Tetrahedron 68 (2012) 4701–4709

Contents lists available at SciVerse ScienceDirect

Tetrahedron

journal homepage: www.elsevier.com/locate/tet

Facile preparation of aromatic esters from aromatic bromides with ethyl formate or DMF and molecular iodine via aryllithium

Sousuke Ushijima, Katsuhiko Moriyama, Hideo Togo *

Graduate School of Science, Chiba University, Yayoi-cho 1-33, Inage-ku, Chiba 263-8522, Japan

ARTICLE INFO

Article history:
Received 9 March 2012
Received in revised form 2 April 2012
Accepted 3 April 2012
Available online 12 April 2012

ABSTRACT

Various aromatic bromides were treated with *n*-BuLi and subsequently with ethyl formate, followed by the reaction with ethanol and molecular iodine in the presence of K_2CO_3 to provide the corresponding aromatic ethyl esters in good yields. Moreover, aromatic bromides could be transformed into the corresponding aromatic methyl esters in good yields by the treatment with *n*-BuLi and subsequently with DMF, followed by the reaction with methanol, molecular iodine, and K_2CO_3. Some aromatics could be also converted into the corresponding aromatic esters in good yields by the treatment with *n*-BuLi, and subsequently with ethyl formate or DMF, followed by the reaction with molecular iodine and K_2CO_3. The present reactions offer a novel route for the transition-metal-free, carbon-monoxide-free, and therefore environmentally benign one-pot conversion of aromatic bromides and aromatics into aromatic esters.

1. Introduction

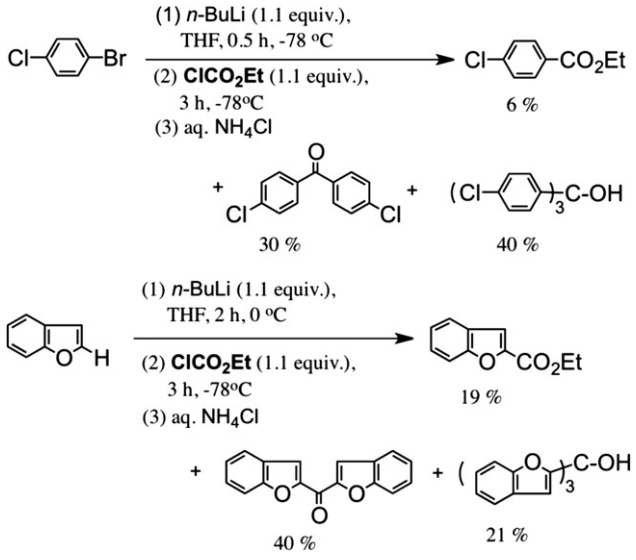
Aromatic esters are very important and useful building blocks or structural elements for the manufacture of pharmaceuticals and agrochemicals.[1] Generally, aromatic esters are prepared by the condensation of aromatic carboxylic acids and alcohols, using the Fischer esterification[2a–c] and the Mitsunobu reaction.[2c–e] In addition, the Favorskii rearrangement of α-haloketones in the presence of a base,[2f] the Baeyer–Villiger oxidation of ketones with peroxides,[2g] and the Pinner reaction of nitriles with an alcohol[2h] are also used. On the other hand, the preparation of aromatic esters from aromatic bromides through carbonylation is very attractive in view of synthetic organic chemistry. Today, transition-metal-catalyzed reactions that yield of aromatic esters from aromatic halides have been well studied[3a–c] and recently, the $Pd(OAc)_2$/dcpp·$2HBF_4$-catalyzed carbonylation of aromatic chlorides in the presence of alcohol under CO atmosphere,[3d] the $Pd(OAc)_2$/xantphos-catalyzed carbonylation of aromatic bromides in the presence of methanol under CO atmosphere,[3e] the $Pd(OAc)_2/Cy_2PCH_2CH_2CH_2PCy_2$-catalyzed carbonylation of aryl tosylates in the presence of *t*-BuOH under CO atmosphere,[3f] the $Pd(TFA)_2$/dppp-catalyzed decarboxylative coupling of potassium oxalate monoester with aromatic bromides,[3g] the $Pd(OAc)_2/Ad_2BuP$-catalyzed carbonylation of aromatic bromides in the presence of phenols under CO atmosphere,[3h] the $PdCl_2$/*rac*-BINAP-catalyzed carbonylation of aromatic bromides in *t*-BuOH under CO atmosphere,[3i] and the $Pd(dba)_2$/[1,1′-bis(diisopropylphosphino)-ferrocene]-catalyzed carbonylation of aromatic bromides with 9-methylfluorene-9-carbonylchloride as the CO precursor,[3j] were reported. However, there are still several drawbacks, such as the use of expensive palladium catalyst, toxic CO gas, the use of complicated operational treatment and equipments, etc. As an alternative method, the halogen-metal exchange of aryl halides, followed by the treatment with ethyl chloroformate,[4a] dimethyl carbonate (preparation of methyl 4-trimethylsilylbenzoate),[4b] or di-*tert*-butyl dicarbonate[4c] was reported. However, there are still some shortcomings, such as variable yields and totally low yields, and the troublesome preparation of ate-complexes. In order to realize an environmentally benign, less toxic, inexpensive, and practical organic synthesis, the preparation of aromatic esters from easily available substrates, such as aromatic bromides, without the use of any transition metals under mild conditions is required. Previously, we reported the conversion of aromatic bromides and iodides into the corresponding aromatic nitriles in good yields by the treatment with *n*-BuLi and subsequently with DMF, followed by the treatment with molecular iodine in aq NH_3.[5] The same treatment of typical aromatics and heteroaromatics with *n*-BuLi and subsequently with DMF, followed by the treatment with molecular iodine in aq NH_3, also provided the corresponding aromatic nitriles in good yields. As part of our ongoing study on the use of molecular iodine for organic synthesis,[6] we would like to report a facile method for the preparation of aromatic esters, which involves the reaction of aromatic bromides or aromatics with *n*-BuLi, followed by the treatment with formate esters or DMF, and finally with molecular iodine in the presence of K_2CO_3 in alcohols.

* Corresponding author. Tel./fax: +81 43 290 2792; e-mail address: togo@faculty.chiba-u.jp (H. Togo).

0040-4020/$ – see front matter © 2012 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tet.2012.04.016

2. Results and discussion

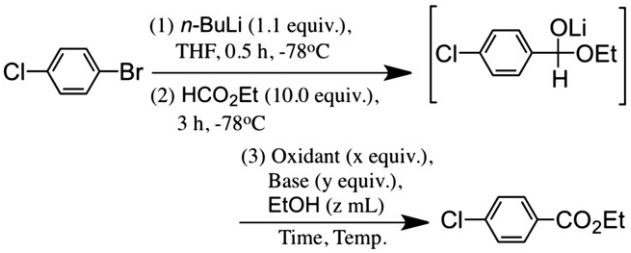
At first, *p*-bromochlorobenzene and benzofuran were treated with *n*-BuLi, followed by the reaction with ethyl chloroformate to generate the corresponding esters, as shown in Scheme 1. However, the esters were obtained in low yields, respectively, and instead, the corresponding diaryl ketones and diarylmethanol were formed as the major products. Thus, the present method is not practical for the preparation of esters from aromatic bromides and aromatics. Then, we looked into the possibility of treating *p*-bromochlorobenzene with *n*-BuLi, followed by the reaction with ethyl formate to generate an adduct. The adduct was subsequently treated with molecular iodine and K_2CO_3 to provide ethyl *p*-chlorobenzoate in 38% yield, together with *p*-chlorobenzaldehyde in 37% yield, as shown in Table 1 (entry 1). As the key step was the third reaction step, i.e., the effective oxidation of the HCO_2Et-adduct, optimization study of the third reaction step was carried out as follows. Organic bases, such as triethylamine, diisopropylethylamine, DBU, and pyridine, showed the same reactivity as K_2CO_3 (entries 4–7). However, the yield of ethyl *p*-chlorobenzoate was increased and that of *p*-chlorobenzaldehyde was decreased when EtOH was added in the third reaction step, together with molecular iodine and K_2CO_3 (entries 8–12). Nevertheless, even if the amount of EtOH was increased to 6 mL and the reaction temperature in the third step was raised, the yield of ethyl *p*-chlorobenzoate could not be improved much (entry 13).



Scheme 1. Introduction of ester group with ethyl chloroformate.

