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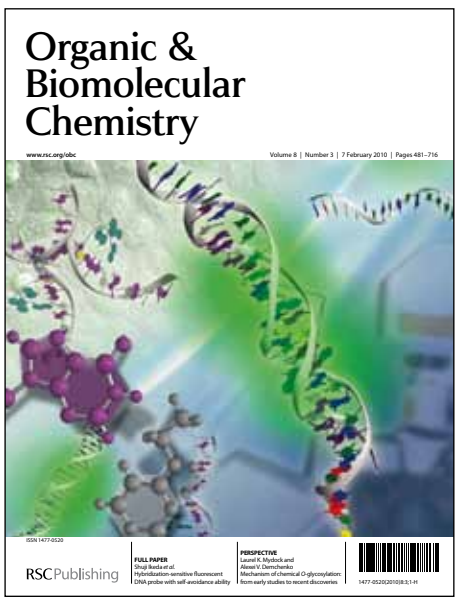

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Rhodium(I)-Catalyzed 1,4-Conjugate Arylation toward β-Fluoroalkylated Electron-Deficient Alkenes: A New Entry to a Construction of a Tertiary Carbon Center Possessing a Fluoroalkyl Group

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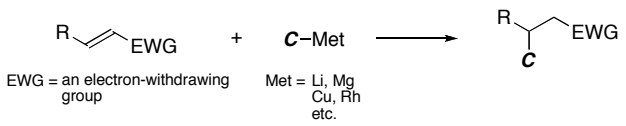
Treatment of β-fluoroalkylated-α,β-unsaturated ketones with 1.2 equiv. of various arylboronic acids in the presence of 5 mol% of $[Rh(C_8H_{12})_2]BF_4$ and 6 mol% of (*S*)-BINAP in toluene/H_2O (v/v=4/1) at the reflux temperature for 3 h gave the corresponding Michael adducts in high yields with over 90% enantioselectivity. Though other electron-deficient alkenes, such as vinyl sulfone and vinylphosphonate, were found to be much less reactive in the rhodium-catalyzed conjugate addition with arylboronic acids, the reaction of various arylstannanes toward such electron-deficient alkenes took place very smoothly to afford the corresponding adducts in high yields.

Introduction

1,4-Conjugate addition reactions of carbon nucleophiles to α,β-unsaturated compounds are among the most widely used methods for carbon-carbon bond formation in organic synthesis (Scheme 1).[1] The versatility for this process is due to the wide variety of donors (organometallic reagents, Michael donors, other carbanions) and acceptors (α,β-unsaturated reagents) that can be employed. In particular, numerous asymmetric version, like copper-,[2] nickel-,[3] cobalt-,[4] rhodium-,[5] alkali metal-catalyzed enantioselective reaction,[6] and others,[7] have been reported in recent years.

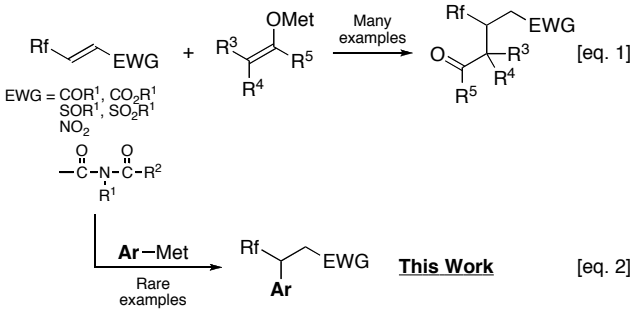


Scheme 1. 1,4-Conjugate addition reaction.

It has been well known that the incorporation of a fluoroalkyl moiety to organic molecules can significantly modify its physicochemical features and consequently its biological properties.[8] Therefore, fluoroalkylated compounds have played a unique and significant role in agricultural and medicinal chemistry.

Hence, it is not surprising that much effort has been devoted to the development of 1,4-conjugate addition reactions of various carbon nucleophiles toward β-fluoroalkylated electron-deficient alkenes for the preparation of various types of fluorine-containing molecules (Scheme 2, [eq. 1]).

To date, there have been considerable studies on the 1,4-conjugate additions toward β-fluoroalkylated α,β-unsaturated ketones,[9] esters,[10] sulfoxides,[11] sulfones,[12] and nitroalkenes[13] using a variety of carbon nucleophiles, such as enolates, stabilized carbanions, etc. However, *very little attention has been focused on the 1,4-conjugate arylation using arylmetals* (Scheme 2, [eq. 2]),[14] although some Friedel-Crafts arylations using heteroaromatics have been reported so far.[15] We report herein that various arylboronic acids or arylstannanes react very smoothly with fluorine-containing α,β-unsaturated compounds in the presence of the rhodium catalyst, particularly in the former case the high enantiocontrol being observed when the catalyst coordinated with (*S*)-BINAP was used.[16]



Scheme 2. Intended program.

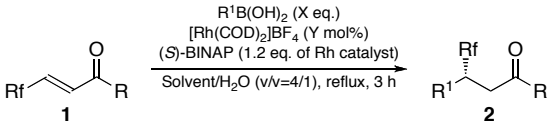
Results and discussion

Initially, we investigated 1,4-conjugate arylation reaction using (*E*)-4,4,4-trifluoro-1-phenyl-2-buten-1-one (**1a**) (Rf = CF_3, R = Ph in Scheme 3), prepared readily according to the reported procedure,[17] and phenylboronic acid as shown in Table 1. Thus,

treatment of 1.0 equiv. of **1a** with 1.2 equiv. of phenylboronic acid in the presence of 0.5 mol% of $[Rh(COD)_2]BF_4$ and 0.6 mol% of (*S*)-BINAP in toluene/H_2O (v/v=4/1) at the reflux temperature for 3 h gave the corresponding 1,4-conjugate arylation product **2a** with 55% enantiomeric excess in 60% yield (Entry 1). In this case, the product with *R* absolute configuration was afforded preferentially (*vide infra*). When 2.4 equiv. of phenylboronic acid was used, the chemical yield and the enantiomeric excess were both increased (Entry 2). Although the employment of 1 mol% of rhodium catalyst did not cause any influence of the reaction (Entry 3), 5 mol% of the catalyst led to a significant improvement of the optical purity, the desired adduct with 85% enantiomeric excess being obtained in 96% yield (Entry 4). Eventually, the best yield was obtained when the reaction was carried out by using 1.2 equiv. of phenylboronic acid in the presence of 5 mol% of $[Rh(COD)_2]BF_4$ and 6 mol% of (*S*)-BINAP (Entry 5). In this case, the product with 90% enantiomeric excess was obtained in 96% yield.

As shown in Entries 6-11, we also examined the solvent effect on the conjugate addition. As a result, hexane, THF, DMF, CH_3OH, and CH_3NO_2 were not the solvent of choice, the corresponding adducts being obtained in very low yields (0–32%). Quite interestingly, 1,4-dioxane, which is generally used in the Rh(I)-catalyzed conjugate addition with nonfluorinated electron-deficient olefins, resulted in the significant decrease of the optical purity of **2a** (23% ee), though the yield was good (Entry 10).

