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Rapid and Slow Generation of 1-Trifluoromethylvinyllithium: Syntheses and Applications of CF_3-Containing Allylic Alcohols, Allylic Amines, and Vinyl Ketones

Ryo Nadano,[b] Kohei Fuchibe,[a] Masahiro Ikeda,[a] Hiroki Takahashi,[a] and Junji Ichikawa*[a]

Abstract: 1-(Trifluoromethyl)vinylation is accomplished in two protocols by the in situ generation of thermally unstable 3,3,3-trifluoroprop-1-en-2-yllithium (**1**): 1) a rapid lithium–halogen-exchange reaction of 2-bromo-3,3,3-trifluoroprop-1-ene (**2**) takes effect with *sec*-BuLi at −105 °C to generate vinyllithium **1**, which reacts with more reactive electrophiles, such as aldehydes and *N*-tosylimines before its decomposition, to afford 2-(trifluoromethyl)allyl alcohols and *N*-[2-(trifluoromethyl)allyl] sulfoamides in good yield; 2) treatment of **2** with *n*BuLi at −100 °C causes a slow lithium–halogen exchange of **2**, which gives rise to a mixture of **1** and *n*BuLi. Vinyllithium **1** is preferentially trapped with less reactive electrophiles, such as *N*,*N*-dimethylamides in the presence of $BF_3{\cdot}OEt_2$, to afford 1-(trifluoromethyl)vinyl ketones in good yield. Versatility of the products toward syntheses of CF_3-containing ring-fused cyclopentenones is also demonstrated by the Pauson–Khand reaction and the Nazarov cyclization.

Keywords: allylic compounds · cyclization · fluorine · ketones · lithium

Introduction

Trifluoromethyl compounds have now become essential in agricultural and medicinal chemistry, and in materials science.[1] It is well-known that the introduction of a trifluoromethyl group into bioactive compounds has a significant effect on their transport, metabolism, and distribution within organisms. An electron-withdrawing trifluoromethyl group is also finding wide use in optical and electronic devices. A building-block strategy is now fully recognized as an efficient approach for the selective introduction of fluorine-containing substituents into bioactive molecules and molecular devices, and trifluoromethylated building blocks have been developed.[2] Among these, the 3,3,3-trifluoroprop-1-en-2-yl group [1-(trifluoromethyl)vinyl group] is very versatile: (trifluoromethyl)vinyl compounds readily undergo cycloaddition with dienes and 1,3-dipoles to construct hetero- and carbocyclic ring systems bearing a trifluoromethyl group.[3] Furthermore, they serve as monomers for the synthesis of trifluoromethyl-containing polymers.[4]

We recognized that a 1-(trifluoromethyl)vinyl group functions as a potential synthetic unit because of its electron-withdrawing CF_3 group, double bond that is reactive toward nucleophiles, and allylic fluorine atoms with leaving-group ability. These properties allow transformations to compounds with fluorinated one-carbon units. Related to this, we have already reported flexible synthetic routes to the following: 1) 1,1-difluoro-1-alkenes by an S_N2'-type reaction[5] of 1-(trifluoromethyl)vinyl compounds,[6] 2) fluorocarbon-substituted heterocycles by intramolecular nucleophilic reactions of functionalized 2-trifluoromethyl-1-alkenes,[7] and 3) 5-trifluoromethyl-2-cyclopentenones by a regioselective Nazarov cyclization of 1-(trifluoromethyl)vinyl ketones.[8]

Because of the synthetic potential of the 1-(trifluoromethyl)vinyl system, extensive efforts have been made to develop synthetic methods for 2-trifluoromethyl-1-alkenes [1-(trifluoromethyl)vinyl compounds].[9–16] Trifluoromethylated

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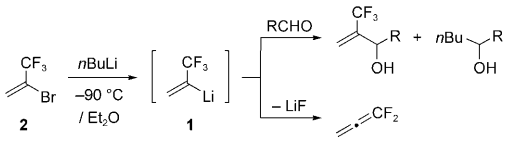
vinylmetal species are straightforward reagents for providing a variety of compounds bearing a (trifluoromethyl)vinyl moiety. 1-(Trifluoromethyl)vinyl compounds with a conjugated system can be prepared by palladium-catalyzed coupling reactions of relatively stable 1-(trifluoromethyl)vinylmetals, such as [1-(trifluoromethyl)vinyl]zinc,[10] -tin,[11] and -boronic acid,[12] with the appropriate unsaturated organohalides. The Suzuki[13a] and the Sonogashira coupling reactions,[13b,c] and a carbonylation reaction[13d] are also amenable to the synthesis of conjugated 1-(trifluoromethyl)vinyl compounds by 1-(trifluoromethyl)vinylpalladium, generated from the corresponding bromide. In contrast, methods for the preparation of nonconjugated 1-(trifluoromethyl)vinyl compounds are still rather limited because of the thermal instability of 1-(trifluoromethyl)vinyl metal species.[14]

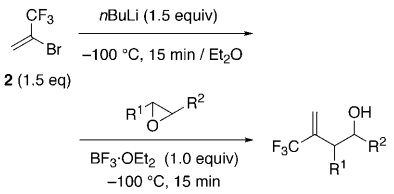
Tarrant reported that 3,3,3-trifluoroprop-1-en-2-yllithium [1-(trifluoromethyl)vinyllithium] (**1**), generated upon treatment of 2-bromo-3,3,3-trifluoropropene (**2**) with *n*BuLi, reacted with aldehydes or ketones to afford 2-(trifluoromethyl)allyl alcohols [Eq. (1)].[15] Although the lithium reagent was sufficiently reactive to allow the preparation of nonconjugated 1-(trifluoromethyl)vinyl compounds, this approach had the following serious drawbacks:[15c] 1) the generated lithium species **1** was highly unstable and readily underwent elimination of lithium fluoride, even at −78 °C, leading to 1,1-difluoroallene [Eq. (1)],[17] and thus, the reaction required the alternate addition of *n*BuLi and a carbonyl substrate to **2** in several aliquots; 2) the product alcohols were obtained only in 30–50 % yields along with butyl carbinols derived from *n*BuLi, indicating incomplete lithium–halogen exchange.

In our previous paper, we reported on the efficient synthesis of 1-(trifluoromethyl)vinyl-substituted alcohols by the



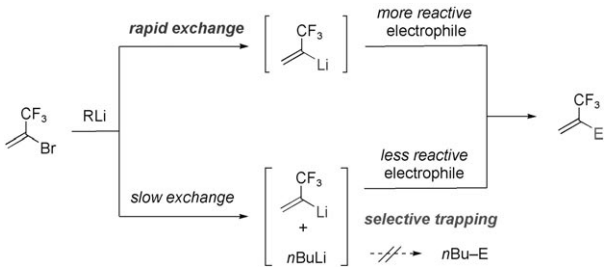
(1)

ring opening of oxiranes or oxetanes with vinyllithium **1** [Eq. (2)].[18a] In this synthesis, the lithium–halogen-exchange reaction takes place upon treatment of bromide **2** with *n*BuLi at −100 °C, under which conditions a slow lithium–halogen exchange gave rise to a mixture of vinyllithium **1** and *n*BuLi. We succeeded, however, in the selective trapping of **1** with appropriate electrophiles, such as oxiranes and oxetanes, in the presence of $BF_3{\cdot}OEt_2$ to obtain the desired alcohols.[19] This selectivity might be explained by the subtle difference between the reactivities of the two lithium species. While *n*BuLi shows lower reactivity, probably because of its high aggregation state,[20] the reactivity of vinyllithium **1** would be relatively enhanced by its low aggregation state, which might be caused by its sp^2-hybridization, the steric effect, and/or the lithium–fluorine interaction[21] of the trifluoromethyl group.



(2)

For general applicability of the 1-(trifluoromethyl)vinylation with vinyllithium **1**, there remained a problem to be solved with regard to its reaction with highly reactive electrophiles. The vinylation of aldehydes led to the nonselective addition of vinyllithium **1** and *n*BuLi, as mentioned above.[15,22] In this paper, we describe full details of the two protocols for the general (trifluoromethyl)vinylation with both more and less reactive electrophiles (Scheme 1): 1) one involving a rapid lithium–halogen exchange for more reactive electrophiles, such as aldehydes and imines,[18b] and 2) the other one involving the combination of a slow lithium–halogen exchange and a selective trapping of vinyllithi-



Scheme 1. Concept for 1-(trifluoromethyl)vinylation.

