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DMAP-catalyzed cascade reaction: one-pot synthesis of benzofurans in water

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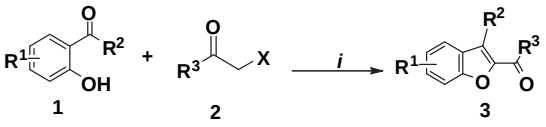
ABSTRACT

A series of benzofurans were efficiently synthesized in good to excellent yields using 4-dimethylaminopyridine (DMAP) catalyzed cascade reaction between salicylaldehydes and halogenated ketones in water at 80 °C opened atmosphere.

1. Introduction

Benzofuran derivatives are important components of those clinically used plant extracts due to their excellent properties, such as antibacterial,[1] antimicrobial,[2] antitumor,[3] and the ability to control calcium level.[4] Many research efforts have been focused on the efficient synthesis of these molecules.[5] Typical approaches including: (1) intramolecular enolated O-arylation[6] and thio-enolated S-arylation,[7] (2) annulation of a furan ring onto a preexisting benzene ring,[8] and (3) catalyzed cyclization-coupling.[9,10] However, the first two approaches generally require multi-step synthesis, while the third one often requires the usage of transition-metals,[11,12] and only limited types of benzofuran derivatives are accessible using these synthetic approaches. The Rap–Stoermer reaction provides opportunity for the direct preparation of benzofurans via base-mediated reaction of salicylaldehydes with haloketones. Recently reported solid state studies on the Rap–Stoermer reaction provided valuable insights into the mechanistic details of this reaction.[13]

DMAP and its analogs have been widely used in many organic synthesis as catalyst, used, for example, in the acylation reactions,[14] aldol reactions,[15] and Baylis–Hillman reactions.[16] Recently, these catalysts have also been used in the Michael-addition[17] and esterification[18] reactions in water. Attracted to the efficiency of these organo-catalysts and the advantages of using water as solvent.[19–22] In the context of our studies aimed for the development of efficient catalytic organic synthsis,[23] we have focused on the utility of DMAP. Herein we report a facile synthesis of a series of benzofurans using DMAP-catalyzed cascade reaction between readily available salicylaldehydes **1** and halogenated ketones **2** in water (Scheme 1).



Scheme 1. Synthesis of benzofuran derivatives conditions: (1) DMAP (0.1 equiv), (2) Na_2CO_3 (1.5 equiv), (3) H_2O (solvent), 80 °C, 5 h.

2. Results and discussion

Initially, DABCO (1, 4-diazabibicyclo [2.2.2] octane) was used as catalyst in the cascade reaction between salicylaldehyde **1** and α-bromoacetophenone **2** in the presence of Na_2CO_3 in water as shown in Table 1 (entry 1). To our delight, the desired benzofuran **3a**[24,25] was obtained in 80% yield after reacting at 80 °C for 5 h. It was characterized by ^1H, ^{13}C NMR and X-ray (Fig. 1). For the optimization of the reaction condition, various catalysts, different solvents, varying temperature, and reaction time were investigated and the results are summarized in Tables 1 and 2.

Among the various catalysts studied (Table 1), 3-HQD (3-hydroxyquinuclidine) (entry 2) and DMAP (4-dimethylaminopyridine) (entry 7) showed higher catalytic activities, and gave

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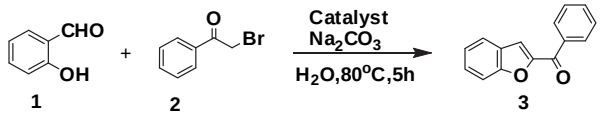
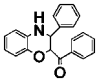
Table 1
Optimization of catalysts[a]



1 2 3

Entry	Catalyst	Yield (%)
1		80
2		82
3		30
4		30
5		42
6		51[b]
7		88
8	—	18

[a] Reaction conditions: salicylaldehydes(1.0 mmol), α-bromoacetophenone (1.0 mmol), catalyst (0.1 mmol), water (5 mL), Na_2CO_3 (1.5 mmol), 80 °C, 5 h.
[b] This catalyst was synthesized in our laboratory.

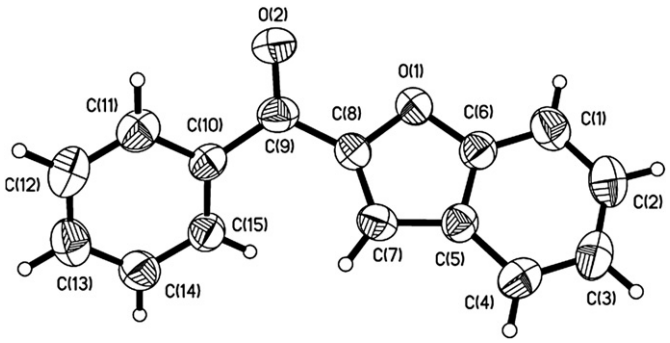
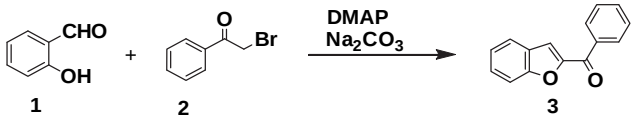


Fig. 1. X-ray crystal structure of **3a**.