With the optimum reaction conditions (Table 1, Entry 5), we next investigated the conjugate addition of various arylboronic acids. The results are summarized in Table 2.



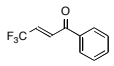
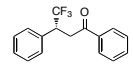
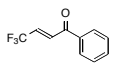
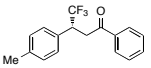
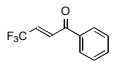
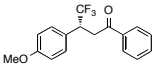
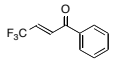
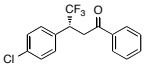
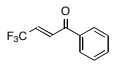
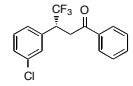
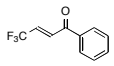
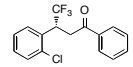
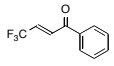
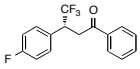
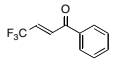
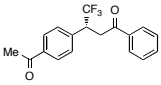
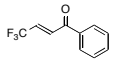
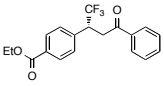
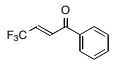
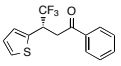
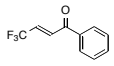
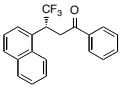
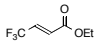
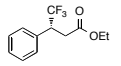
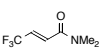
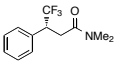
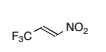
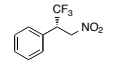
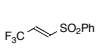
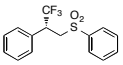
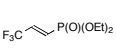
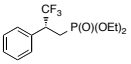
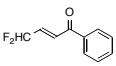
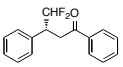
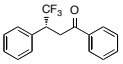
Scheme 3. Rhodium(I)-catalyzed 1,4-conjugate addition using arylboronic acids.

Table 1. Investigation of the reaction conditions (Rf = CF_3, R, R^1 = Ph)

Entry	X/eq	Y/mol%	Solvent	**2a**/%[a]	Ee/%[b]
1	1.2	0.5	Toluene	60	55
2	2.4	0.5	Toluene	91	72
3	2.4	1.0	Toluene	95	74
4	2.4	5.0	Toluene	96	85
5	1.2	5.0	Toluene	96 (90)	90
6	1.2	5.0	Hexane	0	-
7	1.2	5.0	THF	23	34
8[c]	1.2	5.0	DMF	32	2
9	1.2	5.0	CH_3OH	9	4
10	1.2	5.0	1,4-Dioxane	78	23
11	1.2	5.0	CH_3NO_2	22	36

a) Determined by ^{19}F NMR. Value in parentheses is of isolated yield. b) Determined by HPLC (Chiralpac AD). c) Carried out at 100 °C

Table 2. Conjugate addition of various boronic acids toward various fluorinatd electron-deficient alkenes.[a]

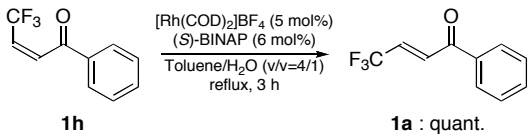
Entry	Substrate		Product		**2**/%[b]	Ee/%[c]
1		**1a**		**2a**	96 (90)	90
2		**1a**		**2b**	95 (91)	92
3		**1a**		**2c**	96 (89)	92
4		**1a**		**2d**	95 (94)	94
5		**1a**		**2e**	89 (81)	91
6		**1a**		**2f**	3	N.D.[d]
7		**1a**		**2g**	84 (80)	90
8		**1a**		**2h**	96 (95)	93
9		**1a**		**2i**	95 (80)	92
10		**1a**		**2j**	79 (65)	90
11		**1a**		**2k**	51[e]	70
12		**1b**		**2l**	60[e]	N.D.[d]
13		**1c**		**2m**	53 (46)	92
14		**1d**		**2n**	60 (45)	5
15		**1e**		**2o**	30 (27)	9
16		**1f**		**2p**	13	N.D.[d]
17		**1g**		**2q**	96 (92)	74
18		**1h**		**2a**	91	90

a) All reaction was carried out by using 1.0 equiv. of the electron-deficient alkene and 1.2 equiv. of boronic acid in the presence of 5 mol% of $[Rh(COD)_2]BF_4$ and 6 mol% of (*S*)-BINAP in toluene/H_2O (v/v=4/1) at the reflux temperature for 3 h. b) Determined by ^{19}F NMR. Values in parentheses are of isolated yield. c) Determined by HPLC (Chiral pac AD-H). d) Not determined. e) The product could not be purified due to some impurities.

As shown in Entries 2-4 and 7-9, various types of arylboronic acids having an electron-donating (CH_3, CH_3O) or an electron-withdrawing group (Cl, F, CH_3CO, EtO_2C) on the benzene ring could participate nicely in the conjugate addition to give the corresponding adducts **2b-d**, **2g-i** in excellent yields (84–96% yield) with high enantioselectivity (90–94% ee). However, the use of *ortho*-substituted arylboronic acid, such as *o*-chlorophenyl- or 1-naphthylboronic acid, resulted in a significant decrease of the reaction efficacy (3% or 51% yield in Entries 6 or 11), while *meta*-substitution of the benzene ring of $R^1B(OH)_2$ did not influence on the reaction at all (Entry 5). 2-Thienylboronic acid was also found to be a good Michael donor in the reaction (Entry 10), though the yield decreased slightly.

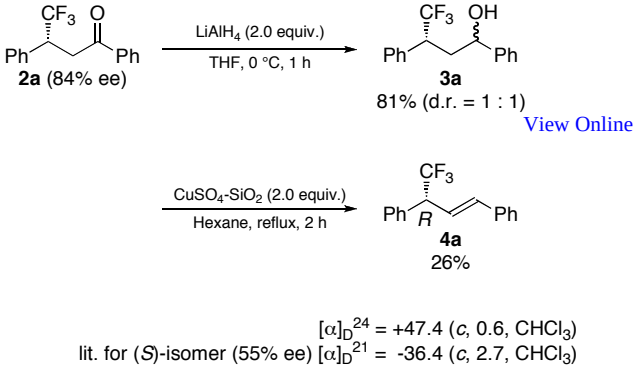
We also examined the conjugate addition reaction using various types of fluorine-containing electron-deficient alkenes. As shown in Entries 12-14, the reaction of various electron-deficient alkenes, such as α,β-unsaturated ester **1b**, amide **1c**, or nitroalkene **1d**[18], proceeded to give the corresponding adducts **2l-n** in good yields. Especially, the high enantioselectivity (92% ee) was observed in the case of the amide (Entry 13). Unfortunately, the vinyl sulfone **1e** and the vinylphosphonate **1f**[19] did not give the satisfactory results, the product being afforded in very low yields as well as in a very low enantioselective manner (Entries 15 and 16). Changing the fluoroalkyl group from a CF_3 group to a CHF_2 group also caused a decrease of the enantiomeric excess. The use of (*Z*)-substrate **1h** afforded the Michael adduct **2a** with the same absolute configuration as in the reaction of (*E*)-substrate **1a** (Entry 1 *vs* Entry 18).

