Available online at www.sciencedirect.com
SCIENCE DIRECT®
Journal of Fluorine Chemistry 126 (2005) 791–795
JOURNAL OF FLUORINE CHEMISTRY
www.elsevier.com/locate/fluor

One-pot synthesis of bromodifluoroacetimidoyl halides and its Suzuki coupling reactions with aryl boronic acids

Yong-Ming Wu *, Ya Li, Juan Deng

Key Laboratory of Organofluorine Chemistry, Shanghai Institute of Organic Chemistry, Chinese Academy of Sciences, 354 Fenglin Road, Shanghai 200032, China

Received 10 January 2005; received in revised form 26 February 2005; accepted 28 February 2005
Available online 19 April 2005

Abstract

N-aryl bromodifluoroacetimidoyl halides were prepared by the reaction of bromodifluoroacetic acid, triphenyl phosphine, *p*-arylaniline and triethylamine in tetrachloromethane in good yields. Palladium-catalyzed cross-coupling reaction of *N*-aryl bromodifluoroimidoyl iodide with arylboronic acids was realized to afford bromodifuoromethyl ketimine in good yields.

Keywords: Suzuki coupling reaction; Bromodifluoroacetimidoyl halide; Arylboronic acids; Imine

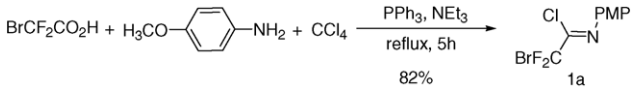
1. Introduction

The Suzuki coupling reaction provides a general method for the formation of carbon–carbon single bond. Palladium-catalyzed cross-coupling reaction of arylboronic acids with alkenyl or aryl halides and acid chlorides have been developed for applications in natural and unnatural products synthesis [1]. The coupling reactions between imidoyl halides and boronic acids tend to be the unit structure of imidoyl halide exsited in a cyclic aromatic compound [2]. However, to our best knowledge, the Suzuki coupling reaction of alkyl or aryl imidoyl halides has not yet been reported. This is probably due to the labile nature of alkyl or aryl imidoyl halides, such as moisture sensitive [3].

In recent years, the introduction of difluoromethylene fragment into organic compounds has proved to be attractive [4]. It has been argued that the difluoromethylene group could be regarded as an isopolar–isosteric replacement for oxygen [5]. Bromodifluoroacetate, chlorodifluomethyl ketones and bromodifluoromethyl acetylene are widely used as reagents to introduce a CF_2 moiety into molecules [6]. In search for new CF_2-containing synthons, we have found that *N*-arylbromodifluoroimidoyl halide is a versatile reactive intermediate in the synthesis of CF_2-containing compounds. Herein, we wish to report a facile approach to bromodifluoromethyl ketimine via palladium-catalyzed Suzuki coupling reaction of bromodifuoroacetimidol halides with arylboronic acids.

2. Results and discussion

N-aryl bromodifluoroacetimidoyl halides were prepared according to Uneyama's One-pot procedure [7]. When the mixture of bromodifluoroacetic acid, triphenyl phosphine, *p*-methoxyaniline and triethylamine in tetrachloromethane was refluxed for 5 h, the desired bromodifluoroacetimidoyl chloride (**1a**) was isolated in 82% yield (Scheme 1). It was worth to note that the carbon–bromine bond in bromodifluoroacetic acid remained intact in the reaction conditions, i.e.:

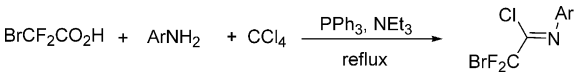


Scheme 1. Preparation of bromodifluoroacetimidoyl chloride (**1**).

* Corresponding author. Tel.: +86 21 54925190; fax: +86 21 64166128.
E-mail address: ymwu@mail.sioc.ac.cn (Y.-M. Wu).

