EurJOC European Journal of Organic Chemistry

FULL PAPER

DOI: 10.1002/ejoc.201301170

Transition-Metal-Free Transformation of Aryl Bromides into Aromatic Esters and Amides via Aryl Trichloromethyl Ketones

Souya Dohi,[a] Katsuhiko Moriyama,[a] and Hideo Togo*[a]

Keywords: Synthetic methods / Grignard reagents / Esters / Amides / Ketones

A variety of aryl bromides have been treated with Mg and then chloral, followed by *t*BuOCl and subsequently alcohols or amines to produce the corresponding aromatic esters or amides in good yields via the formation of aryl trichloromethyl ketones as intermediates. These reactions are examples of a transition-metal-free one-pot preparation of aromatic esters and amides from aryl bromides.

Introduction

Aromatic esters[1] and amides[2] are important and useful building blocks and structural elements of pharmaceuticals and agrochemicals. In general, aromatic esters are prepared by the condensation of aromatic carboxylic acids and alcohols by the Fischer esterification[3a–3c] and Mitsunobu reaction.[3c–3e] The Favorskii rearrangement of α-halo ketones in the presence of a base,[3f] the Baeyer–Villiger oxidation of ketones with peroxides,[3g] and the Pinner reaction of nitriles with an alcohol[3h] can also be used.[3] Aromatic amides are prepared by the Schotten–Baumann reaction between acyl chlorides and amines,[3c,4a,4b] the reaction of carboxylic acids and amines in the presence of $Ph_3P/BrCCl_3$ or $Ph_3P/(PyS)_2$,[3c] the Beckmann rearrangement of oximes,[4c] and the Ritter reaction of nitriles with an *N*-alkylated precursor.[4d] The preparation of aromatic esters and amides from aromatic bromides by a carbonylation reaction is very attractive for synthetic organic chemists.

Transition-metal-catalyzed preparations of aromatic esters from aromatic halides have been well studied[5a] and recently the $Pd(OAc)_2$/dcpp·$2HBF_4$-catalyzed carbonylation of aromatic chlorides in the presence of alcohol under CO,[5b] the $Pd(OAc)_2$/Xantphos-catalyzed carbonylation of aromatic bromides in the presence of methanol under CO,[5c] and related reactions with Pd complexes have been reported.[5d,5e] Aromatic amides can also be prepared by the transition-metal-catalyzed amidation[2] of aryl bromides with amines under CO in the presence of $[PdBr_2(Ph_3P)_2]$[6a] and the amidation of aromatic bromides with carbamoylsilanes in the presence of $[Pd(Ph_3P)_4]$,[6b] and related reactions with Pd or Mo complexes have been reported.[6c–6h] However, these reactions have several drawbacks, such as the use of an expensive palladium catalyst, the requirement of a high temperature (over 100 °C), and the use of complicated equipment and/or toxic CO gas. As alternative methods, the halogen/metal exchange of aryl halides followed by treatment with ethyl chloroformate,[7a] dimethyl carbonate (the preparation of methyl 4-trimethylsilylbenzoate),[7b] di-*tert*-butyl dicarbonate,[7c] and ethyl cyanoformate[7d] have been reported for the synthesis of aromatic esters, and the reactions of arylmagnesium reagents with chlorocarbamate in the presence of $[NiCl_2(Ph_3P)_2]$,[7e] the reactions of arylmagnesium reagents with carbamoyltributylphosphonium chloride,[7f] the reactions of chlorocarbamate with organocuprates,[7g] the reactions of arylmagnesium chlorides with chlorocarbamate,[7h] and the reactions of trichloroacetyl isocyanate with organozinc halides and subsequent treatment with alcohols[7i] have been reported for aromatic amides. However, there are still shortcomings, such as the variable and low yields depending on the substrate, and the troublesome preparation of the complexes. On the other hand, it is known that aryl trichloromethyl ketones, which act as precursors of aromatic esters and amides, cannot be efficiently obtained by the reaction of phenylmagnesium bromide with ethyl trichloroacetate at low temperature. Careful treatment of PhMgBr and ethyl trichloroacetate (1.0 equiv.) at –78 °C gives a trace amount of the desired phenyl trichloromethyl ketone and therefore the direct preparation of aryl trichloromethyl ketones from aryl Grignard reagents and trichloroacetate esters is not practical.[7h]

It would be useful to develop a transition-metal-free, less toxic, inexpensive, and practical organic synthesis of aromatic esters and amides from readily available aromatic bromides under mild conditions. Here, as part of our synthetic study of molecular iodine,[8] we would like to report the transition-metal-free transformation of aryl bromides into aromatic esters and amides via the formation of aryl trichloromethyl ketones. The oxidation of 1-aryl-2,2,2-trichloroethanols and 1-alkyl-2,2,2-trichloroethanol into the

[a] Graduate School of Science, Chiba University,
Yayoi-cho 1-33, Japan
E-mail: togo@faculty.chiba-u.jp
http://reaction-2.chem.chiba-u.jp/index.html

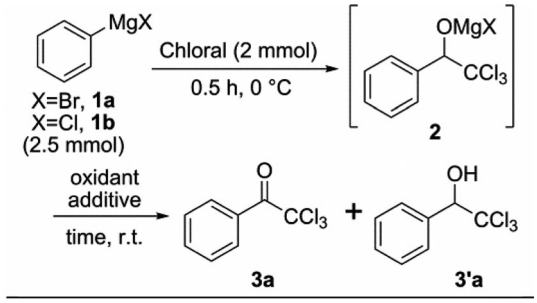
Supporting information for this article is available on the WWW under http://dx.doi.org/10.1002/ejoc.201301170.

corresponding trichloromethyl ketones with chromic acid,[9a,9b] and the oxidation of 1-aryl-2,2,2-trifluoroethanols and 1-alkyl-2,2,2-trifluoroethanols into the corresponding trifluoromethyl ketones with oxoammonium salt[9c] have been reported. In addition, the reactions of aryl trichloromethyl ketones with alcohols and amines have been reported to give the corresponding aromatic esters and amides, respectively.[10] In a related reaction, the preparation of primary aromatic amides from the reactions of aryl methyl ketones or 1-phenylethanols with molecular iodine and aqueous NH_3 at 60 °C have recently been reported.[11] Based on these reports and our previous study,[8] we have examined the one-pot preparation of aromatic esters and amides by the reaction of aryl bromides with Mg followed by treatment with chloral and oxidation to aryl trichloromethyl ketones, and the subsequent reaction with alcohols and amines to provide the corresponding aromatic esters and amides, respectively.

Results and Discussion

First, the reactions of PhMgX [X = Br (**1a**), Cl (**1b**)] and chloral (2,2,2-trichloroethanal), and the subsequent oxidation to phenyl trichloromethyl ketone (**3a**) with less toxic oxidants such as I_2, 1,3-diiodo-5,5-dimethylhydantoin (DIH), *N*-iodosuccinimide (NIS), *N*-bromosuccinimide (NBS), *N*-chlorosuccinimide (NCS), and *tert*-butyl hypochlorite (*t*BuOCl), were investigated (Table 1).

Table 1. Formation of phenyl trichloromethyl ketone by the reactions of PhMgX with chloral and subsequent oxidation.

