Synthesis of Symmetrically and Unsymmetrically Substituted *N*,*N*′-Diarylimidazolin-2-ones by Copper-Catalyzed Arylamidation under Microwave-Assisted and Conventional Conditions

Thomas Hafner, Doris Kunz*

Ruprecht-Karls-Universität Heidelberg, Organisch-Chemisches Institut, Im Neuenheimer Feld 270, 69120 Heidelberg, Germany
Fax +49(6221)544885; E-mail: Doris.Kunz@oci.uni-heidelberg.de

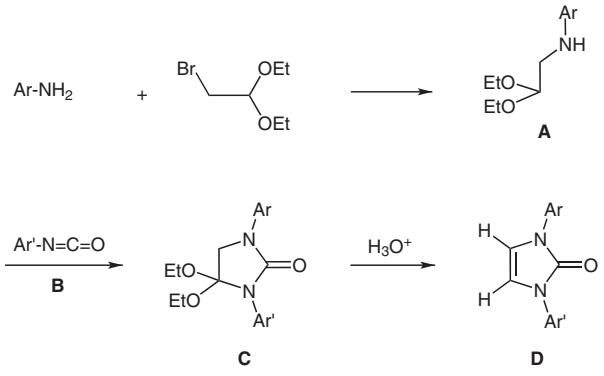
Received 21 July 2006; revised 8 March 2007

Dedicated to Professor Dr. Dr. h.c. Rolf Gleiter on the occasion of his 70th birthday

Abstract: A convenient synthesis of unsymmetrically substituted *N*,*N*′-diarylimidazolin-2-ones is reported. Starting from 2,2-dimethoxyethylamine, the first aryl group was introduced by reaction with arylisocyanate and subsequent cyclization to afford *N*-arylimidazolin-2-ones. The second arylation step was then accomplished by microwave-assisted copper-catalyzed arylamidation of the *N*-arylimidazolin-2-ones with a variety of aryliodides and arylbromides to give unsymmetrically substituted *N*,*N*′-diarylimidazolin-2-ones. Symmetrically substituted *N*,*N*′-diarylimidazolin-2-ones could also be prepared from imidazolin-2-one in a two-fold copper-catalyzed arylamidation, however, the nature of the substrate limits the use of this reaction.

Key words: amination, arylation, copper, homogeneous catalysis, heterocycles

A convenient and straightforward approach to the synthesis of a library of unsymmetrically substituted *N*,*N*′-diarylimidazolin-2-ones has not yet been developed, even though this class of compounds exhibits interesting biological activities[1] and is used in a number of electrophotographic processes.[2] The standard method with which to prepare symmetrically and unsymmetrically diarylsubstituted imidazolin-2-ones is based on the preparation of the respective *N*,*N*′-diaryl-substituted urea acetal **C** by condensation of 1-(*N*-arylamino)ethylacetal **A** with arylisocyanate **B**, followed by cyclization to the *N*,*N*′-diarylimidazolin-2-one **D** (Scheme 1).[3]

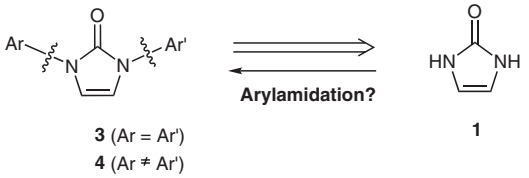


Scheme 1 Typical synthesis of unsymmetrically substituted *N*,*N*′-diarylimidazolin-2-ones **D**

SYNTHESIS 2007, No. 9, pp 1403–1411
Advanced online publication: 18.04.2007
DOI: 10.1055/s-2007-966021; Art ID: T11206SS

Another synthesis involves condensation of unsymmetrically substituted *N*,*N*′-diarylurea with benzoin or 1,2-diols[4] to give the desired imidazolin-2-one. Additional methods are more specific, for example, the preparation of *N*-hydroxyphenyl-substituted urea by reacting benzoxazolones with arylamines,[5] or by oxidative cleavage of quinolines and subsequent ring rearrangement.[6]

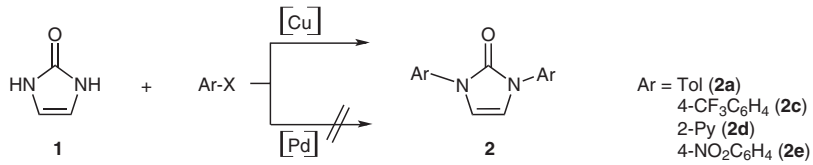
It would, however, be advantageous to introduce at least one of the aryl substituents in the last step of the synthesis. Making use of an arylamination reaction, for example the Buchwald–Hartwig[7] or the Ullmann–Goldberg reaction,[8] could be a successful way with which to achieve this goal. In contrast to regular alkyl or aryl amines, the arylamination of less nucleophilic heteroarylamines or amides is much harder to perform. In these cases, the copper-catalyzed Ullmann–Goldberg reaction seems to be superior to the palladium variants. With ureas as substrate, the reaction is even harder to achieve and only a few examples are known for imidazolidin-2-one, benzimidazolin-2-one or acyclic ureas serving as substrate.[9] It is therefore of no surprise that only one example of the arylamidation of an even less nucleophilic, unsaturated *N*-alkylimidazolin-2-one has been reported.[10] To the best of our knowledge, arylamidation of imidazolin-2-one (**1**) or *N*-arylimidazolin-2-ones **2** have not been reported in the literature (Scheme 2).



Scheme 2 Arylamidation strategy for the synthesis of diarylimidazolinones **3** and **4**

In order to develop such a new approach to diarylated imidazolinones **3**, we chose the reaction of imidazolin-2-one (**1**) with 4-iodotoluene as a test reaction and applied various reaction conditions previously reported in literature for other substrates (Table 1).[11] The palladium-catalyzed reactions (entries 1–7) were not successful, however, in the copper-catalyzed Goldberg reaction at 150 °C, the desired *N*,*N*′-ditolylimidazolin-2-one (**2a**) was formed in satisfactory yield (entry 9). The best results at 120 °C were achieved using the conditions provided by Buch-

Table 1 Conditions Tested for the Catalytic Diarylation of 1,3-Imidazolin-2-one (**1**) with Arylhalides