0022-1139/$ – see front matter © 2005 Elsevier B.V. All rights reserved.
doi:10.1016/j.jfluchem.2005.02.016

Table 1
Synthesis of *N*-aryl-2,2,2-bromodifluoroacetimidoyl chlorides



Entry	Ar	Product	Yield (%)[a]
1	*p*-MeO-C_6H_4	**1a**	82
2	*p*-Cl-C_6H_4	**1b**	72
3	*m*-Me-*p*-Br-C_6H_4	**1c**	70
4	C_6H_5	**1d**	69
5	*p*-NO_2-C_6H_4	**1e**	64
6	*o*-Me-*p*-Br-C_6H_4	**1f**	75
7	*o*-Cl-C_6H_4	**1g**	68
8	*o*-Br-C_6H_4	**1h**	60

[a] Isolated yield.

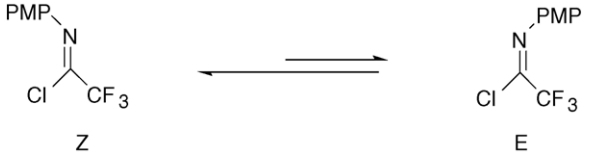
By this method, other *N*-aryl substituted bromodifluoroacetimidoyl chlorides were also synthesized, the results are summarized in Table 1. The configuration of the carbon–nitrogen double bond was also studied. ^{19}F NMR analysis showed that only one of the two possible geometric isomers was obtained. We tentatively assigned *Z* form for the following reason: Fustero have calculated the energy of *Z* and *E* form of trifluoroacetimidoyl chloride by an ab initio smethod and found that the *Z* isomer was 5.6 kcal mol^{-1} lower than the corresponding *E* form (Scheme 2). They considered that trifluoroacetimidoyl chloride is existed in *Z* form [8].

Bromodifluoroacetimidoyl iodide (**2**) was prepared almost in quantitative yields by displacement of the chlorine in imidoyl chloride (**1a**) with iodide in a NaI–acetone system (Scheme 3) [7].

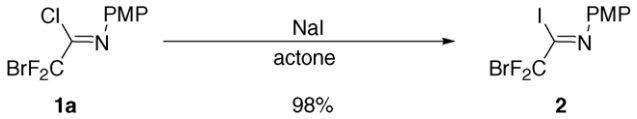
With bromodifluoroimidoyl halides in hand, we then studied Palladium-catalyzed Suzuki coupling reactions. As the carbon–iodide bond was more reactive than carbon–chloride bond [9], the coupling reaction of bromodifluoroimidoyl iodide (**2**) with arylboronic acid was first chosen as a model reaction to opitimize the reaction conditions. The reaction was first carried out in a mixture of bromodifluoroacetimidoyl iodide (**2**), *p*-methoxyphenylboronic acid, $PdCl_2(PPh_3)_2$, K_2CO_3 and THF at 80 °C for 24 h, the desired coupling product was not obtained at all (Table 2, Entry **1**). Different bases (KOH, KF or K_2CO_3) and different solvents (Toluene, DMF or THF) were also tested in this reaction, all the results were not satisfied (Table 2, Entries **2–7**). The fact that Ag_2O dramatically enhanced the rate of some coupling reaction encouraged us to use it to activate the reaction [10]. Fortunately, the reaction's time was decreased to 8 h and the coupling product was obtained in 78% yield after 1.0 equiv. Ag_2O was added to the reaction mixture (Table 2, Entry **8**). Further studies indicated that 0.5 equiv. Ag_2O was sufficient for promoting this reaction (Table 2, Entry **9**). When the reaction was carried out with Ag_2O and using Cs_2CO_3 as a base, the yield was low though bromodifluoroacetimidoyl iodide (**2**) was completely consumed (Table 2, Entries **10–12**). This might be due to the decomposition of **2** under the reaction conditions.

