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Tetrahedron Letters

Tetrahedron Letters 47 (2006) 209–212

Novel synthesis of 1-aryl-1-trifluoromethylallenes

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Received 8 July 2005; revised 30 September 2005; accepted 28 October 2005
Available online 18 November 2005

Abstract—3,3-Bis(phenylthio)-1,1,1,2,2-pentafluorobutane **1** was reacted with aryllithium reagents (6 equiv) in ether at low to room temperature for 1–6 h to provide 2-aryl-1,1,1-trifluoro-3-phenylthio-2-butene **2** in 80–96% yields. Bromination of **2** with NBS in acetonitrile at reflux for 1–7 h afforded the corresponding allylic bromides **3** in 61–96% yields. Treatment of **3** with MCPBA (1.5 equiv) in methylene chloride at reflux temperature for 1–12 h resulted in the formation of 1-aryl-1-trifluoromethylallenes **4** in 74–96% yields.

Allenes are very useful synthetic intermediates in a variety of organic synthetic processes including ionic, radical and concerted reactions because of their unique structural property and reactivity toward cumulated carbon–carbon double bond.[1,2] In contrast to good documentation of nonfluorinated allenic compounds in recent literatures,[3–5] there has been limited synthetic methods for the preparation of fluorinated counterparts. In particular, synthesis of trifluoromethylated allenic compounds as trifluoromethylated building blocks relies on several limited routes. Most of the methods focused on the synthesis of trifluoromethylated allenic compounds containing proton at α-position. S_N2' substitution of propargylic halides or tosylates with CF_3Cu provided the corresponding CF_3-substituted allene compounds.[6,7] CF_3-substituted propargylic mesylates also underwent S_N2' displacement with organozinc reagents in the presence of palladium catalyst to give the corresponding CF_3-substituted allene compounds.[8,9] Direct conversion of CF_3-substituted propargylic alcohol to CF_3-substituted allene compounds containing trifluoromethyl or ethoxycarbonylmethyl group was accomplished by the treatment with sulfur tetrafluoride[10] or ethyl orthoacetate in acidic condition.[11] α-Trifluoromethyl allenol ethers were prepared by the Julia-Lythgoe process involving β-acetoxy sulfone, which undergoes desulfonylation with SmI_2.[12] Recently, α-phenyl-α-trifluoromethylated allene compound was first synthesized by the reaction of four-coordinate rhodium(I) with CO in benzene at 10 °C.[13,14] However, this method exhibited only one example from a tedious procedure. In this letter, we wish to describe an efficient and general preparation of 1-aryl-1-trifluoromethylallenes from 3,3-bis(phenylthio)-1,1,1,2,2-pentafluorobutane.

It has been reported that perfluoroalkyated dithioketals[15] were reacted with a variety of organolithium reagents to give the corresponding β-fluorovinyl or β-trifluoromethylvinyl sulfides.[16] Therefore, the reactions of 3,3-bis(phenylthio)-1,1,1,2,2-pentafluorobutane **1** with aryllithium reagents formed from the reaction of aryl iodides with *n*-BuLi, such as naphthalenyllithium and phenyllithium substituted by proton, trifluoromethyl, methoxy, methyl, fluoro, chloro, bromo on *meta* or *para* position of the benzene ring, in ether at low to room temperature for 1–6 h afforded 2-aryl-1,1,1-trifluoro-3-phenylthio-2-butene **2a**–**m** in 80–96% yields as an *E* and *Z* isomeric mixture. The reaction temperature depends on the stability of generated aryllithium in ether solution. The use of 6 equiv of aryl iodides and 6 equiv of *n*-BuLi to form aryllithium reagents provided the best results for the formation of the corresponding sulfides. The reaction of **1** with *ortho* substituted phenyllithium such as 2-bromo-, 2-fluoro- or 2-methoxyphenyllithium, heteroaromatic lithium reagents such as thienyllithium or pyrazinyllithium, and alkynyllithium reagent did not provide the desired product **2** and the starting material was always recovered. When **1** was reacted with MeLi and *n*-BuLi as alkyllithium reagents at −78 °C, followed by warming to 0 °C, however, the corresponding

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Keywords: 2-Aryl-1,1,1-trifluoro-3-phenylthio-2-butene; Bromination; Oxidation; Trifluoromethylated allenes.

