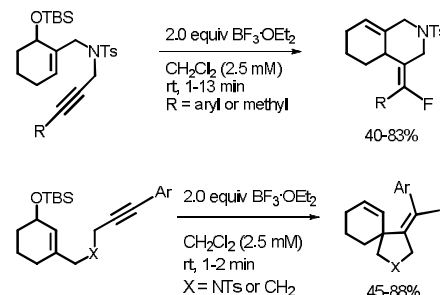


Transition-Metal-Free Carbofluorination of TBS-Protected Nitrogen-Containing Cyclic Enynols: Synthesis of Fluorinated Azabicycles

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ABSTRACT: The synthesis of fluorinated azabicycles from tert-butyldimethylsilyl protected N-containing cyclic enynols using inexpensive $\text{BF}_3 \cdot \text{OEt}_2$ is described. In this reaction, BF_3 reacts as both the Lewis acid and the fluoride source for cyclization/fluorination of the TBS-protected cyclic N-containing enynols. The method provides an easy access to fluorinated azabicycles where a new $\text{C}(\text{sp}^2)\text{-F}$ bond and a new bicyclic skeleton are generated at ambient temperature within 1-13 min under metal-free reaction conditions.



Scheme 1. Synthesis of Ketones 3a-d

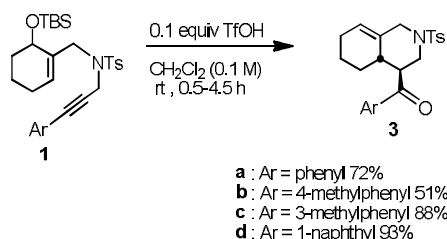
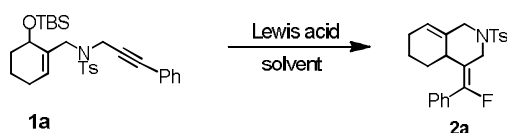


Table 1. Optimizing of Reaction Conditions in the Carbofluorination of 1a with $\text{BF}_3 \cdot \text{OEt}_2$



Entry	Lewis acid	Loading (equiv)	Solvent	Time	Yield (%) ^a
1	$\text{BF}_3 \cdot \text{OEt}_2$	1	0.1 M CH_2Cl_2	1 min	25
2	$\text{BF}_3 \cdot \text{OEt}_2$	2	0.1 M CH_2Cl_2	1 min	48
3	$\text{BF}_3 \cdot \text{OEt}_2$	2	0.1 M DBE	1 min	34
4	$\text{BF}_3 \cdot \text{OEt}_2$	2	0.1 M DCE	1 min	33
5	$\text{BF}_3 \cdot \text{OEt}_2$	2	0.1 M CHCl_3	1 min	34
6	$\text{BF}_3 \cdot \text{OEt}_2$	2	0.1 M toluene	1 min	6
7	$\text{BF}_3 \cdot \text{OEt}_2$	2	0.01 M toluene	15 min	11
8	$\text{BF}_3 \cdot \text{OEt}_2$	2	2.5 mM toluene	35 min	25
9	$\text{BF}_3 \cdot \text{OEt}_2$	2	0.1 M CH_3CN	1 min	0 ^b
10	$\text{BF}_3 \cdot \text{OEt}_2$	10	0.1 M CH_2Cl_2	1 min	50
11	Ph_3CBF_4	2	0.1 M CH_2Cl_2	1 min	26
12	Ph_3CBF_4	5	0.1 M CH_2Cl_2	1 min	27
13	$\text{BF}_3 \cdot \text{OEt}_2$	2	0.1 M THF	10 h	0 ^c
14	<i>n</i> - Bu_4NF	2	0.1 M THF	0.5 h	0 ^c
15	$\text{BF}_3 \cdot \text{OEt}_2$	2	0.01 M THF	36 h	0 ^d
16	$\text{BF}_3 \cdot \text{OEt}_2$	2	0.01 M CH_2Cl_2	1 min	51
17	$\text{BF}_3 \cdot \text{OEt}_2$	2	2.5 mM CH_2Cl_2	1 min	56

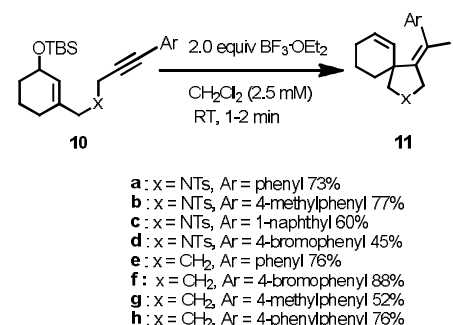
^a Isolated yields by column chromatography. ^b Compound 4 was isolated in 79% yield. ^c Deprotection product 1a' was isolated in good yields. ^d Compound 1a was recovered quantitatively.

Table 2. Substrate scope

Entry	Enynol	R	Product	Yield (%) ^a
1	1a	phenyl	2a ^e	56
2	1b	4-methylphenyl	2b ^e	40
3	1c	3-methylphenyl	2c ^e	50
4	1d	1-naphthyl	2d	56
5	1e	4-nitrophenyl	2e ^e	74
6	1f	3-nitrophenyl	2f ^e	71
7	1g	4-carboxyphenyl	2g ^e	72
8	1h	3-carboxyphenyl	2h ^e	56
9	1i	4-methoxyphenyl	2i	0 ^b
10	1j	4-bromophenyl	2j ^e	52
11	1k	hydrogen	2k	0
12	1l	methyl	2l	83

^a Yields of isolated products. ^b Dienone 5 was isolated in 50% yield. ^c Structures were confirmed by X-ray diffraction analysis.

Scheme 2. Synthesis of (Z)-4-(Arylfluoromethylene)-substituted Aza- and Carbospirocycles



Scheme 3. Postulated Reaction Paths for Formation of 1a and 3a