The reactions of various boronic acids with **2** were explored under the optimized reaction conditions, the results are shown in Table 3. The cross-coupling reaction of **2** with various arylboronicic acids proceeded smoothly with satisfactory yields. It was found that different substituents on benzene ring had a little effect on the result in this reaction. However, *o*-substituted arylboronic acid gave the coupling product in lower yield, obviously, this was due to the steric hindrance. Because of the existing of carbon–nitrogen double bond in products, two possible isomers *Z* and *E* would be presented in the product, their ratio could be determined by ^{19}F NMR spectra. It is interesting to note that when more steric arylboronic acids (e.g.: *o*- or *m*-substituteed) were used as substrates, only one isomer was obtained in their products (Table 3, Entries **5**, **7** and **8**). From the view point of steric effects, this isomer could be easily assigned to *Z* form. For other substrates, the major isomer were also in *Z* form with the ratio from 3:2 to 50:1 of *Z* and *E* form (Table 3).

When bromodifluoroacetimidoyl chloride (**1a**) underwent similar reaction conditions, the reaction was sluggish. After 24 h, **1a** was almost consumed and the coupling product was isolated in only 59% yield. One can envision that prolonged reaction time resulted in the decomposition of more starting material **1a**.

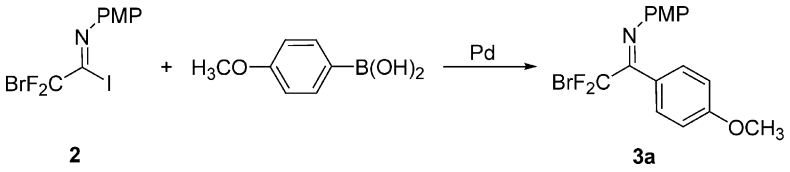


Scheme 2.



Scheme 3. Preparation of bromodifluoroacetimidoyl iodide (**2**).

Table 2
Effect of the bases and solvents on the Suzuki reaction of **2**



2 **3a**

Entry	Conditions	Time (h)	Time (h)[a]
1	$PdCl_2(PPh_3)_2$, K_2CO_3, THF, 70 °C	12	0
2	$PdCl_2(PPh_3)_2$, KOH, THF, 70 °C	24	22
3	$PdCl_2(PPh_3)_2$, KF, THF, 70 °C	24	–
4	$PdCl_2(PPh_3)_2$, K_2CO_3, DMF, 100 °C	24	–
5	$PdCl_2(PPh_3)_2$, K_2CO_3, toluene, 100 °C	22	16
6	$Pd(PPh_3)_4$, K_2CO_3, toluene, 100 °C	24	–
7	$PdCl_2(PPh_3)_2$, K_2CO_3/(0.5 equiv.) Cu_2O, THF, 70 °C	24	30
8	$PdCl_2(PPh_3)_2$, K_2CO_3/(1.0 equiv.) Ag_2O, THF, 70 °C	8	78
9	$PdCl_2(PPh_3)_2$, K_2CO_3/(0.5 equiv.) Ag_2O, THF, 70 °C	12	81
10	$PdCl_2(PPh_3)_2$, K_2CO_3/(0.5 equiv.) Ag_2O, toluene, 100 °C	18	73
11	$PdCl_2(PPh_3)_2$, Cs_2CO_3/(0.5 equiv.) Ag_2O, THF, 70 °C	20	4
12	$PdCl_2(PPh_3)_2$, Cs_2CO_3/(0.5 equiv.) Ag_2O, Dioxane, 90 °C	6	22

[a] Isolated yield.

Table 3
Palladium-catalyzed and Ag_2O-assisted cross-coupling reaction of bromodifluoroacetimidoyl iodide (**2**) with various arylboronic acids

Entry	$ArB(OH)_2$	Product	Isomer ratio[a]	Yield (%)[b]
1	*p*-MeO-$C_6H_4B(OH)_2$	**3a**	4:1	81
2	$C_6H_5B(OH)_2$	**3b**	5:1	79
3	*p*-MeS-$C_6H_4B(OH)_2$	**3c**	37:1	63
4	*p*-Ph-$C_6H_4B(OH)_2$	**3d**	50:1	73
5	*m*-Me-$C_6H_4B(OH)_2$	**3e**	1:0	73
6	*p*-CF_3-$C_6H_4B(OH)_2$	**3f**	3:2	72
7	*m*-CF_3-$C_6H_4B(OH)_2$	**3g**	1:0	61
8	*o*-MeO-$C_6H_4B(OH)_2$	**3h**	1:0	46

[a] Ratio of *Z*:*E*, based on ^{19}F NMR.
[b] Isolated yield.

