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REACTION OF 1,1-DIFLUOROCYCLOPROPANES WITH ORGANOLITHIUM COMPOUNDS

Minoru Suda
Sagami Chemical Research Center
Nishi-Ohnuma 4-4-1, Sagamihara, Kanagawa 229, Japan

Substituted 1,1-difluorocyclopropanes react with organolithium reagents to provide either cyclopropenes or mono-substituted acetylenes depending upon the substitution patterns.

Dichloro- and dibromocyclopropanes, which are easily available by the addition of dihalocarbenes on olefins, are now well known to be lithiated upon treatment with organolithium compounds$^{1)}$, and have been used as the key intermediate in the syntheses of natural products$^{2)}$. On the other hand, the reactivity of the corresponding difluorocyclopropanes has scarcely been examined so far, although some reactions of functionalized difluorocyclopropanes have been reported$^{3)}$. We thought that difluorocyclopropanes would behave differently toward lithium compounds from dichloro- and dibromo-analogs, since the halogen-lithium exchange is not likely to occur. Here we report that 1,1-difluorocyclopropanes react with lithium reagents in completely different ways producing either cyclopropenes or mono-substituted acetylenes depending upon the substitution patterns.

First we examined the reaction of 1,1-difluoro-2-phenylcyclopropane 1 with butyllithium 2a in THF at -70°C. More than two equivalents of 2a was required for the complete disappearance of 1. Subsequent work-up afforded 1-butyl-2-phenylcyclopropene 3a. The product was thermally unstable and polymerized easily upon standing at room temperature. Thus the yield of 3a was calculated by NMR assay of the crude product using tetrachloroethane as the internal standard. Similarly, treatment of 1 with methyllithium 2b and phenyllithium 2c produced cyclopropenes 3b and 3c$^{4)}$, respectively.

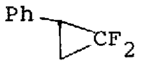
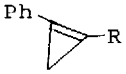
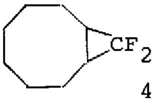
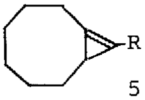
1,4 2a,b,c 3,5

	1, 3	4, 5
R_1	Ph	$(CH_2)_6$
R_2	H	

	R
a	Bu
b	Me
c	Ph

The same transformation took place with 2,3-dialkyl-substituted difluorocyclopropane. Thus, 9,9-difluorobicyclo[6.1.0]nonane 4 gave, upon treatment with 2a,b, 9-substituted bicyclo[6.1.0]non-1(9)-enes 5a,b[5]. The results are summarized in Table together with some spectroscopic features of the products.

Table. Cyclopropenes from difluorocyclopropanes, and characteristic absorptions in IR and NMR spectra of the products.

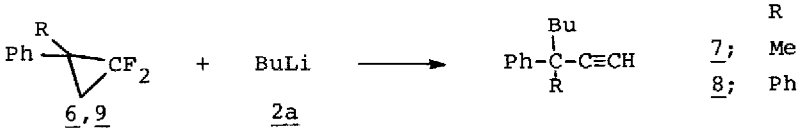
Difluoro-cyclopropane	R in RLi	Cyclopropane	Yield (%)	IR (cm^{-1})	NMR(δ) ring CH_2	H at C_α
 1	Bu	 3	91[a]	1850	1.17	2.63
	Me		68[a]	1855	1.20	2.30
	Ph		63[b]	1820	1.53	-
 4	Bu	 5	85[b]	1860	-	2.2-2.7
	Me		29[b]	1870	-	1.95 2.4-2.7

a) Yields based on NMR assay of crude product using tetrachloroethane as internal standard. b) Isolated yields.

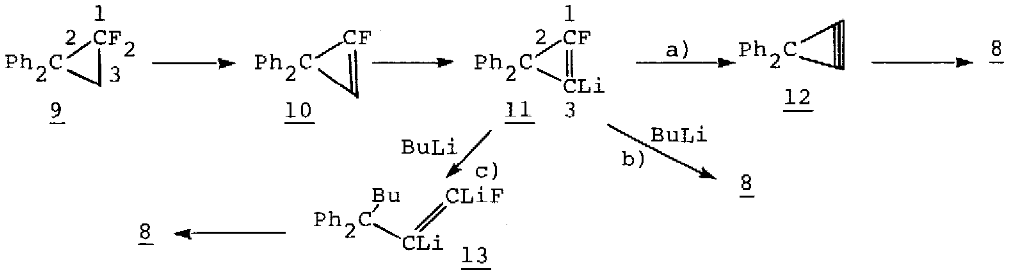
Spectroscopic properties[6] unambiguously support the sturcture of the products. The IR spectra of cyclopropenes exhibit an absorption at 1820-1880 cm^{-1}, and in NMR spectra ring protons on C-3 appear as a sharp singlet, and those on carbon(s) α to ring C-1 and C-2 have absorptions at a fairly low field

Formation of cyclopropenes can be explained as follows. First, difluorocyclopropane is dehydrofluorinated to form an intermediate fluorocyclopropene, which is quite reactive and reacts instantly with lithium compound at fluorine-carrying carbon. And subsequent F^- elimination produces the cyclopropene.