In order to reveal why the same product, (*R*)-stereoisomer **2a** was obtained preferentially in both (*E*)- and (*Z*)-substrates, we treated **1h** with 5 mol% of $[Rh(COD)_2]BF_4$ and 6 mol% of (*S*)-BINAP in toluene/H_2O (v/v = 4/1) at the reflux temperature for 3 h. As a result, **1h** was completely comsumed, **1a** being obtained quantitatively (Scheme 4). This experimental result indicates that rhodium catalyst coordinated with (*S*)-BINAP as a ligand catalyzes the alkene-isomerizaiton much more rapidly than the conjugate addition reaction.[20]



Scheme 4. Rhodium(I)-catalyzed alkene-isomerization.

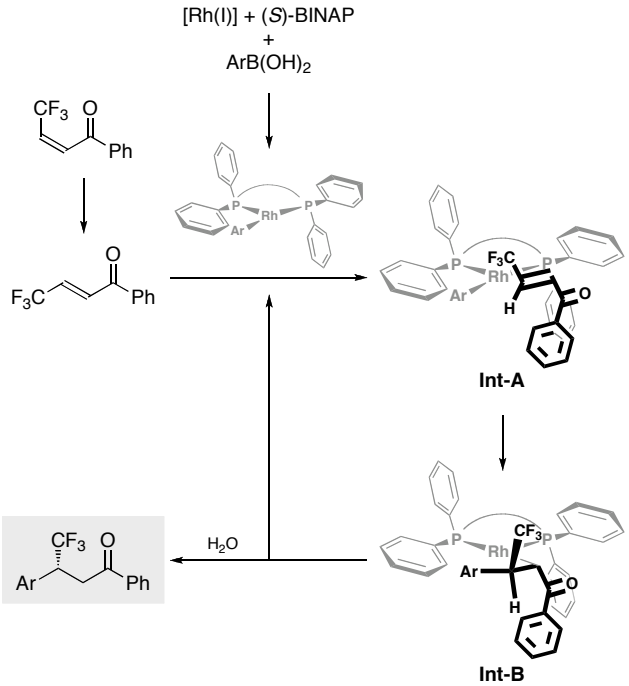
The stereochemical assignment of **2** was made as follows (Scheme 5). Thus, treatment of optically active **2a** with 2.0 equiv. of $LiAlH_4$ in THF at 0 °C for 1 h gave a 1 : 1 diastereomeric mixture of the corresponding alcohol **3a** in 81% yield, which were subjected to 2.0 equiv. of $CuSO_4$-SiO_2 in hexane at the reflux temperature for 2 h,[21] giving the known compound **4a**. The comparison of the observed optical rotation of **4a** with its literature value made it possible to determine the absolute configuration of **2a** as *R*.[22]



Scheme 5. Determination of the absolute configuration of **2a**.

The proposed mechanism for the present reaction is outlined in Scheme 6.[5a, 5b, 5d, 5f]

Thus, (*E*)-substrate (or which was produced *via* isomerization of (*Z*)-isomer) may come close to arylrhodium species coordinated with (*S*)-BINAP (**Int-A**), avoiding the phenyl group on phosphorus atom. Then, *si* face of the alkene may coordinate with aryl-rhodium species, followed by the attack of the aryl group, affording the corresponding rhodium enolate (**Int-B**). Finally, the enolate may react with H_2O to give the corresponding Michael adduct, and the rhodium species coordinated with (*S*)-BINAP may be regenerated.

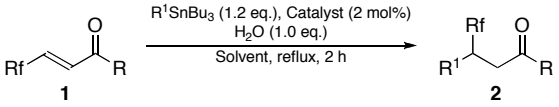


Scheme 6. A plausible reaction mechanism.

Next, our attention was directed toward the conjugate addition of organostannanes into fluorine-containing electron-deficient alkenes.

Initially, screening of the solvent was done in detail as shown in Table 3. Thus, treatment of **1a** (Rf = CF_3, R = Ph) with 1.2 equiv. of phenyltributylstannane in the presence of 2 mol% of $[Rh(COD)_2]BF_4$ in toluene at 90 °C for 2 h gave the corresspponding adduct **2a** in 76% yield (Entry 1). In this case, any trace of the starting α,β-unsaturated ketone was not detected. Changing the solvent from toluene to THF led to an increase of the yield, the desired adduct being afforded in 86% yield (Entry 2). Acetonitrile as well as 1,2-dichloroethane were also found to be the solvent of choice (Entries 3 and 4), while the use of DMF and 1,4-dioxane caused a significant decrease of the yield (Entries 5 and 6). In the absense of catalyst, the reation did not proceed at all (Entry 7).

Then, we next investigated the reaction under the influence of various rhodium catalysts as shown in Entry 8-16. Addition of phosphine ligand, such as PPh_3, P(*o*-Tol)$_3$, P(*t*-Bu)$_3$, PCy_3, did not cause any significant change in the yield (Entries 8-11). In addition, the use of $[RhCl(COD)]_2$ afforded the desired adduct in high yield (Entry 13). However, very disappointingly, the catalyst, $[Rh(COD)_2]BF_4$ + (*S*)-BINAP, which is the catalyst of choice in the conjugate addition with various boronic acids, was found to be less reactive, the adduct being obtained in only 61% yield. Additionally, no enantioselectivity was observed in this case (Entry 12). Furthermore, all of $[Rh(COD)(MeCN)_2]BF_4$, Willkinson catalyst, and $Rh(acac)(C_2H_4)_2$ did not give satisfactory results (Entries 14-16).



Scheme 7. Rhodium(I)-catalyzed 1,4-conjugate addition using arylstannanes.

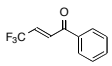
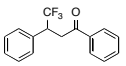
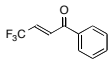
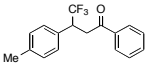
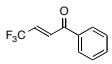
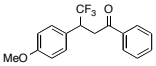
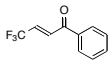
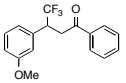
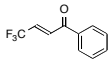
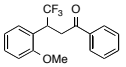
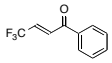
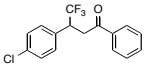
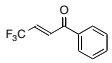
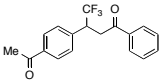
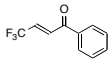
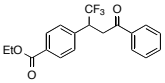
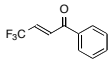
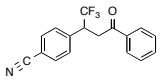
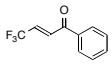
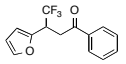
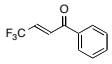
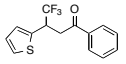
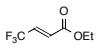
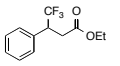
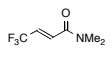
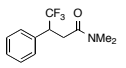
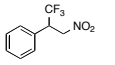
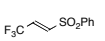
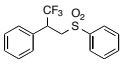
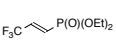
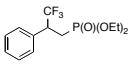
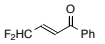
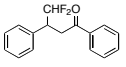
Table 3. Investigation of the reaction conditions (Rf = CF_3, R, R^1 = Ph).

