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Synthesis of unsymmetrical benzils using *N*-heterocyclic carbene catalysis

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ABSTRACT

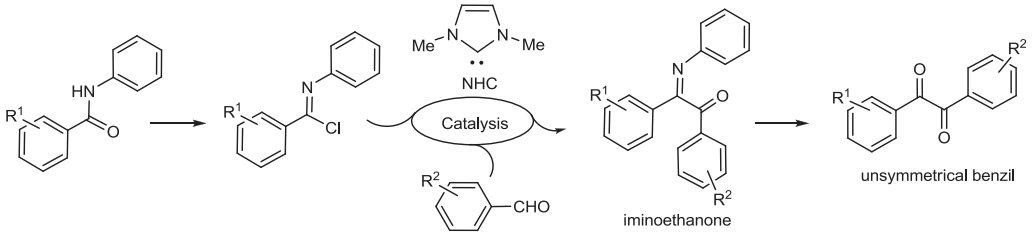
In this paper, we propose a novel and efficient method for the preparation of various unsymmetrical benzils. We first demonstrate the nucleophilic aroylation of *N*-phenylbenzimidoyl chlorides with aromatic aldehydes using *N*-heterocyclic carbene as the catalyst to afford 1-aryl-2-phenyl-2-(phenylimino) ethanones. These iminoethanones were then converted to 1,2-diaryl-1,2-diketones by acid-promoted hydrolysis.

1. Introduction

In the last decade, *N*-heterocyclic carbenes (NHCs) have attracted considerable attention as organocatalysts due to their unique catalytic properties, facile reactions, and selectivities.[1–5] Many reports have indicated the great potential of NHCs as organocatalysts for a variety of organic reactions. In 1992, our former co-workers, Miyashita and his colaborators reported that the NHC generated from 1,3-dimethylimidazolium iodide (30 mol %) catalyzes nucleophilic substitutions at the imino carbon atom of *N*-phenylbenzimidoyl chlorides.[6] In this reaction, the chlorine substituent is replaced by the aroyl groups originating from aromatic aldehydes to afford 1,2-diphenyl-2-(phenylimino)ethanones, and moreover, the hydrolysis of the iminoethanones afforded corresponding benzils (1,2-diaryl-1,2-diketones).

Unsymmetrical benzils are important building blocks in organic synthesis because they are intermediates for the synthesis of biologically active diarylheterocycles.[7–11] Two common methods are primarily employed for the preparation of unsymmetrical benzils. One route involves an addition reaction of the anion derived from cyanohydrins to aromatic aldehydes and the oxidation of the obtained benzoins.[8,12] However, in this method, the use of toxic cyanation reagents is problematic. The other route involves the Friedel–Crafts reaction between benzenes and 2-phenylacetyl chlorides and the oxidation of the products.[9–11,13] In this case, it is difficult to control the regioselectivities in Friedel–Crafts acylation, and moreover, this route is not always applicable to the synthesis due to the directing and activating effects of the substituents.

In this study, we present an alternative synthetic route for unsymmetrical benzils (Scheme 1). Our route consists of NHC-catalyzed aroylation of *N*-phenylbenzimidoyl chlorides with aromatic aldehydes and the hydrolysis of the aroylated products, i.e., iminoethanones. The substrates of the catalytic reaction, *N*-phenylbenzimidoyl chlorides, are easily obtained by the chlorination of



Scheme 1.

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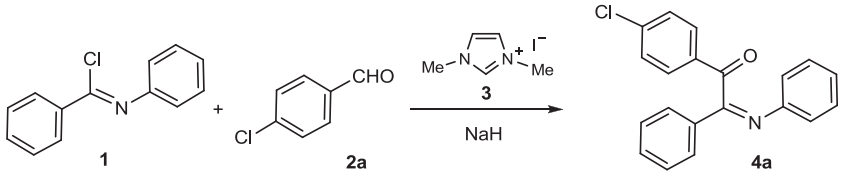
benzanilides. Further, in order to increase the efficiency of the synthesis, we investigated the optimization of the reaction conditions for the NHC catalysis.

2. Results and discussions

In our experiments, we first carried out the reaction according to the procedure previously reported by Miyashita and his co-workers.[6] A mixture of *N*-phenylbenzimidoyl chloride **1**, 4-chlorobenzaldehyde **2a** (1.1 equiv), NaH (1.3 equiv), and 30 mol % of 1,3-dimethylimidazolium iodide **3** in THF was refluxed to afford 1-(4-chlorophenyl)-2-phenyl-2-(phenyl)iminoethanone **4a** in 63% yield (Table 1; entry 1). The reaction was then conducted with the reduced catalyst loadings (entries 2–5). The reduced reaction rate was compensated by using 1.5 equiv of **2a** in the case of the reactions with 10 mol % of **3** (entries 2 and 3). When 3 mol % and 1 mol % of **3** were used, longer reaction times (8 h for 3 mol % and 18 h for 1 mol %) were needed to obtain **4a** in 91% and 75% yields, respectively (entries 4 and 5); further, when DMF and acetonitrile were used instead of THF as the solvent, the yields of **4a** decreased (entries 6 and 7).

Table 1
Aroylation of *N*-phenylbenzimidoyl chloride **1** with 4-chlorobenzaldehyde **2a**



Entry	**2a** (equiv)	**3** (mol %)	Solvent	Temp (°C)	Time (h)	Yield (%)
1[a]	1.1	30	THF	Reflux	3	63
2	1.1	10	THF	Reflux	3	51
3	1.5	10	THF	Reflux	3	78
4	1.5	3	THF	Reflux	8	91
5	1.5	1	THF	Reflux	18	75
6	1.1	30	DMF	60	2	29
7	1.5	3	CH_3CN	60	7	41

[a] The condition reported by Miyashita and his co-workers.[6]

The use of other NHCs and a base was also examined in the reaction of **5** with **2b** (Table 2). When the reaction was carried out using 10 mol % of **3** as a catalyst precursor and NaH as a base, the product **10b** was obtained in 79% yield (entry 1). In contrast, when DBU was used instead of NaH, the reaction did not proceed (entry 2). The NHC originating from **6** is a well-used ligand. However, the bulky *N*-substituents of the NHC seemed to prevent the reaction course (entry 3). On the other hand, the NHC generated from benzimidazolim salt **7** catalyzed the reaction to afford **10a** in 12% yield (entry 4). The attempt to use the NHCs generated from triazolium salt **8** and thiazolium salt **9** as catalysts resulted in the recovery of **2b** (entries 6–9).

