Efficient and Divergent Synthesis of Functionalized Cyclopropanes via Iodoform Reaction

Dingyuan Zhang, Rui Zhang, Dexuan Xiang, Ning Zhang,* Yongjiu Liang, Dewen Dong*

Changchun Institute of Applied Chemistry, Chinese Academy of Sciences, Changchun 130022, P. R. of China
Fax +86(431)85262676; E-mail: zhangningtum@gmail.com; E-mail: dwdong@ciac.jl.cn

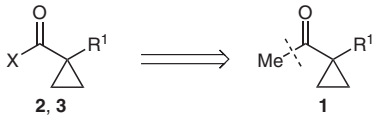
Received 26 November 2011; revised 1 January 2012

Abstract: Efficient and divergent one-pot synthesis of cyclopropyl amides and esters from readily available 1-acetylcyclopropanes via iodoform reaction based on the selection of reaction conditions is reported. A series of substituted cyclopropyl amides were synthesized from 1-acetylcyclopropanes, iodine, and ammonia in water in the presence of K_2CO_3 in good yields, whereas substituted cyclopropyl esters were obtained from the reaction of 1-acetylcyclopropanes with iodine and alcohols in the presence of DBU.

Key words: cyclopropanes, iodoform reaction, iodine, amide, water

The overwhelming importance of cyclopropane derivatives in organic synthesis has been recognized for their presence in numerous natural products and synthetic organic compounds, such as chrysanthemates and cilastatin, along with diverse bio-, physio-, and pharmacological activities.[1,2] Moreover, functionalized cyclopropanes are widely utilized as versatile intermediates in organic transformations to carbo- and heterocyclic systems. So far, extensive work has generated many approaches for the synthesis of a variety of cyclopropanes, from either appropriately acyclic precursors,[3–5] or the modification of the preconstructed cyclopropane rings.[6] Nevertheless, to match the increasing scientific and practical demands, it is still of great importance to develop simple and efficient approaches for the construction of skeleton cyclopropanes, especially those with wide applicability to achieve more elaborate and flexible substitution patterns.

During the course of our studies on the synthesis and utility of cyclopropanes based on β-oxo amides and their derivatives,[7] we developed one-pot synthesis of pyridin-2(1*H*)-ones,[7a] spiro-fused pyrazolin-5-ones,[7b] spiro-fused pyrazolin-5-one *N*-oxides,[7c] 1*H*-pyrazoles, and isoxazoles.[7d] The important synthetic utility of functionalized cyclopropanes and our continuing interest in the synthesis of highly valuable carbo- and heterocycles prompted us to exploit the synthesis of variable and novel cyclopropanes. In the present work, we envisioned that under appropriate conditions the readily available acetylcyclopropanes could be converted into other cyclopropyl systems (Scheme 1). As a result, we developed a facile one-pot synthesis of cyclopropyl amides and esters via iodoform reaction of 1-acetylcyclopropanes under different conditions. Herein, we wish to report our experimental results.



Scheme 1 Proposed synthetic approach for functionalized cyclopropanes

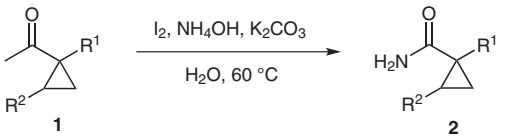
Iodoform reaction is an efficient tool for the conversion of acetyl to carboxylic acid group under basic conditions.[8] Recently, Cao and co-workers reported a modification of classical iodoform reaction using water as a solvent, in which they achieved efficient synthesis of primary amides.[8d] In the present work, we investigated the iodoform reaction of the readily available acetylcyclopropanes **1**.[9] Thus, the reaction of 1-acetyl-*N*-phenylcyclopropane carboxamide (**1a**) with iodine (3.0 equiv) and NH_4OH (3.0 equiv) in the presence of K_2CO_3 (4.0 equiv) was first attempted in DMF at room temperature for 4.5 hours. The reaction proceeded smoothly as monitored by TLC and furnished a white solid after workup and purification by column chromatography of the resulting mixture. The product was identified as *N*-phenylcyclopropane-1,1-dicarboxamide (**2a**) on the basis of the spectral and analytical data.

The results encouraged us to exploit the feasibility of preparation of cyclopropyl amides in water. The use of water as a reaction medium in organic chemistry was rediscovered in the 1980s in Breslow's work, which showed that a hydrophobic effect can strongly enhance the rates of some organic reactions.[10] Organic reactions in water without the use of any organic solvent can also benefit from the fact that water is an easily available, cheap, safe, and environmentally benign solvent.[8d,11,12] After a series of experiments, including variation of reaction temperature, base, and the feed ratio of iodine/base/NH_4OH, the optimal reaction conditions were obtained when the reaction of **1a** was performed with iodine (3.0 equiv) and NH_4OH (2.0 equiv) in the presence of K_2CO_3 (4.0 equiv) in water at 60 °C, whereby the yield of **2a** reached 88% (Table 1, entry 1).

To determine the scope of the iodoform reaction in water, various cyclopropyl ketones **1** were subjected to the identical conditions, and some of the results are summarized in Table 1. It was observed that the reactions of 1-acetyl-

SYNTHESIS 2012, 44, 705–710
Advanced online publication: 03.02.2012
DOI: 10.1055/s-0031-1289693; Art ID: F110811SS

Table 1 Synthesis of Cyclopropyl Amides **2** from 1-Acetylcyclopropanes **1**[a]



1 **2**

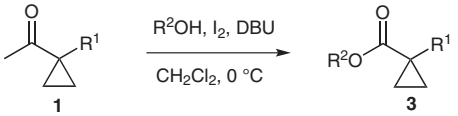
Entry	**1**	R^1	R^2	**2**	Yield (%)[b]
1	**1a**	PhNHCO	H	**2a**	88
2	**1b**	4-MeC_6H_4NHCO	H	**2b**	80
3	**1c**	4-$MeOC_6H_4NHCO$	H	**2c**	82
4	**1d**	4-ClC_6H_4NHCO	H	**2d**	79
5	**1e**	2-MeC_6H_4NHCO	H	**2e**	71
6	**1f**	2-$MeOC_6H_4NHCO$	H	**2f**	62
7	**1g**	2-ClC_6H_4NHCO	H	**2g**	65
8	**1h**	2,4-$Me_2C_6H_3NHCO$	H	**2h**	83
9	**1i**	PhCO	H	**2i**	76
10	**1j**	CO_2Et	H	**2j**	74
11	**1k**	PhNHCO	Me	**2k**	82[c]
12	**1l**	PhNHCO	Ph	**2l**	63[d]