In summary, the palladium-catalyzed cross-coupling reaction of *N*-aryl bromodifluoroacetimidoyl iodides with arylboronic acids was realized affording bromodifluoromethyl ketimine in good yield. This method efficiently and nicely complements the existing methodology based on the condensition reaction of ketone with arylamines.

3. Experimental

Unless otherwise noted, solvents and reagents were commercially available and used as received. ^1H NMR spectra were recorded on a Brucker AM-300 (300 MHz) spectrometer with Me_4Si as internal standard. ^{19}F NMR spectra were taken on Brucher AM-300 (282 MHz) spectrometer with $CFCl_3$ as external standard, downfield shifts being designed as positive. The ^{13}C NMR spectra were measured at Brucker AM-300 (75 MHz) spectrometer with all protons decoupled, and the chemical shifts are reported in ppm downfield of $SiMe_4$. Mass spectra were taken on a HP 5989a spectrometer, accurate mass measurements were performed on Finnigan MAT instrument, and elemental analysis were performed in this institute.

3.1. General procedure for the synthesis of bromodifluoroacetimidoyl chlorides

PPh_3 (48.1 g, 184 mmol), Et_3N (10.4 ml, 61 mmol), CCl_4 (50 ml), $BrCF_2COOH$ (10.7 g, 61 mmol) and *p*-anisidine (8.7 g, 70 mmol) was added to a 250 ml three-necked flask. After stirring for 5 h under refluxing, the solvent was removed under reduced pressure, and the residue was extracted with hexane (3× 50 ml). The filtrate was concentrated under reduced pressure and subsequent column chromatography with 5% ethyl acetate in hexane as elucent to afford **1a** (14.9 g, 82%) as a yellow oil.

*3.1.1. N-(p-anisyl)-2-bromo-2,2-difluoroacetimidoyl chloride (**1a**)*

Yield: 82%, yellow oil. ^{1}H NMR: δ 7.30–7.33 (m, 2H), 6.95–6.98 (m, 2H), 3.85 (s, 3H). ^{19}F NMR: δ −53.17 (s). IR (neat, cm^{-1}): 3006, 2960, 2839, 2056, 1677, 1599, 1505, 1148, 985, 804, 630; *m/z* (EI): 299 (80), 297 (64), 218 (100), 168 (37). Calc. for $C_9H_7BrClF_2NO$: C, 36.21; H, 2.36; N, 4.69; F, 12.73. Found: C, 36.34; H, 2.42; N, 4.92; F, 13.09.

*3.1.2. N-(p-chlorophenyl)-2-bromo-2, 2-difluoroacetimidoyl chloride (**1b**)*

Yield: 72%, yellow oil. ^{1}H NMR: δ 7.42 (ddd, J = 8.70, 2.70, 1.80 Hz, 2H), 7.07 (ddd, J = 8.70, 1.80 Hz, 2H). ^{19}F NMR: δ −54.26 (s). IR (neat, cm^{-1}): 3093, 1890, 1680, 1486, 1233, 1094, 863, 790. *m/z* (EI): 303 (94), 268 (24), 222 (64), 172 (100). Calc. for $C_8H_4BrCl_2F_2N$: C, 31.72; H, 1.33; N, 4.62. Found: C, 31.63; H, 1.55; N, 4.89.

*3.1.3. N-(p-bromo-m-methylphenyl)-2-bromo-2, 2-difluoroacetimidoyl chloride (**1c**)*

Yield: 70%, yellow oil. ^{1}H NMR: δ 7.59 (d, J = 8.70 Hz, 1H), 6.98 (d, J = 2.10 Hz, 1H), 6.82 (dd, J = 8.70, 2.70 Hz, 1H), 2.44 (s, 3H). ^{19}F NMR: δ −54.22 (s). IR (neat, cm^{-1}): 2955, 1880, 1689, 1590, 1472, 1237, 1031, 831, 782. *m/z* (EI): 361 (34), 282 (20), 232 (100), 166 (73), 89 (100). Calc. for $C_9H_6Br_2ClF_2N$: C, 29.91; H, 1.67; N, 3.88. Found: C, 30.11; H, 1.71; N, 4.19.

