JOC The Journal of Organic Chemistry

Article

pubs.acs.org/joc

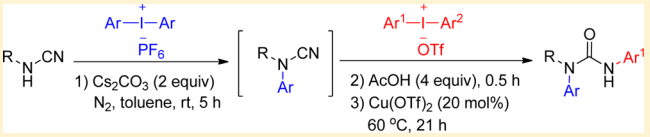
Copper-Catalyzed One-Pot Synthesis of Unsymmetrical Arylurea Derivatives via Tandem Reaction of Diaryliodonium Salts with *N*-Arylcyanamide

Pengfei Li, Guolin Cheng,* Hong Zhang, Xianxiang Xu, Jingyuan Gao, and Xiuling Cui*

Key Laboratory of Xiamen Marine and Gene Drugs, Institutes of Molecular Medicine and School of Biomedical Sciences, Huaqiao University & Engineering Research Center of Molecular Medicine, Ministry of Education, Xiamen 361021, China

Supporting Information

ABSTRACT: An efficient "one-pot" approach to multiple substituted ureas from *N*-arylcyanamide and diaryliodonium salts has been presented. The two-step procedure involved the weak base-promoted chemoselective arylation of secondary amines with diaryliodonium and Cu-catalyzed nucleophilic addition of *N*-arylcyanamide with second diaryliodonium. The diverse unsymmetrical arylureas were obtained in up to 91% yield for 29 examples.

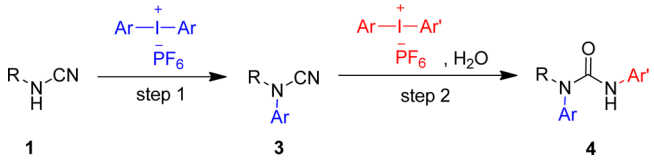


INTRODUCTION

Arylureas are present in natural products and bioactive compounds[1] and have found myriad applications in dyes, pharmaceutics, and industrial chemistry.[2] In particular, some arylureas have been shown a marked inhibiting effect on HIV protease enzyme.[3] Therefore, numerous methods have been developed for building such a structure. Conventionally, phosgene and its derivatives have been used as starting materials.[4] However, the preparation and use of phosgenes usually generates excessive toxicological and environmental waste. The transition-metal-catalyzed reaction of amines with CO as the carbonyl source in the presence of an oxidant have shown an alternative procedure to the ureas.[5] This procedure is limited to the primary arylamines since secondary amines produced formamides.[6] *N*-Aryl- and *N*-heteroarylureas were usually prepared by the reaction of arylamines with isocyanates.[7] The instability of the isocyanates led to the desired products in low yields.[8] From the point of green chemistry and broad generality, the development of an efficient and mild protocol to multiply aryl-substituted ureas from the easily handled starting materials is highly desired.

Diaryliodonium salts have recently gained considerable attention as mild, selective, and environmentally benign regents in organic synthesis.[9,10] Herein we envisioned that triaryl-substituted ureas could be prepared from *N*-arylcyanamides[11] with two different diaryliodonium salts in a "one-pot" manner (Scheme 1).

Scheme 1



RESULTS AND DISCUSSION

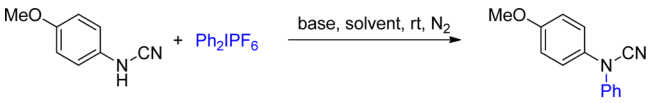
At the outset of the study, the reaction of **1a** and **2a** afforded *N*-(4-methoxyphenyl)cyanamide **3a** in 93% yield in the presence of 3 equiv of K_2CO_3 in DCE at room temperature under N_2 for 5 h (Table 1, entry 1). Inspired by this result, we next screened the solvents, base, temperature, and loading of the reagents to optimize the reaction conditions. First, various solvents were screened at room temperature in the presence of K_2CO_3. When toluene was used as the solvent, the desired product was obtained in 94% yield (Table 1, entry 5). Other solvents (e.g., DMF, DMSO, and 1,4-dioxane) afforded lower yields (Table 1, entries 2−4). We then investigated the influence of the bases. When other bases, such as Na_2CO_3, Li_2CO_3, *t*-BuOLi, and Cs_2CO_3, were used in place of K_2CO_3, Cs_2CO_3 could afford the desired product in 97% yield (Table 1, entry 9). When the amount of base was decreased to 2 and 1.5 equiv, **3a** was provided in 95% and 89% yields, respectively (Table 1, entries 10 and 11). Elevating the reaction temperature did not significantly improve this transformation (Table 1, entry 12). Compound **3a** was not obtained in the air (Table 1, entry 13) since *NH* in *N*-(4-methoxyphenyl)cyanamide might be oxidized by O_2 in the air. The reaction could not proceed well in the absence of base (Table 1, entry 14). The optimized reaction conditions were identified as follows: **1a** (0.5 mmol), **2a** (0.5 mmol), Cs_2CO_3 (2 equiv), toluene (1 mL), room temperature, N_2 atmosphere.

Next, the condensation of **2a** with isolated **3a** was chosen as a model reaction to screen the second reaction parameters (shown in Table 2). When DMSO was used as solvent with $Cu(OTf)_2$ as a catalyst and H_2O as additive, the product **4a** was obtained in 24% yield (Table 2, entry 1). Other polar solvents, such as DMF, 1,4-dioxane, and MeCN, were also ineffective

Received: June 19, 2014
Published: August 10, 2014

dx.doi.org/10.1021/jo501334u | J. Org. Chem. 2014, 79, 8156−8162

Table 1. Optimizing the Reaction Conditions for Arylation of Secondary Amines[a]

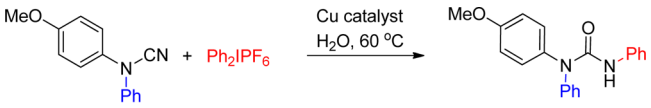


1a 2a 3a

entry	solvent	base	time (h)	yield (%)
1	DCE	K_2CO_3	5	93
2	DMF	K_2CO_3	5	89
3	DMSO	K_2CO_3	5	78
4	1,4-dioxane	K_2CO_3	5	85
5	toluene	K_2CO_3	5	94
6	toluene	Na_2CO_3	5	89
7	toluene	Li_2CO_3	5	trace
8	toluene	*t*-BuOLi	5	62
9	toluene	Cs_2CO_3	5	97
10[b]	toluene	Cs_2CO_3	5	95
11[c]	toluene	Cs_2CO_3	5	89
12[d]	toluene	Cs_2CO_3	4	98
13[e]	toluene	Cs_2CO_3	>24	oxidation
14	toluene		>24	NR

[a]Reaction conditions: **1a** (0.5 mmol), **2a** (0.5 mmol), base (3 equiv), solvent (1 mL) under N_2 at room temperature. NR = no reaction. [b]Cs_2CO_3 (2 equiv). [c]Cs_2CO_3 (1.5 equiv). [d]60 °C. [e]Under air.

