**2a**, the methylene group (δ 3.08 and δ 3.19) bonded to the iodine was enhanced upon irradiation of the methylene group (δ 2.67–2.76 and δ 2.78–2.86) bonded to the perfluoroalkyl group; ^{1}H NMR (400 MHz, CDCl₃): δ 1.99–2.21 (m, 1H), 2.22–2.42 (m, 1H), 2.67–2.76 (m, 1H), 2.78–2.86 (m, 1H), 3.08 (t, J = 9.9 Hz, 1H, *cis*), 3.16–3.22 (m, 1H, *trans*), 3.19 (dd, J = 5.4, 9.9 Hz, 1H, *cis*), 3.32 (dd, J = 4.1, 7.2 Hz, 1H, *trans*), 3.57–3.75 (m, 2H, *trans*), 3.65 (t, J = 8.1 Hz, 1H, *cis*), 3.76 (dd, J = 4.6, 9.0 Hz, 1H, *cis*), 3.98–4.07 (m, 2H, *cis*), 4.20 (m, 1H, *trans*), 4.37 (m, 1H, *trans*); ^{13}C NMR (75 MHz, CDCl₃): [*cis*-**2a**] δ 2.7, 28.3, 35.8, 45.2, 47.9, 71.7, 71.9, 73.4; IR (KBr) 2941, 2866, 1437, 1373, 1344, 1209, 1151, 889, 640 cm⁻¹; HRMS calcd for $C_{16}H_{10}F_{21}IO$: 743.9441, found: 743.9435; Anal. Calcd for $C_{16}H_{10}F_{21}IO$: C, 25.83; H, 1.35. Found: C, 26.30; H, 1.58.

15. $^{n}C_{10}F_{21}I$ exhibits its absorption maximum in 270 nm, and its absorption reaches to 350 nm. Therefore, irradiation with the light of wavelength over 300 nm is enough to generate $^{n}C_{10}F_{21}\cdot$.

16. Most probably, the absorption of **1e** may depress the initiation step (the photoinduced homolysis of $^{n}C_4F_9I$).

17. The *cis/trans* ratio corresponds to both the methylene groups bonded to the iodine and perfluoroalkyl groups. For the stereochemistry of the hydroxy group, both α- and β-isomers were formed in the ratio of ca. 1:1.

18. For the reaction of **6a** or **6b** with $^{n}C_{10}F_{21}I$, acyclic 1,2,6,7-adducts were not obtained at all, and acyclic 1,2-adducts were formed in 15% and 13% yield, respectively.

19. For **7a**, the stereochemistry of the major isomer is (1*E*,6*E*). As to the two minor products, the stereochemistry was tentatively assigned based on the comparison of the signals: (1*E*,6*E*)/(1*E*,6*Z*)/(1*Z*,6*E*) = 80/12/8. For **7b**, similarly, (1*E*,6*E*)/(1*E*,6*Z*) = 91/9.
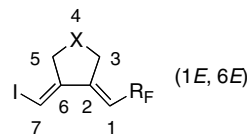
20. The iodoperfluoroalkylation of 1-octyne and 1-octene proceeds with similar rates. Owing to the higher stability of vinylic iodides compared with alkyl iodides, however, the iodoperfluoroalkylation of alkynes sometimes takes place somewhat smoothly, compared with that of alkenes. See Refs. 4b and 12g.

21. The photoinduced reaction of dimethyl allylpropargyl-malonate (**8d**) with $^{n}C_{10}F_{21}I$ under controlled conditions was monitored by ^{1}H NMR. In the initial stage, the ratio of **9d/10d** was 66:34, and was changed to 72:28 upon irradiation for 1 h.