[a] Reaction conditions: **1** (1.0 mmol), I_2 (3.0 mmol), NH_4OH (2.0 mmol), K_2CO_3 (4.0 equiv), H_2O (20 mL), 60 °C, 1.0–4.5 h.
[b] Isolated yield.
[c] For entry 11: *cis*-**1k** was used, *cis*-**2k** was obtained.
[d] For entry 12: *trans*-**1l** was used, *trans*-**2l** was obtained.

cyclopropanes **1b–h** could proceed smoothly to afford the corresponding substituted cyclopropyl amides **2b–h** in good yields (Table 1, entries 2–8). The efficiency of the reaction proved to be suitable for substrates **1i** and **1j** bearing benzoyl and ester groups, respectively (Table 1, entries 9, 10). In the cases of substrates *cis*-**1k** and *trans*-**1l** with a substituent on the cyclopropyl ring, the corresponding cyclopropyl amides *cis*-**2k** and *trans*-**2l** were obtained in moderate to good yields (Table 1, entries 11, 12).[13] All the results demonstrated the efficiency and synthetic interest of the protocol with respect to 1-acetylcyclopropanes **1** bearing variable amide, benzoyl, and ester groups. It should be noted that the richness of the functionality, for example, cyclopropane moiety and amide group of the cyclopropyl amides of type **2** obtained may render them extremely versatile as synthons in other organic transformations. For example, the primary amide group is very reactive group, which can be easily converted into the cyano group,[14] and a variety of ring-opening and ring-enlargement reactions of the functionalized cyclopropanes, for their well-known 'unsaturated' character, may lead to novel carbo- and heterocycles.[7,15]

To extend its scope of the reaction, we subsequently examined the iodoform reaction of 1-acetyl-1-carbamoylcyclopropanes **1** in alcohol. Thus, the reaction of **1a** with iodine (3.0 equiv), K_2CO_3 (4.0 equiv), and methanol (1.0 equiv) was performed in water at room temperature for 4.5 hours. Unfortunately, no reaction was observed as indicated by TLC. When **1a**, methanol (1.2 equiv), and iodine (3.0 equiv) reacted in CH_2Cl_2 (10 mL) in the presence of 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU, 4.0 equiv) at 0 °C for 1 hour, a product was obtained, and characterized as methyl 1-(phenylcarbamoyl)cyclopropanecarboxylate (**3a**) on the basis of the spectral and analytical data (Table 2, entry 1). Under the identical conditions, a range of reactions of 1-acetylcyclopropanes **1b–i** bearing variable aryl amide and benzoyl groups were carried out. As shown in Table 2, the efficiency of the iodoform reaction proved to be suitable to afford the corresponding substituted cyclopropyl esters **3b–i** in good yields (Table 2, entries 2–9). The versatility of the cyclopropyl ester synthesis was evaluated by using other kind of alcohols, such as EtOH and BnOH, as the reactants (Table 2, entries 10–12).

Table 2 Synthesis of Cyclopropyl Esters **3** from 1-Acetylcyclopropanes **1**[a]



1 **3**

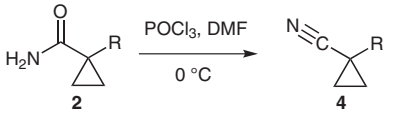
Entry	**1**	R^1	R^2	**3**	Yield (%)[b]
1	**1a**	PhNHCO	Me	**3a**	86
2	**1b**	4-MeC_6H_4NHCO	Me	**3b**	79
3	**1c**	4-$MeOC_6H_4NHCO$	Me	**3c**	80
4	**1d**	4-ClC_6H_4NHCO	Me	**3d**	76
5	**1e**	2-MeC_6H_4NHCO	Me	**3e**	73
6	**1f**	2-$MeOC_6H_4NHCO$	Me	**3f**	82
7	**1g**	2-ClC_6H_4NHCO	Me	**3g**	72
8	**1h**	2,4-$Me_2C_6H_3NHCO$	Me	**3h**	84
9	**1i**	PhCO	Me	**3i**	82
10	**1i**	PhCO	Et	**3j**	84
11	**1e**	2-MeC_6H_4NHCO	Et	**3k**	81
12	**1e**	2-MeC_6H_4NHCO	Bn	**3l**	75

[a] Reaction conditions: **1** (1.0 mmol), R^1OH (1.2 mmol), I_2 (3.0 mmol), DBU (4.0 mmol), CH_2Cl_2 (10 mL), 0 °C, 1.0–6.0 h.
[b] Isolated yield.

Further, we were interested in the utilization of cyclopropyl amides **2** under Vilsmeier conditions.[16] The reaction of **2a** with Vilsmeier reagent, $POCl_3$–DMF (1.5 equiv), was performed at 0 °C for 2 hours, which furnished a white solid. The product was characterized as 1-cyano-*N*-phenylcyclopropanecarboxamide (**4a**) on the basis of its spectral and analytical data (83% yield). When the reaction was conducted with 3.0 equivalents of Vilsmeier reagent at 0 °C, the reaction could be completed within 30

minutes and the yield of **4a** reached 92% (Table 3, entry 1). Some of the selected cyclopropyl amides **2** were subjected to the identical conditions, and the corresponding 1-cyanocyclopropanes **4** were obtained in good to high yields (Table 3, entries 2–7).

Table 3 Synthesis of Cyanocyclopropanes **4** from Cyclopropyl Amides **2** under Vilsmeier Conditions



2 **4**

Entry	2	R	4	Time (h)	Yield (%)[b]
1	**2a**	PhNHCO	**4a**	2.0	92
2	**2b**	4-MeC_6H_4NHCO	**4b**	1.5	90
3	**2c**	4-MeOC_6H_4NHCO	**4c**	2.0	87
4	**2d**	4-ClC_6H_4NHCO	**4d**	2.5	83
5	**2e**	2-MeC_6H_4NHCO	**4e**	1.0	89
6	**2i**	PhCO	**4i**	1.5	86
7	**2j**	CO_2Et	**4j**	1.5	82

[a] Reaction conditions: **2** (1.0 mmol), $POCl_3$ (3.0 mmol), DMF (5 mL), 0 °C, 0.5–2.0 h.
[b] Isolated yield.