In the absence of a base, the ester was obtained in moderate yield (entry 16). Moreover, Na_2CO_3 showed moderate reactivity but was less effective than K_2CO_3 (entry 14). Cs_2CO_3 showed good reactivity; however, K_2CO_3 is much more affordable than Cs_2CO_3 (entry 15). Optimization studies indicated that the treatment of the HCO_2Et-adduct with molecular iodine (3.0 equiv), K_2CO_3 (5.0 equiv), and ethanol (3 mL) in the third reaction step gave the ester in good yield (entry 17). Then, the reactivity of molecular iodine was compared with those of other halogen oxidants, such as *N*-chlorosuccinimide (NCS), *N*-bromosuccinimide (NBS), *N*-iodosuccinimide (NIS), and 1,3-diiodo-5,5-dimethylhydantoin (DIH). The absence of an oxidant and NCS did not work well, NBS and NIS gave ethyl *p*-chlorobenzoate in moderate yields, respectively, whereas DIH gave ethyl *p*-chlorobenzoate in good yield, although DIH is expensive (entries 18–22).

Table 1
Investigation for the third-step reaction conditions



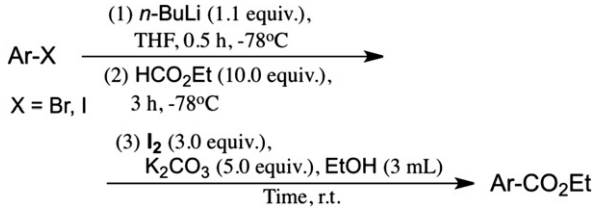
Entry	Oxidant (*x* equiv)	Base (*y* equiv)	EtOH (*z* mL)	Time (h)	Temp (°C)	Yield (%)
1	I_2 (1.2)	K_2CO_3 (1.2)	0	14	rt	38 (37)[a]
2	I_2 (1.2)	K_2CO_3 (1.2)	0	14	50	38 (37)[a]
3	I_2 (1.2)	K_2CO_3 (3.0)	0	42	rt	37 (36)[a]
4	I_2 (1.2)	NEt_3 (1.2)	0	14	rt	18 (50)[a]
5	I_2 (1.2)	$^iPr_2NEt$ (1.2)	0	14	rt	35 (24)[a]
6	I_2 (1.2)	DBU (1,2)	0	14	rt	34 (17)[a]
7	I_2 (1.2)	pyridine (1,2)	0	14	rt	37 (36)[a]
8	I_2 (1.6)	K_2CO_3 (3.0)	0.5	14	rt	59 (18)[a]
9	I_2 (1.6)	K_2CO_3 (3.0)	1.0	14	rt	63 (17)[a]
10	I_2 (1.6)	K_2CO_3 (3.0)	1.0	14	40	57 (19)[a]
11	I_2 (1.6)	K_2CO_3 (3.0)	1.0	14	70	56 (19)[a]
12	I_2 (1.6)	K_2CO_3 (3.0)	3.0	14	rt	68 (12)[a]
13	I_2 (1.6)	K_2CO_3 (3.0)	6.0	14	rt	66 (12)[a]
14	I_2 (1.6)	Na_2CO_3 (3.0)	3.0	14	rt	45 (28)[a]
15	I_2 (1.6)	Cs_2CO_3 (3.0)	3.0	14	rt	70 (6)[a]
16	I_2 (1.6)	—	3.0	14	rt	47 (19)[a]
17	I_2 (1.6)	K_2CO_3 (5.0)	3.0	14	rt	77 (3)[a]
18	—	K_2CO_3 (3.0)	3.0	14	rt	23 (15)[a]
19	NCS (3.0)	K_2CO_3 (5.0)	3.0	14	rt	21 (51)[a]
20	NBS (3.0)	K_2CO_3 (5.0)	3.0	14	rt	55 (18)[a]
21	NIS (3.0)	K_2CO_3 (5.0)	3.0	14	rt	54 (24)[a]
22	DIH (1.5)	K_2CO_3 (5.0)	3.0	14	rt	73 (4)[a]

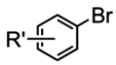
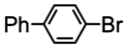
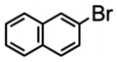
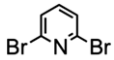
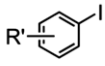
[a] Yield of *p*-chlorobenzaldehyde.

Based on these results, various bromoarenes, such as *p*-dibromobenzene, *p*-bromo(trifluoromethyl)benzene, *p*-bromocyanobenzene, 1,3,5-tribromobenzene, *m*-bromochlorobenzene, 2-bromopyridine, and 2,6-dibromopyridine, could be converted into the corresponding aromatic ethyl esters in good yields by the treatment of aromatic bromides with *n*-BuLi at −78 °C, followed by the reaction with ethyl formate at −78 °C, and subsequently with molecular iodine, K_2CO_3, and ethanol at room temperature, as shown in Table 2 (entries 2–6, 14, 15). On the other hand, when bromobenzene, *p*-bromotoluene, *p*-bromoanisole, 4-bromobiphenyl, 1-bromonaphthalene, and 2-bromonaphthalene were used as the substrate, the yields of ethyl esters were low to moderate (entries 7–13), and aromatic aldehydes and diarylmethanols were obtained, respectively. The reason for this may be the instability of the HCO_2Et-adducts derived from the reaction of aryllithium and ethyl formate under the present conditions; HCO_2Et-adducts decomposed to aromatic aldehydes and lithium ethoxide even if the reactions were carried out at low temperature, and the unfavorable formation of hemiacetals from the formed aromatic aldehydes and ethanol, especially for electron-rich aromatic aldehydes. Once the aromatic aldehydes were formed, they smoothly reacted with aryllithium to generate diarylmethanols. The same treatment of iodobenzene derivatives, such as *p*-chloroiodobenzene, *p*-bromoiodobenzene, 1,4-diiodobenzene, and 3,5-bis(trifluoromethyl)iodobenzene, with *n*-BuLi, followed by the reaction with ethyl formate, and then with molecular iodine, K_2CO_3, and ethanol, also provided the corresponding aromatic ethyl esters in good to moderate yields, respectively (entries 16–19).

Then, the scope for conversion of *p*-bromo(trifluoromethyl) benzene into the corresponding esters by changing formate esters

Table 2
One-pot conversion of aromatic halides into aromatic ethyl esters with ethyl formate

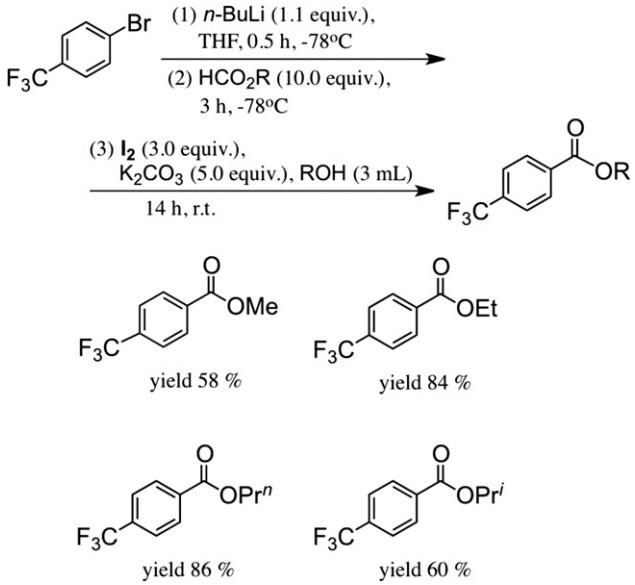


Entry	Ar–X	Time (h)	Yield (%)
			
1	R′=*p*-Cl	14	77
2	R′=*p*-Br	14	80
3	R′=*p*-CF_3	14	84
4	R′=*p*-CN	15	71
5[c]	R′=3,5-diBr	14	90
6	R′=*m*-Cl	14	74
7	R′=H	18	23 (16)[a](32)[b]
8	R′=*p*-Me	14	12 (27)[a](41)[b]
9	R′=*p*-OMe	14	7 (52)[a](21)[b]
10		18	38 (34)[a](14)[b]
11[d]		18	49 (17)[a](14)[b]
12[d]		18	32 (32)[a]
13[d]		18	45 (15)[a](10)[b]
14		14	73
15		14	79
			
16	R′=*p*-Cl	16	57
17	R′=*p*-Br	16	68
18	R′=*p*-I	16	69 (10)[e]
19	R′=3,5-diCF_3	16	55

[a] Yield of aromatic aldehyde.
[b] Yield of diarylmethanol.
[c] Et_2O (9.0 mL) was used instead of THF.
[d] EtOH (3.0 mL) was used at the third step after THF was removed.
[e] Yield of iodobenzene.

and alcohols was studied. The treatment of *p*-bromo(trifluoromethyl)benzene with *n*-BuLi, followed by the reaction with methyl formate, 1-propyl formate, or 2-propyl formate, and subsequently with molecular iodine, K_2CO_3, and methanol, 1-propanol, or 2-propanol, generated methyl *p*-(trifluoromethyl)benzoate in 58% yield, 1-propyl *p*-(trifluoromethyl)benzoate in 86% yield, and 2-propyl *p*-(trifluoromethyl)benzoate in 60% yield, respectively, as shown in Scheme 2. Thus, the esters were obtained in good yields with ethyl formate and ethanol, and with 1-propyl formate and 1-propanol. In contrast, the yields of esters with methyl formate and 2-propyl formate were moderate.

