

Lewis Base-Catalyzed Perfluoroalkylation of Carbonyl Compounds and Imines with (Perfluoroalkyl)trimethylsilane

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Lewis base-catalyzed perfluoroalkylation of carbonyl compounds and aldimines with (perfluoroalkyl)trimethylsilanes ($TMSCF_3$, $TMSC_2F_5$, and $TMSC_3F_7$) is described. The nitrogen- or oxygen-containing anions generated from amides, imides, and carboxylic acids have been found to work as effective Lewis-base catalysts in perfluoroalkylation that proceeds via activation of the carbon–silicon bonds of (perfluoroalkyl)trimethylsilanes. Reactions of carbonyl compounds such as aldehydes, ketones, and esters with $TMSCF_3$ in the presence of a catalytic amount of Lewis bases proceeded smoothly to afford the corresponding adducts in good-to-high yields under mild conditions. Although it was considered difficult, this catalytic perfluoroalkylation of various aldimines with (perfluoroalkyl)trimethylsilane in the presence of Lewis bases such as lithium acetate or benzoate proceeded efficiently to give the corresponding perfluoroalkylated adducts, because the aldimines here were weak electrophiles toward (perfluoroalkyl)trimethylsilanes. The present reaction is, therefore, the first example of a catalytic perfluoroalkylation of aldimines.

Recently, organofluorine compounds have received an increased attention due to their unique physical and biological properties.[1] Fluorine is often regarded as an isostere of hydrogen because the van der Waals radius of fluorine is close to that of hydrogen. Introduction of a fluorine-containing functional group into an organic molecule sometimes brings about notable changes in the physical and chemical properties of the derived fluorinated compounds, and some fluorine-containing drugs and agrochemicals have thus been developed in pharmaceutical industries.[2] One of the most important fluorine-containing functional groups is the trifluoromethyl group, which has an electronegativity similar to that of oxygen and also has a large hydrophobic nature. Syntheses of trifluoromethylated synthons are very important for the introduction of the trifluoromethyl group, which often improves the biological activity and metabolic stability. (Trifluoromethyl)trimethylsilane has been reported as a useful nucleophilic reagent because the trifluoromethyl anion is extremely unstable and liberates difluorocarbene readily along with a fluoride ion.[3] A conventional method for the introduction of the trifluoromethyl group generally employed $TMSCF_3$, which reacted with electrophiles such as aldehydes, ketones,[4,5] esters,[6] imines,[7] and aryl halides.[8] Whereas most of the trifluoromethylation reactions are carried out by using strong bases such as the fluoride ion or metal alkoxides to activate $TMSCF_3$, there have only been a few examples reported that use other catalysts for the effective promotion.[9] There are also few that have reported on effective trifluoromethylation of imines that are weak electrophiles toward $TMSCF_3$, and still less on catalytic trifluoromethylation.[10]

In our previous papers, lithium pyrrolidone, lithium acetate (AcOLi), or tetrabutylammonium benzoate was shown to be an effective Lewis-base catalyst for the activation of the trimethylsilyl (TMS) enolate in aldol, Michael- and Mannich-type reactions[11] (Scheme 1). In order to extend the synthetic utility of the above mentioned Lewis-base catalysts, trifluoromethylation of carbonyl compounds and aldimines via activation of the carbon–silicon bond of $TMSCF_3$ with AcOLi, a mild and inexpensive Lewis base, was considered.[12] In this paper, we describe a convenient method for perfluoroalkylation of carbonyl compounds and imines with (perfluoroalkyl)trimethylsilanes by using weak Lewis-base catalysts such as AcOLi in detail.

Results and Discussion

Lithium Acetate-Catalyzed Trifluoromethylation of Carbonyl Compounds with (Trifluoromethyl)trimethylsilane. At first, a Lewis base-catalyzed trifluoromethylation of an aldehyde, 4-methoxybenzaldehyde (**1**), with $TMSCF_3$ was examined since nitrogen- or oxygen-containing anions are effective catalysts in aldol, Mannich-type, and Michael reactions (Table 1). The reaction of **1** with $TMSCF_3$ was tried in the presence of 5 mol % of AcOLi at 0 °C in DMF, and the corresponding trifluoromethylated adduct **2** was obtained in good yield (Entry 1). Further, the above reaction proceeded smoothly even when only 1 mol % of AcOLi was used (Entry 2). Acetates having such counter cations as sodium, potassium, or ammonium ions also worked effectively and afforded the desired products in high yields (Entries 3–6). Whereas other lithium carboxylates worked as highly active Lewis-base catalysts, lithium trifluoroacetate, a weak nucleophile, did not promote the reaction (Entries 7–9). The oxygen-containing anions generated from carboxylic acids, phenols, or alcohols were shown to be employed as effective catalysts for the activation of $TMSCF_3$. The same reactions were further tried by using nitrogen-containing anions generated from imides or azole derivatives and the desired product was afforded similarly in good

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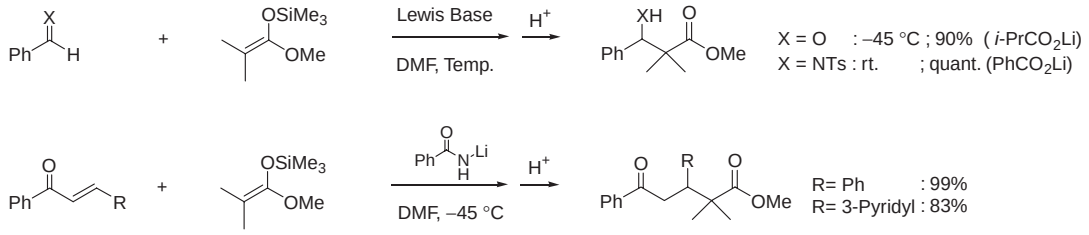
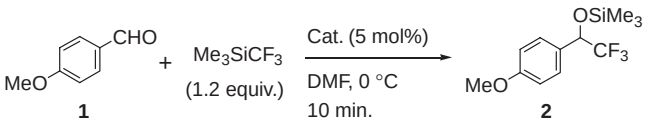


Scheme 1. Lewis base-catalyzed aldol, Mannich-type, and Michael reactions with trimethylsilyl enolate.

Table 1. Screening of Various Catalysts on Trifluoromethylation



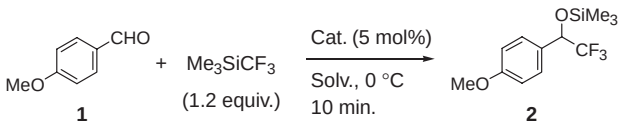
Entry	Cat. (5 mol %)	Yield[a]/%	Entry	Cat. (5 mol %)	Yield[a]/%
1	AcOLi	98 (97)[b]	13	Phthalimide K	98
2	AcOLi	97[c]	14		94
3	AcONa	96			
4	AcOK	99	15		96
5	AcOCs	98	16		98
6	$AcONBu_4$	97			
7	*t*-$BuCO_2Li$	98	17		96
8	$PhCO_2Li$	98	18		97
9	CF_3CO_2Li	0[d]			
10	PhOLi	99	19		91
11	$PhONBu_4$	95			
12	$(CF_3)_2COLi$	92	20	None	0[d]

a) Yield was determined by ^1H NMR analysis (270 MHz) using 1,1,2,2-tetrachloroethane as an internal standard. b) Isolated yield. c) 1 mol % of AcOLi was used. d) Reaction was carried out for 2 h.

yields within 10 min (Entries 13–19). In the absence of a catalyst, the reaction did not proceed at all (Entry 20). These results showed that the nitrogen- or oxygen-containing anions behave as effective Lewis-base catalysts in this trifluoromethylation.

The effect of solvents was examined by taking the reactions of 4-methoxybenzaldehyde (**1**) with $TMSCF_3$ in the presence of AcOLi or tetrabutylammonium acetate ($AcONBu_4$) as model reactions (see Table 2). These reactions proceeded smoothly in DMF or in DMSO if AcOLi was used (AcOLi, Entries 1 and 2), while non-coordinating solvents such as toluene, dichloromethane, or ethyl acetate were not suitable under those conditions because the carbon–silicon bond of $TMSCF_3$ was not sufficiently activated (AcOLi, Entries 3–7). On the other hand, it proceeded smoothly in various other solvents as well when a catalytic amount of $AcONBu_4$ was used ($AcONBu_4$, Entries 1–6). In the case when acetonitrile was used as a solvent, the desired product was obtained in 70% yield along with a small amount of cyanomethylated adduct ($AcONBu_4$, Entry 7).

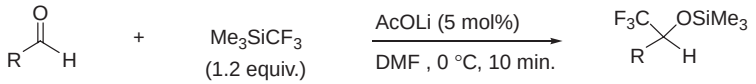
Table 2. Effect of Solvents on Trifluoromethylation

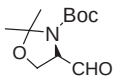


Entry	Solvent	Yield[a]/%	
		AcOLi	$AcONBu_4$
1	DMF	98	97
2	DMSO	96[b]	95[b]
3	THF	0	96
4	AcOEt	0	99
5	CH_2Cl_2	0	95
6	Toluene	0	98
7	CH_3CN	0	70

a) Yield was determined by ^1H NMR analysis (270 MHz) using 1,1,2,2-tetrachloroethane as an internal standard. b) The reaction was carried out at room temperature.

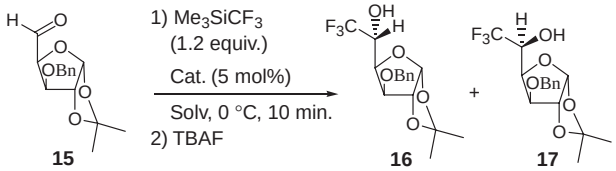
Table 3. AcOLi-Catalyzed Trifluoromethylation of Various Aldehydes



Entry	Aldehyde	Time/min	Product	Yield[a]/%	Entry	Aldehyde	Time/min	Product	Yield[a]/%
1	4-$Me_2NC_6H_4CHO$	10	**3**	97	8	2-PyridylCHO	10	**10**	92
2	PhCHO	10	**4**	91	9	(*E*)-PhCH=CHCHO	10	**11**	93
3	4-BrC_6H_4CHO	10	**5**	94	10	$PhCH_2CH_2CHO$	10	**12**	77
4	4-$MeO_2CC_6H_4CHO$	10	**6**	97	11	*c*-$C_6H_{11}CHO$	10	**13**	81
5	4-$NO_2C_6H_4CHO$	10	**7**	97	12		30	**14**	77[b]
6	2-NaphthylCHO	10	**8**	98	13		30	**14**	86[c,d]
7	AnthracenylCHO	10	**9**	99					

a) Yield was determined by ^{1}H NMR analysis (270 MHz) using 1,1,2,2-tetrachloroethane as an internal standard. b) Major: minor = 58:42 d.r. c) The reaction was carried by using 5 mol % $AcONBu_4$ in toluene. d) Major:minor = 62:38 d.r.

Table 4. Trifluoromethylation of Compound **15**



Entry	Cat.	Solv.	Yield[a]/%	d.r. (**16**:**17**)
1	AcOLi	DMF	55	75:25
2	$AcONBu_4$	DMF	37	75:25
3	$AcONBu_4$	DMF	65	77:23[b]
4	$AcONBu_4$	Toluene	92	73:27
5	$AcONBu_4$	Et_2O	87	68:32
6	$AcONBu_4$	CH_2Cl_2	84	62:38

a) Yield was determined by ^{19}F NMR analysis (270 MHz) using $PhOCF_3$ as an internal standard. b) The reaction was carried out at −20 °C.