Table 2. Optimizing the Reaction Conditions for Arylation of Nitrile[a]



3a 2a 4a

entry	catalyst	solvent	time (h)	yield (%)
1	$Cu(OTf)_2$	DMSO	22	24
2	$Cu(OTf)_2$	DMF	23	27
3	$Cu(OTf)_2$	MeCN	18	19
4	$Cu(OTf)_2$	1,4-dioxane	>24	15
5	$Cu(OTf)_2$	DCE	25	76
6	$Cu(OTf)_2$	toluene	20	77
7	$Cu(OAc)_2$	toluene	>24	NR
8	$CuBr_2$	toluene	>24	NR
9	CuCN	toluene	>24	37
10	$Cu(TFA)_2$	toluene	>24	43
11	CuBr	toluene	23	55
12	CuI	toluene	22	72
13	CuOTf	toluene	22	73
14[b]	$Cu(OTf)_2$	toluene	19	90
15[c]	$Cu(OTf)_2$	toluene	19	86
16[b,d]	$Cu(OTf)_2$	toluene	22	68
17[b,e]	$Cu(OTf)_2$	toluene	17	49
18[b,f]	$Cu(OTf)_2$	toluene	20	77
19[b,g]	$Cu(OTf)_2$	toluene	20	83
20[b]		toluene	>48	NR
21[h]		toluene	>48	NR
22[b,i]	$Cu(OTf)_2$	toluene	>48	NR
23[b,j]	$Cu(OTf)_2$	toluene	19	89

[a]Reaction conditions: **3a** (0.5 mmol), **2a** (0.5 mmol), H_2O (1 equiv), Cu catalyst (0.1 mmol), toluene (1 mL), under air, NR = no reaction. [b]**2a** (0.6 mmol). [c]**2a** (0.7 mmol). [d]Under N_2. [e]90 °C. [f]50 °C. [g]$Cu(OTf)_2$ (0.05 mmol). [h]120 °C. [i]1 equiv of Cs_2CO_3. [j]1 equiv of AcOH.

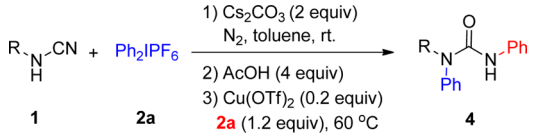
(Table 2, entries 2–4). When this reaction was conducted in DCE and toluene, the desired product was obtained in 76% and 77% yields, respectively (Table 2, entries 5 and 6). Compared to toluene, the waste from halide compounds was difficult to handle. Moreover, the arylation of secondary amines with diaryliodonium salt could proceed well in toluene. Therefore, toluene was chosen as solvent for the second step. Then various copper salts were examined in toluene at 60 °C. No desired product was obtained in the presence of $Cu(OAc)_2$ and $CuBr_2$ (Table 2, entries 7 and 8). When CuCN, $Cu(TFA)_2$, CuBr, CuI, and CuOTf were used as the catalysts, the reaction gave **4a** in 37%, 43%, 55%, 72%, and 73% yields, respectively (Table 2, entries 9–13). $Cu(OTf)_2$ provided the desired product **4a** in 77% yield (Table 2, entry 6). Increasing the loading of **2a** from 0.5 to 0.6 mmol resulted in a higher yield (90%) (Table 2, entry 14). The yield was not improved by increasing the loading of **2a** from 0.6 to 0.7 mmol (Table 2, entry 15), and the reaction under N_2 atmosphere gave lower yield (Table 2, entry 16). Different temperatures were also examined (Table 2, entries 17 and 18). The best result was obtained at 60 °C. The yield of product decreased when the loading of $Cu(OTf)_2$ was reduced (Table 2, entry 19). No reaction was observed in the absence of $Cu(OTf)_2$ (Table 2, entry 20), even when the reaction was carried out at 120 °C (Table 2, entry 21). Considering that the reaction was completely inhibited by base (Table 2, entry 22), and not obviously affected by acid (Table 2, entry 23), a "one-pot" approach to arylureas **4** directed from *N*-arylcyanamide **1** without isolating the intermediates **3** was carried out. When the reaction of **1** with **2** was finished completely, AcOH was added dropwise to neutralize the base and provided enough H_2O to the reaction. Then, the resulting reaction mixture was treated with $Cu(OTf)_2$ and 1.2 equiv of a second diaryliodonium salt **2** and gave **4a** in 89% yield.

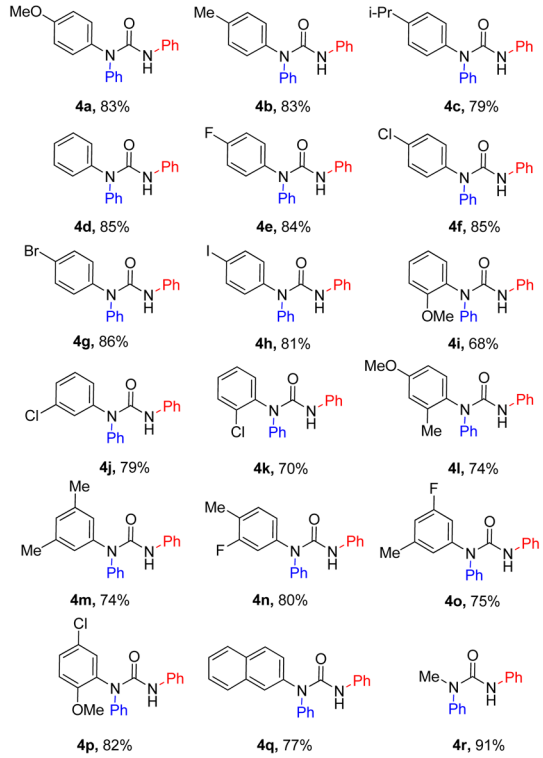
The generality and scope of *N*-arylcyanamide derivatives **1** were explored under the optimal reaction conditions as shown in Table 3. The electronic effects of the substituent at the *N*-arylcyanamide did not affect the reaction significantly. *N*-Arylcyanamide with both electron-donating groups, such as −OMe, −Me, −*i*-Pr, and electron-withdrawing groups, such as −F, −Cl, −Br, and −I, at the *para* position of *N*-benzene performed well, giving the desired products **4a**–**h** in 79–86% yields. The slight influence of the steric hindrance on this transformation was observed. For instance, *N*-(4-chlorophenyl)cyanamide, *N*-(3-chlorophenyl)cyanamide, and *N*-(2-chlorophenyl)cyanamide afforded the corresponding products in 85%, 79%, and 70% yields, respectively (**4f**, **4j**, **4k**). *N*-(2-Methoxyphenyl)cyanamide gave a lower yield than *N*-(4-methoxyphenyl)cyanamide (**4i** vs **4a**), and polysubstituted *N*-arylcyanamide derivatives containing electron-donating or electron-withdrawing groups in the aryl ring provided the corresponding arylureas in good yields (Table 3, **4l**–**p**). Interestingly, *N*-(naphthalen-2-yl)cyanamide was also applicable to this reaction system and gave the product **4q** in 77% yield. *N*-Methylcyanamide was compatible with the reaction conditions and gave the product in 91% yield (Table 3, **4r**).

Next, we explored the generality and scope of diaryliodonium salts **2**.[12] As shown in Table 4, we found that the electronic effect of the substituent on this reaction was also not significant. The diaryliodonium salts containing electron-withdrawing groups such as −Br, −I, $-CF_3$, and $-NO_2$ in the *para* or *meta* positions of the aryl moiety were efficiently coupled with the *N*-(4-methoxyphenyl)cyanamide, producing the corresponding desired products with 70–88% yields (Table 4,

dx.doi.org/10.1021/jo501334u | J. Org. Chem. 2014, 79, 8156–8162

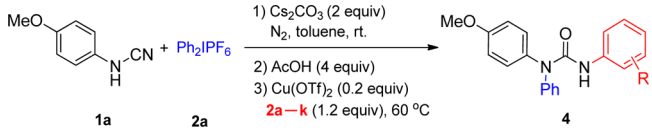
Table 3. Substrate Scope: Variation of the *N*-Arylcyanamides[a]