Then, *n*-BuLi was added dropwise into a solution of benzofuran in THF at 0 °C and the obtained mixture was stirred for 2 h at the same temperature. Thereafter, ethyl formate was added at −78 °C and the obtained mixture was stirred at the same temperature. After 3 h, molecular iodine, K_2CO_3, and ethanol were added and the obtained mixture was stirred for 13 h at room temperature to give

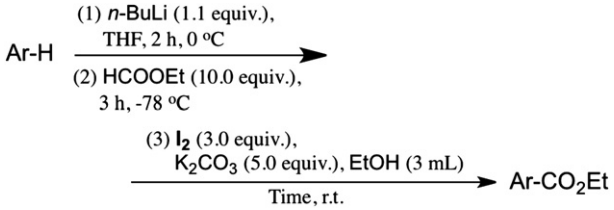


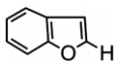
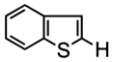
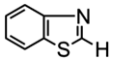
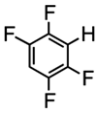
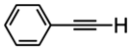
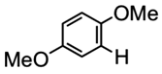
Scheme 2. Preparation of *p*-(trifluoromethyl)benzoate esters with *p*-bromo(trifluoromethyl)benzene and formate esters.

ethyl benzofuran-2-carboxylate in 99% yield, as shown in Table 3 (entry 1). Using the same procedure and conditions, benzothiophene, benzothiazole, *N*-methylimidazole, 1,3-difluorobenzene, 1,2,4,5-tetrafluorobenzene, and phenylacetylene could be converted into the corresponding aromatic ethyl esters in good yields (Table 3, entries 2–7). On the other hand, when 1,3-dimethoxybenzene and 1,4-dimethoxybenzene were used, the corresponding ethyl esters were not obtained (entries 8, 9). Instead, the aldehydes, which were the products of the hydrolysis of the HCO_2Et-adduct, were obtained, together with the starting materials derived from the hydrolysis of the formed aryllithiums. This is due to the smooth decomposition of the HCO_2Et-adduct to the corresponding aldehyde at the second step, and the formation of stable aryllithiums, chelated between the lithium cation and the *o*-methoxy group, at the first step.

Then, the introduction of an ester group with DMF, instead of ethyl formate, to aromatics for the preparation of methyl esters in good yields was studied. *n*-BuLi was added dropwise into a solution of *p*-bromoanisole in THF at −78 °C and the obtained mixture was stirred for 0.5 h at the same temperature. Thereafter, DMF (1.1 equiv) was added at room temperature and the obtained mixture was stirred at the same temperature. After 2 h, methanol (3 mL) was added and the obtained mixture was stirred for 0.5 h at room temperature. Then, molecular iodine (1.6 equiv) and K_2CO_3 (3.0 equiv) were added and the reaction mixture was stirred for 18 h at room temperature to give methyl *p*-methoxybenzoate in 51% yield, together with *p*-methoxybenzaldehyde (23%) and *N*,*N*-dimethyl-*p*-methoxybenzamide (13%), as shown in Table 4 (entry 1). Based on the optimization study, it was found that THF solvent must be removed before the third reaction step and 3.0 equiv of molecular iodine must be added in the fourth reaction step to produce methyl *p*-methoxybenzoate in good yield. Thus, after the reaction of *p*-bromoanisole with *n*-BuLi and subsequently with DMF, THF was removed. The residue was treated with methanol (3 mL), and this was followed by the reaction with molecular iodine (3.0 equiv) and K_2CO_3 for 22 h at room temperature to give methyl *p*-methoxybenzoate in the best yield, as shown in Table 4 (entry 5). On the other hand, when EtOH, *i*-PrOH, and *t*-BuOH were used instead of methanol, the corresponding esters were obtained in low yields (19%, 21%, and 0%) under the same conditions. When the reactivity of molecular iodine was compared with those of NCS, NBS, NIS, and DIH, NCS and NBS did not work at all, whereas NIS

Table 3
One-pot conversion of aromatics into aromatic ethyl esters with ethyl formate



Entry	Ar–H	Time (h)	Yield (%)
1		13	>99
2		15	73
3[c]		18	75
4		14	71
5[c,d]		16	64 (21)[a]
6[c,d]		40	72
7[d,e]		10	72
8		15	0 (48)[a] (26)[b]
9		14	7 (32)[a] (33)[b]

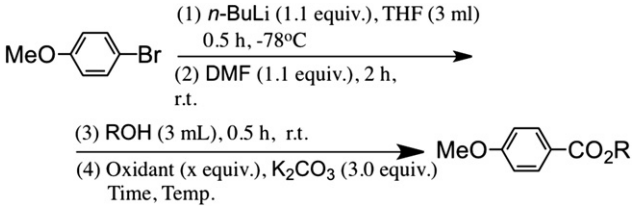
[a] Yield of aromatic aldehyde.
[b] Yield of starting compound.
[c] The first-step reaction was carried out at −78 °C for 1 h.
[d] EtOH (3 mL) was used at the third-step reaction after THF was removed.
[e] The second-step reaction was carried out at −78 °C for 12 h.

and DIH gave the corresponding methyl esters in 66% and 81% yields, respectively.

Based on these results, various aromatic bromides, such as bromobenzene, *p*-bromotoluene, *p*-bromoanisole, *m*-bromotoluene, *m*-bromoanisole, *o*-bromotoluene, *p*-bromochlorobenzene, and *p*-dibromobenzene, could be transformed into the corresponding aromatic methyl esters in good yields, respectively, by the treatment with *n*-BuLi and then with DMF, followed by the reaction with methanol, molecular iodine, and K_2CO_3 after the removal of THF from the reaction mixture, as shown in Table 5 (entries 1–6, 8, 9).

Using the same procedure and conditions, 1-bromonaphthalene, 2-bromonaphthalene, 4-bromobiphenyl, 2-bromothiophene, and 2-bromopyridine were also converted into the corresponding aromatic methyl esters in good yields (entries 10–14). The formation of a small amount of *N*,*N*-dimethyl aromatic amide as the by-product was observed in each reaction. On the other hand, when 2,4,6-trimethyl-1-bromobenzene was used, the yield of methyl 2,4,6-

Table 4
Optimization for the reaction conditions with *p*-bromomethoxybenzene[a]



Entry	ROH	Oxidant (*x* equiv)	Time (h)	Temp	Yield (%)
1[d]	MeOH	I_2 (1.6)	18	0 °C→rt	51 (23)[b](13)[c]
2	MeOH	I_2 (1.6)	16	0 °C→rt	65 (10)[b](6)[c]
3	MeOH	I_2 (1.6)	16	0 °C→60 °C	68 (10)[b](6)[c]
4	MeOH	I_2 (1.6)	45	0 °C→rt	73 (8)[c]
5	MeOH	I_2 (3.0)	22	0 °C→rt	82 (4)[c]
6	EtOH	I_2 (3.0)	20	0 °C→rt	19 (55)[b](8)[c]
7	*i*-PrOH	I_2 (3.0)	20	0 °C→rt	21 (49)[b](3)[c]
8	*t*-BuOH	I_2 (3.0)	20	0 °C→rt	0 (51)[b](28)[c]
9	MeOH	NCS (3.0)	21	0 °C→rt	0 (45)[b](28)[c]
10	MeOH	NBS (3.0)	21	0 °C→rt	Trace (56)[b]
11	MeOH	NIS (3.0)	21	0 °C→rt	66 (14)[b](5)[c]
12	MeOH	DIH (1.5)	21	0 °C→rt	81 (4)[b](3)[c]

[a] Conditions: THF solvent was removed before the third-step reaction.
[b] Yield of *p*-methoxybenzaldehyde.
[c] Yield of *N*, *N*-dimcthyl-*p*-methoxybenzamide.
[d] Conditions: THF was not removed before the third-step reaction.

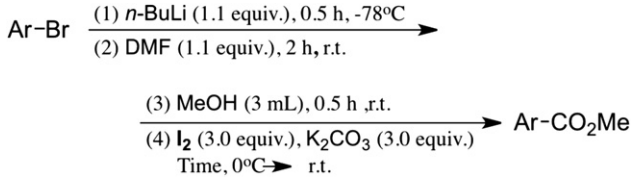
trimethyl-1-benzoate was low (entry 7) and the product of the hydrolysis of the DMF-adduct, 2,4,6-trimethyl-1-benzaldehyde, was obtained as the main product. This is due to the steric hindrance in the reaction of the DMF-adduct with methanol at the third step.