We then examined the reaction of 1,1-difluoro-2-methyl-2-phenylcyclopropane 6 with butyllithium 2a(three equivalents)[7] in THF. No cyclopropene derivative was formed; instead, 3-methyl-3-phenyl-1-heptyne 7[8] was obtained in 33% yield as the sole isolable product. Similarly, 3,3-diphenyl-1-heptyne 8[9] was isolated in 38% yield when 1,1-difluoro-2,2-diphenylcyclopropane 9 was treated similarly. Mechanistically, several pathways seem to explain the formation of acetylene derivatives. Dehydrofluorination of 9 produces a fluorocyclopropene 10. In the cases of 1 and 4, which carry no hydrogen on the ring double bond, lithium reagent attacks on fluorine-carrying carbon



of the intermediate fluorocyclopropene. On the other hand, in this case, a hydrogen on the double bond, which is expected to be quite acidic[6), is preferentially abstracted by lithium reagent to give a lithium compound 11. The fate of 11 to provide the final product 8 seems to have three possibilities a) Elimination of LiF affords cyclopropyne 12, which is then attacked by butyllithium at C-2 (bond 1-2 or 2-3 fission). b) Butyllithium attacks C-2 of 11, and subsequent (or concerted) F^- elimination gives rise to lithium salt of 8 (bond 2-3 fission). And c) butyllithium adds on bond 1-2 to give dilithium intermediate 13. Subsequent elimination of LiF produces the lithium salt of 8 (bond 1-2 fission).



In order to distinguish these possibilities, ^{13}C-labelling experiments were performed. Thus, 9 having about 40% ^{13}C- at C-3 was prepared from acetic acid-2-^{13}C by 1) diazomethane, 2) phenylmagnesium bromide, 3) dehydration, and 4) sodium chlorodifluoroacetate, and treated similarly with butyllithium. The ^{13}C-NMR spectrum of produced 8 exhibited only one strong absorption at δ 73.6 [$J(^{13}C\text{-}H)=248Hz$]. This result clearly supports that bond 2-3 fission occurred (mechanism b).

Formation of cyclopropyne, which has been the target of theoretical calculations[10), seems to be thermodynamically unfavorable, since LiF elimination cannot take place prior to the attack of butyllithium.

In summary, substituted 1,1-difluorocyclopropanes react with lithium reagents in two different manners depending upon the substitution pattern, and either cyclopropene or mono-substituted acetylene is formed. In the latter transformation, intermediacy of cyclopropyne was excluded by ^{13}C-labelling experiments. Observed reactivity of difluorocyclopropanes is completely different from that of dichloro- and dibromo-analogs.

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2) K. Kitatani, T. Hiyama, and H. Nozaki, J. Am. Chem. Soc., 98, 2362 (1976).

3) Y. Kobayashi, T. Taguchi, T. Morokawa, T. Takase, and H. Takanashi, Tetrahedron Lett., 1980, 1047, and references cited therein.

4) D. T. Longone and D. M. Stehouwer, Tetrahedron Lett., 1970, 1017.

5) Phenyllithium did not react with 4. Also, in an attempt to prepare a trisubstituted difluorocyclopropane, reaction of difluorocarbene intermediate generated by the thermal decomposition of sodium chlorodifluoroacetate and 1,1-diphenylpropene was unsuccessful in our hand.

6) G. L. Closs, "Advances in Alicyclic Chemistry", Academic Press, Vol 1, p53 (1966). A. J. Schipperijn and P. Smael, Rec. Trav. Chim., 92, 1159 (1973).

7) Addition of three equivalents of 2a is necessary to cause the complete disappearance of 6. When progress of the reaction was monitored by glc, no other peaks were observed besides the product, suggesting that the reactivity of intermediate is much higher than that of 6.

8) ^{1}H-NMR ($CDCl_3$) δ 0.84(3H), 1.1-1.4(4H), 1.58(3H), 1.6-1.9(2H), 2.35(1H), 7.2-7.6(5H). IR(neat) 3320, 2110 cm^{-1}. Mass Spec., m/e 186(M^+, 3%), 144 (3%), 143(3%), 130(13%), 129(100%). Correct elemental analysis.

9) ^{1}H-NMR($CDCl_3$) δ 0.88(3H), 1.2-1.6(4H), 2.25(2H), 2.54(1H), 7.1-7.6(10H). ^{13}C-NMR($CDCl_3$) δ 14.0(CH_3), 23.0(CH_2), 27.6(CH_2), 41.2(CH_2), 49.3(C), 73.6 ($\equiv$CH), 88.2(C$\equiv$), 126.5(Ar), 127.2(Ar), 128.1(Ar), 145.0(Ar). IR(neat) 3310, 2100 cm^{-1}. Mass Spec., m/e 248(M^+,3%), 247(9%), 205(5%), 192(18%), 191(100%) Correct elemental analysis.

10) W. J. Hehre, J. A. Pople, W. A. Lathan, L. Radom, E. Wasserman, and A. R. Wasserman, J. Am. Chem. Soc., 98, 4378 (1976). P. Saxe and H. F. Schaefer, III, J. Am. Chem. Soc., 102, 3239 (1980).

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