The results of the aroylation reaction of **1** and other *N*-phenylimidoyl chlorides **5**, **11**, and **12** with various aromatic aldehydes **2a**–**j** are shown in Table 3. Imidoyl chlorides **1**, **5**, **11**, and **12** were prepared by the chlorination of the corresponding *N*-phenylarenecarboxamides.[14–18] All the reactions were performed in the presence of 3 mol % of catalysts using 1.5 equiv of aldehydes to *N*-phenylimidoyl chlorides in refluxing THF. The reaction of **1** with aldehydes **2b**, **c**, and **e**–**g** afforded iminoethanones **4b**, **c**, and **e**–**g** in good yields (entries 1–7). On the other hand, the yields of **4d** and **h** were moderate, presumably due to the steric hindrances caused by the *o*-methyl substituent of **4d** and bulky naphthalene of **4h**. The aroylation reaction is considered to proceed through a common intermediate with NHC-catalyzed benzoin condensation, i.e., the 'acyl anion equivalent.'[6,19] It is well known that the benzoin condensation process is significantly affected by the nature of the substituents in the aldehydes.[20,21] The aroylation of **5** and **11** with various aldehydes also afforded iminoethanones **10** and **13** in good to moderate yields. In the case of **12**, the reaction yield increased from 69% to 80% when imidazolium salt **15** was used instead of **3**.

In order to prepare the unsymmetrical benzils, iminoethanones **4**, **10**, **13**, and **14** were hydrolyzed under acidic conditions; the results are shown in Table 4. Treatment of **4**, **10**, **13**, and **14** with 10% HCl in THF at room temperature for 3 h afforded benzils **16**–**19** in good to excellent yields (entries 1, 2, and 4–14), except for the product with the furyl substituent **16f** (entry 3). The acidic condition damaged the furan nucleus of **4f** and/or **16f**. A milder hydrolysis condition is required for **4f** to prevent the decomposition.

3. Conclusion

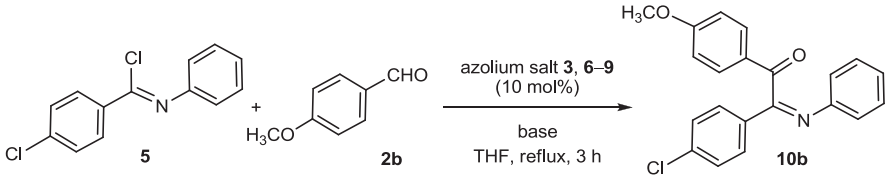
We have developed an efficient method for the synthesis of unsymmetrical benzils **16**–**19** using the NHC-catalyzed aroylation of *N*-phenylimidoyl chlorides **1**, **5**, **11**, and **12** with aromatic aldehydes **2a**–**j** followed by acidic hydrolysis. The aroylation was catalyzed with only 3 mol % of **3** and **15**. The substrates of the first reaction, *N*-phenylimidoyl chlorides **1**, **5**, **11**, and **12** were prepared by the chlorination of the corresponding *N*-phenylarenecarboxamides. Note that various aromatic aldehydes are applicable to the aroylation. Moreover, a large variety of aldehydes and *N*-phenylarenecarboxamides are easily accessible. By combining *N*-phenylarenecarboxamides and aldehydes appropriately, it is possible to prepare various unsymmetrical benzils by employing our method.

4. Experimental section

4.1. General procedure for the synthesis of iminoethanones

To a mixture of the *N*-phenylbenzimidoyl chlorides **1**, **5**, **11**, and **12** (1 mmol), aromatic aldehyde **2a**–**j** (1.5 mmol), and 1,3-dimethylimidazolium iodide **3** (6.7 mg, 0.03 mol) in THF (20 ml), NaH (60% in oil, 52 mg, 1.3 mmol) was added with stirring under argon atmosphere. The reaction mixture was then refluxed for the indicated time (shown in Table 3) and poured into ice water. Subsequently, the products were extracted with ethyl acetate and washed with brine; the solvent was then evaporated. The residue was purified by silica gel column chromatography (*n*-hexane/ethyl acetate) to obtain iminoethanones **4**, **10**, **13**, and **14**.

Table 2
Aroylation of *N*-phenylbenzimidoyl chloride **5** with 4-methoxybenzaldehyde **2b**



Entry	Azolium salt	Base	Yield (%)
1	**3**	NaH	79
2[a]	**3**	DBU	—
3	**6**	NaH	—
4	**7**	NaH	12[b]
5[a]	**7**	DBU	—
6	**8**	NaH	—
7[a]	**8**	DBU	—
8	**9**	NaH	—
9[a]	**9**	DBU	—

[a] The reaction was carried out using **5** (1 mmol), **2b** (1.5 mmol), and DBU (10 mmol) in THF (20 ml).
[b] The hydrolyzed product, 1-(4-chlorolphenyl)-2-(4-methoxyphenyl)ethane-1,2-dione was also obtained in 7% yield.

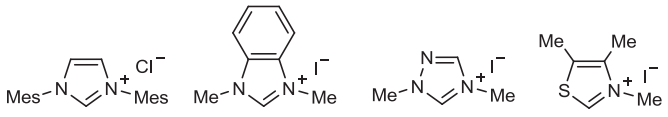
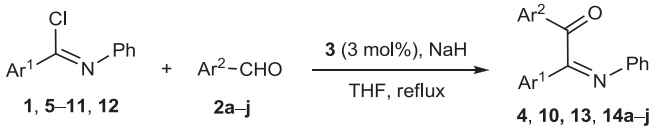


Table 3
Aroylation of imidoyl chlorides **1**, **5**, **11**, and **12** with aldehydes **2a**–**j**



Entry	Imidoyl chloride	Aldehyde	Time (h)	Iminoethanone	Yield (%)
1	**1**	**2b**	7	**4b**	80
2	**1**	**2c**	6	**4c**	74
3	**1**	**2d**	7	**4d**	60
4	**1**	**2e**	7	**4e**	76
5	**1**	**2f**	7	**4f**	90
6	**1**	**2g**	7	**4g**	86
7	**1**	**2h**	7	**4h**	51
8	**5**	**2b**	6	**10b**	75
9	**5**	**2c**	6	**10c**	82
10	**5**	**2f**	6	**10f**	80
11	**5**	**2i**	6	**10i**	90
12	**5**	**2j**	6	**10j**	91
13	**11**	**2a**	9	**13a**	49
14	**11**	**2b**	10	**13b**	42
15	**11**	**2e**	9	**13e**	36
16	**11**	**2f**	10	**13f**	74
17	**11**	**2g**	10	**13g**	81
18	**11**	**2i**	9	**13i**	85
19	**12**	**2b**	6	**14b**	69
20[a]	**12**	**2b**	6	**14b**	80

[a] Imidazolium salt **15** was used instead of **3**.