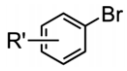
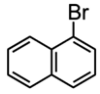
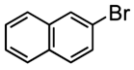
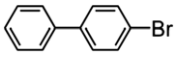
Then, *n*-BuLi was added dropwise into a solution of 1,4-dimethoxybenzene in THF at 0 °C and the obtained mixture was stirred for 2 h at the same temperature. Thereafter, DMF was added at 0 °C and the obtained mixture was stirred at room temperature. After 2 h, THF was removed, MeOH was added to the residue, and then, the obtained mixture was stirred for 0.5 h at room temperature. Then, molecular iodine (3.0 equiv) and K_2CO_3 (3.0 equiv) were added and the obtained mixture was stirred at room temperature to give methyl 2,5-dimethoxy-1-benzoate in 70% yield, as shown in Table 6 (entry 2). Using the same procedure and conditions, anisole, 1,2-dimethoxybenzene, 1,3-difluorobenzene, 2-methoxynaphthalene, *N*-methylimidazole, benzofuran, and benzothiophene, could be converted into the corresponding aromatic methyl esters in good to moderate yields (entries 1, 3, 6–10). On the other hand, when 1,3-dimethoxybenzene and 1,3,5-trimethoxybenzene were used, the yields of methyl esters were low (entries 4, 5) and the aldehydes were obtained as the main product of each reaction. This is due to the smooth decomposition of the DMF-adducts to the corresponding aromatic aldehydes at the third reaction step, and the unfavorable formation of hemiacetals from the formed aromatic aldehydes and methanol, especially for electron-rich aromatic aldehydes.

A plausible reaction mechanism is shown in Scheme 3. Aromatic bromide or arene reacts with *n*-BuLi to form aryllithium (**a**). Aryllithium (**a**) reacts with formate ester to form adduct (**b**), which further reacts with ethanol to generate hemiacetal (**c**). Hemiacetal (**c**) reacts with molecular iodine to give hemiacetal-hypoiodite (**d**).[7]

Once hemiacetal-hypoiodite (**d**) is formed, HI elimination smoothly occurs in the presence of K_2CO_3 to provide aromatic ester. When DMF is used instead of formate ester, aryllithium (**a**) reacts with DMF to form adduct (**b′**), which further reacts with methanol to generate hemiacetal (**c′**) through the formation of hemiaminal (**e**) and aldehyde (**f**). Hemiacetal (**c′**) reacts with molecular iodine to give hemiacetal-hypoiodite (**d′**). Once hemiacetal-hypoiodite (**d′**) is formed, HI elimination smoothly occurs in the presence of K_2CO_3 to provide aromatic methyl ester. On the other hand, hemiaminal (**e**) may directly react with molecular iodine to form hemiaminal-

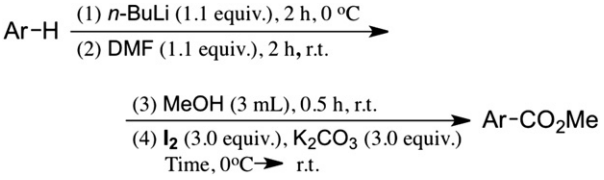
Table 5
One-pot conversion of aromatic bromides into aromatic methyl esters with DMF

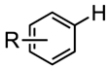
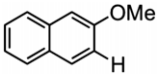
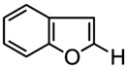
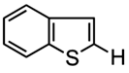


Entry	Ar–Br	Time (h)[a]	Yield (%)
			
1	R′=H	21	71 (12)[b]
2	R′=*p*-Me	21	79 (10)[b]
3	R′=*p*-OMe	22	82 (4)[b]
4	R′=*m*-Me	20	81 (12)[b]
5	R′=*m*-OMe	20	86 (8)[b]
6	R′=*o*-Me	20	78 (7)[b]
7	R′=2,4,6-triMe	22	4 (65)[c]
8	R′=*p*-Cl	16	71 (15)[b]
9	R′=*p*-Br	16	71 (12)[b]
10		20	61 (7)[b]
11		22	72 (6)[b]
12		20	69 (5)[b]
13		20	61 (13)[b]
14		20	63 (11)[b]

[a] Conditions: solvent was removed before the third-step reaction.
[b] Yield of *N*,*N*-dimethyl aromatic amide.
[c] Yield of aromatic aldehyde.

Table 6
One-pot conversion of aromatics into aromatic mehtyl esters with DMF



Entry	Ar–H	Time (h)[a]	Yield (%)
			
1	R=2-OMe	41	53 (6)[b]
2	R=2,5-diOMe	41	70 (5)[b]
3	R=2,3-diOMe	41	55 (5)[b]
4	R=2,6-diOMe	41	13 (63)[b]
5	R=2,4,6-triOMe	41	0 (55)[b](44)[c]
6[e]	R=2,6-diF	18	58 (10)[d]
7		41	66 (5)[b]
8		18	79 (14)[d]
9		18	64 (5)[d]
10		18	70 (18)[d]

[a] Conditions: solvent was removed before the third-step reaction.
[b] Yield of aromatic aldehyde.
[c] Yield of 1-iodo-2,4,6-trimethoxybenzene.
[d] Yield of *N*,*N*-dimenthyl aromatic amide.
[e] The first-step reaction was carried out at −78 °C for 1 h.

hypoiodite (**g**), and HI elimination may occur in the presence of K_2CO_3 to provide *N*,*N*-dimethyl aromatic amide. Practically, in the DMF system, the formation of *N*,*N*-dimethyl aromatic amide partly occurs depending on the substrate.

3. Conclusion

Various aromatic bromides were treated with *n*-BuLi, and subsequently with ethyl formate, followed by the reaction with ethanol and molecular iodine in the presence of K_2CO_3 to provide the corresponding aromatic ethyl esters in good to moderate yields. Moreover, aromatic bromides could be transformed into the corresponding aromatic methyl esters in good yields by the treatment with *n*-BuLi and subsequently with DMF, followed by the reaction with methanol, molecular iodine, and K_2CO_3. The latter method is more effective than the former method, and both electron-deficient and electron-rich aromatic bromides could be smoothly converted into the corresponding aromatic methyl esters in good yields, except for 2,6-disubstituted aromatic bromides. Some aromatics could be also converted into the corresponding aromatic esters in good yields by these two methods, and the latter method is more effective than the former method again. The present reactions offer a novel route for the transition-metal-free, carbon-monoxide-free, and therefore environmentally benign one-pot conversion of aromatic bromides and aromatics into the aromatic esters.

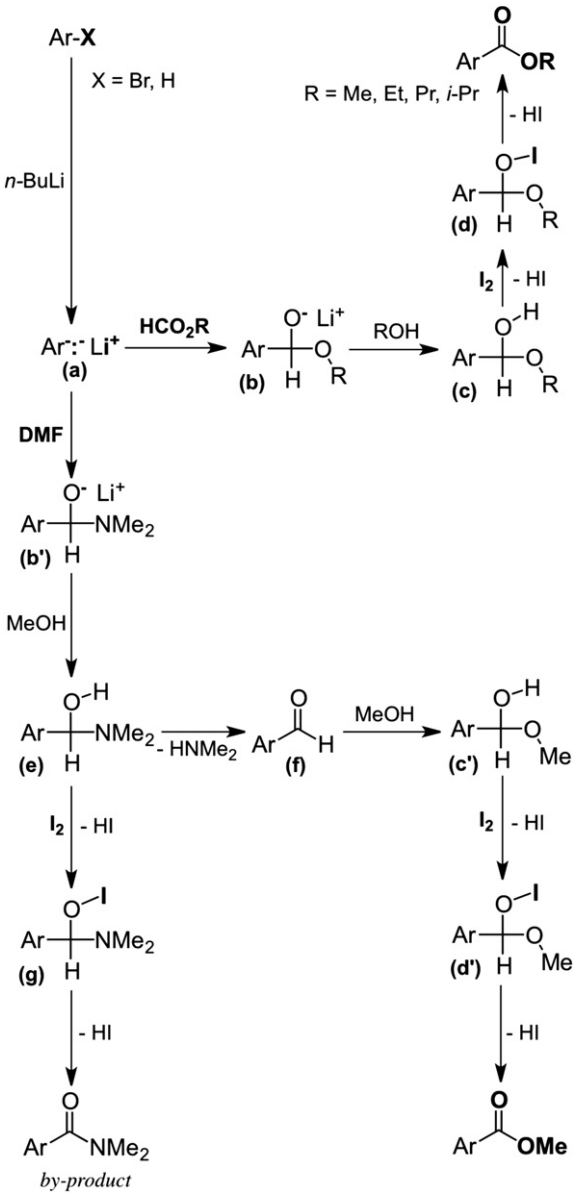
4. Experimental section

4.1. General

^{1}H NMR and ^{13}C NMR spectra were obtained with JEOL-JNM-ECX400, JEOL-JNM-ECS400, and JEOL-JNM-ECA500 spectrometers. Chemical shifts were expressed in parts per million downfield from TMS in δ units. Mass spectra were recorded on JMS-T100GCV, JMS-HX110, and Thermo LTQ Orbitrap spectrometers. IR spectra were measured with a JASCO FT/IR-4100 spectrometer. Melting points were determined with Yamato Melting Point Apparatus Model MP-21. Silica gel 60 (Kanto Kagaku Co.) was used for column chromatography and Wakogel B-5F was used for preparative TLC.