Abstract in Japanese:

熱的に不安定な 1-(トリフルオロメチル)ビニルリチウムの調製法 2 種を開発し、1-(トリフルオロメチル)ビニル基の導入を達成した。2-ブロモ-3,3,3-トリフルオロプロペンに−105 °C で *sec*-ブチルリチウムを作用させると速やかなリチウム–ハロゲン交換が進行し、3,3,3-トリフルオロプロパ-1-エン-2-イルリチウム [1-(トリフルオロメチル)ビニルリチウム]が生成した。これにアルデヒドやイミンなど反応性の高い求電子剤を作用させることで、対応するトリフルオロメチル基含有アリルアルコール誘導体およびアリルアミン誘導体が得られた。また、2-ブロモ-3,3,3-トリフルオロプロペンに −100 °C でブチルリチウムを作用させるとリチウム–ハロゲン交換がゆっくり進行し、1-(トリフルオロメチル)ビニルリチウムと未反応のブチルリチウムの混合物を与えた。この混合物に対して三フッ化ホウ素エーテル錯体存在下、反応性の低い求電子剤である α,β-不飽和アミドを作用させることでビニルリチウムのみが優先的に反応し、(トリフルオロメチル)ビニルケトンを収率良く得ることができた。得られたトリフルオロメチル基含有アリルアルコール誘導体、アリルアミン誘導体、ならびにビニルケトンは Pauson–Khand 反応や Nazarov 環化の良い基質であり、トリフルオロメチル基を有する種々の縮環シクロペンテノンへ誘導することができた。

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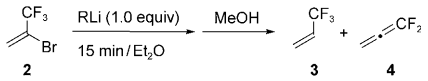
um **1** with less reactive electrophiles other than oxiranes and oxetanes,[18a] namely, carboxamides. Furthermore, 1-(trifluoromethyl)vinyl compounds obtained by using the two methods mentioned above were used to construct more complex structures bearing a trifluoromethyl group, such as pyrrolidine ring-fused or furan ring-fused cyclopentenones and indanones by the Pauson–Khand reaction and the Nazarov cyclization, respectively.

Results and Discussion

Generation of 1-(Trifluoromethyl)vinyllithium 1 by the Rapid Lithium–Halogen-Exchange Reaction: Synthesis of 2-(Trilfuoromethyl)allyl Alcohols 5

We first re-examined the generation of vinyllithium **1** from bromotrifluoropropene **2** upon treatment with several alkyllithiums at temperatures ranging from −78 °C to −105 °C over 15 min. After quenching with methanol, the product distributions were observed by ^{19}F NMR (Table 1).[23] When

Table 1. Generation of 1-(trifluoromethyl)vinyllithium **1**.



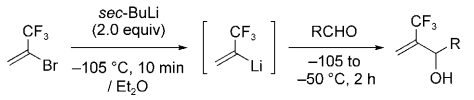
2 **3** **4**

Entry	R	*T* [°C]	**3** [%]	**4** [%]	Recovery of **2** [%]
1	*n*Bu	−78	20	54	17
2	*n*Bu	−96	31	11	58
3	*n*Bu	−105	14	1	76
4	*sec*-Bu	−105	60	26	10
5	*tert*-Bu	−105	50	35	5

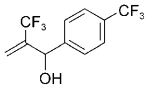
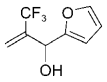
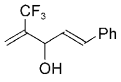
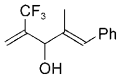
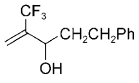
the reaction was carried out with *n*BuLi at −78 °C, the decomposition of vinyllithium **1** took place to afford 1,1-difluoroallene (**4**) in 54 % yield by the elimination of lithium fluoride (Entry 1). On the other hand, performing the reaction at −105 °C suppressed the decomposition; here, we observed only a 14 % yield of 3,3,3-trifluoroprop-1-ene (**3**), along with a 76 % recovery of **2** (Entry 3). These results indicate that either incomplete conversion of **2** or decomposition of **1** is inevitable in the reaction with *n*BuLi, because of the slow exchange rate of **2** and the thermal instability of **1**. In contrast, the lithium–halogen-exchange reaction with *sec*-BuLi proceeded rapidly even at −105 °C to consume 90 % of **2**, which generated **1** in at least 60 % yield along with 26 % of **4** (Entry 4).

We then attempted the reaction of vinyllithium **1** with aldehydes. Vinyllithium **1** was generated in situ from excess amounts of vinyl bromide **2** (2.0 equiv) and *sec*-BuLi (2.0 equiv), taking the partial decomposition of **1** into consideration. Treatment of the ether solution of **1** with benzaldehyde afforded the desired 2-(trifluoromethyl)allyl alcohol[14] **5a** in 73 % yield (Table 2, Entry 1). Aryl, heteroaryl, alkenyl, and alkyl aldehydes reacted in a similar manner to give the corresponding allylic alcohols **5b–f** in high yield

Table 2. Synthesis of 2-(trifluoromethyl)allyl alcohols **5**.



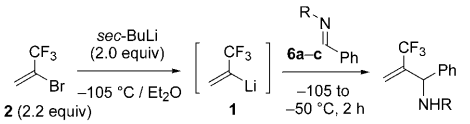
2 (2.0 equiv) **1** **5**

Entry	R	Product		Yield [%]
1	Ph		**5a**	73
2	C_6H_4(*p*-CF_3)		**5b**	82
3	2-furyl		**5c**	58
4	(*E*)-cinnamyl		**5d**	93
5	(*E*)-α-methylcinnamyl		**5e**	92
6	CH_2CH_2Ph		**5f**	76

(Entries 2–6). Thus, the more rapid lithium–halogen exchange allowed the reaction with reactive electrophiles.

Synthesis of *N*-[2-(Trifluoromethyl)allyl] Amines 7

Allyl amine derivatives have been used as useful components for the synthesis of *N*-heterocycles.[24] This fact prompted us to investigate the reaction of vinyllithium **1** with imines (as other, more reactive, electrophiles), leading to the synthesis of 2-(trifluoromethyl)allyl amine derivatives **7** [Eq. (3)].[9c–e] Although *N*-benzylimine **6a** was not sufficiently reactive toward **1**, $BF_3{\cdot}OEt_2$ promoted the desired reaction to afford allyl amine **7a** in 81 % yield. When much more reactive electrophiles, *N*-benzoylimine[25] **6b** and *N*-tosylimine[26] **6c**, were used, the corresponding allyl amines **7b** and **7c** were obtained in 97 % and 90 % yield, respectively.



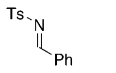
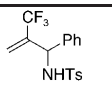
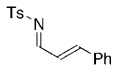
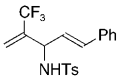
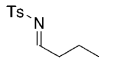
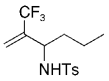
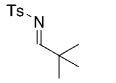
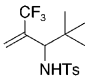
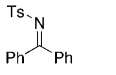
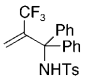
2 (2.2 equiv) **1** (3)

R = $CH_2C_6H_5$ **7a** 81 %[a]
COC_6H_5 **7b** 97 %
$SO_2C_6H_4CH_3$ **7c** 90 %

[a] Bromide **2** (2.0 equiv) and $BF_3{\cdot}OEt_2$ (1.5 equiv) were used.

We further examined the 1-(trifluoromethyl)vinylation of several other imines **6d–g**. We chose *N*-tosylimines in view of their availability, ease of handling, and the synthetic applicability of the products. The results are summarized in Table 3. All examined *N*-tosylimines **6c–g** provided the corresponding *N*-[2-(trifluoromethyl)allyl] amines **7c–g** in good

Table 3. Synthesis of *N*-[2-(trifluoromethyl)allyl] amines **7**.

Entry	*N*-Tosylimine		Product		Yield [%]
1		**6c**		**7c**	90
2		**6d**		**7d**	89
3		**6e**		**7e**	77
4		**6f**		**7f**	96
5		**6g**		**7g**	76, 91[a]

[a] Bromide **2** (3.5 equiv) and *sec*-BuLi (3.2 equiv) were used.

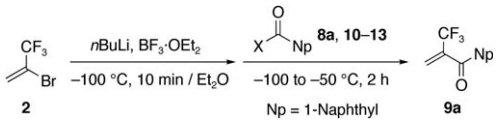
to excellent yield (Entries 1–5). Butanimine **6e** gave **7e** in good yield, even though it had acidic α-protons (Entry 3). Although 1,1-diphenylmethanimine **6g** showed modest reactivity, the yield of **7g** was improved to 91% when using greater amounts of **1**, generated from **2** (3.5 equiv) and *sec*-BuLi (3.2 equiv) (Entry 5).