Entry	Catalyst	Solvent	**2a**/%[a]
1[b]	$[Rh(COD)_2]BF_4$	Toluene	76
2	$[Rh(COD)_2]BF_4$	THF	86 (68)
3[b]	$[Rh(COD)_2]BF_4$	DMF	64
4[b]	$[Rh(COD)_2]BF_4$	1,4-Dioxane	66[c]
5	$[Rh(COD)_2]BF_4$	MeCN	80
6[b]	$[Rh(COD)_2]BF_4$	$ClCH_2CH_2Cl$	87
7	None	THF	0
8	$[Rh(COD)_2]BF_4$ + $2PPh_3$	THF	84
9	$[Rh(COD)_2]BF_4$ + 2P(*o*-Tol)$_3$	THF	88
10	$[Rh(COD)_2]BF_4$ + 2P(*t*-Bu)$_3$	THF	86
11	$[Rh(COD)_2]BF_4$ + $2PCy_3$	THF	87
12	$[Rh(COD)_2]BF_4$ + (*S*)-BINAP	THF	61[d]
13	1/2$[RhCl(COD)_2]$	THF	88
14	$[Rh(COD)(MeCN)_2]$	THF	41
15	$RhCl(PPh_3)_3$	THF	0
16	$Rh(acac)(C_2H_4)_2$	THF	0

a) Determined by ^{19}F NMR. Value in parentheses is of isolated yield.
b) Carried out at 90 °C (bath temp).
c) The starting α,β-unsaturated ketone was recovered in 7% yield.
d) No enantioselectivity was observed.

With the best reaction conditions in hand (Table 3, Entry 2), we next examined the reaction using various organostannanes as shown in Table 4.

Table 4. Conjugate addition of various organostannanes toward various fluorinated electron-deficient alkenes.

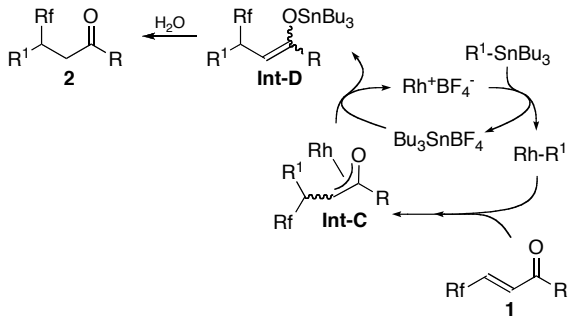
Entry	Substrate		Product		**2**/%[a]	**1**/%[a]
1		**1a**		**2a**	86 (68)	trace
2		**1a**		**2b**	75	0
3		**1a**		**2c**	87 (56)	trace
4		**1a**		**2r**	87 (66)	trace
5		**1a**		**2s**	31	26
6		**1a**		**2d**	75 (67)	0
7		**1a**		**2h**	89 (54)	0
8		**1a**		**2i**	78 (59)	0
9		**1a**		**2t**	39 (13)	38
10		**1a**		**2u**	14	29
11		**1a**		**2j**	10	25
12		**1b**		**2l**	65	0
13		**1c**		**2m**	23	20
14		**1d**		**2n**	19	16
15[b]		**1e**		**2o**	77 (61)	8
16[b]		**1f**		**2p**	82 (47)	0
17		**1g**		**2q**	86 (60)	trace

a) Determined by ^{19}F NMR. Values in parentheses are of isolatd yield.
b) Five mol% of rhodium catalyst were used.

As shown in Entries 2, 3 and 6-8, various types of arylstannanes having an electron-donating (CH_3, CH_3O) or an electron-withdrawing group (Cl, EtO_2C, CH_3CO) on the benzene ring could participate nicely in the conjugate addition to give the corresponding adducts **2b-d**, **2h, i** in high yields (75-89% yield). However, the use of *ortho*-substituted and *para*-cyano-substituted arylstannanes resulted in a significant decrease of the reaction efficacy (31% and 39% yield in Entries 5 and 9). Additionally, 2-furyl and 2-thienyl functionalities were all found to be somewhat less reactive, the desired adducts being afforded in less than 20% yield (Entries 10 and 11).

We also examined the conjugate addition reaction using various types of fluorine-containing electron-deficient olefins. As shown in Entry 12, the reaction with α,β-unsaturated ester **1b** proceeded smoothly to give the corresponding adducts **2l** in good yields, while α,β-unsaturated amide as well as nitroalkene did not give any satisfactory results (Entries 13 and 14). It is noteworthy that both trifluoromethylated vinyl sulfone and vinylphosphonate could react with phenylstannane very smoothly to give the corresponding 1,4-adducts **2o**, **2p** in high yields, because the reaction with arylboronic acids did not afford the 1,4-adducts in good yields (Entries 15 and 16 in Table 2). Changing a fluoroalkyl group from a CF_3 group to a CHF_2 group did not influence on the reaction at all (Entry 17).

As shown in Scheme 8, the reaction mechanism, which is similar to that in the reaction with boronic acids, may be proposed.[5c, 5e] Thus, the transmetalation of the cationic rhodium complex with organostannane produces the organorhodium intermediate Rh-R^1 and Bu_3SnBF_4. Addition of Rh-R^1 toward electron-deficient alkenes **1** leads to the η^3-oxa-π-allylrhodium complex **Int-C**, which then reacts with Bu_3SnBF_4 to afford stannyl enol ether **Int-D** and to regenerate the cationic rhodium complex. The stannyl enol ether **Int-D** is easily hydrolyzed to afford product **2**.



Scheme 8. A plausible reaction mechanism.

Conclusions

In summary, we have demonstrated the rhodium-catalyzed conjugate addition reaction of various arylboronic acids as well as arylstannanes toward various β-fluoroalkylated electron-deficient olefins. As a result, α,β-unsaturated ketones and amide, not vinylsulfone and vinylphosphonate, could participate in the highly enantioselective conjugate addition very well. In sharp contrast, organostannanes were found to be more reactive in the case of vinylsulfone and vinylphosphonate as Michael donor, the corresponding adducts being given in high yields.

Notes and references

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Experimental

General information: Infrared spectra (IR) were taken on a JASCO FT/IR-4100typeA spectrometer as film on a NaCl plate. ^1H and ^{13}C NMR spectra were measured with a Bruker DRX-500 NMR spectrometer and a JEOL JNM- AL 400 NMR spectrometer in a chloroform-*d* ($CDCl_3$) solution with tetramethylsilane (Me_4Si) as an internal reference. A JEOL JNM-EX90A (84.21 MHz) FT-NMR spectrometer and a JEOL JNM-AL 400 NMR spectrometer were used for determining the yield of the products with hexafluorobenzene (C_6F_6). ^{19}F NMR (376.05 MHz) spectra was measured with a JEOL JNM-AL 400 NMR spectrometer in a chloroform-*d* ($CDCl_3$) solution with trichlorofluoromethane ($CFCl_3$) as an internal standard. High-resolution mass spectra (HRMS) were taken on a Hitachi M-80B mass spectrometer by electron impact (EI), chemical ionization (CI), and fast atom bombardment (FAB) methods. Thin-layer chromatography (TLC) was done on aluminium sheets coated with silica gel (Merck 60 F_{254}), and column chromatography was carried out using silica gel (Wacogel C-200) as adsorbent. Liquid choromatographic analysis were conducted on a Shimadzu LC-10Avp instrument equipped with model SPD-10Avp spectrometers as an ultra violet light (254 nm) and chiral column (Daicel CHIRALPAC AD-H). Optical rotations were measured on a Horiba high sensitive polarimeter SEPA-200. Specific rotations, $[\alpha]_D$, were reported in degree and the concentration (*c*) was given in gram per 100 mL of the indicated solvent.

