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Silver-Mediated Direct sp^3 C–H Bond Functionalization

Taigang Zhou and Zhang-Jie Shi

Abstract Direct sp^3 C–H bond functionalization is an efficient, straightforward, and powerful method to construct new C–X (X=C, N, F, S) bonds from nonfunctionalized aliphatic motif of organic molecules, which has been used in late-stage modification of complex molecules. In this chapter, the recent developments of silver-mediated direct sp^3 C–H functionalizations are reviewed, categorized by C–C bond formation (C–H insertion), C–N bond formation (intramolecular and intermolecular amination/amidation), C–F bond formation, and C–S bond formation.

Keywords C–X (X=C, N, F, S) formation • Silver • sp^3 C–H functionalization

Contents

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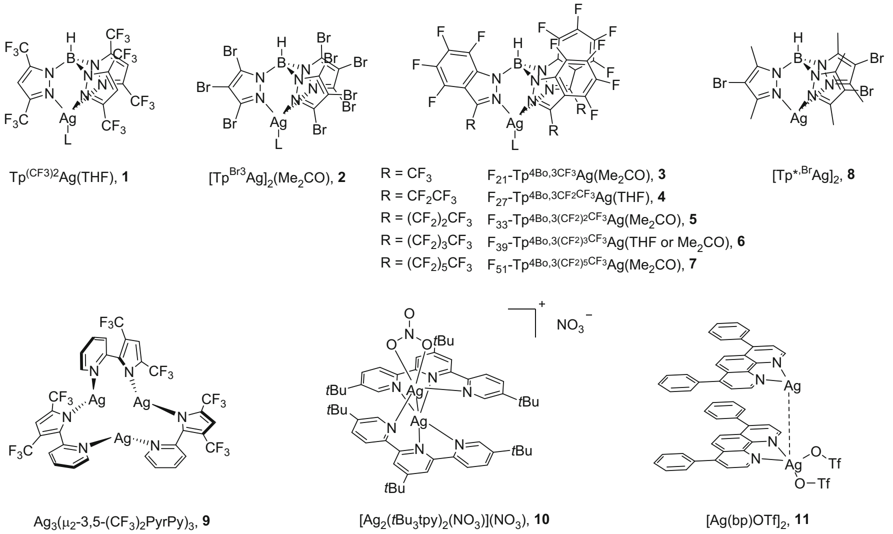
Abbreviations

BHT	2,6-Di-tert-butyl-4-methylphenol
Bo	Benzo
bp	4,7-Diphenyl-1,10-phenanthroline
d.r.	Diastereoselectivity ratio
DCE	Dichloroethane
DCM	Dichloromethane
EDA	Ethyl diazoacetate
h	Hour(s)
L	Ligand
L-Men	L-Menthyl
Me	Methyl
Ns	*p*-Nitrosulfonyl
Ph	Phenyl
Py	Pyridine
Pyr	Pyrrole
rt	Room temperature
$scCO_2$	Supercritical carbon dioxide
^{t}Bubipy	4,4′-Di-*tert*-butyl-2,2′-bipyridine
THF	Tetrahydrofuran
Tp	Tris(pyrazolyl)borate
tpa	Tris(2-pyridylmethyl)amine
Ts	*p*-Toluenesulfonyl

1 Introduction

As a noble metal, silver becomes one of the most important metals in the life of human beings, which has been used as currency and ornaments by humans for thousands of years. Nowadays, silver and its salts have been widely used in photography, electrical equipment, jewelry, as well as transition metal for catalysis in chemistry. In chemical research, silver complexes were usually thought to be low activity and used as either co-catalysts [1, 2] or Lewis acids [3] for decades. In recent years, a wide range of important organic transformation has been catalyzed by silver complexes, including C–H insertion, amination/amidation, fluorination, hydrosilylation, decarboxylation, and so on [4–12].

Direct sp^3 C–H bond functionalization has attracted much attention in the past few decades, which presents high efficient, atom-economical pathways to construct new functional groups from easily available chemicals. Most of present C–H bond transformations need to use expensive metals, such as palladium, rhodium, iridium, etc. [13]. Compared to these metals, silver is relatively economically attractive and has been proved highly efficient for C–H activation in recent years, in particular, silver-mediated sp^3 C–H bond transformation. Diverse Ag complexes exhibited



$Tp^{(CF_3)2}Ag(THF)$, **1**

$[Tp^{Br3}Ag]_2(Me_2CO)$, **2**

R = CF_3 F_{21}-$Tp^{4Bo,3CF_3}Ag(Me_2CO)$, **3**
R = CF_2CF_3 F_{27}-$Tp^{4Bo,3CF_2CF_3}Ag(THF)$, **4**
R = $(CF_2)_2CF_3$ F_{33}-$Tp^{4Bo,3(CF_2)_2CF_3}Ag(Me_2CO)$, **5**
R = $(CF_2)_3CF_3$ F_{39}-$Tp^{4Bo,3(CF_2)_3CF_3}Ag$(THF or Me_2CO), **6**
R = $(CF_2)_5CF_3$ F_{51}-$Tp^{4Bo,3(CF_2)_5CF_3}Ag(Me_2CO)$, **7**

$[Tp^{*,Br}Ag]_2$, **8**

$Ag_3(\mu_2\text{-}3,5\text{-}(CF_3)_2PyrPy)_3$, **9**

$[Ag_2(tBu_3tpy)_2(NO_3)](NO_3)$, **10**

$[Ag(bp)OTf]_2$, **11**

Scheme 1 Silver complexes involved in sp^3 C–H bond transformation

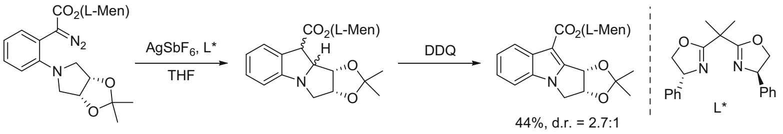
their unprecedented reactivity in this field, which will be discussed in the text (Scheme 1). This chapter will focus on a variety of sp^3 C–H functionalizations catalyzed by different silver complexes.