Table 2
Optimization of reaction conditions[a]



1 2 3

Entry	Solvent	Temp (°C)	Time(h)	Yield (%)
1	Toluene	Reflux	5	83
2	THF	Reflux	5	85
3	DMF	Reflux	5	80
4	CH_2Cl_2	Reflux	8	20
5	CH_3CN	Reflux	4	87
6	H_2O	100	5	87
7	H_2O	80	5	88
8	H_2O	80	5	87[b]
9	H_2O	60	8	40
10	H_2O	40	10	36
11	H_2O	rt	12	20

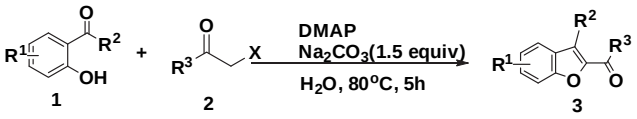
[a] Reaction conditions: salicylaldehydes (1.0 mmol), α-bromoacetophenone (1.0 mmol), solvent (5 mL), catalyst (0.1 mmol), and Na_2CO_3 (1.5 mmol).
[b] Catalyst (0.2 mmol).

compound **3** in 82% and 88% yields, respectively. We thus chose DMAP as catalyst, and further optimized the reaction condition as summarized in Table 2.

This reaction was carried out in a variety of solvents, such as THF, DMF, toluene, and water. In this study, benzofuran **3** was obtained in 80% and 85% yield with DMF, THF as solvent at reflux for 5 h (entries 2 and 3), but it obtained in 88% yield with water as solvent at 80 °C at the same time (entry 7). Thus, water turns out to be the best solvent for this reaction. And then we optimized the reaction with water as solvent (entries 6–11). At room temperature, compound **3** was obtained in low yield in water (entry 11). When the temperature increased to 80 °C, the yield increased to 88%, and the reaction time reduced to 5 h (entry 7). Further increasing the temperature to 100 °C, a comparable result was obtained (entry 6). Thus, we eventually settle down the optimized reaction condition to be the combination of 10 mol % of DMAP as catalyst, water as solvent and Na_2CO_3 as base.

Utilizing the optimized reaction condition, various salicylaldehydes **1** and halogenated ketones **2** were used to test the versatility of this reaction, and the results were summarized in Table 3. Many functionalities were able to survive from this reaction. Among various salicylaldehydes **1** investigated (entries 1, 11, and 17), molecules with electron-withdrawing groups (Br and Cl) attached generally provides higher yields. Among various halogenated aromatic ketones **2** investigated, molecules with electron-donating group attached on the benzene rings of R_3 often gave higher yields, while those with electron-withdrawing groups attached, such as **3d** led to lower yields. Compared with α-bromoacetophenone (entry 1), chloroacetophenone gave lower yield (82%, entry 10).

Table 3
DMAP-catalyzed cascade reaction for the formation of benzofurans[a]

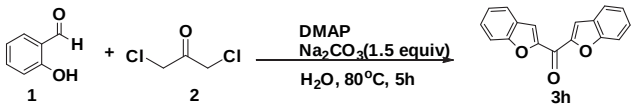


1 2 3

Entry	R^1	R^2	R^3	X	Yield (%)	
1	H	H	C_6H_5	Br	**3a**	88
2	H	H	$CH_3C_6H_4$	Br	**3b**	81
3	H	H	$CH_3OC_6H_4$	Br	**3c**	90
4	H	H	BrC_6H_4	Br	**3d**	60
5	H	H	*p*-$NO_2C_6H_4$	Br	**3e**	71
6	H	H	*m*-$NO_2C_6H_4$	Br	**3f**	75
7	H	H	OCH_2CH_3	Cl	**3g**	60
8	H	H	$ClCH_2$	Cl	**3h**	80
9	H	H	CH_3	Cl	**3i**	80
10	3-Br	H	C_6H_5	Br	**3j**	95
11	3-Br	H	$CH_3C_6H_4$	Br	**3k**	83
12	3-Br	H	$CH_3OC_6H_4$	Br	**3l**	73
13	3-Br	H	BrC_6H_4	Br	**3m**	70
14	3-Br	H	*p*-$NO_2C_6H_4$	Br	**3n**	71
15	3-Br	H	*m*-$NO_2C_6H_4$	Br	**3o**	68
16	3-Cl	H	C_6H_5	Br	**3p**	90
17	3-Cl	H	$CH_3C_6H_4$	Br	**3q**	87
18	3-Cl	H	$CH_3OC_6H_4$	Br	**3r**	91
19	3-Cl	H	BrC_6H_4	Br	**3s**	82
20	3-Cl	H	*p*-$NO_2C_6H_4$	Br	**3t**	72
21	3-Cl	H	*m*-$NO_2C_6H_4$	Br	**3u**	65
22	H	CH_3	C_6H_5	Br	**3v**	72
23	H	CH_3	BrC_6H_4	Br	**3w**	70
24	H	CH_3	*p*-$NO_2C_6H_4$	Br	**3x**	70

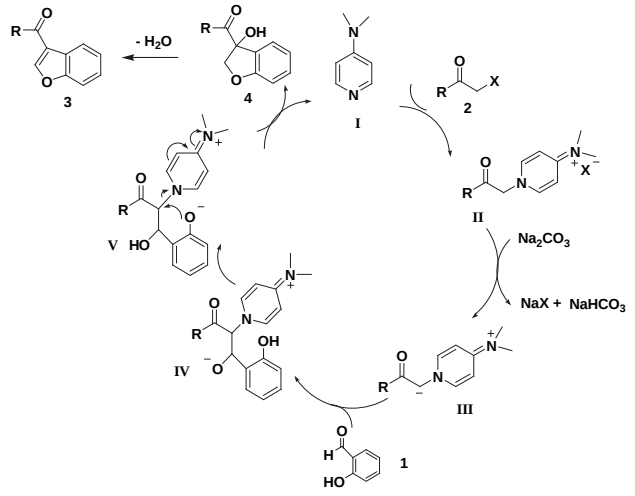
[a] Reaction conditions: salicylaldehydes (1.0 mmol), α-bromoacetophenone (1.0 mmol), water (5 mL), DMAP (0.1 mmol), and Na_2CO_3 (1.5 mmol), 80 °C, 5 h.