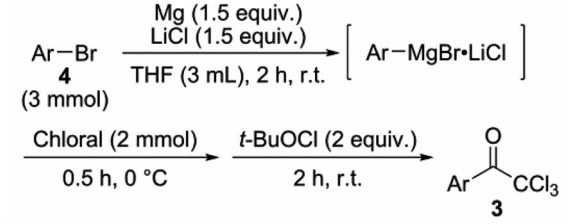


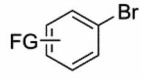
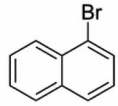
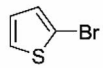
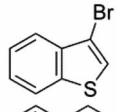
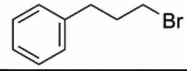
Entry	Oxidant (2 equiv.)	X	Additive (0.1 equiv.)	Time (h)	Yield (%)[a]	
					3a	**3'a**
1	I_2	Br	–	1	1	86
2	DIH	Br	–	1	1	90
3	NIS	Br	–	1	<1	95
4	NBS	Br	–	1	21	68
5	NCS	Br	–	1	43	46
6	*t*BuOCl	Br	–	1	89	<1
7	*t*BuOCl	Br	I_2	1	90	<1
8	*t*BuOCl	Cl	–	4	19	66
9	*t*BuOCl	Cl	KBr	4	66	8
10	*t*BuOCl	Cl	KI	4	82	8
11	*t*BuOCl	Cl	I_2	4	91	<1

[a] The yields were determined based on the amount of chloral.

The oxidation of adduct **2a** derived from PhMgBr and chloral by *t*BuOCl (entry 6) or by *t*BuOCl with I_2 as an additive (entry 7) proved to be the best choice. When PhMgCl was used instead of PhMgBr, *t*BuOCl alone was not effective for the oxidation, but *t*BuOCl with KI or I_2 as an additive showed high reactivity to give the corresponding trichloromethyl ketone in good yields (entries 8–11). The formation of ArMgBr from ArBr is more practical than that of ArMgCl from ArCl in terms of the ease of formation of Grignard reagents. On the basis of these results, the aryl bromides **4a**–**4j**, that is, phenyl bromide, 4-methylphenyl bromide, 3-methylphenyl bromide, 2-methylphenyl bromide, 4-methoxyphenyl bromide, 4-chlorophenyl bromide, 4-(trifluoromethyl)phenyl bromide, 1-bromonaphthalene, 2-bromothiophene, and 3-bromobenzothiophene, were treated with Mg and then chloral followed by the oxidation with *t*BuOCl to provide aryl tri-

Table 2. Formation of aryl trichloromethyl ketones by the reactions of ArBr with Mg, chloral, and subsequent oxidation with *t*BuOCl.



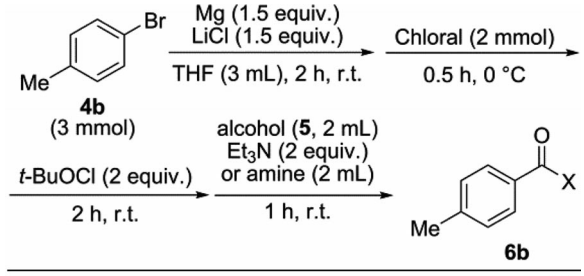
Entry	Bromide		Product	Yield (%)[a]
				
1	FG = H	**4a**	**3a**	82
2	FG = 4-Me	**4b**	**3b**	90
3	FG = 3-Me	**4c**	**3c**	89
4[b]	FG = 2-Me	**4d**	**3d**	86
5[c]	FG = 4-OMe	**4e**	**3e**	85
6[d]	FG = 4-Cl	**4f**	**3f**	96
7[d]	FG = 4-CF_3	**4g**	**3g**	60
8		**4h**	**3h**	90
9		**4i**	**3i**	78
10		**4j**	**3j**	85
11		**4k**	**3k**	0

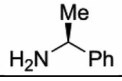
[a] The yields were determined based on the amount of chloral. [b] I_2 (10 mol-%) was added in the third step. [c] Et_2O (4 mL) was added to the THF solution in the first step, the second step was carried out at –20 °C, and Et_2O was removed before the third step. [d] Conditions for the third step: *t*BuOCl (2.0 equiv.) and I_2 (10 mol-%) were added and the mixture was stirred for 2 h at 0 °C.

chloromethyl ketones **3a**–**3j** in good yields (Table 2, entries 1–10). LiCl was added as it is known to be effective for the smooth formation of Grignard reagents from aryl bromides with Mg.[12] The yield of compound **3g** was low (60%) because the trichloromethyl ketone formed partly decomposed during purification by column chromatography due to its high sensitivity to nucleophiles. On the other hand, the reaction between 3-phenylpropylmagnesium bromide and chloral did not occur smoothly (entry 11) because the alkyl Grignard reagent reacts with one of the chlorine atoms of chloral.

Next, the one-pot transformation of 4-methylphenyl bromide **4b** with Mg in the presence of LiCl and then chloral, followed by the treatment with *t*BuOCl and then various nucleophiles (2 mL), such as methanol (**5a**), ethanol (**5b**), 2-propanol (**5c**), benzyl alcohol (**5d**), aq. NH_3 (**5e**), aq. methylamine (**5f**), piperidine (**5g**), and benzylamine (**5h**), was carried out to give the corresponding esters and amides **6ba**–**6bh** in good yields, respectively (Table 3, entries 1–4 and 6–9). When the amount of benzyl alcohol (**5d**) and benzylamine (**5h**) was reduced to 1.2 equiv., the corresponding aromatic ester and amide were also obtained in good yields,

Table 3. Formation of esters and amides from the reactions of 4-MeC_6H_4Br with Mg, chloral, *t*BuOCl, and nucleophiles.



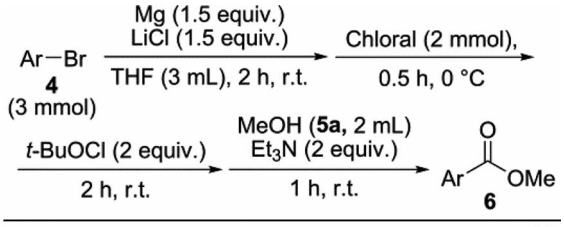
Entry	Nucleophile		Product	Yield (%)[a]
1	MeOH	**5a**	**6ba**	76
2	EtOH	**5b**	**6bb**	79
3[b]	*i*PrOH	**5c**	**6bc**	74
4	BnOH	**5d**	**6bd**	82
5[c]	BnOH	**5d**	**6bd**	75
6	aq. NH_3	**5e**	**6be**	75
7	aq. $MeNH_2$	**5f**	**6bf**	88
8	Piperidine	**5g**	**6bg**	90
9	$BnNH_2$	**5h**	**6bh**	73
10[d]	$BnNH_2$	**5h**	**6bh**	79
11[e]		**5i** (>99% *ee*)	**6bi**	73 (>99% *ee*)

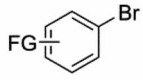
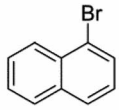
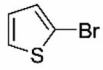
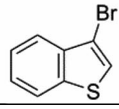
[a] The yields were determined based on the amount of chloral. [b] DMAP (10 mol-%) was used in the fourth step. [c] Conditions for the fourth step: BnOH (1.2 equiv.) and Et_3N (2.0 equiv.) were added and the mixture was stirred for 2 h at room temp. [d] Conditions for the fourth step: $BnNH_2$ (1.2 equiv.) and Et_3N (1.0 equiv.) were added and the mixture was stirred for 2 h at room temp. [e] Conditions for the fourth step: Amine (1.2 equiv.) and Et_3N (1.0 equiv.) were added and the mixture was stirred for 2 h at room temp.

respectively, although the reaction time was 2 h for the last step (entries 5 and 10). Thus, the nucleophiles in the last step in these reactions can be reduced to 1.2 equiv. to provide the corresponding aromatic esters and amides in good yields.

When chiral (*S*)-1-phenylethylamine (**5i**, 1.2 equiv.) was used as the nucleophile, the corresponding amide **6bi** was obtained in good yield with high *ee* (>99%, entry 11). Based on these procedures and conditions, aryl bromides **4a**–**4j** were treated with Mg in the presence of LiCl and then chloral, followed by *t*BuOCl and subsequently methanol to provide aromatic methyl esters **6aa**–**6da** and **6ha**–**6ja** in good yields (Table 4, entries 1–4 and 11–13). When 4-methoxyphenyl bromide was used, it was necessary to use a mixture of THF and diethyl ether as the solvent and the reaction with chloral was carried out at –20 °C to give amide

Table 4. Formation of aromatic methyl esters from the reactions of ArBr with Mg, chloral, *t*BuOCl, and MeOH.