2 Silver-Mediated Direct sp^3 C–H Transformations

2.1 *Direct C–C Bond Formation*

C–C bond formation is a major task in synthetic chemistry, and direct C–C bond formation through sp^3 C–H transformation is an ideal method. Up to date, only a few examples were reported via silver catalysts in this field. In 1996, Burgess and coworkers described the earliest work of silver-mediated intramolecular carbene insertion toward C–H bonds (Scheme 2) [14]. They examined 96 potential systems of ligand/metal/solvent combinations to optimize such a C–H insertion reaction. Silver hexafluoroantimonate(V) ($AgSbF_6$) together with bis(oxazolidine) ligand L* in THF showed an unexpected activity and gave desired insertion products in moderate yield (44%) and diastereoselectivity (2.7:1).

A family of tris(pyrazolyl)borate (Tp) silver complexes (Scheme 1, catalysts **1**–**7**) have been independently developed by Dias and Pérez's groups, which proved to be efficient for carbene insertion in sp^3 C–H bonds with diazoacetates [8, 15–24]. For example, in 2004, Dias, Lovely, and coworkers reported early examples of carbene insertion into sp^3 C–H bond of alkanes and ethers by silver with tris (pyrazolyl)borate complex **1** [18, 19]. In this reaction, using neat alkane as substrate



Scheme 2 Intramolecular carbene insertion into C–H bond with silver catalyst

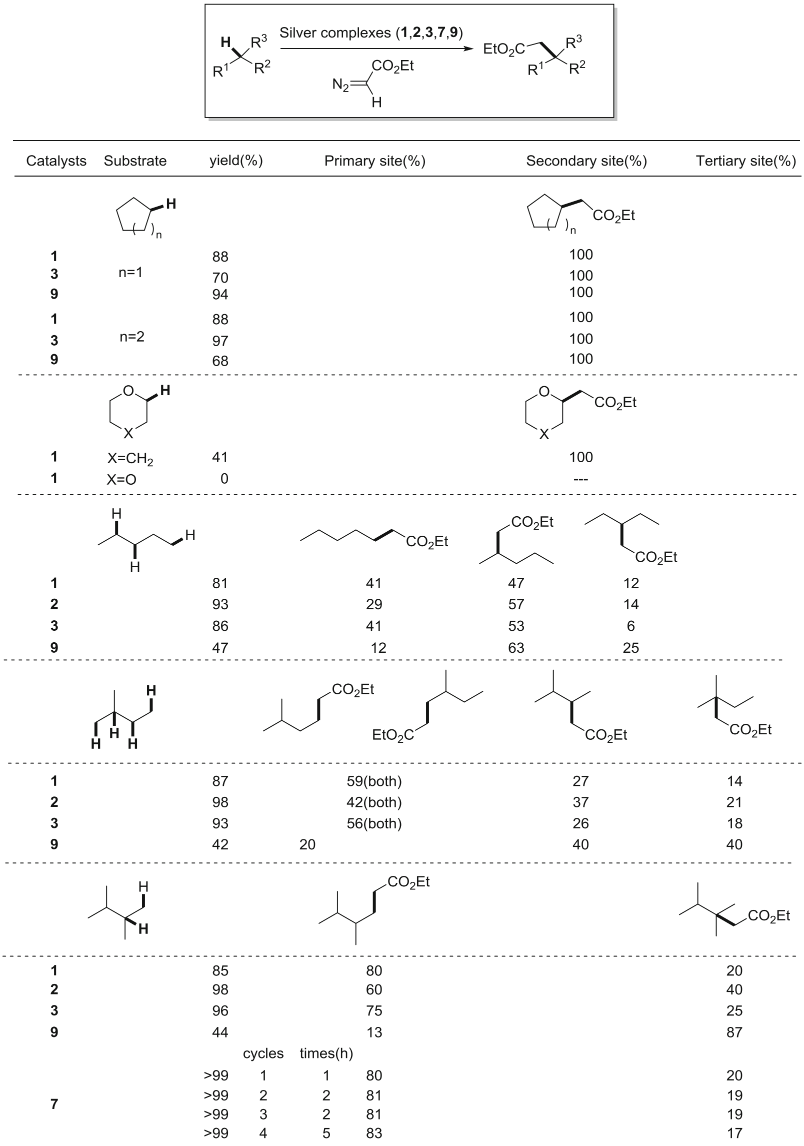
and solvent, 5 mol% $[\mathrm{Tp}^{(\mathrm{CF3})2}]\mathrm{Ag(THF)}$ **1** as catalyst (Scheme 1), and ethyl diazoacetate (EDA) as a carbene source, the desired carbene insertion products were observed with moderate to excellent yield (41–88%, Scheme 3). All primary, secondary, and tertiary sp^3 C–H bonds of alkanes worked well in this transformation. The regioselectivity for the carbene insertion was favored at the primary and secondary sites. However, cyclic ethers were not suitable substrates and showed low activity, presumably due to highly coordinating ability of cyclic ethers.

Pérez's group has focused on modification of tris(pyrazolyl)borate silver complexes for several years. In 2005, Pérez and coworkers developed a highly active silver catalyst $[\mathrm{Tp}^{\mathrm{Br3}}\mathrm{Ag}]_2(\mathrm{Me_2CO})$ **2** for the transformation of sp^3 C–H bond of alkanes with carbene species (Scheme 3) [20]. Compared to silver catalyst **1**, the substitution of ligand in silver catalysts **2** was changed from CF_3 (catalyst **1**) to Br (catalyst **2**) and showed higher efficiency of carbene insertion into sp^3 C–H bonds of various alkanes with EDA. However, the drawback of these silver catalysts is the high catalyst loading (5%) with quite a low turnover numbers. Thus, efficient silver complexes for this transformation were still highly appealing.

After developing the promising catalyst **2**, Pérez and coworkers further reported a new silver complex with perfluorinated tris(pyrazolyl)borate ligand $[\mathrm{F}_{21}\text{-}\mathrm{Tp}^{4\mathrm{Bo},3\mathrm{CF3}}]\mathrm{Ag(Me_2CO)}$ **3**, which can catalyze carbene insertion into sp^3 C–H bond of alkanes with EDA [21]. A variety of alkanes and cycloalkanes were evaluated in the reaction (Scheme 3). Compared to catalyst **1** and **2**, the similar results were achieved with catalyst **3**, while with a low catalyst loading (0.5%) and high turnover numbers.