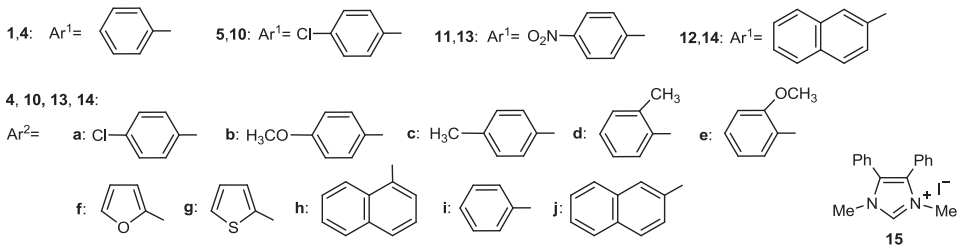
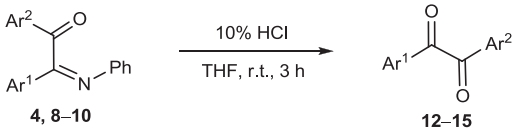
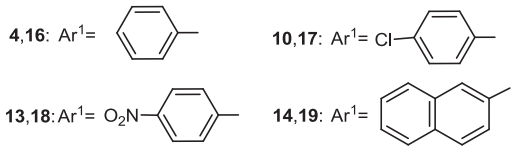


Table 4
Hydrolysis of iminoethanones **4**, **10**, **13**, and **14** to unsymmetrical benzils **16**–**19**



Entry	Iminoethanone	1,2-Diaryl-1,2-diketone	Yield (%)
1	**4a**	**16a**	100
2	**4b**	**16b**	100
3	**4f**	**16f**	47
4	**4g**	**16g**	100
5	**4h**	**16h**	100
6	**10b**	**17b**	88
7	**10f**	**17f**	100
8	**10i**	**16a** (**17i**)	63
9	**10j**	**17j**	86
10	**13a**	**18a**	100
11	**13f**	**18f**	82
12	**13g**	**18g**	100
13	**13i**	**18i**	100
14	**14b**	**19b**	90



*4.1.1. 1-(4-Chlorophenyl)-2-phenyl-2-(phenylimino)ethanone (**4a**)*[6]. Yellow oil, 91%; IR (ATR) cm^{-1}: 1670 (C=O); ^1H NMR ($CDCl_3$) δ: 6.86 (2H, d, J=7.5 Hz), 6.96 (1H, t, J=7.5 Hz), 7.14 (2H, t, J=7.5 Hz), 7.29–7.32 (2H, m), 7.44 (2H, t, J=7.5 Hz), 7.49–7.52 (1H, m), 7.67–7.70 (2H, m), 7.85 (2H, dd, J=7.5, 1.7 Hz); ^{13}C NMR ($CDCl_3$) δ: 120.5, 125.0, 128.2, 128.8, 129.0, 129.4, 130.7, 132.0, 133.0, 134.9, 141.0, 149.1, 165.9, 196.6.

*4.1.2. 1-(4-Methoxyphenyl)-2-phenyl-2-(phenylimino)ethanone (**4b**)*[6]. Yellow granules (recrystallized from *n*-hexane/acetone); 80%, mp 73–74 °C; IR (ATR) cm^{-1}: 1657 (C=O); ^1H NMR ($CDCl_3$) δ: 3.79 (3H, s), 6.80 (2H, dt, J=8.0, 1.7 Hz), 6.90–6.96 (3H, m), 7.15 (2H, t, J=7.5 Hz), 7.42 (2H, td, J=8.0, 1.7 Hz), 7.48 (1H, td, J=7.5, 1.1 Hz), 7.73 (2H, dt, J=9.2, 2.3 Hz), 7.87 (2H, dd, J=7.5, 1.1 Hz); ^{13}C NMR ($CDCl_3$) δ: 55.6, 114.2, 120.5, 124.7, 127.9, 128.2, 128.7, 128.8, 131.7, 131.9, 135.3, 149.5, 164.5, 166.6, 195.9.

*4.1.3. 1-(4-Methylphenyl)-2-phenyl-2-(phenylimino)ethanone (**4c**).* Yellow oil, 74%; IR (ATR) cm^{-1}: 1665 (C=O); ^1H NMR ($CDCl_3$) δ: 2.32 (3H, s), 6.89 (2H, d, J=7.5 Hz), 6.94 (1H, t, J=7.5 Hz), 7.12–7.15 (4H, m), 7.43 (2H, t, J=7.5 Hz), 7.48 (1H, td, J=7.5, 1.1 Hz), 7.66 (2H, d, J=8.6 Hz), 7.86 (2H, dt, J=7.5, 1.1 Hz); ^{13}C NMR ($CDCl_3$) δ: 21.9, 120.6, 124.7, 128.2, 128.7, 128.9, 129.6, 129.7, 131.7, 132.3, 135.3, 145.6, 149.4, 166.5, 197.2; HRMS (FAB) calcd for $C_{21}H_{18}NO$ (M+1): 300.1388. Found: 300.1389.

*4.1.4. 1-(2-Methylphenyl)-2-phenyl-2-(phenylimino)ethanone (**4d**).* Yellow oil, 60%; IR (ATR) cm^{-1}: 1667 (C=O); ^1H NMR ($CDCl_3$) δ: 2.41 (3H, s), 6.78 (2H, d, J=7.5 Hz), 6.91 (1H, t, J=7.5 Hz), 7.08–7.13 (4H, m), 7.28 (1H, td, J=7.5, 1.1 Hz), 7.46 (2H, t, J=7.5 Hz), 7.49–7.55 (2H, m), 7.92 (2H, dd, J=7.5, 1.1 Hz); ^{13}C NMR ($CDCl_3$) δ: 21.9, 120.6, 124.7, 128.2, 128.7, 128.9, 129.6, 129.7, 131.7, 132.3, 135.3, 145.6, 149.4, 166.5, 197.2; HRMS (FAB) calcd for $C_{21}H_{18}NO$ (M+1): 300.1388. Found: 300.1394.