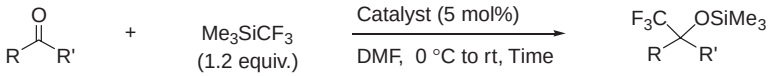
Since metal carboxylates were found useful in the reaction with 4-methoxybenzaldehyde (**1**), trifluoromethylation of various carbonyl compounds with $TMSCF_3$ was then tried in the presence of AcOLi (Table 3). Aldehydes worked as good acceptors of $TMSCF_3$ under the above reaction conditions and aromatic aldehydes having either an electron-donating or -withdrawing group and aliphatic aldehydes reacted rapidly in a similar manner to afford the corresponding trifluoromethylated products **3**–**14** in good-to-high yields (Entries 1–13). In the case when substrates possessing a *t*-butoxycarbonyl (Boc) or ester groups within the same molecule were used, these adducts were also obtained (Entries 4, 12, and 13). A diastereoselective trifluoromethylation of the pentodialdose derivatives **15**[13,14] was examined in the presence of a catalytic amount of a Lewis base (Table 4). The corresponding products were obtained in good yields as a mixture of the L-*ido* and D-*gluco* epimers **16** and **17** with moderate selectivities when the reactions were carried out in the presence of $AcONBu_4$ in toluene (Entry 4).

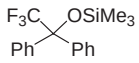
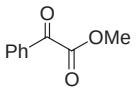
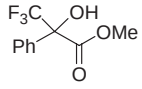
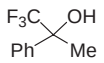
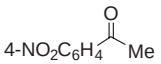
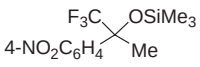
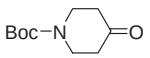
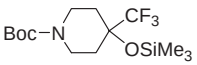
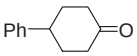
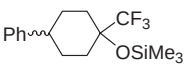
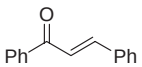
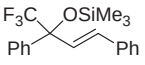
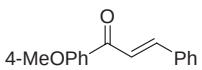
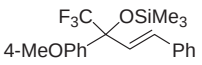
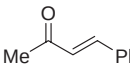
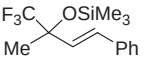
Next, the possible applications of trifluoromethylation to ketones were examined and the reactions also proceeded smoothly to afford the corresponding adducts in high yields (Table 5). It was found that easily enolizable ketones worked as a good acceptor of this reaction as well (Entries 3–6). When α,β-unsaturated ketones were employed, 1,2-addition products were obtained in good yields and 1,4-addition products were not detected in all cases (Entries 7–9).

The present reaction system was next applied to the trifluoromethylation of esters by using methyl 4-chlorobenzoate (**27**) as a model substrate (Table 6). However, the trifluoromethyl adducts **28** and **29** were obtained in 20% yield only when the reaction was carried out in the presence of AcOLi in DMF. Since the solvent showed a crucial effect on this reaction, various solvents were reexamined for further optimization.[6a,6b] It was found then that nonpolar aprotic solvents such as toluene and Et_2O were effective, and the trifluoromethyl adducts **28** and **29** were obtained in good yields. When pentane was used, the corresponding adducts were obtained along with considerable amounts of the bis-trifluoromethylated compounds **30** and **31** formed by double addition reactions.

Next, the trifluoromethylation of various esters was tried in order to generalize the reaction (Table 7). A reaction of methyl 4-chlorobenzoate (**27**) was carried out at 0 °C in dry toluene in the presence of $TMSCF_3$, and the reaction mixture was then allowed to warm slowly up to the room temperature for 1 h, followed by the treatment with a 4 M HCl solution, which resulted in the formation of the desired trifluoromethyl ketone **29** in good yield (Entry 1). It is remarkable that aromatic esters having both electron-donating groups and aliphatic esters reacted smoothly to afford the corresponding trifluoromethylated ketones in good yields (Entries 2–4, 6, and 7). Contrary to the case in which an ester having electron-withdrawing groups such as methyl 4-nitrobenzoate were used, the desired trifluoromethylated ketone[15] was obtained as its hydrate in moderate yield along with the formation of the double addition products at the same time. The structure of compound **34** was determined by X-ray analysis (Fig. 1). Then, reaction conditions were optimized in order to improve the yield and the desired product **34** was obtained in good yield when the reaction was carried out in Et_2O at temperatures ranging from −78 °C to room temperature (Entry 5). These results indicate that

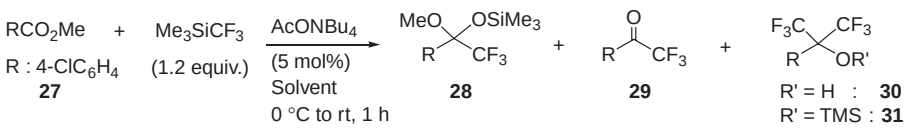
Table 5. Trifluoromethylation of Various Ketones



Entry	Ketone	Product		Catalyst	Time/h	Yield[a]/%
1			**18**	AcOLi	2	84
2			**19**	AcOLi	1	87[b]
3			**20**	AcOLi	2	84[b]
4			**21**	AcOLi	1	95
5			**22**	AcOLi	1	80
				$AcONBu_4$	1	96[c]
6			**23**	AcOLi	1	81
				$AcONBu_4$	1	87[c]
7			**24**	AcOLi	1	97
				$AcONBu_4$	1	97[c]
8			**25**	AcOLi	2	92
9			**26**	AcOLi	2	91[d]

a) Yield was determined by ^{1}H NMR analysis (270 MHz) using 1,1,2,2-tetrachloroethane as an internal standard. b) The product was obtained after desilylation. c) The reaction was carried out in THF. d) 1.5 equivalents of $TMSCF_3$ were used.

Table 6. Trifluoromethylation of Ester



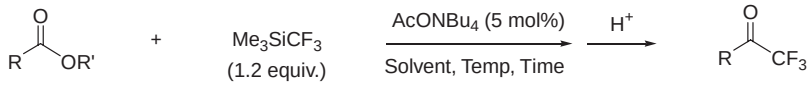
Entry	Solvent	Time/h	Yield[a]/%		
			28	**29**	**30 + 31**
1	Pentane	1	69	5	26
2	Toluene	1	93	N.D.	1
3	Et_2O	1	50	34	11
4	THF	1	N.D.	33	43
5	CH_2Cl_2	3	N.D.	4	N.D.
6	DMF	3	N.D.	20	4

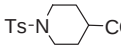
a) Yield was determined by ^{19}F NMR analysis (270 MHz) using $PhOCF_3$ as an internal standard.

the desired products could be obtained in high yields by a suitable choice of solvents according to the nature of the substrates. It is noteworthy that the reactions proceeded rapidly and gave the corresponding trifluoromethyl ketones in excellent yields even when carboxylic esters with decreased reactivities were used.

Lewis Base-Catalyzed Perfluoroalkylation of Aldimines with (Perfluoroalkyl)trimethylsilane. Although the catalytic trifluoromethylation of carbonyl compounds using $TMSCF_3$ has already been reported, few methods of trifluoromethylation of imines are known due to their weakly electrophilic character toward $TMSCF_3$. Of the few, Prakash and Olah showed an ex-

Table 7. $AcONBu_4$-Catalyzed Trifluoromethylation of Various Esters



Entry	Ester	Solvent	Temp/°C	Time/h	Product		Yield[a]/%
1	$4\text{-}ClC_6H_4CO_2Me$	Toluene	0–rt	1	$4\text{-}ClC_6H_4COCF_3$	**29**	90
2	$4\text{-}ClC_6H_4CO_2iPr$	Toluene	0–rt	1	$4\text{-}ClC_6H_4COCF_3$	**29**	64
3	$4\text{-}MeOC_6H_4CO_2Me$	Toluene	0–rt	1	$4\text{-}MeOC_6H_4COCF_3$	**32**	83[b]
4	(*E*)-$PhCH{=}CHCO_2Me$	Toluene	0–rt	1	(*E*)-$PhCH{=}CHCOCF_3$	**33**	84
5	$4\text{-}NO_2C_6H_4CO_2Me$	Et_2O	−78–rt	1	$4\text{-}NO_2C_6H_4C(OH)_2CF_3$	**34**	78
6	$PhCH_2CH_2CO_2Et$	Toluene	0–rt	1	$PhCH_2CH_2COCF_3$	**35**	82
7		Toluene	0–rt	4		**36**	76

a) Yield was determined by ^{19}F NMR analysis (270 MHz) using $PhOCF_3$ as an internal standard. b) 1.5 equiv of $TMSCF_3$ was used.

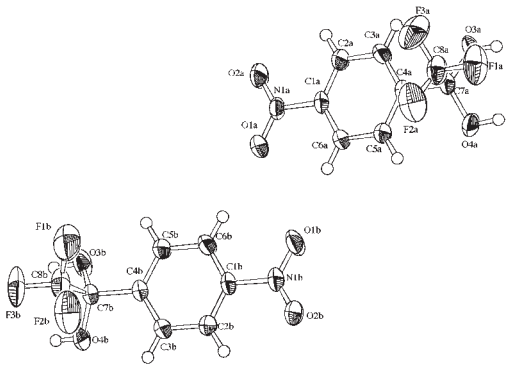
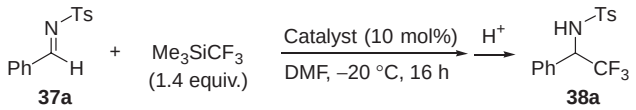


Fig. 1.

cellent trifluoromethylation of aldimines with $TMSCF_3$ in the presence of an equimolar amount of tetrabutylammonium-triphenylsilyl difluorosilicate.[7g] However, this method leaves the following synthetic problems: (i) an equimolar amount of a catalyst is required, and (ii) isolation of the desired products from a co-product such as triphenylsilyl fluoride is not easy. For these reasons, it was strongly desired to develop a catalytic trifluoromethylation of imines. In order to extend the applicability of this Lewis base-catalyzed trifluoromethylation, the use of imines instead of the above-mentioned carbonyl compounds was examined. *N*-Phenylsulfonylaldimines were prepared from the corresponding aldehydes and *N*-sulfonamides according to the literature procedures.[11,12] At first, various Lewis-base catalysts were examined by taking the reaction of the *N*-tosylaldimines **37a** with $TMSCF_3$ in the presence of 10 mol % of a catalyst at −20 °C in DMF as a model (Table 8). In the absence of a catalyst, the trifluoromethylated adduct was not detected (Entry 1). On the other hand, several lithium carboxylates such as lithium benzoate, acetate, and pivalate worked as effective Lewis-base catalysts in the reaction with aldimines, although long reaction times were required before completion (Entries 3–6). It is noted here that the lithium ion was an effective counter cation of the carboxylates (Entries 7–9). However, weakly nucleophilic lithium trifluoroacetate did not promote this reaction (Entry 2). Also, trifluoromethylation reactions did not proceed effectively when they were carried out in the presence of CsF or BnOLi (Entries 10 and 11).

Next, the reactions of various *N*-tosylaldimines, **37b–37m**,

Table 8. Screening of Various Catalysts on Trifluoromethylation



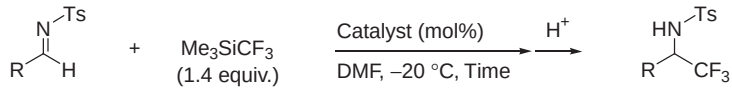
Entry	Catalyst	Yield[a]/%	Entry	Catalyst	Yield[a]/%
1	None	N.D.[b]	7	AcONa	86
2	CF_3CO_2Li	N.D.	8	AcOK	67
3	$PhCO_2Li$	94	9	$AcONn\text{-}Bu_4$	79
4	$t\text{-}BuCO_2Li$	87[b]	10	BnOLi	37[b]
5	AcOLi	93 (91)[c]	11	CsF	30[b]
6	AcOLi	95[b]			

a) Each yield was determined by ^1H NMR analysis (270 MHz) using 1,1,2,2-tetrachloroethane as an internal standard. b) The reaction was carried out for 40 h. c) Isolated yield.

with $TMSCF_3$ were tried by using 10 mol % of AcOLi in DMF (Table 9). Aromatic aldimines having electron-donating or -withdrawing groups on the aromatic ring reacted smoothly to afford the trifluoromethylated adducts **38b–38j** in good yields (Entries 1–9). Whereas aliphatic aldimines having no protons adjacent to the imino group reacted smoothly to afford the desired adduct **38k** in high yields, those with α-protons did not undergo the trifluoromethylation because of the competitive abstraction of the protons taking place at the same time (Entries 10 and 11). Then, various Lewis bases were screened and the reaction conditions were optimized in order to improve the yields. Consequently, the corresponding trifluoromethylated adducts **38l** and **38m** were obtained in moderate to high yields when the reactions were carried out in the coexistence of an equimolar amount of PhOLi (Entries 12 and 13).