In 2011, Asensio, Etienne, Pérez, and coworkers reported a first example of carbene insertion into methane sp^3 C–H bond by silver catalysts (Scheme 4) [22]. The reaction was performed using $\mathrm{Tp}^{\mathrm{X}}\mathrm{Ag}$ (silver complexes **2**, **3**, **4**) as the catalysts and ethyl diazoacetate as a carbene source. $ScCO_2$ as the solvent was the key for the success of this transformation. Although silver catalyst was only sparingly soluble in mixture of methane/$scCO_2$, silver complexes **3** or **4** gave approximately 7% desired insertion product, respectively, whereas complex **2** led to a trace amount of product. Nineteen percent yield of ethyl propionate was obtained after the optimization of conditions. Ethane and *n*-pentane also underwent this transformation in $scCO_2$. Additionally, in 2014, Pérez and coworkers also developed a catalytic method for functionalization of methane and light alkanes with EDA in $scCO_2$ based with these fluorinated silver complexes (catalysts **3**–**7**) [23].

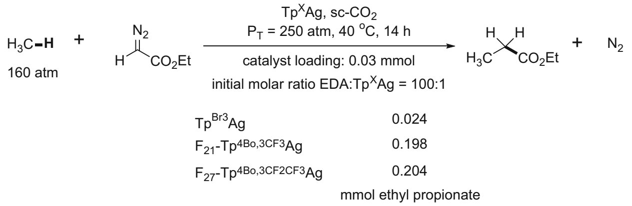
Later on, more fluorinated silver complexes (catalysts **5**–**7**) were developed by Pérez and coworkers [24]. Most of those complexes efficiently catalyzed carbene



Catalysts	Substrate	yield(%)			Primary site(%)		Secondary site(%)		Tertiary site(%)
1	n=1	88					100		
3		70					100		
9		94					100		
1	n=2	88					100		
3		97					100		
9		68					100		
1	X=CH$_2$	41					100		
1	X=O	0					---		
1		81			41		47	12	
2		93			29		57	14	
3		86			41		53	6	
9		47			12		63	25	
1		87			59(both)		27		14
2		98			42(both)		37		21
3		93			56(both)		26		18
9		42			20		40		40
1		85			80				20
2		98			60				40
3		96			75				25
9		44			13				87
			cycles	times(h)					
7		>99	1	1	80				20
		>99	2	2	81				19
		>99	3	2	81				19
		>99	4	5	83				17

Scheme 3 Silver complex-catalyzed carbene insertion into sp^3 C–H bonds

insertion into alkane sp^3 C–H bond with EDA in quantitative yield. More importantly, those silver complexes could be separated and reused several times without loss of efficacy and chemo- and regioselectivities under a fluorous phase (Fomblin or perfluorophenanthrene). For example, by using 2,3-dimethylbutane (1 mL, 7.6 mmol) as the substrate, silver complex **7** (0.005 mmol) F$_{51}$-Tp$^{4Bo,3(CF2)}$ ^{5CF3}Ag(acetone) as the catalyst, ethyl diazoacetate (10.5 μL, 0.1 mmol) as a carbene

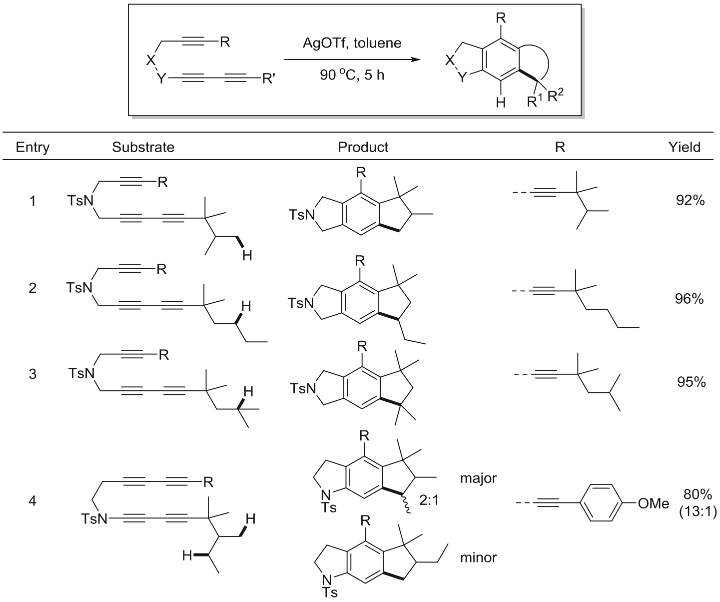


Scheme 4 Silver-mediated methane sp^3 C–H transformation by Pérez et al.

source, and Fomblin HVAC 140/13 (4.0 mL, 1.2 mmol) as the fluorous medium, the desired product and starting material were collected by trap-to-trap vacuum distillation at room temperature after the first catalytic cycle run in good efficiency. Then the fresh starting material (1 mL) and EDA (10.5 μL) were added to the distillation which contained soluble catalyst and the fluorous phase for the second run. This procedure could be repeated several times. The results were shown in Scheme 3. The catalyst **7** was used 4 times and observed identical chemo- and regioselectivity with a slight increase of the reaction time.

Besides a series of tris(pyrazolyl)borate silver complexes, another type of silver complex **9**, discovered by Caulton, Mindiola, and coworkers, could also catalyze carbene insertion into alkane sp^3 C–H bonds [25]. This silver complex was easily prepared from Ag_2O with a bidentated ligand (H(3,5-$(CF_3)_2$PyrPy). This complex was an air- and water-stable complex, existing as a trinuclear form. A series of alkanes, including cyclic, linear, and branched alkanes, were functionalized with complex **9** at 25°C in moderate to excellent yield (Scheme 3). Interestingly, compared with the results from Dias and Pérez's groups by using Tp^XAg complexes, the opposite regioselectivity was observed from Mindiola's group by using complex **9**. For example, the regioselectivity for the carbene insertion into 2,3-dimethylbutane C–H bond with complex **9** favored at the tertiary site over the primary site (ratio 6.7:1, Scheme 3), whereas complex **3** favored at the primary site over tertiary site (ratio 3:1). The yields of functionalization of linear and branched alkanes with complex **9** were moderate due to the formation of fumarate, maleate from EDA, and some unreacted EDA.

In 2013, Lee and coworkers reported silver-mediated intramolecular carbene insertion to sp^3 C–H from alkyne building blocks, mediated by aryne intermediates [26]. In this reaction, using silver trifluoromethanesulfonate (AgOTf, 10 mol%) or $AgSbF_6$ (10 mol%) as the catalyst and toluene as the solvent at 90°C for 5 h, good to excellent yields were obtained for various unsymmetrical and symmetrical bis-1,3-diyne substrates. All primary, secondary, and tertiary C–H bonds could be activated to generate the desired five-membered ring product, and secondary C–H bond was more reactive than primary C–H bond when substrates had two different kinds of available sp^3 C–H bonds (Scheme 5). For example, sp^3 C–H insertion in substrate with two different C–H bonds (entry 4) afforded a mixture of secondary and primary insertion products in high yield (80%) and ratio (13:1).