All chemicals were of reagent grade and, if necessary, were purified in the usual manner prior to use.

Typical experimental procedure for the conjugate addition of aryl- and alkenylboronic acids to electron deficient ofefins

A mixture of phenylboronic acid (37 mg, 3.00 mmol), bis(1,5-cyclooctadiene)rhodium tetrafluoroborate (5.00 mg, 5 mol%), (*S*)-2,2'-bis(diphenylphosphino)-1,1'-binaphtyl [(*S*)-BINAP] (9.00 mg, 6 mol%) and the 4,4,4-trifluoro-1-phenyl-2-butenone (**1a**) (50 mg, 0.25 mmol) were placed in a flask and then a distilled toluene/water mixture (4 mL/0.5 mL) was added at room temperature. The flask was heated in a preheated oil bath at 120 °C and the mixture was stirred for 3 h. After filtration through silica (eluting ethyl acetate), the solvent was removed under reduced pressure. The residue was purified by silica gel column chromatography to give 4,4,4-trifluoro-1,3-diphenylbutan-1-one (**2a**) (63 mg, 90% yield). (**Method A**)

Typical procedure for the 1,4-addition of aryl- and alkenylstannanes to electron deficient ofefins

To a solution of $[Rh(COD)_2]BF_4$ (5.00 mg, 2 mol%) in THF (1

mL) were added 4,4,4-trifluoro-1-phenyl-2-butenone (**1a**) (100 mg, 0.50 mmol) and tributylphenylstannane (220 mg, 0.60 mmol) and water (9.00 mg, 0.50 mmol). After addition was completed, the reaction mixture was heated reflux temperature and stirred at that temperature for 2 h. After the reaction was quenched with sat. NH_4Cl aq., the whole was extracted with ethyl acetate three times, and combined organic layers were dried over andydrous Na_2SO_4, concentrated in *vacuo*. The residue was purified by silica gel column chromatography to give 4,4,4-trifluoro-1,3-diphenylbutan-1-one (**2a**) (120 mg, 86% yield). (**Method B**)

(3*R*)-4,4,4-Trifluoro-1,3-diphenylbutan-1-one (2a)

Yield : 90%; $[\alpha]^{34}_{D}$ = +36.6 (*c* = 1.04, CCl_4), ee = 90%, AD-H, Hexane : *i*-PrOH = 99.6 : 0.4, 0.7 mL/m (**Method A**); M.P. : 61-63 °C; ^{1}H NMR ($CDCl_3$) δ = 3.60 (dd, *J* = 4.01, 17.76 Hz, 1H), 3.70 (dd, *J* = 9.22, 17.76 Hz, 1H), 4.21-4.30 (m, 1H), 7.26-7.35 (m, 3H), 7.39-7.41 (m, 2H), 7.44-7.48 (m, 2H), 7.56-7.59 (m, 2H), 7.92-7.94 (m, 1H); ^{13}C NMR ($CDCl_3$) δ = 38.25, 44.77 (q, *J* = 27.45 Hz), 126.95 (q, *J* = 279.49 Hz), 128.01, 128.27, 128.67, 128.69, 129.00, 133.52, 134.71 (q, *J* = 1.38 Hz), 136.27, 195.25; ^{19}F NMR ($CDCl_3$) δ = –70.17 (d, *J* = 8.83 Hz 3F); IR (KBr) 3065, 3038, 2963, 2910, 1717, 1686, 1595, 1497, 1474, 1450, 1427, 1375, 1362, 1339, 1319, 1308, 1256, 1227, 1153, 1001, 961, 922, 880, 779 cm^{-1}.; HRMS calcd for $C_{16}H_{13}F_3O$ (M^+) 278.0918, found 278.0923.

(3*R*)-4,4,4-Trifluoro-3-(4-methylphenyl)-1-phenylbutan-1-one (2b)

Yield : 91%; $[\alpha]^{36}_{D}$ = +12.3 (*c* = 1.01, CCl_4), ee = 92%, AD-H, Hexane : *i*-PrOH = 99.6 : 0.4, 0.7 mL/m (**Method A**); M.P. : 80-81 °C; ^{1}H NMR ($CDCl_3$) δ = 2.31 (s, 3H), 3.58 (dd, *J* = 3.94, 17.73 Hz, 1H), 3.68 (dd, *J* = 9.33, 17.73 Hz, 1H), 4.15-4.26 (m, 1H), 7.14-7.15 (m, 2H), 7.26-7.29 (m, 2H), 7.44-7.47 (m, 2H), 7.56-7.59 (m, 1H), 7.92-7.94 (m, 2H); ^{13}C NMR ($CDCl_3$) δ = 21.01, 38.23, 44.42 (q, *J* = 27.37 Hz), 127.02 (q, *J* = 279.44 Hz), 128.00, 128.66, 128.82, 129.37, 131.51, 133.46, 136.33, 138.02, 195.33; ^{19}F NMR ($CDCl_3$) δ = –70.29 (d, *J* = 11.02 Hz, 3F); IR (KBr) 3036, 2963, 2907, 1686, 1595, 1578, 1520, 1508, 1423, 1373, 1306, 1259, 1200, 1153, 1119, 1097, 1020, 1003, 961, 885,, 814 cm^{-1}.; HRMS calcd for $C_{17}H_{15}F_3O$ (M^+) 292.1075, found 292.1068.

(3*R*)-4,4,4-Trifluoro-3-(4-methoxyphenyl)-1-phenylbutan-1-one (2c)

Yield : 89%; $[\alpha]^{35}_{D}$ = +12.6 (*c* =1.00, CCl_4), ee = 92% AD-H, Hexane : *i*-PrOH = 99 : 1, 0.7 mL/m (**Method A**); M.P. : 65-66 °C; ^{1}H NMR ($CDCl_3$) δ = 3.56 (dd, *J* = 3.93, 17.67 Hz, 1H), 3.66 (dd, *J* = 9.38, 17.67 Hz, 1H), 3.78 (s, 3H), 4.15-4.23 (m, 1H), 6.85-6.87 (m, 2H), 7.30-7.32 (m, 2H), 7.44-7.47 (m, 2H), 7.56-7.59 (m, 1H), 7.92-7.93 (m, 2H); ^{13}C NMR ($CDCl_3$) δ = 38.31, 44.54 (q, *J* = 27.53 Hz), 55.16, 114.07, 126.50 (q, *J* = 1.38 Hz), 127.02 (q, *J* = 279.19 Hz), 128.00, 128.68, 130.04, 133.49, 136.34, 159.43, 195.41; ^{19}F NMR ($CDCl_3$) δ = –69.80 (d, *J* = 8.83 Hz, 3F); IR (KBr) 3026, 2961, 2839, 1682, 1614, 1595, 1518, 1450, 1431, 1371, 1308, 1246, 1227, 1207, 1184, 1153, 1121, 1099, 1036, 1001, 961, 883, 818, 764, 685 cm^{-1}.; HRMS calcd for $C_{17}H_{15}F_3O_2$ (M^+) 308.1024, found 308.1026