In summary, an efficient and divergent one-pot synthesis of functionalized cyclopropanes **2** and **3** from readily available 1-acetylcyclopropanes **1** via iodoform reaction based on the selection of reaction conditions is reported. Moreover, synthetic transformation of cyclopropyl amides **2** provided an alternative synthetic approach to cyanocyclopropanes **4**. These protocols for functionalized cyclopropanes are associated with readily available starting materials, mild conditions, high yields, and potential utility of the products.

All reagents were purchased from commercial sources and used without treatment, unless otherwise indicated. The products were purified by column chromatography over silica gel. Petroleum ether (PE) refers to a hydrocarbon mixture with a boiling range of 60–90 °C. ^{1}H NMR and ^{13}C NMR spectra were recorded at 300 (or 400) MHz and 75 (or 100) MHz, respectively, with TMS as internal standard at 25 °C. IR spectra (KBr) were recorded on a FTIR spectrophotometer in the range of 400–4000 cm^{-1}.

1-Acetyl-1-carbamoylcyclopropanes 1

Cyclopropanes **1a–l** were prepared according to a known literature procedure.[9] Products **1a–j** are known compounds; their analytical and spectral data are in good agreement with those reported in the literature.[9] The data for the new derivatives *cis*-**1k** and *trans*-**1l** are given below.

cis-1-Acetyl-2-methyl-*N*-phenylcyclopropanecarboxamide (*cis*-1k)

Yield: 91 mg (42%); white solid; mp 87–89 °C.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.29 (d, *J* = 3.0 Hz, 3 H), 1.68–1.72 (m, 1 H), 1.84–1.96 (m, 1 H), 1.98–2.02 (m, 1 H), 2.11 (s, 3 H), 7.10 (t, *J* = 7.5 Hz, 1 H), 7.33 (t, *J* = 7.5 Hz, 2 H), 7.57 (d, *J* = 7.5 Hz, 2 H), 10.06 (s, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 12.7, 22.1, 26.2, 27.7, 42.3, 120.2 (2 C), 124.2, 128.9 (2 C), 138.1, 165.1, 206.9.

Anal. Calcd for $C_{13}H_{15}NO_2$: C, 71.87; H, 6.96; N, 6.45. Found: C, 71.64; H, 6.89; N, 6.49.

trans-1-Acetyl-*N*,2-diphenylcyclopropanecarboxamide (*trans*-1l)

Yield: 109 mg (39%); white solid; mp 125–127 °C.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.60 (s, 3 H), 2.20 (dd, *J* = 8.0, 5.5 Hz, 1 H), 2.53 (dd, *J* = 9.0, 5.0 Hz, 1 H), 3.40 (t, *J* = 9.0 Hz, 1 H), 7.12 (t, *J* = 7.5 Hz, 1 H), 7.26–7.37 (m, 7 H), 7.62 (d, *J* = 7.5 Hz, 2 H), 10.73 (s, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 21.0, 30.1, 38.2, 41.9, 120.2 (2 C), 124.2, 127.8, 128.8 (2 C), 128.9 (2 C), 129.4 (2 C), 135.1, 138.1, 166.7, 208.0.

Anal. Calcd for $C_{18}H_{17}NO_2$: C, 77.40; H, 6.13; N, 5.01. Found: C, 77.61; H, 6.09; N, 5.06.

Substituted Cyclopropyl Amides; *N*-Phenylcyclopropane-1,1-dicarboxamide (2a); Typical Procedure

To a solution of K_2CO_3 (553 mg, 4.0 mmol) in H_2O (25 mL) was added **1a** (203 mg, 1.0 mmol), I_2 (761 mg, 3.0 mmol), and NH_4OH (25%, 0.38 mL, 2.0 mmol). The mixture was stirred at 60 °C for 2.0 h (TLC monitoring; eluent: PE–EtOAc, 1:1). After completion, the reaction mixture was cooled down to r.t. and poured slowly into sat. aq $Na_2S_2O_3$ (50 mL), and extracted with EtOAc (3 × 20 mL). The combined organic phases were washed with H_2O (3 × 20 mL), dried ($MgSO_4$), filtered, and concentrated in vacuo. The crude product was purified by flash chromatography (silica gel, PE–EtOAc, 1:1) to give **2a** as a white solid; yield: 180 mg (88%); mp 106–107 °C.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.39–1.43 (m, 2 H), 1.77–1.81 (m, 2 H), 5.65 (br s, 2 H), 7.11 (t, *J* = 7.5 Hz, 1 H), 7.32 (t, *J* = 7.5 Hz, 2 H), 7.55 (d, *J* = 9.0 Hz, 2 H), 10.46 (s, 1 H).

^{13}C NMR (75 MHz, DMSO-d_6): δ = 17.7 (2 C), 29.1, 120.5 (2 C), 124.4, 129.6 (2 C), 139.3, 168.9, 174.8.

Anal. Calcd for $C_{11}H_{12}N_2O_2$: C, 64.69; H, 5.92; N, 13.72. Found: C, 64.84; H, 5.83; N, 13.79.

N-(*p*-Tolyl)cyclopropane-1,1-dicarboxamide (2b)

Yield: 175 mg (80%); white solid; mp 140–141 °C.

IR (KBr): 3338, 3072, 2920, 2798, 1656, 1589, 1544, 1411, 1112, 1031, 968, 810 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.38–1.42 (m, 2 H), 1.73–1.77 (m, 2 H), 2.31 (s, 3 H), 5.77 (br s, 2 H), 7.12 (d, *J* = 8.0 Hz, 2 H), 7.41 (d, *J* = 8.5 Hz, 2 H), 10.23 (s, 1 H).

^{13}C NMR (75 MHz, DMSO-d_6): δ = 16.9 (2 C), 20.4, 28.1, 119.7, 119.8, 129.1 (2 C), 132.5, 136.1, 167.9, 174.1.

Anal. Calcd for $C_{12}H_{14}N_2O_2$: C, 66.04; H, 6.47; N, 12.84. Found: C, 66.23; H, 6.53; N, 12.72.