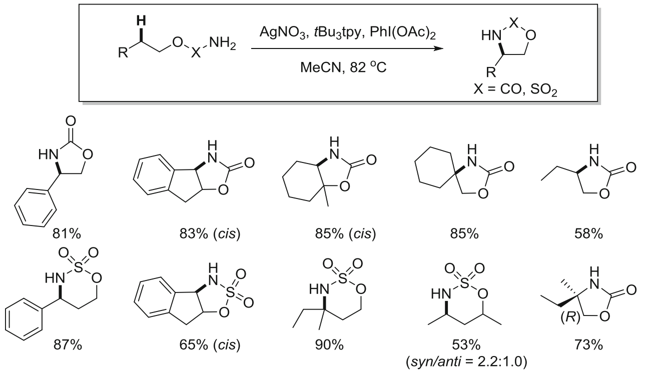
Scheme 5 Silver-mediated sp^3 C–H insertion through aryne intermediates by Lee et al.

2.2 *Direct C–N Bond Formation*

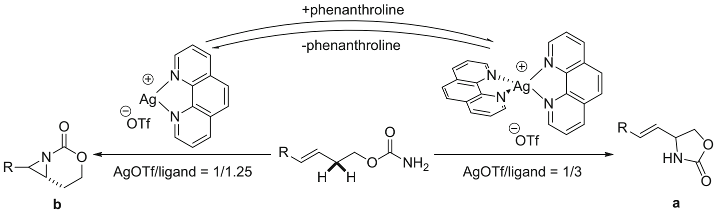
Nitrogen-containing functional groups are basic and important structural motifs, exiting in biologically active compounds and natural products [27]. The development of new and efficient methods to construct C–N bonds through C–H activation attracted much attention in medicinal chemistry and organic chemistry. Usually, there are two ways to introduce C–N bonds via C–H activation, intramolecular and intermolecular amination/amidation.

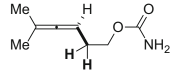
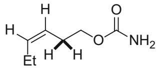
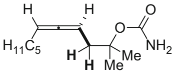
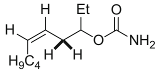
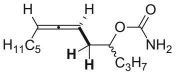
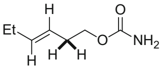
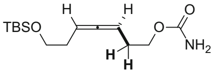
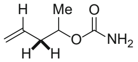
2.2.1 Intramolecular Amination/Amidation

In 2004, He and coworkers reported that a disilver (I) complex **10** (Scheme 1) catalyzed intramolecular amidation of sp^3 C–H bonds in both carbamates and sulfamates [28]. Using $AgNO_3$ (4 mol%) with *t*Bu$_3$tpy (4-6 mol%) as the catalyst and $PhI(OAc)_2$ (2.0 equiv.) as the oxidant in MeCN, the intramolecular amidation products were obtained in good to excellent yields (53–90%, Scheme 6). The reaction worked for a range of carbamates and sulfamates, generated five-membered ring and six-membered ring products. In addition, the optical rotation of product will remain as an enantiomerically pure sample during the reaction. This result indicated that the reaction is stereospecific and also provided the evidence to show that the amination involved a silver-mediated nitrene-transfer mechanism.



Scheme 6 Silver-mediated intramolecular amination of sp^3 C–H bonds



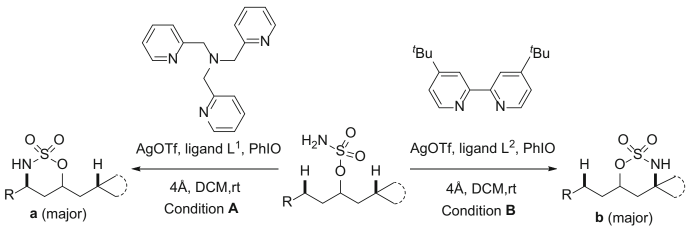
Substrate (AgOTf/ligand = 1/3)	Product a	Product b	Substrate (AgOTf/ligand = 1/3)	Product a	Product dr(*cis:trans*)	Product b
	81%	0		93%	---	0
	76%	1%		87%	3:1	4%
	76%	0		73%	---	11%
	36%	0		68%	2.4:1	0

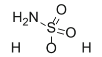
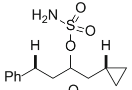
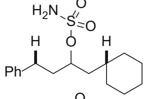
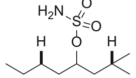
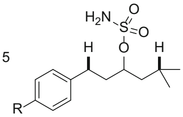
Scheme 7 Silver-catalyzed tunable, chemoselective sp^3 C–H amination

However, the substrate scope could not be expanded to amides. Several amides were tried under various reaction conditions; no desired product was obtained.

In 2013, Schomaker and coworkers reported highly chemoselective amidation of C=C and sp^3 C–H bonds by silver catalyst (Scheme 7) [29]. AgOTf was used as the catalyst with phenanthroline as ligand set in the presence of PhIO as the oxidant and 4 Å molecular sieves as additive in DCM. The reaction ran at room temperature. The ratio of AgOTf/ligand is critical since it controlled the reaction pathways to form either aziridination or C–H insertion product. The substrate scopes were explored to homoallenic and homoallylic carbamates with various substituents. Excellent chemoselectivity and high yields were obtained for this amidation of sp^3 C–H bonds when a 1:3 ratio of AgOTf/ligand was used, while for aziridination when a 1:1.25 ratio of AgOTf/ligand was used.