Interestingly, the usage of 1,3-dichlorin acetone as the starting material led to the formation of **3h** (Scheme 2), containing two benzofuran rings, in 80% yield using the optimized reaction condition (entry 8).



Scheme 2. DMAP-catalyzed one-pot synthesis of the dibenzofuran-2-ylmethanone (**3h**).

The mechanism for this reaction is complicated, however it is reasonable to propose the following explanation as shown in Scheme 3 for this reaction based on our experimental results and literature reports.[25] We reasoned that DMAP may has an increased efficiency for this reaction for two reasons. The DMAP could lead to more efficient ammonium salt to enhance its solubility in water. The hydrogen activity of the ammonium salt would be more higher and it would be taken away by sodium carbonate in water to generate a carbanion to enhance its nucleophilic properties. The nitrogen of the catalyst **I** displaces the halogen of compound **2** to generate the corresponding ammonium salt **II**. The enolate form of the ammoniumylide **III** nucleophilic attack at the carbonyl group of salicylaldehyde **1** to generate intermediate **IV**, which was further converted to the intermediate **V** via proton-transfer process. The key precursor-compound **4** was generated from the intramolecular nucleophilic addition within intermediate **V**, and was further converted to the desired target compound **3** through dehydration process. Meanwhile, catalyst **I** was regenerated.



Scheme 3. Possible mechanism for the synthesis of benzofurans.

3. Conclusions

In conclusion, we have developed an efficient DMAP-catalyzed Rap–Stoermer reaction for the efficient generation of a series of 2-aryl-benzofurans in excellent yields. This reaction contains certain value from a green-chemistry viewpoint, as well as in terms of practicality. This reaction features with mild reaction condition and wide access of the starting materials. This mild annulation strategy developed here may find application in the synthesis of other hetero-containing aromatic compounds.

4. Experimental section

4.1. General methods

All reagents involved in the experiments were commercially available and used without further purification. ^{1}H NMR and ^{13}C NMR spectra (300 MHz) were recorded on a Bruker spectrospin 300 MHz. All NMR samples were run in $CDCl_3$ and chemical shifts are expressed as parts per million relative to internal Me_4Si and the metallic nature of the particles was confirmed with a UV spectrophotometer (Shimadzo). Column chromatography was carried out with the use of silica gel (200–300 mesh), purchased from Qingdao Haiyang Chemical Plang, China.

4.2. General procedure for the synthesis of benzofurans

To DMAP (10% mmol) and Na_2CO_3 (1.5 mmol) in water, halogenated ketone (1 mmol) and salicylaldehyde (1 mmol) were added. The resulting mixture was stirred at 80 °C for 5 h. The mixture was extracted with CH_2Cl_2 (30 mL), washed with water. The organic layers were combined, dried over anhydrous Na_2SO_4, and evaporated in vacuum. The residue was purified by column chromatography on silica gel (200–300 mesh) (EtOAc/petroleum=1/20, v/v) to give the pure product **3**.

*4.2.1. Compound **3a**[24].* ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.06 (d, J=7.6 Hz, 1H, C_6H_4), 8.03 (d, J=8.0 Hz, 1H, C_6H_4), 7.67–7.75 (m, J=8.0 Hz, 2H, C_6H_4), 7.62–7.66 (m, 2H, C_6H_4CO), 7.57 (s, 1H, C_4HO), 7.51–7.54 (m, 2H, C_6H_4CO), 7.37–7.49 (s, 1H, C_6H_4CO) ppm; ^{13}C NMR ($CDCl_3$, 75 MHz) δ 184.4, 155.9, 152.1, 137.1, 132.9, 129.6, 129.4, 128.5, 128.4, 126.7, 123.9, 123.3, 116.6, 112.5 ppm.

*4.2.2. Compound **3b**[24].* ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.98 (d, J=7.8 Hz, 1H, C_6H_4), 7.74 (d, J=8.1 Hz, 1H, C_6H_4), 7.71–7.74 (m, J=8.0 Hz, 2H, C_6H_4), 7.63–7.66 (m, 2H, $CH_3C_6H_4CO$), 7.50 (s, 1H, C_4HO), 7.31–7.47 (m, 2H, $CH_3C_6H_4CO$), 2.47 (s, 3H, $CH_3C_6H_4CO$) ppm; ^{13}C NMR ($CDCl_3$, 75 MHz) δ 183.7, 154.3, 153.3, 144.1, 129.7, 129.5, 129.3, 128.5, 128.3, 122.5, 115.0, 113.6, 21.8 ppm.

*4.2.3. Compound **3c**[24].* ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.09 (d, J=9.0 Hz, 2H, $CH_3OC_6H_4CO$), 7.71 (d, J=8.1 Hz, 1H, C_6H_4), 7.62 (d, J=8.7 Hz, 1H, C_6H_4), 7.50 (s, 1H, C_4HO), 7.44–7.49 (m, 1H, C_6H_4), 7.30–7.33 (m, 1H, C_6H_4), 6.97–7.02 (m, 2H, $CH_3OC_6H_4CO$), 3.89 (s, 3H, $CH_3OC_6H_4CO$) ppm; ^{13}C NMR ($CDCl_3$, 75 MHz) δ 182.9, 163.6, 155.5, 152.7, 134.7, 131.9, 128.3, 127.1, 123.9, 123.2, 115.6, 113.9, 112.5, 55.6 ppm.