Entry	ArX (1.5 equiv)	**1** (mmol)	Catalyst precursor (mol%)	Ligand (mol%)[a]	Base (equiv)	Solvent (*c* of **1** in mmol/mL)	Temp (°C)	Time (h)	Product	Yield (%)[b]
1	4-Iodotoluene	0.50	$Pd(OAc)_2$ (2.0)	dppf (10.0)	*t*-BuOK (2.0)	Dioxane (0.38)	120	10	**2a**	–
2	4-Iodotoluene	0.50	$Pd(OAc)_2$ (2.0)	SIPr·BF_4 (2.0)	*t*-BuOK (2.0)	Dioxane (0.38)	120	10	**2a**	–
3	4-Iodotoluene	0.50	$Pd_2(dba)_3$ (2.0)	IPr·HCl (2.0)	*t*-BuOK (2.0)	Dioxane (0.38)	120	10	**2a**	–
4	4-Iodotoluene	1.0	$Pd_2(dba)_3$ (0.5)	Xantphos (1.0)	Cs_2CO_3 (2.4)	Dioxane (0.25)	100	44	**2a**	–
5	4-Bromotoluene	1.0	$Pd_2(dba)_3$ (0.5)	Xantphos (1.0)	Cs_2CO_3 (2.4)	Dioxane (0.25)	100	44	**2a**	–
6	4-Iodotoluene	1.0	$Pd_2(dba)_3$ (2.5)	Xantphos (5.0)	Cs_2CO_3 (2.4)	Dioxane (0.25)	150	15	**2a**	–
7	4-Bromotoluene	1.0	$Pd_2(dba)_3$ (2.5)	Xantphos (5.0)	Cs_2CO_3 (2.4)	Dioxane (0.25)	150	15	**2a**	3
8	4-Iodotoluene	0.50	Cu_2O (20.0)	–	K_2CO_3 (4.0)	DMSO (1.00)	150	15	**2a**	–
9	4-Iodotoluene	0.50	CuO (10.0)	–	K_2CO_3 (4.0)	DMSO (1.00)	150	15	**2a**	61
10	4-Bromotoluene	0.50	CuO (10.0)	–	K_2CO_3 (4.0)	DMSO (1.00)	150	15	**2a**	–
11	2-Bromopyridine	0.50	CuO (10.0)	–	K_2CO_3 (4.0)	DMSO (1.00)	150	15	**2d**	76
12	4-Iodotoluene	1.0	$(CuOTf)_2·C_6H_6$ (10.0)	phen (2 equiv)[d]	Cs_2CO_3 (2.0)	Dioxane (0.5)	120	15	**2a**	50[c]
13	4-Bromotoluene	1.0	$(CuOTf)_2·C_6H_6$ (10.0)	phen (2 equiv)[d]	Cs_2CO_3 (2.0)	Dioxane (0.38)	120	15	**2a**	–
14	2-Bromopyridine	1.0	$(CuOTf)_2·C_6H_6$ (10.0)	phen (2 equiv)[d]	Cs_2CO_3 (2.0)	Dioxane (0.5)	120	15	**2d**	61[c]
15	4-Iodonitro-benzene	1.0	$(CuOTf)_2·C_6H_6$ (10.0)	phen (2 equiv)[d]	Cs_2CO_3 (2.0)	Dioxane (0.5)	120	15	**2e**	–
16	4-Iodotoluene	1.0	$(CuOTf)_2·C_6H_6$ (5.0)	DACy (50)	Cs_2CO_3 (2.2)	Dioxane (0.25)	120	15	**2a**	67[c]
17	4-Bromotoluene	1.0	$(CuOTf)_2·C_6H_6$ (5.0)	DACy (50)[d]	Cs_2CO_3 (2.2)	Dioxane (0.25)	120	15	**2a**	17[c]
18	4-Bromo(trifluo-romethyl)benzene	1.0	$(CuOTf)_2·C_6H_6$ (5.0)	DACy (10)	Cs_2CO_3 (2.2)	Dioxane (0.25)	120	15	**2c**	52[c]
19	4-Bromo(trifluo-romethyl)benzene	1.0	$(CuOTf)_2·C_6H_6$ (5.0)	DACy (50)[d]	Cs_2CO_3 (2.2)	Dioxane (0.25)	120	15	**2c**	56[c]
20	4-Iodonitro-benzene	1.0	$(CuOTf)_2·C_6H_6$ (5.0)	DACy (50)	Cs_2CO_3 (2.2)	Dioxane (0.5)	120	15	**2e**	trace
21	4-Iodotoluene	1.0	CuI (5.0)	DACy (50)	K_3PO_4 (4.0)	Dioxane (0.25)	120	15	**2a**	56[c]
22	4-Iodotoluene	1.0	CuI (10.0)	DACy (10)	K_3PO_4 (2.0)	Dioxane (0.25)	120	15	**2a**	80[c]
23	4-Iodotoluene	1.0	CuI (10.0)	DACy (20)	Cs_2CO_3 (2.2)	Dioxane (0.25)	120	15	**2a**	41[c]

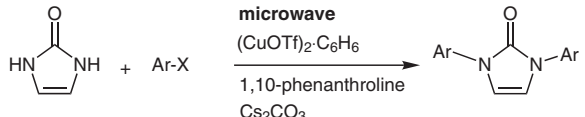
[a] Abbreviations used: 1,1-bis(diphenylphosphino)ferrocene (dppf), 1,3-bis(2,6-diisopropylphenyl)-4,5-dihydroimidazoliumtetrafluoroborate (SIPr·BF_4), 1,3-bis(2,6-diisopropylphenyl)imidazoliumchloride (IPr·HCl), 9,9-dimethyl-4,5-bis(diphenylphosphino)xanthene (Xantphos), 1,10-phenanthroline (phen), *trans*-1,2-diaminocyclohexane (DACy).
[b] Yield determined by NMR with dodecahydrotriphenylene as internal standard.
[c] Isolated yield.
[d] Addition of 10.0 mol% dibenzylideneacetone (dba).

wald {bis[copper(I)triflate]benzene [$(CuOTf)_2{\cdot}C_6H_6$; 10 mol%], dibenzylideneacetone [dba; 10 mol%], 1,10-phenanthroline [2 equiv] and Cs_2CO_3 as a base [entry 12][12] or with CuI, 1,2-*trans*-diaminocyclohexane and K_3PO_4 [entry 22]}.[11d] We also found the combination of $(CuOTf)_2{\cdot}C_6H_6$, 1,2-*trans*-diaminocyclohexane and Cs_2CO_3 to be of similar activity (entry 16).

However, the spectrum of substrates was quite limited for this reaction, with 4-bromotoluene or 4-iodonitrobenzene, for example, giving only poor yields or none at all, whereas electron-deficient arylhalides such as 4-bromo(trifluoromethyl)benzene or 2-bromopyridine (entries 11, 14, 18, 19) gave satisfactory yields. Following the progress of the reaction by analyzing NMR samples from the reaction mixture showed that, though low amounts of product were formed, the starting imidazolin-2-one (**1**) was consumed during the reaction. It seems that **1** decomposes under the basic conditions applied, however, no decomposition product could be observed either by NMR spectroscopy or GC.

We therefore tried to reduce the extent of decomposition of **1** by shortening the reaction time and conducted the C–N coupling reaction under microwave irradiation (Table 2).[13] The reactions were carried out at a range of temperatures between 80 °C and 210 °C for 30 minutes. At 150 °C the reaction rate with 4-iodotoluene remained very slow (entry 3) but was increased by raising the temperature. Optimal yields were obtained at 180 °C with 4-iodotoluene (44%) and 2-bromopyridine (54%) as substrates (entries 4 and 9). At higher temperatures (entries 5 and 10) the yield decreased, possibly due to faster decomposition of imidazolin-2-one (**1**) and/or the catalyst. This is consistent with the observation that longer reaction times did not lead to an increase in the yield (entry 11). However, the reaction remained sensitive to both the arylhalide and the catalyst precursor used; with 4-bromotoluene, for example, no product could be detected at all (entries 7 and 8) whereas with copper(I) iodide (entries 12 and 13), the yields obtained were much lower than those obtained through conventional heating. It seems that the reaction is best carried out by conventional heating, however, the reduced reaction time of microwave-assisted reactions can be useful for faster screening of various substrates.