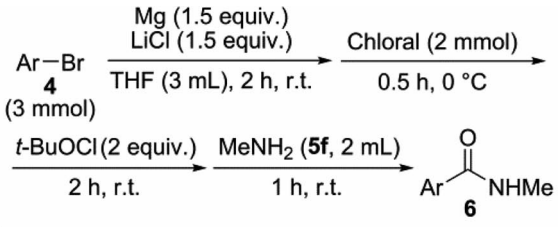
Entry	Bromide		Product	Yield (%)[a]
				
1	FG = H	**4a**	**6aa**	72
2	FG = 4-Me	**4b**	**6ba**	76
3	FG = 3-Me	**4c**	**6ca**	88
4[b]	FG = 2-Me	**4d**	**6da**	85
5	FG = 4-OMe	**4e**	**6ea**	27 (18)[c]
6[d]	FG = 4-OMe	**4e**	**6ea**	80
7	FG = 4-Cl	**4f**	**6fa**	55 (43)[e]
8[f]	FG = 4-Cl	**4f**	**6fa**	53 (23)[c]
9[g]	FG = 4-Cl	**4f**	**6fa**	96
10[g]	FG = 4-CF_3	**4g**	**6ga**	87
11		**4h**	**6ha**	90
12		**4i**	**6ia**	70
13		**4j**	**6ja**	83

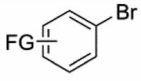
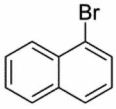
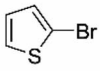
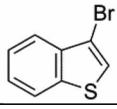
[a] The yields were determined based on the amount of chloral. [b] I_2 (10 mol-%) was added in the third step. [c] Yield of alcohol. [d] Et_2O (4 mL) was added to the THF solution in the first step, the second step was carried out at –20 °C, Et_2O was removed before the third step. [e] Yield of *tert*-butyl ester. [f] The third step was carried out at 0 °C. [g] Conditions for the third step: *t*BuOCl (2.0 equiv.) and I_2 (10 mol-%) were added and the mixture was stirred for 2 h at 0 °C.

6ea in good yield because the corresponding Grignard reagent was rather reactive (entries 5 and 6). Moreover, when 4-chlorophenyl bromide and 4-(trifluoromethyl)phenyl bromide were used, *t*BuOCl and I_2 were added in the third step for effective oxidation to the trichloromethyl ketones at 0 °C, and the high reactivity of the trichloromethyl ketones towards nucleophiles, such as *t*BuOH, furnished esters **6fa** and **6ga** in good yields (entries 7–10).

Similarly, aryl bromides **4a**–**4j** were treated with Mg in the presence of LiCl and then chloral, followed by *t*BuOCl and subsequently methylamine (2 mL) to provide the aromatic *N*-methylamides **6af**–**6df** and **6hf**–**6jf** in good yields (Table 5, entries 1–4 and 8–10). When 4-methoxyphenyl bromide was used, it was necessary to use a mixture of THF and diethyl ether as the solvent and the reaction with chloral was again carried out at –20 °C to improve the yield of amide **6ef** (entry 5). Moreover, when 4-chlorophenyl bromide and 4-(trifluoromethyl)phenyl bromide were used, *t*BuOCl and I_2 were again added in the third step for the effective oxidation to ketones at 0 °C to give amides **6ff** and **6gf** in good yields (entries 6 and 7).

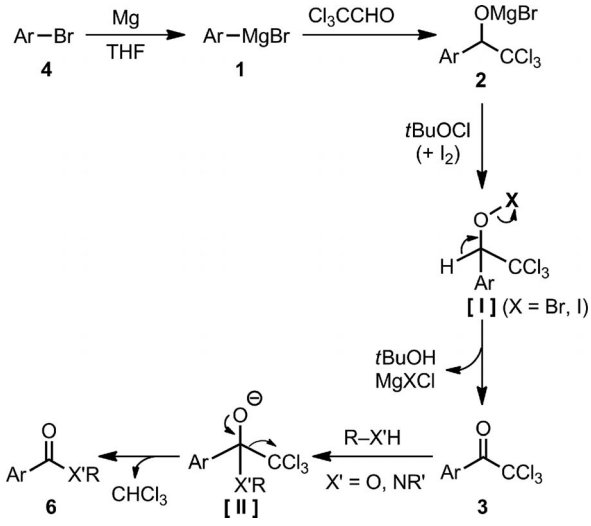
Table 5. Formation of aromatic *N*-methylamides by the the reactions of ArBr with Mg, chloral, *t*BuOCl, and $MeNH_2$.



Entry	Bromide		Product	Yield (%)[a]
				
1	FG = H	**4a**	**6af**	76
2	FG = 4-Me	**4b**	**6bf**	88
3	FG = 3-Me	**4c**	**6cf**	91
4[b]	FG = 2-Me	**4d**	**6df**	86
5[c]	FG = 4-OMe	**4e**	**6ef**	82
6[d]	FG = 4-Cl	**4f**	**6ff**	93
7[d]	FG = 4-CF_3	**4g**	**6gf**	87
8		**4h**	**6hf**	83
9		**4i**	**6if**	77
10		**4j**	**6jf**	85

[a] The yields were determined based on the amount of chloral. [b] I_2 (10 mol-%) was added in the third step. [c] Et_2O (4 mL) was added in the first step, the second step was carried out at –20 °C, and Et_2O was removed before the third step. [d] Conditions for the third step: *t*BuOCl (2.0 equiv.) and I_2 (10 mol-%) were added and the mixture was stirred for 2 h at 0 °C.

The reaction developed in this work proceeds by the addition of aryl Grignard reagents **1** to chloral, the oxidation of the adducts **2** to aryl trichloromethyl ketones **3** by *t*BuOCl via the formation of hypobromites **I** and its β-elimination, and finally the nucleophilic substitution of aryl trichloromethyl ketones **3** by alcohols or amines to provide aromatic esters or amides **6** with the generation of chloroform (Scheme 1). The key point in this reaction is the oxidation of adducts **2** by *t*BuOCl with β-elimination of hypobromite **I** to generate aryl trichloromethyl ketones **3**. When I_2 or KI is added to the solution of adducts **2** and *t*BuOCl, hypoiodite is formed and its β-elimination occurs smoothly to give aryl trichloromethyl ketones **3**. Once the aryl trichloromethyl ketones **3** have formed, they react smoothly with alcohols and amines to give aromatic esters and amides **6**, respectively. The in situ formation of *t*BuOI from *t*BuOK and KI and its synthetic use have been reported previously.[13] On the other hand, when ArMgCl instead of ArMgBr was used in the addition reaction with chloral, treatment of the reaction mixture with *t*BuOCl alone does not generate the trichloromethyl ketone effectively due to the poor β-elimination ability of the formed hypochlorite.



Scheme 1. Reaction pathway.

Conclusions

A variety of aryl bromides have been treated with Mg in the presence of LiCl and then chloral, followed by *t*BuOCl or *t*BuOCl with I_2 as an additive, and subsequently alcohols or amines to form the corresponding aromatic esters and amides, respectively, in good yields via the formation of aryl trichloromethyl ketones under mild conditions. We believe the present reactions are useful for the transition-metal-free one-pot preparation of aromatic esters and amides from aryl bromides.

Experimental Section

General: ^1H and ^{13}C NMR spectra were obtained with JEOL JNM-ECX400, JNM-ECS400, and JNM-ECA500 spectrometers. Chemi-

cal shifts are expressed in ppm downfield from TMS in units of δ. ^{19}F NMR spectra were recorded with a 471 MHz spectrometer. High-resolution mass spectra (HRMS) were recorded with an Orbitrap mass spectrometer. Mass spectra were recorded with JMS-T100GCV, JMS-HX110, and Thermo LTQ Orbitrap XL spectrometers. IR spectra were recorded with a JASCO FT/IR-4100 spectrometer. Melting points were determined with a Yamato Melting Point Apparatus Model MP-21. Silica gel $60F_{254}$ (Merck) was used for TLC and silica gel 60 (Kanto Kagaku Co.) was used for short column chromatography. *t*BuOCl was commercially available from Tokyo Kasei Co, (purity over 98%) and was used without further purification.