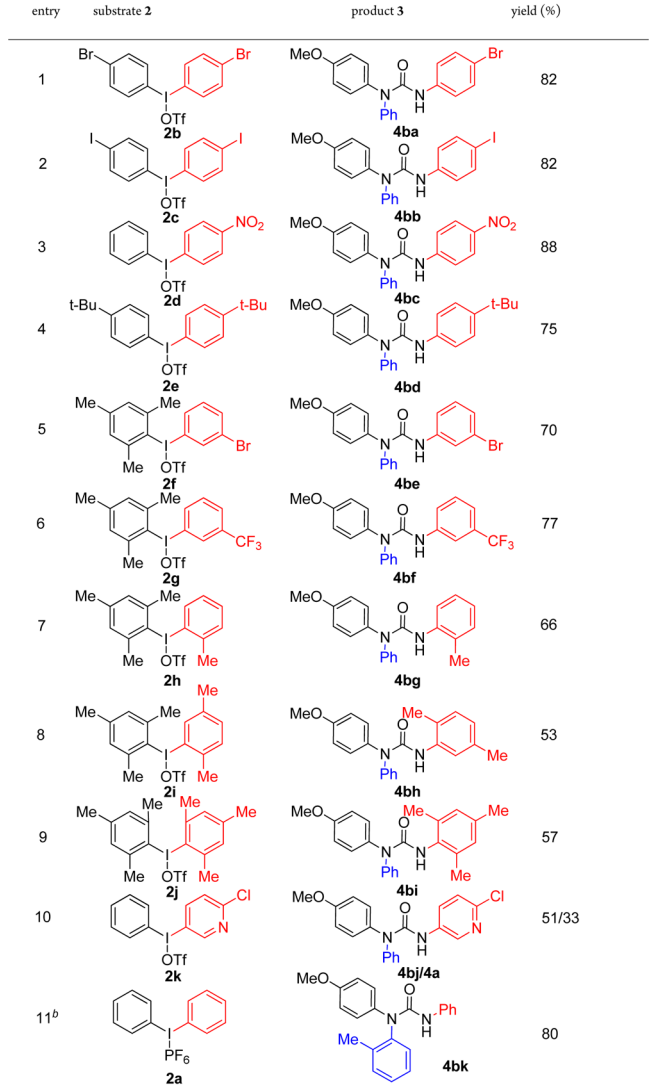




[a]Reaction conditions: first step, **1** (0.5 mmol), **2a** (0.5 mmol), Cs_2CO_3 (2 equiv) in toluene (1 mL) under N_2 at room temperature for 5 h; second step, AcOH (4 equiv), 30 min; third step, **2a** (0.6 mmol), $Cu(OTf)_2$ (0.2 equiv) at 60 °C for 21 h.

Table 4. Substrate Scope: Variation of the Diaryliodonium Salts[a]





[a]Reaction conditions: first step, **1** (0.5 mmol), **2a** (0.5 mmol), Cs_2CO_3 (2 equiv) in toluene (1 mL) under N_2 at room temperature for 5 h; second step, AcOH (4 equiv), 30 min; thrid step, **2a**–**k** (0.6 mmol), $Cu(OTf)_2$ (0.2 equiv) at 60 °C for 21 h. [b]First step, **2h** alternative **2a**.

entries 1–5). The diaryliodonium salts with electron-donating groups provided **4bf** in 77% yield (Table 4, entry 6). However, the steric hindrance of diaryliodonium salts affected this reaction slightly. Compounds **4bg**, **4bh**, and **4bi** were obtained in 66%, 53%, and 57% yields, respectively. It was valuable to note that only one aryl group was transferred preferentially in case of unsymmetrical iodonium salts, such as **2f**, **2h**, **2i**, and **2j**. A heteroaryl group, such as pyridyl, could be tolerated. However, the chemoselectivity was poor. Mixtures of **4bj** and **4a** were obtained and isolated in 51% and 33% yields, respectively. When unsymmetrical iodonium salt (**2h**) was used in the first step, **4bk** was obtained in good yield (Table 4, entry 11).

Finally, a gram experiment with 14 mmol (2.07 g) of **1a**, 30.8 mmol (13.12 g) of **2a**, 28 mmol (9.12 g) of Cs_2CO_3, 56 mmol (3.36 g) of AcOH, and toluene (40 mL) was employed. Compound **4a** was obtained in 69% yield. Iodobenzene (yellow oil) was obtained in 77% yield (4.84 g).

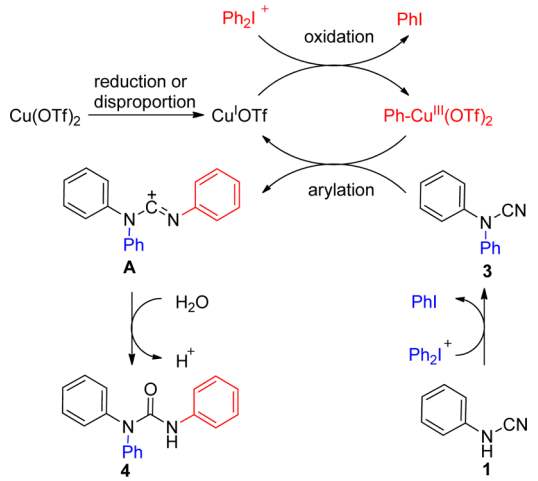
According to the literature and the results obtained above,[10,13] a plausible reaction mechanism was proposed and is shown in Scheme 2. Initially, Cs_2CO_3-promoted *N*-arylation of *N*-phenylcyanamide with 1 equiv of diaryliodonium salts gave the intermediate **3**, and $Cu(OTf)_2$ was converted into Cu(I)OTf by either a reduction or disproportion. Oxidative addition to the Cu(I)OTf species by the diaryliodonium salt gave a Ph–Cu(III) species, which transferred the aryl group to the cyano of the *N*,*N*-diphenylcyanamide to produce intermediate **A**, which generated the *N*,*N*,*N*′-triphenylurea **4** as the desired product by hydrolysis. In this process, the Cu(I)OTf was regenerated for the next cycle.

CONCLUSION

In summary, we have presented an efficient, operationally simple and chemoselective protocol to synthesize triarylurea derivatives using *N*-arylcyanamide and two different diaryliodonium salts as starting materials in a "one-pot" process. In

dx.doi.org/10.1021/jo501334u | J. Org. Chem. 2014, 79, 8156–8162

Scheme 2. Proposed Mechanism



comparison to the methods reported in the literature using isocyanates and phosgene as starting reagents, diaryliodonium salts are more stable, easy handle, and beneficial to the environment, which made this protocol more attractive and highly practical for the synthesis of the fundamentally important arylurea derivatives.

EXPERIMENTAL SECTION

General Methods. All commercial materials and solvents were used directly without further purification. Melting points were determined on a melting point apparatus and were uncorrected. ^{1}H and ^{13}C{^{1}H} NMR spectra were measured on a 400 MHz spectrometer (^{1}H 400 MHz, ^{13}C 100 MHz) using $CDCl_3$ as the solvent with tetramethylsilane (TMS) as the internal standard at room temperature. HRMS ESI spectra were obtained on Q-TOF spectrometer.

Preparation of *N*-Arylcyanamide 1. Aniline (10 mmol, 46.6 mg/mL, 1 equiv) and $NaHCO_3$ (35 mmol, 147.02 mg/mL, 3.5 equiv) were added in 20 mL of toluene with cyanogen bromide (20 mmol, 105.92 mg/mL, 2 equiv) under N_2. The mixture was stirred for 3 h at room temperature, quenched with water, and extracted with EtOAc (3 × 40 mL). The organic layers were combined, washed with H_2O and brine, dried by $MgSO_4$, and concentrated under reduced pressure to give a residue, which was purified by flash chromatography (SiO_2, eluent: DCM/heptane = 1/1).