4.2. Typical procedure for one-pot conversion of aromatic bromides into aromatic ethyl esters with ethyl formate

n-BuLi (1.67 M solution in hexane, 1.32 mL, 2.2 mmol) was added dropwise into a solution of *p*-bromochlorobenzene (383 mg, 2.0 mmol) in THF (3 mL) at −78 °C for 30 min. Then, ethyl formate (1.6 mL, 20 mmol) was added to the mixture and the obtained mixture was stirred at −78 °C. After 3 h at the same temperature, I_2 (1523 mg, 6 mmol), K_2CO_3 (1382 mg, 10 mmol) and EtOH (3 mL)



Scheme 3. Plausible reaction mechanism.

were added at −78 °C and the mixture was stirred for 14 h at rt. The reaction mixture was quenched with satd aq Na_2SO_3 (5 mL) and was extracted with $CHCl_3$ (3×20 mL). The organic layer was washed with brine and dried over Na_2SO_4 to provide ethyl 4-chlorobenzoate in 77% yield. If necessary, the product was purified by short column chromatography (SiO_2:hexane:EtOAc=9:1) to give pure ethyl 4-chloro-1-benzoate as a colorless oil.

4.2.1. Ethyl 4-chloro-1-benzoate. Oil (commercial, oil); IR (neat) 1719 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ 1.39 (t, 3H, J=7.2 Hz), 4.37 (q, 2H, J=7.2 Hz), 7.39 (d, 2H, J=8.3 Hz), 7.97 (d, 2H, J=8.9 Hz); ^{13}C NMR (125 MHz, $CDCl_3$): δ 14.2, 61.1, 128.6, 128.9, 130.9, 139.1, 165.6.

4.2.2. Ethyl 4-bromo-1-benzoate. Oil (commercial, oil); IR (neat) 1719 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ 1.39 (t, 3H, J=7.2 Hz), 4.37 (q, 2H, J=7.2 Hz), 7.57 (d, 2H, J=8.3 Hz), 7.90 (d, 2H, J=8.3 Hz); ^{13}C NMR (125 MHz, $CDCl_3$): δ 14.2, 61.2, 127.8, 129.3, 131.0, 131.6, 165.8.

4.2.3. Ethyl 4-(trifluoromethyl)-1-benzoate. Oil (lit.[3g] oil); IR (neat) 1725 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ 1.42 (t, 3H, J=7.2 Hz), 4.42 (q, 2H, J=7.2 Hz), 7.70 (d, 2H, J=8.3 Hz), 8.16 (d, 2H, J=8.9 Hz); ^{13}C NMR (125 MHz, $CDCl_3$): δ 14.9, 61.5, 123.6 (q, J_{C-F}=271.9 Hz), 125.3 (q, J_{C-F}=3.6 Hz), 129.9, 133.7, 134.3 (q, J_{C-F}=32.4 Hz), 165.4.

4.2.4. Ethyl 4-cyano-1-benzoate. Mp 52–53 °C (commercial, mp 52–54 °C); IR (Nujol) 1716, 2228 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 1.42 (t, 3H, J=7.2 Hz), 4.42 (q, 2H, J=7.2 Hz), 7.75 (d, 2H, J=8.6 Hz), 8.15 (d, 2H, J=8.6 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 14.1, 61.7, 116.2, 117.9, 130.0, 132.1, 134.2, 164.8.

4.2.5. Ethyl 3,5-dibromo-1-benzoate. Mp 54–56 °C (lit.[8] mp 50–51 °C); IR (Nujol) 1730 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ 1.40 (t, 3H, J=7.2 Hz), 4.38 (q, 2H, J=7.2 Hz), 7.84 (s, 1H), 8.10 (s, 2H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 14.2, 61.8, 122.9, 131.3, 133.6, 138.1, 164.0.

4.2.6. Ethyl 3-chloro-1-benzoate. Oil (commercial, oil); IR (neat) 1721 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 1.40 (t, 3H, J=7.2 Hz), 4.38 (q, 2H, J=7.2 Hz), 7.38 (t, 1H, J=7.9 Hz), 7.52 (d, 1H, J=7.9 Hz), 7.92 (d, 1H, J=7.9 Hz), 8.01 (s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 14.2, 61.3, 127.6, 129.5, 129.6, 132.2, 132.8, 134.4, 165.3.

4.2.7. Ethyl benzoate. Oil (commercial, oil); IR (neat) 1718 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 1.38 (t, 3H, J=7.2 Hz), 4.36 (q, 2H, J=7.2 Hz), 7.37 (t, 2H, J=7.7 Hz), 7.48 (t, 1H, J=7.3 Hz), 8.04 (d, 2H, J=8.5 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 13.8, 60.3, 127.8, 129.0, 130.0, 132.2, 165.9.

4.2.8. Ethyl 4-methyl-1-benzoate. Oil (commercial, oil); IR (neat) 1717 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 1.37 (t, 3H, J=7.2 Hz), 2.37 (s, 3H), 4.34 (q, 2H, J=7.2 Hz), 7.20 (d, 2H, J=7.0 Hz), 7.93 (d, 2H, J=7.3 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 14.2, 21.4, 60.6, 127.6, 128.8, 129.4, 143.2, 166.5.

4.2.9. Ethyl 4-phenyl-1-benzoate. Mp 45–46 °C (lit.[9] mp 46–48 °C); IR (Nujol) 1724 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 1.39 (t, 3H, J=7.2 Hz), 4.38 (q, 2H, J=7.2 Hz), 7.33–7.45 (m, 3H), 7.56–7.63 (m, 4H), 8.10 (d, 2H, J=8.4 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 14.2, 60.8, 126.8, 127.1, 128.0, 128.8, 129.1, 129.9, 139.9, 145.3, 166.3.

4.2.10. Ethyl 1-naphthoate. Oil (commercial, oil); IR (neat) 1713 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 1.42 (t, 3H, J=7.2 Hz), 4.45 (q, 2H, J=7.2 Hz), 7.41–7.50 (m, 2H), 7.52 (t, 1H, J=7.0 Hz), 7.82 (d, 1H, J=8.2 Hz), 7.95 (d, 1H, J=8.2 Hz), 8.16 (d, 1H, J=7.3 Hz), 8.92 (d, 1H, J=8.6 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 14.3, 60.9, 124.4, 125.7, 126.0, 127.3, 127.6, 128.4, 129.9, 131.2, 133.1, 133.7, 167.5.

4.2.11. Ethyl 2-naphthoate. Mp 33–34 °C (lit.[10] mp 35.5–36.2 °C); IR (Nujol) 1722 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 1.43 (t, 3H, J=7.2 Hz), 4.43 (q, 2H, J=7.2 Hz), 7.49–7.58 (m, 2H), 7.85 (d, 2H, J=8.6 Hz), 7.93 (d, 1H, J=7.9 Hz), 8.06 (dd, 1H, J=8.6, 1.6 Hz), 8.60 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 14.3, 61.0, 125.2, 126.5, 127.7 (2C), 128.01, 128.07, 129.3, 130.9, 132.4, 135.4, 166.7.

4.2.12. Ethyl picolinate. Oil (commercial, oil); IR (neat) 1716 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 1.45 (t, 3H, J=7.2 Hz), 4.49 (q, 2H, J=7.2 Hz), 7.48 (ddd, 1H, J=7.7, 4.8, 1.1 Hz), 7.85 (td, 1H, J=7.7, 1.8 Hz), 8.14 (dt, 1H, J=7.9, 1.1 Hz), 8.77 (ddd, 1H, J=4.8, 1.8, 0.9 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 14.1, 61.8, 124.9, 126.7, 136.8, 148.1, 149.6, 165.0.

4.2.13. Ethyl 6-bromopicolinate. Mp 41–42 °C (commercial, mp 41 °C); IR (Nujol) 1713 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.33 (t, J=7.2 Hz, 3H), 4.38 (q, 2H, J=7.2 Hz), 7.26–7.70 (m, 2H), 7.96–8.03 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.0, 62.0, 123.8, 131.5, 139.1, 141.8, 148.7, 163.6.