*4.2.4. Compound **3d**[24].* ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.96 (d, J=8.4 Hz, 1H, C_6H_4), 7.93 (d, J=8.1 Hz, 2H, BrC_6H_4CO),7.73–7.76 (m, 1H, C_6H_4), 7.70–7.72 (m, 2H, BrC_6H_4CO), 7.68 (s, 1H, C_4HO), 7.49–7.56 (m, 1H, C_6H_4), 7.32–7.37 (m, 1H, C_6H_4) ppm; ^{13}C NMR ($CDCl_3$, 75 MHz) δ 182.9, 154.3, 153.0, 136.5, 131.9, 131.6, 129.8, 128.9, 128.4, 128.1, 122.7, 115.4, 113.7 ppm.

*4.2.5. Compound **3e**.* Unknown, ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.42 (d, J=6.90 Hz, 2H, $NO_2C_6H_4CO$), 8.25 (d, J=6.91 Hz, 2H, $NO_2C_6H_4CO$), 7.83 (d, J=8.1 Hz, 1H, C_6H_4), 7.63–7.71 (m, 2H, C_6H_4), 7.60 (s, 1H, C_4HO), 7.33–7.59 (m, 1H, C_6H_4) ppm; ^{13}C NMR ($CDCl_3$, 75 MHz) δ 181.2, 154.7, 152.4, 148.2, 137.8, 135.3, 135.1, 133.9, 131.6, 129.9, 128.5, 127.6, 127.4, 126.1, 125.9, 124.9, 124.8, 124.5, 117.4, 115.8, 115.7, 114.1, 111.6 ppm; IR (KBr): ν 3753, 3666, 3201, 2958, 2922, 2850, 2349, 2308, 1651, 1598, 1556, 1519, 1469, 1454, 1336, 1301, 1263, 1190, 1128, 1101, 972, 866, 850, 758 cm^{-1}; HRMS (ESI) calcd for $C_{15}H_9NO_4$ ($[M+H]^+$) 267.0532, found 267.1674.

*4.2.6. Compound **3f**.* Unknown, ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.42 (d, J=8.7 Hz, 1H, $NO_2C_6H_4CO$), 8.38 (d, J=8.3, 1H, $NO_2C_6H_4CO$), 8.24 (d, J=8.4 Hz, 1H, $NO_2C_6H_4CO$), 8.20–8.24 (m, 1H, $NO_2C_6H_4CO$), 7.85 (d, J=7.8 Hz, 1H, C_6H_4), 7.67–7.82 (m, 1H, C_6H_4), 7.64 (s, 1H, C_4HO), 7.53–7.62 (m, 1H, C_6H_4), 7.35–7.40 (m, 1H, C_6H_4) ppm; ^{13}C NMR ($CDCl_3$, 75 MHz) δ 181.8, 154.7, 141.5, 132.1, 130.5, 128.5, 123.7, 117.4, 123.3, 116.1, 115.9, 114.1 ppm; IR (KBr): ν 3672, 3278, 2958, 2924, 2852, 2349, 2308, 1651, 1606, 1548, 1525, 1475, 1355, 1332, 1300,

1261, 1190, 1134, 1085, 997, 921, 848, 756, 725 cm^{-1}; HRMS (ESI) calcd for $C_{15}H_9NO_4$ ($[M+H]^+$) 268.0565, found 268.0599.

4.2.7. Compound ***3g***[26]. ^1H NMR ($CDCl_3$, 300 MHz) δ 7.67 (d, J=7.5 Hz, 1H, C_6H_4), 7.59 (d, J=7.8 Hz, 1H, C_6H_4), 7.52 (s, 1H, C_4HO), 7.41–7.46 (m, 1H, C_6H_4), 7.27–7.32 (m, 1H, C_6H_4), 4.45 (t, J=6.9, 2H, CH_2CH_3), 1.43 (q, J=6.6, 3H, CH_2CH_3) ppm; ^{13}C NMR ($CDCl_3$, 75 MHz) δ 159.6, 155.7, 145.7, 127.6, 126.9, 123.8, 122.8, 113.8, 112.4, 61.5, 14.3 ppm.

4.2.8. Compound ***3h***. Unknown, ^1H NMR ($CDCl_3$, 300 MHz) δ 8.01 (s, 2H, C_4HO), 7.76–7.90 (m, 2H, C_6H_4), 7.64–7.67 (m, 2H, C_6H_4), 7.49–7.54 (m, 2H C_6H_4), 7.32–7.37 (m, 2H, C_6H_4) ppm; ^{13}C NMR ($CDCl_3$, 75 MHz) δ 171.6, 155.9, 151.6, 128.7, 127.1, 124.1, 123.5, 116.2, 112.5 ppm; IR (KBr): ν 3745, 3666, 3304, 2924, 2349, 2308, 1768, 1714, 1651, 1631, 1612, 1543, 1473, 1359, 1332, 1303, 1257, 1155, 1134, 987, 939, 889, 866, 748 cm^{-1}; HRMS (ESI) calcd for $C_{17}H_{10}O_3$ ($[M+H]^+$) 263.0663, found 263.0692.