Preparation of Diaryliodonium Salts 2. 3-Chloroperoxybenzoic acid (65%, 660 mg, 2.6 mmol) and aryl iodide were dissolved in CH_2Cl_2 (10 mL) in a sealed tube. The arene (2.6 mmol) was added. The solution was cooled to 0 °C, and then TfOH was added dropwise. The reaction was stirred at the indicated temperature for 0.2−22 h. The solvent was concentrated under vacuum. Et_2O (10 mL) was added, and the mixture was stirred at room temperature for 10 min to precipitate out an off-white solid. To ensure complete precipitation, the flask was stored in the freezer for 30 min before the solid was filtered off, washed with Et_2O, and dried under vacuum to give diaryliodonium salts **2**.

Preparation of N,N,N′-Triphenylurea **4.** A mixture of diaryliodonium salts **2** (0.5 mmol, 213 mg/mL, 1 equiv), *N*-phenylcyanamide **1** (0.5 mmol, 74 mg/mL, 1 equiv), and Cs_2CO_3 (1 mmol, 325.8 mg/mL, 2 equiv) in toluene (1 mL) were stirred at room temperature in a glass flask under N_2 atmosphere for 5 h. Then AcOH (2 mmol, 120.1 mg/mL, 4 equiv) was added dropwise and the mixture stirred for 30 min. Cs_2CO_3 was neutralized. The second diaryliodonium salts **2** (0.6 mmol, 255.6 mg/mL, 1.2 equiv) and $Cu(OTf)_2$ (0.1 mmol, 36.2 mg/mL, 0.2 equiv) were added. The resulting mixture was stirred at 60 °C for 21 h. After the reaction was complete (monitored by TLC), the solvent was evaporated and the residue was purified by chromatography (silica gel, eluent: EtOAc/PE = 1/15) to give **4**.

*1-(1-Methoxyphenyl)-1,3-diphenylurea (**4a**):* 130 mg (83%); white solid; mp 111−112 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37−7.32 (m, 6H), 7.27 (ddd, J = 16.9, 8.2, 5.3 Hz, 5H), 7.03 (d, J = 7.3 Hz, 1H), 6.96−6.93 (m, 2H), 6.45 (s, 1H), 3.83 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 158.5, 153.7, 142.7, 138.6, 134.8, 129.3, 126.7, 126.0, 123.2, 119.3, 115.1, 77.3, 77.0, 76.7, 55.5; HRMS (ESI) m/z calcd for $C_{20}H_{18}N_2O_2$ $[M + H]^+$ 319.1447, found 319.1443; IR (KBr) cm^{-1} 2958, 1684, 1597, 1507, 1440, 1315, 1242, 1031, 753, 695.

*1,3-Diphenyl-1-(p-tolyl)urea (**4b**):* 126 mg (83%); white solid; mp 131−132 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38−7.32 (m, 6H), 7.28−7.22 (m, 7H), 7.04−7.00 (m, 1H), 6.47 (s, 1H), 2.38 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 153.6, 142.6, 139.6, 138.5, 137.0, 130.4, 129.3, 128.8, 127.7, 127.0, 126.2, 123.2, 119.3, 77.3, 77.0, 76.7, 21.0; HRMS (ESI) m/z calcd for $C_{20}H_{18}N_2O$ $[M + H]^+$ 303.1497, found 303.1495; IR (KBr) cm^{-1} 1681, 1598, 1523, 1493, 1439, 1318, 1297, 1232, 755, 695.

*1-(4-Isopropylphenyl)-1,3-diphenylurea (**4c**):* 132 mg (79%); yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39−7.32 (m, 6H), 7.28−7.23 (m, 7H), 7.02 (s, 1H), 6.46 (s, 1H), 2.93 (s, 1H), 1.27 (d, J = 6.9 Hz, 6H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 153.6, 147.7, 142.5, 139.7, 138.6, 129.4, 128.8, 127.6, 127.2, 126.3, 123.2, 119.3, 77.3, 77.0, 76.7, 33.7, 23.9; HRMS (ESI): m/z calcd for $C_{22}H_{22}N_2O$ $[M + H]^+$ 331.1810, found 331.1809; IR (KBr) cm^{-1} 2960, 1687, 1597, 1522, 1440, 1315, 1234, 750, 694.

*1,1,3-Triphenylurea (**4d**):*[14] 98 mg (85%); white solid; mp133−136 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.42−7.38 (m, 5H), 7.35 (d, J = 1.5 Hz, 3H), 7.32 (d, J = 1.2 Hz, 2H), 7.28−7.26 (m, 5H), 6.44 (s, 1H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 153.5, 142.3, 138.4, 129.6, 128.9, 127.5, 126.6, 123.3, 119.3, 77.3, 77.0, 76.7; IR (KBr) cm^{-1} 2922, 1678, 1594, 1516, 1489, 1438, 1326, 1229, 1025, 758, 703, 567.

*1-(4-Fluorophenyl)-1,3-diphenylurea (**4e**):* 132 mg (84%); white solid; mp 112−114 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.42 (dd, J = 10.5, 5.0 Hz, 2H), 7.35−7.29 (m, 7H), 7.25 (t, J = 4.2 Hz, 2H), 7.09−7.01 (m, 3H), 6.42 (s, 1H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 162.1, 159.6, 153.5, 142.1, 138.3 (d, J = 8.9 Hz), 129.9, 129.1, 129.0, 128.9, 127.6, 127.1, 123.4, 119.4, 116.4, 116.2, 77.3, 77.0, 76.7; HRMS (ESI) m/z calcd for $C_{19}H_{15}FN_2O$ $[M + H]^+$ 307.1247, found 307.1247; IR (KBr) cm^{-1} 3245, 1661, 1596, 1528, 1503, 1440, 1324, 754, 693.

*1-(4-Chlorophenyl)-1,3-diphenylurea (**4f**):* 137 mg (85%); white solid; mp 145−146 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.49−7.42 (m, 4H), 7.34−7.31 (m, 4H), 7.29−7.24 (m, 3H), 7.20−7.16 (m, 2H), 7.04 (dd, J = 7.7, 6.8 Hz, 1H), 6.41 (s, 1H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 153.3, 141.8, 141.1, 138.2, 131.6, 130.1, 129.4, 128.9, 128.0, 127.5, 123.5, 119.5, 77.3, 77.0, 76.7; HRMS (ESI) m/z calcd for $C_{19}H_{15}ClN_2O$ $[M + H]^+$ 323.0951, found 323.0948; IR (KBr) cm^{-1} 3242, 1663, 1596, 1532, 1489, 1440, 1325, 691, 672, 653.

*1-(4-Bromophenyl)-1,3-diphenylurea (**4g**):* 157 mg (86%); yellow solid; mp 146−148 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.49−7.42 (m, 4H), 7.34−7.31 (m, 4H), 7.29−7.24 (m, 3H), 7.20−7.16 (m, 2H), 7.04 (dd, J = 7.7, 6.8 Hz, 1H), 6.41 (s, 1H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 153.2, 141.7, 138.2, 132.3, 130.1, 128.9, 128.3, 128.0, 127.5, 123.6, 119.4, 77.3, 77.0, 76.7; HRMS (ESI): m/z calcd for $C_{19}H_{15}BrN_2O$ $[M + H]^+$ 367.0446, found 367.0440; IR (KBr) cm^{-1} 3239, 2923, 1663, 1596, 1531, 1487, 1440, 1326, 1277, 1245, 755, 694.

