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REACTIONS OF 2,2-DIFLUOROALKENYLBORANES WITH HALOGENS IN THE PRESENCE OF BASE. NOVEL SYNTHESES OF SYMMETRICALLY DISUBSTITUTED 1,1-DIFLUORO-1-ALKENES AND 1,1-DIFLUORO-2-IODO-1-ALKENES

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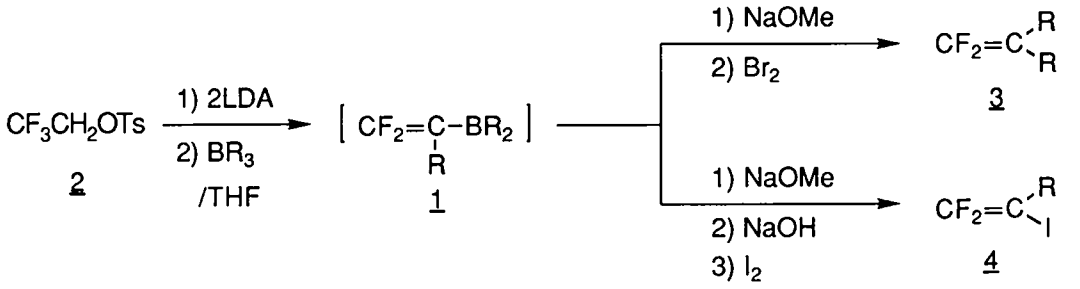
Summary: Treatment of 2,2-difluoroalkenylboranes with bromine and iodine causes coupling reaction and halogenolysis to afford the title compounds in a reverse manner to nonfluorinated counterpart.

The utility of alkenylboranes in organic synthesis is now fully recognized.[1] Among their valuable applications, there are the reactions with halogens to afford alkenyl halides by halogenolysis[1,2] and alkenes by boron-mediated coupling reaction.[1,3]

In the course of our recent study on the synthesis of 1,1-difluoro-1-alkenes, we have found that 2,2-difluoroalkenylboranes 1 could be readily prepared from 2,2,2-trifluoroethyl *p*-toluenesulfonate (2) and trialkylboranes.[4] Then, we examined the reaction of 1 with halogens for the purpose of extending the utility of 1 as a synthetic intermediate for fluorine-containing compounds. In this communication, we report unique results of the reaction of 1 with bromine and iodine, which permit convenient syntheses of symmetrically disubstituted 1,1-difluoro-1-alkenes 3 and 1,1-difluoro-2-iodo-1-alkenes 4, respectively.

We attempted to synthesize the 1,1-difluoroalkenyl bromides from 1 in a similar manner as that of the brominolysis of nonfluorinated alkenylboranes: Treatment of 1 (R=$(CH_2)_4Ph$) with bromine followed by sodium methoxide,



however, yielded no expected bromide, but induced 1,2-migration of the alkyl group on boron to afford symmetrically disubstituted 1,1-difluoro-1-alkene 3 in 10% yield along with a 58% yield of the protonolyzed product, 1,1-difluoro-6-phenyl-1-hexene. Re-examination on the reaction conditions demonstrated that the use of an excess amount of bromine in the presence of methanol-free sodium methoxide suppressed protonolysis to improve the yield of 3 up to 65%.

Several other 1,1-difluoroalkenylboranes 1 underwent the reaction with bromine in the same manner to give 3 as summarized in Table 1. The results are in contrast to occurrence of brominolysis in the case of nonfluorinated alkenyldialkylboranes, of which bromination are known to afford the corresponding alkenyl bromides.[5,6,1,2]

Table 1. Synthesis of 1,1-Difluoro-1-alkenes[a]

Entry	R	BR_3/2	NaOMe/2	Yield of 3/%[b]
1	$-(CH_2)_4Ph$	1.1	3.8	65
2	$-CH_2CH(CH_3)Ph$	1.1	3.1	68(67)[c]
3	10-Pinanyl	1.1	4.6	54
4	Cyclooctyl	1.1	3.4	48
5	Bicyclo[2.2.1]hept-2-yl	1.5	3.0[d]	65

[a]Unless otherwise noted, all reactions were carried out under conditions described in the text. [b]^{19}F NMR yield relative to internal $C_6H_5CF_3$ standard. All products gave satisfactory ^1H, ^{19}F, ^{13}C NMR, and IR spectra. [c]Isolated yield is given in parentheses. [d]A methanol solution of sodium methoxide (1M) was added instead of solid one 30 min before treatment with bromine.