N-(4-Methoxyphenyl)cyclopropane-1,1-dicarboxamide (2c)

Yield: 192 mg (82%); yellowish solid; mp 159–161 °C.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.39–1.43 (m, 2 H), 1.73–1.77 (m, 2 H), 3.79 (s, 3 H), 5.77 (br s, 2 H), 6.85 (d, *J* = 9.0 Hz, 2 H), 7.44 (d, *J* = 9.0 Hz, 2 H), 10.16 (s, 1 H).

^{13}C NMR (100 MHz, DMSO-d_6): δ = 16.8 (2 C), 28.3, 55.3, 114.0 (2 C), 121.6 (2 C), 131.8, 155.6, 168.0, 174.1.

Anal. Calcd for $C_{12}H_{14}N_2O_3$: C, 61.53; H, 6.02; N, 11.96. Found: C, 61.46; H, 6.07; N, 12.08.

***N*-(4-Chlorophenyl)cyclopropane-1,1-dicarboxamide (2d)**
Yield: 189 mg (79%); yellowish solid; mp 154–155 °C.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.37–1.41 (m, 2 H), 1.81–1.86 (m, 2 H), 5.48 (br s, 2 H), 7.28 (d, *J* = 9.0 Hz, 2 H), 7.52 (d, *J* = 9.0 Hz, 2 H), 10.84 (s, 1 H).

^{13}C NMR (100 MHz, DMSO-d_6): δ = 16.9 (2 C), 28.6, 121.4 (2 C), 127.2, 128.7 (2 C), 137.5, 168.3, 173.8.

Anal. Calcd for $C_{11}H_{11}ClN_2O_2$: C, 55.36; H, 4.65; N, 11.74. Found: C, 55.71; H, 4.59; N, 11.63.

***N*-(*o*-Tolyl)cyclopropane-1,1-dicarboxamide (2e)**
Yield: 155 mg (71%); yellowish solid; mp 123–124 °C.

IR (KBr): 3434, 3348, 3122, 1639, 1548, 1456, 1413, 1166, 960, 752 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.39–1.43 (m, 2 H), 1.79–1.83 (m, 2 H), 2.34 (s, 3 H), 5.68 (br s, 2 H), 7.07 (t, *J* = 6.0 Hz, 1 H), 7.20 (t, *J* = 6.0 Hz, 2 H), 7.93 (d, *J* = 8.0 Hz, 1 H), 10.51 (s, 1 H).

^{13}C NMR (100 MHz, DMSO-d_6): δ = 17.8, 18.0 (2 C), 27.1, 121.8, 124.1, 126.4, 128.3, 130.4, 136.8, 168.1, 175.3.

Anal. Calcd for $C_{12}H_{14}N_2O_2$: C, 66.04; H, 6.47; N, 12.84. Found: C, 65.88; H, 6.41; N, 12.91.

***N*-(2-Methoxyphenyl)cyclopropane-1,1-dicarboxamide (2f)**
Yield: 145 mg (62%); yellowish solid; mp 174–176 °C.

IR (KBr): 3419, 3276, 2962, 2839, 1650, 1600, 1541, 1465, 1413, 1232, 1114, 1029, 738 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.52–1.57 (m, 2 H), 1.60–1.65 (m, 2 H), 3.92 (s, 3 H), 5.50 (br s, 1 H), 6.88–6.91 (m, 1 H), 6.93–6.98 (m, 1 H), 7.04–7.09 (m, 1 H), 8.27–8.30 (m, 1 H), 9.62 (s, 1 H).

^{13}C NMR (100 MHz, DMSO-d_6): δ = 18.0 (2 C), 27.2, 56.0, 111.1, 119.8, 120.6, 123.8, 127.8, 148.6, 167.8, 175.1.

Anal. Calcd for $C_{12}H_{14}N_2O_3$: C, 61.53; H, 6.02; N, 11.96. Found: C, 61.81; H, 6.08; N, 11.83.

***N*-(2-Chlorophenyl)cyclopropane-1,1-dicarboxamide (2g)**
Yield: 155 mg (65%); yellowish solid; mp 160–162 °C.

IR (KBr): 3434, 3346, 3095, 3035, 1645, 1591, 1544, 1440, 1301, 1166, 1035, 962, 750 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.47–1.51 (m, 2 H), 1.77–1.82 (m, 2 H), 5.77 (br s, 2 H), 7.02–7.07 (m, 1 H), 7.22–7.28 (m, 1 H), 7.37–7.40 (m, 1 H), 8.29–8.33 (m, 1 H), 10.72 (s, 1 H).

^{13}C NMR (100 MHz, DMSO-d_6): δ = 18.7 (2 C), 26.9, 122.2, 123.0, 124.9, 127.8, 129.2, 135.3, 168.6, 175.2.

Anal. Calcd for $C_{11}H_{11}ClN_2O_2$: C, 55.36; H, 4.65; N, 11.74. Found: C, 55.29; H, 4.54; N, 11.86.

***N*-(2,4-Dimethylphenyl)cyclopropane-1,1-dicarboxamide (2h)**
Yield: 193 mg (83%); white solid; mp 130–131 °C.

IR (KBr): 3367, 3184, 3033, 2916, 2794, 1650, 1589, 1541, 1409, 1218, 1027, 1180, 970, 765 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.40–1.44 (m, 2 H), 1.76–1.80 (m, 2 H), 2.29 (s, 6 H), 5.68 (br s, 2 H), 6.99 (d, *J* = 6.5 Hz, 2 H), 7.74 (d, *J* = 9.0 Hz, 1 H), 10.16 (s, 1 H).

^{13}C NMR (75 MHz, DMSO-d_6): δ = 18.4, 18.6 (2 C), 21.2, 27.7, 122.6, 127.4, 129.1, 131.6, 133.8, 134.9, 168.7, 175.9.

Anal. Calcd for $C_{13}H_{16}N_2O_2$: C, 67.22; H, 6.94; N, 12.06. Found: C, 67.06; H, 6.98; N, 12.11.

1-Benzoylcyclopropanecarboxamide (2i)
Yield: 144 mg (76%); white solid; mp 169–171 °C.