*3.1.4. N-phenyl-2-bromo-2,2-difluoroacetimidoyl chloride (**1d**)*

Yield: 69%, yellow oil. ^{1}H NMR: δ 7.42–7.48 (m, 2H), 7.27–7.33 (m, 1H), 7.09–7.12 (m, 2H). ^{19}F NMR: δ −54.08 (s). IR (neat, cm^{-1}): 3068, 3038, 2930, 1943, 1680, 1594, 1488, 1228, 1150, 859, 784. *m/z* (EI): 269 (21), 232 (9), 188 (24), 138 (67), 77 (100). Calc. for $C_8H_5BrClF_2N$: C, 35.79; H, 1.88; N, 5.22. Found: C, 35.59; H, 1.99; N, 5.39.

*3.1.5. N-phenyl-2-bromo-2,2-difluoroacetimidoyl chloride (**1e**)*

Yield: 64%, yellow oil. ^{1}H NMR: δ 8.34 (dd, J = 8.70, 1.80 Hz, 2H), 7.14 (dd, J = 8.70, 2.40 Hz, 2H). ^{19}F NMR: δ −55.04 (s). IR (neat, cm^{-1}): 3110, 3080, 2937, 2453, 1686, 1606, 1525, 1487, 1345, 1153, 875, 756. *m/z* (EI): 314 (24), 183 (100), 75 (54). Calc. for $C_8H_4BrClF_2N_2O_2$: C, 30.65; H, 1.29; N, 8.94. Found: C, 30.81; H, 1.54; N, 9.26.

*3.1.6. N-(p-bromo-o-methylphenyl)-2-bromo-2, 2-difluoroacetimidoyl chloride (**1f**)*

Yield: 75%, yellow oil. ^{1}H NMR:δ 7.42 (s, 1H), 7.38 (dd, J = 8.40, 2.10 Hz, 1H), 6.81 (d, J = 8.40 Hz, 1H), 2.17 (s, 3H). ^{19}F NMR: δ −54.19 (s). IR (neat, cm^{-1}): 2930, 1687, 1586, 1479, 1235, 996, 839, 665. m/z (EI): 361 (100), 232 (33), 151 (41), 89 (79). Calc. for $C_9H_6Br_2ClF_2N$: C, 29.91; H, 1.67; N, 3.88. Found: C, 30.15; H, 1.82; N, 4.07.

*3.1.7. N-(o-chlorophenyl)-2-bromo-2, 2-difluoroacetimidoyl chloride (**1g**)*

Yield: 68%, yellow oil. ^{1}H NMR: δ 7.49 (dd, J = 8.10, 1.20 Hz, 1H), 7.36 (td, J = 7.50, 1.50 Hz, 1H), 7.23 (td, J = 7.50, 1.80 Hz, 1H), 6.97 (dd, J = 7.80, 1.80 Hz, 1H). ^{19}F NMR: δ −54.71 (s). IR (neat, cm^{-1}): 3069, 1913, 1686, 1587, 1471, 1232, 1061, 868, 722. *m/z* (EI): 303 (23), 222 (25), 172 (100), 137 (22). Calc. for $C_8H_4BrCl_2F_2N$: C, 31.72; H, 1.33; N, 4.62. Found: C, 31.57; H, 1.81; N, 4.92.