A typical reaction procedure is as follows: To a tetrahydrofuran (THF, 2 ml) solution of 2,2-difluoro-1-tosyloxyvinyllithium, generated from 2 (87 mg, 0.34 mmol) and lithium diisopropylamide (LDA, 0.72 mmol), was added tris(2-phenylpropyl)borane (0.38 mmol) in THF (1 ml) at -78 °C under an argon atmosphere.[4] After 30 min at -78 °C, sodium methoxide (57 mg, 1.06 mmol) was added in solid form. The mixture was brought to room temperature and stirred for 12 h. A dichloromethane (1 ml) solution of bromine (181 mg, 1.13 mmol) was added at -78 °C. The mixture was stirred for 1 h at -78 °C and an additional 1 h at room temperature, then quenched with aqueous sodium thiosulfate. After usual workup, 1,1-dilfuoro-4-phenyl-2-(2-phenylpropyl)-

1-pentene (5, 69 mg, 67%) was isolated by column chromatography on silica gel (pentane).[7]

On the other hand, treatment of 1 (R=$(CH_2)_4Ph$) with iodine in the presence of aqueous sodium hydroxide brought about iodinolysis to give 1,1-difluoroalkenyl iodide 4 in 50% yield along with only a trace amount of the coupling product 3. Detailed examination on the reaction showed that the yield was raised up to 76% in the following procedure; after the addition of sodium methoxide (25 mg, 0.46 mmol)[8] in a similar manner as above to 1 generated from 2 (87 mg, 0.34 mmol) and tris(4-phenylbutyl)borane (0.37 mmol), the mixture was warmed to room temperature and stirred for 12 h. Aqueous sodium hydroxide (6N, 0.19 ml) and a THF (1 ml) solution of iodine (350 mg, 1.38 mmol) was added successively at -10 °C. The stirring was continued for 1 h at -10 °C and an additional 1 h at room temperature. Similar workup as described above provided a 76% yield of 1,1-difluoro-2-iodo-6-phenyl-1-hexene (6).[9]

The results of several other 2,2-difluoroalkenylboranes 1 are summarized in Table 2. These observations are of interest because i) fluorinated alkenyl iodides are potentially important intermediates in the synthesis of fluorine-containing compounds; ii) treatment of nonfluorinated alkenylalkylboranes with iodine is known to induce migration of B-alkyl group in preference to iodinolysis.[3,10,1]

Table 2. Synthesis of 1,1-Difluoro-2-iodo-1-alkenes[a]

Entry	R	BR_3/2	NaOMe/2	I_2/2	Yield of 4/%[b]
1	$-(CH_2)_4Ph$	1.1	1.4	4.1	76(76)[c]
2	$-CH_2CH(CH_3)Ph$	1.1	1.3	3.8	69
3	10-Pinanyl	1.1	1.4	3.5	64
4[d]	Cyclooctyl	1.5	---	5.5	51
5[d]	Bicyclo[2.2.1]-hept-2-yl	1.5	---	5.0	58

[a]Unless otherwise noted, all reactions were carried out under conditions described in the text. [b]^{19}F NMR yield relative to internal $C_6H_5CF_3$ standard. All products gave satisfactory ^1H, ^{19}F, ^{13}C NMR, and IR spectra. [c]Isolated yield is given in parentheses. [d]Molar ratio of 2:NaOH(6N) = 1:4.5.