Later in 2014, ligand-controlled tunable, site-selective silver-catalyzed intramolecular amination/amidation between two different types of C–H bonds has been described by Schomaker and coworkers (Scheme 8) [30]. In the reaction, AgOTf with 4,4′-di-*tert*-butyl-2,2′-bipyridine (^{t}Bubipy) or tris(2-pyridylmethyl)amine (tpa) as the catalyst, PhIO as the oxidant, and 4 Å molecular sieves as additive were used. The sulfamate substrates contained two different types of C–H bonds, including a benzylic C–H bond and an electron-rich tertiary C–H bond. The reactions ran in DCM at room temperature. When AgOTf with ^{t}Bubipy (AgOTf/ligand=1:3) was used as a catalyst, the reaction preferred at an electron-rich tertiary C–H bond. Interestingly, when tpa was used as ligand (AgOTf/ligand=1:1.25), the amidation was favored at a benzylic C–H bond. However, there also were some exceptions. For example, substrate only gave benzylic C–H bond activation with both catalysts, while a higher yield was obtained with (tpa)AgOTf, presumably due to the low bond dissociation energy of benzylic C–H bond (~89 kcal/mol)

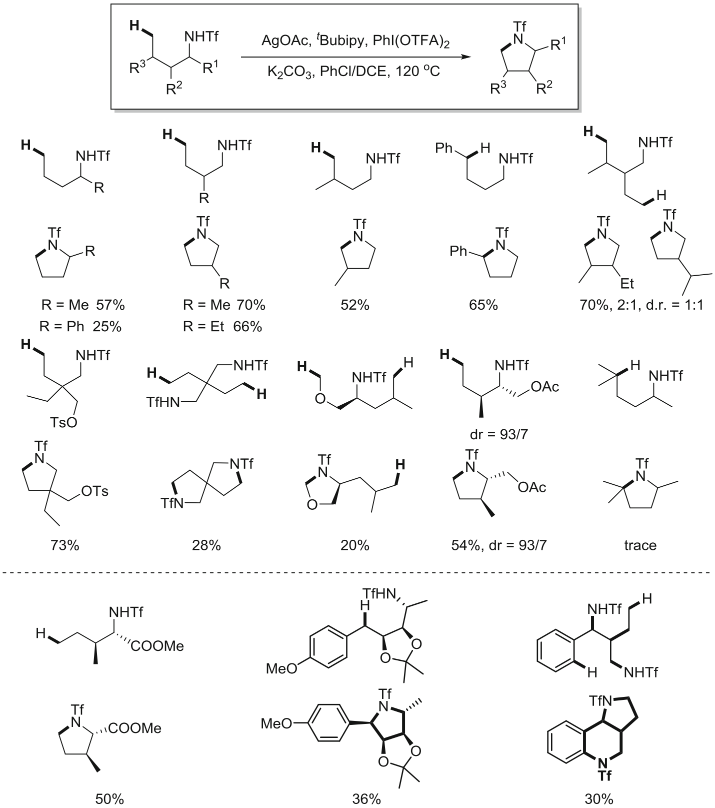


Entry	Substrate		Conditlon A (yield)		Condition B (yield)	
			a	**b**	**a**	**b**
1			60%	24%	19%	56%
2			63%	0	28%	0
3			73%	20%	9%	72%
4			0	94%	0	64%
5		R=OMe	70%	15%	31%	38%
		R=CF$_3$	42%	54%	11%	69%

Scheme 8 Silver-catalyzed, ligand-controlled sp^3 C–H amination by Schomaker et al.

compared to the cyclopropyl C–H bond (~106 kal/mol) (entry 2). The amidation with both catalysts again was obtained at tertiary C–H bond, and similarly (tpa) AgOTf was superior to (^{t}Bubipy)$_2$AgOTf (entry 4).

Very recently, Shi and coworkers reported another beautiful example of silver-catalyzed direct intramolecular amination (Scheme 9) [31]. Primary sp^3 C–H bonds are much less reactive than secondary and tertiary C–H bonds, and activation of primary sp^3 C–H bonds is high challenge and needs to develop a new silver-based catalytic system. In their report, primary sp^3 C–H bond was found preferred to secondary and tertiary C–H bonds. Notably, secondary benzylic C–H and aryl C–H bonds were suitable in the reaction; by using AgOAc (20 mol%) with ^{t}Bubipy (20 mol%) as the catalyst, PhI(OTFA)$_2$ (2.0–4.0 equiv.) as the oxidant, K$_2$CO$_3$ (2.0 equiv.) as the base, and PhCl/DCE (1/1) as the solvent at 120°C for 12 h, this amination worked for various triflic amide derivatives and generated only five-membered ring products, while six-membered products were generated through sp^2 C–H amidation. Moderate to good yields are obtained (20–73%). Secondary and tertiary C–H bonds have shown quite a low reactivity in the reaction. The substrates with β-substitution were favorable for amination and usually good yields were

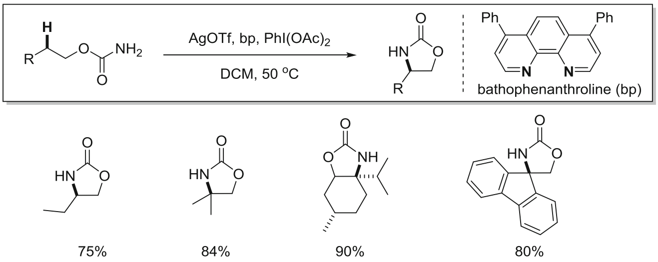


Scheme 9 Silver-mediated directed amination of primary and benzylic C–H bonds by Shi et al.

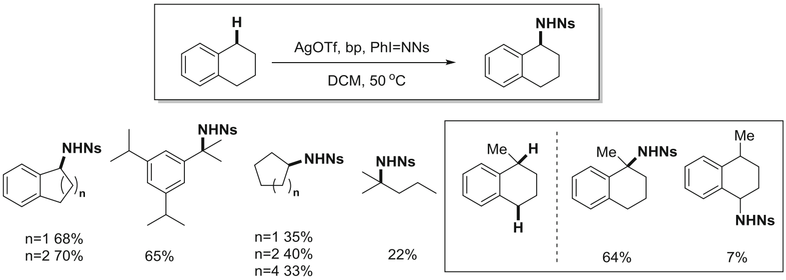
obtained. However, α-substitution decreased the yields, possibly due to the steric effect. Furthermore, protected linear amino acid ester underwent this transformation and formed 3-methylproline with 50% yield. More complicated core structure of (−)-codonophsinine and (−)-martinellic acid was easily constructed using this powerful method with moderate yields.

2.2.2 Intermolecular Amination

In comparison, intermolecular reaction met high challenges due to both enthalpy and entropy reasons. In 2007, He and coworkers developed a disilver-based new catalyst **11** which showed high efficiency for intramolecular C–H amination reaction (Scheme 10) [32]. Such an intermolecular C–H amination/amidation ran at mild condition. The new catalyst set has successfully been applied to intermolecular amination reaction for the first time (Scheme 11). In the reaction, the catalyst was added in two portions in order to increase the yield. Under typical reaction condition, AgOTf (2 mol%) and ligand (2.4 mol%) were mixed in DCM in a tube for 20 min. Then the substrate (5.0 or 10.0 equiv.), PhI=NNs (1.0 equiv.) and 4 Å molecular sieves (2 g/mmol) were added under N_2 atmosphere. The tube was sealed and heated to 50°C for 2 h before another AgOTf (2 mol%) and ligand (2.4 mol%) mixed in DCM were added. The reaction was carried out at 50°C



Scheme 10 Silver-mediated intramolecular amination of sp^3 C–H bonds by He et al.