*4.1.5. 1-(2-Methoxyphenyl)-2-phenyl-2-(phenylimino)ethanone (**4e**).* Yellow granules (recrystallized from *n*-hexane/acetone); 76%, mp 79–81 °C; IR (ATR) cm^{-1}: 1647 (C=O); ^1H NMR ($CDCl_3$) δ: 3.65 (3H, s), 6.85–6.91 (2H, m), 7.09 (2H, td, J=7.5, 1.1 Hz), 7.39–7.46 (4H, m), 7.61 (2H, dd, J=7.5, 1.1 Hz), 7.85 (2H, dt, J=6.9, 1.7 Hz); ^{13}C NMR ($CDCl_3$) δ: 55.5, 111.8, 120.1, 121.0, 124.1, 125.8, 128.1, 128.6, 130.5, 130.9, 135.3, 135.7, 149.9, 159.5, 167.9, 195.6; HRMS (FAB) calcd for $C_{21}H_{18}NO_2$ (M+1): 316.1338. Found: 316.1328.

*4.1.6. 1-(Furan-2-yl)-2-phenyl-2-(phenylimino)ethanone (**4f**).* Brown needles (recrystallized from *n*-hexane/acetone); 90%, mp 134–136 °C; IR (ATR) cm^{-1}: 1655 (C=O); ^1H NMR ($CDCl_3$) δ: 6.41 (1H, dd, J=3.4, 1.1 Hz), 6.92 (2H, dt, J=7.5, 1.2 Hz), 6.98–7.01 (2H, m), 7.19 (2H, td, J=7.5, 1.7 Hz), 7.43–7.46 (2H, m), 7.50–7.52 (2H, m), 7.89 (2H, dt, J=7.5, 1.7 Hz); ^{13}C NMR ($CDCl_3$) δ: 112.8, 120.4, 121.4, 124.9, 128.2, 128.8, 128.9, 129.0, 130.2, 131.8, 134.8, 148.3, 149.2, 151.3, 164.7, 184.4; HRMS (FAB) calcd for $C_{18}H_{14}NO_2$ (M+1): 276.1025. Found: 276.1023.

*4.1.7. 2-Phenyl-2-(phenylimino)-1-(thiophen-2-yl)ethanone (**4g**)*[6]. Yellow prisms (recrystallized from *n*-hexane/acetone); 86%, mp 116–118 °C; IR (ATR) cm^{-1}: 1640 (C=O); ^1H NMR ($CDCl_3$) δ: 6.94 (2H, d, J=8.0 Hz), 6.97–7.00 (2H, m), 7.18 (2H, t, J=8.0 Hz), 7.43–7.46 (3H, m), 7.49 (1H, td, J=7.5, 2.3 Hz), 7.62 (1H, dd, J=5.1, 1.1 Hz), 7.90 (2H, dd, J=8.6, 1.1 Hz); ^{13}C NMR ($CDCl_3$) δ: 120.6, 125.0, 128.3, 128.6, 128.8, 128.9, 131.8, 135.0, 136.0, 136.2, 142.3, 149.3, 165.3, 189.3.

*4.1.8. 1-(Naphthalen-1-yl)-2-phenyl-2-(phenylimino)ethanone (**4h**).* Yellow powder (recrystallized from *n*-hexane/acetone); 47%, mp 143–145 °C; IR (ATR) cm^{-1}: 1655 (C=O); ^1H NMR ($CDCl_3$) δ: 6.76 (1H, t, J=7.5 Hz), 6.88 (2H, d, J=7.5 Hz), 7.01 (2H, t, J=7.5 Hz), 7.35 (1H, t, J=7.5 Hz), 7.45 (2H, td, J=7.5, 1.7 Hz), 7.52 (2H, td, J=7.5, 1.1 Hz), 7.60 (1H, td, J=6.9, 1.1 Hz), 7.79 (1H, d, J=8.0 Hz), 7.87 (1H, dd, J=7.5, 1.1 Hz), 7.98 (1H, d, J=8.0 Hz), 7.95 (2H, dd, J=6.9, 1.7 Hz), 9.04 (1H, d, J=8.6 Hz); ^{13}C NMR ($CDCl_3$) δ: 120.4, 124.4, 124.5, 125.8, 126.9, 128.4, 128.6, 128.6, 128.9, 129.1, 130.3, 131.2, 131.7, 133.8, 135.4, 135.7, 149.4, 167.1, 199.5; HRMS (FAB) calcd for $C_{24}H_{18}NO$ (M+1): 336.1388. Found: 336.1353.

*4.1.9. 2-(4-Chlorophenyl)-1-(4-methoxyphenyl)-2-(phenylimino) ethanone (**10b**)*[6]. Yellow oil; 75%; IR (ATR) cm^{-1}: 1660 (C=O); ^1H NMR ($CDCl_3$) δ: 3.81 (3H, s), 6.81 (2H, d, J=8.5 Hz), 6.90 (2H, dd, J=8.5, 1.0 Hz), 6.96 (1H, t, J=7.5 Hz), 7.15 (2H, t, J=7.5 Hz), 7.41 (2H, d, J=8.5 Hz), 7.74 (2H, d, J=9.0 Hz), 7.85 (2H, d, J=8.5 Hz).

*4.1.10. 2-(4-Chlorophenyl)-2-(phenylimino)-1-p-tolylethanone (**10c**).* Yellow needles (recrystallized from ether/hexane); 82%; mp 100–102 °C; ^1H NMR ($CDCl_3$) δ: 2.33 (3H, s), 6.89 (2H, d, J=7.5 Hz), 6.95 (1H, t, J=7.5 Hz), 7.14 (2H, d, J=8.0 Hz), 7.14 (2H, t, J=7.5 Hz), 7.41 (2H, d, J=8.5 Hz), 7.64 (2H, d, J=8.5 Hz), 7.82 (2H, d, J=8.5 Hz); ^{13}C NMR ($CDCl_3$) δ: 21.9, 120.5, 124.9, 128.7, 129.1, 129.5, 129.5, 129.7, 132.1, 133.7, 138.0, 145.9, 149.1, 165.2, 196.8; HRMS (FAB) calcd for $C_{21}H_{17}ClNO$ (M+1): 334.0999. Found: 334.1005.