Typical Experimental Procedure for the One-Pot Transformation of Aryl Bromides into Aryl Trichloromethyl Ketones 3: Magnesium turnings (72.9 mg, 3.0 mmol) and LiCl (127 mg, 3.0 mmol) were dried with a heat gun for 10 min in vacuo. Under argon, THF (1.0 mL) was added to a flask. Then a solution of 4-bromotoluene (**4b**; 513 mg, 3.0 mmol) in dry THF (2.0 mL) was added at room temp. and the mixture was stirred for 2 h at room temp. Chloral (195 μL, 2.0 mmol) was slowly added at 0 °C and the reaction mixture was stirred for 30 min at 0 °C. Then *t*BuOCl (452 μL, 4.0 mmol) was added and the mixture was stirred for 2 h at room temp. The reaction mixture was quenched with 1 M HCl (2 mL) and a satd. Na_2SO_3 solution (1 mL), and then extracted with EtOAc (3 × 15 mL). The organic layer was washed with brine and dried with Na_2SO_4. Purification by short column chromatography (silica gel, EtOAc/hexane = 0:1 to 1:50) yielded 4-methylphenyl trichloromethyl ketone (**3b**; 428 mg, 90%) as a colorless oil.

Typical Experimental Procedure for the One-Pot Transformation of Aryl Bromides into Aromatic Methyl Esters 6: Magnesium turnings (72.9 mg, 3.0 mmol) and LiCl (127 mg, 3.0 mmol) were dried with a heat gun for 10 min in vacuo. Under argon, THF (1.0 mL) was added to a flask. Then a solution of 4-bromotoluene (**4b**; 513 mg, 3.0 mmol) in dry THF (2.0 mL) was added at room temp. and the mixture was stirred for 2 h at room temp. Chloral (195 μL, 2.0 mmol) was slowly added at 0 °C and the mixture was stirred for 30 min at 0 °C. Then *t*BuOCl (452 μL, 4.0 mmol) was added and the reaction mixture was stirred for 2 h at room temp. Methanol (**5a**; 2 mL) and triethylamine (556 μL, 4 mmol) were added and the mixture was stirred for 1 h at room temp. The reaction mixture was quenched with NH_4Cl (4 mL) and satd. Na_2SO_3 (1 mL), and then extracted with EtOAc (3 × 15 mL). The organic layer was washed with brine and dried with Na_2SO_4. Purification by short column chromatography (silica gel, EtOAc/hexane = 0:1 to 1:10) yielded methyl 4-methylbenzoate (**6ba**; 228 mg, 76%) as a white solid.

Typical Experimental Procedure for the One-Pot Transformation of Aryl Bromides into Aromatic *N*-Methyl Amides 6: Magnesium turnings (72.9 mg, 3.0 mmol) and LiCl (127 mg, 3.0 mmol) were dried with a heat gun for 10 min in vacuo. Under argon, THF (1.0 mL) was added to a flask. Then a solution of 4-bromotoluene (**4b**; 513 mg, 3.0 mmol) in dry THF (2.0 mL) was added at room temp. and the mixture was stirred for 2 h at room temp. Chloral (195 μL, 2.0 mmol) was slowly added at 0 °C and the mixture was stirred for 30 min at 0 °C. Then *t*BuOCl (452 μL, 4.0 mmol) was added and the reaction mixture was stirred for 2 h at room temp. Methylamine (**5f**; 40% in water, 2 mL) was added and the mixture was stirred for 1 h at room temp. The reaction mixture was quenched with 1 M HCl (until neutrality) and satd. Na_2SO_3 (1 mL), and then extracted with EtOAc (3 × 15 mL). The organic layer was washed with brine and dried with Na_2SO_4. Purification by short column chromatography (silica gel, EtOAc/hexane = 1:3 to 4:1) yielded *N*,4-dimethylbenzamide (**5bf**; 263 mg, 88%) as a white solid.

Typical Experimental Procedure for the One-Pot Transformation of Aryl Bromides into Aromatic Esters 6 with Alcohol (1.2 equiv.): Magnesium turnings (72.9 mg, 3.0 mmol) and LiCl (127 mg, 3.0 mmol) were dried with a heat gun for 10 min in vacuo. Under argon, THF (1.0 mL) was added to a flask. Then a solution of 4-bromotoluene (**4b**; 513 mg, 3.0 mmol) in dry THF (2.0 mL) was added at room temp. and the mixture was stirred for 2 h at room temp. Chloral (195 μL, 2.0 mmol) was slowly added at 0 °C and the mixture stirred for 30 min at 0 °C. Then *t*BuOCl (452 μL, 4.0 mmol) was added and the reaction mixture was stirred for 2 h at room temp. Benzyl alcohol (**5d**; 248 μL, 2.4 mmol) and triethylamine (556 μL, 4 mmol) were added and the mixture was stirred for 2 h at room temp. The reaction mixture was quenched with NH_4Cl (4 mL) and satd. Na_2SO_3 (1 mL), and then extracted with EtOAc (3 × 15 mL). The organic layer was washed with brine and dried with Na_2SO_4. Purification by short column chromatography (silica gel, EtOAc/hexane = 0:1 to 1:10) yielded benzyl 4-methylbenzoate (**6bd**; 339 mg, 75%) as a white solid.

Typical Experimental Procedure for the One-Pot Transformation of Aryl Bromides into Aromatic Amides 6 with Amine (1.2 equiv.): Magnesium turnings (72.9 mg, 3.0 mmol) and LiCl (127 mg, 3.0 mmol) were dried with a heat gun for 10 min in vacuo. Under argon, THF (1.0 mL) was added to a flask. Then a solution of 4-bromotoluene (**4b**; 513 mg, 3.0 mmol) in dry THF (2.0 mL) was added at room temp. and the mixture was stirred for 2 h at room temp. Chloral (195 μL, 2.0 mmol) was slowly added at 0 °C and the mixture stirred for 30 min at 0 °C. Then *t*BuOCl (452 μL, 4.0 mmol) was added and the reaction mixture stirred for 2 h at room temp. Benzylamine (**5h**; 262 μL, 2.4 mmol) and triethylamine (278 μL, 2 mmol) were added and the mixture stirred for 2 h at room temp. The reaction mixture was quenched with 1 M HCl (3 mL) and satd. Na_2SO_3 (1 mL), and then extracted with EtOAc (3 × 15 mL). The organic layer was washed with brine and dried with Na_2SO_4. Purification by short column chromatography (silica gel, EtOAc/hexane = 1:3 to 4:1) yielded *N*-benzyl-4-methylbenzamide (**6bh**; 356 mg, 79%) as a white solid.

Compounds **3h**, **3i**, **3j**, **6ja**, and **6jf** are new compounds and compounds **3b**, **3c**, **3d**, **3e**, **3f**, **3g**, **6bc**, **6bd**, **6bg**, **6bi**, **6gf**, and **6if** are known. The other aromatic esters and amides were commercially available and were identified by comparison with authentic compounds.

2,2,2-Trichloroacetophenone (3a) (commercially available): Colorless oil (367 mg, 82% yield). IR (neat): $\tilde{\nu}$ = 1710 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ = 7.50 (t, J = 7.5 Hz, 2 H), 7.64 (t, J = 7.5 Hz, 1 H), 8.27 (d, J = 7.5 Hz, 2 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 95.4, 128.4, 129.0, 131.5, 134.3, 181.2 ppm.