Table 2 Microwave-Assisted Copper-Catalyzed Diarylation of 1,3-Imidazolin-2-one (**1**)[a]



1 **2**

Entry	ArX	Ligand (mol%)	Product	Temp (°C)	Yield (%)[b]
1	4-Iodotoluene	phen (2 equiv)	**2a**	80[c]	–
2	4-Iodotoluene	phen (2 equiv)	**2a**	120	trace
3	4-Iodotoluene	phen (2 equiv)	**2a**	150	8
4	4-Iodotoluene	phen (2 equiv)	**2a**	180	44
5	4-Iodotoluene	phen (2 equiv)	**2a**	210	28[d]
6	4-Iodotoluene	DACy (80)[f]	**2a**	180	31[d]
7	4-Bromotoluene	phen (2 equiv)	**2a**	180	–
8	4-Bromotoluene	phen (2 equiv)	**2a**	210	–
9	2-Bromopyridine	phen (2 equiv)	**2d**	180	54
10	2-Bromopyridine	phen (2 equiv)	**2d**	210	33 32[d]
11	2-Bromopyridine	phen (2 equiv)	**2d**	210[c]	30
12	4-Iodotoluene	DACy (30)[e,f]	**2a**	150	8[d]
13	4-Iodotoluene	DACy (30)[e,f]	**2a**	180	11[d]

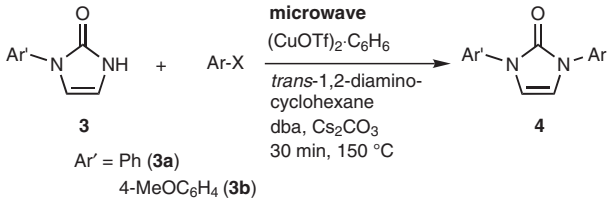
[a] *Reagents and conditions*: **1** (0.500 mmol), arylhalide (1.50 mmol), $(CuOTf)_2{\cdot}C_6H_6$ (10 mol%), Cs_2CO_3 (1.10 mmol), dioxane (2 mL).
[b] Yield determined by NMR with dodecahydrotriphenylene as internal standard.
[c] Reaction time: 1 h.
[d] Isolated yield.
[e] Based on 1.00 mmol **1**.
[f] CuI (10 mol%), dioxane (4 mL).

As the monosubstituted *N*-arylimidazolin-2-one **3** was never observed in any of these experiments, we concluded that the diarylation proceeds much faster than the monoarylation and/or **3** is more stable under the applied conditions. It seemed beneficial to first synthesize the monoarylated imidazolin-2-one **3** by the known reaction of arylisocyanate with amino(dimethoxy)ethylacetal and subsequent acid-induced cyclization.[14] This substrate could be then arylated by means of copper catalysis to give a library of unsymmetrically substituted *N*,*N*′-diarylimidazolin-2-ones **4**. This route would also be attractive as it avoids the necessity of protecting groups.

Table 3 summarizes the reaction of phenylimidazolin-2-one (**3a**) with various activated and deactivated aryliodides, arylbromides and 2-bromopyridine under microwave-assisted conditions. We found good to very good yields of the unsymmetrically N,N′-disubstituted arylation products **4**, due to the higher nucleophilicity of the imidazolinone. A combination of the bis[copper(I)triflate]benzene complex and *trans*-1,2-diaminocyclohexane resulted in a very active catalytic system for this purpose, so that the temperature could be reduced to 150 °C under microwave irradiation conditions. Use of 4-methoxyphenylimidazolinone (**3b**), a slightly more nucleophilic imidazolinone, led to comparable results (entries 11–14).

After we had screened various substrates and conditions under microwave-assisted conditions, we undertook the same reactions using conventional heating (Table 4). A catalyst to ligand ratio of 1:3 was found to give the best results. However, increasing the amount of ligand did not affect the reaction rate. The yields of the microwave-

Table 3 Synthesis of Unsymmetrically Substituted *N*,*N*′-Diarylimidazolinones **4** by Microwave-Assisted Copper-Catalyzed N-Arylation of Arylimidazolin-2-ones **3a** and **3b**[a]



3

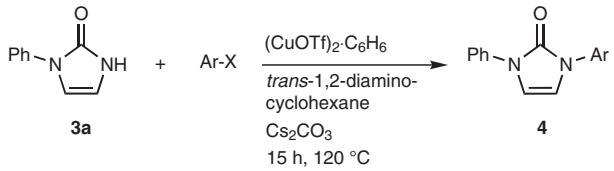
Ar′ = Ph (**3a**)
4-MeOC$_6$H$_4$ (**3b**)

4

Entry	Imidazolinone	Ar	X	Product	Yield (%)[b]
1	**3a**	4-Tolyl	I	**4a**	76[c]
2	**3a**	4-Tolyl	I	**4a**	97
3	**3a**	4-Tolyl	I	**4a**	66[d]
4	**3a**	4-Tolyl	Br	**4a**	35[e]
5	**3a**	4-Methoxyphenyl	Br	**4b**	58
6	**3a**	4-(Trifluoro-methyl)-phenyl	I	**4c**	83
7	**3a**	2-Pyridyl	Br	**4d**	96
8	**3a**	4-Nitrophenyl	I	**4e**	100
9	**3a**	4-Nitrophenyl	Br	**4e**	96
10	**3a**	3-Nitrophenyl	I	**4f**	73
11	**3b**	4-Tolyl	I	**4g**	86[f]
12	**3b**	4-Tolyl	Br	**4g**	84[f]
13	**3b**	4-Methoxyphenyl	I	**4h**	63[f]
14	**3b**	4-Nitrophenyl	I	**4i**	74[f]
15	**3a**	4-Tolyl	I	**4a**	–[g]

[a] *Reagents and conditions*: **3** (1.00 mmol), arylhalide (1.50 mmol), (CuOTf)$_2$·C$_6$H$_6$ (10 mol%), Cu:ligand:dba = 1:5:1, Cs_2CO_3 (1.10 mmol), dioxane (4 mL).
[b] Yield of isolated product.
[c] Ligand: 1,10-phenanthroline (2 mmol).
[d] Catalyst (2.5 mol%), dba (2.5 mol%), *trans*-1,2-diaminocyclohexane (5 mol%).
[e] Yield determined by NMR with dodecahydrotriphenylene as internal standard.
[f] Without dba.
[g] Without Cu-catalyst and ligand, but with Cs_2CO_3 (1.00 mmol).

Table 4 Synthesis of Unsymmetrically Substituted Diarylimidazolinones **4** by Copper-Catalyzed N-Arylation of Phenylimidazolin-2-one (**3a**) with Conventional Heating[a]



3a **4**

Entry	Ar	X	Ratio (Cu:L)	Product	Yield (%)[b]
1	4-Tolyl	I	1:5	**4a**	83
2	4-Tolyl	I	1:1	**4a**	53[c]
3	4-Tolyl	I	1:2	**4a**	83[c]
4	4-Tolyl	I	1:3	**4a**	92[c]
5	4-Tolyl	I	1:5	**4a**	90[c]
6	4-Methoxyphenyl	Br	1:5	**4b**	89
7	2-Pyridyl	Br	1:3	**4d**	85[d]
8	4-Nitrophenyl	I	1:5	**4e**	91

[a] *Reagents and conditions*: **3** (1.00 mmol), arylhalide (1.50 mmol), $(CuOTf)_2{\cdot}C_6H_6$ (10 mol%), Cu:ligand:dba = 1:5:1, dioxane (4 mL).
[b] Isolated yield.
[c] $(CuOTf)_2{\cdot}C_6H_6$ (5.0 mol%).
[d] $(CuOTf)_2{\cdot}C_6H_6$ (2.5 mol%).

assisted reactions and those using conventional heating were comparable, thus, both procedures should be synthetically useful.