4.2.9. Compound ***3i***[27]. ^1H NMR ($CDCl_3$, 300 MHz) δ 8.20 (d, J=7.8 Hz, 1H, C_6H_4), 7.63 (s, 1H, C_4HO), 7.43–7.47 (m, 1H, C_6H_4), 7.25–7.37 (m, 2H, C_6H_4), 2.49 (s, 3H, $COCH_3$) ppm; ^{13}C NMR ($CDCl_3$, 75 MHz) δ 181.7, 153.6, 146.7, 142.5, 130.8, 130.5, 130.3, 128.1, 127.5, 126.8, 1376.7, 123.4, 123.0, 122.4, 120.5, 117.1, 115.9, 115.7, 111.2, 9.1 ppm.

4.2.10. Compound ***3j***[24]. ^1H NMR ($CDCl_3$, 300 MHz) δ 8.07 (s, 1H, BrC_6H_3), 7.88 (d, J=7.8 Hz, 2H, C_6H_5CO), 7.68 (d, J=7.7 Hz, 2H, C_6H_5CO), 7.64–7.66 (m, 1H, C_6H_5CO), 7.58 (s, 1H, C_4HO), 7.47–7.55 (m, 2H, BrC_6H_3) ppm; ^{13}C NMR ($CDCl_3$, 75 MHz) δ 184.0, 154.6, 153.3, 136.6, 133.2, 131.3, 129.5, 128.9, 128.6, 125.7, 123.4, 117.0, 115.3, 114.0 ppm.

4.2.11. Compound ***3k***[24]. ^1H NMR($CDCl_3$, 300 MHz) δ 7.98 (s, 1H, BrC_6H_3), 7.96 (d, J=8.0 Hz, 2H, $CH_3C_6H_4CO$), 7.86 (d, J=8.1 Hz, 1H, $CH_3C_6H_4CO$), 7.62–7.65 (m, 1H, $CH_3C_6H_4CO$), 7.53–7.57 (m, 1H, BrC_6H_3), 7.45 (s, 1H, C_4HO), 7.33–7.36 (m, 1H, BrC_6H_3), 2.47 (s, 3H, $CH_3C_6H_4CO$) ppm; ^{13}C NMR ($CDCl_3$, 75 MHz) δ 183.5, 154.2, 153.3, 144.1, 134.1, 131.1, 129.6, 129.3, 128.9, 125.6, 116.9, 114.8, 114.0, 21.7 ppm.

4.2.12. Compound ***3l***[24]. ^1H NMR ($CDCl_3$, 300 MHz) δ 8.08 (s, 1H, BrC_6H_3), 8.06 (d, J=8.5 Hz, 2H, $CH_3OC_6H_4CO$), 7.66 (d, J=7.7 Hz, 1H, BrC_6H_3), 7.51 (s, 1H, C_4HO), 7.41–7.43 (m, 1H, BrC_6H_3), 6.96–7.01 (m, 2H, $CH_3OC_6H_4CO$), 3.89 (s, 3H, $CH_3OC_6H_4CO$) ppm; ^{13}C NMR ($CDCl_3$, 75 MHz) δ 182.4, 163.8, 154.0, 134.9, 132.0, 129.5, 129.4, 128.2, 122.5, 114.4, 113.9, 113.5, 55.6 ppm.

4.2.13. Compound ***3m***[24]. ^1H NMR($CDCl_3$, 300 Hz) δ 7.96 (s, 1H, BrC_6H_3), 7.93 (d, J=8.5 Hz, 2H, BrC_6H_4CO), 7.70 (d, J=8.1 Hz, 2H, BrC_6H_4CO), 7.67–7.69 (m, 1H, BrC_6H_3), 7.58 (s, 1H, C_4HO), 7.45–7.49 (m, 1H, BrC_6H_3) ppm; ^{13}C NMR ($CDCl_3$, 75 MHz) δ 183.2, 154.3, 153.0, 135.6, 135.5, 131.9, 131.0, 129.8, 128.9, 128.4, 128.1, 122.7, 115.4, 113.8 ppm.

4.2.14. Compound ***3n***. Unknown, ^1H NMR ($CDCl_3$, 300 MHz) δ 8.41 (d, J=8.3 Hz, 2H, $NO_2C_6H_4CO$), 8.20–8.25 (m, 2H, $NO_2C_6H_4CO$), 7.91 (s, 1H, BrC_6H_3), 7.66 (s, 1H, C_4HO), 7.63–7.65 (m, 1H, BrC_6H_3), 7.52–7.56 (m, 1H, BrC_6H_3) ppm; ^{13}C NMR ($CDCl_3$, 75 MHz) δ 181.4, 154.3, 152.8, 148.2, 137.8, 135.1, 130.1, 129.9, 129.4, 127.9, 127.4, 124.4, 122.8, 116.0, 113.7 ppm; IR (KBr): ν 3745, 3670, 3280, 3103, 2924, 1852, 2349, 2308, 1699, 1651, 1598, 1523, 1436, 1340, 1309, 1267, 1186, 1134, 1105, 1045, 975, 898, 850, 812, 775 cm^{-1}; HRMS (ESI) calcd for $C_{15}H_8BrNO_4$ ($[M+H]^+$) 346.9616, found 346.3323.