*1-(4-Iodophenyl)-1,3-diphenylurea (**4h**):* 172 mg (81%); white solid; mp 151−153 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.47−7.42 (m, 2H), 7.36−7.23 (m, 9H), 7.07−7.03 (m, 3H), 6.42 (s, 1H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 153.2, 142.5, 141.6, 138.3, 138.2, 130.1, 128.9, 128.5, 128.1, 127.6, 123.6, 119.5, 90.4, 77.3, 77.0, 76.7; HRMS (ESI) m/z calcd for $C_{19}H_{15}IN_2O$ $[M + H]^+$ 415.0307, found 415.0304; IR (KBr) cm^{-1} 2921, 1662, 1596, 1528, 1485, 1440, 1325, 1247, 756, 693.

*1-(2-Methoxyphenyl)-1,3-diphenylurea (**4i**):* 111 mg (68%); yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36−7.31 (m, 8H), 7.24 (dd, J = 11.0, 4.9 Hz, 3H), 7.04−6.98 (m, 3H), 6.44 (s, 1H), 3.83 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 156.1, 153.8, 142.4, 138.8, 130.9, 130.6, 129.6, 129.0, 128.8, 126.5, 125.9, 123.0, 121.5, 119.3,

dx.doi.org/10.1021/jo501334u | J. Org. Chem. 2014, 79, 8156−8162

112.6, 77.3, 77.0, 76.7, 55.9; HRMS (ESI) m/z calcd for $C_{20}H_{18}N_2O_2$ $[M + H]^+$ 319.1447, found 319.1443; IR (KBr) cm^{-1} 2918, 2849, 1686, 1595, 1522, 1497, 1440, 1313, 1275, 1235, 1026, 753, 693.

*1-(3-Chlorophenyl)-1,3-diphenylurea (**4j**):* 124 mg (79%); orange solid; mp 123−125 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 7.46 (dt, J = 9.6, 2.1 Hz, 2H), 7.39−7.30 (m, 6H), 7.30−7.24 (m, 3H), 7.19 (dddd, J = 7.7, 6.7, 1.9, 1.1 Hz, 2H), 7.07−7.02 (m, 1H), 6.42 (s, 1H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 153.2, 143.8, 141.5, 138.2, 134.7, 130.1, 128.9, 128.2, 127.7, 126.8, 126.0, 124.7, 123.6, 119.5, 77.3, 77.0, 76.7; HRMS (ESI) m/z calcd for $C_{19}H_{15}ClN_2O$ $[M + H]^+$ 323.0951, found 323.0948; IR (KBr) cm^{-1} 3246, 2921, 1664, 1594, 1531, 1442, 1321, 1244, 1092, 1029, 756, 690.

*1-(2-Chlorophenyl)-1,3-diphenylurea (**4k**):* 117 mg (70%); yellow solid; mp 121−123 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 7.43−7.41 (m, 1H), 7.39−7.34 (m, 8H), 7.29−7.24 (m, 4H), 7.04 (t, J = 7.4 Hz, 1H), 6.45 (s, 1H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 152.9, 141.6, 139.5, 138.3, 134.0, 131.2, 131.0, 129.5, 129.2, 128.9, 128.2, 126.6, 123.4, 119.5, 77.3, 77.0, 76.7; HRMS (ESI) m/z calcd for $C_{19}H_{15}ClN_2O$ $[M + H]^+$ 323.0951, found 323.0949; IR (KBr) cm^{-1} 3248, 1672, 1597, 1531, 1496, 1441, 1326, 1248, 1030, 751, 692.

*1-(4-Methoxy-2-methylphenyl)-1,3-diphenylurea (**4l**):* 124 mg (74%); yellow oil; ^1H NMR (400 MHz, $CDCl_3$) δ 7.33 (dd, J = 8.6, 1.2 Hz, 2H), 7.30−7.25 (m, 8H), 7.03 (d, J = 7.3 Hz, 1H), 6.87 (t, J = 3.4 Hz, 2H), 6.38 (s, 1H), 3.84 (s, 3H), 2.25 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 159.5, 153.6, 142.2, 138.8, 138.6, 132.6, 130.9, 128.9, 128.8, 124.8, 124.7, 123.2, 119.4, 117.0, 113.1, 77.3, 77.0, 76.7, 55.5, 18.2; HRMS (ESI) m/z calcd for $C_{21}H_{20}N_2O_2$ $[M + H]^+$ 333.1603, found 333.1601; IR (KBr) cm^{-1} 2923, 1686, 1598, 1520, 1497, 1439, 1312, 1294, 1233, 753, 693.

*1-(3,5-Dimethylphenyl)-1,3-diphenylurea (**4m**):* 117 mg (74%); white solid; mp 102−104 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 7.40−7.32 (m, 6H), 7.25 (dd, J = 12.9, 4.8 Hz, 3H), 7.02 (t, J = 7.3 Hz, 1H), 6.97 (s, 2H), 6.94 (s, 1H), 6.46 (s, 1H), 2.31 (s, 6H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 153.6, 142.6, 141.9, 139.5, 138.6, 129.3, 128.9, 127.1, 126.2, 125.6, 123.1, 119.3, 77.3, 77.0, 76.7, 21.2; HRMS (ESI) m/z calcd for $C_{21}H_{20}N_2O$ $[M + H]^+$ 317.1654, found 317.1654; IR (KBr) cm^{-1} 3294, 2959, 2922, 1664, 1594, 1523, 1495, 1440, 1316, 1293, 1239, 754, 694.

*1-(3-Fluoro-4-methylphenyl)-1,3-diphenylurea (**4n**):* 130 mg (80%); yellow solid; mp 97−99 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 7.42 (tt, J = 4.2, 1.9 Hz, 2H), 7.34−7.31 (m, 4H), 7.29−7.24 (m, 3H), 7.17 (t, J = 8.4 Hz, 1H), 7.05−6.98 (m, 3H), 6.43 (s, 1H), 2.26 (d, J = 1.8 Hz, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 162.4, 160.0, 153.3, 141.9, 138.3, 131.7 (d, J = 6.2 Hz), 129.9, 128.9, 127.7, 127.2, 123.4 (d, J = 17.1 Hz), 122.4, 119.4, 114.1, 113.9, 77.3, 77.0, 76.7, 14.2; HRMS (ESI) m/z calcd for $C_{20}H_{17}FN_2O$ $[M + H]^+$ 321.1403, found 321.1402; IR (KBr) cm^{-1} 2920, 1663, 1596, 1532, 1502, 1441, 1323, 1245, 757, 695.

*1-(3-Fluoro-5-methylphenyl)-1,3-diphenylurea (**4o**):* 118 mg (75%); white solid; mp 131−132 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 7.47−7.42 (m, 2H), 7.36−7.31 (m, 5H), 7.29−7.24 (m, 2H), 7.06−7.02 (m, 1H), 6.94 (s, 1H), 6.82 (dt, J = 9.9, 2.1 Hz, 1H), 6.75 (d, J = 9.2 Hz, 1H), 6.42 (s, 1H), 2.32 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 164.1, 161.6, 153.3, 143.6 (d, J = 10.5 Hz), 141.8, 141.0 (d, J = 9.0 Hz), 138.2, 130.0, 128.9, 128.0, 127.4, 123.5, 123.1 (d, J = 2.5 Hz), 119.5, 114.0, 113.7, 111.4, 111.1, 77.3, 77.0, 76.7, 21.4; HRMS (ESI) m/z calcd for $C_{20}H_{17}FN_2O$ $[M + H]^+$ 321.1403, found 321.1402; IR (KBr) cm^{-1} 2924, 1663, 1618, 1595, 1531, 1496, 1443, 1322, 1288, 1243, 757, 693.