(3*R*)-3-(4-Chlorophenyl)-4,4,4-trifluoro-1-phenylbutan-1-one (2d)

Yield : 94%; $[\alpha]^{37}_{D}$ = +16.5 (*c* = 1.00, CCl_4), ee = 94%, AD-H, Hexane : *i*-PrOH = 99.6 : 0.4, 0.7 mL/m (**Method A**); M.P. : 66-68 °C; ^{1}H NMR ($CDCl_3$) δ = 3.59 (dd, *J* = 3.86, 17.80 Hz, 1H), 3.67 (dd, *J* = 9.47, 17.80 Hz, 1H), 4.18-4.26 (m, 1H), 7.28-7.35 (m, 4H), 7.45-7.48 (m, 2H), 7.57-7.60 (m, 1H), 7.91-7.93 (m, 2H); ^{13}C NMR ($CDCl_3$) δ = 38.14, 44.30 (q, *J* = 27.73 Hz), 126.68 (q, *J* = 279.31 Hz), 128.00, 128.75, 129.00, 130.34, 133.04 (q, *J* = 1.26 Hz), 133.67, 134.30, 136.11, 194.96; ^{19}F NMR ($CDCl_3$) δ = –70.20 (d, *J* = 8.83 Hz, 3F); IR (KBr) 2963, 2956, 1670, 1595, 1580, 1497, 1450, 1425, 1319, 1310, 1281, 1250, 1207, 1184, 1157, 1103, 1092, 1069, 1015, 961, 924, 822, 804, 779 cm^{-1}; HRMS calcd for $C_{16}H_{13}ClF_3O$ (M+H) 313.0607, found 313.0618.

(3*R*)-3-(3-Chlorophenyl)-4,4,4-trifluoro-1-phenylbutan-1-one (2e)

Yield : 81%; $[\alpha]^{34}_{D}$ = +13.3 (*c* = 1.10, CCl_4), ee = 91% AD-H, Hexane : *i*-PrOH = 99.6 : 0.4, 0.7 mL/m (**Method A**); ^{1}H NMR ($CDCl_3$) δ = 3.62 (dd, *J* = 4.20, 17.92 Hz, 1H), 3.68 (dd, *J* = 9.05, 17.92 Hz, 1H), 4.21-4.29 (m, 1H), 7.20-7.67 (m, 7H), 7.90-8.03 (m, 2H); ^{13}C NMR ($CDCl_3$) δ = 38.13, 44.50 (q, *J* = 27.68 Hz), 126.62 (q, *J* = 279.44 Hz), 127.39, 128.00, 128.56, 128.74, 129.07, 129.93, 133.68, 134.51, 136.05, 136.54, 194.81; ^{19}F NMR ($CDCl_3$) δ = –70.05 (d, *J* = 11.02 Hz, 3F); IR (neat) 3065, 2961, 1692, 1597, 1578, 1479, 1450, 1435, 1420, 1371, 1346, 1307, 1258, 1223, 1158, 1109 , 1001, 989, 972, 783, 756 cm^{-1}.; HRMS calcd for $C_{16}H_{13}ClF_3O$ (M+H) 313.0607, found 313.0607.

(3*R*)-4,4,4-Trifluoro-3-(4-fluorophenyl)-1-phenylbutan-1-one (2g)

Yield : 80%; $[\alpha]^{35}_{D}$ = +6.4 (*c* = 0.85, CCl_4), ee = 90%, AD-H, Hexane : *i*-PrOH = 99 : 1, 0.7 mL/m (**Method A**); M.P. : 94-95 °C; ^{1}H NMR ($CDCl_3$) δ = 3.51 (dd, *J* = 3.99, 17.76 Hz, 1H), 3.59 (dd, *J* = 9.40, 17.76 Hz, 1H), 4.12-4.20 (m, 1H), 6.90-6.98 (m, 2H), 7.28-7.51 (m, 5H), 7.83-7.85 (m, 2H); ^{13}C NMR ($CDCl_3$) δ = 38.30, 44.17 (q, *J* = 27.65 Hz), 115.66 (d, *J* = 21.38 Hz), 126.80 (q, *J* = 279.56 Hz), 127.99, 128.75, 130.63, 130.70, 133.63, 136.21, 162.57 (d, *J* = 247.24 Hz), 195.10; ^{19}F NMR ($CDCl_3$) δ = –69.88 (d, *J* = 8.83 Hz, 3F), –114.68 (s, 1F); IR (KBr) 2926, 2856, 1693, 1659, 1599, 1580, 1514, 1448, 1423, 1350, 1306, 1259, 1165, 1109, 1067, 1016, 962, 922, 831, 791, 689 cm^{-1}.; HRMS calcd for $C_{16}H_{13}F_4O$ (M+H) 297.0903, found 297.0905.

(3*R*)-3-(4-Acetylphenyl)-4,4,4-trifluoro-1-phenylbutan-1-one (2h)

Yield ; 95%; $[\alpha]^{18}_{D}$= +32.4 (*c* = 0.98, CCl_4), ee = 93%, AD-H, Hexane : *i*-PrOH = 80 : 20, 0.7 mL/m (**Method A**); M.P. : 96-97 °C; ^{1}H NMR ($CDCl_3$) δ = 2.36 (s, 3H), 3.64 (dd, *J* = 3.73, 17.89 Hz, 1H), 3.74 (dd, *J* = 9.81, 17.89 Hz, 1H), 4.27-4.35 (m, 1H), 7.45-7.52 (m, 4H), 7.57-7.60 (m, 1H), 7.91-7.94 (m, 4H); ^{13}C NMR ($CDCl_3$) δ = 26.48, 37.98, 44.79 (q, *J* = 27.67 Hz), 126.57 (q, *J* = 279.44 Hz), 127.95, 128.58, 128.72, 129.28, 133.68, 135.98, 136.90, 139.65 (q, *J* = 1.38 Hz), 194.84, 197.36; ^{19}F NMR ($CDCl_3$) δ = –69.82 (d, *J* = 9.04 Hz, 3F); IR (KBr) 2964, 1738, 1684, 1609, 1595, 1578, 1448, 1427, 1319, 1310, 1250, 1221, 1161, 1123, 1101, 1016, 945, 924, 831, 779, 687 cm^{-}

^{1}.; HRMS calcd for $C_{18}H_{16}F_3O_2$ (M+H) 321.1102, found 321.1110.