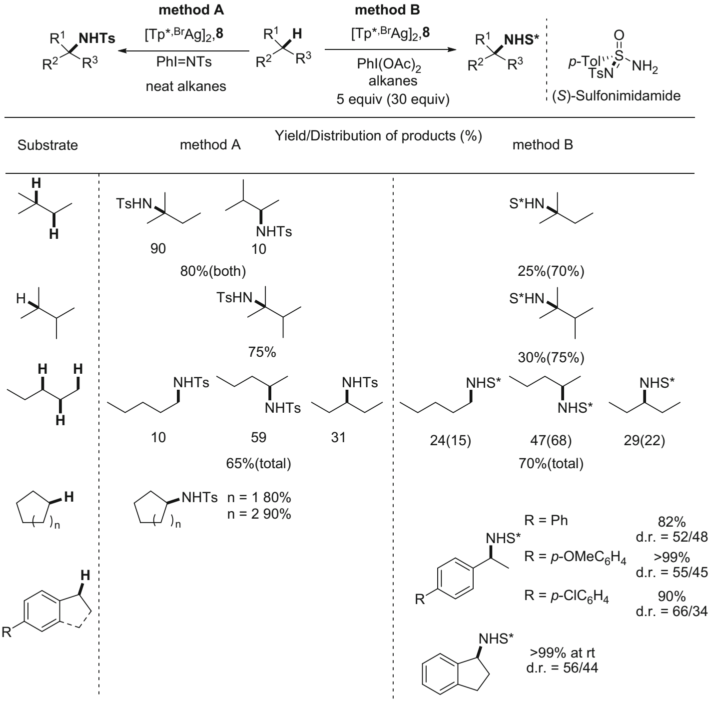


Scheme 11 Silver-mediated intermolecular amination of sp^3 C–H bonds by He et al.

overnight. Good yields were obtained for activating the benzylic C–H bond, while only moderate yields were obtained for inert C–H bond of cyclic alkanes.

In 2008, Díaz-Requejo, Pérez, and coworkers developed a new silver-based catalytic system which proceeded the direct intermolecular amination of alkanes [33]. This new catalyzed system employed complexes $[Tp^{*,Br}Ag]_2$ **8** as catalyst and PhI=NTs ([Ag]/[PhI=NTs]=1/20) as the nitrene source. The reaction was carried out in neat alkane at 80°C for 4 h. Linear and branched alkanes were converted to corresponding isomeric mixtures of amides in moderate to excellent yields (Scheme 12). The amination/amidation was favored at tertiary sites over secondary and primary sp^3 C–H bonds of alkanes, and only a few examples were observed at primary sp^3 C–H bonds. The reaction was inhibited when 2,6-di-*tert*-butyl-4-methylphenol (BHT) was present . Chloroalkanes were observed when CCl_4 was used as solvent. These evidences indicated that the mechanism involved radical species.

Although good results were observed for amination/amidation of alkanes, the reaction needed to carry out in neat substrates. In 2013, Dauban, Díaz-Requejo, Pérez, and coworkers have developed a highly efficient nitrene source sulfonimidamide. Based on their previous studies, complexes $[Tp^{*,Br}Ag]_2$ **8** could catalyze amination/amidation of alkanes (Scheme 12) [34]. In this report, a chiral sulfonimidamide was used as the nitrene source instead of PhI=NTs. High

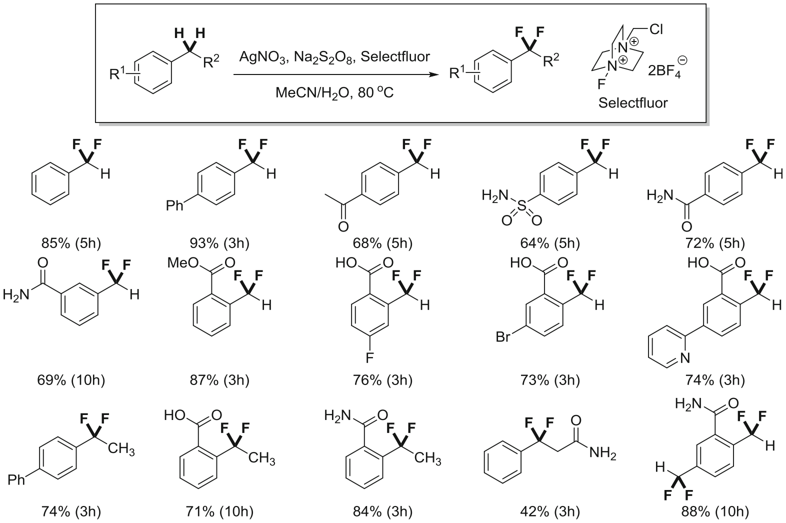


Scheme 12 Sp^3 C–H bond amination using silver complex **8** as catalyst

conversion was obtained for benzylic sp^3 C–H transformation. Important to note, for sp^3 C–H bond of alkane, the silver catalyst **8** showed high activity and gave better yields by using much lower amounts of alkanes.