In order to extend the scope of this reaction, the effects of substituents on the nitrogen atom of aldimines were next examined by using various aldimines in the presence of a catalytic amount of AcOLi in DMF (Table 10). It was then found that the reactivity of this reaction was greatly influenced by the electrophilicities of these imines. For example, when a weak electrophile such as the *N*-phenylaldimine **43** or *N*-benzylaldimines **44** was used as a substrate, no desired products were detected (Entries 6 and 7). On the other hand, it proceeded

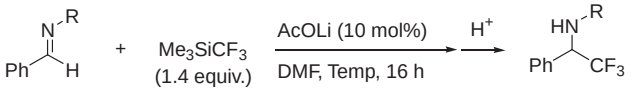
Table 9. Trifluoromethylation of Various Aldimines



Entry	R		Catalyst (mol %)	Time/h	Product	Yield[a]/%
1	4-$MeOC_6H_4$	**37b**	AcOLi (10)	40	**38b**	83
2	4-MeC_6H_4	**37c**	AcOLi (10)	40	**38c**	82
3	4-ClC_6H_4	**37d**	AcOLi (10)	16	**38d**	93
4	4-BrC_6H_4	**37e**	AcOLi (10)	16	**38e**	80
5	4-$NO_2C_6H_4$	**37f**	AcOLi (10)	16	**38f**	92
6	2-Naphthyl	**37g**	AcOLi (10)	16	**38g**	92
7	2-Furyl	**37h**	AcOLi (10)	16	**38h**	86
8	4-Pyridyl	**37i**	AcOLi (10)	16	**38i**	89
9	*trans*-PhCH=CH	**37j**	AcOLi (10)	16	**38j**	78[b]
10	*t*-Bu	**37k**	AcOLi (10)	40	**38k**	90
11	*c*-C_6H_{11}	**37l**	AcOLi (10)	40	**38l**	trace
12	*c*-C_6H_{11}	**37l**	PhOLi (100)	1	**38l**	80[c,d]
13	$PhCH_2CH_2$	**37m**	PhOLi (100)	1	**38m**	35[c,d]

a) Each yield was determined by ^{1}H NMR analysis (270 MHz) using 1,1,2,2-tetrachloroethane as an internal standard. b) 2.0 equiv of $TMSCF_3$ were used. c) The combined solution of imine and $TMSCF_3$ in DMF was added slowly to the DMF solution of PhOLi. d) The reaction was carried out at 0 °C.

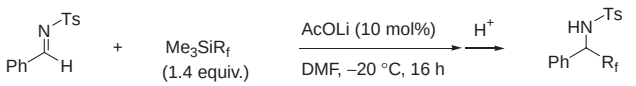
Table 10. Effect of Substituents on the Nitrogen of Aldimine



Entry	R		Temp /°C	Product	Yield[a] /%
1	4-$MeC_6H_4SO_2$	**37a**	−20	**38a**	93
2	4-$ClC_6H_4SO_2$	**39**	−20	**45**	82
3	4-$NO_2C_6H_4SO_2$	**40**	−20	**46**	93
4	2-$NO_2C_6H_4SO_2$	**41**	−20	**47**	87
5	$P(O)Ph_2$	**42**	rt	**48**	75[b]
6	Ph	**43**	rt	**49**	N.D.
7	Bn	**44**	rt	**50**	N.D.

a) Each yield was determined by ^{1}H NMR analysis (270 MHz) using 1,1,2,2-tetrachloroethane as an internal standard. b) 2.0 equiv of $TMSCF_3$ were used.

Table 11. Perfluoro- and Difluoroalkylation of Aldimines



Entry	Me_3SiR_f		Temp /°C	Product	Yield[a] /%
1	Me_3SiCF_3	**37a**	−20	**38a**	93
2	$Me_3SiC_2F_5$	**51**	−20	**55**	91
3	$Me_3SiC_3F_7$	**52**	−20	**56**	87
4	$Me_3SiCF_2CO_2Et$	**53**	rt	**57**	85
5	Me_3SiCF_2–C$_6$H$_4$–CF_3	**54**	rt	**58**	82[b]

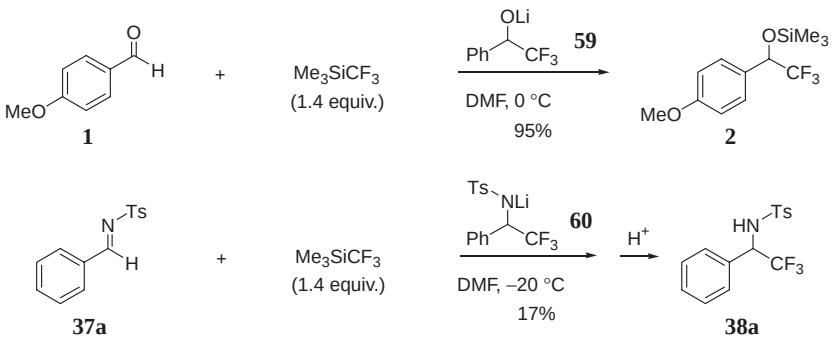
a) Each yield was determined by ^{1}H NMR analysis (270 MHz) using 1,1,2,2-tetrachloroethane as an internal standard. b) 2.0 equiv of $TMSCF_2C_6H_4CF_3$ were used.

smoothly under the same reaction conditions and the desired products **45**–**48** were obtained in good to moderate yields when the *N*-phenylsulfonylaldimines **39**–**41** and *N*-phosphinoylaldimines **42** were employed (Entries 2–5).

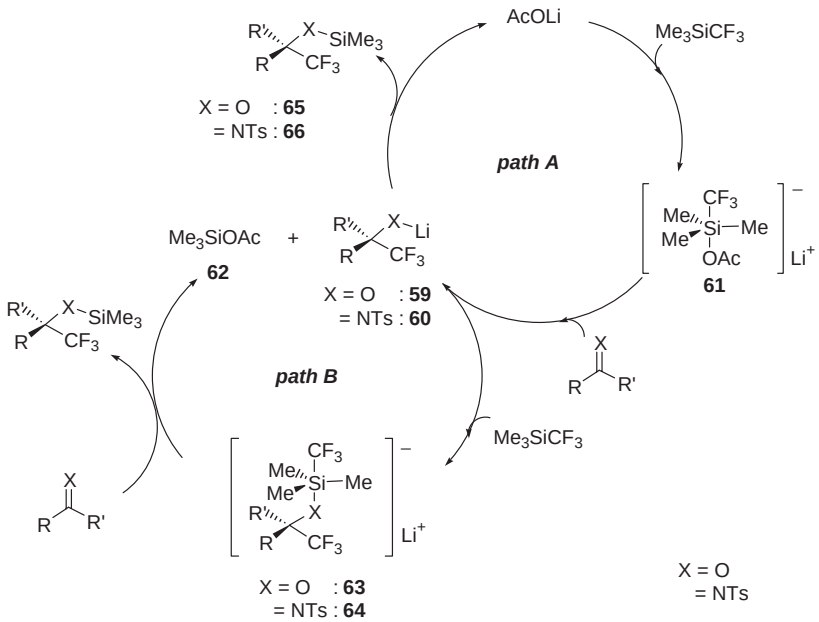
Finally, various (perfluoroalkyl)trimethylsilane or difluorotrimethylsilane derivatives were applied to this reaction (Table 11). Nucleophilic reagents such as (pentafluoroethyl)trimethylsilane ($Me_3SiCF_2CF_3$) or (heptafluoropropyl)trimethylsilane ($Me_3SiCF_2CF_2CF_3$) were also worked under the same conditions (Entries 2 and 3). This method is quite effective since the reaction proceeded smoothly in the presence of a catalytic amount of a Lewis base.

Mechanisms for Lewis Base-Catalyzed Trifluoromethylation. In order to study the mechanism of the trifluoromethylation, the reaction was examined by using the trifluoromethylated alkoxide anion intermediate **59** as a catalyst since the reaction was known to be catalyzed by the in situ formed trifluoromethylated alkoxide when a fluoride ion such as cesium fluoride or tetrabutylammonium fluoride was used.[4] As a result, the trifluoromethylation of the carbonyl compound **1** in the presence of the intermediate **59** proceeded smoothly to afford the corresponding adduct **2** in good yield as expected, whereas the yield was low when the *N*-tosylaldimine **37a** was employed in the presence of the intermediate **60** (Scheme 2). Based on these two experimental results, these reactions were considered to proceed via different mechanisms.

The assumed catalytic cycle of Lewis base-catalyzed trifluoromethylation of carbonyl compounds or imines is illustrated in Scheme 3. In the first step, a Lewis base and DMF coordinate to the silicon atom of $TMSCF_3$ to form the hypervalent silicate **61**. The nucleophilicity of the silicate **61** is sufficient for the reaction with carbonyl compounds and it forms the trifluoromethylated alkoxy anion **59** together with trimethylsilyl acetate (TMSOAc). Subsequent silylation of **59** by the thus formed TMSOAc **62** affords the *O*-silyl ether **65** along with regeneration of the catalyst because the trimethylsilyl acetate is a powerful silylating reagent (path A). Actually, the silyl ether **65** is produced when the lithium alkoxide **59** is treated



Scheme 2. Autocatalytic process.



Scheme 3. Assumed catalytic cycle of AcOLi-catalyzed trifluoromethylation of carbonyl compounds or imines.

with trimethylsilyl acetate in DMF at 0 °C. Further, the trifluoromethylated alkoxy anion **59** can also catalyze the subsequent reaction via the hypervalent silicon intermediate **63** (path B). Thus, it is considered that the reaction proceeds by both path A and path B. On the other hand, the *N*-amide anion of the produced trifluoromethyl-adduct **60** did not effectively activate the carbon–silicon bond of $TMSCF_3$ as a Lewis-base catalyst in the case when *N*-tosylaldimines were used as a substrate. This result indicates that the reaction does not proceed via path B. For this reason, it is considered that the reaction proceeds via path A to complete the reaction when *N*-tosylaldimines were used.[8]

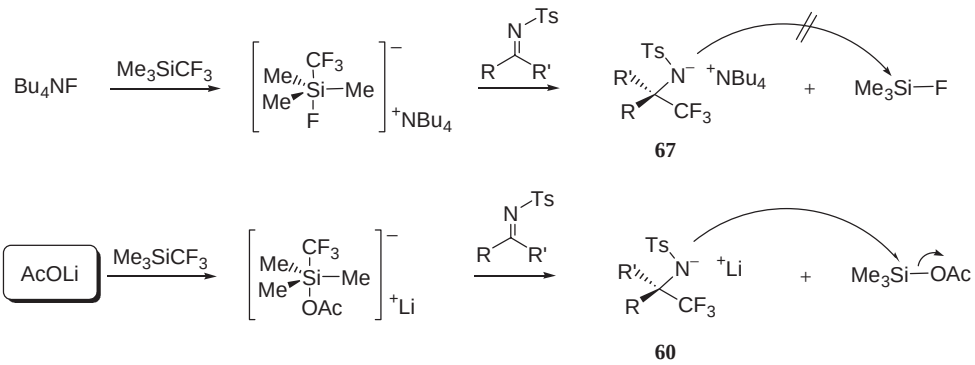
When *N*-tosylaldimines were used as substrates, metal carboxylates such as AcOLi worked as catalysts more effectively when compared with metal fluorides such as CsF. These results are explained by considering the fact that the reaction using a fluoride ion could not regenerate the catalyst; more specifically, the silyl group transfer from the formed trimethylsilyl fluoride to the intermediate **67** never took place because of the highly-stable fluorine–silicon bond (Scheme 4).