*1-(5-Chloro-2-methoxyphenyl)-1,3-diphenylurea (**4p**):* 146 mg (82%); yellow oil; ^1H NMR (400 MHz, $CDCl_3$) δ 7.38−7.32 (m, 6H), 7.30 (t, J = 2.4 Hz, 1H), 7.27−7.23 (m, 4H), 7.03 (d, J = 7.3 Hz, 1H), 6.93 (d, J = 8.6 Hz, 1H), 6.45 (s, 1H), 3.83 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 154.8, 153.4, 141.9, 138.5, 131.9, 130.4, 129.5, 129.0, 128.9, 127.0, 126.8, 125.7, 123.2, 119.3, 113.5, 77.3, 77.0, 76.7, 56.2; HRMS (ESI) m/z calcd for $C_{20}H_{17}ClN_2O_2$ $[M + H]^+$ 353.1057, found 353.1055; IR (KBr) cm^{-1} 2919, 1684, 1597, 1524, 1495, 1440, 1285, 1237, 1026, 752, 696.

*1-(Naphthalen-2-yl)-1,3-diphenylurea (**4q**):* 127 mg (77%); yellow solid; mp 121−123 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 7.89−7.83 (m, 2H), 7.79−7.75 (m, 2H), 7.51−7.48 (m, 2H), 7.42−7.33 (m, 6H), 7.31−7.24 (m, 4H), 7.03 (t, J = 7.3 Hz, 1H), 6.55 (s, 1H); $^{13}C\{^1H\}$NMR (100 MHz, $CDCl_3$) δ 153.6, 142.4, 139.8, 138.4, 133.8, 131.8, 129.6, 128.9, 127.9, 127.3, 126.7, 126.3, 125.8, 125.6, 123.3, 119.4, 77.3, 77.0, 76.7; HRMS (ESI) m/z calcd for $C_{23}H_{18}N_2O$ $[M + H]^+$ 339.1497, found 339.1496; IR (KBr) cm^{-1} 3055, 2923, 1663, 1595, 1526, 1495, 1440, 1316, 1240, 752, 694, 670.

*1-Methyl-1,3-diphenylurea (**4r**):* 103 mg (91%); white solid; mp 80−81 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 7.48 (dd, J = 10.5, 4.8 Hz, 2H), 7.39−7.32 (m, 3H), 7.29−7.21 (m, 4H), 7.00−6.96 (m, 1H), 6.25 (s, 1H), 3.34 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 154.4, 142.9, 138.8, 130.3, 128.7, 127.8, 127.4, 122.8, 119.2, 77.3, 77.0, 76.7, 37.2; HRMS (ESI): m/z calcd for $C_{14}H_{14}N_2O$ $[M + H]^+$ 227.1184, found 227.1184; IR (KBr) cm^{-1} 3285, 1648, 1594, 1527, 1496, 1444, 1349, 752, 698.

*3-(4-Bromophenyl)-1-(4-methoxyphenyl)-1-phenylurea (**4ba**):* 160 mg (82%); white solid; mp 148−149 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 7.37−7.34 (m, 4H), 7.32−7.28 (m, 3H), 7.26−7.22 (m, 4H), 6.95−6.93 (m, 2H), 6.45 (s, 1H), 3.82 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 158.7, 153.5, 142.5, 137.7, 134.5, 131.7, 129.3, 129.3, 126.8, 126.2, 120.8, 115.6, 115.1, 77.3, 77.0, 76.7, 55.5; HRMS (ESI) m/z calcd for $C_{20}H_{17}BrN_2O_2$ $[M + H]^+$ 397.0552, found 397.0546; IR (KBr) cm^{-1} 2962, 2923, 1661, 1588, 1513, 1489, 1393, 1310, 1243, 1098, 1034, 801, 750, 692, 667.

*3-(4-Iodophenyl)-1-(4-methoxyphenyl)-1-phenylurea (**4bb**):* 182 mg (82%); yellow solid; mp 138−140 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 7.55−7.52 (m, 2H), 7.35 (d, J = 7.2 Hz, 2H), 7.29 (dt, J = 5.9, 1.8 Hz, 4H), 7.22 (s, 1H), 7.14−7.11 (m, 2H), 6.96−6.92 (m, 2H), 6.42 (s, 1H), 3.83 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 158.7, 153.4, 138.5, 137.7, 129.4, 129.3, 126.8, 126.3, 121.1, 115.2, 77.3, 77.0, 76.7, 55.5; HRMS (ESI): m/z calcd for $C_{20}H_{17}IN_2O_2$ $[M + H]^+$ 445.0413, found 445.0410; IR (KBr) cm^{-1} 2918, 2849, 1662, 1583, 1509, 1486, 1392, 1312, 1285, 1245, 1035, 793, 752, 691, 669.

*1-(4-Methoxyphenyl)-3-(4-nitrophenyl)-1-phenylurea (**4bc**):* 161 mg (88%); yellow oil; ^1H NMR (400 MHz, $CDCl_3$) δ 7.33 (dd, J = 9.0, 4.4 Hz, 6H), 7.29 (d, J = 2.2 Hz, 1H), 7.25 (dd, J = 10.4, 6.6 Hz, 5H), 6.95−6.92 (m, 2H), 6.44 (s, 1H), 3.82 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 158.5, 153.8, 142.8, 136.0, 134.9, 132.7, 129.3, 129.2, 128.8, 126.7, 125.9, 119.4, 115.0, 77.3, 77.0, 76.7, 55.5; HRMS (ESI) m/z calcd for $C_{20}H_{17}N_3O_4$ $[M + H]^+$ 364.1297, found 364.1294; IR (KBr) cm^{-1} 3041, 2953, 2930, 1634, 1617, 1572, 1473, 1446, 1375, 1340, 1296, 1262, 1227, 1197, 1199, 1029, 795, 772, 715, 690.

*3-(4-tert-Butylphenyl)-1-(4-methoxyphenyl)-1-phenylurea (**4bd**):* 146 mg (75%); yellow oil; ^1H NMR (400 MHz, $CDCl_3$) δ 7.34(dd, J = 11.2, 2.4 Hz, 7H), 7.29−7.28 (m, 1H), 7.26 (s, 1H), 6.96−6.92 (m, 2H), 6.85 (s, 2H), 5.73 (s, 1H), 3.82 (s, 3H), 1.60 (d, J = 8.1 Hz, 9H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 158.5, 154.4, 143.2, 139.3, 135.4, 131.9, 129.4, 129.1, 128.8, 126.2, 125.5,115.0, 114.1, 77.3, 77.0, 76.7, 55.5, 33.8, 31.9; HRMS (ESI) m/z calcd for $C_{24}H_{26}N_2O_2$ $[M + H]^+$ 375.2073, found 375.2072; IR (KBr) cm^{-1} 2959, 2925, 2854, 1685, 1491, 1289, 12471032, 831, 750, 696.

*3-(3-Bromophenyl)-1-(4-methoxyphenyl)-1-phenylurea (**4be**):* 140 mg (70%); yellow oil; ^1H NMR (400 MHz, $CDCl_3$) δ 7.59 (t, J = 1.9 Hz, 1H), 7.36 (dd, J = 10.3, 5.1 Hz, 2H), 7.33−7.28 (m, 3H), 7.25 (ddd, J = 7.2, 3.8, 1.9 Hz, 3H), 7.15−7.07 (m, 2H), 6.96−6.93 (m, 2H), 6.46 (s, 1H), 3.83 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 158.7, 153.4, 142.4, 139.9, 134.4, 130.1, 129.3, 129.3, 126.7, 126.3, 126.0, 122.5, 122.0, 117.6, 115.1, 77.3, 77.0, 76.7, 55.5; HRMS (ESI) m/z calcd for $C_{20}H_{17}BrN_2O_2$ $[M + H]^+$ 397.0552, found 397.0546; IR (KBr) cm^{-1} 2920, 2850, 1725, 1679, 1586, 1509, 1480, 1417, 1292, 1245, 1031, 775, 750, 695.