*4.1.11. 2-(4-Chlorophenyl)-1-(furan-2-yl)-2-(phenylimino)-ethanone (**10f**).* Yellow needles (recrystallized from ethyl acetate/*n*-hexane); 80%, mp 106–107 °C; ^1H NMR ($CDCl_3$) δ: 6.41 (1H, dd, J=4.0, 2.0 Hz), 6.91 (2H, dd, J=8.5, 1.0 Hz), 6.99–7.02 (2H, m), 7.20 (2H, t, J=7.5 Hz), 7.42 (2H, d, J=8.5 Hz), 7.52 (1H, d, J=1.0 Hz), 7.83 (2H, d, J=8.5 Hz); ^{13}C NMR ($CDCl_3$) δ: 112.9, 120.4, 121.4, 125.1, 128.9, 129.1, 129.5, 133.2, 138.1, 148.5, 148.9, 151.1, 163.4, 183.9; HRMS (FAB) calcd for $C_{18}H_{13}NO_2$ (M+1): 310.0635. Found: 310.0661.

*4.1.12. 2-(4-Chlorophenyl)-1-phenyl-2-(phenylimino)ethanone (**10i**)*[6]. Yellow prisms (recrystallized from methanol); 90%, mp 106–107 °C; IR (ATR) cm^{-1}: 1670 (C=O); ^1H NMR ($CDCl_3$) δ: 6.88 (2H, dd, J=8.5, 1.0 Hz), 6.94 (1H, t, J=7.5 Hz), 7.14 (2H, t, J=8.5 Hz),

7.35 (2H, t, *J*=8.5 Hz), 7.42 (2H, d, *J*=8.5 Hz), 7.50 (1H, t, *J*=7.5 Hz), 7.73 (2H, d, *J*=8.5 Hz), 7.83 (2H, d, *J*=8.5 Hz).

*4.1.13. 2-(4-Chlorophenyl)-1-(naphthalen-2-yl)-2-(phenylimino)-ethanone (**10j**).* Yellow needles (recrystallized from ether/hexane); 91%, mp 124–126 °C; ^{1}H NMR ($CDCl_3$) δ: 6.89 (1H, t, *J*=7.5 Hz), 6.93 (2H, dd, *J*=8.5, 1.0 Hz), 7.10 (2H, t, *J*=7.5 Hz), 7.42 (2H, d, *J*=8.5 Hz), 7.52 (1H, td, *J*=7.5, 1.0 Hz), 7.59 (1H, td, *J*=7.5, 1.0 Hz), 7.80 (2H, t, *J*=8.5 Hz), 7.85 (2H, td, *J*=8.5, 1.0 Hz), 7.87 (2H, d, *J*=8.5 Hz), 8.21 (1H, s); ^{13}C NMR ($CDCl_3$) δ: 120.5, 123.5, 125.0, 127.2, 128.0, 128.8, 129.1, 129.2, 129.5, 129.6, 129.9, 131.8, 132.4, 132.7, 133.8, 136.2, 138.1, 149.1, 165.1, 197.4; HRMS (FAB) calcd for $C_{24}H_{17}ClNO$ (M+1): 370.0999. Found: 370.1002.

*4.1.14. 1-(4-Chlorophenyl)-2-(4-nitrophenyl)-2-(phenylimino)-ethanone (**13a**)*[6]. Yellow needles (recrystallized from *n*-hexane/acetone); 49%, mp 164–166 °C; IR (ATR) cm^{-1}: 1665 (C=O), 1514, 1341 (NO_2); ^{1}H NMR ($CDCl_3$) δ: 6.91 (2H, dd, *J*=7.5, 1.1 Hz), 7.00–7.03 (1H, m), 7.17–7.20 (2H, m), 7.31–7.34 (2H, m), 7.64–7.67 (2H, m), 8.04–8.06 (2H, m), 8.28–8.31 (2H, m); ^{13}C NMR ($CDCl_3$) δ: 120.5, 124.1, 126.0, 129.1, 129.1, 129.6, 130.6, 132.3, 140.2, 141.6, 148.3, 149.6, 163.4, 195.8.

*4.1.15. 1-(4-Methoxyphenyl)-2-(4-nitrophenyl)-2-(phenylimino)-ethanone (**13b**)*[6]. Yellow granules (recrystallized from *n*-hexane/acetone); 42%, mp 99–101 °C; IR (ATR) cm^{-1}: 1655 (C=O), 1520, 1343 (NO_2); ^{1}H NMR ($CDCl_3$) δ: 3.80 (3H, s), 6.81 (2H, d, *J*=9.2 Hz), 6.95 (2H, dd, *J*=7.5, 1.2 Hz), 7.00 (1H, t, *J*=7.5 Hz), 7.18 (2H, t, *J*=7.5 Hz) 7.70–7.72 (2H, m), 8.05–8.07 (2H, m), 8.26–8.28 (2H, m); ^{13}C NMR ($CDCl_3$) δ: 55.7, 114.5, 120.5, 124.0, 125.7, 127.2, 129.0, 129.2, 132.0, 140.8, 148.7, 149.5, 164.2, 165.0, 195.0.

*4.1.16. 1-(2-Methoxyphenyl)-2-(4-nitrophenyl)-2-(phenylimino)-ethanone (**13e**).* Yellow granules (recrystallized from *n*-hexane/acetone); 36%, mp 122–124 °C; IR (ATR) cm^{-1}: 1655 (C=O), 1520, 1344 (NO_2); ^{1}H NMR ($CDCl_3$) δ: 3.65 (3H, s), 6.75–6.80 (3H, m), 6.88 (1H, t, *J*=7.5 Hz), 6.93 (1H, t, *J*=7.5 Hz), 7.12 (2H, t, *J*=7.5 Hz), 7.45 (1H, dt, *J*=8.6, 1.7 Hz), 7.60 (1H, dd, *J*=7.5, 1.7 Hz), 8.04 (2H, dt, *J*=8.6, 1.7 Hz), 8.27 (2H, dt, *J*=8.6, 1.7 Hz); ^{13}C NMR ($CDCl_3$) δ: 55.5, 111.7, 119.8, 123.8, 124.9, 125.3, 128.7, 129.0, 130.5, 136.3, 141.0, 149.1, 149.1, 159.4, 165.6, 194.8; HRMS (FAB) calcd for $C_{21}H_{17}N_2O_4$ (M+1): 361.1188. Found: 361.1175.