Generation of 1-(Trifluoromethyl)vinyllithium 1 by the Slow Lithium-Halogen-Exchange Reaction: Synthesis of 1-(Trifluoromethyl)vinyl Ketones 9

Recently, α,β-unsaturated carbonyl compounds with an α-trifluoromethyl group have been attracting much attention, especially in the field of materials science. While many trifluoromethacrylic acid derivatives were developed as building blocks[27] and monomers,[4] reports on the corresponding ketones are rather limited.[28] Huang and co-workers reported the synthesis of 1-(trifluoromethyl)vinyl ketones by the Stille coupling of 1-(trifluoromethyl)vinyltin with acyl chlorides.[11] The disadvantages associated with this reaction were toxicity and low atom economy, attributed to the trialkyltin group. We therefore focused on the (trifluoromethyl)vinylation of amide electrophiles using the slow lithium–halogen-exchange protocol, expecting to synthesize 1-(trifluoromethyl)vinyl ketones **9**. Amides, like oxiranes,[18] are less reactive electrophiles and might react preferentially with vinyllithium **1** in the presence of *n*BuLi.

Vinyl bromide **2** (1.5 equiv) was treated with *n*BuLi (1.5 equiv) to generate **1**, which was in turn trapped with *N*,*N*-dimethyl-1-naphthylcarboxamide (**8a**) at −100 °C in the presence of $BF_3{\cdot}OEt_2$ (1.0 equiv), to afford the desired ketone **9a** but in only 7% yield. No products were obtained in the absence of Lewis acid (Table 4, Entries 1 and 2). To improve the yield of **9a**, we investigated the effect of the molar ratio of reagents. By using 3 equiv each of **2** and *n*BuLi, the yield was increased to 44%, while 2 equiv of $BF_3{\cdot}OEt_2$ gave a poor result (Entries 5 and 6). To avoid side reactions, 5 equiv of **2** was used, which improved the yield of **9a** to 55% (Entry 7). In this reaction, only a trace amount of butyl adduct 1-(1-naphthyl)pentan-1-one was observed, which indicated that vinyllithium **1** was selectively trapped with amide **8a**. When **8a** was treated with **1** generated from **2** and *sec*-BuLi at −105 °C in the presence of $BF_3{\cdot}OEt_2$, the reaction gave an inferior result (29% yield of **9a**), compared with the result with *n*BuLi (Entry 4). The rapid lithium–halogen exchange would cause competitive decomposition of vinyllithium **1**, when the reaction with electrophiles is not facile.

Table 4. (Trifluoromethyl)vinylation of amides and thioester **8a**, **10**–**13**.[a]



Entry	**2** (equiv)	*n*BuLi (equiv)	$BF_3{\cdot}OEt_2$ (equiv)	X	Electrophile	Yield [%]
1	1.5	1.5	0	NMe_2	**8a**	0
2	1.5	1.5	1.0	NMe_2	**8a**	7
3[b]	2.0	2.0	1.0	NMe_2	**8a**	39
4	2.2	2.0[c]	1.0	NMe_2	**8a**	29
5[b]	3.0	3.0	1.0	NMe_2	**8a**	44
6	3.0	3.0	2.0	NMe_2	**8a**	9
7	5.0	2.0	1.0	NMe_2	**8a**	55
8	3.0	3.0	1.0		**10**	35
9	3.0	3.0	1.0	NMePh	**11**	5
10	3.0	3.0	1.0	NMe(OMe)	**12**	23
11	3.0	3.0	1.0		**13**	–

[a] Reagents were added in the following order: **2**, $BF_3{\cdot}OEt_2$, *n*BuLi, and **8a**. [b] Amide **8a** was recovered in 42% (Entry 3) and in 23% (Entry 5). [c] *sec*-BuLi was used instead of *n*BuLi. Reagents were added in the following order: **2**, *sec*-BuLi, **8a**, and $BF_3{\cdot}OEt_2$.

Several other amides and thioesters **10**–**13** were examined, in vain, as shown in Table 4.[29] *N*-Acylmorpholine **10** resulted in a nonselective reaction of vinyllithium **1** and *n*BuLi (Entry 8). *N*-Methy-*N*-phenylamide **11** afforded only 5% yield of ketone **9a**. This is probably arising from its bulkiness, which prevents an attack of the lithium species (Entry 9). The Weinreb amide **12** afforded **9a** in 23% yield, together with its conjugate addition product of *N*-methoxymethanamine (Entry 10). The reaction of 2-pyridylthioester **13** gave a complex mixture of trifluoromethyl compounds (Entry 11).

We examined other substrates **8** to synthesize 1-(trifluoromethyl)vinyl ketones **9** under the reaction conditions described above (Table 4, Entry 7). The results are summarized in Table 5. The reactions of **8a**–**d** bearing aryl groups afforded the corresponding ketenes **9** in moderate to good

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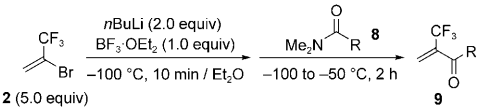
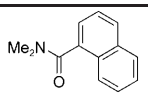
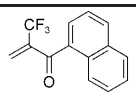
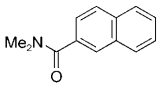
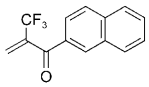
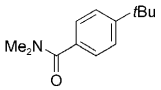
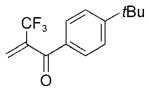
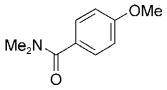
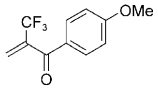
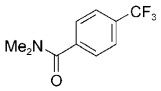
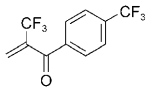
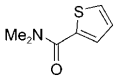
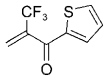
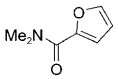
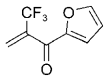
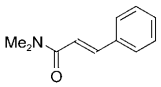
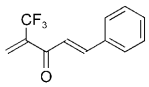
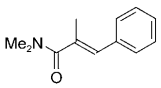
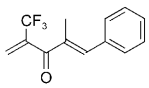
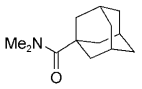
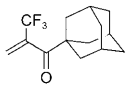
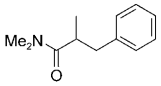
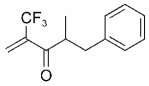
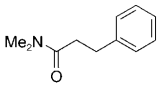
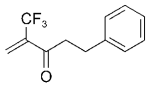
Table 5. Synthesis of 1-(trifluoromethyl)vinyl ketones **9**.



Entry	Dimethylamide		Product	Yield [%]
1		**8a**		**9a**, 55
2		**8b**		**9b**, 61
3		**8c**		**9c**, 65
4		**8d**		**9d**, 57
5		**8e**		**9e**, 24[a]
6		**8f**		**9f**, 65
7		**8g**		**9g**, 51[a]
8		**8h**		**9h**, 38
9		**8i**		**9i**, 66
10[a,b]		**8j**		**9j**, 73
11[c]		**8k**		**9k**, 78
12[c]		**8l**		**9l**, 42[a]

[a] ^{19}F NMR yield relative to internal $CF_3C_6H_5$ standard. [b] Vinyl bromide **2** (2.0 equiv) was used. [c] $BF_3{\cdot}OEt_2$ (1.3 equiv) was used.

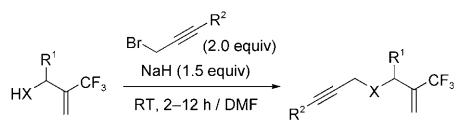
yield. 4-(Trifluoromethyl)benzamide **8e** resulted in 24% yield of **9e**. This is probably arising from the high reactivity of the product **9e**, caused by the strong electron-withdrawing CF_3 group. Ketones **9f** and **9g** bearing a heteroaryl group, such as the 2-thienyl and 2-furyl groups, were obtained in 65% and 51% yield, respectively. (Trifluoromethyl)vinylation of cinnamamide **8h** afforded **9h** in 38% yield. The reason for this is the susceptibility of the styryl group to nucleophilic attack. Introduction of a methyl group at the α-position suppressed the attack on the product **9i**, leading to an improved yield of 66%. Among the alkyl ketone products, adamantyl ketone **9j** and 1-phenylpropan-2-yl ketone **9k** were obtained in 73% and 78% yield, respectively, and amide **8l** bearing a primary alkyl group gave vinyl alkyl ketone **9l** in 42% yield. Highly electrophilic 1-(trifluoromethyl)vinylketones **9** were efficiently prepared by a nucleophilic addition reaction of vinyllithium species, without affecting the products.