2.3 Direct C–F Bond Formation

Fluorine-containing compounds have unique physical and chemical properties, and they are widely used in material chemistry and medicinal chemistry [35–37]. For example, ^{18}F-labeled organic compounds are used as biological imaging agents for positron emission tomography (PET) [38, 39]. In 2014, Tang and coworkers reported a silver-mediated difluorination of benzylic C–H bonds [40]. In this reaction, they used $AgNO_3$ as catalyst, $Na_2S_2O_8$ as oxidant, and 1-(chloromethyl)-4-fluoro-1,4-diazoniabicyclo[2.2.2]octane bis(tetrafluoroborate) as Selectfluor fluorinating reagent, which is commercially available. Under standard condition, substrate (1.0 equiv.), $AgNO_3$ (10 mol%), $Na_2S_2O_8$ (0.5 equiv.), Selectfluor (3.0 equiv.), and $MeCN/H_2O$ under N_2 were heated to 80°C for several hours. Moderate to excellent yields were achieved (42–93%, Scheme 13). The reaction was tolerating various functional groups, including ketone, ester, carboxylic acid, amide, sulfonamide, aromatic derivatives, and heteroaromatic derivatives. However, higher catalyst loading and excess reagents were needed for some cases. For example, substrates without *ortho*-substituents reacted slowly and usually needed high catalyst loading and large amount of Selectfluor. Obviously, this



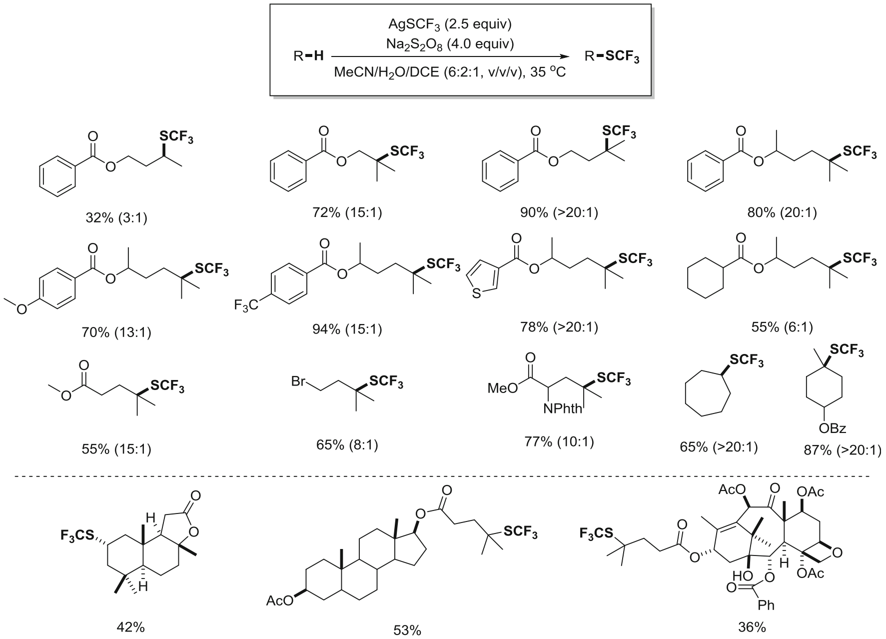
Scheme 13 Silver-mediated difluorination of sp^3 C–H bonds

method provided the most straightforward way to produce 1,1-difluoro substituents at benzylic position.

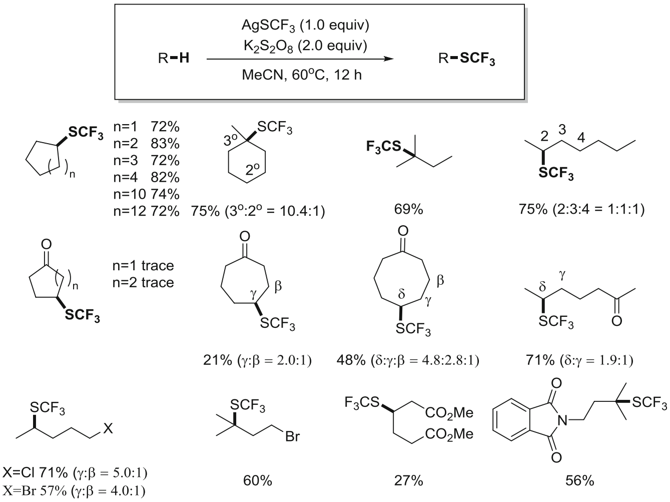
2.4 Direct C–SCF$_3$ Bond Formation

Trifluoromethylthio group (SCF$_3$) is an important structural moiety in new drugs and agrochemicals owing to its strong electronegativity and high lipophilicity [41–44]. Very recently, both Tang and Chen groups have reported direct sp^3 C–H trifluoromethylthiolation using silver (I) trifluoromethanethiolate and persulfate [45, 46]. These developed methods were applied for the late-stage trifluoromethylthiolation of pharmaceutical and agrochemical compounds.

In Tang's work [45], AgSCF$_3$ was used as trifluoromethylthiolation reagent and $Na_2S_2O_8$ as the oxidant. The reaction was carried out under aqueous conditions in air. As standard condition, the substrates (1.0 equiv.), AgSCF$_3$ (2.5 equiv.), $Na_2S_2O_8$ (4.0 equiv.), and MeCN/H$_2$O/DCE (6:2:1, v/v/v) in 2.00 mL sealed in a vial were warmed to 35°C for 12 h. Moderate to excellent yields (32–94%) of desired products are obtained. The reaction can be carried out at gram scale (Scheme 14). The reaction tolerated various functional groups, including ethers, esters, amino acid derivatives, bromides, and aromatic derivatives. This reaction was favored occurring selectively at tertiary and secondary C–H bonds. Otherwise,



Scheme 14 Silver-mediated trifluoromethylthiolation of sp^3 C–H bonds and applications



Scheme 15 Silver-mediated trifluoromethylthiolation of sp^3 C–H bonds

this transformation gave a much lower selectivity of trifluoromethylthiolation products. It is important to note that more complex natural products were successfully applied in this trifluoromethylthiolation, exhibiting the potential of this method in medicinal chemistry.

Almost at the same time, Chen and coworkers also reported the similar direct trifluoromethylthiolation of sp^3 C–H bonds by $AgSCF_3/K_2S_2O_8$ [46]. They also used $AgSCF_3$ as trifluoromethylthiolation reagent, but $K_2S_2O_8$ as the oxidant. The reaction was carried out under argon atmosphere. Moderate to excellent yields (18–83%) were obtained under mild conditions (Scheme 15). Similarly, the trifluoromethylthiolation were showed with a better selectivity at tertiary C–H than secondary C–H bonds. Many functional groups were also well tolerated, including ketones, esters, bromides, tertiary alcohols, and phthalimides. However, the presence of the primary and secondary aliphatic alcohols terminated the reaction. The substrates with alkene and alkyne groups were also not workable and resulted in a complicated reaction mixture.