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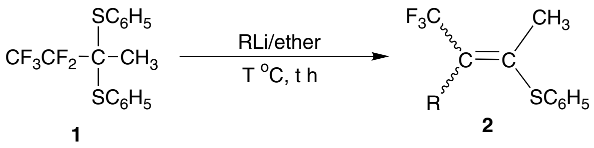
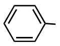
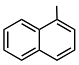
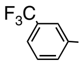
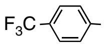
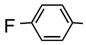
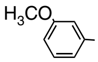
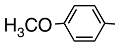
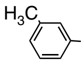
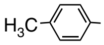
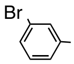
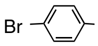
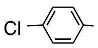
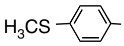
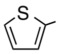
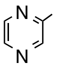
doi:10.1016/j.tetlet.2005.10.166

products **2n** and **2o** were obtained in 78% and 82% yield as an *E* and *Z* isomeric mixture. The reaction pathway seems likely that the initial attack of sulfur atom of **1** by aryllithium generates a carbanion bearing pentafluoroethyl group, which undergoes β-defluorination to give β-fluoro-β-trifluoromethylated vinyl sulfides. These vinyl sulfides quickly undergo addition–elimination reaction with another equiv of aryllithium to afford **2**. The assignment of stereoisomer of **2** was based on the H–F homoallylic coupling constant, in which *cis* H–F coupling constant is bigger than *trans* one.[17] The results of these reactions are summarized in Table 1.

Subsequence allylic bromination of **2** with *N*-bromosuccinimide (1.2 equiv) in the presence of catalytic amount of AIBN at reflux temperature of acetonitrile for 1–7 h

Table 1. Preparation of 2-aryl-1,1,1-trifluoro-3-phenylthio-2-butene **2**



Compounds	R	*T*	*t* (h)	Yield (%)[a]	*E*/*Z*[b]
2a		0 °C → rt	3	87	70/30
2b		rt	1	87	82/18
2c		0 °C → rt	6	96	76/24
2d		−50 °C → rt	1	87	70/30
2e		−50 °C → rt	5	90	80/20
2f		rt	1	86	70/30
2g		rt	1	88	70/30
2h		rt	2	88	67/33
2i		rt	1	84	66/34
2j		0 °C → rt	2	84	74/26
2k		0 °C → rt	1	80	81/19
2l		rt	1	86	56/44
2m		0 °C → rt	1	96	70/30
2n	CH_3	−78 °C → 0 °C	1	78	62/38
2o	n-C_4H_9	−78 °C → 0 °C	1	82	65/35
2p	n-$C_6H_{13}C{\equiv}C$—	0 °C → rt	24	—[c]	
2q		0 °C → rt	24	—[c]	
2r		0 °C → rt	24	—[c]	

[a] Isolated yield.

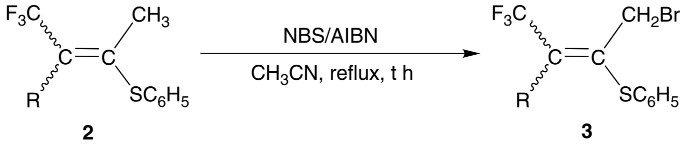
[b] *E*/*Z* ratio was determined by ^1H and ^{19}F NMR spectroscopy.

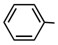
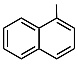
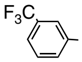
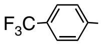
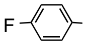
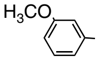
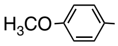
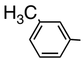
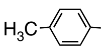
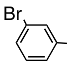
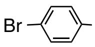
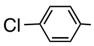
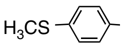
[c] Starting material **1** was recovered.

resulted in the formation of the corresponding allylic bromide **3** as an *E* and *Z* isomeric mixture in 61–96% yields. Although **2n** and **2o** have two allylic positions, only allylic methyl proton connected to vinyl carbon having phenylthio group was brominated regioselectively. The use of acetonitrile as a solvent provided much better result than use of CCl_4. *E*/*Z* ratio was assigned in a similar manner as assignment of **2**. The results of these reactions are summarized in Table 2.

Initially, we tried to prepare vinyl sulfones via oxidation of **3** with MCPBA, but 1-aryl-trifluoromethylallenes **4a**–**m** were obtained in 61–96% yields. The use of 1.5 equiv of MCPBA was enough to yield **4** except for formation of **4m**, in which 2 equiv of MCPBA was used to oxidize methylthio group connected to benzene ring and the reaction was shown to be temperature dependent since the reaction of **3** with MCPBA at room temperature did not provide any desired product **4**. Methylene chloride having low boiling point was enough solvent system to afford allenes **4**. However, **3n** and **3o** did not undergo debromosulfinylation with MCPBA to give the corresponding allenes under several reaction conditions such as reflux in CH_2Cl_2 or CCl_4 for the longer reaction time, but the corresponding vinyl sulfoxides were obtained in 90% and 92% yield, respectively. Although debromosulfinylation of β-sulfinylated allylic bromide in the presence of excess amount of AIBN and tris(trimethylsilyl)silane at reflux temperature of benzene was successfully carried out to give the corre-