4.2.14. Ethyl 4-iodo-1-benzoate. Oil (commercial, oil); IR (neat) 1718 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 1.38 (t, 3H, J=7.2 Hz), 4.36

(q, 2H, J=7.2 Hz), 7.71–7.80 (m, 4H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 14.2, 61.1, 100.5, 129.8, 130.9, 137.5, 165.9.

4.2.15. Ethyl 3,5-bis(trifluoromethyl)-1-benzoate. Oil (lit.[11] oil); IR (neat) 1733 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.45 (t, 3H, J=7.2 Hz), 4.47 (q, 2H, J=7.2 Hz), 8.06 (s, 1H), 8.50 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 14.2, 62.2, 122.9 (q, J_{C-F}=271.2 Hz), 126.2 (q, J_{C-F}=3.3 Hz), 129.7, 132.1 (q, J_{C-F}=33.2 Hz), 132.7, 163.9.

4.2.16. Methyl 4-(trifluoromethyl)-1-benzoate. Oil (lit.[12] oil); IR (neat) 1741 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ 3.96 (s, 3H), 7.71 (d, 2H, J=8.6 Hz), 8.15 (d, 2H, J=8.0 Hz); ^{13}C NMR (125 MHz, $CDCl_3$): δ 52.4, 123.6 (q, J_{C-F}=270.7 Hz), 125.3 (d, J_{C-F}=3.6 Hz), 129.9, 133.3, 134.3 (q, J_{C-F}=32.4 Hz), 165.8.

4.2.17. 1′-Propyl 4-(trifluoromethyl)-1-benzoate. Oil; IR (neat) 1726 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.04 (t, 3H, J=7.2 Hz), 1.81 (sextet, 2H, J=7.2 Hz), 4.32 (t, 2H, J=6.7 Hz), 7.70 (d, 2H, J=8.4 Hz), 8.16 (d, 2H, J=8.2 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 10.4, 22.0, 67.1, 123.6 (q, J_{C-F}=272.8 Hz), 125.3 (q, J_{C-F}=3.8 Hz), 129.9, 133.7, 134.3 (q, J_{C-F}=32.4 Hz), 165.4; HRMS (ESI) $[M]^+$, Calcd for $C_{11}H_{11}O_2F_3$=232.0706, observed=232.0697.

4.2.18. Isopropyl 4-(trifluoromethyl)-1-benzoate. Oil (lit.[13] oil); IR (neat) 1731 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ 1.39 (d, 6H, J=6.3 Hz), 5.28 (septet, 1H, J=6.3 Hz), 7.69 (d, 2H, J=8.0 Hz), 8.15 (d, 2H, J=8.0 Hz); ^{13}C NMR (125 MHz, $CDCl_3$): δ 21.8, 69.1, 123.7 (q, J_{C-F}=272.3 Hz), 125.3 (q, J_{C-F}=3.6 Hz), 129.9, 134.1 (q, J_{C-F}=32.4 Hz), 134.2, 164.8.

4.2.19. Ethyl benzofuran-2-carboxylate. Oil (lit.[14] mp 30 °C); IR (neat) 1731 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.43 (t, 3H, J=7.2 Hz), 4.44 (q, 2H, J=7.2 Hz), 7.30 (t, 1H, J=7.8 Hz), 7.44 (t, 1H, J=7.8 Hz), 7.52 (s, 1H), 7.59 (d, 1H, J=8.0 Hz), 7.67 (d, 1H, J=8.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 14.3, 61.5, 112.3, 113.7, 122.7, 123.7, 126.9, 127.5, 145.7, 155.6, 159.5.

4.2.20. Ethyl benzo[b]thiophene-2-carboxylate. Mp 34–35 °C (lit.[15] mp 36–38 °C); IR (Nujol) 1715 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.42 (t, 3H, J=7.2 Hz), 4.41 (q, 2H, J=7.2 Hz), 7.36–7.47 (m, 2H), 7.83–7.89 (m, 2H), 8.06 (s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 14.2, 61.5, 122.7, 124.8, 125.4, 126.8, 130.3, 133.8, 138.6, 142.1, 162.7.

4.2.21. Ethyl benzo[d]thiazole-2-carboxylate. Mp 68–71 °C (lit.[16] mp 68–70 °C); IR (Nujol) 1749 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.49 (t, 3H, J=7.2 Hz), 4.56 (q, 2H, J=7.2 Hz), 7.52–7.61 (m, 2H), 7.98 (d, 1H, J=7.6 Hz), 8.25 (d, 1H, J=7.7 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 14.3, 63.1, 122.0, 125.5, 127.0, 127.5, 136.8, 153.2, 158.5, 160.6.

4.2.22. Ethyl 1-methyl-1H-imidazole-2-carboxylate. Mp 44–46 °C (lit.[17] mp 43–45 °C); IR (Nujol) 1715 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.43 (t, 3H, J=7.2 Hz), 4.02 (s, 3H), 4.41 (q, 2H, J=7.2 Hz), 7.05 (d, 1H, J=1.3 Hz), 7.13 (d, 1H, J=1.3 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 14.0, 35.6, 61.1, 126.0, 129.1, 136.5, 159.0.

4.2.23. Ethyl 2,6-difluoro-1-benzoate. Oil; IR (neat) 1736 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ 1.39 (t, 3H, J=7.2 Hz), 4.42 (q, 2H, J=7.2 Hz), 6.94 (t, 2H, J=8.2 Hz), 7.37–7.43 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 14.0, 61.9, 111.3 (t, J_{C-F}=18.0 Hz), 118.2 (dd, J_{C-F}=21.0, 4.2 Hz), 132.4 (t, J_{C-F}=10.8 Hz), 160.5 (dd, J_{C-F}=254.0, 6.0 Hz), 161.5; HRMS (ESI) $[M+Na]^+$, Calcd for $C_9H_8O_2F_2Na$=209.0385, observed=209.0384.

4.2.24. Ethyl 2,3,5,6-tetrafluoro-1-benzoate. Oil; IR (neat) 1741 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ 1.41 (t, 3H, J=7.2 Hz), 4.46 (q, 2H, J=7.2 Hz), 7.19–7.23 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 13.9, 62.7, 108.4 (t, J_{C-F}=22.8 Hz), 113.9 (t, J_{C-F}=16.8 Hz), 144.3 (ddt, J_{C-F}=254.6, 14.3, 4.8 Hz), 145.9 (dtd J_{C-F}=248.1, 12.0, 4.8 Hz), 159.5; HRMS (ESI) $[M+Na]^+$, Calcd for $C_9H_6O_2F_4Na$=245.0196, observed=245.0193.

4.2.25. Ethyl 3-phenylpropiolate. Oil (commercial. oil); IR (neat) 1708, 2211 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.35 (t, 3H, J=7.2 Hz), 4.29 (q, 2H, J=7.2 Hz), 7.33–7.47 (m, 3H), 7.58 (d, 2H, J=8.3 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 14.0, 62.0, 80.7, 86.0, 119.6, 128.5, 130.5, 132.9, 154.0.

4.3. Typical procedure for one-pot conversion of aromatic bromides into aromatic methyl esters with DMF

n-BuLi (1.67 M solution in hexane, 1.3 mL, 2.2 mmol) was added dropwise into a solution of *p*-bromoanisole (383 mg, 2.0 mmol) in THF (3 mL) at −78 °C for 30 min. Then, DMF (0.22 mL, 2.2 mmol) was added to the mixture and the obtained mixture was stirred at rt. After 2 h at the same temperature, THF was removed. Then, MeOH (3 mL) was added to the residue and the mixture was stirred at room temperature. After 30 min, I_2 (1523 mg, 6 mmol) and K_2CO_3 (829 mg, 6 mmol) were added at 0 °C and the obtained mixture was stirred for 22 h at rt. The reaction mixture was quenched with satd aq Na_2SO_3 (5 mL) and was extracted with $CHCl_3$ (3×20 mL). The organic layer was washed with brine and dried over Na_2SO_4 to provide methyl 4-methoxy-1-benzoate in 82% yield. If necessary, the product was purified by short column chromatography (SiO_2:hexane:EtOAc=9:1) to give pure methyl 4-methoxybenzoate as a colorless oil.

4.3.1. Methyl benzoate. Oil (commercial, oil); IR (neat) 1722 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.90 (s, 3H), 7.42 (t, 2H, J=7.7 Hz), 7.54 (t, 1H, J=7.3 Hz), 8.04 (d, 2H, J=8.5 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 52.0, 128.2, 129.5, 130.1, 132.8, 167.0.

4.3.2. Methyl 4-methyl-1-benzoate. Mp 33–34 °C (commercial, mp 32 °C); IR (Nujol) 1729 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.38 (s, 3H), 3.88 (s, 3H), 7.21 (d, 2H, J=8.0 Hz), 7.92 (d, 2H, J=8.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 21.5, 51.8, 127.3, 129.0, 129.5, 143.4, 167.0.