Conclusion

Lewis base-catalyzed perfluoroalkylation of carbonyl compounds or *N*-tosylaldimines with (perfluoroalkyl)trimethylsilane (Me_3SiR_f) has been established. The nitrogen- or oxygen-containing anions that were generated from amides, imides, and carboxylic acids were found to work as Lewis-base catalysts effectively in perfluoroalkylation that proceeds via the activation of the carbon–silicon bonds of Me_3SiR_f. Trifluoromethylated alcohols or amines were synthesized in good to high yields by a trifluoromethylation of carbonyl compounds or *N*-tosylaldimines in the presence of a catalytic amount of Lewis bases such as lithium acetate or benzoate. This method is a quite practical one since the reaction proceeded smoothly when a readily available and easy to handle catalyst such as AcOLi was used.

Experimental

General. All melting points were determined on a Yanagimoto micro melting apparatus (Yanaco MP-S3) and remain uncorrected. Infrared (IR) spectra were recorded by an attenuated total reflection (ATR) method on a SensIR Technologies Travel *IR*™ spectrometer. ^{1}H NMR spectra were recorded on a JEOL JNM-EX270L (270 MHz) spectrometer; chemical shifts (δ) are reported in parts per million relative to tetramethylsilane. Splitting patterns are designated as s, singlet; d, doublet; t, triplet; q, quartet;



Scheme 4.

h, heptet; m, multiplet; brs, broad singlet. ^{13}C NMR spectra were recorded on an EX270L (68 MHz) spectrometer with complete proton decoupling. Chemical shifts are reported in parts per million relative to tetramethylsilane, with the solvent resonance as the internal standard ($CDCl_3$; $\delta = 77.0$ ppm, DMSO-d_6; $\delta =$ 39.5 ppm). High-resolution mass spectra (HRMS) were recorded on a JMS-SX102A mass spectrometer or LCT premier. Elemental analyses were conducted using a Yanaco MT-5 CHN corder. Analytical TLC was performed on Merck preparative TLC plates (silica gel 60 GF254, 0.25 mm). Column chromatography was carried out on Merck silica gel 60 (0.063–0.200 mm) or Kanto silica gel 60 N (neutral). Preparative thin-layer chromatography (PTLC) was carried out on silica gel Wakogel B-5F. Reactions in anhydrous DMF were carried out under an argon atmosphere in dried glassware, unless otherwise noted. Dehydrated DMF, THF, Et_2O, CH_2Cl_2, AcOEt, and CH_3CN were purchased from Kanto Chemical. Other dry solvents were prepared by distillation under appropriate drying agents. Lithium acetate and lithium benzoate were purchased from Wako Pure Chemical Industries. Tetrabutylammonium acetate was purchased from Aldrich Chemical. Other Lewis-base catalysts were prepared from corresponding precursors and *n*-BuLi in THF at 0 °C. After the solvent had been removed under reduced pressure, the residue was used without further purification. (Trifluoromethyl)trimethylsilane was purchased from Tokyo Kasei Kogyo and used without further purification. All reagents were purchased from Tokyo Kasei Kogyo, Kanto Chemical, Kokusan Chemical, Wako Pure Chemical Industries, Fluka, or Aldrich Chemical. Aldehydes were used after purification by distillation or recrystallization. *N*-Sulfonylaldimines **37a**–**37m** and **39**–**41** were prepared by the literature procedures.[16] The *N*-diphenylphosphinoylaldimine **42** was also synthesized by a known procedure.[17]

Catalyst Preparation. To a mixture of the alcohol **4** or amide **38a** (1.05 mmol) in THF (4.37 mL) was added *n*-BuLi in hexane (1.58 M, 0.63 mL, 1.0 mmol) at 0 °C, and the mixture was stirred for 30 min to prepare a 0.2 M solution of lithium alkoxide **59** or lithium amide **60**.

Typical Experimental Procedure for Trifluoromethylation of Carbonyl Compounds. To a stirred solution of AcOLi (1.3 mg, 0.02 mmol) in DMF (0.6 mL) were added successively a solution of 4-methoxybenzaldehyde (52.5 mg, 0.4 mmol) in DMF (0.6 mL) and $TMSCF_3$ (74.8 μL, 0.48 mmol, 95% content) at 0 °C. The mixture was stirred for 10 min at the same temperature, and then quenched with saturated aqueous NH_4Cl. The mixture was extracted with Et_2O and the organic layer was washed with brine and dried over anhydrous Na_2SO_4. After filtration and evaporation of the solvent, the crude product was purified by preparative TLC to afford the corresponding adduct **2** (111.3 mg, 98%).

2,2,2-Trifluoro-1-(4-methoxyphenyl)-1-(trimethylsilyloxy)-ethane (2):[5d] Colorless oil; IR (ATR) 2960, 1614, 1514, 1250, 1125, 840 cm^{-1}; ^{1}H NMR (270 MHz, $CDCl_3$) δ 7.35 (d, $J = 8.6$ Hz, 2H), 6.89 (d, $J = 8.6$ Hz, 2H), 4.85 (q, $J = 6.5$ Hz, 1H), 3.15 (s, 3H), 0.10 (s, 9H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 160.0, 128.7, 127.4, 124.2 (q, $J_{C-F} = 281$ Hz), 113.6, 72.9 (q, $J_{C-C-F} = 32$ Hz), 55.2, −0.15.

1-(4-*N*,*N*-Dimethylaminophenyl)-2,2,2-trifluoro-1-(trimethylsilyloxy)ethane (3):[5d] Colorless solid; mp 55–56 °C; IR (ATR) 2899, 1618, 1529, 1357, 1252, 1097, 868 cm^{-1}; ^{1}H NMR (270 MHz, $CDCl_3$) δ 7.28 (d, $J = 8.6$ Hz, 2H), 6.69 (d, $J = 8.6$ Hz, 2H), 4.81 (q, $J = 6.8$ Hz, 1H), 2.96 (s, 6H), 0.10 (s, 9H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 150.8, 128.4, 124.4 (q, $J_{C-F} = 281$ Hz), 122.7, 111.7, 73.1 (q, $J_{C-C-F} = 32$ Hz), 40.4, −0.08.

2,2,2-Trifluoro-1-phenylethanol (4):[5a] The desired product was obtained after acid hydrolysis (1 M HCl solution). Colorless oil; IR (ATR) 3383, 1263, 1167, 1122, 701 cm^{-1}; ^{1}H NMR (270 MHz, $CDCl_3$) δ 7.49–7.36 (m, 5H), 4.99 (dq, $J = 6.8$, 4.3 Hz, 1H), 2.78 (d, $J = 4.3$ Hz, 1H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 133.9, 129.5, 128.5, 127.3, 124.2 (q, $J_{C-F} = 281$ Hz), 72.9 (q, $J_{C-C-F} = 32$ Hz).

1-(4-Bromophenyl)-2,2,2-trifluoro-1-(trimethylsilyloxy)ethane (5):[9c] Colorless oil; IR (ATR) 2960, 1256, 1169, 1129, 842 cm^{-1}; ^{1}H NMR (270 MHz, $CDCl_3$) δ 7.51 (d, $J = 8.6$ Hz, 2H), 7.32 (d, $J = 8.6$ Hz, 2H), 4.87 (q, $J = 6.5$ Hz, 1H), 0.12 (s, 9H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 134.4, 131.4, 129.1, 123.7 (q, $J_{C-F} =$ 281 Hz), 123.2, 74.7 (q, $J_{C-C-F} = 32$ Hz), −0.19.

2,2,2-Trifluoro-1-(4-methoxycarbonylphenyl)-1-(trimethylsilyloxy)ethane (6): Colorless oil; IR (ATR) 2958, 1725, 1268, 1170, 1129, 843 cm^{-1}; ^{1}H NMR (270 MHz, $CDCl_3$) δ 8.15 (d, $J =$ 8.1 Hz, 2H), 7.63 (d, $J = 8.1$ Hz, 2H), 5.06 (q, $J = 6.5$ Hz, 1H), 4.02 (s, 3H), 0.22 (s, 9H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 166.5, 140.2, 130.8, 129.5, 127.5, 123.8 (q, $J_{C-F} = 282$ Hz), 72.9 (q, $J_{C-C-F} = 32$ Hz), 52.2, −0.21; HRMS (FAB+) calcd for $C_{13}H_{18}F_3O_3Si$ $[M + H]^+$ 307.0977, found 307.0979.

2,2,2-Trifluoro-1-(4-nitrophenyl)-1-(trimethylsilyloxy)ethane (7): Pale yellow oil; IR (ATR) 2961, 1526, 1349, 1259, 1171, 1130, 843 cm^{-1}; ^{1}H NMR (270 MHz, $CDCl_3$) δ 8.25 (d, $J = 8.6$ Hz, 2H), 7.66 (d, $J = 8.6$ Hz, 2H), 5.03 (q, $J = 6.2$ Hz, 1H), 0.16 (s, 9H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 148.4, 142.2, 128.4, 123.5 (q, $J_{C-F} = 281$ Hz), 123.5, 72.5 (q, $J_{C-C-F} = 33$ Hz), −0.23; HRMS (FAB+) calcd for $C_{11}H_{15}F_3NO_3Si$ $[M + H]^+$ 293.0695, found 293.0786.

2,2,2-Trifluoro-1-(2-naphthyl)-1-(trimethylsilyloxy)ethane (8):[9c] White powder; mp 56–58 °C; IR (ATR) 2958, 1362, 1257,

1169, 1124, 848 cm^{-1}; ^{1}H NMR (270 MHz, $CDCl_3$) δ 7.92–7.80 (m, 4H), 7.61–7.45 (m, 3H), 5.08 (q, $J = 6.5$ Hz, 1H), 0.13 (s, 9H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 133.6, 132.8, 132.8, 128.1, 128.0, 127.6, 127.2, 126.5, 126.2, 124.7, 124.2 (q, $J_{C-F} = 281$ Hz), 73.5 (q, $J_{C-C-F} = 32$ Hz), −0.11.

1-(9-Anthracenyl)-1-(trimethylsilyloxy)-2,2,2-trifluoroethane (9):[9c] White powder; mp 99–101 °C; IR (ATR) 2963, 1160, 1116, 839 cm^{-1}; ^{1}H NMR (270 MHz, $CDCl_3$) δ 9.04 (d, $J = 8.4$ Hz, 1H), 8.52 (s, 1H), 8.17 (d, $J = 8.9$ Hz, 1H), 8.12–7.94 (m, 2H), 7.65–7.44 (m, 4H), 6.53 (q, $J = 8.1$ Hz, 1H), −0.02 (s, 9H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 131.8, 131.1, 130.9, 130.4, 130.2, 129.6, 128.6, 127.8 (q, $J_{C-C-C-F} = 3$ Hz), 127.0, 125.4, (q, $J_{C-F} = 283$ Hz), 125.4, 125.2, 125.0, 124.5, 122.2, 70.4 (q, $J_{C-C-F} = 33$ Hz), −0.39.

2,2,2-Trifluoro-1-(2-pyridyl)-1-(trimethylsilyloxy)ethane (10):[9c] Colorless oil; IR (ATR) 2961, 1174, 1128, 841 cm^{-1}; ^{1}H NMR (270 MHz, $CDCl_3$) δ 8.58 (d, $J = 4.3$ Hz, 1H), 7.80–7.72 (m, 1H), 7.63 (d, $J = 7.8$ Hz, 1H), 7.33–7.23 (m, 1H), 5.09 (q, $J = 6.5$ Hz, 1H), 0.13 (s, 9H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 155.5, 148.7, 136.7, 123.9 (q, $J_{C-F} = 282$ Hz), 123.8, 122.2, 74.8 (q, $J_{C-C-F} = 31$ Hz), −0.22.