2-(Trifluoromethyl)allyl Alcohols, *N*-[2-(Trifluoromethyl)allyl] Amides, and 1-(Trifluoromethyl)vinyl Ketones as Trifluoromethyl-group-containing Synthones

The (trifluoromethyl)vinylated compounds obtained above, 2-(trifluoromethyl)allyl alcohols **5**, *N*-[2-(trifluoromethyl)allyl] amides **7**, and 1-(trifluoromethyl)vinyl ketones **9**, were expected to serve as versatile synthones for creating a variety of valuable trifluoromethyl-substituted compounds because of their reactive vinyl groups. To demonstrate the viability of this building-block strategy, we converted the products to trifluoromethylated cyclopentenone derivatives by an intramolecular Pauson–Khand reaction or the Nazarov cyclization.

Synthesis of Bicyclic Cyclopentenones with an Angular Trifluoromethyl Group by an Intramolecular Pauson–Khand Reaction

In steroid and alkaloid syntheses, much effort has been devoted to the construction of fused-ring systems involving an angular methyl group,[30] as exemplified by dendrobine,[31] the framework of which is formed by an intramolecular Pauson–Khand reaction.[32] Whereas the introduction of an angular trifluoromethyl group is one of the most promising approaches for the analog synthesis of steroids and alkaloids, it remains a challenging task.[3,33] Furthermore, there is only one example of the Pauson–Khand reaction of enynes bearing a trifluoromethyl group on the vinylic carbons, and it gave an unsuccessful result.[34] These facts prompted us to investigate the Pauson–Khand reaction of 1,6-enynes bearing a trifluoromethyl group. The enyne substrates *N*-allyl-*N*-propargylamides **14a–c** and allyl propargyl ether **14d** were prepared from 2-(trifluoromethyl)allyl amides **7c**,**e** and alcohol **5a**, respectively, simply by propargylation [Eq. (4)].

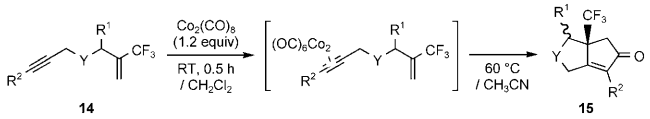


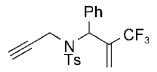
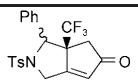
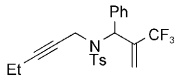
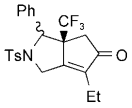
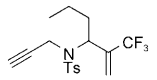
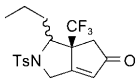
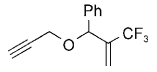
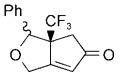
(4)

X = NTs, R^1 = Ph	**7c**	X = NTs, R^1 = Ph, R^2 = H	**14a** 92%
X = NTs, R^1 = propyl	**7e**	X = NTs, R^1 = Ph, R^2 = Et	**14b** 90%
X = O, R^1 = Ph	**5a**	X = NTs, R^1 = propyl, R^2 = H	**14c** 84%
		X = O, R^1 = Ph, R^2 = H	**14d** 81%

Enyne **14a** was treated with dicobalt octacarbonyl to afford the cobalt alkyne complex, which was then heated in CH_3CN. The expected intramolecular Pauson–Khand reaction smoothly proceeded to afford the desired angularly trifluoromethylated cyclopentenone **15a** in high yield (81%) and with high diastereoselectivity (*anti*/*syn* = 94:6) (Table 6,

Table 6. Synthesis of angularly trifluoromethylated cyclopentenones **15**.

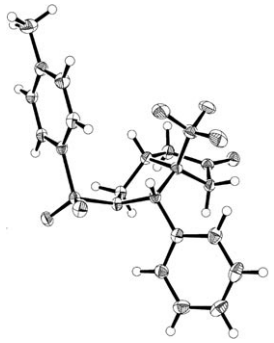


Entry	1,6-Enyne		*t* [h]	Product		Yield [%]	*anti*/*syn*[a]
1		**14a**	3		**15a**	81	94:6[b]
2		**14b**	2		**15b**	85	83:17
3		**14c**	3		**15c**	71	86:14
4[c]		**14d**	5		**15d**	53	64:36

[a] Isomer ratio was determined by ^{19}F NMR. [b] Configuration of the major isomer was determined to be *anti*. See text. [c] Substrate **14d** was treated with $Co_2(CO)_8$ in toluene at room temperature for 1 h, and then heated at reflux.

Entry 1). The cyclization of internal alkyne substrate **14b** and substrate **14c** with an alkyl group at the allylic position yielded pyrrolidine ring-fused cyclopentenones **15b** and **15c** in 85% and 71% yield, respectively (Entries 2 and 3). Although enyne **14d** bearing an ether linkage instead of a sulfonamide linkage gave a poorer result under the above conditions, refluxing the cobalt complex in toluene improved the yield of the desired furan ring-fused cyclopentenone **15d** to 53%.

The configuration of the major isomer of **15a** was determined to be *anti* by X-ray crystallography of **16**, which is derived from **15a** by hydrogenation of the double bond (Figure 1).[35] The relative configurations of **15b–d** were assigned by analogy with **15a**, and supported by comparing the ^1H and ^{19}F NMR data of each isomer.



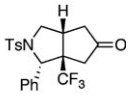


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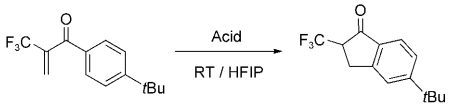
Figure 1. X-ray crystal structure of cyclopentanone **16**.

Synthesis of 2-Trifluoromethylindanones 17 by the Nazarov Cyclization

As an application of the aryl (trifluoromethyl)vinyl ketones **9** obtained above, we attempted the Nazarov cyclization,[8,36] which would provide 1-indanones bearing a trifluoromethyl group at the α-position of the carbonyl group. α-Trifluoromethylation of ketones has been accomplished by radical[37] and electrophilic[38] trifluoromethylation of enolate derivatives. As these methods are often inefficient, a method for the preparation of α-trifluoromethylated cyclopentanones would be valuable.

A solution of ketone **9c** was treated with several Lewis and Brønsted acids in 1,1,1,3,3,3-hexafluoropropan-2-ol (HFIP) as a solvent at room temperature.[8,39] Whereas Lewis acids, such as ferric chloride and trimethylsilyl trifluoromethanesulfonate (TMSOTf), hardly promoted the reaction and gave only a trace amount of the desired 2-trifluoromethylindan-1-one **17c** (Table 7, Entries 1 and 2), 10 equiv of trifluoromethanesulfonic acid (TfOH) successfully afforded **17c** in 87% yield (Entry 4).[40]

Table 7. The Nazarov cyclization of 1-(trilfuoromethyl)vinyl ketone **9c**.



Entry	Acid (equiv)	*t* [h]	Yield [%]
1	$FeCl_3$ (3.0)	20	3
2	TMSOTf (3.0)	20	trace
3	TfOH (3.0)	20	18
4	TfOH (10)	3 days	87

The synthesis of several other substituted indanones was achieved by the TfOH-mediated Nazarov cyclization (Table 8). The cyclization of naphthyl ketones **9a,b** proceeded considerably faster than that of phenyl ketone **9c** (Entries 1,2 vs 3). The cyclization of naphthyl ketones proceeded in a regioselective manner. Treatment of 1-naphthyl ketone **9a** with TfOH exclusively gave the Nazarov product **17a** in 73% yield without the formation of dihydrophenalenone **18**, which suggests that the Nazarov cyclization is preferred to a Friedel–Crafts-type cyclization. When 2-naphthyl isomer **9b** was subjected to the reaction conditions, indanone **17b** was regioselectively obtained in quantitative yield. Thiophene-fused cyclopentenone was also synthesized in moderate yield (Entry 4). Divinylketone **9h**, without substituent at the α position, underwent the ring formation by the use of TfOH, whereas the cyclization of methylated **9i** proceeded smoothly with TMSOTf (Entries 5–7).[8a]

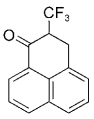


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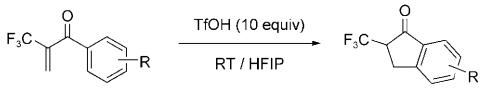
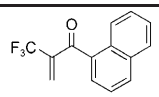
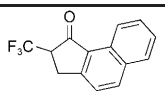
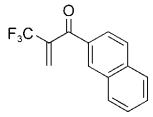
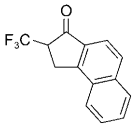
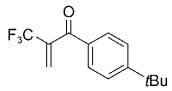
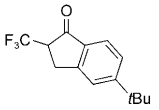
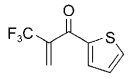
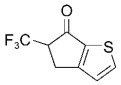
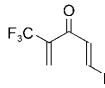
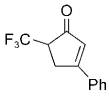
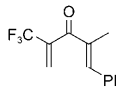
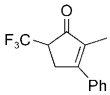
Table 8. Synthesis of trifluoromethylated indanones **17**.