*3.1.8. N-(o-bromophenyl)-2-bromo-2, 2-difluoroacetimidoyl chloride (**1h**)*

Yield: 60%, yellow oil. ^{1}H NMR: δ 7.64 (d, J = 8.10 Hz, 1H), 7.37 (t, J = 7.50 Hz, 1H), 7.15 (td, J = 7.50, 1.50 Hz, 1H), 6.93 (dd, J = 7.80, 1.50 Hz, 1H). ^{19}F NMR: δ −54.65 (s). IR (neat, cm^{-1}): 3067, 1686, 1467, 1231, 1155, 999, 793, 717. *m/z* (EI): 347 (35), 312 (20), 218 (100), 155 (47). HRMS (EI): M^+, found 344.83670. $C_8H_4Br_2ClF_2N$ requires 344.83850.

*3.2. Procedure for the preparation of N-(p-Anisyl)-2-bromo-2,2-difluoroace-timidoyl idide (**2**)*

A mixture of **1a** (1.49 g, 5 mmol) and NaI (2.25 g, 15 mmol) in 10 ml acetone was stirred under N_2 atmosphere at room temperature for 10 h. The mixture was washed with saturated $Na_2S_2O_3$ and extracted with Et_2O (2× 15 ml). The extracts were dried with Mg_2SO_4 and concentrated under reduced pressure. Flash column chromatography with hexane as elucent gave 2 (1.91 g, 98%). Yield: 98%, yellow oil. ^{1}H NMR: δ 6.96–7.04 (m, 4H), 3.86 (s, 3H). ^{19}F NMR: δ −49.76 (s). IR (neat, cm^{-1}): 2959, 2837, 1670, 1601, 1504, 1251, 965, 832, 734. *m/z* (EI): 389 (9), 262 (100), 183 (48), 133 (56). Calc. for $C_9H_7BrF_2INO$: C, 27,72; H, 1.81, N, 3.59. Found: C, 27.69; H, 1.79; N, 3.88.

*3.3. General procedure for the palladium-catalyzed cross-coupling reaction of bromodifluoacetimidoyl iodide (**2**) with arylboronic acids*

A mixture of **2** (156 mg, 0.4 mmol), 4-methoxyl-boronic acid (73 mg, 0.48 mmol), $PdCl_2(PPh_3)_2$ (14 mmg, 0.02 mmol), K_2CO_3 (111 mg, 0.8 mmol) and Ag_2O (46 mg, 0.2 mmol) was stirred in THF at 70 °C under N_2 atmosphere for 8 h. The mixture was filtered and the filtrate was concentrated under reduced pressure. The residue was purified by flash column chromatography with 2% ethyl acetate in hexanes as elucent affording to **3a** (120 mg, 81%).

*3.3.1. Bromodifluoromethyl-4-methoxyphenyl-keton-4-methoxyphenylimine (**3a**)*

Yield: 81%. Yellowish solid. Mp: 64–65 °C. ^{1}H NMR: δ 7.21 (d, J = 8.40 Hz, 2H), 6.84 (d, J = 9.00 Hz, 2H), 6.74 (s, 4H), 3.81 (s, 3H), 3.75 (s, 3 H). ^{19}F NMR: δ −52.97 (s):−57.31 (s) = 4:1. ^{13}C NMR: δ 160.65, 159.41 (t, J = 24.4 Hz), 157.60, 139.90, 130.96, 130.74, 123.41,

123.30, 122.61, 117.49 (t, J = 302.0 Hz), 114.06, 113.99, 55.32, 55.24. IR (film, cm^{-1}): 3052, 2970, 2840, 1593, 1504, 1253, 1127, 989, 835, 656. *m/z* (EI): 369 (4), 240 (100), 77 (23). HRMS (EI): M^+, found 369.0180. $C_{16}H_{14}BrF_2NO_2$ requires 369.0176.

3.3.2. Bromodifluoromethyl-phenylketon-4-methoxyphenylimine (**3b**)

Yield: 79%. Yellowish solid. Mp: 52–53 °C. ^{1}H NMR: δ 7.32–7.40 (m, 3H), 7.26–7.28 (m, 2H), 6.74 (d, J = 9.30 Hz, 2H), 6.70 (d, J = 9.30 Hz, 2H), 3.74 (s, 3H). ^{19}F NMR: δ −50.37 (s):−57.60 (s) = 5:1; ^{13}C NMR: δ 159.55 (t, J = 23.9 Hz), 157.82, 139.51, 130.88, 129.92, 129.28, 129.01, 128.64, 123.63, 123.52, 117.27 (t, J = 308.7 Hz), 113.93, 55.30. IR (film, cm^{-1}): 3060, 2963, 2839, 2049, 1646, 1606, 1506, 1250, 1031,840. *m/z* (EI): 339 (9), 210 (100), 77 (24). HRMS (EI): M^+, found 339.0055. $C_{19}H_{12}BrF_2NO$ requires 339.0070.