*4.1.17. 1-(Furan-2-yl)-2-(4-nitrophenyl)-2-(phenylimino)-ethanone (**13f**).* Yellow needles (recrystallized from *n*-hexane/acetone); 74%, mp 137–139 °C; IR (ATR) cm^{-1}: 1647 (C=O), 1516, 1346 (NO_2); ^{1}H NMR ($CDCl_3$) δ: 6.43–6.44 (1H, m), 6.95 (2H, dd, *J*=8.6, 1.1 Hz), 7.03–7.06 (2H, m), 7.22 (2H, t, *J*=7.5 Hz), 7.53 (1H, s), 8.08 (2H, dt, *J*=6.9, 1.7 Hz), 8.28 (1H, dt, *J*=6.9, 1.7 Hz); ^{13}C NMR ($CDCl_3$) δ: 113.2, 120.4, 121.6, 124.0, 125.9, 129.0, 129.2, 140.1, 148.5, 148.8, 149.5, 150.9, 162.4, 183.3; HRMS (FAB) calcd for $C_{18}H_{13}N_2O_4$ (M+1): 321.0875. Found: 321.0870.

*4.1.18. 2-(4-Nitrophenyl)-2-(phenylimino)-1-(thiophen-2-yl)-ethanone (**13g**)*[6]. Yellow columns (recrystallized from *n*-hexane/acetone), 81%, mp 119–121 °C; IR (ATR) cm^{-1}: 1638 (C=O), 1518, 1346 (NO_2); ^{1}H NMR ($CDCl_3$) δ: 6.98–7.00 (3H, m), 7.04 (1H, t, *J*=7.5 Hz), 7.22 (2H, t, *J*=7.5 Hz), 7.40 (1H, dd, *J*=4.0, 1.1 Hz), 7.68 (1H, dd, *J*=4.0, 1.1 Hz), 8.09–8.12 (2H, m), 8.28–8.31 (2H, m); ^{13}C NMR ($CDCl_3$) δ: 120.6, 124.0, 128.0, 128.8, 129.1, 129.2, 136.1, 137.1, 140.3, 141.5, 148.5, 149.6, 162.9, 188.3.

*4.1.19. 1-(Naphthalen-1-yl)-2-(4-nitrophenyl)-2-(phenylimino)ethanone (**13i**)*[6]. Orange prisms (recrystallized from *n*-hexane/acetone); 85%, mp 134–136 °C; IR (ATR) cm^{-1}: 1668 (C=O), 1516, 1343 (NO_2); ^{1}H NMR ($CDCl_3$) δ: 6.91 (2H, dd, *J*=8.6, 1.2 Hz), 6.97–7.00 (1H, m), 7.16 (2H, t, *J*=7.5 Hz), 7.36 (2H, t, *J*=7.5 Hz), 7.50–7.53 (1H, m), 7.72 (2H, dd, *J*=8.0, 1.2 Hz), 8.05–8.08 (2H, m), 8.27–8.30 (2H, m); ^{13}C NMR ($CDCl_3$) δ: 120.5, 124.1, 125.8, 129.0, 129.2, 129.4, 134.1, 135.0, 140.5, 148.5, 149.6, 164.0, 196.9.

*4.1.20. 1-(4-Methoxyphenyl)-2-(naphthalen-2-yl)-2-(phenylimino) ethanone (**14b**).* Yellow oil; 80%; ^{1}H NMR ($CDCl_3$) δ: 3.84 (3H), 6.81 (2H, d, *J*=8.5 Hz), 6.95 (2H, d, *J*=8.5 Hz), 7.17 (1H, t, *J*=8.5 Hz), 7.49 (1H, td, *J*=8.0, 1.0 Hz), 7.55 (1H, td, *J*=8.0, 1.0 Hz), 7.79 (2H, d, *J*=8.5 Hz), 7.82 (2H, d, *J*=8.5 Hz), 7.87 (1H, d, *J*=8.5 Hz), 7.93 (1H, d, *J*=8.5 Hz), 8.11 (1H, s), 8.23 (1H, dd, *J*=8.0, 1.0 Hz); ^{13}C NMR ($CDCl_3$) δ: 55.8, 114.1, 120.4, 123.7, 124.6, 126.6, 127.7, 127.8, 127.8, 128.6, 128.7, 130.0, 131.9, 132.6, 134.8, 136.2, 149.4, 164.4, 166.5, 195.8; HRMS (FAB) calcd for $C_{25}H_{20}NO_2$ (M+1): 366.1494. Found: 366.1513.

4.2. Hydrolysis of iminoethanones

To a stirring solution of iminoethanones **4**, **10**, **13**, and **14** (0.2 mmol) in THF (3 ml), 10% HCl (1 ml) was added. The reaction mixture was then stirred at room temperature for 3 h and poured into water. The products were extracted with ethyl acetate, washed with brine, and dried over $MgSO_4$. The solvent was evaporated and the residue was purified by silica gel column chromatography (*n*-hexane/ethyl acetate=4:1) to obtain benzils **16**–**19**.

*4.2.1. 1-(4-Chlorophenyl)-2-phenylethane-1,2-dione (**16a**)*[6]. Yellow needles (recrystallized from methanol/water); quant., mp 67–70 °C; IR (ATR) cm^{-1}: 1663 (C=O); ^{1}H NMR ($CDCl_3$) δ: 7.50 (2H, dt, *J*=8.6, 1.9 Hz), 7.53 (2H, d, *J*=8.6 Hz), 7.68 (1H, m), 7.93 (2H, dt, *J*=8.6, 1.9 Hz), 7.97 (2H, dd, *J*=8.6, 1.2 Hz); ^{13}C NMR ($CDCl_3$) δ: 129.2, 129.5, 130.0, 131.3, 131.4, 132.9, 135.2, 141.7, 193.2, 194.0.

*4.2.2. 1-(4-Methoxyphenyl)-2-phenylethane-1,2-dione (**16e**)*[6]. Yellow oil, quant.; IR (ATR) cm^{-1}: 1670, 1659 (C=O); ^{1}H NMR ($CDCl_3$) δ: 3.88 (3H, s), 6.97 (2H, dt, *J*=9.5, 1.7 Hz), 7.50 (2H, t, *J*=7.5 Hz), 7.64 (1H, t, *J*=7.5 Hz), 7.93–7.97 (4H, m); ^{13}C NMR ($CDCl_3$) δ: 55.8, 114.5, 126.2, 129.1, 130.0, 132.5, 133.3, 134.9, 165.1, 193.3, 195.0.