4.2.15. Compound ***3o***. Unknown, ^1H NMR ($CDCl_3$, 300 MHz) δ 8.41 (s, 1H, $NO_2C_6H_4CO$), 8.36 (d, J=8.7 Hz, 1H, $NO_2C_6H_4CO$), 8.23 (d, J=8.1 Hz, 1H, $NO_2C_6H_4CO$), 7.91 (s, 1H, BrC_6H_3), 7.85–7.91 (m, 1H, $NO_2C_6H_4CO$), 7.84 (s, 1H, C_4HO), 7.61–7.66 (m, 1H, BrC_6H_3), 7.50–7.56 (m, 1H, BrC_6H_3) ppm; ^{13}C NMR ($CDCl_3$, 75 MHz) δ 181.6, 155.0, 152.7, 148.5, 138.1, 135.6, 135.4, 134.2, 132.3, 128.8, 127.9, 127.7, 126.3, 125.3, 125.2, 124.8, 117.8, 116.2, 116.1, 114.5 ppm; IR (KBr): ν 3743, 3672, 3105, 2924, 2854, 2349, 2308, 1651, 1597, 1523, 1442, 1404, 1342, 1309, 1269, 1213, 1186, 1136, 1105, 1058, 985, 900, 850, 815, 777 cm^{-1}; HRMS (ESI) calcd for $C_{15}H_8BrNO_4$ ($[M+H]^+$) 346.9616, found 346.4251.

4.2.16. Compound ***3p***[24]. ^1H NMR ($CDCl_3$, 300 MHz) δ 8.03 (d, J=6.8 Hz, 2H, C_6H_5CO), 7.69 (s, 1H, ClC_6H_3), 7.68 (s, 1H, C_4HO), 7.62–7.65 (m, 2H, C_6H_5CO), 7.54–7.56 (m, 1H, C_6H_5CO), 7.41–7.52 (m, 2H, ClC_6H_3) ppm; ^{13}C NMR ($CDCl_3$, 75 MHz) δ 184.3, 154.2, 153.1, 136.8, 133.2, 129.6, 129.5, 128.6, 128.2, 122.6, 115.5, 113.6 ppm.

4.2.17. Compound ***3q***[24]. ^1H NMR($CDCl_3$, 300 Hz) δ 7.94 (d, J=8.0 Hz, 2H, $CH_3C_6H_4CO$), 7.67 (s, 1H, C_4HO), 7.55 (s, 1H, ClC_6H_3), 7.39–7.43 (m, 2H, ClC_6H_3), 7.31–7.34 (m, 2H, $CH_3C_6H_4CO$), 2.45 (s, 3H, $C_6H_4CH_3$) ppm; ^{13}C NMR ($CDCl_3$, 75 MHz) δ 183.5, 154.3, 153.5, 144.2, 134.2, 129.7, 129.5, 129.3, 128.5, 128.3, 122.6, 115.0, 113.6, 21.7 ppm.

4.2.18. Compound ***3r***[24]. ^1H NMR ($CDCl_3$, 300 MHz) δ 8.09 (d, J=8.16 Hz, 2H, $CH_3OC_6H_4CO$), 7.67 (s, 1H, C_4HO), 7.56 (s, 1H, ClC_6H_3), 7.40–7.44 (m, 2H, ClC_6H_3), 6.99–7.02 (m, 2H, $CH_3OC_6H_4CO$), 3.90 (s, 3H, $CH_3OC_6H_4CO$) ppm; ^{13}C NMR ($CDCl_3$, 75 MHz) δ 182.4, 163.8, 154.0, 132.0, 129.4, 128.3, 122.5, 114.5, 114.0, 113.6, 55.6 ppm.

4.2.19. Compound ***3s***[24]. ^1H NMR ($CDCl_3$, 300 MHz) δ 7.91–7.96 (m, 2H, BrC_6H_4CO), 7.70 (s, 1H, C_4HO), 7.68 (s, 1H, ClC_6H_3), 7.48–7.58 (m, 2H, BrC_6H_4CO), 7.44–7.48 (m, 2H, ClC_6H_3) ppm; ^{13}C NMR ($CDCl_3$, 75 MHz) δ 182.1, 154.5, 152.7, 150.3, 141.6, 130.5, 130.1, 129.5, 127.9, 123.8, 123.6, 122.9, 116.3, 113.7 ppm.

4.2.20. Compound ***3t***. Unknown, ^1H NMR ($CDCl_3$, 300 MHz) δ 8.40 (d, J=7.8 Hz, 2H, $NO_2C_6H_4CO$), 8.22 (d, J=7.8 Hz, 2H, $NO_2C_6H_4CO$), 7.74 (s, 1H, C_4HO), 7.60 (s, 1H, ClC_6H_3), 7.48–7.57 (m, 2H, ClC_6H_3) ppm; ^{13}C NMR ($CDCl_3$, 75 MHz) δ 182.2, 154.2, 152.8, 150.6, 141.6, 130.5, 130.3, 129.5, 127.9, 123.8, 123.6, 122.8, 116.3, 113.8 ppm; IR (KBr): ν 3670, 3136, 3103, 2920, 2850, 2349, 2308, 1732, 1645, 1598, 1523, 1454, 1340, 1309, 1263, 1184, 1134, 1103, 974, 850, 812, 775 cm^{-1}; HRMS (ESI) calcd for $C_{15}H_8ClNO_4$ ($[M+H]^+$) 301.0142, found 301.1378.