In conclusion, we have found a very useful and easy route to a library of unsymmetrically substituted *N*,*N*′-diarylimidazolinones, without the need for protecting groups, by reacting monoarylated imidazolin-2-ones **3** in a copper-catalyzed arylamidation reaction. This can either be achieved in short reaction times under microwave-assisted conditions (180 °C, 30 min) or under conventional heating conditions at lower temperature but prolonged reaction times (120 °C, 15 h). The advantage to alternative syntheses of such compounds is that the second aryl substituent is introduced in the last step, using readily available arylhalides. We have also found copper-catalyzed conditions with which to react imidazolin-2-one (**1**) in a double C–N arylation, to form the symmetrically substituted *N*,*N*′-diarylimidazolin-2-ones **2**. This reaction is more limited to electron-poor arylhalides as a substrate because decomposition of the imidazolin-2-one (**1**) becomes a competing side reaction in the case of less reactive substrates. Further investigations aiming to find more active catalytic systems and milder reaction conditions are a current goal in our laboratory.

All starting materials are commercially available or were synthesized according to the procedures described herein. Solvents were dried and purified by conventional methods prior to use. Where used, petroleum ether (PE) had a boiling range of 30–70 °C. The microwave experiments were conducted in a CEM DISCOVER, single mode microwave reactor with a maximum power of 300 W, using the POWERMAX cooling function in all experiments.[15] Standard CEM vials (5 mL) and standard caps were used. The microwave experiments involving imidazolin-2-one (**1**) were conducted in a monomode SmithCreator microwave reactor with a maximal power of 300 W using Biotage vials (5 mL); the vials were charged in a glovebox under nitrogen atmosphere. Preparative column chromatography was carried out using silica gel 60. ^1H and ^{13}C NMR spectra were measured on a Bruker ARX250 or Bruker DRX300 spectrometer. Chemical shifts are given in ppm relative to the residual proton solvent peak (δ = 2.51 ppm for DMSO-d_6 and δ = 5.32 ppm for CD_2Cl_2). The assignment of the NMR signals is based on 2-D ^1H–^1H and ^1H–^{13}C correlation experiments. IR spectra were recorded on a Bruker 55 FT-IR Equinox spectrometer and mass spectra on a Jeol JMS-700 spectrometer. Microanalyses were performed by the Microanalytical Laboratory of the Institute of Chemistry at the University of Heidelberg. Melting Points were measured on a Büchi Melting Point B-540 and are uncorrected. Imidazolin-2-one (**1**) (Marckwald's method),[16] 1-(2,2-diethoxyethyl)urea[17] and 1-(2,2-dimethoxyethyl)-3-phenylurea[14] were synthesized according to literature procedures.

Copper-Catalyzed C–N Coupling of Imidazolin-2-one (1); General Procedure

A Schlenk tube was charged under nitrogen atmosphere with dioxane (0.5 mL), imidazolin-2-one (**1**; 41.9 mg, 0.500 mmol), $(CuOTf)_2{\cdot}C_6H_6$ (25.2 mg, 10.0 mol%), dibenzylideneacetone (12.0 mg, 10.0 mol%), Cs_2CO_3 (326 mg, 1.00 mmol), arylhalide (1.50 mmol) and 1,10-phenanthroline (180 mg, 1.0 mmol). Additional dioxane (1.5 mL) was added and the suspension was thoroughly stirred. The suspension was heated in an oil bath at the given temperature for the given time (see Table 1). The crude solution was filtered through silica gel and the residue was washed with CH_2Cl_2 (40 mL). The filtrate is concentrated to dryness in vacuo and further purified by flash chromatography over silica gel.

1,3-Di-*p*-tolylimidazolin-2-one (2a)

Purified by flash chromatography (cyclohexane–acetone, 7:1).

Yield: 67% (isolated yield from 4-iodotoluene); colorless crystals; mp 198 °C.

IR (KBr): 2918 (w), 2852 (w), 1683 (s), 1521 (s), 1426 (s), 1275 (m), 1221 (m), 1185 (w), 1127 (w), 1096 (w), 919 (m), 839 (m), 818 (s), 767 (m), 664 (s), 588 (w), 508 (m) cm^{-1}.

^1H NMR (250 MHz, DMSO-d_6): δ = 2.32 (s, 6 H, CH_3), 7.19 (s, 2 H, H-4), 7.26 (d, *J* = 8.4 Hz, 4 H, H-3′), 7.60 (d, *J* = 8.4 Hz, 4 H, H-2′).

^{13}C NMR (75 MHz, DMSO-d_6): δ = 20.4 (CH_3), 111.0 (C-4), 121.1 (C-2′), 129.4 (C-3′), 134.5 (C-1′), 134.8 (C-4′), 149.6 (C-2).

HRMS (EI): *m*/*z* calcd for $C_{16}H_{16}N_2O$: 264.1263; found (%): 264.1251 (100), 235.1224 (16), 221.1094 (25), 118.0652 (25), 91.0571 (35).

Anal. Calcd for $C_{16}H_{16}N_2O$: C, 77.25; H, 6.10; N, 10.60. Found: C, 77.29; H, 6.11; N, 10.49.

1,3-Bis(4-trifluoromethylphenyl)imidazolin-2-one (2c)

Purified by flash chromatography (cyclohexane–acetone, 3:1).

Yield: 30% (isolated yield); colorless crystals, mp 165 °C.

IR (KBr): 3123 (m), 1692 (s), 1618 (m), 1526 (m), 1431 (m), 1322 (s), 1285 (m), 1130 (s), 918 (s), 668 (w) cm^{-1}.

^1H NMR (300 MHz, CD_2Cl_2): δ = 6.88 (s, 2 H, H-4), 7.74 (d, *J* = 8.6 Hz, 4 H, H-3′), 7.85 (d, *J* = 8.6 Hz, 4 H, H-2′).

^{13}C NMR (75 MHz, CD_2Cl_2): δ = 111.5 (C-4), 121.9 (C-2′), 124.7 (q, J_{C-F} = 271.6 Hz, CF_3), 127.0 (q, J_{C-F} = 3.8 Hz, C-3′), 128.2 (q, J_{C-F} = 32.9 Hz, C-4′), 140.6 (C-1′), 150.7 (C-2).

HRMS–FAB: *m/z* calcd for $C_{17}H_{10}F_6N_2O$: 372.0697; found (%): 373.0748 (100) $[M + H]^+$, 372.0677 (84) $[M]^+$, 353.0717 (8).

Anal. Calcd for $C_{17}H_{10}F_6N_2O$: C, 54.85; H, 2.71; N, 7.53. Found: C, 54.83; H, 2.93; N, 7.34.

1,3-Di(pyrid-2′-yl)imidazolin-2-one (2d)
Purified by flash chromatography (cyclohexane–acetone, 20:1).

Yield: 61%; colorless crystals; mp 120 °C.

IR (KBr): 3167 (m), 1708 (s), 1575 (s), 1469 (s), 1438 (s), 1403 (s), 1277 (m), 1222 (m), 922 (s), 783 (s), 678 (s) cm^{-1}.