***trans*-1,1,1-Trifluoro-4-phenyl-2-(trimethylsilyloxy)-3-butene (11):**[9c] Colorless oil; IR (ATR) 2961, 1265, 1256, 1167, 1127, 840 cm^{-1}; ^{1}H NMR (270 MHz, $CDCl_3$) δ 7.44–7.23 (m, 5H), 6.75 (d, $J = 15.9$ Hz, 1H), 6.17 (dd, $J = 15.9$, 6.2 Hz, 1H), 4.61–4.49 (m, 1H), 0.20 (s, 9H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 135.6, 134.9, 128.6, 128.3, 126.7, 124.1 (q, $J_{C-F} = 282$ Hz), 122.3, 72.2 (q, $J_{C-C-F} = 32$ Hz), 0.05.

1,1,1-Trifluoro-4-phenyl-2-(trimethylsilyloxy)butane (12):[9c] Pale yellow oil; IR (ATR) 2961, 1254, 1128, 841 cm^{-1}; ^{1}H NMR (270 MHz, $CDCl_3$) δ 7.36–7.12 (m, 5H), 3.95–3.83 (m, 1H), 2.80–2.52 (m, 2H), 2.08–1.83 (m, 2H), 0.15 (s, 9H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 140.6, 128.4, 128.3, 126.1, 125.0 (q, $J_{C-F} = 282$ Hz), 70.5 (q, $J_{C-C-F} = 31$ Hz), 32.2 (q, $J_{C-C-C-F} = 1$ Hz), 31.2, 0.11.

1-Cyclohexyl-2,2,2-trifluoroethanol (13):[5a] The desired product was obtained after acid hydrolysis (1 M HCl solution). Colorless oil; IR (ATR) 3402, 2927, 1086 cm^{-1}; ^{1}H NMR (270 MHz, $CDCl_3$) δ 3.78–3.62 (m, 1H), 2.76 (brs, 1H), 1.95–1.64 (m, 6H), 1.39–1.05 (m, 5H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 125.3 (q, $J_{C-F} = 282$ Hz), 74.3 (q, $J_{C-C-F} = 29$ Hz), 38.3, 29.3 (q, $J_{C-C-C-F} = 1$ Hz), 26.9 (q, $J_{C-C-C-F} = 1$ Hz), 26.1, 26.0, 25.8.

(*S*)-3-*t*-Butoxycarbonyl-2,2-dimethyl-4-(2,2,2-trifluoro-1-trimethylsilyloxyethyl)-1,3-oxazolidine (14): Mixture of diastereomers; isomer A/isomer B = 61:39. Colorless oil; IR (ATR) 2977, 1690, 1366, 1171, 843 cm^{-1}; ^{1}H NMR (270 MHz, $CDCl_3$) δ 4.87 (d, $J = 7.6$ Hz, 0.61H, A), 4.39 (d, $J = 7.6$ Hz, 0.39H, B), 4.32–3.88 (m, 3H), 1.70–1.41 (m, 15H), 0.18 (s, 5.5H, A), 0.16 (s, 3.5H, B); ^{13}C NMR (68 MHz, $CDCl_3$) δ 152.5, 151.8, 124.5 (q, $J_{C-F} = 283$ Hz), 94.2, 93.7, 80.7, 80.6, 70.3 (q, $J_{C-C-F} = 30$ Hz), 67.9 (q, $J_{C-C-F} = 29$ Hz), 62.6, 62.0, 57.2, 56.9, 28.4, 28.3, 26.2, 25.8, 0.03; HRMS (FAB+) calcd for $C_{15}H_{28}F_3NO_4Si$ $[M + H]^+$ 372.1818, found 372.1799.

3-*O*-Benzyl-6-deoxy-6,6,6-trifluoro-1,2-*O*-isopropylidene-β-L-idofuranose (16):[14] Colorless oil; IR (ATR) 3466, 2989, 1262, 1134, 1073, 1026 cm^{-1}; ^{1}H NMR (270 MHz, $CDCl_3$) δ 7.42–7.26 (m, 5H), 5.99 (d, $J = 3.8$ Hz, 1H), 4.69 (d, $J = 11.6$ Hz, 1H), 4.65 (d, $J = 3.8$ Hz, 1H), 4.51 (d, $J = 11.3$ Hz, 1H), 4.39–4.28 (m, 2H), 4.07 (d, $J = 3.0$ Hz, 1H), 3.33 (brs, 1H), 1.49 (s, 3H), 1.33 (s, 3H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 136.3, 128.6, 128.3, 127.8, 123.9 (q, $J_{C-F} = 281$ Hz), 112.4, 104.9, 82.8, 81.9, 76.4 (q, $J_{C-C-C-F} = 2$ Hz), 72.3, 68.5 (q, $J_{C-C-F} = 31$ Hz), 26.9, 26.3.

3-*O*-Benzyl-6-deoxy-6,6,6-trifluoro-1,2-*O*-isopropylidene-α-D-glucofuranose (17):[14] Colorless plate; mp 93–95 °C; IR (ATR) 3404, 2934, 1270, 1134, 1068, 1025 cm^{-1}; ^{1}H NMR (270 MHz, $CDCl_3$) δ 7.40–7.26 (m, 5H), 6.02 (d, $J = 3.8$ Hz, 1H), 4.68 (d, $J = 11.1$ Hz, 1H), 4.64 (d, $J = 3.8$ Hz, 1H), 4.55 (d, $J = 11.1$ Hz, 1H), 4.47–4.35 (m, 1H), 4.31 (dd, $J = 4.3$, 3.2 Hz, 1H), 4.25 (d, $J = 2.4$ Hz, 1H), 4.11 (brs, 1H), 1.55 (s, 3H), 1.33 (s, 3H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 135.8, 128.7, 128.6, 128.1, 124.3 (q, $J_{C-F} = 282$ Hz), 112.1, 104.8, 84.0, 81.6, 75.4, 72.8, 70.2 (q, $J_{C-C-F} = 31$ Hz), 26.7, 26.1.

2,2,2-Trifluoro-1,1-diphenyl-1-(trimethylsilyloxy)ethane (18):[5a] Colorless oil; IR (ATR) 2960, 1157, 840 cm^{-1}; ^{1}H NMR (270 MHz, $CDCl_3$) δ 7.46–7.27 (m, 10H), −0.06 (s, 9H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 140.8, 128.2, 128.1 (q, $J_{C-C-C-F} = 2$ Hz), 127.7, 125.1 (q, $J_{C-F} = 286$ Hz), 81.9 (q, $J_{C-C-F} = 29$ Hz), 1.4.

Methyl 3,3,3-Trifluoro-2-hydroxy-2-phenylpropanoate (19): The desired product was obtained after acid hydrolysis (1 M HCl solution). Colorless oil; IR (ATR) 3489, 2961, 1743, 1167 cm^{-1}; ^{1}H NMR (270 MHz, $CDCl_3$) δ 7.82–7.72 (m, 2H), 7.44–7.34 (m, 3H), 4.33 (s, 1H), 3.94 (s, 3H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 169.3, 132.7, 129.5, 128.3, 126.6, 122.9 (q, $J_{C-F} = 285$ Hz), 77.9 (q, $J_{C-C-F} = 30$ Hz), 54.6; Anal. Calcd for $C_{10}H_9F_3O_3$: C, 51.29; H, 3.88%. Found: C, 51.34; H, 4.09%.

2,2,2-Trifluoro-1-methyl-1-phenylethanol (20):[5a] The desired product was obtained after acid hydrolysis (1 M HCl solution). Colorless oil; IR (ATR) 3429, 1673, 1148, 1071 cm^{-1}; ^{1}H NMR (270 MHz, $CDCl_3$) δ 7.62–7.52 (m, 2H), 7.44–7.32 (m, 3H), 2.60 (brs, 1H), 1.78 (s, 3H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 138.3, 128.5, 128.2, 126.0, 125.5 (q, $J_{C-F} = 284$ Hz), 74.8 (q, $J_{C-C-F} = 29$ Hz), 23.9.

2,2,2-Trifluoro-1-methyl-1-(4-nitrophenyl)-1-(trimethylsilyloxy)ethane (21): Colorless oil; IR (ATR) 2962, 1525, 1163, 840 cm^{-1}; ^{1}H NMR (270 MHz, $CDCl_3$) δ 8.23 (d, $J = 8.6$ Hz, 2H), 7.73 (d, $J = 8.6$ Hz, 2H), 1.87 (s, 3H), 0.20 (s, 9H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 147.9, 147.0, 127.8, 124.6 (q, $J_{C-F} = 285$ Hz), 123.1, 77.1 (q, $J_{C-C-F} = 30$ Hz), 22.8, 2.1; Anal. Calcd for $C_{12}H_{16}F_3NO_3Si$: C, 46.90; H, 5.25; N, 4.56%. Found: C, 46.82; H, 5.38; N, 4.58%.

***N*-(*t*-Butoxycarbonyl)-4-(trifluoromethyl)-4-trimethylsilyloxypiperidine (22):** Colorless oil; IR (ATR) 2971, 1699, 1150, 1099 cm^{-1}; ^{1}H NMR (270 MHz, $CDCl_3$) δ 4.14–3.92 (m, 2H), 3.08–2.85 (m, 2H), 1.78–1.62 (m, 4H), 1.47 (s, 9H), 0.18 (s, 9H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 154.5, 125.6 (q, $J_{C-F} = 284$ Hz), 79.8, 74.1 (q, $J_{C-C-F} = 28$ Hz), 38.6, 30.8, 28.5, 1.8; Anal. Calcd for $C_{14}H_{26}F_3NO_3Si$: C, 49.25; H, 7.68; N, 4.10%. Found: C, 49.19; H, 7.41; N, 3.88%.

4-Phenyl-1-(trifluoromethyl)-1-(trimethylsilyloxy)cyclohexane (23): Mixture of diastereomers; isomer A/isomer B = 91:9. Colorless oil; IR (ATR) 2956, 1140, 1124, 839 cm^{-1}; ^{1}H NMR (270 MHz, $CDCl_3$) δ 7.38–7.18 (m, 5H), 2.80–2.66 (m, 0.91H, A), 2.62–2.48 (m, 0.09H, B), 2.27–2.14 (m, 2H), 2.05–1.62 (m, 6H), 0.24 (s, 0.81, B), 0.22 (s, 8.19, A); ^{13}C NMR (68 MHz, $CDCl_3$) δ 146.4, 145.1, 128.4, 128.3, 126.8, 126.6, 126.6 (q, $J_{C-F} = 286$ Hz), 126.2, 126.0, 75.0 (q, $J_{C-C-F} = 29$ Hz), 74.7 (q, $J_{C-C-F} = 29$ Hz), 43.3, 41.0, 32.7, 31.1, 28.7, 28.1, 2.3, 1.9; Anal. Calcd for $C_{16}H_{23}F_3OSi$: C, 60.73; H, 7.33%. Found: C, 60.56; H, 7.44%.

***trans*-4,4,4-Trifluoro-1,3-diphenyl-3-trimethylsilyloxy-1-butene (24):**[5c] Colorless oil; IR (ATR) 2961, 1650, 1254, 1159, 839 cm^{-1}; ^{1}H NMR (270 MHz, $CDCl_3$) δ 7.65–7.56 (m, 2H), 7.44–7.24 (m, 8H), 6.70 (d, $J = 16.2$ Hz, 1H), 6.55 (d, $J = 16.2$ Hz, 1H), 0.15 (s, 9H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 137.9,

135.6, 135.1, 128.7, 128.5, 128.4, 127.8, 126.8, 126.7, 124.9 (q, $J_{C-F} = 286$ Hz), 79.9 (q, $J_{C-C-F} = 28$ Hz), 2.1.