4.2.21. Compound ***3u***. Unknown, ^1H NMR ($CDCl_3$, 300 MHz) δ 8.41 (s, 1H, $NO_2C_6H_4CO$), 8.38 (d, J=8.7 Hz, 2H, $NO_2C_6H_4CO$), 8.22 (d, J=8.7 Hz, 1H, $NO_2C_6H_4CO$), 7.68–7.74 (m, 1H, ClC_6H_3), 7.57 (s, 1H, C_4HO), 7.56 (s, 1H, ClC_6H_3), 7.50–7.52 (m, 1H, ClC_6H_3) ppm; ^{13}C NMR ($CDCl_3$, 75 MHz) δ 181.5, 154.4, 152.8, 148.2, 137.8, 135.1, 129.9, 129.4, 127.9, 127.4124.5, 122.8, 116.0, 113.7 ppm; IR (KBr): ν 3672, 3134, 3089, 2956, 2924, 2850, 2349, 2320, 1651, 1612, 1537, 1521, 1471, 1440, 1361, 1317, 1215, 1190, 1138, 1093, 1062, 987, 912, 879, 710, 715 cm^{-1}; HRMS (ESI) calcd for $C_{15}H_8ClNO_4$ ($[M+H]^+$) 301.0142, found 301.1412.

4.2.22. Compound ***3v***. Unknown, ^1H NMR ($CDCl_3$, 300 MHz) δ 8.07–8.12 (m, 2H, C_6H_5CO), 7.59–7.62 (m, 2H, C_6H_5CO), 7.54–7.55 (m, 1H, C_6H_5CO), 7.52–7.53 (m, 1H, C_6H_4), 7.49–7.52 (m, 2H, C_6H_4), 7.34–7.39 (m, 1H, C_6H_4), 2.65 (s, 3H, CH_3C_4O) ppm; ^{13}C NMR ($CDCl_3$, 75 MHz) δ 185.9, 154.3, 148.3, 137.9, 132.6, 129.8, 129.2, 128.3, 128.2, 127.6, 127.5, 126.9, 123.3, 121.5, 112.3, 10.1 ppm; IR (KBr): ν 3665, 3198, 2958, 2850, 2349, 2308, 1748, 1672, 1587, 1545, 1512, 1457, 1412, 1296, 1258, 1090, 1025, 987, 875, 835, 756, 721 cm^{-1}; HRMS (ESI) calcd for $C_{16}H_{12}O_2$ ($[M+H]^+$) 237.0871, found 237.0818.

4.2.23. Compound ***3w***. Unknown, ^1H NMR ($CDCl_3$, 300 MHz) δ 8.37 (d, J=8.1, 2H, $NO_2C_6H_4CO$), 8.25 (d, J=8.1, 2H, $NO_2C_6H_4CO$),

7.73–7.76 (m, 2H, C_6H_4), 7.36–7.54 (m, 2H, C_6H_4), 2.71 (s, 3H, CH_3C_4O) ppm; ^{13}C NMR ($CDCl_3$, 75 MHz) δ 183.7, 154.5, 149.8, 142.8, 130.7, 130.2, 129.8, 129.0, 123.7, 123.5, 122.9, 122.6, 121.8, 121.5, 112.3, 10.2 ppm; IR (KBr): ν 3645, 3278, 2958, 2924, 2852, 2349, 2308, 1732, 1651, 1602, 1548, 1521, 1454, 1394, 1302, 1261, 1121, 1054, 987, 898, 848, 756 cm^{-1}; HRMS (ESI) calcd for $C_{16}H_{11}NO_4$ ($[M+H]^+$) 281.0688, found 281.0493.

4.2.24. Compound ***3x****.* Unknown, ^1H NMR ($CDCl_3$, 300 MHz) δ 7.97 (d, J=8.6, 2H, BrC_6H_4CO), 7.68–7.71 (m, 2H, BrC_6H_4CO), 7.64–7.67 (m, 1H, C_6H_4), 7.49–7.52 (m, 2H, C_6H_4), 7.25–7.34 (m, 1H, C_6H_4), 2.65 (s, 3H, CH_3C_4O) ppm; ^{13}C NMR ($CDCl_3$, 75 MHz) δ 184.6, 154.0, 151.1, 136.3, 131.6, 131.3, 128.5, 127.7, 123.5, 121.5, 112.3, 10.1 ppm; IR (KBr): ν 3645, 3194, 2962, 2916, 2850, 2349, 2308, 1732, 1651, 1587, 1556, 1504, 1454, 1394, 1296, 1263, 1070, 1012, 931, 875, 833, 742 cm^{-1}; HRMS (ESI) calcd for $C_{16}H_{11}BrO_2$ ($[M+H]^+$) 314.9976, found 315.0018.