3.3.3. Bromodifluoromethyl-4-methylthiophenyl-keton-4-methoxyphenylimine (**3c**)

Yield: 63%. Yellowish solid. Mp: 82–84 °C. ^{1}H NMR: δ 7.17 (s, 4H), 6.74 (s, 4 H), 3.75 (s, 3H), 2.48 (s, 3H). ^{19}F NMR: δ −53.01 (s):57.31 (s) = 37:1. IR (film, cm^{-1}): 3064, 2973, 2841, 1638, 1593, 1504, 1250, 1124, 837; *m/z* (EI): 385 (7), 256 (100), 241 (16). Calc. for $C_{16}H_{14}BrF_2NOS$: C, 49.75; H, 3.65; N, 3.63. Found: C, 50.17; H, 3.70; N, 3.63.

3.3.4. Bromodifluoromethy-4-phenylphenylketon-4-methoxyphenylimine (**3d**)

Yield: 73%. Yellowish solid. Mp: 105–105 °C. ^{1}H NMR: δ 7.56–7.61 (m, 4H), 7.34–7.48 (m, 5H), 6.71–6.80 (m, 4H); ^{19}F NMR: δ −53.17 (s):−57.29 (s) = 50:1. IR (film, cm^{-1}): 3028, 2841, 1636, 1594, 1504, 1299, 1251, 1125, 835. *m/z* (EI): 415 (17), 286 (100), Calc. for $C_{21}H_{16}BrF_2NO$: C, 60.59; H, 3.87; N, 3.36. Found: C, 60.96; H, 3.95; N, 3.41.

3.3.5. Bromodifluoromethyl-3-methylphenylketon-4-methoxyphenylimine (**3e**)

Yield: 73%. Yellowish solid. Mp: 65–66 °C. ^{1}H NMR: δ 7.20–7.22 (m, 2H), 6.75 (d, J = 8.70 Hz, 2H), 6.73(d, J = 8.70 Hz, 4H), 3.74(s, 3H), 2.32(s, 3H). ^{19}F NMR: δ −53.02 (s). IR (film, cm^{-1}): 3024, 2966, 2839, 1637, 1593, 1504, 1251, 1126, 884, 659. *m/z* (EI): 353 (5), 224 (100). Calc. for $C_{16}H_{14}BrF_2NO$: C, 54.26; H, 3.98; N, 3.95. Found: C, 54.33; H, 4.08; N, 4.04.

3.3.6. Bromodifluoromethyl-4-trifluoromethylphenylketon-4-methoxyphenylimine (**3f**)

Yield: 72%. Yellowish solid. Mp: 71–72 °C. ^{1}H NMR: δ 7.63 (d, J = 8.40 Hz, 2H), 7.42 (d, J = 8.40 Hz, 2H), 6.72 (s, 4H), 3.75 (s, 3H). ^{19}F NMR: δ −53.37 (s):−63.38 (s) = 2:3. IR (film, cm^{-1}): 3052, 2911, 2840, 1667, 1618, 1503, 1324, 1179, 998, 886. *m/z* (EI): 407 (1), 278 (14), 77 (18), 40 (100). Calc. for $C_{16}H_{11}BrF_5NO$: C, 47.08; H, 2.72; N, 3.43. Found: C, 47.48; H, 2.78; N, 3.35.