*1-(4-Methoxyphenyl)-1-phenyl-3-(3-(trifluoromethyl)phenyl)urea (**4bf**):* 147 mg (77%); yellow oil; ^1H NMR (400 MHz, $CDCl_3$) δ 7.66 (s, 1H), 7.37 (dd, J = 9.1, 2.0 Hz, 3H), 7.34−7.30 (m, 3H), 7.29−7.23 (m, 4H), 6.97−6.94 (m, 2H), 6.57 (s, 1H), 3.83 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 167.7, 158.8, 153.5, 142.3, 139.1, 134.3, 130.9, 129.4 (d, J = 10.5 Hz), 128.8, 126.8, 126.4, 122.2, 119.7 (d, J = 3.7 Hz), 115.9 (d, J = 3.8 Hz), 115.2, 77.3, 77.0, 76.7, 55.5; HRMS (ESI) m/z calcd for $C_{21}H_{17}F_3N_2O_2$ $[M + H]^+$ 387.1320, found

dx.doi.org/10.1021/jo501334u | J. Org. Chem. 2014, 79, 8156−8162

387.1315; IR (KBr) cm^{-1} 2959, 2921, 1724, 1681, 1601, 1535, 1509, 1442, 1316, 1247, 1168, 1125, 794, 744, 697.

*1-(4-Methoxyphenyl)-1-phenyl-3-(o-tolyl)urea (**4bg**):* 114 mg (66%); yellow oil; ^1H NMR (400 MHz, $CDCl_3$) δ 7.98 (s, 1H), 7.37 (s, 6H), 7.14 (d, J = 51.4 Hz, 3H), 6.96 (s, 3H), 6.35 (s, 1H), 3.84 (s, 3H), 1.91 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 158.6, 153.7, 136.8, 134.8, 130.1, 129.3, 126.9, 126.7, 126.0, 123.5, 120.9, 115.1, 77.3, 77.0, 76.7, 55.5, 31.4, 17.3; HRMS (ESI) m/z calcd for $C_{21}H_{20}N_2O_2$ $[M + H]^+$ 333.1603, found 333.1601; IR (KBr) cm^{-1} 2959, 1690, 1588, 1509, 1453, 1307, 1245, 1184, 1032, 967, 752, 695.

*3-(2,5-Dimethylphenyl)-1-(4-methoxyphenyl)-1-phenylurea (**4bh**):* 92 mg (53%); yellow oil; ^1H NMR (400 MHz, $CDCl_3$) δ 7.40–7.32 (m, 6H), 7.25 (dd, J = 12.9, 4.8 Hz, 3H), 7.02 (t, J = 7.3 Hz, 1H), 6.97 (s, 2H), 6.94 (s, 1H), 6.46 (s, 1H), 2.31 (s, 6H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 158.6, 153.8, 142.7, 136.6, 134.8, 129.9, 129.3, 126.7, 126.0, 124.2, 123.8, 121.5, 115.0, 77.3, 77.0, 76.7, 55.5, 21.2, 16.8; HRMS (ESI) m/z calcd for $C_{22}H_{22}N_2O_2$ $[M + H]^+$ 347.1760, found 347.1758; IR (KBr) cm^{-1} 2926, 1689, 1582, 1534, 1508, 1485, 1456, 1290, 1246, 1176, 1032, 805, 746, 696.

*3-Mesityl-1-(4-methoxyphenyl)-1-phenylurea (**4bi**):* 105 mg (57%); yellow oil; ^1H NMR (400 MHz, $CDCl_3$) δ 7.34 (d, J = 8.7 Hz, 7H), 6.96–6.93 (m, 2H), 6.85 (s, 2H), 5.73 (s, 1H), 3.82 (s, 3H), 2.23 (s, 3H), 2.22 (s, 6H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 158.4, 154.4, 143.2, 136.4, 135.4, 135.2, 131.9, 129.4, 129.1, 128.8, 126.2, 125.4, 115.0, 77.3, 77.0, 76.7, 55.5, 20.9, 18.4; HRMS (ESI) m/z calcd for $C_{23}H_{24}N_2O_2$ $[M + H]^+$ 361.1916, found 361.1914; IR (KBr) cm^{-1} 2958, 2924, 1684, 1490, 1290, 1246, 1183, 1033, 750, 694.

*3-(6-Chloropyridin-3-yl)-1-(4-methoxyphenyl)-1-phenylurea (**4bj**):* 90.5 mg (51%); white solid; mp 153–155 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 8.12 (d, J = 2.6 Hz, 1H), 7.35–7.27 (m, 9H), 6.99–6.97 (m, 2H), 6.52 (s, 1H), 3.85 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 158.9, 153.4, 144.9, 142.1, 140.0, 134.6, 134.1, 129.6, 129.5, 129.3, 126.8, 126.6, 124.1, 115.3, 77.3, 77.0, 76.7, 55.6; HRMS (ESI) m/z calcd for $C_{19}H_{16}ClN_3O_2$ $[M + H]^+$ 354.8096, found 354.8092; IR (KBr) cm^{-1} 2924, 1690, 1509, 1490, 1290, 1245, 1183, 1032, 750, 695.

*1-(4-Methoxyphenyl)-3-phenyl-1-(o-tolyl)urea (**4bk**):* 133.4 mg (80%); yellow oil; ^1H NMR (400 MHz, $CDCl_3$) δ 7.31–7.21 (m, 10H), 7.03–6.99 (m, 1H), 6.88–6.85 (m, 2H), 6.37 (s, 1H), 3.79 (s, 3H), 2.31 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 157.3, 153.5, 140.4, 138.6, 136.9, 134.8, 131.9, 129.5, 128.9, 128.3, 127.6, 127.2, 123.1, 119.3, 114.3, 77.3, 77.0, 76.7, 55.5, 18.1; HRMS (ESI) m/z calcd for $C_{21}H_{20}N_2O_2$ $[M + H]^+$ 333.4031, found 333.4029; IR (KBr) cm^{-1} 2959, 2854, 1690, 1509, 1481, 1290, 1245, 1183, 1032, 752, 696.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

^1H and ^{13}C NMR spectra for all compounds and X-ray crystallographic data for compound **4m** (CIF). This material is available free of charge via the Internet at http://pubs.acs.org.

■ AUTHOR INFORMATION

Corresponding Authors

*E-mail: glcheng@hqu.edu.cn.

*E-mail: cuixl@hqu.edu.cn.

Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

This work was supported by Minjiang Scholar Program (10BS216), Xiamen Southern Oceanographic Center (13GYY003NF16), the Natural Science Foundation of Fujian Province, China (2013J01050), and Fundamental Research Funds of Huaqiao University.

■ REFERENCES

(1) (a) Gallou, I. *Org. Prep. Proced. Int.* **2007**, *4*, 355–383. (b) Looker, A. R.; Littler, B. J.; Blythe, T. A.; Snoonian, J. R.; Ansell, G. K.; Jones, A. D.; Nyce, P.; Chen, M.; Neubert, B. J. *Org. Process Res. Dev.* **2008**, *12*, 666–673. (c) Dai, Y.; Hartandi, K.; Ji, Z.; Ahmed, A. A.; Albert, D. H.; Bauch, J. L.; Bouska, J. J.; Bousquet, P. F.; Cunha, G. A.; Glaser, K. B.; Harris, C. M.; Hickman, D.; Guo, J.; Li, J.; Marcotte, P. A.; Marsh, K. C.; Moskey, M. D.; Martin, R. L.; Olson, A. M.; Osterling, D. J.; Pease, L. J.; Soni, N. B.; Stewart, K. D.; Stoll, V. S.; Tapang, P.; Reuter, D. R.; Davidsen, S. K.; Michaelides, M. R. *J. Med. Chem.* **2007**, *50*, 1584–1597. (d) Flipo, M.; Charton, J.; Hocine, A.; Dassonneville, S.; Deptez, B.; Deprez-Poulain, R. *J. Med. Chem.* **2009**, *52*, 6790–6802.