9 **17**

Entry	**9**		*t*	Product		Yield [%]
1		**9a**	1 h		**17a**	73[a]
2		**9b**	1 h		**17b**	Quant.
3		**9c**	3 days		**17c**	87
4		**9f**	3 days		**17f**	30[b]
5		**9h**	3 days		**17h**	46
6		**9h**	3 days		**17h**	–[c]
7		**9i**	10 min		**17i**	86[c]

[a] Dihydrophenalenone **18** was not observed. [b] (Trifluoromethyl)vinyl ketone **9f** was recovered in 21% yield. [c] TMSOTf (1 equiv) was used in place of TfOH (CH_2Cl_2/HFIP = 1:1, RT).

Conclusions

We develop two protocols for the synthesis of 1-(trifluoromethyl)vinyl compounds by rapid and slow lithium–halogen-exchange processes that generate thermally unstable 1-(trifluoromethyl)vinyllithium (**1**). The rapid lithium–halogen-exchange reaction of 2-bromo-3,3,3-trifluoroprop-1-ene (**2**) takes place by using *sec*-BuLi at −105 °C to suppress the decomposition of **1**. The reaction with more reactive electrophiles, aldehydes and *N*-tosylimines, can now proceed to afford 2-(trifluoromethyl)allyl alcohols **5** and amines **7** in good to excellent yield. The slow lithium–halogen exchange of **2** with *n*BuLi gives a mixture of vinyllithium **1** and *n*BuLi, in which **1** is preferentially trapped by *N*,*N*-dimethylamide to yield 1-(trifluoromethyl)vinyl ketones **9** efficiently. These two (trifluoromethyl)vinylation methods are considered to be complementary, which broadens their applicability to various electrophiles.

Furthermore, we succeed in the construction of pyrrolidine ring-fused or furan ring-fused cyclopentenones **15** bearing an angular trifluoromethyl group and 2-trifluoromethyl-substituted indanones **17** by: 1) the cobalt octacarbonyl-mediated Pauson–Khand reaction of 1,6-enynes **14**, derived from 2-(trifluoromethyl)allyl amides **7** or alcohols **5**, and 2) the Nazarov cyclization of aryl 1-(trifluoromethyl)vinyl ketones **9**, respectively. These complex trifluoromethyl-containing structures are constructed in a couple of steps from 2-bromo-3,3,3-trifluoroprop-1-ene (**2**), which is a versatile fluorinated C3 building block.

Experimental Section

General

IR spectra were recorded by ATR (attenuated total reflectance) method. NMR spectra were recorded in $CDCl_3$ at 500 MHz (^{1}H NMR), 126 MHz (^{13}C NMR), and 470 MHz (^{19}F NMR). Chemical shift values were given in ppm relative to internal Me_4Si (for ^{1}H NMR: $\delta = 0.00$), $CDCl_3$ (for ^{13}C NMR: $\delta = 77.0$), and C_6F_6 (for ^{19}F NMR: $\delta = 0.0$). Column chromatography and preparative thin-layer chromatography (PTLC) were performed on silica gel. Diethylether (Et_2O), *N*,*N*-dimethylformamide (DMF), and CH_2Cl_2 were dried by passing over a column of activated alumina (A-2, Purity) followed by a column of Q-5 scavenger (Engelhard). 1,1,1,3,3,3-Hexafluoropropan-2-ol (HFIP) was distilled from molecular sieves 4 Å, and stored over molecular sieves 4 Å. Acetonitrile (CH_3CN) was distilled from P_2O_5 and then from CaH_2, and stored over molecular sieves 3 Å. 2-Bromo-3,3,3-trifluoroprop-1-ene (**2**) was distilled prior to use. $BF_3{\cdot}OEt_2$ was distilled from CaH_2 prior to use. All reactions were conducted under argon. *n*BuLi (hexane solution), *sec*-BuLi (cyclohexane solution), CF_3SO_3H, NaH (55% dispersion in mineral oil), propargyl bromide, $Co_2(CO)_8$, and palladium on activated charcoal (5% Pd/C) were purchased and used without further purification. *N*,*N*-Dimethylcarboxamides were prepared by the reaction of the corresponding acyl chlorides with dimethylamine (50% solution in water) in CH_2Cl_2, and purified by distillation with bulb-to-bulb apparatus under reduced pressure. *N*-benzoylimine **6b**[25] and *N*-(4-*m*ethylbenzenesulfonyl)imine **6c**–**g**[26] were prepared according to the literatures.

Syntheses

2-(Trifluoromethyl)allyl alcohols (5): To a solution of 2-bromo-3,3,3-trifluoroprop-1-ene (**2**, 2.0 mmol) in Et_2O (10 mL) was added a solution of *sec*-BuLi (1.07 M in cyclohexane, 2.0 mmol) in Et_2O (2 mL, pre-chilled with a −78 °C bath) at −105 °C (internal temperature) over 5 min. After stirring for an additional 5 min, a solution of an aldehyde (1.0 mmol) in Et_2O (2 mL) was transferred by using a cannula into the solution of the generated vinyllithium reagent. The reaction mixture was allowed to warm up to −50 °C over 2 h. After the reaction was quenched with phosphate buffer (pH 7, 10 mL), organic materials were extracted with Et_2O. The combined extracts were washed with brine, and dried over $MgSO_4$. After removal of the solvent under reduced pressure, the residue was purified by column chromatography (hexane-EtOAc, 10:1) to give **5**.

1-Phenyl-2-trifluoromethylprop-2-en-1-ol (5a): A colorless liquid (73%). IR (neat): $\tilde{\nu} = 3357, 3066, 3035, 2922, 2850, 1321, 1167, 1115, 1022, 957, 698\ cm^{-1}$; ^{1}H NMR (500 MHz, $CDCl_3$, 25 °C, TMS): $\delta = 2.20$–2.22 (m, 1H; OH), 5.43 (d, $^3J_{(H,H)} = 2.9$ Hz, 1H; CH), 5.80 (q, $^4J_{(H,F)} = 1.4$ Hz, 1H; =CH_2), 5.93 (q, $^4J_{(H,F)} = 0.7$ Hz, 1H; =CH_2), 7.33–7.39 ppm (m, 5H; ArH); ^{13}C NMR (126 MHz, $CDCl_3$, 25 °C): $\delta = 71.3$, 119.8 (q, $^3J_{(C,F)} = 5$ Hz), 123.1 (q, $^1J_{(C,F)} = 275$ Hz), 126.8, 128.6, 128.7, 140.2, 140.8 ppm (q, $^2J_{(C,F)} = 28$ Hz); ^{19}F NMR (470 MHz, $CDCl_3$, 25 °C, C_6F_6): $\delta = 96.5$ ppm (br s); HRMS (FAB): *m*/*z* (%) calcd for $C_{10}H_{10}F_3O$: 203.0684 $[M+H]^+$; found: 203.0687.

[2-(Trifluoromethyl)allyl] amines (7b–g): To a solution of **2** (0.88 mmol) in Et_2O (8 mL), was added a solution of *sec*-BuLi (1.07 M in cyclohexane, 0.80 mmol) in Et_2O (2 mL) at −105 °C. After stirring for 10 min, a solution of *N*-benzoylimine **6b**[25] or *N*-(4-*m*ethylbenzenesulfonyl)imine **6c**–**g**[26] (0.40 mmol) in Et_2O (5–20 mL) was added dropwise. The reaction mixture was allowed to warm up to −50 °C over 2 h. The reaction was quenched with phosphate buffer (pH 7, 10 mL), and organic materials were extracted with EtOAc. The combined extracts were washed with brine, and dried over $MgSO_4$. After removal of the solvent under reduced pressure, the residue was purified by column chromatography to give **7b**–**g**.