IR (KBr): 3381, 3302, 3194, 1659, 1541, 1440, 1324, 1246, 756, 694 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.42–1.46 (m, 2 H), 1.64–1.68 (m, 2 H), 5.66 (br s, 1 H), 5.86 (br s, 1 H), 7.47 (t, *J* = 7.5 Hz, 2 H), 7.59 (t, *J* = 7.0 Hz, 1 H), 7.93 (d, *J* = 7.0 Hz, 2 H).

^{13}C NMR (125 MHz, DMSO-d_6): δ = 13.8 (2 C), 34.8, 128.3 (2 C), 128.4 (2 C), 132.8, 136.7, 171.7, 195.9.

Anal. Calcd for $C_{11}H_{11}NO_2$: C, 69.83; H, 5.86; N, 7.40. Found: C, 69.68; H, 5.91; N, 7.49.

***cis*-2-Methyl-*N*-phenylcyclopropane-1,1-dicarboxamide (*cis*-2k)**
Yield: 179 mg (82%); white solid; mp 142–145 °C.

IR (KBr): 3346, 1767, 1670, 1548, 1447, 1173, 758 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.21 (d, *J* = 5.5 Hz, 3 H), 1.43–1.46 (m, 1 H), 1.61–1.69 (m, 2 H), 5.69 (br s, 1 H), 6.59 (br s, 1 H), 7.12 (t, *J* = 7.0 Hz, 1 H), 7.32 (t, *J* = 8.0 Hz, 2 H), 7.54 (d, *J* = 8.0 Hz, 2 H), 9.20 (s, 1 H).

^{13}C NMR (100 MHz, DMSO-d_6): δ = 13.8, 19.4, 22.1, 36.6, 119.8 (2 C), 123.4, 128.5 (2 C), 139.0, 166.4, 172.4.

Anal. Calcd for $C_{12}H_{14}N_2O_2$: C, 66.04; H, 6.47; N, 12.84. Found: C, 66.21; H, 6.53; N, 12.78.

***trans*-*N*,2-Diphenylcyclopropane-1,1-dicarboxamide (*trans*-2l)**
Yield: 177 mg (63%); yellow solid; mp 182–183 °C.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.80 (dd, *J* = 8.0, 6.0 Hz, 1 H), 2.32 (dd, *J* = 9.0, 6.0 Hz, 1 H), 3.23 (t, *J* = 8.0 Hz, 1 H), 5.30 (br s, 2 H), 7.11 (t, *J* = 7.0 Hz, 1 H), 7.26–7.36 (m, 7 H), 7.60 (d, *J* = 8.0 Hz, 2 H), 10.53 (s, 1 H).

^{13}C NMR (100 MHz, DMSO-d_6): δ = 15.4, 32.7, 38.6, 119.6 (2 C), 123.5, 126.8, 127.8 (2 C), 128.7 (2 C), 128.9 (2 C), 135.5, 138.5, 167.1, 169.6.

Anal. Calcd for $C_{17}H_{16}N_2O_2$: C, 72.84; H, 5.75; N, 9.99. Found: C, 72.68; H, 5.84; N, 9.94.

Substituted Cyclopropyl Esters 3; Methyl 1-(Phenylcarbamoyl)cyclopropanecarboxylate (3a); Typical Procedure
To a solution of **1a** (203 mg, 1.0 mmol) in CH_2Cl_2 (10 mL) was added MeOH (0.049 mL, 1.2 mmol), I_2 (761 mg, 3.0 mmol), and DBU (609 mg, 4.0 mmol) under stirring at 0 °C. The mixture was stirred for 1 h at 0 °C (TLC monitoring; eluent: PE–EtOAc, 3:1). After completion, the reaction mixture was poured slowly into sat. aq $Na_2S_2O_3$ (50 mL), and extracted with EtOAc (3 × 20 mL). The combined organic phases were washed with H_2O (3 × 20 mL), dried ($MgSO_4$), filtered, and concentrated in vacuo. The crude product was purified by chromatography (silica gel, PE–EtOAc, 4:1) to give **3a** as a yellow solid, yield: 189 mg (86%); mp 54–55 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.64–1.67 (m, 2 H), 1.80–1.83 (m, 2 H), 3.74 (s, 3 H), 7.08 (t, *J* = 7.5 Hz, 1 H), 7.32 (t, *J* = 7.5 Hz, 2 H), 7.58 (d, *J* = 8.0 Hz, 2 H), 10.83 (s, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 20.7 (2 C), 26.4, 52.4, 120.0 (2 C), 124.0, 128.8 (2 C), 138.0, 166.6, 174.3.

Anal. Calcd for $C_{12}H_{13}NO_3$: C, 65.74; H, 5.98; N, 6.39. Found: C, 65.57; H, 5.90; N, 6.55.

Methyl 1-(*p*-Tolylcarbamoyl)cyclopropanecarboxylate (3b)
Yield: 184 mg (79%); white solid; mp 120–121 °C.

IR (KBr): 3273, 1709, 1599, 1545, 1444, 1354, 1202, 1153, 974, 822, 721, 519 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.60–1.67 (m, 2 H), 1.79–1.83 (m, 2 H), 2.31 (s, 3 H), 3.73 (s, 3 H), 7.12 (d, *J* = 8.0 Hz, 2 H), 7.46 (d, *J* = 8.0 Hz, 2 H), 10.75 (s, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 20.6 (2 C), 20.8, 26.4, 52.4, 120.1 (2 C), 129.4 (2 C), 133.6, 135.6, 166.5, 174.4.

Anal. Calcd for $C_{13}H_{15}NO_3$: C, 66.94; H, 6.48; N, 6.00. Found: C, 66.78; H, 6.53; N, 6.08.

Methyl 1-[(4-Methoxyphenyl)carbamoyl]cyclopropanecarboxylate (3c)
Yield: 199 mg (80%); white solid; mp 105–107 °C.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.63–1.67 (m, 2 H), 1.79–1.82 (m, 2 H), 3.73 (s, 3 H), 3.79 (s, 3 H), 6.86 (d, *J* = 7.5 Hz, 2 H), 7.49 (d, *J* = 7.5 Hz, 2 H), 10.70 (s, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 20.4 (2 C), 26.2, 52.3, 55.3, 113.9 (2 C), 121.6 (2 C), 131.3, 156.1, 166.3, 174.3.