*4.2.3. 1-(Furan-2-yl)-2-phenylethane-1,2-dione (**16f**)*[7]. Yellow oil, 47%; IR (ATR) cm^{-1}: 1655 (C=O); ^{1}H NMR ($CDCl_3$) δ: 6.62–6.63 (1H, m), 7.37 (1H, d, *J*=3.5 Hz), 7.51 (2H, t, *J*=8.0 Hz), 7.66 (1H, m), 7.75 (1H, m), 8.01–8.03 (2H, m); ^{13}C NMR ($CDCl_3$) δ: 113.1, 123.5, 129.0, 130.3, 132.6, 135.0, 149.4, 150.0, 180.5, 191.7.

*4.2.4. 1-Phenyl-2-(thiophen-2-yl)ethane-1,2-dione (**16g**).* Yellow oil, quant.; IR (ATR) cm^{-1}: 1674, 1643 (C=O); ^{1}H NMR ($CDCl_3$) δ: 7.18 (1H, dt, *J*=8.6, 1.1 Hz), 7.51 (2H, t, *J*=7.5 Hz), 7.66 (1H, m), 7.80 (1H, dd, *J*=6.9, 1.1 Hz), 7.83 (1H, dd, *J*=6.9, 1.1 Hz), 8.03 (2H, dd, *J*=8.6, 1.1 Hz); ^{13}C NMR ($CDCl_3$) δ: 129.0, 129.1, 130.4, 132.7, 135.0, 137.9, 137.1, 140.0, 185.7, 192.2.

*4.2.5. 1-(Naphthalen-1-yl)-2-phenylethane-1,2-dione (**16h**).* Yellow needles, quant.; mp 98–99 °C; IR (ATR) cm^{-1}: 1670, 1651 (C=O); ^{1}H NMR ($CDCl_3$) δ: 7.48 (1H, d, *J*=7.5 Hz), 7.52 (2H, t, *J*=8.1 Hz), 7.61–7.67 (2H, m), 7.75 (1H, t, *J*=7.5 Hz), 7.91 (1H, dd, *J*=7.5, 1.2 Hz), 7.94 (1H, d, *J*=8.6 Hz), 8.03 (2H, d, *J*=7.5 Hz), 8.12 (1H, d, *J*=8.0 Hz), 9.31 (1H, d, *J*=8.6 Hz); ^{13}C NMR ($CDCl_3$) δ: 124.6, 126.0, 127.3, 128.7, 128.9, 129.2, 129.6, 130.1, 131.0, 133.4, 134.2, 134.9, 135.3, 136.1, 194.7, 197.3.

*4.2.6. 1-(4-Chlorophenyl)-2-(4-methoxyphenyl)ethane-1,2-dione (**17b**)*[6]. Yellow needles (recrystallized from ether/hexane), 88%; mp

102–103 °C; ^{1}H NMR ($CDCl_3$) δ: 3.90 (3H, s), 6.99 (2H, d, J=8.5 Hz), 7.48 (2H, d, J=8.5 Hz), 7.93 (4H, t, J=8.5 Hz).

*4.2.7. 1-(4-Chlorophenyl)-2-(furan-2-yl)ethane-1,2-dione (**17f**).* Yellow needles (recrystallized from ether/hexane), 100%; mp 115–116 °C; ^{1}H NMR ($CDCl_3$) δ: 6.65 (1H, dd, J=4.0, 2.0 Hz), 7.42 (1H, d, J=4.0 Hz), 7.50 (2H, d, J=8.5 Hz), 7.78 (1H, d, J=1.5 Hz), 8.00 (2H, d, J=8.5 Hz); HRMS (FAB) calcd for $C_{12}H_8ClO_3$ (M+1): 235.0162. Found: 235.0176.

*4.2.8. 1-(4-Chlorophenyl)-2-(naphthalen-2-yl)ethane-1,2-dione (**17j**).* Yellow needles (recrystallized from ether/hexane), 100%; mp 130–132 °C; ^{1}H NMR ($CDCl_3$) δ: 7.51 (2H, d, J=8.5 Hz), 7.58 (1H, td, J=7.5, 1.5 Hz), 7.67 (1H, td, J=7.5, 1.0 Hz), 7.92 (2H, t, J=8.5 Hz), 7.98 (2H, d, J=8.5 Hz), 8.09 (2H, dd, J=8.5, 1.5 Hz), 8.40 (1H, s); ^{13}C NMR ($CDCl_3$) δ: 123.7, 127.4, 128.1, 129.4, 129.6, 129.8, 130.1, 130.2, 131.4, 131.5, 132.0, 132.4, 133.8, 136.5, 141.7, 193.3, 194.1; HRMS (FAB) calcd for $C_{18}H_{12}ClO_2$ (M+1): 295.0526. Found: 295.0537.

*4.2.9. 1-(4-Chlorophenyl)-2-(4-nitrophenyl)ethane-1,2-dione (**18a**)*[6]. Yellow needles, quant.; mp 201–203 °C; IR (ATR) cm^{-1}: 1672, 1653 (C=O), 1522, 1348 (NO_2); ^{1}H NMR ($CDCl_3$) δ: 7.53 (2H, d, J=8.6 Hz), 7.94 (2H, d, J=8.6 Hz), 8.16 (2H, d, J=9.2 Hz), 8.36 (2H, d, J=9.2 Hz); ^{13}C NMR ($CDCl_3$) δ: 124.3, 129.8, 130.8, 131.2, 131.5, 137.2, 142.4, 151.3, 191.4, 191.5.

*4.2.10. 1-(Furan-2-yl)-2-(4-nitrophenyl)ethane-1,2-dione (**18f**).* Yellow needles, 82%; mp 126–128 °C; IR (ATR) cm^{-1}: 1678, 1651 (C=O); ^{1}H NMR ($CDCl_3$) δ: 6.67–6.68 (1H, m), 7.50 (1H, d, J=7.5 Hz), 7.82 (1H, s), 8.23 (2H, dt, J=8.6, 1.7 Hz), 8.35 (2H, dt, J=8.6, 1.7 Hz); ^{13}C NMR ($CDCl_3$) δ: 113.5, 124.1, 124.6, 131.5, 137.2, 149.6, 150.1, 151.2, 178.2, 189.2; HRMS (FAB) calcd for $C_{12}H_8NO_5$ (M+1): 246.0402. Found: 246.0432.