4-Methyl-*N*-[1-phenyl-2-(trifluoromethyl)prop-2-en-1-yl]benzenesulfonamide (7c): Colorless crystals (90%); m.p.: 111–114 °C; IR (neat): $\tilde{\nu} =$

3261, 3064, 2929, 1435, 1323, 1159, 1115, 1090, 968, 914, 771, 660 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$, 25 °C, TMS): δ = 2.41 (s, 3H; CH_3), 5.12 (d, $^2J_{(H,H)}$ = 7.2 Hz, 1H; =CH_2), 5.43 (d, ^2J(H,H) = 7.2 Hz, 1H; =CH_2), 5.73 (s, 1H), 5.88 (s, 1H), 7.04 (d, $^3J_{(H,H)}$ = 6.5 Hz, 2H; ArH), 7.18–7.25 (m, 5H; ArH), 7.63 ppm (d, $^3J_{(H,H)}$ = 8.2 Hz, 2H; ArH); ^{13}C NMR (126 MHz, $CDCl_3$, 25 °C): δ = 21.5, 56.5, 121.6 (q, $^3J_{(C,F)}$ = 5 Hz), 122.8 (q, $^1J_{(C,F)}$ = 275 Hz), 127.1, 127.2, 128.4, 128.8, 129.5, 136.8, 137.2, 138.0 (q, $^2J_{(C,F)}$ = 29 Hz), 143.7 ppm; ^{19}F NMR (470 MHz, $CDCl_3$, 25 °C, C_6F_6): δ = 96.5 ppm (br s); elemental analysis: calcd (%) for $C_{17}H_{16}F_3NO_2S$ (341.4): C 57.46, H 4.54, N 3.94; found: C 57.72, H 4.73, N 3.74.

1-(Trifluoromethyl)vinylketones (9): To a solution of $BF_3{\cdot}OEt_2$ (1.0 mmol) and **2** (5.0 mmol) in Et_2O (10 mL) was added a solution of *n*BuLi (1.53 M in hexane, 2.0 mmol) in Et_2O (3 mL) at −100 °C. After stirring for 10 min, a solution of *N*,*N*-dimethylcarboxamide **8** (1.0 mmol) in Et_2O (5 mL) was added. The reaction mixture was allowed to warm up to −50 °C over 2 h. Phosphate buffer (pH 7, 10 mL) was added to quench the reaction, and organic materials were extracted with EtOAc. The combined extracts were washed with brine, and dried over $MgSO_4$. After removal of the solvent under reduced pressure, the residue was purified by column chromatography (hexane-EtOAc, 10:1) to give **9**.

1-(1-Naphthyl)-2-(trifluoromethyl)prop-2-en-1-one (9a): A pale brown liquid (55%). IR (neat): $\tilde{\nu}$ = 3059, 1668, 1508, 1340, 1132, 1055, 793 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$, 25 °C, TMS): δ = 6.14 (q, $^4J_{(H,F)}$ = 1.6 Hz, 1H), 6.67 (s, 1H; =CH_2), 7.50 (dd, $^3J_{(H,H)}$ = 8.2, 7.2 Hz, 1H; ArH), 7.56 (dd, $^3J_{(H,H)}$ = 7.4, 7.4 Hz, 1H; ArH), 7.59 (dd, $^3J_{(H,H)}$ = 7.4, 7.4 Hz, 1H; ArH), 7.62 (d, $^3J_{(H,H)}$ = 7.2 Hz, 1H; ArH), 7.91 (d, $^3J_{(H,H)}$ = 7.4 Hz, 1H; ArH), 8.02 (d, $^3J_{(H,H)}$ = 8.2 Hz, 1H; ArH), 8.18 ppm (d, $^3J_{(H,H)}$ = 7.4 Hz, 1H; ArH); ^{13}C NMR (126 MHz, $CDCl_3$, 25 °C): δ = 121.8 (q, $^1J_{(C,F)}$ = 276 Hz), 124.1, 125.1, 126.8, 127.9, 128.4, 128.5, 130.5, 132.6, 133.7 (q, $^3J_{(C,F)}$ = 5 Hz), 133.7, 134.2, 139.4 (q, $^2J_{(C,F)}$ = 29 Hz), 192.7 ppm; ^{19}F NMR (470 MHz, $CDCl_3$, 25 °C, C_6F_6): δ = 96.9 ppm (br s); HRMS (FAB): *m*/*z* (%) calcd for $C_{14}H_{10}F_3O$: 251.0684 $[M+H]^+$; found: 251.0691.

The Pauson–Khand reaction of *N*-propargyl-*N*-[2-(trifluoromethyl)allyl] amines (14a-c): To a solution of **14a–c** (0.339 mmol) in CH_2Cl_2 (10 mL) was added $Co_2(CO)_8$ (0.41 mmol), and the solution was stirred for 30 min at room temperature. The solvent was removed under reduced pressure, and then acetonitrile (15 mL) was added. After heating the solution at 60 °C for 2–3 h, the solvent was removed under reduced pressure. The residue was purified by column chromatography (hexane/EtOAc, 3:1) to give **15a–c**.

2-(4-Methylbenzenesulfonyl)-3-phenyl-3a-(trifluoromethyl)-2,3,3a,4-tetrahydrocyclopenta[*c*]pyrrol-5(1*H*)-one (15a): A pale yellow liquid (81%; *anti*/*syn* = 94:6). **Major product**: *anti* isomer: IR (neat): $\tilde{\nu}$ = 3032, 2943, 2868, 1730, 1348, 1147, 1059, 912, 802, 667, 563, 542 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$, 25 °C, TMS): δ = 1.58 (d, $^2J_{(H,H)}$ = 18.0 Hz, 1H; CH_2), 2.37 (d, $^2J_{(H,H)}$ = 18.0 Hz, 1H; CH_2), 2.40 (s, 3H; CH_3), 4.41 (d, $^2J_{(H,H)}$ = 15.0 Hz, 1H; CH_2), 4.58 (d, $^2J_{(H,H)}$ = 15.0 Hz, 1H; CH_2), 5.34 (s, 1H; CH), 6.32 (s, 1H; =CH), 6.75–6.82 (m, 1H; ArH), 7.11–7.23 (m, 2H; ArH), 7.23 (d, $^3J_{(H,H)}$ = 8.1 Hz, 2H; ArH), 7.29 (t, $^3J_{(H,H)}$ = 7.4 Hz, 1H; ArH), 7.34–7.41 (m, 1H; ArH), 7.57 ppm (d, $^3J_{(H,H)}$ = 8.1 Hz, 2H; ArH); ^{13}C NMR (126 MHz, $CDCl_3$, 25 °C): δ = 21.5, 41.4, 47.8, 62.2 (q, $^2J_{(C,F)}$ = 26 Hz), 64.0, 125.1 (br s), 125.9 (q, $^1J_{(C,F)}$ = 284 Hz), 127.2, 127.5 (br s), 128.8, 129.0 (br s), 129.2 (br s), 129.6, 131.5, 135.0, 136.8, 143.9, 168.3, 203.1 ppm; ^{19}F NMR (470 MHz, $CDCl_3$, 25 °C, C_6F_6): δ = 87.6 ppm (br s); HRMS (FAB): *m*/*z* (%) calcd for $C_{21}H_{19}F_3NO_3S$: 422.1038 $[M+H]^+$; found: 422.1050. **Minor product**: *syn* isomer: IR (neat): $\tilde{\nu}$ = 3066, 3033, 2922, 2852, 1732, 1354, 1165, 1092, 1032 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$, 25 °C, TMS): δ = 2.43 (s, 3H; CH_3), 2.47 (d, $^2J_{(H,H)}$ = 17.8 Hz, 1H; CH_2), 2.72 (d, $^2J_{(H,H)}$ = 17.8 Hz, 1H; CH_2), 4.45 (s, 1H; CH), 4.57 (d, $^2J_{(H,H)}$ = 16.0 Hz, 1H; CH_2), 4.69 (d, $^2J_{(H,H)}$ = 16.0 Hz, 1H; CH_2), 6.13 (s, 1H; =CH), 7.07–7.18 (m, 1H; ArH), 7.27 (d, $^3J_{(H,H)}$ = 8.3 Hz, 2H; ArH), 7.28–7.35 (m, 3H; ArH), 7.54 (d, $^3J_{(H,H)}$ = 8.3 Hz, 2H; ArH), 7.54–7.64 ppm (m, 1H; ArH); ^{13}C NMR (126 MHz, $CDCl_3$, 25 °C): δ = 21.6, 43.5, 49.3, 62.4 (q, $^2J_{(C,F)}$ = 26 Hz), 71.0, 124.9 (q, $^1J_{(C,F)}$ = 285 Hz), 127.9, 128.1 (br s), 128.1 (br s), 128.8, 129.8, 130.0, 133.3, 133.7, 144.6, 168.9, 202.9 ppm; ^{19}F NMR (470 MHz, $CDCl_3$, 25 °C, C_6F_6): δ = 94.0 ppm (br s); HRMS (FAB): *m*/*z* (%) calcd for $C_{21}H_{19}F_3NO_3S$: 422.1038 $[M+H]^+$; found: 422.1010.