Anal. Calcd for $C_{13}H_{15}NO_4$: C, 62.64; H, 6.07; N, 5.62. Found: C, 62.85; H, 6.21; N, 5.67.

Methyl 1-[(4-Chlorophenyl)carbamoyl]cyclopropanecarboxylate (3d)
Yield: 193 mg (76%); yellow solid; mp 115–116 °C.

IR (KBr): 3279, 1707, 1664, 1593, 1537, 1441, 1398, 1198, 829, 708, 501 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.66–1.70 (m, 2 H), 1.79–1.83 (m, 2 H), 3.74 (s, 3 H), 7.28 (d, *J* = 9.0 Hz, 2 H), 7.54 (d, *J* = 9.0 Hz, 2 H), 10.91 (s, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 20.8 (2 C), 26.4, 52.5, 121.2 (2 C), 128.8 (2 C), 136.7, 166.8, 174.3.

Anal. Calcd for $C_{12}H_{12}ClNO_3$: C, 56.81; H, 4.77; N, 5.52. Found: C, 56.62; H, 4.72; N, 5.59.

Methyl 1-(*o*-Tolylcarbamoyl)cyclopropanecarboxylate (3e)
Yield: 170 mg (73%); white solid; mp 83–84 °C.

IR (KBr): 3282, 1715, 1587, 1553, 1144, 972, 854, 716, 598, 488 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.66–1.69 (m, 2 H), 1.81–1.85 (m, 2 H), 2.39 (s, 3 H), 3.74 (s, 3 H), 7.03 (t, *J* = 7.5 Hz, 1 H), 7.20 (t, *J* = 6.0 Hz, 2 H), 8.04 (d, *J* = 6.0 Hz, 1 H), 10.77 (s, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 18.0, 20.8 (2 C), 26.5, 52.4, 121.7, 124.3, 126.6, 128.0, 130.3, 136.5, 166.6, 174.5.

Anal. Calcd for $C_{13}H_{15}NO_3$: C, 66.94; H, 6.48; N, 6.00. Found: C, 67.16; H, 6.40; N, 6.05.

Methyl 1-[(2-Methoxyphenyl)carbamoyl]cyclopropanecarboxylate (3f)
Yield: 204 mg (82%); yellow solid; mp 93–96 °C.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.63–1.67 (m, 2 H), 1.79–1.82 (m, 2 H), 3.75 (s, 3 H), 3.96 (s, 3 H), 6.92 (t, *J* = 7.5 Hz, 2 H), 7.04 (t, *J* = 7.5 Hz, 1 H), 8.34 (d, *J* = 7.5 Hz, 1 H), 11.19 (s, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 20.4 (2 C), 26.7, 52.2, 55.8, 109.9, 120.0, 120.7, 123.5, 127.9, 148.5, 166.3, 173.6.

Anal. Calcd for $C_{13}H_{15}NO_4$: C, 62.64; H, 6.07; N, 5.62. Found: C, 62.41; H, 6.14; N, 5.57.

Methyl 1-[(2-Chlorophenyl)carbamoyl]cyclopropanecarboxylate (3g)
Yield: 183 mg (72%); yellowish solid; mp 77–79 °C.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.69–1.73 (m, 2 H), 1.81–1.84 (m, 2 H), 3.77 (s, 3 H), 7.03 (t, *J* = 8.0 Hz, 1 H), 7.22 (t, *J* = 7.0 Hz, 1 H), 7.40 (d, *J* = 8.0 Hz, 1 H), 8.37 (d, *J* = 8.0 Hz, 1 H), 11.33 (s, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 21.0 (2 C), 26.7, 52.5, 121.8, 123.3, 124.3, 127.3, 129.0, 135.2, 166.9, 173.7.

Anal. Calcd for $C_{12}H_{12}ClNO_3$: C, 56.81; H, 4.77; N, 5.52. Found: C, 56.98; H, 4.74; N, 5.48.

Methyl 1-[(2,4-Dimethylphenyl)carbamoyl]cyclopropanecarboxylate (3h)
Yield: 208 mg (84%); yellowish solid; mp 93–94 °C.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.64–1.68 (m, 2 H), 1.80–1.84 (m, 2 H), 2.28 (s, 3 H), 2.34 (s, 3 H), 3.73 (s, 3 H), 6.99 (d, *J* = 7.0 Hz, 1 H), 7.01 (s, 1 H), 7.86 (d, *J* = 8.0 Hz, 1 H), 10.67 (s, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 17.7, 20.4 (2 C), 20.6, 26.3, 52.2, 121.6, 126.8, 127.9, 130.7, 133.6, 133.8, 166.3, 174.2.

Anal. Calcd for $C_{14}H_{17}NO_3$: C, 68.00; H, 6.93; N, 5.66. Found: C, 68.12; H, 6.87; N, 5.70.

Ethyl 1-(*o*-Tolylcarbamoyl)cyclopropanecarboxylate (3k)
Yield: 200 mg (81%); yellowish solid; mp 66–69 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.28 (t, *J* = 7.0 Hz, 3 H), 1.65–1.67 (m, 2 H), 1.80–1.83 (m, 2 H), 2.38 (s, 3 H), 4.21 (q, *J* = 7.0 Hz, 2 H), 7.03 (t, *J* = 8.0 Hz, 1 H), 7.19 (t, *J* = 7.0 Hz, 2 H), 8.03 (d, *J* = 8.0 Hz, 1 H), 10.79 (s, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 13.9, 17.9, 20.6 (2 C), 26.5, 61.4, 121.6, 124.1, 126.4, 127.9, 130.2, 136.5, 166.7, 173.9.

Anal. Calcd for $C_{14}H_{17}NO_3$: C, 68.00; H, 6.93; N, 5.66. Found: C, 68.16; H, 6.99; N, 5.61.

Benzyl 1-(*o*-Tolylcarbamoyl)cyclopropanecarboxylate (3l)
Yield: 232 mg (75%); white solid; mp 86–87 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.69–1.71 (m, 2 H), 1.82–1.85 (m, 2 H), 2.37 (s, 3 H), 5.18 (s, 2 H), 7.03 (t, *J* = 8.0 Hz, 1 H), 7.19 (t, *J* = 6.0 Hz, 2 H), 7.33 (d, *J* = 8.0 Hz, 2 H), 7.39 (d, *J* = 6.0 Hz, 3 H), 8.01 (d, *J* = 8.0 Hz, 1 H), 10.73 (s, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 18.0, 20.9 (2 C), 26.6, 67.0, 121.8, 124.3, 126.5, 128.0 (2 C), 128.6, 128.7 (2 C), 130.2, 134.9, 136.4, 166.5, 173.8.