^{1}H NMR (300 MHz, CD_2Cl_2): δ = 7.17 (dd, *J* = 5.3, 6.8 Hz, 2 H, H-5′), 7.54 (s, 2 H, H-4), 7.82 (dd, *J* = 6.8, 8.6 Hz, 2 H, H-4′), 8.43 (d, *J* = 5.3 Hz, 2 H, H-6′), 8.45 (d, *J* = 8.6 Hz, 2 H, H-3′).

^{13}C NMR (75 MHz, CD_2Cl_2): δ = 109.7 (C-4), 114.3 (C-3′), 121.1 (C-5′), 138.9 (C-4′), 148.6 (C-6′), 149.9 (C-2′), 150.7 (C-2).

HRMS (EI): *m/z* calcd for $C_{13}H_{10}N_4O$: 238.0855; found (%): 238.0848 (100), 209.0824 (6), 79.0443 (12).

Anal. Calcd for $C_{13}H_{10}N_4O$: C, 65.54; H, 4.23; N, 23.52. Found: C, 65.36; H, 4.32; N, 23.28.

Microwave-Assisted Copper-Catalyzed C–N Coupling of Imidazolin-2-one (1); General Procedure
A microwave reaction vial was charged under a nitrogen atmosphere with dioxane (0.5 mL), imidazolin-2-one (**1**; 41.9 mg, 0.500 mmol), copper(I)triflate–benzene complex (25.2 mg, 10.0 mol%), Cs_2CO_3 (326 mg, 1.00 mmol), arylhalide (1.50 mmol) and 1,10-phenanthroline (180 mg, 1.00 mmol). Additional dioxane (1.5 mL) was added and the suspension was thoroughly stirred. The reaction was conducted in a microwave reactor at the given temperature and a maximum power of 300 W for 30 min (Table 2). The crude solution was filtered through silica gel and the residue was washed with CH_2Cl_2 (50 mL). The filtrate is concentrated to dryness in vacuo and further purified by flash chromatography over silica gel.

1,3-Di(pyrid-2′-yl)imidazolin-2-one (2d)
Yield: 32%.

All physical and spectroscopic properties were found to be identical to **2d** obtained through conventional heating (see above).

1-Phenylimidazolin-2-one (3a)
Finely powdered 1-(2,2-dimethoxyethyl)-3-phenylurea (4.80 g, 20.1 mmol) was cooled to 0 °C and suspended in H_2SO_4 (1 N, 10.0 mL). The reaction mixture was allowed to warm slowly to r.t. and then heated to 50 °C for 3 h. The reaction mixture was adjusted to pH 8 with KOH (1 N), stirred for 1 h and extracted with CH_2Cl_2 (4 × 50 mL). The combined organic phases were dried over Na_2SO_4 and the solvent was evaporated in vacuo to afford 1-phenylimidazolin-2-one (**3a**).

Yield: 100%; colorless crystalline solid; mp 127 °C (Lit. 123 °C,[17] 126 °C,[18] 136–139 °C[19]).

^{1}H NMR (250 MHz, DMSO-d_6): δ = 6.58 (d, *J* = 2.5 Hz, 1 H, H-4/H-5), 6.93 (d, *J* = 2.5 Hz, 1 H, H-4/H-5), 7.20 (t, *J* = 7.6 Hz, 1 H, H-1), 7.41 (dd, *J* = 8.0, 7.6 Hz, 2 H, H-2), 7.70 (d, *J* = 8.0 Hz, 2 H, H-3), 10.28 (s, 1 H, NH).

1-(4-Methoxyphenyl)imidazolin-2-one (3b)
Aminoacetaldehyde dimethylacetal (3.55 g, 33.8 mmol) was added dropwise to 4-methoxyphenylisocyanate (5.03 g, 33.7 mmol). The reaction vessel was put into an ultrasonic bath for 20 min during which the solution turned completely solid. The colorless product was washed with PE (1 × 50 mL), finely powdered and cooled to 0 °C in an ice bath. H_2SO_4 (1 N, 10 mL) was added and the suspension was stirred for 1 h at r.t. then for 3 h at 50 °C. The reaction mixture was adjusted to pH 8 with KOH (1 N, ~10 mL) and extracted with CH_2Cl_2 (3 × 100 mL). Separation of the organic phase, drying with Na_2SO_4 and evaporation of the solvent in vacuo afforded 1-methoxyphenylimidazolin-2-one as a colorless solid, which was recrystallized from EtOH.

Yield: 89%; mp 143 °C.

IR (KBr): 3149 (m), 2962 (m), 1681 (s), 1516 (s), 1428 (m), 1250 (s), 1031 (s), 996 (s), 845 (m), 661 (s) cm^{-1}.

^{1}H NMR (300 MHz, CD_2Cl_2): δ = 3.83 (s, 3 H, OCH_3), 6.40 (d, *J* = 2.6 Hz, 1 H, H-5), 6.50 (d, *J* = 2.6 Hz, 1 H, H-4), 6.96 (d, *J* = 8.9 Hz, 2 H, H-3′), 7.47 (d, *J* = 8.9 Hz, 2 H, H-2′), 10.7 (s, 1 H, NH).

^{13}C NMR (75 MHz, CD_2Cl_2): δ = 56.1 (OCH_3), 109.6 (C-4), 112.0 (C-5), 114.8 (C-3′), 124.5 (C-2′), 130.8 (C-1′), 154.5 (C-2), 158.5 (C-4′).

Copper-Catalyzed C–N Coupling of Arylimidazolin-2-one (3); General Procedure
A Schlenk tube was charged under a nitrogen atmosphere with 1-arylimidazolin-2-one (**3**; 1.00 mmol), copper(I)triflate–benzene complex (50.4 mg, 10.0 mol%), dibenzylideneacetone (24.0 mg, 10.0 mol%), Cs_2CO_3 (358.4 mg, 1.10 mmol) and the mixture was suspended in dioxane (2.0 mL). *trans*-1,2-Diaminocyclohexane (120 μL, 114 mg, 100 mol%) and arylhalide (1.50 mmol) dissolved in dioxane (2.0 mL) was added and the suspension was heated at 120 °C for 15 h. The crude solution was filtered through silica gel and the residue was washed with CH_2Cl_2 (50 mL). The filtrate was concentrated to dryness in vacuo and further purified by flash chromatography over silica gel.

Microwave-Assisted Copper-Catalyzed Amidation of 1-Arylimidazolin-2-ones 3a and 3b with Arylhalides; General Procedure
A microwave reaction vial was charged under a nitrogen atmosphere with 1-phenylimidazolin-2-one (**3a**; 160 mg, 1.00 mmol) or 1-(4-methoxyphenyl)imidazolin-2-one (**3b**; 190 mg, 1.00 mmol), copper(I)triflate–benzene complex (50.4 mg, 10.0 mol%), dibenzylideneacetone (if required; 24.0 mg 10.0 mol%), Cs_2CO_3 (358.4 mg, 1.10 mmol) and arylhalide (1.50 mmol) and the mixture was suspended in dioxane (2 mL). *trans*-1,2-Diaminocyclohexane (120 μL, 114 mg, 100 mol%) dissolved in dioxane (2.0 mL) was added and the reaction was conducted in a microwave reactor at 150 °C and 300 W for 30 min. The crude solution was filtered through silica gel and the residue was washed with CH_2Cl_2 (50 mL). The filtrate was concentrated to dryness in vacuo and further purified by flash chromatography over silica gel.

1-Phenyl-3-*p*-tolylimidazolin-2-one (4a)
Purified by flash chromatography (cyclohexane–acetone, 5:1).