Table 2. Bromination of 2-aryl-1,1,1-trifluoro-3-phenylthio-2-butene **2**



Compounds	R	*t* (h)	Yield (%)[a]	*E*/*Z*[b]
3a		1	87	58/42
3b		5	76	56/44
3c		3	96	63/37
3d		3	61	62/38
3e		3	74	57/43
3f		3	79	56/44
3g		3	72	59/41
3h		3	71	59/41
3i		3	79	56/44
3j		7	76	56/44
3k		7	70	61/39
3l		7	75	57/43
3m		5	96	73/27
3n	CH_3	1	85	65/35
3o	*n*-C_4H_9	1	80	62/38

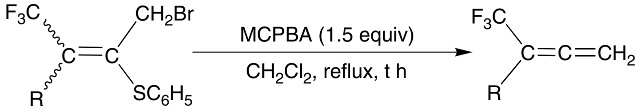
[a] Isolated yield.

[b] *E*/*Z* ratio was determined by ^1H and ^{19}F NMR spectroscopy.

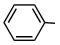
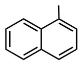
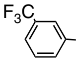
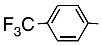
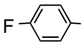
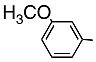
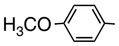
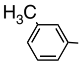
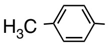
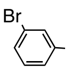
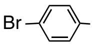
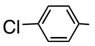
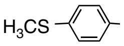
sponding allene derivatives in the nonfluorinated system,[18] there has been no report on the synthesis of trifluoromethylated allenes directly from trifluoromethylated β-phenylthio substituted allylic bromides. It seems likely that the reaction mechanism involves the formation of β-sulfinylated allylic bromides, which quickly provides the corresponding allylic radical to form 1-aryl-1-trifluoromethylallenes **4** via β-elimination of sulfinyl radical. The results of these reactions are summarized in Table 3.

A typical reaction procedure for the preparation of **4g** is as follows. A 25 mL two-neck round bottomed flask equipped with a magnetic stirrer bar, a septum and nitrogen tee connected to an argon source was charged with 4-bromo-1,1,1-trifluoro-2-(4′-methoxy)phenyl-3-phenylthio-2-butene **3g** (0.202 g, 0.5 mmol), MCPBA (0.260 g, 0.75 mmol, 50% technical purity) and methylene chloride (5 mL) and then heated to reflux for 12 h. After the reaction mixture was quenched with saturated $NaHCO_3$, and 10% $NaHSO_3$, the reaction mixture was extracted with methylene chloride twice. The methylene chloride solution was dried over anhydrous K_2CO_3 and chromatographed on SiO_2 column. Elution with a mixture of hexane and ethyl acetate (4:1) provided 0.190 g of **4g** in 87% yield. **4g**:oil:^1H NMR ($CDCl_3$) δ 7.90–6.67 (m, 4H), 4.77 (s, 2H), 3.85 (s, 3H); ^{19}F NMR ($CDCl_3$, internal standard $CFCl_3$) δ −59.98 (s, 3F); MS, *m*/*z* (relative intensity) 214 (M^+, 100), 199 (7), 171 (13), 151 (28), 145 (71), 130 (10), 102 (18); IR (neat) 3079, 2927, 2871, 1959, 1596, 1579, 1497, 1384, 1261, 1156, 834 cm^{-1}. Anal. Calcd for $C_{11}H_9F_3O$: C, 61.66; H, 4.24. Found: C, 61.58; H, 4.21.

Table 3. Preparation of 1-aryl-1-trifluoromethylallenes **4**



3 **4**

Compounds	R	*t* (h)	Yield (%)[a]
4a		2	96
4b		5	78
4c		6	74
4d		6	88
4e		1	79
4f		12	81
4g		12	87
4h		6	87
4i		6	87
4j		6	83
4k		6	86
4l		6	81
4m[b]		3	84
4n	CH_3	18	—[c]
4o	*n*-C_4H_9	18	—[c]

[a] Isolated yield.

[b] 3.5 equiv of MCPBA was used.

[c] Allene was not obtained, but vinyl sulfoxide was formed in high yield.

Acknowledgements

This work was supported by Korea Research Foundation Grant (KRF-2003-041-C00199).

References and notes

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