4.3.3. Methyl 4-methoxy-1-benzoate. Mp 49–51 °C (commercial, mp 48–52 °C); IR (Nujol) 1725 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.85 (s, 3H), 3.88 (s, 3H), 6.91 (d, 2H, J=8.8 Hz), 7.99 (d, 2H, J=9.1 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 51.8, 55.4, 113.6, 122.6, 131.5, 163.3, 166.8.

4.3.4. Methyl 3-methyl-1-benzoate. Oil (commercial, oil); IR (neat) 1723 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ 2.36 (s, 3H), 3.87 (s, 3H), 7.25–7.35 (m, 2H), 7.79–7.86 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 21.1, 51.8, 126.5, 128.1, 130.0 (2C), 133.5, 137.9, 167.1.

4.3.5. Methyl 3-methoxy-1-benzoate. Oil (commercial, oil); IR (neat) 1721 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.84 (s, 3H), 3.91 (s, 3H), 7.09 (d, 1H, J=8.3 Hz), 7.33 (t, 1H, J=7.9 Hz), 7.55 (s, 1H), 7.63 (d, 1H, J=8.2 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 52.1, 55.3, 113.9, 119.9, 121.9, 129.3, 131.4, 159.5, 166.9.

4.3.6. Methyl 2-methyl-1-benzoate. Oil (commercial, oil); IR (neat) 1722 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.60 (s, 3H), 3.88 (s, 3H), 7.21–7.25 (m, 2H), 7.38 (t, 1H, J=7.5 Hz), 7.90 (d, 1H, J=8.2 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 21.6, 51.7, 125.6, 129.5, 130.5, 131.6, 131.9, 140.1, 168.0.

4.3.7. Methyl 4-chloro-1-benzoate. Mp 43 °C (commercial, mp 42–44 °C); IR (Nujol) 1732 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ 3.91

(s, 3H), 7.40 (d, 2H, *J*=8.6 Hz), 7.96 (d, 2H, *J*=8.9 Hz); ^{13}C NMR (125 MHz, $CDCl_3$): δ 52.2, 128.5, 128.6, 130.9, 139.3, 166.1.

4.3.8. Methyl 4-bromo-1-benzoate. Mp 77–79 °C (commercial, mp 77–81 °C); IR (Nujol) 1734 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ 3.91 (s, 3H), 7.57 (d, 2H, *J*=8.6 Hz), 7.90 (d, 2H, *J*=8.9 Hz); ^{13}C NMR (125 MHz, $CDCl_3$): δ 52.2, 128.0, 129.0, 131.1, 131.7, 166.3.

4.3.9. Methyl 1-naphthoate. Oil (commercial, oil); IR (neat) 1715 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.96 (s, 3H), 7.40–7.51 (m, 2H), 7.58 (t, 1H, *J*=7.0 Hz), 7.82 (d, 1H, *J*=8.2 Hz), 7.95 (d, 1H, *J*=8.4 Hz), 8.15 (d, 1H, *J*=7.3 Hz), 8.92 (d, 1H, *J*=8.6 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 52.0, 124.4, 125.7, 126.1, 126.9, 127.6, 128.4, 130.1, 131.2, 133.2, 133.7, 167.9.

4.3.10. Methyl 2-naphthoate. Mp 75–76 °C (commercial, mp 75–77 °C); IR (Nujol) 1730 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.98 (s, 3H), 7.50–7.61 (m, 2H), 7.87 (d, 2H, *J*=8.6 Hz), 7.95 (d, 1H, *J*=8.2 Hz), 8.06 (dd, 1H, *J*=8.6, 1.8 Hz), 8.61 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 52.2, 125.2, 126.6, 127.4, 127.7, 128.1, 128.2, 129.3, 131.0, 132.5, 135.5, 167.2.

4.3.11. Methyl 4-phenyl-1-benzoate. Mp 110–112 °C (lit.[18] mp 112–114 °C); IR (Nujol) 1703 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.93 (s, 3H), 7.38 (t, 1H, *J*=7.4 Hz), 7.46 (t, 2H, *J*=7.4 Hz), 7.59–7.67 (m, 4H), 8.10 (d, 2H, *J*=8.6 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 52.1, 127.0, 127.2, 128.1, 128.9 (2C), 130.1, 140.0, 145.6, 167.0.

4.3.12. Methyl thiophene-2-carboxylate. Oil (commercial oil); IR (neat) 1703 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ 3.89 (s, 3H), 7.10 (dd, 1H, *J*=5.0, 4.3 Hz), 7.55 (dd, 1H, *J*=5.0, 1.2 Hz), 7.80 (dd, 1H, *J*=4.3, 1.2 Hz); ^{13}C NMR (125 MHz, $CDCl_3$): δ 52.1, 127.7, 132.3, 133.4, 133.6, 162.7.

4.3.13. Methyl picolinate. Oil (commercial oil); IR (neat) 1703 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ 4.02 (s, 3H), 7.50 (ddd, 1H, *J*=7.7, 4.7, 1.2 Hz), 7.86 (td, 1H, *J*=7.7, 1.7 Hz), 8.15 (dt, 1H, *J*=7.7, 1.2 Hz), 8.76 (ddd, 1H, *J*=4.7, 1.7, 0.9 Hz); ^{13}C NMR (125 MHz, $CDCl_3$): δ 52.8, 125.0, 126.8, 136.9, 147.8, 149.7, 165.6.

4.3.14. Methyl 2-methoxy-1-benzoate. Oil (commercial, oil); IR (neat) 1731 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ 3.89 (s, 3H), 3.90 (s, 3H), 6.95–6.99 (m, 2H), 7.46 (t, 1H, *J*=7.9 Hz), 7.79 (d, 1H, *J*=8.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 51.9, 55.9, 111.9, 119.9, 120.0, 131.6, 133.4, 159.0, 166.6.

4.3.15. Methyl 2,5-dimethoxy-1-benzoate. Oil (lit.[19] oil); IR (neat) 1732 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ 3.79 (s, 3H), 3.86 (s, 3H), 3.89 (s, 3H), 6.92 (d, 1H, *J*=8.9 Hz), 7.02 (dd, 1H, *J*=8.9, 3.2 Hz), 7.33 (d, 1H, *J*=3.2 Hz); ^{13}C NMR (125 MHz, $CDCl_3$): δ 52.0, 55.7, 56.7, 113.7, 115.9, 119.5, 120.4, 152.9, 153.4, 166.4.

4.3.16. Methyl 2,3-dimethoxy-1-benzoate. Mp 48–49 °C (commercial, mp 48–52 °C); IR (Nujol) 1725 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.88 (s, 3H), 3.90 (s, 3H), 3.91 (s, 3H), 7.04–7.09 (m, 2H), 7.32 (d, 1H, *J*=7.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 52.1, 56.0, 61.4, 115.7, 122.1, 123.7, 126.0, 149.0, 153.4, 166.7.

4.3.17. Methyl 2,6-dimethoxy-1-benzoate. Mp 86–88 °C (commercial, mp 87–90 °C); IR (Nujol) 1732 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ 3.80 (s, 6H), 3.89 (s, 3H), 6.54 (d, 2H, *J*=8.6 Hz), 7.27 (t, 1H, *J*=8.4 Hz); ^{13}C NMR (125 MHz, $CDCl_3$): δ 52.3, 55.9, 103.8, 112.9, 131.0, 157.2, 167.0.

4.3.18. Methyl 2,6-difluoro-1-benzoate. Oil (commercial, oil); IR (neat) 1725 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ 3.95 (s, 3H), 6.92–6.98 (m, 2H), 7.38–7.45 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 52.6, 110.9 (t, J_{C-F}=17.9 Hz), 111.67 (dd, J_{C-F}=20.9, 4.2 Hz), 132.7 (t, J_{C-F}=10.1 Hz), 160.6 (dd, J_{C-F}=255.2, 6.0 Hz), 161.9.

4.3.19. Methyl 3-methoxy-2-naphthoate. Mp 48–49 °C (commercial, mp 48–51 °C); IR (Nujol) 1732 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ 3.93 (s, 3H), 3.95 (s, 3H), 7.16 (s, 1H), 7.34 (t, 1H, *J*=7.6 Hz), 7.48 (t, 1H, *J*=7.6 Hz), 7.69 (d, 1H, *J*=8.3 Hz), 7.78 (d, 1H, *J*=8.3 Hz), 8.28 (s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 52.1, 55.8, 106.6, 121.6, 124.2, 126.3, 127.4, 128.3, 128.5, 135.6, 135.9, 155.5, 166.5.

4.3.20. Methyl 1-methyl-1H-imidazole-2-carboxylate. Oil (lit.[20] oil); IR (neat) 1725 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.92 (s, 3H), 4.01 (s, 3H), 7.07 (d, 1H, *J*=1.3 Hz), 7.13 (d, 1H, *J*=1.3 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 35.3, 51.7, 126.0, 129.0, 136.1, 159.2.