***trans*-4,4,4-Trifluoro-3-(4-methoxyphenyl)-1-phenyl-3-trimethylsilyloxy-1-butene (25):** Colorless oil; IR (ATR) 2959, 1610, 1511, 1252, 1157, 837 cm^{-1}; ^{1}H NMR (270 MHz, $CDCl_3$) δ 7.51 (d, $J = 8.9$ Hz, 2H), 7.44–7.24 (m, 5H), 6.91 (d, $J = 8.9$ Hz, 2H), 6.71 (d, $J = 16.5$ Hz, 1H), 6.53 (d, $J = 16.5$ Hz, 1H), 3.82 (s, 3H), 0.13 (s, 9H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 159.6, 135.7, 135.0, 129.2, 128.7, 128.5, 127.0, 126.7, 125.0 (q, $J_{C-F} =$ 286 Hz), 113.2, 79.7 (q, $J_{C-C-F} = 29$ Hz), 2.1; HRMS (FAB+) calcd for $C_{20}H_{23}F_3O_2Si$ M^+ 380.1419, found 380.1404.

***trans*-4,4,4-Trifluoro-3-methyl-1-phenyl-3-trimethylsilyloxy-1-butene (26):** Colorless oil; IR (ATR) 2961, 1254, 1158, 1093, 839 cm^{-1}; ^{1}H NMR (270 MHz, $CDCl_3$) δ 7.42–7.24 (m, 5H), 6.75 (d, $J = 16.2$ Hz, 1H), 6.25 (d, $J = 16.2$ Hz, 1H), 1.59 (s, 3H), 0.19 (s, 9H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 135.8, 132.4, 128.6, 128.2, 127.6, 126.7, 125.2 (q, $J_{C-F} = 285$ Hz), 76.4 (q, $J_{C-C-F} = 30$ Hz), 21.8, 2.3; HRMS (FAB+) calcd for $C_{14}H_{19}F_3OSi$ M^+ 288.1157, found 288.1150.

Typical Experimental Procedure for Trifluoromethylation of Esters. To a stirred solution of $AcONBu_4$ (6.0 mg, 0.02 mmol) in toluene (0.6 mL) were added successively a solution of 4-$ClC_6H_4CO_2Me$ (70.4 mg, 0.4 mmol) in toluene (0.6 mL) and $TMSCF_3$ (74.8 μL, 0.48 mmol, 95% content) at 0 °C. The reaction mixture slowly warmed to room temperature. The mixture was stirred for 1 h at the same temperature and quenched with saturated aqueous NH_4Cl (1.0 mL). The mixture was extracted with Et_2O and dried over anhydrous Na_2SO_4, and then evaporated. The residue was dissolved in a mixture of HCl (1.0 M, 1.0 mL) and THF (1 mL), and the mixture was stirred for 16 h. The mixture was extracted with AcOEt and the organic layer was washed with brine, dried over anhydrous Na_2SO_4, and then evaporated. After filtration and evaporation of the solvent, the crude product was purified by preparative TLC to afford the corresponding adduct (75.1 mg, 90%).

4′-Chloro-2,2,2-trifluoroacetophenone (29):[18] Colorless oil; IR (ATR) 1717, 1588, 1141, 1091 cm^{-1}; ^{1}H NMR (270 MHz, $CDCl_3$) δ 8.06–7.97 (m, 2H), 7.56–7.50 (m, 2H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 179.3 (q, $J_{C-C-F} = 36$ Hz), 142.4, 131.3 (q, $J_{C-C-C-F} = 2$ Hz), 129.5, 128.1, 116.4 (q, $J_{C-F} = 290$ Hz).

1-(4-Chlorophenyl)-2,2,2-trifluoro-1-methoxy-1-trimethylsilyloxyethane (28): Colorless oil; IR (ATR) 2961, 1255, 1174, 1087, 844 cm^{-1}; ^{1}H NMR (270 MHz, $CDCl_3$) δ 7.52 (d, $J = 8.4$ Hz, 2H), 7.36 (d, $J = 8.4$ Hz, 2H), 3.20 (s, 3H), 0.27 (s, 9H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 135.6, 134.1, 129.7, 128.2, 122.3 (q, $J_{C-F} = 288$ Hz), 98.1 (q, $J_{C-C-F} = 32$ Hz), 50.5, 1.2; HRMS (FAB+) calcd for $C_{12}H_{16}ClF_3O_2Si$ M^+ 312.0560, found 312.0593.

2-(4-Chlorophenyl)-1,1,1,3,3,3-hexafluoro-2-trimethylsilyloxypropane (30): Colorless oil; IR (ATR) 2963, 1198, 1154, 846 cm^{-1}; ^{1}H NMR (270 MHz, $CDCl_3$) δ 7.57 (d, $J = 8.6$ Hz, 2H), 7.44–7.37 (m, 2H), 0.24 (s, 9H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 136.1, 130.4, 128.5, 128.4, 122.4 (q, $J_{C-C-F} = 289$ Hz), 79.6 (h, $J_{C-F} = 30$ Hz), 1.45.

2-(4-Chlorophenyl)-1,1,1,3,3,3-hexafluoropropan-2-ol (31): Colorless oil; IR (ATR) 3325, 1212, 1166, 1097, 924 cm^{-1}; ^{1}H NMR (270 MHz, $CDCl_3$) δ 7.66 (d, $J = 8.9$ Hz, 2H), 7.48–7.40 (m, 2H), 3.84 (brs, 1H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 136.5, 128.8, 128.0 (h, $J_{C-C-C-F} = 2$ Hz), 127.7, 122.4 (q, $J_{C-C-F} = 288$ Hz), 76.8 (h, $J_{C-F} = 30$ Hz); HRMS (ESI) calcd for $C_9H_4ClF_6O$ $[M - H]^-$ 276.9855, found 276.9856.

2,2,2-Trifluoro-4′-methoxyacetophenone (32):[19] Colorless oil; IR (ATR) 2940, 1705, 1600, 1161 cm^{-1}; ^{1}H NMR (270 MHz, $CDCl_3$) δ 8.13–7.95 (m, 2H), 7.08–6.93 (m, 2H), 3.91 (s, 3H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 178.7 (q, $J_{C-C-F} = 35$ Hz), 165.2, 132.6, 122.7, 116.8 (q, $J_{C-F} = 291$ Hz), 114.4, 55.7.

***trans*-1,1,1-Trifluoro-4-phenyl-3-buten-2-one (33):**[6b,20] Colorless oil; IR (ATR) 3066, 1608, 1139, 1053 cm^{-1}; ^{1}H NMR (270 MHz, $CDCl_3$) δ 7.96 (d, $J = 15.9$ Hz, 1H), 7.68–7.60 (m, 2H), 7.55–6.40 (m, 3H), 7.01 (d, $J = 15.9$ Hz, 1H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 179.8 (q, $J_{C-C-F} = 35$ Hz), 150.0, 133.2, 132.2, 129.1, 116.5, 116.3 (q, $J_{C-F} = 291$ Hz).

2,2,2-Trifluoro-1-(4-nitrophenyl)ethan-1,1-diol (34):[21] Pale yellow prisms; mp 105–107 °C; IR (ATR) 3433, 1512, 1283, 1154, 1058, 852 cm^{-1}; ^{1}H NMR (270 MHz, DMSO-d_6) δ 8.27 (d, $J = 8.6$ Hz, 2H), 7.95 (brs, 2H), 7.86 (d, $J = 8.6$ Hz, 2H); ^{13}C NMR (68 MHz, DMSO-d_6) δ 147.9, 145.2, 128.8, 123.0 (q, $J_{C-F} = 288$ Hz), 122.8, 92.2 (q, $J_{C-C-F} = 31$ Hz).

1,1,1-Trifluoro-4-phenyl-2-butanone (35):[6b] Colorless oil; IR (ATR) 2931, 1716, 1150 cm^{-1}; ^{1}H NMR (270 MHz, $CDCl_3$) δ 7.33–7.14 (m, 5H), 3.07–2.92 (m, 4H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 190.4 (q, $J_{C-C-F} = 35$ Hz), 139.1, 128.5, 128.1, 126.5, 115.4 (q, $J_{C-F} = 291$ Hz), 38.0, 28.2.

***N*-(4-Tolylsulfonyl)-4-(2,2,2-trifluoroacetyl)piperidine (36):** White solid; mp 98–100 °C; IR (ATR) 3378, 2849, 1322, 1148 cm^{-1}; ^{1}H NMR (270 MHz, $CDCl_3$) δ 7.65 (d, $J = 8.4$ Hz, 2H), 7.32 (d, $J = 8.4$ Hz, 2H), 3.89–3.71 (m, 2H), 2.51 (s, 3H), 2.30–2.10 (m, 2H), 2.05–1.52 (m, 4H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 192.1 (q, $J_{C-C-F} = 34$ Hz), 134.8, 132.7, 129.7, 127.6, 115.5 (q, $J_{C-F} = 292$ Hz), 45.1, 42.1, 26.5, 21.6; HRMS (FAB+) calcd for $C_{14}H_{16}F_3NO_3SLi$ $[M + Li]^+$ 342.0963, found 342.0935.

Typical Experimental Procedure for Trifluoromethylation of *N*-Ts-aldimines. To a stirred solution of AcOLi (2.6 mg, 0.04 mmol) in DMF (1.0 mL) were added successively a solution of *N*-tosylbenzaldimine (103.7 mg, 0.4 mmol) in DMF (0.2 mL) and $TMSCF_3$ (87.3 μL, 0.56 mmol, 95% content) at −20 °C. The mixture was stirred for 16 h at the same temperature and quenched with saturated aqueous NH_4Cl. The mixture was extracted with AcOEt, and the organic layer was washed with brine and dried over anhydrous Na_2SO_4. After filtration and evaporation of the solvent, the resulting residue was purified by preparative TLC to give the desired product (119.9 mg, 91%).

4-Methyl-*N*-(2,2,2-trifluoro-1-phenylethyl)benzenesulfonamide (38a):[22] Colorless granulars; mp 156–158 °C; IR (ATR) 3250, 1601, 1452, 1329, 1263, 1179, 1121, 1093 cm^{-1}; ^{1}H NMR (270 MHz, $CDCl_3$) δ 7.60 (d, $J = 8.1$ Hz, 2H), 7.34–7.12 (m, 7H), 5.94 (d, $J = 9.2$ Hz, 1H), 4.97–4.82 (m, 1H), 2.35 (s, 3H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 143.7, 136.9, 131.8 (d, $J_{C-C-C-F} =$ 1 Hz), 129.4, 129.2, 128.7, 127.7, 126.9, 123.8 (q, $J_{C-F} =$ 281 Hz), 59.2 (q, $J_{C-C-F} = 32$ Hz), 21.5. Anal. Calcd for $C_{15}H_{14}F_3NO_2S$: C, 54.70; H, 4.28; N, 4.25%. Found: C, 54.53; H, 4.27; N, 4.06%.

4-Methyl-*N*-[2,2,2-trifluoro-1-(4-methoxyphenyl)ethyl]benzenesulfonamide (38b):[8] Colorless granulars; mp 148–149 °C; IR (ATR) 3252, 1613, 1455, 1347, 1252, 1178, 1124, 1082 cm^{-1}; ^{1}H NMR (270 MHz, $CDCl_3$) δ 7.60 (d, $J = 8.4$ Hz, 2H), 7.17 (d, $J = 8.9$ Hz, 2H), 7.10 (d, $J = 8.9$ Hz, 2H), 6.76 (d, $J = 8.4$ Hz, 2H), 5.54 (d, $J = 9.2$ Hz, 1H), 4.93–4.79 (m, 1H), 3.77 (s, 3H), 2.38 (s, 3H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 160.1, 143.6, 136.9, 129.4, 128.9 (d, $J_{C-C-C-F} = 1$ Hz), 126.9, 123.9 (q, $J_{C-F} = 281$ Hz), 123.8 (d, $J_{C-C-C-F} = 1$ Hz), 114.1, 58.7 (q, $J_{C-C-F} = 32$ Hz), 55.3, 21.6. Anal. Calcd for $C_{16}H_{16}F_3NO_3S$: C, 53.48; H, 4.49; N, 3.90%. Found: C, 53.16; H, 4.36; N, 3.57%.