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Supplementary data

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References and notes

1. Bevinakatti, H. S.; Badiger, V. V. *Arch. Pharm. (Weinheim)* **1981**, *314*, 162–167.
2. Ward, R. S. *Nat. Prod. Rep.* **1999**, *16*, 57–59.
3. Gangjee, A.; Devraj, R.; McGuire, J. J.; Kisliuk, R. L. *J. Med. Chem.* **1995**, *38*, 3798–3805.
4. Kozikowsky, A. P.; Ma, D.; Du, L.; Lewin, N. E.; Blumberg, P. M. *J. Am. Chem. Soc.* **1995**, *117*, 6666–6672.
5. (a) Kadieva, M. G.; Oganesyan, E. T. *Chem. Heterocycl. Compd.* **1997**, *33*, 1245–1258; (b) Xie, X.-G.; Chen, B.; Lu, J.-P.; Han, J.-J.; She, X.-G.; Pan, X.-F. *Tetrahedron Lett.* **2004**, *45*, 6235–6237; (c) Yan, Z.; Liu, H.-B.; Lee, C. M.; Chang, H.-M.; Wong, H. N. *J. Org. Chem.* **1992**, *57*, 7248–7257; (d) Katritzky, A. R.; Ji, Y.; Fang, Y.; Prakash, I. *J. Org. Chem.* **2001**, *66*, 5613–5615; (e) Hou, X.-L.; Yang, Z.; Wong, H. N. C. Furans and Benzofurans In. *Progress in Heterocyclic Chemistry*; Gribble, G. W., Gilchrist, T. L., Eds.; Pergamon: Oxford, England, 2002; Vol. 14, pp 139–179.
6. Eidamshaus, C.; Burch, D. J. *Org. Lett.* **2008**, 4211–4214.
7. Willis, M. C.; Taylor, D.; Gillmore, A. T. *Tetrahedron* **2006**, *62*, 11513–11520.
8. (a) Thielges, S.; Meddah, E.; Bisseret, P.; Eustache, J. *Tetrahedron Lett.* **2004**, *45*, 907–910; (b) Zhan, Z.-P.; Wang, S.-P.; Cai, X.-B.; Liu, H.-J.; Yu, J.-L.; Cui, Y.-Y. *Adv. Synth. Catal.* **2007**, *349*, 2097–2102.
9. (a) Cacchi, S.; Fabrizi, G.; Goggiomani, A. *Heterocycles* **2002**, *56*, 613–615; (b) Alonso, F.; Sánchez, D.; Soler, T.; Yus, M. *Adv. Synth. Catal.* **2008**, *350*, 2118–2126.
10. (a) José, B.; Henar, V.-V.; Alfredo, B.; José, M. G. *Adv. Synth. Catal.* **2005**, *347*, 526–530; (b) Xiao, Y.-J.; Zhang, J.-L. *Adv. Synth. Catal.* **2009**, *351*, 617–629.
11. Zhang, H.; Feneira, E. M.; Stoltz, B. M. *Angew. Chem., Int. Ed.* **2004**, *43*, 6144–6146.
12. (a) Colobert, F.; Castanet, A. S.; Abillard, O. *Eur. J. Org. Chem.* **2005**, 3334–3341; (b) Anderson, K. W.; Ikawa, T.; Tundel, R. E.; Buchwald, S. L. *J. Am. Chem. Soc.* **2006**, *128*, 10694–10695.
13. Yoshizawa, K.; Toyota, S.; Toda, F.; Csoregh, I. *Green Chem.* **2003**, *5*, 353–356.
14. (a) Ragnarsson, U.; Grehn, L. *Acc. Chem. Res.* **1998**, *31*, 494–501; (b) Wang, Y.-Z.; Kataeva, O.; Metz, P. *Adv. Synth. Catal.* **2009**, *351*, 2075–2080.
15. Hagiwara, H.; Inoguchi, H.; Fukushima, M.; Hoshi, T.; Suzuki, T. *Tetrahedron Lett.* **2006**, *47*, 5371–5373.
16. Zhao, G.-L.; Huang, J. W.; Shi, M. *Org. Lett.* **2003**, *24*, 4737–4739.
17. Ko, K.; Nakano, K.; Watanabe, S.; Ichikawa, Y.; Kotsuki, H. *Tetrahedron Lett.* **2009**, 4037–4041.
18. Sakakura, A.; Kawajiri, K.; Ohkubo, T.; Kosugi, Y.; Ishihara, K. *J. Am. Chem. Soc.* **2007**, *129*, 14775–14779.
19. (a) Lindström, U. M. *Chem. Rev.* **2002**, *102*, 2751–2772; (b) Li, C.-J. *Chem. Rev.* **2005**, *105*, 3095–3166.
20. (a) Berkessel, A.; Gröger, H. *Asymmetric Organocatalysis*; Wiley-VCH: New York, NY, 2005; (b) *Enantioselective Organocatalysis*; Dalko, P. I., Ed.; Wiley-VCH: New York, NY, 2007.
21. Sheldon, R. A.; Ardens, I.; Hanefeld, U. *Green Chemistry and Catalysis*; Wiley-VCH: Weinheim, Germany, 2007.
22. For the controversy regarding organocatalysis in aqueous media, see: (a) Brogan, A. P.; Dickerson, T. J.; Janda, K. D. *Angew. Chem., Int. Ed.* **2006**, *45*, 8100–8102; (b) Hayashi, Y. *Angew. Chem., Int. Ed.* **2006**, *45*, 8103–8104; (c) Blackmond, D. G.; Armstrong, A.; Coombe, V.; Wells, A. *Angew. Chem., Int. Ed.* **2007**, *46*, 3798–3800.
23. Shang, Y.-J.; He, X.-W.; Hu, J.-S.; Wu, J.-W.; Zhang, M.; Yu, S.-Y.; Zhang, Q.-Q. *Adv. Synth. Catal.* **2009**, *351*, 2709–2713.
24. Rao, M. L.; Awasthi, D. K.; Banerjee, B. *Tetrahedron Lett.* **2007**, *48*, 431–434.
25. (a) Anniina, E.; Inkeri, M.; Petri, M. P. *Chem. Rev.* **2007**, *107*, 5416–5470; (b) Anniina, E.; Petri, M. P. *J. Org. Chem.* **2006**, *71*, 2538–2541; (c) Mauro, M.; Johan, F.; Thomas, B. P.; Wei, Z.; Karl, A. J. *J. Am. Chem. Soc.* **2005**, *127*, 6964–6965; (d) Constantinos, R.; William, D. W. *J. Am. Chem. Soc.* **2008**, *130*, 13524–13525.
26. Korthals, K. A.; Wulff, W. D. *J. Am. Chem. Soc.* **2008**, *130*, 2898–2899.
27. Chen, T.; Jiang, J.-J.; Xu, Q.; Shi, M. *Org. Lett.* **2007**, *9*, 865–868.