2,2,2-Trichloro-4′-methylacetophenone (3b):[9a] Colorless oil (428 mg, 90% yield). IR (neat): $\tilde{\nu}$ = 1711 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ = 2.45 (s, 3 H), 7.30 (d, J = 8.6 Hz, 2 H), 8.17 (d, J = 8.6 Hz, 2 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 21.8, 95.6, 126.3, 129.1, 131.7, 145.6, 180.9 ppm.

2,2,2-Trichloro-3′-methylacetophenone (3c):[9a] Colorless oil (423 mg, 89% yield). IR (neat): $\tilde{\nu}$ = 1710 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ = 2.44 (s, 3 H), 7.38 (t, J = 7.7 Hz, 1 H), 7.45 (d, J = 7.7 Hz, 1 H), 8.04 (s, 1 H), 8.07 (d, J = 7.7 Hz, 1 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 21.4, 95.5, 128.2, 128.6, 129.1, 131.9, 135.1, 138.4, 181.5 ppm.

2,2,2-Trichloro-2′-methylacetophenone (3d):[9a] Colorless oil (409 mg, 86% yield). IR (neat): $\tilde{\nu}$ = 1730 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ = 2.42 (s, 3 H), 7.26 (t, J = 7.7 Hz, 1 H), 7.32 (d, J = 7.7 Hz, 1 H), 7.43 (t, J = 7.7 Hz, 1 H), 7.91 (d, J =

7.7 Hz, 1 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 20.7, 96.0, 125.0, 128.3, 131.5, 131.7, 132.1, 138.7, 186.1 ppm.

2,2,2-Trichloro-4′-methoxyacetophenone (3e):[9a] White solid (431 mg, 85% yield); m.p. 33–34 °C (ref.[9a] 33–34 °C). IR (neat): $\tilde{\nu}$ = 1697 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 3.91 (s, 3 H), 6.97 (d, J = 8.9 Hz, 2 H), 8.28 (d, J = 8.9 Hz, 2 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 55.6, 95.7, 113.7, 121.1, 134.2, 164.3, 179.8 ppm.

2,2,2-Trichloro-4′-chloroacetophenone (3f):[9a] White solid (495 mg, 96% yield); m.p. 27–28 °C (ref.[9a] oil). IR (neat): $\tilde{\nu}$ = 1713 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.48 (d, J = 8.9 Hz, 2 H), 8.21 (d, J = 8.9 Hz, 2 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 95.1, 127.3, 128.8, 132.9, 141.0, 180.2 ppm.

2,2,2-Trichloro-4′-(trifluoromethyl)acetophenone (3g):[14] Colorless oil (350 mg, 60% yield). IR (neat): $\tilde{\nu}$ = 1719 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.78 (d, J = 8.3 Hz, 2 H), 8.37 (d, J = 8.3 Hz, 2 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 94.8, 123.2 (q, $J_{C,F}$ = 273.5 Hz), 125.5 (q, $J_{C,F}$ = 3.6 Hz), 131.8, 132.3, 135.3 (q, $J_{C,F}$ = 32.4 Hz), 180.5 ppm. ^{19}F NMR (471 MHz, $CDCl_3$): δ = –63.3 ppm.

2,2,2-Trichloro-1′-acetonaphthone (3h): White solid (493 mg, 90% yield); m.p. 40–41 °C. IR (neat): $\tilde{\nu}$ = 1716 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.51 (t, J = 7.7 Hz, 1 H), 7.56 (t, J = 7.7 Hz, 1 H), 7.61 (t, J = 7.7 Hz, 1 H), 7.91 (d, J = 7.7 Hz, 1 H), 7.97 (d, J = 7.7 Hz, 1 H), 8.03 (d, J = 7.7 Hz, 1 H), 8.16 (d, J = 7.7 Hz, 1 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 96.2, 123.8, 125.1, 126.8, 127.3, 128.0, 128.7, 130.0, 131.0, 132.6, 133.6, 186.0 ppm. $C_{12}H_7Cl_3O$ (273.54): C 52.69, H 2.58; found C 52.83, H 2.58.

2-(2,2,2-Trichloroacetyl)thiophene (3i): Colorless oil (358 mg, 78% yield). IR (neat): $\tilde{\nu}$ = 1683 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.20 (dd, J = 4.9, 4.0 Hz, 1 H), 7.81 (dd, J = 4.9, 0.9 Hz, 1 H), 8.18 (dd, J = 4.0, 0.9 Hz, 1 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 95.0, 128.4, 134.0, 136.7, 137.1, 175.1 ppm. $C_6H_3Cl_3OS$ (229.50): C 31.40, H 1.32; found C 31.49, H 1.31.

3-(2,2,2-Trichloroacetyl)benzo[*b*]thiophene (3j): White solid (475 mg, 85% yield); m.p. 65–66 °C. IR (neat): $\tilde{\nu}$ = 1684 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.48 (t, J = 8.0 Hz, 1 H), 7.56 (t, J = 8.0 Hz, 1 H), 7.91 (d, J = 8.0 Hz, 1 H), 8.70 (d, J = 8.0 Hz, 1 H), 8.92 (s, 1 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 96.0, 122.4, 124.0, 125.4, 125.9, 126.4, 137.9, 138.7, 141.1, 176.0 ppm. $C_{10}H_5Cl_3OS$ (279.56): C 42.96, H 1.80; found C 43.00, H 1.75.

Methyl 4-Methylbenzoate (6ba, commercially available): White solid (228 mg, 76% yield); m.p. 33–34 °C. IR (neat): $\tilde{\nu}$ = 1704 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 2.38 (s, 3 H), 3.88 (s, 3 H), 7.21 (d, J = 8.0 Hz, 2 H), 7.91 (d, J = 8.0 Hz, 2 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 21.6, 51.8, 127.4, 129.0, 129.5, 143.5, 167.1 ppm.

Ethyl 4-Methylbenzoate (6bb) (commercially available): Colorless oil (259 mg, 79% yield). IR (neat): $\tilde{\nu}$ = 1714 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.39 (t, J = 7.2 Hz, 3 H), 2.41 (s, 3 H), 4.36 (q, J = 7.2 Hz, 2 H), 7.23 (d, J = 8.0 Hz, 2 H), 7.94 (d, J = 8.0 Hz, 2 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 14.3, 21.6, 60.7, 127.7, 129.0, 129.5, 143.4, 166.7 ppm.

Isopropyl 4-Methylbenzoate (6bc):[15] Colorless oil (264 mg, 74% yield). IR (neat): $\tilde{\nu}$ = 1711 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.36 (d, J = 6.3 Hz, 6 H), 2.40 (s, 3 H), 5.24 (sept, J = 6.3 Hz, 1 H), 7.23 (d, J = 8.3 Hz, 2 H), 7.93 (d, J = 8.3 Hz, 2 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 21.6, 21.9, 68.1, 128.1, 128.9, 129.5, 143.3, 166.2 ppm.

Benzyl 4-Methylbenzoate (6bd):[15] White solid (371 mg, 82% yield); m.p. 44–45 °C (ref.[14] 45–46 °C). IR (neat): $\tilde{\nu}$ = 1612 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 2.40 (s, 3 H), 5.35 (s, 2 H), 7.32 (d, J = 8.0 Hz, 2 H), 7.33 (t, J = 7.5 Hz, 1 H), 7.38 (t, J = 7.5 Hz, 2 H), 7.44 (d, J = 7.5 Hz, 2 H), 7.97 (d, J = 8.0 Hz, 2 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 21.6, 66.5, 127.3, 128.08, 128.14, 128.5, 129.1, 129.7, 136.2, 143.7, 166.5 ppm.

4-Methylbenzamide (6be) (commercially available): White solid (203 mg, 75% yield); m.p. 158–159 °C. IR (neat): $\tilde{\nu}$ = 3340, 3158, 1667 cm^{-1}. ^{1}H NMR (500 MHz, [D$_6$]DMSO): δ = 2.32 (s, 3 H), 7.28 (d, J = 8.3 Hz, 2 H), 7.28 (br. s, 1 H), 7.77 (d, J = 8.3 Hz, 2 H), 7.90 (br. s, 1 H) ppm. ^{13}C NMR (125 MHz, [D$_6$]-DMSO): δ = 21.0, 127.5, 128.8, 131.5, 141.1, 167.9 ppm.