4-Methyl-*N*-[2,2,2-trifluoro-1-(4-methylphenyl)ethyl]benzene-

sulfonamide (38c):[8] Colorless granulars; mp 186–188 °C; IR (ATR) 3256, 1457, 1325, 1263, 1181 cm^{-1}; ^{1}H NMR (270 MHz, $CDCl_3$) δ 7.61 (d, J = 8.1 Hz, 2H), 7.16 (d, J = 8.1 Hz, 2H), 7.05 (s, 4H), 5.73 (d, J = 9.5 Hz, 1H), 4.93–4.79 (m, 1H), 2.37 (s, 3H), 2.30 (s, 3H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 143.6, 139.2, 136.9, 129.4, 129.3, 128.9, 127.5 (d, $J_{C-C-C-F}$ = 1 Hz), 126.9, 123.9 (q, J_{C-F} = 281 Hz), 58.9 (q, J_{C-C-F} = 32 Hz), 21.6, 21.2. Anal. Calcd for $C_{16}H_{16}F_3NO_2S$: C, 55.97; H, 4.70; N, 4.08%. Found: C, 55.70; H, 4.60; N, 3.68%.

***N*-[1-(4-Chlorophenyl)-2,2,2-trifluoroethyl]-4-methylbenzenesulfonamide (38d):**[22] Colorless granulars; mp 196–198 °C; IR (ATR) 3250, 1603, 1499, 1336, 1185, 1091 cm^{-1}; ^{1}H NMR (270 MHz, $CDCl_3$) δ 7.59 (d, J = 7.8 Hz, 2H), 7.28–7.08 (m, 6H), 6.06 (d, J = 9.5 Hz, 1H), 4.97–4.82 (m, 1H), 2.39 (s, 3H); ^{13}C NMR (68 MHz, DMSO-d_6) δ 142.6, 137.7, 131.1, 130.0, 129.1, 128.0, 126.2, 125.4, 123.7 (q, J_{C-F} = 281 Hz), 57.1 (q, J_{C-C-F} = 31 Hz), 20.8. Anal. Calcd for $C_{15}H_{13}ClF_3NO_2S$: C, 49.52; H, 3.60; N, 3.85%. Found: C, 49.26; H, 3.61; N, 4.07%.

***N*-[1-(4-Bromophenyl)-2,2,2-trifluoroethyl]-4-methylbenzenesulfonamide (38e):**[22] Colorless granulars; mp 221–223 °C; IR (ATR) 3250, 1600, 1495, 1333, 1183, 1135 cm^{-1}; ^{1}H NMR (270 MHz, DMSO-d_6) δ 9.20 (d, J = 9.7 Hz, 1H), 7.51 (d, J = 8.1 Hz, 2H), 7.43 (d, J = 8.6 Hz, 2H), 7.32 (d, J = 8.6 Hz, 2H), 7.18 (d, J = 8.1 Hz, 2H), 5.40–5.24 (m, 1H), 2.29 (s, 3H); ^{13}C NMR (68 MHz, DMSO-d_6) δ 142.6, 137.6, 131.5, 131.0, 130.3, 129.1, 126.2, 123.9 (q, J_{C-F} = 281 Hz), 122.1, 57.2 (q, J_{C-C-F} = 31 Hz), 20.9; Anal. Calcd for $C_{15}H_{13}BrF_3NO_2S$: C, 44.13; H, 3.21; N, 3.43%. Found: C, 44.01; H, 3.10; N, 3.50%.

4-Methyl-*N*-[2,2,2-trifluoro-1-(4-nitrophenyl)ethyl]benzenesulfonamide (38f): Colorless granulars; mp 164–165 °C; IR (ATR) 3254, 1537, 1349, 1263, 1183, 1166, 1086 cm^{-1}; ^{1}H NMR (270 MHz, $CDCl_3$) δ 8.12 (d, J = 8.4 Hz, 2H), 7.62 (d, J = 8.4 Hz, 2H), 7.43 (d, J = 8.4 Hz, 2H), 7.19 (d, J = 8.4 Hz, 2H), 6.05 (d, J = 8.9 Hz, 1H), 5.12–4.95 (m, 1H), 2.38 (s, 3H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 148.3, 144.4, 138.5, 136.4, 129.7, 129.0, 126.9, 123.8, 123.3 (q, J_{C-F} = 281 Hz), 58.6 (q, J_{C-C-F} = 32 Hz), 21.6; Anal. Calcd for $C_{15}H_{13}F_3N_2O_4S$: C, 48.13; H, 3.50; N, 7.48%. Found: C, 47.93; H, 3.34; N, 7.32%.

4-Methyl-*N*-[2,2,2-trifluoro-1-(2-naphthyl)ethyl]benzenesulfonamide (38g):[3g] Colorless granulars; mp 154–155 °C; IR (ATR) 3252, 1598, 1454, 1336, 1267, 1191, 1126 cm^{-1}; ^{1}H NMR (270 MHz, DMSO-d_6) δ 9.28 (d, J = 10.3 Hz, 1H), 7.89–7.72 (m, 4H), 7.55–7.46 (m, 5H), 7.03 (d, J = 8.6 Hz, 2H), 5.46–5.30 (m, 1H), 2.07 (s, 3H); ^{13}C NMR (68 MHz, DMSO-d_6) δ 142.4, 137.7, 132.5, 132.0, 129.4, 128.9, 128.0, 127.8, 127.3, 126.5, 126.4, 126.3, 126.1, 125.0, 124.3 (q, J_{C-F} = 281 Hz), 58.1 (q, J_{C-C-F} = 31 Hz), 20.9; Anal. Calcd for $C_{19}H_{16}F_3NO_2S$: C, 60.15; H, 4.25; N, 3.69%. Found: C, 59.86; H, 4.23; N, 3.68%.

4-Methyl-*N*-[2,2,2-trifluoro-1-(2-furyl)ethyl]benzenesulfonamide (38h): Colorless granulars; mp 140–142 °C; IR (ATR) 3244, 1454, 1330, 1268, 1184, 1167, 1091 cm^{-1}; ^{1}H NMR (270 MHz, $CDCl_3$) δ 7.66 (d, J = 8.4 Hz, 2H), 7.27 (d, J = 7.8 Hz, 1H), 7.23 (d, J = 8.4 Hz, 2H), 6.27 (s, 2H), 5.39 (d, J = 9.7 Hz, 1H), 5.12–4.98 (m, 1H), 2.40 (s, 3H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 144.2, 143.8, 143.5, 136.7, 129.5, 126.8, 122.8 (q, J_{C-F} = 281 Hz), 110.6, 110.4, 53.3 (q, J_{C-C-F} = 34 Hz), 21.6; Anal. Calcd for $C_{13}H_{12}F_3NO_3S$: C, 48.90; H, 3.79; N, 4.39%. Found: C, 48.84; H, 3.56; N, 4.22%.

4-Methyl-*N*-[2,2,2-trifluoro-1-(4-pyridyl)ethyl]benzenesulfonamide (38i): Colorless granulars; mp 194–197 °C (dec.); IR (ATR) 3045, 2738, 1607, 1339, 1183, 1164 cm^{-1}; ^{1}H NMR (270 MHz, DMSO-d_6) δ 9.37 (d, J = 10.3 Hz, 1H), 8.44 (d, J = 5.1 Hz, 2H), 7.54 (d, J = 8.1 Hz, 2H), 7.40 (d, J = 8.1 Hz, 2H), 7.19 (d, J = 5.1 Hz, 2H), 5.52–5.36 (m, 1H), 2.27 (s, 3H); ^{13}C NMR (68 MHz, DMSO-d_6) δ 149.4, 142.8, 140.7, 137.5, 129.1, 126.2, 123.8 (q, J_{C-F} = 281 Hz), 123.0, 56.8 (q, J_{C-C-F} = 31 Hz), 20.9; Anal. Calcd for $C_{14}H_{13}F_3N_2O_2S$: C, 50.90; H, 3.97; N, 8.48%. Found: C, 50.83; H, 3.98; N, 8.39%.

4-Methyl-*N*-(1,1,1-trifluoro-4-phenylbut-3-en-2-yl)benzenesulfonamide (38j):[8] Colorless granulars; mp 116–118 °C; IR (ATR) 3253, 1598, 1452, 1265, 1185, 1127 cm^{-1}; ^{1}H NMR (270 MHz, $CDCl_3$) δ 7.76 (d, J = 8.1 Hz, 2H), 7.34–7.16 (m, 7H), 6.49 (d, J = 15.9 Hz, 1H), 5.90 (dd, J = 15.9, 7.0 Hz, 1H), 5.26 (d, J = 9.2 Hz, 1H), 4.65–4.50 (m, 1H), 2.34 (s, 3H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 143.9, 137.2, 136.8, 134.8, 129.6 (d, $J_{C-C-C-F}$ = 1 Hz), 128.7, 128.5, 127.0, 126.7, 123.8 (q, J_{C-F} = 281 Hz), 118.1 (q, $J_{C-C-C-F}$ = 2 Hz), 57.5 (q, J_{C-C-F} = 32 Hz), 21.5; Anal. Calcd for $C_{17}H_{16}F_3NO_2S$: C, 57.46; H, 4.54; N, 3.94%. Found: C, 57.35; H, 4.50; N, 3.56%.

***N*-[1-(*t*-Butyl)-2,2,2-trifluoroethyl]-4-methylbenzenesulfonamide (38k):** Colorless needles; mp 178–179 °C; IR (ATR) 3296, 2985, 1477, 1327, 1265, 1173, 1094 cm^{-1}; ^{1}H NMR (270 MHz, $CDCl_3$) δ 7.74 (d, J = 8.1 Hz, 2H), 7.28 (d, J = 8.1 Hz, 2H), 5.13 (d, J = 10.0 Hz, 1H), 3.84–3.66 (m, 1H), 2.42 (s, 3H), 1.05 (s, 9H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 143.4, 138.0, 129.4, 126.7, 125.2 (q, J_{C-F} = 283 Hz), 62.7 (q, J_{C-C-F} = 28 Hz), 34.0, 27.2 (q, $J_{C-C-C-F}$ = 2 Hz), 21.6; Anal. Calcd for $C_{13}H_{18}F_3NO_2S$: C, 50.47; H, 5.86; N, 4.53%. Found: C, 50.16; H, 5.62; N, 4.27%.

***N*-(1-Cyclohexyl-2,2,2-trifluoroethyl)-4-methylbenzenesulfonamide (38l):** White solid; mp 130–132 °C; IR (ATR) 3279, 2936, 1454, 1332, 1175, 1122 cm^{-1}; ^{1}H NMR (270 MHz, $CDCl_3$) δ 7.74 (d, J = 8.1 Hz, 2H), 7.29 (d, J = 8.1 Hz, 2H), 4.94 (d, J = 10.3 Hz, 1H), 3.88–3.72 (m, 1H), 2.42 (s, 3H), 1.85–1.55 (m, 6H), 1.35–0.95 (m, 5H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 143.5, 137.9, 129.4, 126.9, 124.8 (q, J_{C-F} = 283 Hz), 59.5 (q, J_{C-C-F} = 29 Hz), 37.7, 29.9, 27.0 (q, $J_{C-C-C-F}$ = 1 Hz), 26.0, 25.8, 25.7, 21.6; Anal. Calcd for $C_{15}H_{20}F_3NO_2S$: C, 53.72; H, 6.01; N, 4.18%. Found: C, 53.37; H, 5.78; N, 3.96%.