(2) (a) Bigi, F.; Maggi, R.; Sartori, G. *Green Chem.* **2000**, *2*, 140–148. (b) Vishnyakova, T. P.; Golubeva, I. A.; Glebova, E. V. *Russ. Chem. Rev. (Engl. Ed.)* **1985**, *54*, 249–261. (c) Seebach, D.; Beck, A. K.; Bierbaum, D. J. *Chem. Biodiversity* **2004**, *1*, 1111–1239.

(3) Lam, P. Y.; Jadhav, P. K.; Eyermann, C. J.; Hodge, C. N.; Ru, Y.; Bacheler, L. T.; Meek, J. L.; Otto, M. J.; Rayner, M. M.; Wong, Y. N.; Chang, C. H.; Weber, P. C.; Jackson, D. A.; Sharpe, T. R. *Science* **1994**, *263*, 380–384.

(4) (a) Ozaki, S. *Chem. Rev.* **1972**, *72*, 457–496. (b) Dudic, M.; Lhotak, P.; Stibor, I.; Lang, K.; Proskova, P. *Org. Lett.* **2003**, *5*, 149–152. (c) Molina, P.; Fresneda, P. M.; Delgado, S. *J. Org. Chem.* **2003**, *68*, 489–499. (d) McElroy, N. R.; Jurs, P. C.; Morisseau, C.; Hammock, B. D. *J. Med. Chem.* **2003**, *46*, 1066–1080. (e) Arduini, A.; Calzavacca, F.; Pochini, A.; Secchi, A. *Chem.—Eur. J.* **2003**, *9*, 793–799.

(5) (a) Nudelman, N. S.; Lewkowicz, E. S.; Pérez, D. G. *Synthesis.* **1990**, *1990*, 917–920. (b) Yang, Y.; Lu, S. *Tetrahedron Lett.* **1999**, *40*, 4845–4846.

(6) McCusker, J. E.; Abboud, K. A.; McElwee-White, L. *Organometallics* **1997**, *16*, 3863–3866.

(7) (a) Sartori, G.; Maggi, R. In *Science of Synthesis*; Ley, S. V., Knight, J. G., Eds.; Thieme: Stuttgart, 2005; Vol. *18*, pp 665–758. (b) Hegarty, A. F.; Drennan, L. J. In *Comprehensive Organic Functional Group Transformations*; Katritzky, A. R., Meth-Cohn, O., Rees, C. W., Eds.; Pergamon: Oxford, 1995; Vol. *6*, pp 499–526.

(8) Nowick, J. S.; Powell, N. A.; Nguyen, T. M.; Noronha, G. *J. Org. Chem.* **1992**, *57*, 7364–7366.

(9) For reviews on diaryliodonium salts, see: (a) Yusubov, M. S.; Maskaev, A. V.; Zhdankin, V. V. *ARKIVOC* **2011**, 370–409. (b) Merritt, E. A.; Olofsson, B. *Angew. Chem., Int. Ed.* **2009**, *48*, 9052–9070. (c) Zhdankin, V. V.; Stang, P. J. *Chem. Rev.* **2008**, *108*, 5299–5358. (d) Zhdankin, V. V.; Stang, P. J. *Chem. Rev.* **2002**, *102*, 2523–2584. (e) Grushin, V. V. *Chem. Soc. Rev.* **2000**, *29*, 315–324. (f) Stang, P. J.; Zhdankin, V. V. *Chem. Rev.* **1996**, *96*, 1123–1178.

(10) (a) Castro, S.; Fernandez, J. J.; Vicente, R.; Fananas, F. J.; Rodríguez, F. *Chem. Commun.* **2012**, *48*, 9089–9091. (b) Hickman, A. J.; Sanford, M. S. *ACS Catal.* **2011**, *1*, 170–174. (c) Chen, B.; Hou, X. L.; Li, Y. X.; Wu, Y. D. *J. Am. Chem. Soc.* **2011**, *133*, 7668–7671. (d) Wagner, A. M.; Sanford, M. S. *Org. Lett.* **2011**, *13*, 288–291. (e) Xiao, B.; Fu, Y.; Xu, J.; Gong, T. J.; Dai, J. J.; Yi, J.; Liu, L. *J. Am. Chem. Soc.* **2010**, *132*, 468–469. (f) Deprez, N. R.; Sanford, M. S. *J. Am. Chem. Soc.* **2009**, *131*, 11234–11241. (g) Phipps, R. J.; Gaunt, M. J. *Science* **2009**, *323*, 1593–1597. (h) Phipps, R. J.; Grimster, N. P.; Gaunt, M. J. *J. Am. Chem. Soc.* **2008**, *130*, 8172–8174. (i) Deprez, N. R.; Kalyani, D.; Krause, A.; Sanford, M. S. *J. Am. Chem. Soc.* **2006**, *128*, 4972–4973. (j) Wang, Y.; Chen, C.; Zhang, S.; Lou, Z. B.; Su, X.; Wen, L. R.; Li, M. *Org. Lett.* **2013**, *15*, 4794–4797. (k) Wang, Y.; Chen, C.; Peng, J.; Li, M. *Angew. Chem., Int. Ed.* **2013**, *52*, 5323–5327. (l) Su, X.; Chen, C.; Wang, Y.; Peng, J.; Lou, Z.; Li, M. *Chem. Commun.* **2013**, *49*, 6752–6754. (m) Peng, J.; Chen, C.; Wang, Y.; Lou, Z.; Li, M.; Xi, C.; Chen, H. *Angew. Chem., Int. Ed.* **2013**, *52*, 7574–7578. (n) Wang, F.; Chen, C.; Deng, G.; Xi, C. *J. Org. Chem.* **2012**, *77*, 4148–4151. (o) Tang, D. T. D.; Collins, K. D.; Ernst, J. B.; Glorius, F. *Angew. Chem., Int. Ed.* **2014**, *53*, 1809–1813. (p) Ackermann, L.; Dell'Acqua, M.; Fenner, S.; Vicente, R.; Sandmann, R. *Org. Lett.* **2011**, *13*, 2358–2360.

(11) (a) Basavaprabhu, H.; Sureshbabu, V. V. *Org. Biomol. Chem.* **2012**, *10*, 2528–2533. (b) Panduranga, V.; Sureshbabu, V. V.

Tetrahedron Lett. **2013**, *54*, 975−979. (c) Li, J. H.; Neuville, L. *Org. Lett.* **2013**, *15*, 6124−6127.
(12) (a) Bielawski, M.; Zhu, M. Z.; Olofsson, B. *Adv. Synth. Catal.* **2007**, *349*, 2610−2618. (b) Bielawski, M.; Aili, D.; Olofsson, B. *J. Org. Chem.* **2008**, *73*, 4602−4607. (c) Phipps, R. J.; Grimster, N. P.; Gaunt, M. J. *J. Am. Chem. Soc.* **2008**, *130*, 8172−8174.
(13) Phipps, R. J.; McMurray, L.; Ritter, S.; Duong, H. A.; Gaunt, M. J. *J. Am. Chem. Soc.* **2012**, *134*, 10773−10776.
(14) Barrett, A. G. M.; Boorman, T. C.; Crimmin, M. R.; Hill, M. S.; Kociok-Köhn, G.; Procopiou, P. A. *Chem. Commun.* **2008**, *41*, 5206−5208.