(3*R*)-3-(4-Ethoxycarbonylphenyl)-4,4,4-trifluoro-1-phenylbutan-1-one (2i)

Yield : 80%; $[\alpha]^{19}_D$ = +31.6 (*c* = 0.77, CCl_4), ee = 92%, AD-H, Hexane : *i*-PrOH = 95 : 5, 0.7mL/m (**Method A**); M.P. : 85-86 °C; ^{1}H NMR ($CDCl_3$) δ = 1.37 (t, *J* = 7.12 Hz, 3H), 3.62 (dd, *J* = 3.82, 17.86 Hz, 1H) , 3.72 (dd, *J* = 9.53, 17.86 Hz, 1H), 4.25-4.35 (m, 1H), 4.36 (q, *J* = 7.12 Hz, 2H), 7.40-7.52 (m, 4H), 7.53-7.61 (m, 1H), 7.86-7.94 (m, 2H), 7.96-8.04 (m, 2H); ^{13}C NMR ($CDCl_3$) δ = 14.26, 38.10, 44.85 (q, *J* = 27.79 Hz), 61.01, 126.62 (q, *J* = 279.69 Hz), 128.00, 128.76, 129.07, 129.87, 130.55, 133.69, 136.10, 139.41, 166.05, 194.92; ^{19}F NMR ($CDCl_3$) δ = –69.73 (d, *J* = 8.83 Hz, 3F); IR (KBr) 2963, 1711, 1684, 1614, 1450, 1433, 1369, 1311, 1286, 1250, 1207, 1168, 1151, 1103, 1022, 964, 851, 766, 754, 714, 690, 644, 629, 594 cm^{-1}.; HRMS calcd for $C_{19}H_{18}F_3O_3$ (M+H) 351.1208, found 351.1214.

(3*S*)-4,4,4-Trifluoro-1-phenyl-3-(2-thienyl)butan-1-one (2j)

Yield : 65%; $[\alpha]^{36}_D$ = –4.4 (*c* = 0.98, CCl_4), ee = 90%, AD-H, Hexane : *i*-PrOH = 99.6 : 0.4, 0.7 mL/m (**Method A**); M.P. : 89-91 °C; ^{1}H NMR ($CDCl_3$) δ = 3.54 (dd, *J* = 4.12, 17.60 Hz, 1H), 3.62 (dd, *J* = 9.03, 17.60 Hz, 1H), 4.38-4.46 (m, 1H), 7.11-7.12 (m, 1H), 7.28-7.30 (m, 2H), 7.45-7.48 (m, 2H), 7.59-7.60 (m, 1H), 7.92-7.94 (m, 2H); ^{13}C NMR ($CDCl_3$) δ = 38.58, 40.26 (q, *J* = 28.37 Hz), 124.16, 126.02, 126.66 (q, *J* = 279.19 Hz), 127.42, 128.00, 128.70, 133.54, 134.75, 136.25, 195.19; ^{19}F NMR ($CDCl_3$) δ = –70.64 (d, *J* = 8.75 Hz, 3F); IR (KBr) 3749, 3107, 3090, 3061, 2964, 2941, 1717, 1684, 1595, 1578, 1541, 1448, 1433, 1331, 1308, 1295, 1219, 1146, 1094, 1016, 978 cm^{-1}.; HRMS calcd for $C_{14}H_{12}F_3OS$ (M+H) 285.0561, found 285.0555.

(3*R*)-*N*,*N*-Dimethyl-4,4,4-trifluoro-3-phenylbutanamide (2m)

Yield : 46%; $[\alpha]^{35}_D$ = –44.0 (*c* = 1.01, CCl_4), ee = 92% AD-H, Hexane : *i*-PrOH = 97 : 3, 0.7 mL/m (**Method A**); M.P. : 68-69 ℃; ^{1}H NMR ($CDCl_3$) δ = 2.87 (s, 3H), 2.94 (d, *J* = 6.72 Hz, 2H), 2.97 (s, 3H), 4.10-4.18 (m, 1H), 7.29-7.37 (m, 5H); ^{13}C NMR ($CDCl_3$) δ = 33.11 (q, *J* = 1.50 Hz), 35.60, 37.03, 46.01 (q, *J* = 27.13 Hz), 127.00 (q, *J* = 279.52 Hz), 128.13, 128.58, 128.93, 134.95 (q, *J* = 1.51 Hz), 168.72; ^{19}F NMR ($CDCl_3$) δ = –70.19 (d, *J* = 8.83 Hz, 3F); IR (KBr) 2928, 1637, 1499, 1458, 1354, 1286, 1256, 1211, 1163, 1101, 1059, 966, 880, 804, 783, 758, 706, 687, 613 cm^{-1}; HRMS calcd for $C_{12}H_{15}F_3NO$ (M+H) 246.1107, found 246.1102.

3,3,3-Trifluoro-1-nitro-2-phenylpropane (2n)

Yield : 45%; $[\alpha]^{26}_D$ = +2.8 (*c* = 0.85, CCl_4), ee = 5% , AD-H, Hexane : *i*-PrOH = 99.6 : 0.4, 0.5 mL/m (**Method A**); ^{1}H NMR ($CDCl_3$) δ = 4.29-4.37 (m, 1H), 4.84 (dd, *J* = 8.98, 13.76 Hz, 1H), 4.98 (dd, *J* = 5.73, 13.76 Hz, 1H), 7.30-7.36 (m, 2H), 7.37-7.44 (m, 3H); ^{13}C NMR ($CDCl_3$) δ = 48.06 (q, *J* = 28.47 Hz), 73.84, 124.95 (q, *J* = 280.30 Hz), 128.75, 129.26, 129.57, 129.99; ^{19}F NMR ($CDCl_3$) δ = –69.47 (d, *J* = 8.75 Hz, 3F); IR (neat) 3040, 2961, 1568, 1458, 1437, 1377, 1304, 1259, 1177, 1119, 1005, 984, 795, 762, 698, 665, 500 cm^{-1}; HRMS calcd for $C_9H_8F_3NO_2$ (M^+) 219.0507, found 219.0503.

Phenyl 3,3,3-trifluoro-2-phenylsulfone (2o)

Yield : 27%; $[\alpha]^{35}_D$= –6.1 (*c* = 1.09, CCl_4), ee = 9%, AD-H, Hexane : *i*-PrOH = 97 : 3, 0.7 mL/m (**Method A**); Yield : 61% (**Method B**), M.P. : 91-92 °C; ^{1}H NMR ($CDCl_3$) δ = 3.74 (dd, *J* = 3.48, 14.69 Hz, 1H), 3.79 (dd, *J* = 9.93, 14.69 Hz, 1H), 3.93-4.02 (m, 1H), 7.11-7.13 (m, 2H), 7.18-7.21 (m, 2H) 7.23-7.26 (m, 1H), 7.33-7.36 (m, 2H), 7.49-7.52 (m, 1H), 7.58-7.60 (m, 2H); ^{13}C NMR ($CDCl_3$) δ = 45.81 (q, *J* = 28.64 Hz), 55.34, 125.37 (q, *J* = 280.44 Hz), 127.79, 128.73, 128.88, 129.05, 129.08, 131.00, 133.63, 138.95; ^{19}F NMR ($CDCl_3$) δ = –70.55 (d, *J* = 6.64 Hz, 3F); IR (KBr) 2986, 1558, 1418, 1310, 1259, 1188, 1157, 1142, 1105, 1082, 1030, 870, 795, 754, 698, 689, 592, 550 cm^{-1}; HRMS calcd for $C_{15}H_{13}F_3O_2S$ (M^+) 314.0588, found 314.0593.

