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Iodine Atom-Transfer Ring-Opening of 1,1-Difluoro-2-(1-iodoalkyl)cyclopropanes by Free-Radical Reaction

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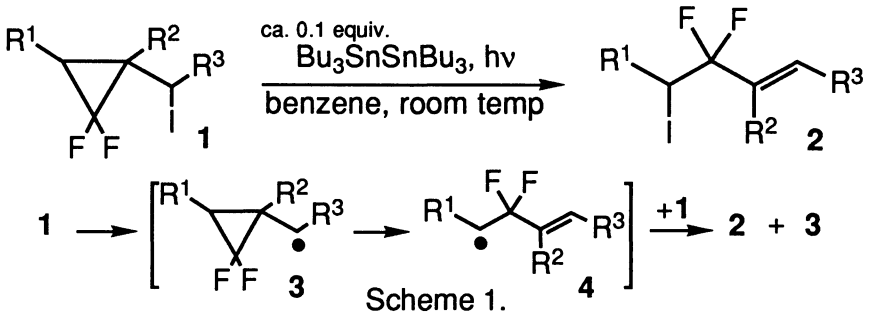
Free-radical chain reaction of 1,1-difluoro-2-(1-iodoalkyl)cyclopropanes with hexabutylditin and irradiation gave (E)-difluorohomoallyl iodides via iodine atom-transfer ring-opening.

Free-radical chain reactions involving iodine atom-transfer from the starting iodide into the product have been used effectively for addition and cyclization reactions.[1] These nonreductive processes via atom-transfer hold promise for serving as a complement to the reductive radical reactions by the tin hydride method. Recently, we reported the tin hydride mediated radical ring-opening of 1,1-difluorocyclopropane derivatives via deiodination or deoxygenation to give (E)-difluoroallylic compounds selectively.[2] As an extension of that work, we examined the functionalization of the intermediary difluorohomoallyl radical by iodine atom-transfer reaction. This paper describes the iodine atom-transfer ring-opening of 1,1-difluoro-2-(1-iodoalkyl)-cyclopropanes (**1**) conducted by hexabutylditin ($Bu_3SnSnBu_3$) and irradiation.



Scheme 1.

When a benzene solution of **1a**[2] and hexabutylditin (0.15 equiv.) was irradiated with a high pressure mercury lamp (100 W) through a Pyrex filter at room temperature for 4 h, ring-opening by iodine atom-transfer proceeded smoothly to give (E)-difluorohomoallyl iodide (**2a**) in 60% yield.[3] The absence of hexabutylditin (room temperature, 4 h) retarded the ring-opening reaction (**1a** : **2a** = ca. 9 : 1 by ^{19}F NMR). Thermal reactions were also attempted. Refluxing in benzene in the presence of hexabutylditin (0.1 equiv.) and azobisisobutyronitrile (0.1 equiv.) for 5 h was carried out but the ring-opening of **1a** failed to occur. Initiation with benzoyl peroxide (0.075 equiv., benzene, reflux, 6 h) brought about the conversion of **1a** to **2a** at less than 50%, according to ^{19}F NMR analysis.

Table 1. Iodine Atom-Transfer Reaction (1 → 2)[a)]

	R^1	R^2	R^3	Yield of 2/%[b, c)]
1a	H	CH_3	$PhCH_2CH_2$	60[d)]
1b	H	H	$PhCH_2CH_2$	60
1c	CH_3	H	$PhCH_2CH_2$	50
1d	$PhCH_2CH_2$	H	H	52
1e	$PhCH_2CH_2$	H	CH_3	52
(1f	Ph	H	H	none)

a) Reaction conditions: $Bu_3SnSnBu_3$ (0.11 - 0.15 equiv.), high pressure mercury lamp (100 W), room temp, 1.3 - 4 h. b) Isolated yield. c) E-Selective. d) The stereochemistry of **2a** was determined through NOE difference analysis.

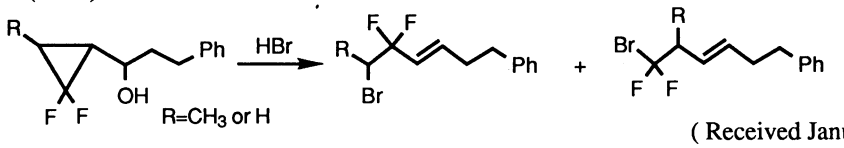
As shown in Table 1, difluorocyclopropanes (**1b** - **1e**) gave **2b** - **2e** in 50 - 60% yields, respectively. In all cases, ^{19}F NMR of the crude reaction mixture indicated a signal assignable only to **2**. These atom-transfer ring-openings were regio- and stereoselective. In the case of **1f**, no reaction occurred and the recovery of **1f** was detected by ^{19}F NMR.[4)]

The reaction pathway for the formation of **2** via iodine atom-transfer is outlined in the Scheme. Initiation by hexabutylditin and irradiation produced the cyclopropylmethyl radical (**3**), which rapidly underwent ring-opening to give the homoallyl radical (**4**). The key chain transfer step is the iodine atom abstraction from **1** by **4** to give **2** and regenerate **3**. This is a novel example of an iodine atom-transfer chain reaction which involves cyclopropane ring-opening in the chain propagation step.[5)]

From the results presented above, it is evident that the free-radical promoted iodine atom-transfer is applicable to the ring-opening reaction of difluorocyclopropane derivatives to obtain difluorohomoallyl iodides.[6)]

References

1) D. P. Curran, *Synthesis*, **1988**, 489; D. P. Curran and C.-T. Chang, *J. Org. Chem.*, **54**, 3140 (1989); D. P. Curran, M.-H. Chen, and D. Kim, *J. Am. Chem. Soc.*, **111**, 6265 (1989). 2) T. Morikawa, M. Uejima, and Y. Kobayashi, *Chem. Lett.*, **1988**, 1407. 3) **2a**: ^1H NMR ($CDCl_3$) δ 1.62 (3H, bs), 2.43 (2H, td, J=7.69 and 7.3 Hz), 2.73 (2H, t, J=7.69 Hz), 3.45 (2H, t, J=14.8 Hz), 5.94 (1H, tq, J=7.3 and 1.57 Hz), 7.14-7.33 (5H, m); ^{19}F NMR ($CDCl_3$, benzotrifluoride as an internal standard) δ -33.0 (t, J=14.8 Hz); MS m/z 336 (M^+). 4) Stability of the intermediary benzyl radical and/or instability of the product seemed to inhibit the radical chain reaction. 5) M. T. Crimmins and S. W. Mascarella, *Tetrahedron Lett.*, **28**, 5063 (1987). 6) The ring-opening reaction of difluorocyclopropylmethanol derivatives leading to the corresponding difluorohomoallyl bromide is not selective. Y. Kobayashi, T. Morikawa, and T. Taguchi, *Chem. Pharm. Bull.*, **31**, 2616 (1983).



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