Yield: 35% (NMR yield based on 40.0 mg of dodecahydrotriphenylene as NMR standard, from 4-bromotoluene); 97% (isolated yield from 4-iodotoluene); colorless crystals; mp 158 °C.

IR (KBr): 3156 (w), 2856 (w), 1686 (s), 1597 (m), 1519 (s), 1502 (s), 1426 (s), 1276 (s), 1224 (s), 1181 (w), 1126 (m), 919 (s), 819 (s), 758 (s), 663 (s), 509 (s) cm^{-1}.

^{1}H NMR (300 MHz, CD_2Cl_2): δ = 2.39 (s, 3 H, CH_3), 6.72 (d, *J* = 3.2 Hz, 1 H, H-4/H-5), 6.75 (d, *J* = 3.2 Hz, 1 H, H-4/H-5), 7.27 (d, *J* = 8.2 Hz, 2 H, H-3′), 7.29 (t, *J* = 8.1 Hz, 1 H, H-*para*), 7.47 (dd, *J* = 8.1, 7.5 Hz, 2 H, H-*meta*), 7.52 (d, *J* = 8.2 Hz, 2 H, H-2′) 7.66 (d, *J* = 7.5 Hz, 2 H, H-*ortho*).

^{13}C NMR (75 MHz, CD_2Cl_2): δ = 21.2 (CH_3), 111.1 and 111.7 (C-4/C-5), 122.4 (C-*ortho*), 122.5 (C-2′), 126.4 (C-*para*), 129.6

(C-*meta*), 130.2 (C-3′), 135.3 (C-1′), 136.5 (C-4′), 137.9 (C-*ipso*), 151.1 (C-2).

HRMS (EI): *m*/*z* calcd for $C_{16}H_{14}N_2O$: 250.1106; found (%): 250.1132 (100), 221.1087 (39), 207.0913 (30), 118.0651 (13), 104.0503 (13), 91.0551 (23), 77.0396 (19).

Anal. Calcd for $C_{16}H_{14}N_2O$: C, 76.78; H, 5.64; N, 11.19. Found: C, 76.59; H, 5.63; N, 11.15.

3-(4-Methoxyphenyl)-1-phenylimidazolin-2-one (4b)
Purified by flash chromatography (PE–EtOAc, 3:1).

Yield: 58% (isolated yield from bromo-4-methoxybenzene); colorless crystals; mp 144 °C.

IR (KBr): 3154 (w), 2934 (w), 1690 (s), 1598 (m), 1520 (s), 1425 (s), 1359 (w), 1253 (s), 1177 (w), 1034 (s), 917 (s), 833 (s), 778 (s), 657 (s) cm^{-1}.

^1H NMR (300 MHz, CD_2Cl_2): δ = 3.83 (s, 3 H, OCH_3), 6.68 (d, *J* = 3.2 Hz, 1 H, C-4/C-5), 6.73 (d, *J* = 3.2 Hz, 1 H, C-4/C-5), 6.98 (d, *J* = 9.0 Hz, 2 H, H-3′), 7.28 (t, *J* = 7.6 Hz, 1 H, H-*para*), 7.46 (dd, *J* = 8.1, 7.6 Hz, 2 H, H-*meta*), 7.52 (d, *J* = 9.0 Hz, 2 H, H-2′), 7.65 (d, *J* = 8.1 Hz, 2 H, H-*ortho*).

^{13}C NMR (75 MHz, CD_2Cl_2): δ = 56.1 (OCH_3), 110.9 and 112.1 (C-4/C-5), 114.8 (C-3′), 122.4 (C-*ortho*), 124.4 (C-2′), 126.4 (C-*para*), 129.7 (C-*meta*), 130.9 (C-1′), 138.0 (C-*ipso*), 151.2 (C-2), 158.5 (C-4′).

HRMS (EI): *m*/*z* calcd for $C_{16}H_{14}N_2O_2$: 266.1055; found (%): 266.1048 (100), 251.0817 (6), 237.1007 (23), 223.0874 (11), 134.0599 (13).

Anal. Calcd for $C_{16}H_{14}N_2O_2$: C, 72.16; H, 5.30; N, 10.52. Found: C, 72.07; H, 5.29; N, 10.50.

3-(3′-Trifluoromethylphenyl)-1-phenylimidazolin-2-one (4c)
Purified by flash chromatography (PE–acetone, 5:1).

Yield: 83% (isolated yield from iodo-3-trifluorobenzene); colorless crystals; mp 140 °C.

IR (KBr): 3184 (w), 3155 (w), 1685 (s), 1598 (m), 1509 (s), 1460 (s), 1423 (s), 1362 (s), 1329 (s), 1290 (s), 1225 (s), 1170 (s), 1117 (s), 889 (w), 808 (s), 762 (s), 698 (s) cm^{-1}.

^1H NMR (300 MHz, CD_2Cl_2): δ = 6.81 (s, 2 H, H-4/H-5), 7.31 (t, *J* = 7.5 Hz, 1 H, H-*para*), 7.48 (dd, *J* = 7.8, 7.5 Hz, 2 H, H-*meta*), 7.54 (d, *J* = 7.9 Hz, 1 H, H-4′), 7.61 (t, *J* = 7.9 Hz, 1 H, H-5′), 7.65 (d, *J* = 7.8 Hz, 2 H, H-*ortho*), 7.92 (d, *J* = 7.9 Hz, 1 H, H-6′), 8.00 (s, 1 H, H-2′).

^{13}C NMR (75 MHz, CD_2Cl_2): δ = 110.7 and 112.3 (C-4/C-5), 118.8 (q, J_{C-F} = 4.0 Hz, C-2′), 122.5 (C-*ortho*), 122.9 (q, J_{C-F} = 4.0 Hz, C-4′), 124.5 (q, J_{C-F} = 272.4 Hz, CF_3), 125.3 (C-6′), 126.8 (C-*para*), 129.8 (C-*meta*), 130.5 (C-5′), 131.9 (q, J_{C-F} = 32.5 Hz, C-3′), 137.6 and 138.4 (C-*ipso*/C-1′), 150.9 (C-2).

HRMS (EI): *m*/*z* calcd for $C_{16}H_{11}F_3N_2O$: 304.0823; found (%): 304.0844 (100), 285.0836 (5), 275.0803 (17), 145.0264 (6), 104.0501 (15), 77.0394 (13).

Anal. Calcd for $C_{16}H_{11}F_3N_2O$: C, 63.16; H, 3.64; N, 9.21. Found: C, 63.23; H, 3.72; N, 9.17.

1-Phenyl-3-(pyridin-2′-yl)imidazolin-2-one (4d)
Purified by flash chromatography (cyclohexane–acetone, 10:1).

Yield: 96% (isolated yield from 2-bromopyridine); colorless crystals; mp 137 °C.

IR (KBr): 3117 (w), 2919 (w), 1707 (s), 1602 (m), 1477 (s), 1450 (s), 1286 (m), 1227 (s), 922 (m), 783 (s), 682 (s) cm^{-1}.