***N*,4-Dimethylbenzamide (6bf) (commercially available):** White solid (263 mg, 88% yield); m.p. 144–145 °C. IR (neat): $\tilde{\nu}$ = 3334, 1628 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 2.38 (s, 3 H), 2.97(I)/2.98(II) (s, 3 H), 6.48 (br. s, 1 H), 7.20 (d, J = 8.0 Hz, 2 H), 7.67 (d, J = 8.0 Hz, 2 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 21.4, 26.7, 126.8, 129.1, 131.7, 141.6, 168.2 ppm.

***N*-(4-Methylbenzoyl)piperidine (6bg):**[16] White solid (366 mg, 90% yield); m.p. 53–54 °C (ref.[16] 53.5–54.0 °C). IR (neat): $\tilde{\nu}$ = 1610 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.51 (br. s, 2 H), 1.67 (br. s, 4 H), 2.37 (s, 3 H), 3.36(I)/3.70(II) (br. s, 4 H), 7.19 (d, J = 8.0 Hz, 2 H), 7.29 (d, J = 8.0 Hz, 2 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 21.3, 24.6, 25.6, 26.5, 43.1, 48.8, 126.8, 128.9, 133.5, 139.3, 170.4 ppm.

***N*-Benzyl-4-methylbenzamide (6bh) (commercially available):** White solid (329 mg, 73% yield); m.p. 133–134 °C. IR (neat): $\tilde{\nu}$ = 3308, 1638 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 2.38 (s, 3 H), 4.62 (d, J = 5.7 Hz, 2 H), 6.52 (br. s, 1 H), 7.20 (d, J = 8.3 Hz, 2 H), 7.26–7.31 (m, 1 H), 7.32–7.36 (m, 4 H), 7.68 (d, J = 8.3 Hz, 2 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 21.4, 44.0, 126.9, 127.6, 127.9, 128.7, 129.2, 131.5, 138.3, 141.9, 167.2 ppm.

(*S*)-4-Methyl-*N*-(1-phenylethyl)benzamide (6bi):[17] White solid (335 mg, 73% yield, >99% *ee*); m.p. 135–136 °C (ref.[17] 127–128 °C, *rac*). IR (neat): $\tilde{\nu}$ = 3341, 1633 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.60 (d, J = 6.9 Hz, 3 H), 2.38 (s, 3 H), 5.33 (quint., J = 6.9 Hz, 1 H), 6.34 (br. s, 1 H), 7.21 (d, J = 8.0 Hz, 2 H), 7.27 (t, J = 7.5 Hz, 1 H), 7.35 (t, J = 7.5 Hz, 2 H), 7.39 (d, J = 7.5 Hz, 2 H), 7.67 (d, J = 8.0 Hz, 2 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 21.4, 21.7, 49.1, 126.2, 126.9, 127.4, 128.7, 129.2, 131.7, 141.8, 143.2, 166.4 ppm. HPLC analysis (Chiralcel OD-H, 1.0 mL/min, 230 nm, hexane/*i*PrOH = 9:1): t_R = 11.0 (minor, *R*), 13.2 min (major, *S*).

Methyl Benzoate (6aa) (commercially available): Colorless oil (196 mg, 72% yield). IR (neat): $\tilde{\nu}$ = 1719 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 3.92 (s, 3 H), 7.44 (t, J = 7.5 Hz, 2 H), 7.56 (t, J = 7.5 Hz, 1 H), 8.04 (d, J = 7.5 Hz, 2 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 52.1, 128.3, 129.5, 130.1, 132.9, 167.1 ppm.

Methyl 3-Methylbenzoate (6ca) (commercially available): Colorless oil (264 mg, 88% yield). IR (neat): $\tilde{\nu}$ = 1718 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 2.40 (s, 3 H), 3.91 (s, 3 H), 7.32 (m, 1 H), 7.37 (d, J = 7.7 Hz, 1 H), 7.84 (d, J = 7.5 Hz, 1 H), 7.86 (s, 1 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 21.2, 52.0, 126.7, 128.2, 130.0, 130.1, 133.7, 138.1, 167.3 ppm.

Methyl 2-Methylbenzoate (6da) (commercially available): Colorless oil (255 mg, 85% yield). IR (neat): $\tilde{\nu}$ = 1719 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 2.60 (s, 3 H), 3.89 (s, 3 H), 7.21–7.27 (m, 2 H), 7.40 (dt, J = 7.7, 1.4 Hz, 1 H), 7.91 (dd, J = 7.4, 1.4 Hz, 1 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 21.7, 51.8, 125.7, 129.5, 130.5, 131.7, 131.9, 140.2, 168.1 ppm.

Methyl 4-Methoxybenzoate (6ea) (commercially available): White solid (266 mg, 80% yield); m.p. 48–49 °C. IR (neat): $\tilde{\nu}$ = 1705 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ = 3.84 (s, 3 H), 3.89 (s, 3 H), 6.91 (d, J = 8.9 Hz, 2 H), 7.99 (d, J = 8.9 Hz, 2 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 51.8, 55.3, 113.5, 122.5, 131.5, 163.2, 166.8 ppm.

Methyl 4-Chlorobenzoate (6fa) (commercially available): White solid (328 mg, 96% yield); m.p. 44–45 °C. IR (neat): $\tilde{\nu}$ = 1718 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ = 3.91 (s, 3 H), 7.41 (d, J = 8.6 Hz, 2 H), 7.97 (d, J = 8.6 Hz, 2 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 52.2, 128.5, 128.7, 130.9, 139.3, 166.2 ppm.

Methyl 4-(Trifluoromethyl)benzoate (6ga) (commercially available): Colorless oil (355 mg, 87% yield). IR (neat): $\tilde{\nu}$ = 1726 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ = 3.96 (s, 3 H), 7.71 (d, J = 8.3 Hz, 2 H), 8.18 (d, J = 8.3 Hz, 2 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 52.5, 123.6 (q, $J_{C,F}$ = 273.3 Hz), 125.4 (q, $J_{C,F}$ = 3.6 Hz), 130.0, 133.3, 134.4 (q, $J_{C,F}$ = 32.4 Hz), 165.9 ppm. ^{19}F NMR (471 MHz, $CDCl_3$): δ = –63.0 ppm.

Methyl 1-Naphthoate (6ha) (commercially available): Colorless oil (335 mg, 90% yield). IR (neat): $\tilde{\nu}$ = 1712 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ = 4.00 (s, 3 H), 7.50 (dd, J = 8.0, 7.5 Hz, 1 H), 7.53 (dd, J = 8.3, 6.9 Hz, 1 H), 7.62 (dd, J = 8.6, 6.9 Hz, 1 H), 7.88 (d, J = 8.3 Hz, 1 H), 8.02 (d, J = 8.0 Hz, 1 H), 8.19 (d, J = 7.5 Hz, 1 H), 8.91 (d, J = 8.6 Hz, 1 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 52.2, 124.5, 125.8, 126.2, 127.0, 127.7, 128.5, 130.2, 131.3, 133.4, 133.8, 168.0 ppm.

Methyl Thiophene-2-carboxylate (3ia) (commercially available): Colorless oil (199 mg, 70% yield). IR (neat): $\tilde{\nu}$ = 1706 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ = 3.89 (s, 3 H), 7.10 (dd, J = 4.6, 4.1 Hz, 1 H), 7.55 (dd, J = 4.6, 0.6 Hz, 1 H), 7.81 (dd, J = 4.1, 0.6 Hz, 1 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 52.1, 127.7, 132.3, 133.4, 133.5, 162.7 ppm.