3 Conclusions and Perspective

Although much attention has been paid to silver catalysis in the past several years and significant progress has been achieved in this field of silver-mediated sp^3 C–H bond transformations, compared to the catalysis with other transition metals, the reports in this field are still very limited. In this chapter, we have reviewed a variety of important silver-catalyzed sp^3 C–H transformations, including C–C bond formation, C–N bond formation, C–F bond formation, and C–S bond formation. A family of tris(pyrazolyl)borate silver complexes and other unique silver complexes were designed, synthesized, and characterized and further proved to be efficient catalysts in this field. Fascinating methodologies were developed for functionalization of different aliphatic C–H bonds, particularly, methane and short alkanes with EDA by perfluorinated tris(pyrazolyl)borate silver complexes in $scCO_2$. Silver-catalyzed/silver-mediated sp^3 C–H amination/amidation, difluorination, and trifluoromethylthiolation provided a great potential for future late-stage functionalization of pharmaceutical and agrochemical compounds. All these developments will blossom a new field to approach the direct aliphatic C–H functionalization. As a cheap noble metal, silver exhibited an exciting feature in catalysis, tunable by the different ligands. We believe that silver will play more and more important roles in direct C–H functionalization with the development of new processes.

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References

1. Ladd CL, Sustac Roman D, Charette AB (2013) Org Lett 15:1350
2. Maestre L, Sameera WMC, Díaz-Requejo MM, Maseras F, Pérez PJ (2013) J Am Chem Soc 135:1338
3. Naodovic M, Yamamoto H (2008) Chem Rev 108:3132
4. Yanagisawa A, Takeshita S, Izumi Y, Yoshida K (2010) J Am Chem Soc 132:5328
5. Li Z, He C (2006) Eur J Org Chem 2006:4313
6. Álvarez-Corral M, Muñoz-Dorado M, Rodríguez-García I (2008) Chem Rev 108:3174
7. Yamamoto Y (2008) Chem Rev 108:3199
8. Dias HVR, Lovely CJ (2008) Chem Rev 108:3223
9. Díez-González S, Nolan SP (2008) Acc Chem Res 41:349
10. Munoz MP (2014) Chem Soc Rev 43:3164
11. Weibel J-M, Blanc A, Pale P (2008) Chem Rev 108:3149
12. Harmata M (ed) (2010) Silver in organic chemistry. Wiley, Hoboken
13. Cheng C, Hartwig JF (2015) Chem Rev. doi:10.1021/cr5006414
14. Burgess K, Lim H-J, Porte AM, Sulikowski GA (1996) Angew Chem Int Ed 35:220
15. Doyle MP (2011) ChemCatChem 3:1681
16. Pérez PJ (ed) (2012) Alkane C–H activation by single-site metal catalysis. Springer, Netherlands
17. Rangan K, Fianchini M, Singh S, Dias HVR (2009) Inorg Chim Acta 362:4347
18. Dias HVR, Browning RG, Richey SA, Lovely CJ (2004) Organometallics 23:1200
19. Dias HVR, Browning RG, Richey SA, Lovely CJ (2005) Organometallics 24:5784
20. Urbano J, Belderraín TR, Nicasio MC, Trofimenko S, Díaz-Requejo MM, Pérez PJ (2005) Organometallics 24:1528
21. Despagnet-Ayoub E, Jacob K, Vendier L, Etienne M, Álvarez E, Caballero A, Díaz-Requejo MM, Pérez PJ (2008) Organometallics 27:4779
22. Caballero A, Despagnet-Ayoub E, Mar Díaz-Requejo M, Díaz-Rodríguez A, González-Núñez ME, Mello R, Muñoz BK, Ojo W-S, Asensio G, Etienne M, Pérez PJ (2011) Science 332:835

23. Fuentes MÁ, Olmos A, Muñoz BK, Jacob K, González-Núñez ME, Mello R, Asensio G, Caballero A, Etienne M, Pérez PJ (2014) Chem Eur J 20:11013
24. Fuentes MÁ, Muñoz BK, Jacob K, Vendier L, Caballero A, Etienne M, Pérez PJ (2013) Chem Eur J 19:1327
25. Flores JA, Komine N, Pal K, Pinter B, Pink M, Chen C-H, Caulton KG, Mindiola DJ (2012) ACS Catal 2:2066
26. Yun SY, Wang K-P, Lee N-K, Mamidipalli P, Lee D (2013) J Am Chem Soc 135:4668
27. Lawrence SA (2004) Amines: synthesis, properties and applications. Cambridge University, New York
28. Cui Y, He C (2004) Angew Chem Int Ed 43:4210
29. Rigoli JW, Weatherly CD, Alderson JM, Vo BT, Schomaker JM (2013) J Am Chem Soc 135:17238
30. Alderson JM, Phelps AM, Scamp RJ, Dolan NS, Schomaker JM (2014) J Am Chem Soc 136:16720
31. Yang M, Su B, Wang Y, Chen K, Jiang X, Zhang Y-F, Zhang X-S, Chen G, Cheng Y, Cao Z, Guo Q-Y, Wang L, Shi Z-J (2014) Nat Commun 5
32. Li Z, Capretto DA, Rahaman R, He C (2007) Angew Chem Int Ed 46:5184
33. Gómez-Emeterio BP, Urbano J, Díaz-Requejo MM, Pérez PJ (2008) Organometallics 27:4126
34. Beltran A, Lescot C, Mar Diaz-Requejo M, Perez PJ, Dauban P (2013) Tetrahedron 69:4488
35. O'Hagan D (2008) Chem Soc Rev 37:308
36. Purser S, Moore PR, Swallow S, Gouverneur V (2008) Chem Soc Rev 37:320
37. Wang J, Sánchez-Roselló M, Aceña JL, del Pozo C, Sorochinsky AE, Fustero S, Soloshonok VA, Liu H (2014) Chem Rev 114:2432
38. Ametamey SM, Honer M, Schubiger PA (2008) Chem Rev 108:1501
39. Miller PW, Long NJ, Vilar R, Gee AD (2008) Angew Chem Int Ed 47:8998
40. Xu P, Guo S, Wang L, Tang P (2014) Angew Chem Int Ed 53:5955
41. Leo A, Hansch C, Elkins D (1971) Chem Rev 71:525
42. Leroux F, Jeschke P, Schlosser M (2005) Chem Rev 105:827
43. Manteau B, Pazenok S, Vors J-P, Leroux FR (2010) J Fluor Chem 131:140
44. Xu X-H, Matsuzaki K, Shibata N (2015) Chem Rev 115:731
45. Guo S, Zhang X, Tang P (2015) Angew Chem Int Ed 54:4065
46. Wu H, Xiao Z, Wu J, Guo Y, Xiao J-C, Liu C, Chen Q-Y (2015) Angew Chem Int Ed 54:4070