Anal. Calcd for $C_{19}H_{19}NO_3$: C, 73.77; H, 6.19; N, 4.53. Found: C, 73.54; H, 6.14; N, 4.56.

Substituted Cyclopropanecarbonitriles 4; 1-Cyano-*N*-phenylcyclopropanecarboxamide (4a); Typical Procedure
The Vilsmeier reagent was prepared by adding $POCl_3$ (460 mg, 3.0 mmol) dropwise to anhyd DMF (5 mL) under stirring at 0 °C. The mixture was then stirred for 10–15 min at 0 °C. To the above Vilsmeier reagent was added **2a** (204 mg, 1.0 mmol) as a solution in DMF (5 mL). The mixture was stirred for 0.5 h (TLC monitoring, eluent: PE–EtOAc, 7:1), poured into brine (50 mL), and extracted with CH_2Cl_2 (3 × 20 mL). The combined organic phases were washed with H_2O (3 × 20 mL), dried ($MgSO_4$), filtered, and concentrated in vacuo. The crude product was purified by flash chromatography (silica gel, PE–Et_2O, 4:1) to give **4a** as a white solid; yield: 171 mg (92%).

Cyanocyclopropanes **4** are known compounds; their analytical data are in good agreement with those reported in the literature.[17]

Supporting Information for this article is available online at http://www.thieme-connect.com/ejournals/toc/synthesis.

Acknowledgment

Financial support of this research by the National Natural Science Foundation of China (20872136 and 21172211) is greatly acknowledged.

References

(1) For reviews on cyclopropanes, see: (a) Wong, H. N. C.; Hon, M. Y.; Tse, C. W.; Yip, Y. C.; Tanko, J.; Hudlicky, T. *Chem. Rev.* **1989**, *89*, 165. (b) Kulinkovich, O. G. *Chem. Rev.* **2003**, *103*, 2597. (c) Brackmann, F.; de Meijere, A. *Chem. Rev.* **2007**, *107*, 4493. (d) Gnad, F.; Reiser, O. *Chem. Rev.* **2003**, *103*, 1603. (e) Noyori, R. *Angew. Chem. Int. Ed.* **2002**, *41*, 2008.

(2) (a) Vinogradov, M. G.; Kaigorodova, L. N.; Chel'tsova-Bebutova, G. V.; Gorshkova, L. S.; Starostin, E. K.; Nikishin, G. L.; Ignatenko, A. V.; Shapiro, E. A. *Russ. Chem. Bull.* **1995**, *44*, 167. (b) Kaneko, H. *J. Agric. Food Chem.* **2011**, *59*, 2786. (c) Graham, D. W.; Ashton, W. T.; Barash, L.; Brown, J. E.; Brown, R. D.; Canning, L. F.; Chen, A.; Springer, J. P.; Rogers, E. F. *J. Med. Chem.* **1987**, *30*, 1074. (d) Krief, A.; Froidbisea, A. *Tetrahedron* **2004**, *60*, 7637.

(3) For reviews, see: (a) Hoveyda, A. H.; Evans, D. A.; Fu, G. C. *Chem. Rev.* **1993**, *93*, 1307. (b) Charette, A. B.; Marcoux, J.-F. *Synlett* **1995**, 1197. (c) Lautens, M.; Klute, W.; Tam, W. *Chem. Rev.* **1996**, *96*, 49. (d) Charette, A. B.; Lebel, H. In *Comprehensive Asymmetric Catalysis*; Jacobsen, E. N.; Pfaltz, A.; Yamamoto, H., Eds.; Springer-Verlag: Berlin, **1999**, Chap. 16.3. (e) Lebel, H.; Marcoux, J.-F.; Molinaro, C.; Charette, A. B. *Chem. Rev.* **2003**, *103*, 977.

(4) For references, see: (a) Simmons, H. E.; Smith, R. D. *J. Am. Chem. Soc.* **1958**, *80*, 5323. (b) Simmons, H. E.; Smith, R. D. *J. Am. Chem. Soc.* **1959**, *81*, 4256. (c) Rawson, R. J.; Harrison, I. T. *J. Org. Chem.* **1970**, *35*, 2057. (d) Nishimura, J.; Furukawa, J.; Kawabata, N.; Kitayama, M. *Tetrahedron* **1971**, *27*, 1799. (e) Friedrich, E. C.; Lunetta, S. E.; Lewis, E. J. *J. Org. Chem.* **1989**, *54*, 2388. (f) Charette, A. B.; Marcoux, J.-F.; Molinaro, C.; Beauchemin, A.; Brochu, C.; Isabel, E. *J. Am. Chem. Soc.* **2000**, *122*, 4508.

(5) (a) Shimamoto, K.; Ishida, M.; Shinozaki, H.; Ohfune, Y. *J. Org. Chem.* **1991**, *56*, 4167. (b) Shimamoto, K.; Ohfune, Y. *Tetrahedron Lett.* **1989**, *30*, 3802. (c) Hanessian, S.; Murray, P. J. *J. Org. Chem.* **1987**, *52*, 1170. (d) Vangveravong, S.; Nichols, D. E. *J. Org. Chem.* **1995**, *60*, 3409. (e) Pietruszka, J.; Widenmeyer, M. *Synlett* **1997**, 977. (f) Luithle, J. E. A.; Pietruszka, J. *J. Org. Chem.* **1999**, *64*, 8287. (g) Pietruszka, J.; Witt, A. *J. Chem. Soc., Perkin Trans. 1* **2000**, 4293. (h) Luithle, J. E. A.; Pietruszka, J. *J. Org. Chem.* **2000**, *65*, 9194.