4.3.21. Methyl benzofuran-2-carboxylate. Mp 53–54 °C (lit.[21] mp 53–55 °C); IR (Nujol) 1731 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ 3.98 (s, 3H), 7.30 (t, 1H, *J*=7.2 Hz), 7.45 (t, 1H, *J*=7.2 Hz), 7.53 (s, 1H), 7.59 (d, 1H, *J*=8.3 Hz), 7.68 (d, 1H, *J*=8.0 Hz); ^{13}C NMR (125 MHz, $CDCl_3$): δ 52.3, 112.3, 114.0, 122.8, 123.8, 126.9, 127.6, 145.3, 155.7, 160.0.

4.3.22. Methyl benzo[b]thiophene-2-carboxylate. Mp 70–71 °C (commercial, mp 70–74 °C); IR (Nujol) 1725 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.94 (s, 3H), 7.37–7.48 (m, 2H), 7.84–7.88 (m, 2H), 8.06 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 52.5, 122.7, 124.9, 125.5, 126.9, 130.6, 133.3, 138.6, 142.2, 163.2.

References and notes

1. The Art of Drug Synthesis: (a) Johnson, D. S., Li, J. J., Eds. ; John Wiley and Sons.: Hoboken, NJ, 2007; (b) Zapf, A.; Beller, M. *Top. Catal.* **2002**, *19*, 101; (c) Stetter, J.; Lieb, F. *Angew. Chem., Int. Ed.* **2000**, *39*, 1724.
2. Fischer ester synthesis: (a) Fischer, E.; Speier, A. *Ber. Dtsch. Chem. Ges.* **1895**, *28*, 3252; (b) Bew, S. P.; Hughs, D. L.; Sharma, S. V. *J. Org. Chem.* **2006**, *71*, 7881; (c) Larock, R. C. *Comprehensive Organic Transformations*, 2nd ed.; VCH: New York, NY, U.S., 1989, pp 881–958. Mitsunobu Reaction; (d) Mitsunobu, O. *Synthesis* **1981**, 1; (e) Watterson, M. P.; Fleet, G. W. J. *Tetrahedron Lett.* **2003**, *44*, 5853; (f) Favorskii, A. E. *J. Prakt. Chem.* **1895**, *51*, 533 **1913**, *88*, 658; (g) Baeyer, A.; Villiger, V. *Chem. Ber.* **1899**, *32*, 3625; (h) Pinner, A.; Klein, F. *Chem. Ber.* **1883**, *16*, 1643.
3. (a) Schoenberg, A.; Bartoletti, I.; Heck, R. F. *J. Org. Chem.* **1974**, *39*, 3318 recent reviews; (b) Skoda-Foldes, R.; Koller, L. *Curr. Org. Chem.* **2002**, *6*, 1097; (c) Barnard, C. F. J. *Organometallics* **2008**, *27*, 5402 recent papers; (d) Watson, D. A.; Fan, X.; Buchwald, S. L. *J. Org. Chem.* **2008**, *73*, 7096; (e) Martinelli, J. R.; Watson, D. A.; Freckmann, D. M. M.; Barder, T. E.; Buchwald, S. L. *J. Org. Chem.* **2008**, *73*, 7102; (f) Munday, R. H.; Martinelli, J. R.; Buchwald, S. L. *J. Am. Chem. Soc.* **2008**, *130*, 2754; (g) Shang, R.; Fu, Y.; Li, J.; Zhang, S.; Guo, Q.; Liu, L. *J. Am. Chem. Soc.* **2009**, *131*, 5738; (h) Wu, X.; Neumann, H.; Matthlas, B. *ChemCatChem* **2010**, *2*, 509; (i) Yang, W.; Han, W.; Zhang, W.; Shan, L.; Sun, J. *Synlett* **2011**, 2253; (j) Xin, Z.; Gogsig, T. M.; Lindhardt, A. T.; Skrydstrup, T. *Org. Lett.* **2012**, *14*, 284.
4. (a) Bratton, L. D.; Huh, H.; Bartsch, R. A. *J. Heterocycl. Chem.* **2000**, *37*, 2599; (b) Amedio, J. C. J.; Lee, G. T.; Prasad, K.; Repic, O. *Synth. Commun.* **1995**, *25*, 2599; (c) Li, H.; Balsells, J. *Tetrahedron Lett.* **2008**, *49*, 2034.
5. (a) Ushijima, S.; Togo, H. *Synlett* **2010**, 1562; (b) Ushijima, S.; Moriyama, K.; Togo, H. *Tetrahedron* **2011**, *67*, 958.
6. Reviews: (a) Togo, H.; Iida, S. *Synlett* **2006**, 2159; (b) Togo, H. J. *Synth. Org. Chem. (Japanese)* **2008**, *66*, 652 Papers; (c) Mori, N.; Togo, H. *Synlett* **2004**, 880; (d) Mori, N.; Togo, H. *Synlett* **2005**, 1456; (e) Mori, N.; Togo, H. *Tetrahedron* **2005**, *61*, 5915; (f) Ishihara, M.; Togo, H. *Synlett* **2006**, 227; (g) Iida, S.; Togo, H. *Synlett* **2006**, 2633; (h) Ishihara, M.; Togo, H. *Tetrahedron* **2007**, *63*, 1474; (i) Iida, S.; Togo, H. *Tetrahedron* **2007**, *63*, 8274; (j) Iida, S.; Togo, H. *Synlett* **2007**, 407; (k) Iida, S.; Togo, H. *Synlett* **2008**, 1639; (l) Iida, S.; Ohmura, R.; Togo, H. *Tetrahedron* **2009**, *65*, 6257; (m) Ushujima, S.; Togo, H. *Synlett* **2010**, 1067; (n) Ishii, G.; Moriyama, K.; Togo, H. *Tetrahedron Lett.* **2011**, *52*, 2404; (o) Baba, H.; Moriyama, K.; Togo, H. *Tetrahedron Lett.* **2011**, *52*, 4303; (p) Suzuki, Y.; Yoshino, T.; Moriyama, K.; Togo, H. *Tetrahedron* **2011**, *67*, 3809; (q) Suzuki, Y.; Moriyama, K.; Togo, H. *Tetrahedron* **2011**, *67*, 7956; (r) Ushijima, S.; Dohi, S.; Moriyama, K.; Togo, H. *Tetrahedron* **2012**, *68*, 1346.
7. (a) Yamada, S.; Morizono, D.; Yamamoto, K. *Tetrahedron Lett.* **1992**, *3*, 4329; (b) Kiran, Y. B.; Ikeda, R.; Sakai, N.; Konakahara, T. *Synthesis* **2010**, 276.
8. Motrenko, T. I.; Sevbo, D. P.; Nekhoroshev, A. A.; Ginzberg, O. F. *Z. Org. Khm.* **1978**, *14*, 1669.
9. Chen, X.; Hou, Y.; Wang, H.; Cao, Y.; He, J. *J. Phys. Chem. C* **2008**, *112*, 8172.
10. Palmelund, A.; Myers, E. L.; Tai, L. R.; Tisserand, S.; Butts, C. P.; Aggarwal, V. K. *Chem. Commun.* **2007**, 4128.
11. Al-Aseer, M. A. *J. Org. Chem.* **1985**, *50*, 2715.

12. Knauber, T.; Arikan, F.; Roeschenthaler, G.; Goossen, L. J. *Chem.—Eur. J.* **2011**, *17*, 2689.
13. Liu, Q.; Li, G.; He, J.; Liu, J.; Li, P.; Lei, A. *Angew. Chem., Int. Ed.* **2010**, *49*, 3371.
14. Saiser, S.; Smidt, S. P.; Pfaltz, A. *Angew. Chem., Int. Ed.* **2006**, *45*, 5194.
15. Guo, H.; Shao, H.; Yang, Z.; Xue, S.; Li, X.; Liu, Z.; He, X.; Jiang, J.; Zhang, Y.; Si, S.; Li, Z. *J. Med. Chem.* **2010**, *53*, 1819.
16. Rajeeva, B.; Srinivasulu, N.; Shantakumar, S. M. *Eur. J. Chem.* **2009**, *6*, 775.
17. Gautier, F. *Org. Biomol. Chem.* **2009**, *7*, 229.
18. Chaturbhuj, G. U.; Akamanchi, K. G. *Tetrahedron Lett.* **2011**, *52*, 4950.
19. Mazzini, F.; Alpi, E.; Salvadori, P.; Netscher, T. *Eur. J. Org. Chem.* **2003**, *15*, 2840.
20. Regel, E.; Buechel, K. H. *Justus Liebigs Ann. Chem.* **1977**, *1*, 145.
21. Yamamoto, Y. *Adv. Synth. Catal.* **2010**, *352*, 478.