^1H NMR (300 MHz, CD_2Cl_2): δ = 6.76 (d, *J* = 3.3 Hz, 1 H, H-5), 7.16 (ddd, *J* = 1.0, 4.9, 7.4 Hz, 1 H, H-5′), 7.30 (tt, *J* = 1.4, 7.5 Hz, 1 H, H-*para*), 7.47 (m, 2 H, H-*meta*), 7.54 (d, *J* = 3.3 Hz, 1 H, H-4), 7.65 (dd, *J* = 1.1, 8.6 Hz, 2 H, H-*ortho*), 7.81 (ddd, *J* = 1.9, 7.4, 8.4 Hz, 1 H, H-4′), 8.42 (ddd, *J* = 1.0, 1.9, 4.9 Hz, 1 H, H-6′), 8.48 (dt, *J* = 1.0, 8.4 Hz, 1 H, H-3′).

^{13}C NMR (75 MHz, CD_2Cl_2): δ = 109.5 (C-4), 111.8 (C-5), 114.2 (C-3′), 121.1 (C-5′), 122.6 (C-*ortho*), 126.3 (C-*para*), 129.7 (C-*meta*), 137.6 (C-*ipso*), 138.9 (C-4′), 148.6 (C-6′), 150.0 (C-2′), 150.8 (C-2).

HRMS (EI): *m*/*z* calcd for $C_{14}H_{11}N_3O$: 237.0902; found (%): 237.0909 (100), 234.1030 (24), 208.0870 (5).

Anal. Calcd for $C_{14}H_{11}N_3O$: C, 70.87; H, 4.67; N, 17.71. Found: C, 70.67; H, 4.71; N, 17.52.

3-(4′-Nitrophenyl)-1-phenylimidazolin-2-one (4e)
Purified by flash chromatography (PE–EtOAc, 3:1).

Yield: 100% (isolated yield from iodo-4-nitrobenzene); 96% (isolated yield from bromo-4-nitrobenzene); yellow crystals; mp 195 °C.

IR (KBr): 3163 (w), 2921 (w), 1689 (s), 1596 (s), 1518 (s), 1427 (s), 1346 (s), 1274 (m), 1225 (m), 1182 (m), 917 (m), 855 (s), 788 (s), 762 (s) cm^{-1}.

^1H NMR (300 MHz, CD_2Cl_2): δ = 6.85 (d, *J* = 3.4 Hz, 1 H, H-4/H-5), 6.89 (d, *J* = 3.4 Hz, 1 H, H-4/H-5), 7.33 (dd, *J* = 7.4, 1.3 Hz, 1 H, H-*para*), 7.49 (dd, *J* = 7.4, 8.0 Hz, 2 H, H-*meta*), 7.63 (dd, *J* = 8.0, 1.3 Hz, 2 H, H-*ortho*), 7.95 (d, *J* = 9.4 Hz, 2 H, H-2′), 8.32 (d, *J* = 9.4 Hz, 2 H, H-3′).

^{13}C NMR (75 MHz, CD_2Cl_2): δ = 109.9 and 113.4 (C-4/C-5), 121.2 (C-2′), 122.7 (C-*ortho*), 125.5 (C-3′), 127.1 (C-*para*), 129.8 (C-*meta*), 137.3 (C-*ipso*), 143.2 (C-1′), 145.2 (C-4′), 150.8 (C-2).

HRMS (EI): *m*/*z* calcd for $C_{15}H_{11}N_3O_3$: 281.0800; found (%): 281.0809 (100), 252.0777 (33), 235.0869 (30), 207.0897 (7), 104.0507 (49), 77.0412 (62).

Anal. Calcd for $C_{15}H_{11}N_3O_3$: C, 64.05; H, 3.94; N, 14.96. Found: C, 63.93; H, 4.01; N, 14.84.

3-(3′-Nitrophenyl)-1-phenylimidazolin-2-one (4f)
Purified by flash chromatography (PE–EtOAc, 2:1).

Yield: 73% (isolated yield from iodo-3-nitrobenzene); yellow crystals; mp 156 °C.

IR (KBr): 3157 (s), 2923 (w), 1688 (s), 1617 (m), 1526 (s), 1424 (s), 1353 (s), 1283 (s), 1230 (s), 1200 (m), 1131 (w), 1095 (s), 759 (s), 653 (s) cm^{-1}.

^1H NMR (300 MHz, CD_2Cl_2): δ = 6.84 (d, *J* = 3.5 Hz, 1 H, H-4/H-5), 6.87 (d, *J* = 3.5 Hz, 1 H, H-4/H-5), 7.32 (t, *J* = 7.4 Hz, 1 H, H-*para*), 7.48 (dd, *J* = 8.3, 7.4 Hz, 2 H, H-*meta*), 7.63–7.67 (m, 2 H, H-*ortho*), 7.65 (t, *J* = 8.2 Hz, 1 H, H-5′), 8.11 (dt, *J* = 8.2, 2.0 Hz, 1 H, H-4′), 8.12 (dt, *J* = 8.2, 2.0 Hz, 1 H, H-6′), 8.58 (t, *J* = 2.0 Hz, 1 H, H-2′).

^{13}C NMR (75 MHz, CD_2Cl_2): δ = 110.1 and 112.6 (C-4/C-5), 116.3 (C-2′), 120.5 (C-4′), 122.4 (C-*ortho*), 126.7 (C-*para*), 127.2 (C-6′), 129.6 (C-*meta*), 130.5 (C-5′), 137.2 (C-*ipso*), 138.7 (C-1′), 149.2 (C-3′), 150.6 (C-2).

HRMS (EI): *m*/*z* calcd for $C_{15}H_{11}N_3O_3$: 281.0800; found (%): 281.0804 (100), 252.0776 (18), 235.0865 (13), 104.0516 (24), 77.0405 (24).

Anal. Calcd for $C_{15}H_{11}N_3O_3$: C, 64.05; H, 3.94; N, 14.94. Found: C, 63.95; H, 3.95; N, 14.86.

1-(4-Methoxyphenyl)-3-*p*-tolyl-1*H*-imidazol-2(3*H*)-one (4g)
Purified by flash chromatography (cyclohexane–acetone, 3:1).

Yield: 86% (isolated yield); colorless crystals; mp 166 °C.

IR (KBr): 3156 (w), 2959 (m), 1683 (s), 1516 (s), 1427 (s), 1250 (s), 1038 (m), 919 (m), 834 (m), 692 (m) cm^{-1}.

^1H NMR (300 MHz, CD_2Cl_2): δ = 2.38 (s, 3 H, CH_3), 3.83 (s, 3 H, OCH_3), 6.67 (d, *J* = 3.2 Hz, 1 H, H-5), 6.69 (d, *J* = 3.2 Hz, 1 H, H-4), 6.97 (d, *J* = 9.0 Hz, 2 H, H-3′), 7.26 (d, *J* = 8.2 Hz, 2 H, H-3″), 7.52 (d, *J* = 9.0 Hz, 4 H, H-2′/H-2″).

^{13}C NMR (75 MHz, CD_2Cl_2): δ = 21.0 (CH_3), 55.9 (OCH_3), 111.0 (C-5), 111.6 (C-4), 114.6 (C-3′), 122.2 (C-2″), 124.3 (C-2′), 130.0 (C-3″), 130.8 (C-1′), 135.3 (C-4″), 136.2 (C-1″), 151.0 (C-2), 158.2 (C-4′).

HRMS (EI): *m/z* calcd for $C_{17}H_{16}N_2O_2$: 280.1215; found (%): 280.1215 (100), 251.1176 (13), 237.1024 (17), 161.9893 (11), 150.9994 (12).