4-Methyl-*N*-(3-phenyl-1-trifluoromethylpropyl)benzenesulfonamide (38m): White solid; mp 109–111 °C; IR (ATR) 3255, 2938, 1454, 1342, 1129 cm^{-1}; ^{1}H NMR (270 MHz, $CDCl_3$) δ 7.74 (d, J = 8.4 Hz, 2H), 7.33–7.05 (m, 7H), 4.93 (d, J = 9.7 Hz, 1H), 4.04–3.84 (m, 1H), 2.86–2.57 (m, 2H), 2.43 (s, 3H), 2.16–2.02 (m, 1H), 1.86–1.66 (m, 1H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 143.8, 139.7, 137.5, 129.6, 128.5, 128.3, 126.9, 126.3, 124.6 (q, J_{C-F} = 281 Hz), 55.0 (q, J_{C-C-F} = 29 Hz), 31.1 (q, $J_{C-C-C-F}$ = 2 Hz), 31.0, 21.7; HRMS (FAB+) calcd for $C_{17}H_{19}F_3NO_2S$ $[M+H]^+$ 358.1089, found 358.1082.

4-Chloro-*N*-(2,2,2-trifluoro-1-phenylethyl)benzenesulfonamide (45): Colorless needles; mp 172–174 °C; IR (ATR) 3251, 1461, 1346, 1265, 1174, 1127 cm^{-1}; ^{1}H NMR (270 MHz, DMSO-d_6) δ 9.40 (brs, 1H), 7.64 (d, J = 8.6 Hz, 2H), 7.44 (d, J = 8.6 Hz, 2H), 7.40–7.34 (m, 2H), 7.32–7.18 (m, 3H), 5.35–5.22 (m, 1H); ^{13}C NMR (68 MHz, DMSO-d_6) δ 139.4, 137.1, 131.8, 128.7, 128.6, 128.1, 126.6, 124.1 (q, J_{C-F} = 281 Hz), 57.8 (q, J_{C-C-F} = 31 Hz); Anal. Calcd for $C_{14}H_{11}ClF_3NO_2S$: C, 48.08; H, 3.17; N, 4.00%. Found: C, 48.01; H, 3.27; N, 3.80%.

4-Nitro-*N*-(2,2,2-trifluoro-1-phenylethyl)benzenesulfonamide (46): Colorless granulars; mp 153–154 °C; IR (ATR) 3268, 1524, 1351, 1190, 1134 cm^{-1}; ^{1}H NMR (270 MHz, DMSO-d_6) δ 9.71 (d, J = 10.0 Hz, 1H), 8.21 (d, J = 8.6 Hz, 2H), 7.89 (d, J = 8.6 Hz, 2H), 7.48–7.36 (m, 2H), 7.28–7.16 (m, 3H), 5.48–5.32 (m, 1H); ^{13}C NMR (68 MHz, DMSO-d_6) δ 149.1, 146.0, 131.7, 129.0, 128.1, 128.1, 127.8, 124.1 (q, J_{C-F} = 281 Hz), 124.0, 57.9 (q,

$J_{C-C-F} = 31$ Hz); Anal. Calcd for $C_{14}H_{11}F_3N_2O_4S$: C, 46.67; H, 3.08; N, 7.77%. Found: C, 46.59; H, 3.11; N, 7.60%.

2-Nitro-*N*-(2,2,2-trifluoro-1-phenylethyl)benzenesulfonamide (47): Colorless needles; mp 105–106 °C; IR (ATR) 3309, 1537, 1360, 1183, 1130 cm^{-1}; ^{1}H NMR (270 MHz, $CDCl_3$) δ 7.86 (dd, $J = 7.6$, 1.6 Hz, 1H), 7.79 (dd, $J = 7.6$, 1.4 Hz, 1H), 7.62 (dd, $J = 7.6$, 1.4 Hz, 1H), 7.52 (dd, $J = 7.6$, 1.6 Hz, 1H), 7.26–7.18 (m, 5H), 6.41 (d, $J = 10.0$ Hz, 1H), 5.11 (dq, $J = 10.0$, 7.6 Hz, 1H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 147.1, 133.9, 133.6, 132.8, 130.9, 130.4, 129.5, 128.8, 127.6, 125.3, 123.6 (q, $J_{C-F} = 281$ Hz), 60.0 (q, $J_{C-C-F} = 32$ Hz); Anal. Calcd for $C_{14}H_{11}F_3N_2O_4S$: C, 46.67; H, 3.08; N, 7.77%. Found: C, 46.36; H, 3.08; N, 7.43%.

***N*-(2,2,2-Trifluoro-1-phenylethyl)diphenylphosphinamide (48):** White solid; mp 214–216 °C; IR (ATR) 3192, 1438, 1253, 1187, 1119 cm^{-1}; ^{1}H NMR (270 MHz, $CDCl_3$) δ 7.92–7.82 (m, 2H), 7.77–7.67 (m, 2H), 7.58–7.26 (m, 11H), 4.79–4.60 (m, 1H), 3.83 (dd, $J = 11.3$, 7.8 Hz, 1H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 134.5, 132.4, 132.3, 132.2, 132.2, 132.1, 132.1, 132.0, 131.9, 130.5, 130.3, 128.9, 128.7, 128.6, 128.5, 128.4, 128.3, 127.6, 124.7 (dq, $J_{C-F} = 281$, 8 Hz), 56.8 (q, $J_{C-C-F} = 31$ Hz); Anal. Calcd for $C_{20}H_{17}F_3NOP$: C, 64.00; H, 4.57; N, 3.73%. Found: C, 64.01; H, 4.40; N, 3.53%.

4-Methyl-*N*-(2,2,3,3,3-pentafluoro-1-phenylpropyl)benzenesulfonamide (55): Colorless needles; mp 180–182 °C; IR (ATR) 3261, 1462, 1335, 1189, 1169, 1029 cm^{-1}; ^{1}H NMR (270 MHz, $CDCl_3$) δ 7.52 (d, $J = 8.4$ Hz, 2H), 7.30–7.16 (m, 3H), 7.13–7.04 (m, 4H), 5.71 (d, $J = 10.5$ Hz, 1H), 4.96 (dt, $J = 16.2$, 10.5 Hz, 1H), 2.32 (s, 3H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 143.6, 136.7, 131.3, 129.3, 129.1, 128.6, 128.0, 126.9, 120.7, 116.6, 116.4, 112.8 (121–112 ppm: multiple peaks), 57.7 (dd, $J_{C-C-F} =$ 26, 21 Hz), 21.5; Anal. Calcd for $C_{16}H_{14}F_5NO_2S$: C, 50.66; H, 3.72; N, 3.69%. Found: C, 50.36; H, 3.55; N, 3.47%.

***N*-(2,2,3,3,4,4,4-Heptafluoro-1-phenylbutyl)-4-methylbenzenesulfonamide (56):** Colorless needles; mp 114–115 °C; IR (ATR) 3280, 1460, 1347, 1224, 1167 cm^{-1}; ^{1}H NMR (270 MHz, $CDCl_3$) δ 7.52 (d, $J = 8.1$ Hz, 2H), 7.28–7.01 (m, 7H), 6.09 (d, $J = 10.8$ Hz, 1H), 5.05 (dt, $J = 15.9$, 10.8 Hz, 1H), 2.31 (s, 3H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 143.6, 136.7, 131.3, 129.3, 129.2, 128.6, 128.1, 126.9, 120.1, 119.6, 118.9, 118.5, 115.4, 115.1, 114.9, 114.6, 114.2, 113.2, 112.7, 110.8, 110.4, 109.9, 109.3, 108.8, 108.2, 104.9 (121–104 ppm: multiple peaks), 57.9 (dd, $J_{C-C-F} = 26$, 22 Hz), 21.5; Anal. Calcd for $C_{17}H_{14}F_7NO_2S$: C, 47.56; H, 3.29; N, 3.26%. Found: C, 47.55; H, 3.14; N, 2.97%.

Ethyl 2,2-Difluoro-3-phenyl-3-(4-tolylsulfonylamino)propionate (57): Colorless granulars; mp 105–106 °C; IR (ATR) 3251, 1782, 1326, 1169, 1058 cm^{-1}; ^{1}H NMR (270 MHz, $CDCl_3$) δ 7.53 (d, $J = 8.1$ Hz, 2H), 7.28–7.06 (m, 7H), 5.45 (d, $J = 9.7$ Hz, 1H), 5.02 (dt, $J = 16.2$, 9.7 Hz, 1H), 4.22 (q, $J = 7.0$ Hz, 2H), 2.33 (s, 3H), 1.25 (t, $J = 7.0$ Hz, 3H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 162.4 (dd, $J_{C-C-F} = 32$, 31 Hz), 143.4, 137.0, 131.8, 129.3, 128.9, 128.4, 128.1 (t, $J_{C-C-C-F} = 1$ Hz), 126.9, 113.5 (dd, $J_{C-F} = 256$, 258 Hz), 63.5, 59.7 (dd, $J_{C-C-F} = 27$, 24 Hz), 21.5, 13.8; Anal. Calcd for $C_{18}H_{19}F_2NO_4S$: C, 56.39; H, 5.00; N, 3.65%. Found: C, 56.24; H, 4.93; N, 3.39%.

***N*-[2,2-Difluoro-1-phenyl-2-(4-trifluoromethylphenyl)ethyl]-4-methylbenzenesulfonamide (58):** Colorless granulars; mp 156–157 °C; IR (ATR) 3313, 1326, 1157, 1088 cm^{-1}; ^{1}H NMR (270 MHz, $CDCl_3$) δ 7.51 (d, $J = 8.1$ Hz, 2H), 7.48–7.40 (m, 2H), 7.32 (d, $J = 8.1$ Hz, 2H), 7.26–7.09 (m, 3H), 7.08 (d, $J = 8.1$ Hz, 2H), 7.02–6.96 (m, 2H), 5.61 (d, $J = 9.5$ Hz, 1H), 4.87 (dt, $J = 12.7$, 9.5 Hz, 1H), 2.32 (s, 3H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 143.3, 137.0, 129.2, 128.6, 128.3, 128.2, 128.1, 128.1, 126.8, 126.5 (t, $J_{C-C-F} = 24$ Hz), 125.1 (q, $J_{C-C-F} = 4$ Hz), 123.5 (q, $J_{C-F} = 272$ Hz), 119.9, 63.1 (t, $J_{C-C-F} = 29$ Hz), 21.4; Anal. Calcd for $C_{22}H_{18}F_5NO_2S$: C, 58.02; H, 3.98; N, 3.08%. Found: C, 58.11; H, 3.90; N, 2.78%.

X-ray Crystal Structure Analyses of 34. $C_8H_6F_3NO_4$ (FW = 237.13), monoclinic, $P1$, $a = 9.686(5)$ Å, $b = 11.341(3)$ Å, $c = 8.730(3)$ Å, $\alpha = 103.47(2)°$, $\beta = 96.95(3)°$, $\gamma = 91.78(3)°$, $V = 924.0(6)$ Å^3, $Z = 4.0$, $D_{calcd} = 1.705$ g cm^{-3}, $T = 295$ K. X-ray intensities were measured on a Rigaku AFC-5S diffractometer with graphite-monochromated Mo Kα radiation. The final R factors was 0.066 ($Rw = 0.156$ for all data) for 4255 reflections with $I > 2\sigma(I)$. Crystallographic data have been deposited with Cambridge Crystallographic Data Centre: Deposition number CCDC-601469. Copies of the data can be obtained free of charge via http://www.ccdc.cam.ac.uk/conts/retrieving.html (or from the Cambridge Crystallographic Data Centre, 12, Union Road, Cambridge, CB2 1EZ, UK; Fax: +44 1223 336033; e-mail: deposit@ccdc.cam.ac.uk).

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