*4.2.11. 1-(4-Nitrophenyl)-2-(thiophen-2-yl)ethane-1,2-dione (**18g**).* Yellow needles, quant.; mp 142–144 °C; IR (ATR) cm^{-1}: 1676, 1635 (C=O); ^{1}H NMR ($CDCl_3$) δ: 7.23 (1H, m), 7.90 (2H, td, J=6.9, 1.1 Hz), 8.23 (2H, dt, J=6.9, 1.1 Hz), 8.34 (2H, dt, J=9.1, 1.7 Hz); ^{13}C NMR ($CDCl_3$) δ: 124.1, 129.2, 131.5, 137.2, 137.5, 138.1, 139.1, 151.2, 183.5, 189.7.

*4.2.12. 1-(4-Nitrophenyl)-2-phenylethane-1,2-dione (**18i**)*[6]. Yellow needles, quant.; mp 137–139 °C; IR (ATR) cm^{-1}: 1674, 1661 (C=O), 1526, 1346 (NO_2); ^{1}H NMR ($CDCl_3$) δ: 7.55 (2H, t, J=7.5 Hz), 7.71 (1H, t, J=7.5 Hz), 7.99 (2H, d, J=7.5 Hz), 8.17 (2H, dt, J=8.6, 1.7 Hz), 8.36 (2H, d, J=8.6 Hz); ^{13}C NMR ($CDCl_3$) δ: 124.3, 129.4, 130.2, 131.1, 132.4, 135.6, 137.4, 151.2, 192.2, 193.0.

*4.2.13. 1-(4-Methoxyphenyl)-2-(naphthalen-2-yl)ethane-1,2-dione (**19b**).* Yellow oil, 90%; ^{1}H NMR ($CDCl_3$) δ: 3.88 (3H, s), 6.98 (2H, d, J=8.5 Hz), 7.54 (1H, t, J=7.5 Hz), 7.63 (1H, t, J=8.0 Hz), 7.89 (1H, t, J=8.5 Hz), 7.95 (1H, d, J=8.5 Hz), 8.00 (2H, d, J=8.5 Hz), 8.09 (2H, dd, J=8.5, 1.5 Hz), 8.15 (1H, d, J=8.5 Hz), 8.41 (1H, d, J=8.5 Hz); ^{13}C NMR ($CDCl_3$) δ: 55.6, 114.3, 123.7, 125.3, 126.1, 127.1, 127.9, 129.1, 129.9, 130.4, 132.4, 133.4, 136.3, 165.0, 193.2, 194.9; HRMS (FAB) calcd for $C_{19}H_{15}O_3$ (M+1): 291.1021. Found: 291.1022.

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References and notes

1. *N-Heterocyclic Carbenes in Synthesis*; Nolan, S. P., Ed.; WILEY-VCH GmbH & KGaA: Weinheim, 2006.
2. Enders, D.; Niemeier, O.; Henseler, A. *Chem. Rev.* **2007**, *107*, 5606–5655.
3. Marion, N.; Díe-Gonzále, S.; Nolan, S. P. *Angew. Chem., Int. Ed.* **2007**, *46*, 2988–3000.
4. Enders, D.; Balensiefer, T. *Acc. Chem. Res.* **2004**, *37*, 534–541.
5. Nair, V.; Bindu, S.; Sreekumar, V. *Angew. Chem., Int. Ed.* **2004**, *43*, 5130–5135.
6. Miyashita, A.; Matsuda, H.; Higashino, T. *Chem. Pharm. Bull.* **1992**, *40*, 2627–2631.
7. Katritzky, A. R.; Zhang, D.; Kirichenko, K. *J. Org. Chem.* **2005**, *70*, 3271–3274.
8. Barta, T. E.; Stealey, M. A.; Collins, P. W.; Weier, R. M. *Bioorg. Med. Chem. Lett.* **1998**, *8*, 3443–3448.
9. Singh, S. K.; Saibaba, V.; Ravikumar, V.; Rudrawar, S. V.; Daga, P.; Rao, C. S.; Akhila, V.; Hegde, P.; Rao, Y. K. *Bioorg. Med. Chem. Lett.* **2004**, *12*, 1881–1893.
10. Bostrom, J.; Berggren, K.; Elebring, T.; Greasley, P. J.; Wilstermann, M. *Bioorg. Med. Chem.* **2007**, *15*, 4077–4084.
11. Wilsterman, J. M.; Berggren, A. I. K. PCT Int. Appl., 2003, 27 pp.
12. Deuchert, K.; Hertenstein, U.; Huenig, S.; Wehner, G. *Chem. Ber.* **1979**, *112*, 2045–2061.
13. Fuson, R. C.; Hoch, P. E. *J. Am. Chem. Soc.* **1949**, *71*, 1585–1586.
14. Ugi, I.; Beck, F.; Fetzer, U. *Chem. Ber.* **1962**, *95*, 126–135.
15. Eloy, F.; Deryckere, A.; Maffrand, J. P. *Eur. J. Med. Chem.* **1974**, *9*, 602–606.
16. Houghton, P. G.; Pipe, D. F.; Rees, C. W. *J. Chem. Soc., Perkin Trans. 1* **1985**, 1471–1479.
17. Van den Nieuwendijk, A. M. C. H.; Pietra, D.; Heitman, L.; Goeblyoes, A.; IJzerman, A. P. *J. Med. Chem.* **2004**, *47*, 663–672.
18. Haeger, I.; Froehlich, R.; Wuerthwein, E.-U. *Eur. J. Inorg. Chem.* **2009**, 2415–2428.
19. Miyashita, A.; Kurachi, A.; Matsuoka, Y.; Tanabe, N.; Suzuki, Y.; Iwamoto, K.; Higashino, T. *Heterocycles* **1997**, *44*, 417–426.
20. Ide, W. S.; Buck, J. S. In *Organic Reactions*; Bachmann, W. E., Fieser, L. F., Blatt, A. H., Johnson, J. R., Eds.; John Wiley: New York, NY, USA, 1948; Vol. 4, pp 278–434.
21. Miyashita, A.; Suzuki, Y.; Iwamoto, K.; Higashino, T. *Chem. Pharm. Bull.* **1994**, *42*, 2633–2635.