Diethyl (2-phenyl-2-trifluoromethylethyl)phosphonate (2p)

Yield : 47% (**Method B**), ^{1}H NMR ($CDCl_3$) δ = 1.01 (t, *J* = 7.06 Hz, 3H), 1.13 (t, *J* = 7.05 Hz 3H), 2.31-2.44 (m, 2H), 3.53-3.60 (m, 1H), 3.70-3.96 (m, 4H), 7.53 (s, 5H); ^{13}C NMR ($CDCl_3$) δ = 15.97 (d, *J* = 6.29 Hz), 16.02 (d, *J* = 6.54 Hz), 26.03 (dq, *J* = 147.48, 1.46 Hz), 45.09 (dq, *J* = 28.37, 1.92 Hz), 61.63 (d, *J* = 5.85 Hz), 61.67 (d, *J* = 5.33 Hz), 126.28 (dq, *J* = 280.19, 22.89 Hz), 128.51, 128.52, 129.17, 133.58; ^{19}F NMR ($CDCl_3$) δ = –71.55 (d, *J* = 9.78 Hz, 3F). IR (neat) 3037, 2984, 2932, 1723, 1497, 1457, 1416, 1393, 1367, 1257, 1176, 1147, 1109, 1061, 1026, 969, 900, 864, 812, 752 cm^{-1}.

(3*R*)-4,4-Difluoro-1,3-diphenylbutan-1-one (2q)

Yield : 92%; $[\alpha]^{36}_D$ = –12.6 (*c* = 0.99, CCl_4), ee = 74%, AD-H, Hexane : *i*-PrOH = 99 : 1, 0.7 mL/m (**Method A**); M.P. : 56-58 °C; ^{1}H NMR ($CDCl_3$) δ = 3.54 (dd, *J* = 7.99, 17.82 Hz, 1H), 3.62 (dd, *J* = 5.47, 17.82 Hz, 1H), 3.91-4.00 (m, 1H), 6.05 (dt, *J* = 2.81, 56.61 Hz, 1H), 7.26-7.59 (m, 8H), 7.95-7.97 (m, 2H); ^{13}C NMR ($CDCl_3$) δ = 37.37 (t, *J* = 2.82 Hz), 44.56 (t, *J* = 19.97 Hz), 117.24 (t, *J* = 244.35 Hz), 127.75, 128.01, 128.64, 128.68, 128.90, 133.35, 136.44 (m), 136.65, 196.72; ^{19}F NMR ($CDCl_3$) δ = –120.18 (ddd, *J* = 14.12, 56.61, 276.75 Hz, 1F), -123.34 (ddd, *J* = 18.36, 56.61, 276.75, 1F); IR (KBr) 3064, 2963, 2926, 1693, 1597, 1477, 1435, 1418, 1348, 1298, 1258, 1223, 1157, 1084, 1065, 1001, 989, 974, 783, 756, 714, 648 cm^{-1}.; HRMS calcd for $C_{16}H_{14}F_2O$ (M+H) 261.1091, found 261.1088.

4,4,4-Trifluoro-3-(3-methoxyphenyl)-1-phenylbutan-1-one (2r)

Yield : 66% (**Method B**); M.P. : 69-70 °C; ^{1}H NMR ($CDCl_3$) δ = 3.58 (dd, *J* = 4.10, 17.73 Hz, 1H), 3.68 (dd, *J* = 9.12, 17.73 Hz, 1H), 3.80 (s, 3H), 4.19-4.27 (m, 1H), 6.83-6.85 (m, 1H), 6.93 (s, 1H), 6.98 (d, *J* = 22.70 Hz, 1H), 7.25 (t, *J* = 8.16 Hz, 1H), 7.46 (m, 2H), 7.57 (m, 1H), 7.93 (m, 2H); ^{13}C NMR ($CDCl_3$) δ = 38.28, 44.77 (q, *J* = 27.54 Hz), 55.21, 113.39, 115.18, 121.29, 126.91 (q, *J* = 284.09 Hz), 128.04, 128.71, 129.65, 133.53, 136.05 (q, *J* = 1.63 Hz), 136.32, 159.65, 195.24; ^{19}F NMR ($CDCl_3$) δ = –70.08 (d, *J* = 9.78 Hz, 3F); IR (KBr) 3073, 3007, 2969, 2942, 2842, 1686, 1602, 1496, 1466, 1450, 1440, 1376, 1317, 1304, 1265, 1251, 1222, 1199, 1160, 1105 cm^{-1}.; HRMS calcd for $C_{17}H_{16}F_3O_2$ (M+H) 309.1102, found 309.1109.

4,4,4-Trifluoro-3-(4-cyanophenyl)-1-phenylbutan-1-one (2t)

Yield : 13% (**Method B**); ^{1}H NMR ($CDCl_3$) δ = 3.64 (dd, *J* = 3.96, 18.00 Hz, 1H), 3.70 (dd, *J* = 9.47, 18.00 Hz, 1H), 4.25-4.33 (m, 1H), 7.47 (t, *J* = 7.59 Hz, 2H), 7.52 (d, *J* = 8.21 Hz, 2H),

7.57-7.64 (m, 3H), 7.91 (d, J = 7.59 Hz, 2H); ^{13}C NMR ($CDCl_3$) δ = 37.99, 44.98 (q, J = 28.06 Hz), 118.25, 126.37 (q, J = 279.69 Hz), 127.99, 128.84, 129.90, 132.44, 133.04, 133.90, 135.85, 139.81, 194.60; ^{19}F NMR ($CDCl_3$) δ = –69.71 (d, J = 9.78 Hz, 3F); IR (neat) 3063, 2927, 2231, 1691, 1597, 1581, 1507, 1449, 1421, 1369, 1307, 1257, 1225, 1159, 1108, 1066, 1022, 1002, 961, 925 cm^{-1}.

Determination of the absolute stereochemistry

To a suspension of lithium aluminium hydride (19 mg, 0.50 mmol) in THF (2 mL) was dropwise added a THF solution of **2a** (69 mg, 0.25 mmol) at 0 °C. The reaction mixture was stirred at that temperature for 1 h, and then the reaction was quenched with sturated aqueous NH_4Cl. The whole was extracted with EtOAc three times. The combined organic layers were dried over anhydrous Na_2SO_4, filtered, and concentrated *in vacuo*. The residue was purified by silica gel column chromatography to give the corresponding alcohols **3a** as a diastereomeric mixture in a ratio of 1 : 1 (57 mg, 0.20 mmol, 81% yield).

To a suspension of $CuSO_4$-SiO_2 (136 mg)[21] in hexane (2 mL) was added the alcohols 4a (56 mg, 0.20 mmol) at room temperature. Then the reaction was refluxed for 1 h. After the reaction was allowed to cool to roomtemperature, the mixture was fitered, and concentrated in vacuo. The residue was purified by silica gel column chromatography to afford the dehydrated product **4a** (known compound) in 26% yield (14 mg, 0.052 mmol).

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