Methyl Benzo[*b*]thiophene-3-carboxylate (6ja): Colorless oil (319 mg, 83% yield). IR (neat): $\tilde{\nu}$ = 1707 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ = 3.96 (s, 3 H), 7.40–7.44 (m, 1 H), 7.47–7.52 (m, 1 H), 7.88 (d, J = 8.0 Hz, 1 H), 8.38 (s, 1 H), 8.60 (d, J = 8.0 Hz, 1 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 51.7, 122.5, 124.7, 125.0, 125.4, 127.0, 136.6, 136.7, 140.0, 163.2 ppm. HRMS (APCI): calcd. for $C_{10}H_9O_2S$ $[M]^+$ 193.0318; found 193.0316.

***N*-Methylbenzamide (6af) (commercially available):** White solid (205 mg, 76% yield); m.p. 78–79 °C. IR (neat): $\tilde{\nu}$ = 3675, 3327, 1636 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ = 3.00(I)/3.01(II) (s, 3 H), 6.30 (br. s, 1 H), 7.42 (t, J = 7.2 Hz, 2 H), 7.48 (t, J = 7.2 Hz, 1 H), 7.76 (d, J = 7.2 Hz, 2 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 26.8, 126.8, 128.5, 131.3, 134.6, 168.2 ppm.

***N*,3-Dimethylbenzamide (6cf) (commercially available):** White solid (272 mg, 91% yield); m.p. 45–46 °C. IR (neat): $\tilde{\nu}$ = 3257, 1632 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ = 2.38 (s, 3 H), 2.99(I)/3.00(II) (s, 3 H), 6.32 (br. s, 1 H), 7.28–7.32 (m, 2 H), 7.51–7.56 (m, 1 H), 7.59 (s, 1 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 21.3, 26.8, 123.7, 127.6, 128.3, 132.0, 134.5, 138.3, 168.4 ppm.

***N*,2-Dimethylbenzamide (6df) (commercially available):** White solid (257 mg, 86% yield); m.p. 76–77 °C. IR (neat): $\tilde{\nu}$ = 3675, 3291, 1633 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ = 2.39 (s, 3 H), 2.92(I)/2.93(II) (s, 3 H), 5.99 (br. s, 1 H), 7.11–7.20 (m, 2 H), 7.24–7.31 (m, 2 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 19.7, 26.5, 125.6, 126.6, 129.7, 130.8, 135.9, 136.4, 170.8 ppm.

***N*-Methyl-4-methoxybenzamide (6ef, commercially available):** White solid (271 mg, 82% yield); m.p. 118–119 °C. IR (neat): $\tilde{\nu}$ = 3351, 1628 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ = 2.96(I)/2.97(II) (s, 3 H), 3.83 (s, 3 H), 6.46 (br. s, 1 H), 6.89 (d, J = 8.9 Hz, 2 H), 7.74 (d, J = 8.9 Hz, 2 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 26.7, 55.3, 113.6, 126.8, 128.6, 161.9, 167.9 ppm.

4-Chloro-*N*-methylbenzamide (6ff) (commercially available): White solid (315 mg, 93% yield); m.p. 157–158 °C. IR (neat): $\tilde{\nu}$ = 3334, 1633 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ = 3.00(I)/3.01(II) (s, 3 H), 6.27 (br. s, 1 H), 7.39 (d, J = 8.6 Hz, 2 H), 7.70 (d, J = 8.6 Hz, 2 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 26.9, 128.3, 128.8, 132.9, 137.5, 167.2 ppm.

***N*-Methyl-4-(trifluoromethyl)benzamide (6gf):**[18] White solid (354 mg, 87% yield); m.p. 155–156 °C. IR (neat): $\tilde{\nu}$ = 3301, 1647 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ = 3.02(I)/3.03(II) (s, 3 H), 6.47 (br. s, 1 H), 7.68 (d, J = 8.3 Hz, 2 H), 7.87 (d, J = 8.3 Hz, 2 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 26.9, 123.6 (q, $J_{C,F}$ = 272.3 Hz), 125.6 (q, $J_{C,F}$ = 3.6 Hz), 127.3, 133.1 (q, $J_{C,F}$ = 32.4 Hz), 137.8, 167.0 ppm. ^{19}F NMR (471 MHz, $CDCl_3$): δ = –62.8 ppm.

***N*-Methyl-1-naphthamide (6hf) (commercially available):** White solid (307 mg, 83% yield); m.p. 160–161 °C. IR (neat): $\tilde{\nu}$ = 3675, 3271, 1632 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ = 2.97(I)/2.98(II) (s, 3 H), 6.23 (br. s, 1 H), 7.35 (dd, J = 8.0, 7.0 Hz, 1 H), 7.44–7.52 (m, 3 H), 7.79–7.87 (m, 2 H), 8.20–8.26 (m, 1 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 26.7, 124.6, 124.8, 125.4, 126.3, 126.9, 128.2, 130.0, 130.3, 133.5, 134.4, 170.2 ppm.

***N*-Methylthiophene-2-carboxamide (6if):**[18] White solid (217 mg, 77% yield); m.p. 111–112 °C. IR (neat): $\tilde{\nu}$ = 3285, 1613 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ = 2.99(I)/2.30(II) (s, 3 H), 6.27 (br. s, 1 H), 7.06 (dd, J = 4.9, 3.7 Hz, 1 H), 7.45 (dd, J = 4.9, 1.2 Hz, 1 H), 7.52 (dd, J = 3.7, 1.2 Hz, 1 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 26.7, 127.6, 127.9, 129.6, 138.9, 162.6 ppm.

***N*-Methylbenzo[*b*]thiophene-3-carboxamide (6jf):** White solid (325 mg, 85% yield); m.p. 131–132 °C. IR (neat): $\tilde{\nu}$ = 3300, 1633 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ = 2.95(I)/2.96(II) (s, 3 H), 7.33–7.42 (m, 2 H), 7.80–7.84 (m, 2 H), 8.35 (d, J = 7.7 Hz, 1 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 26.4, 122.4, 124.2, 124.9, 124.9, 128.9, 131.9, 136.7, 140.0, 164.9 ppm. HRMS (APCI): calcd. for $C_{10}H_{10}ONS$ $[M]^+$ 192.0478; found 192.0474.

Supporting Information (see footnote on the first page of this article): ^1H, ^{13}C, and ^{19}F NMR spectra of all esters and amides, and a chiral HPLC chart.

Acknowledgments

Financial support from the Japanese Ministry of Education, Culture, Sports, Science, and Technology (MEXT) in the form of a Grant-in-Aid for Scientific Research (grant number 25105710) and the Iodine Research Project of Chiba University is gratefully acknowledged.

[1] a) D. S. Johnson, J. J. Li, (Eds.), *The Art of Drug Synthesis* Wiley, Hoboken, NJ, **2007**; b) A. Zapf, M. Beller, *Top. Catal.* **2002**, *19*, 101–109; c) J. Stetter, F. Lieb, *Angew. Chem.* **2000**, *112*, 1792; *Angew. Chem. Int. Ed.* **2000**, *39*, 1724–1744.

[2] For recent reviews, see: a) A. Roy, S. Roy, G. W. Gribble, *Tetrahedron* **2012**, *68*, 9867–9923; b) L. R. Odell, F. Russo, M. Larhed, *Synlett* **2012**, *23*, 685–698, and references cited therein.

[3] For the Fischer ester Synthesis see: a) E. Fischer, A. Speier, *Ber. Dtsch. Chem. Ges.* **1895**, *28*, 3252–3258; b) S. P. Bew, D. L. Hughs, S. V. Sharma, *J. Org. Chem.* **2006**, *71*, 7881–7884; c) R. C. Larock, *Comprehensive Organic Transformations*, 2nd ed., Wiley, New York, **1999**, p. 1625–1993; for the Mitsunobu reac-

tion, see: d) O. Mitsunobu, *Synthesis* **1981**, 1–28; e) M. P. Watterson, G. W. J. Fleet, *Tetrahedron Lett.* **2003**, *44*, 5853–5857; f) A. E. Favorskii, *J. Prakt. Chem.* **1895**, *51*, 533–563; A. E. Favorskii, *J. Prakt. Chem.* **1913**, *88*, 641–698; g) A. Baeyer, V. Villiger, *Ber. Dtsch. Chem. Ges.* **1899**, *32*, 3625–3633; h) A. Pinner, F. Klein, *Ber. Dtsch. Chem. Ges.* **1883**, *16*, 352; i) A. Pinner, F. Klein, *Ber. Dtsch. Chem. Ges.* **1883**, *16*, 1643–1655.