3.3.7. Bromodifluoromethyl-3-trifluoromethylphenylketon-4-methoxyphenylimine (**3g**)

Yield: 61%. Yellow oil. ^{1}H NMR: δ 7.67 (d, J = 7.20 Hz, 1H), 7.42-7.56 (m, 3H), 6.68–6.75 (m, 4H), 3.74 (s, 3H). ^{19}F NMR: δ −53.45 (s, 2H), −63.15 (s, 3H). IR (film, cm^{-1}): 2951, 2840, 1647, 1601, 1504, 1466, 1533, 1133, 1076, 840. *m/z* (EI): 407 (9.22), 328 (7.98), 278 (100.00), 263 (3.59). HRMS (MALDI): M^+ + 1 found 408.0034. $C_{16}H_{12}BrF_5NO$ 408.0028;

3.3.8. Bromodifluoromethyl-2-methoxyphenylketon-4-methoxyphenyliamine (**3h**)

Yield: 46%. Yellow oil. ^{1}H NMR: δ 7.33–7.39 (m, 1 H), 7.20 (d, J = 7.20 Hz, 1H), 6.93 (t, J = 7.20 Hz, 1H), 6.84 (d, J = 8.70 Hz, 1H), 6.74–6.83 (m, 2H), 6.67–6.70 (m, 2H), 3.72 (s, 3H), 3.67 (s, 3H). ^{19}F NMR: δ −53.43 (d, J = 265.1 Hz). IR (film, cm^{-1}): 3004, 2838, 1650, 1599, 1504, 1490, 1464, 1249, 1112, 990, 836. *m/z* (EI): 369 (7), 240 (100.00); HRMS(MALDI): M^+ + 1, found 370.0262. $C_{16}H_{15}BrF_2NO_2$ requires 370.0249.

Acknowledgment

The authors thank the National Natural Science Foundation of China (NNSFC) (No. 20472104) for financial support.

References

[1] (a) N. Miyaura, T. Yano, A. Suzuki, Tetrahedron Lett. 21 (1980) 2865;
(b) A. Suzuki, Pure Appl. Chem. 66 (1994) 213;
(c) M. Haddach, J.R. McCarthy, Tetrahedron Lett. 40 (1999) 3109;
(d) P.G. Schultz, S. Ding, Org. lett. 5 (2003) 3587.
[2] (a) Y. Gong, W. He, Org Lett. 4 (2002) 3803;
(b) J.Q. Tan, J.H. Chang, M.Z. Deng, Chin. J. Chem. 22 (2004) 941.
[3] (a) I. Ugi, F. Beck, U. Fetzer, Chem. Ber. 95 (1962) 126;
(b) K. Tamura, H. Mizukami, K. Uneyama, J. Org. Chem. 58 (1993) 32.
[4] (a) S. Fustero, J.F. Sanz-Cervera, Org. Lett. 5 (2003) 2523;
(b) A. Suzuki, M. Mae, K. Uneyama, J. Org. Chem. 69 (2004) 5132;
(c) G.Q. Shi, W.L. Cai, J. Org. Chem. 60 (1995) 6289.
[5] K.E. Stremler, C.D. Poulter, J. Am. Chem. Soc. 109 (1987) 5542.
[6] (a) D.J. Burton, Z.Y. Yang, Tetrahedron 48 (1992) 189;
(b) Z.Y. Yang, D.J. Burton, J. Org. Chem. 56 (1991) 5125.
[7] K. Tamura, H. Mizukami, K. Uneyama, J. Org. Chem. 58 (1993) 32.
[8] S. Fustero, A. Navarro, A. Asensio, Tetrahedron Lett. 38 (1997) 4891.
[9] H. Watanabe, Y. Hashizume, K. Uneyama, Tetrahedron Lett. 33 (1992) 4333.
[10] (a) J. Uenishi, J.-M. Beau, R.W. Armstrong, Y. Kish, J. Am. Chem. Soc. 109 (1987) 4756;
(b) J.C. Anderson, H. Namli, C.A. Roberts, Tetrahedron 53 (1997) 15123;
(c) K. Hirabayashi, J. Kawashima, Y. Nishihara, A. Mori, T. Hiyama, Org. Lett. 1 (1999) 299.