The Nazarov cyclization of 9: To a solution of **9** (0.29 mmol) in HFIP (1 mL) was added TfOH (3 mmol) at room temperature. After stirring for 1 h, the reaction was quenched with phosphate buffer (pH 7, 5 mL). Organic materials were extracted with EtOAc. The combined extracts were washed with brine, and dried over $MgSO_4$. After removal of the solvent under reduced pressure, the residue was purified by column chromatography (hexane/EtOAc, 10:1) to give **17**.

2-(Trifluoromethyl)-2,3-dihydro-1*H*-cyclopenta[*a*]naphthalen-1-one (17a): m.p.: 102–104 °C; IR (neat): $\tilde{\nu}$ = 3059, 2945, 1705, 1574, 1514, 1439, 1344, 1250, 1184, 1153, 1088, 955 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$, 25 °C, TMS): δ = 3.34–3.43 (m, 1H), 3.48–3.57 (m, 2H), 7.53 (d, $^3J_{(H,H)}$ = 8.4 Hz, 1H; ArH), 7.60 (dd, $^3J_{(H,H)}$ = 7.8, 7.8 Hz, 1H; ArH), 7.71 (dd, $^3J_{(H,H)}$ = 7.8, 7.8 Hz, 1H; ArH), 7.91 (d, $^3J_{(H,H)}$ = 7.8 Hz, 1H; ArH), 8.10 (d, $^3J_{(H,H)}$ = 8.4 Hz, 1H; ArH), 9.09 ppm (d, $^3J_{(H,H)}$ = 7.8 Hz, 1H; ArH); ^{13}C NMR (126 MHz, $CDCl_3$, 25 °C): δ = 27.9 (q, $^3J_{(C,F)}$ = 2 Hz), 50.1 (q, $^2J_{(C,F)}$ = 27 Hz), 123.3, 123.9, 125.0 (q, $^1J_{(C,F)}$ = 279 Hz), 127.2, 128.3, 129.3, 129.6, 130.1, 132.8, 137.1, 155.7, 197.1 ppm; ^{19}F NMR (470 MHz, $CDCl_3$, 25 °C, C_6F_6): δ = 93.9 ppm (d, ^3J(F,H) = 9 Hz); elemental analysis: calcd (%) for $C_{14}H_9F_3O$ (250.2): C 67.20, H 3.63; found: C 67.18, H 3.83.

Acknowledgements

We thank Dr. N. Kano (the University of Tokyo) for the X-ray crystal structure analysis. We are grateful to the Ogasawara Foundation for the Promotion of Science and Engineering and Central Glass Co., Ltd. for financial support, and to Tosoh F-Tech, Inc. for a generous gift of 2-bromo-3,3,3-trifluoroprop-1-ene.

[1] a) P. Kirsch, *Modern Fluoroorganic Chemistry: Synthesis, Reactivity, Applications*, Wiley-VCH, Weinheim, **2004**; b) T. Hiyama, *Organofluorine Compounds: Chemistry and Applications*, Springer, Berlin, **2000**; c) *Organofluorine Chemistry, Principles and Commercial Applications* (Eds.: R. E. Banks, B. E. Smart, J. C. Tatlow), Plenum, New York, **1994**; d) J. T. Welch, S. Eswarakrishnan, *Fluorine in Bioorganic Chemistry*, Wiley, New York, **1991**.

[2] a) K. Uneyama, *Organofluorine Chemistry*, Blackwell, Oxford, **2006**; b) M. Shimizu, T. Hiyama, *Angew. Chem.* **2005**, *117*, 218–234; *Angew. Chem. Int. Ed.* **2005**, *44*, 214–231; c) J. M. Percy, *Top. Curr. Chem.* **1997**, *193*, 131–195.

[3] For a review, see: P. Lin, J. Jiang, *Tetrahedron* **2000**, *56*, 3635–3671.

[4] For examples, see: a) H. Ito, *Adv. Polym. Sci.* **2005**, *172*, 37–245; b) H. Ito, H. D. Truong, M. Okazaki, R. A. DiPietro, *J. Photopolym. Sci. Technol.* **2003**, *16*, 523–536.

[5] For the S_N2' reaction of 1-(trifluoromethyl)vinyl compounds [CH_2=$C(Y)CF_3$], see [Y = CO_2R, CO_2H]: a) T. Kitazume, T. Ohnogi, H. Miyauchi, T. Yamazaki, *J. Org. Chem.* **1989**, *54*, 5630–5632; b) T. Fuchikami, Y. Shibata, Y. Suzuki, *Tetrahedron Lett.* **1986**, *27*, 3173–3176; [Y = SPh, SePh]: c) A. E. Feiring, *J. Org. Chem.* **1980**, *45*, 1962–1964; [Y = Ph]: d) J.-P. Bégué, D. Bonnet-Delpon, M. H. Rock, *J. Chem. Soc. Perkin Trans. 1* **1996**, 1409–1413. [Y = H, Me] e) D. A. Kendrick, M. Kolb, *J. Fluorine Chem.* **1989**, *45*, 265–272; f) T. Hiyama, M. Obayashi, M. Sawahata, *Tetrahedron Lett.* **1983**, *24*, 4113–4116; g) D. E. Bergstrom, M. W. Ng, J. J. Wong, *J. Org. Chem.* **1983**, *48*, 1902–1903.

[6] a) J. Ichikawa, M. Yokota, T. Kudo, S. Umezaki, *Angew. Chem.* **2008**, *120*, 4948–4951; *Angew. Chem. Int. Ed.* **2008**, *47*, 4870–4873; b) J. Ichikawa, H. Fukui, Y. Ishibashi, *J. Org. Chem.* **2003**, *68*, 7800–7805.

[7] a) J. Ichikawa, M. Ikeda, M. Hattori, *Heterocycles* **2009**, *77*, 1285–1296; b) J. Ichikawa, Y. Iwai, R. Nadano, T. Mori, M. Ikeda, *Chem. Asian J.* **2008**, *3*, 393–406; c) R. Nadano, Y. Iwai, T. Mori, J. Ichikawa, *J. Org. Chem.* **2006**, *71*, 8748–8754; d) T. Mori, Y. Iwai, J. Ichikawa, *Chem. Lett.* **2005**, *34*, 778–779; e) T. Mori, J. Ichikawa, *Chem. Lett.* **2004**, *33*, 1206–1207.

[8] a) J. Ichikawa, M. Fujiwara, T. Okauchi, T. Minami, *Synlett* **1998**, 927–929. See also: J. Ichikawa, S. Miyazaki, M. Fujiwara, T. Minami, *J. Org. Chem.* **1995**, *60*, 2320–2321.

[9] a) H. Lebel, M. Davi, G. T. Stoklosa, *J. Org. Chem.* **2008**, *73*, 6828–6830; b) H. Lebel, V. Paquet, *Org. Lett.* **2002**, *4*, 1671–1674 and references therein; c) V. De Matteis, F. L. van Delft, J. Tiebes, F. P. J. T. Rutjes, *Synlett* **2008**, 351–354; d) V. De Matteis, O. Dufay, D. C. J. Waalboer, F. L. van Delft, J. Tiebes, F. P. J. T. Rutjes, *Eur. J. Org. Chem.* **2007**, 2667–2675; e) V. De Matteis, F. L. van Delft, H. Jakobi, S. Lindell, J. Tiebes, F. P. J. T. Rutjes, *J. Org. Chem.* **2006**, *71*, 7527–7532; f) T. Yamazaki, N. Ishikawa, *Chem. Lett.* **1984**, *13*, 521–524.

[10] a) B. Jiang, Y. Xu, *J. Org. Chem.* **1991**, *56*, 7336–7340; b) B. Jiang, Y. Xu, *Tetrahedron Lett.* **1992**, *33*, 511–514.

[11] Y. Xu, F. Jin, W. Huang, *J. Org. Chem.* **1994**, *59*, 2638–2641.

[12] B. Jiang, Q. Wang, C. Yang, M. Xu, *Tetrahedron Lett.* **2001**, *42*, 4083–4085.