[4] a) C. Schotten, *Ber. Dtsch. Chem. Ges.* **1884**, *17*, 2544–2547; b) E. Baumann, *Ber. Dtsch. Chem. Ges.* **1886**, *19*, 3218–3222; c) E. Beckmann, *Ber. Dtsch. Chem. Ges.* **1886**, *19*, 988–993; d) J. J. Ritter, P. P. Minieri, *J. Am. Chem. Soc.* **1948**, *70*, 4045–4048.

[5] a) A. Schoenberg, I. Bartoletti, R. F. Heck, *J. Org. Chem.* **1974**, *39*, 3318–3326; for recent papers, see: b) D. A. Watson, X. Fan, S. L. Buchwald, *J. Org. Chem.* **2008**, *73*, 7096–7101; c) J. R. Martinelli, D. A. Watson, D. M. M. Freckmann, T. E. Barder, S. L. Buchwald, *J. Org. Chem.* **2008**, *73*, 7102–7107; d) R. H. Munday, J. R. Martinelli, S. L. Buchwald, *J. Am. Chem. Soc.* **2008**, *130*, 2754–2755; e) R. Shang, Y. Fu, J. Li, S. Zhang, Q. Guo, L. Liu, *J. Am. Chem. Soc.* **2009**, *131*, 5738–5739.

[6] a) A. Schoenberg, R. F. Heck, *J. Org. Chem.* **1974**, *39*, 3327–3331; for recent papers, see: b) R. F. Cunico, B. Maity, *Org. Lett.* **2002**, *4*, 4357–4359; c) J. Ju, M. Jeong, J. Moon, H. M. Jung, S. Lee, *Org. Lett.* **2007**, *9*, 4615–4618; d) X. Wu, H. Neumann, M. Beller, *Chem. Asian J.* **2010**, *5*, 2168–2172; e) X. Wu, H. Neumann, M. Beller, *Chem. Eur. J.* **2010**, *16*, 9750–9753; f) B. Roberts, D. Liptrot, L. Alcaraz, T. Luker, M. J. Stocks, *Org. Lett.* **2010**, *12*, 4280–4283; g) D. N. Sawant, Y. S. Wagh, K. D. Bhatte, B. M. Bhanage, *J. Org. Chem.* **2011**, *76*, 5489–5494; h) T. T. Dang, Y. Zhu, S. C. Ghosh, A. Chen, C. L. L. Chai, A. M. Seayad, *Chem. Commun.* **2012**, *48*, 1805–1807.

[7] a) L. D. Bratton, H. Huh, R. A. Bartsch, *J. Heterocycl. Chem.* **2000**, *37*, 815–819; b) J. C. J. Amedio, G. T. Lee, K. Prasad, O. Repic, *Synth. Commun.* **1995**, *25*, 2599–2612; c) H. Li, J. Balsells, *Tetrahedron Lett.* **2008**, *49*, 2034–2037; d) M. Mosrin, N. Boudet, P. Knochel, *Org. Biomol. Chem.* **2008**, *6*, 3237–3239; e) L. Lemoucheux, J. Rouden, M. Lasne, *Tetrahedron Lett.* **2000**, *41*, 9997–10001; f) L. Lemoucheux, T. Seitz, J. Rouden, M. Lasne, *Org. Lett.* **2004**, *6*, 3703–3706; g) C. Dunst, P. Knochel, *Synlett* **2011**, 2064–2068; h) T. Yamazaki, T. Terajima, T. Kawasaki-Taskasuka, *Tetrahedron* **2008**, *64*, 2419–2424; i) M. A. Schade, G. Manolikakes, P. Knochel, *Org. Lett.* **2010**, *12*, 3648–3650.

[8] For reviews, see: a) H. Togo, S. Iida, *Synlett* **2006**, 2159–2175; b) H. Togo, *J. Synth. Org. Chem.* **2008**, *66*, 652–663; for recent papers, see: c) S. Ushijima, S. Dohi, K. Moriyama, H. Togo, *Tetrahedron* **2012**, *68*, 1436–1442; d) H. Baba, K. Moriyama, H. Togo, *Synlett* **2012**, *23*, 1175–1180; e) S. Ushijima, K. Moriyama, H. Togo, *Tetrahedron* **2012**, *68*, 4701–4709; f) S. Ushijima, K. Moriyama, H. Togo, *Tetrahedron* **2012**, *68*, 4588–4595; g) S. Dohi, K. Moriyama, H. Togo, *Tetrahedron* **2012**, *68*, 6557–6564.

[9] a) C. Gallina, C. Giordano, *Synthesis* **1989**, 466–468; b) E. J. Corey, J. O. Link, Y. Shao, *Tetrahedron Lett.* **1992**, *33*, 3435–3438; c) C. B. Kelly, M. A. Mercadante, T. A. Hamlin, M. H. Fletcher, *J. Org. Chem.* **2012**, *77*, 8131–8141.

[10] a) R. A. Rebelo, M. C. Rezende, F. Nome, C. Zucco, *Synth. Commun.* **1987**, *17*, 1741–1748; b) S. C. Hess, F. Nome, C. Zucco, M. C. Rezende, *Synth. Commun.* **1989**, *19*, 3037–3045; c) R. N. Ram, V. K. Soni, D. K. Gupta, *Tetrahedron* **2012**, *68*, 9068–9075.

[11] L. Cao, J. Ding, M. Gao, Z. Wang, J. Li, A. Wu, *Org. Lett.* **2009**, *11*, 3810–3813.

[12] F. M. Piller, P. Appokkuttan, A. Gavryushin, M. Helm, P. Knochel, *Angew. Chem.* **2008**, *120*, 6907; *Angew. Chem. Int. Ed.* **2008**, *47*, 6802–6806.

[13] a) Y. Takeda, S. Okumura, S. Minakata, *Synthesis* **2013**, *45*, 1029–1033; b) S. Minakata, S. Okumura, T. Nagamachi, Y. Takeda, *Org. Lett.* **2011**, *13*, 2966–2969; c) S. Minakata, I. Sasaki, T. Ide, *Angew. Chem.* **2010**, *122*, 1331; *Angew. Chem. Int. Ed.* **2010**, *49*, 1309–1311; d) Y. Takeda, S. Okumura, S. Minakata, *Angew. Chem.* **2012**, *124*, 7924; *Angew. Chem. Int. Ed.* **2012**, *51*, 7804–7808; e) Y. Takeda, S. Enokijima, T. Nagamachi, K. Nakayama, S. Minakata, *Asian J. Org. Chem.* **2013**, *2*, 91–97.

[14] T. Imanishi, Y. Fujiwara, Y. Sawama, Y. Monguchi, H. Sajiki, *Adv. Synth. Catal.* **2012**, *354*, 771–776.

[15] X. Jia, H. Wang, Q. Huang, L. Kong, W. Zhang, *J. Chem. Res.* **2006**, 135–138.

[16] Y. Otani, O. Nagae, Y. Naruse, S. Inagaki, M. Ohno, K. Yamaguchi, G. Yamamoto, M. Uchiyama, T. Ohwada, *J. Am. Chem. Soc.* **2003**, *125*, 15191–15199.

[17] W. Songa, L. Maa, L. Huab, *Synth. Commun.* **2011**, *41*, 3186–3196.

[18] T. K. Hyster, T. Rovis, *J. Am. Chem. Soc.* **2010**, *132*, 10565–10569.

Received: August 2, 2013
Published Online: October 9, 2013