(6) (a) de Meijere, A.; Bagutski, V.; Zeuner, F.; Fischer, U. K.; Rheinberger, V.; Moszner, N. *Eur. J. Org. Chem.* **2004**, 3669. (b) Yang, Y.; Shi, M. *J. Org. Chem.* **2005**, *70*, 8645. (c) Su, J.; Xiong, J.; Liang, S.; Qiu, G.; Feng, X.; Teng, H.; Wu, L.; Hu, X. *Synth. Commun.* **2006**, *36*, 693. (d) Ronsisvalle, G.; Marrazzo, A.; Prezzavento, O.; Pasquinucci, L.; Falcucci, B.; Toro, R. D.; Spampinato, S. *Bioorg. Med. Chem.* **2000**, *8*, 1503.

(7) (a) Pan, W.; Dong, D.; Wang, K.; Zhang, J.; Wu, R.; Xiang, D.; Liu, Q. *Org. Lett.* **2007**, *9*, 2421. (b) Fu, X.; Huang, P.; Zhou, G.; Hu, Y.; Dong, D. *Tetrahedron* **2011**, *67*, 6347. (c) Wang, K.; Fu, X.; Liu, J.; Liang, Y.; Dong, D. *Org. Lett.* **2009**, *11*, 1015. (d) Wang, K.; Xiang, D.; Liu, J.; Pan, W.; Dong, D. *Org. Lett.* **2008**, *10*, 1691.

(8) For Iodoform reactions, see: (a) Fuson, R. C.; Bull, B. A. *Chem. Rev.* **1934**, *15*, 275. (b) Fuson, R. C.; Tullock, C. W. *J. Am. Chem. Soc.* **1934**, *56*, 1638. (c) Arnold, R. T.; Buckles, R.; Stoltenberg, J. *J. Am. Chem. Soc.* **1944**, *66*, 208. For the conversion of acetyl into amide and ester group, see: (d) Cao, L.; Ding, J.; Gao, M.; Wang, Z.; Li, J.; Wu, A. *Org. Lett.* **2009**, *11*, 3810. (e) Yin, G.; Gao, M.; Wang, Z.; Wu, Y.; Wu, A. *Bull. Chem. Soc. Jpn.* **2008**, *81*, 369.

(9) For the preparation of 1-acetyl-1-carbamoylcyclopropanes, see: Zhang, Z.; Zhang, Q.; Sun, S.; Xiong, T.; Liu, Q. *Angew. Chem. Int. Ed.* **2007**, *46*, 1726.

(10) (a) *Aqueous-Phase Organometallic Catalysis: Concepts and Applications*; Cornils, B.; Herrmann, W. A., Eds.; Wiley-VCH: Weinheim, **1998**. (b) *Organic Synthesis in Water*; Grieco, P. A., Ed.; Blackie Academic and Professional: London, **1998**. (c) *Organic Reactions in Aqueous Media*; Li, C.-J.; Chan, T.-H., Eds.; Wiley: New York, **1997**. (d) Kobayashi, S.; Manabe, K. In *Stimulating Concepts in Chemistry*; Shibasaki, M.; Stoddart, J. F.; Vögtle, F., Eds.; Wiley-VCH: Weinheim, **2000**.

(11) (a) Li, C. J. *Chem. Rev.* **1993**, *93*, 2023. (b) Fringuelli, F.; Piermatti, O.; Pizzo, F.; Vaccaro, L. *Eur. J. Org. Chem.* **2001**, 439. (c) Kobayashi, S.; Manabe, K. *Acc. Chem. Res.* **2002**, *35*, 209.

(12) (a) Manabe, K.; Mori, Y.; Kobayashi, S. *Synlett* **1999**, 1401. (b) Manabe, K.; Kobayashi, S. *Org. Lett.* **1999**, *1*, 1965. (c) Otto, S.; Engberts, J. B. S. N.; Kwak, J. C. T. *J. Am. Chem. Soc.* **1998**, *120*, 9517. (d) Rispens, T.; Engberts, J. B. S. N. *Org. Lett.* **2001**, *3*, 941. (e) Manabe, K.; Sun, X. M.; Kobayashi, S. *J. Am. Chem. Soc.* **2001**, *123*, 10101. (f) Ouyang, Y.; Dong, D.; Yu, H.; Liang, Y.; Liu, Q. *Adv. Synth. Catal.* **2006**, *348*, 206.

(13) The relative configurations of *cis*-**1k**, *trans*-**1l**, *cis*-**2k**, and *trans*-**2l** were determined by NOESY, see Supporting Information.

(14) For selected work on the conversion of amide into cyano group, see: (a) Mowry, D. T. *Chem. Rev.* **1948**, *42*, 189. (b) Rickborn, B.; Jensen, F. R. *J. Org. Chem.* **1962**, *27*, 4608. (c) Lehnert, W. *Tetrahedron Lett.* **1971**, *19*, 1501. (d) Ellzey, S. E.; Mack, C. H.; Connick, W. J. *J. Org. Chem.* **1967**, *32*, 846.

(15) For selected examples on ring-opening or ring-enlargement reactions of cyclopropanes, see: (a) Bernard, A. M.; Frongia, A.; Piras, P. P.; Secci, F.; Spiga, M. *Org. Lett.* **2005**, *7*, 4565. (b) Ogoshi, S.; Nagata, M.; Kurosawa, H. *J. Am. Chem. Soc.* **2006**, *128*, 5350. (c) Liu, L.; Montgomery, J. *J. Am. Chem. Soc.* **2006**, *128*, 5348. (d) Ma, S.; Zhang, J. *Angew. Chem. Int. Ed.* **2003**, *42*, 183.

(16) For selected references on Vilsmeier reagents, see: (a) Marson, C. M. *Tetrahedron* **1992**, *48*, 3659. (b) Meth-Cohn, O.; Tarnowski, B. *Adv. Heterocycl. Chem.* **1982**, *31*, 207. (c) Reichardt, C. *J. Prakt. Chem.* **1999**, *341*, 609. (d) Gangadasu, B.; Narender, P.; Kumar, S. B.; Ravinder, M.; Rao, B. A.; Ramesh, C.; Raju, B. C.; Rao, V. J. *Tetrahedron* **2006**, *62*, 8398. (e) Thomas, A. D.; Asokan, C. V. *Tetrahedron* **2004**, *60*, 5069.

(17) (a) Johnson, C. R.; Lockard, J. P.; Kennedy, E. R. *J. Org. Chem.* **1980**, *45*, 264. (b) Zhang, Z.; Xue, C.; Liu, X.; Zhang, Q.; Liu, Q. *Tetrahedron* **2011**, *67*, 7081.