[13] a) R. Pan, X. Liu, M. Deng, *J. Fluorine Chem.* **1999**, *95*, 167–170; b) C.-M. Hu, F. Hong, Y.-Y. Xu, *J. Fluorine Chem.* **1993**, *64*, 1–4; c) C.-M. Hu, F. Hong, Y. Xu, *J. Fluorine Chem.* **1993**, *63*, 1–3; d) T. Fuchikami, A. Yamanouchi, I. Ojima, *Synthesis* **1984**, 766–767.

[14] a) S. Peng, F.-L. Qing, *J. Chem. Soc. Perkin Trans. 1* **1999**, 3345–3348; b) S. Peng, F.-L. Qing, Y. Guo, *Synlett* **1998**, 859–860; c) F. Hong, X. Tang, C. Hu, *J. Chem. Soc. Chem. Commun.* **1994**, 289–290.

[15] a) Q. Chen, F.-L. Qing, *Tetrahedron* **2007**, *63*, 11965–11972; b) K. Iseki, Y. Kuroki, T. Nagai, Y. Kobayashi, *J. Fluorine Chem.* **1994**, *69*, 5–6; c) F. G. Drakesmith, O. J. Stewart, P. Tarrant, *J. Org. Chem.* **1968**, *33*, 280–285.

[16] For recent reports on the synthesis of 1-trifluoromethyl-1-alkenes [2-(trifluoromethyl)vinyl compounds], see: a) I. Nowak, M. J. Robins, *J. Org. Chem.* **2007**, *72*, 2678–2681; b) T. Konno, J. Chae, T. Tanaka, T. Ishihara, H. Yamanaka, *J. Fluorine Chem.* **2006**, *127*, 36–43; c) T. Hanamoto, N. Morita, K. Shindo, *Eur. J. Org. Chem.* **2003**, 4279–4285; d) T. Kobayashi, T. Eda, O. Tamura, H. Ishibashi, *J. Org. Chem.* **2002**, *67*, 3156–3159; e) X. Liu, M. Shimizu, T. Hiyama, *Angew. Chem.* **2004**, *116*, 897–900; *Angew. Chem. Int. Ed.* **2004**, *43*, 879–882; f) T. Yamazaki, T. Kawasaki-Takasuka, A. Furuta, S. Sakamoto, *Tetrahedron* **2009**, *65*, 5945–5948.

[17] W. R. Dolbier, Jr., C. R. Burkholder, C. A. Piedrahita, *J. Fluorine Chem.* **1982**, *20*, 637–647.

[18] a) R. Nadano, J. Ichikawa, *Synthesis* **2006**, 128–132; b) R. Nadano, J. Ichikawa, *Chem. Lett.* **2007**, *36*, 22–23.

[19] a) M. Yamaguchi, I. Hirao, *Tetrahedron Lett.* **1983**, *24*, 391–394; b) M. Yamaguchi, Y. Nobayashi, I. Hirao, *Tetrahedron Lett.* **1983**, *24*, 5121–5122; c) M. J. Eis, J. E. Wrobel, B. Ganem, *J. Am. Chem. Soc.* **1984**, *106*, 3693–3694. See also: d) H. C. Brown, U. R. Racherla, S. M. Singh, *Tetrahedron Lett.* **1984**, *25*, 2411–2415.

[20] a) R. Waack, M. A. Doran, *J. Am. Chem. Soc.* **1969**, *91*, 2456–2461; b) J. Clayden, *Organolithiums: Selectivity for Synthesis*, Elsevier, Oxford, **2002**.

[21] a) E. Castagnetti, M. Schlosser, *Eur. J. Org. Chem.* **2001**, 691–695 and references therein; b) T. Yamazaki, S. Hiraoka, T. Kitazume, *J. Org. Chem.* **1994**, *59*, 5100–5103.

[22] When the 1:1 mixture of **2** and *n*BuLi was kept at −100 °C for 15 min and then treated with benzaldehyde, alcohol **5**, and 1-phenylpentan-1-ol, the adducts of vinyllithium **1** and *n*BuLi were obtained in 25 % and 64 % yields, respectively.

[23] Trifluoropropene and 1,1-difluoroallene were identified by ^{19}F NMR chemical shifts; a) M. Hanack, J. Ullmann, *J. Org. Chem.* **1989**, *54*, 1432–1435; b) Ref. [17].

[24] For example, see: a) S. Nag, S. Madapa, S. Batra, *Synthesis* **2008**, 101–109 and references therein; b) F.-X. Felpin, J. E. Lebreton, *Eur. J. Org. Chem.* **2003**, *19*, 3693–3712.

[25] R. Kupfer, S. Meier, E.-U. Würthwein, *Synthesis* **1984**, 688–690.

[26] a) F. Chemla, V. Hebbe, J.-F. Normant, *Synthesis* **2000**, 75–77; b) J. L. Garcia Ruano, J. Alemán, M. B. Cid, A. Parra, *Org. Lett.* **2005**, *7*, 179–182.

[27] a) A. Avenoza, J. H. Busto, G. Jiménez-Osés, J. M. Peregrina, *J. Org. Chem.* **2005**, *70*, 5721–5724; b) M. Sani, L. Bruché, G. Chiva, S. Fustero, J. Piera, A. Volonterio, M. Zanda, *Angew. Chem.* **2003**, *115*, 2106–2109; *Angew. Chem. Int. Ed.* **2003**, *42*, 2060–2063; c) U. Matteoli, C. Botteghi, F. Sbrogiò, V. Beghetto, S. Paganelli, A. Scrivanti, *J. Mol. Catal. A* **1999**, *143*, 287–295; d) T. Kitazume, T. Ohnogi, *Synthesis* **1988**, 614–615.

[28] H. Nemoto, A. Satoh, K. Fukumoto, *Tetrahedron* **1995**, *51*, 10159–10174.

[29] C. T. Clark, B. C. Milgram, K. A. Scheidt, *Org. Lett.* **2004**, *6*, 3977–3980.

[30] a) K. C. Nicolaou, E. J. Sorensen, *Classics in Total Synthesis*, VCH, Weinheim, **1995**; b) E. J. Corey, X.-M. Cheng, *The Logic of Chemical Synthesis* Wiley, New York, **1989**; c) F. J. Zeelen, *Nat. Prod. Rep.* **1994**, *11*, 607–612.

[31] J. Cassayre, S. Z. Zard, *J. Organomet. Chem.* **2001**, *624*, 316–326.

[32] For recent reviews on the Pauson–Khand reaction, see: a) S. E. Gibson, M. Mainolfi, *Angew. Chem.* **2005**, *117*, 3082–3097; *Angew. Chem. Int. Ed.* **2005**, *44*, 3022–3037; b) M. R. Rivero, J. Adrio, J. C. Carretero, *Synlett* **2005**, 26–41; c) S. E. Gibson (née Thomas), A. Stevenazzi, *Angew. Chem.* **2003**, *115*, 1844–1854; *Angew. Chem. Int. Ed.* **2003**, *42*, 1800–1810.

[33] T. Barhoumi-Slimi, B. Crousse, M. Ourevitch, M. E. Gaied, J.-P. Bégué, D. Bonnet-Delpon, *J. Fluorine Chem.* **2002**, *117*, 137–141.

[34] M. Ishizaki, D. Suzuki, O. Hoshino, *J. Fluorine Chem.* **2001**, *111*, 81–90.

[35] CCDC 772077 contains the supplementary crystallographic data for compound **16**. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre at www.ccdc.cam.ac.uk/data_request/cif.

[36] For recent reviews on the Nazarov cyclization, see: a) A. J. Frontiera, C. Collison, *Tetrahedron* **2005**, *61*, 7577–7606; b) H. Pellissier, *Tetrahedron* **2005**, *61*, 6479–6517; c) M. A. Tius, *Eur. J. Org. Chem.* **2005**, 2193–2206.

[37] a) B. R. Langlois, E. Laurent, N. Roidot, *Tetrahedron Lett.* **1992**, *33*, 1291–1294; b) K. Miura, Y. Takeyama, K. Oshima, K. Utimoto, *Bull. Chem. Soc. Jpn.* **1991**, *64*, 1542–1553.

[38] T. Umemoto, K. Adachi, *J. Org. Chem.* **1994**, *59*, 5692–5699 and references therein.

[39] For recent reports on the cationic reactions conducted in HFIP, see: a) T. Saitoh, S. Yoshida, J. Ichikawa, *J. Org. Chem.* **2006**, *71*, 6414–6419 and references therein; b) I. A. Shuklov, N. V. Dubrovina, A. Börner, *Synthesis* **2007**, 2925.

[40] T. Suzuki, T. Ohwada, K. Shudo, *J. Am. Chem. Soc.* **1997**, *119*, 6774–6780.

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