It should be noted that i) 1 reacts with bromine and iodine in the

presence of base in a reverse manner to nonfluorinated counterpart,[11] ii) the present reactions provide useful methods for preparing symmetrically disubstituted 1,1-difluoro-1-alkenes and 1,1-difluoro-1-alkenyl iodides.

References and Notes

1. For example: A. Pelter, K. Smith, and H. C. Brown, "Borane Reagents," Academic Press, London (1988); E. Negishi, "Comprehensive Organometallic Chemistry," ed by G. Wilkinson, F. G. A. Stone, and E. W. Abel, Pergamon Press, Oxford (1982), Vol. 7, pp. 303-322.
2. H. C. Brown and N. G. Bhat, Tetrahedron Lett., 29, 21 (1988) and references cited therein.
3. H. C. Brown, D. Basavaiah, S. U. Kulkarni, N. G. Bhat, and J. V. N. V. Prasad, J. Org. Chem., 53, 239 (1988) and references cited therein.
4. J. Ichikawa, T. Sonoda, and H. Kobayashi, Tetrahedron Lett., 30, 1641 (1989).
5. H. C. Brown, D. H. Bowman, S. Misumi, and M. K. Unni, J. Am. Chem. Soc., 89, 4531 (1967).
6. Such a bromine-induced migration of B-alkyl group occurred very rarely, except the case reported by Negishi on 2-ethoxycarbonylvinylboranes. E. Negishi, G. Lew, and T. Yoshida, J. Org. Chem., 39, 2321 (1974).
7. 5 (*meso*:*dl* = 1:1) : IR (neat): ν 1745 cm^{-1}; ^{1}H NMR ($CDCl_3$/TMS): δ 1.20 (6H, d, J=8 Hz), 1.98-2.20 (4H, m), 2.58-3.02 (2H, m), and 6.98-7.36 ppm (10H, m); ^{19}F NMR ($CDCl_3/C_6F_6$): δ 67.5 ppm (2F, br s); ^{13}C NMR ($CDCl_3$/ TMS): δ 21.1, 21.5, 34.5, 34.6, 37.7, 37.8, 86.6 (t, J_{CF}=17 Hz), 86.7 (t, J_{CF}=17 Hz), 126.2, 126.8, 128.4, 146.4, 146.5, 154.5 (t, J_{CF}=284 Hz), and 154.6 ppm (t, J_{CF}=284 Hz); Found: m/z 300.1696. Calcd for $C_{20}H_{22}F_2$: 300.1688.
8. Sodium methoxide suppressed protonolysis of 1.
9. 6: IR (neat): ν 1725 cm^{-1}; ^{1}H NMR ($CDCl_3$/TMS): δ 1.22-1.78 (4H, m), 2.14-2.40 (2H, m), 2.44-2.72 (2H, m), and 6.96-7.34 ppm (5H, m); ^{19}F NMR ($CDCl_3/C_6F_6$): δ 79.0 (1F, d, J=39 Hz) and 85.9 ppm (1F, d, J=39 Hz); ^{13}C NMR ($CDCl_3$/TMS): δ 28.2 (t, J_{CF}=2 Hz), 29.9, 32.4, 35.5, 51.2, (dd, J_{CF}=32 Hz, 24 Hz), 125.8, 128.3, 128.4, 142.1, and 152.9 ppm (dd, J_{CF}=292 Hz, 281 Hz); Found: m/z 322.0012. Calcd for $C_{12}H_{13}F_2I$: 322.0031.
10. G. Zweifel, H. Arzoumanian, and C. C. Whitney, J. Am. Chem. Soc., 89, 3652 (1967); D. A. Evans, R. C. Thomas, and J. A. Walker, Tetrahedron Lett., 1976, 1427.
11. Although definite mechanistic studies are lacking, the observed reversal of the reaction pathways is presumably due to the electronic effect of the geminal fluorine substituents to the intermediary dibromide and iodonium ion from 1.

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