Anal. Calcd for $C_{17}H_{16}N_2O_2$: C, 72.84; H, 5.75; N, 9.99. Found: C, 72.36; H, 5.74; N, 9.75.

1,3-Bis(4-methoxyphenyl)-1*H*-imidazol-2(3*H*)-one (4h)
Purified by flash chromatography (cyclohexane–acetone, 3:1).

Yield: 63% (isolated yield); off-white crystals; mp 197 °C.

IR (KBr): 3152 (w), 3014 (w), 2954 (m), 2835 (m), 1688 (s), 1613 (m), 1525 (s), 1425 (s), 1257 (s), 1035 (s), 918 (m), 834 (s), 766 (s), 656 (s) cm^{-1}.

^1H NMR (300 MHz, CD_2Cl_2): δ = 6.65 (s, 2 H, H-4, 5-H), 6.97 (d, *J* = 8.9 Hz, 4 H, H-3′), 7.51 (d, *J* = 8.9 Hz, 4 H, H-2′).

^{13}C NMR (75 MHz, CD_2Cl_2): δ = 56.1 (OCH_3), 111.5 (C-4), 114.8 (C-3′), 124.3 (C-2′), 131.0 (C-1′), 151.3 (C-2), 158.4 (C-4′).

HRMS (EI): *m/z* calcd for $C_{17}H_{16}N_2O_3$: 296.1161; found (%): 296.1155 (100), 267.1124 (14), 253.0976 (13).

Anal. Calcd for $C_{17}H_{16}N_2O_3$: C, 68.91; H, 5.44; N, 9.45. Found: C, 68.92; H, 5.47; N, 9.27.

1-(4-Methoxyphenyl)-3-(4-nitrophenyl)-1*H*-imidazol-2(3*H*)-one (4i)
Purified by flash chromatography (cyclohexane–acetone, 3:1).

Yield: 74% (isolated yield); yellow crystals; mp 175 °C.

IR (KBr): 3127 (m), 3006 (w), 2966 (w), 2836 (w), 1688 (s), 1604 (m), 1517 (s), 1428 (m), 1341 (s), 1251 (s), 1170 (s), 1115 (m), 1029 (m), 918 (m), 851 (m), 779 (m) cm^{-1}.

^1H NMR (300 MHz, CD_2Cl_2): δ = 3.84 (s, 3 H, OCH_3), 6.76 (d, *J* = 3.2 Hz, 2 H, H-5), 6.85 (d, *J* = 3.2 Hz, 2 H, H-4), 6.99 (d, *J* = 9.0 Hz, 1 H, H-3′), 7.49 (d, *J* = 9.0 Hz, 1 H, H-2′), 7.95 (d, *J* = 9.2 Hz, 2 H, H-2″), 8.31 (d, *J* = 9.2 Hz, 2 H, H-3″).

^{13}C NMR (75 MHz, CD_2Cl_2): δ = 56.1 (OCH_3), 109.4 (C-4), 113.9 (C-5), 115.0 (C-3′), 119.4 (C-2″), 120.8 (C-3″), 124.3 (C-2′), 130.3 (C-1′), 142.5 (C-1″), 145.6 (C-4″), 151.3 (C-2), 158.4 (C-4′).

HRMS (EI): *m/z* calcd for $C_{16}H_{13}N_3O_4$: 311.0906; found (%): 311.0905 (100), 282.0883 (6), 265.0972 (11), 134.0605 (16).

Anal. Calcd for $C_{16}H_{13}N_3O_4$: C, 61.73; H, 4.21; N, 13.50. Found: C, 61.53; H, 4.27; N, 13.50.

Acknowledgment

Financial support for this research by the Deutsche Forschungsgemeinschaft (KU 1473/2-1) and the Fonds der Chemischen Industrie is gratefully acknowledged. We thank Prof. Peter Hofmann for his constant and generous support, Prof. Thomas J. J. Müller for the use of the SmithCreator microwave and Johnson Matthey for a loan of Pd-complexes.

References

(1) (a) Muchmore, S. W.; Souers, A. J.; Akritopoulou-Zanze, I. *Chem. Biol. Drug Design.* **2006**, *67*, 174. (b) Schwink, L.; Stengelin, S.; Gossel, M.; Boehme, T.; Hessler, G.; Rosse, G.; Walser, A. PCT Int. Appl. WO 2004011438, **2004**; *Chem. Abstr.* **2004**, *140*, 163866. (c) Wilde, R. G.; Takasugi, J. J.; Hwang, S.; Welch, E. M.; Chen, G. PCT Int. Appl. WO 2004009558, **2004**; *Chem. Abstr.* **2004**, *140*, 146137. (d) Himmelsbach, F.; Pieper, H.; Austel, V.; Linz, G.; Weisenberger, J.; Eisert, W.; Mueller, T. U.S. Patent US 5852192, **1998**; *Chem. Abstr.* **1999**, *130*, 665504. (e) Felix, R. A. U.S. Patent US 4724261, **1988**; *Chem. Abstr.* **1988**, *108*, 167475.

(2) (a) Tanaka, K.; Doi, M. Japan Patent JP 4343365, **1992**; *Chem. Abstr.* **1993**, *118*, 263846. (b) Klüpfel, K. W.; Stumpf, H. R.; Behmenburg, H.; Neugebauer, W.; Süs, O.; Tomanek, M. German Patent Appl. DE 1060713, **1959**; *Chem. Abstr.* **1961**, *55*, 110603.

(3) (a) Brazier, S. A.; McCombie, H. *J. Chem. Soc.* **1912**, *101*, 2352. (b) Schönherr, H. J.; Wanzlick, H. W. *Chem. Ber.* **1970**, *103*, 1037.

(4) Watabe, Y.; Kondo, T.; Watabe, Y. Japan Patent JP 5004970, **1993**; *Chem. Abstr.* **1993**, *118*, 254934.

(5) Lozanova, K.; Kalcheva, V.; Simov, D. *Chem. Heterocycl. Compd. (Engl. Transl.)* **1988**, *24*, 1129.

(6) Wendeborn, S.; Winkler, T.; Foisy, I. *Tetrahedron Lett.* **2000**, *41*, 6387.

(7) (a) Mann, G.; Hartwig, J. F.; Driver, M. S.; Fernández-Rivas, C. *J. Am. Chem. Soc.* **1998**, *120*, 827. (b) Yang, B. H.; Buchwald, S. L. *J. Organomet. Chem.* **1999**, *576*, 125. (c) Shekhar, S.; Ryberg, P.; Hartwig, J. F.; Mathew, J. S.; Blackmond, D. G.; Strieter, E. R.; Buchwald, S. L. *J. Am. Chem. Soc.* **2006**, *128*, 3584.

(8) (a) Ullmann, F. *Ber. Dtsch. Chem. Ges.* **1903**, *36*, 2382. (b) Goldberg, I. *Ber. Dtsch. Chem. Ges.* **1906**, *39*, 1691. (c) Sugahara, M.; Ukita, T. *Chem. Pharm. Bull.* **1997**, *45*, 719. (d) Strieter, E. R.; Blackmond, D. G.; Buchwald, S. L. *J. Am. Chem. Soc.* **2005**, *127*, 4120. (e) Haider, J.; Kunz, K.; Scholz, U. *Adv. Synth. Catal.* **2004**, *346*, 717. (f) Beletskaya, I. P.; Cheprakov, A. V. *Coord. Chem. Rev.* **2004**, *248*, 2337.

(9) For examples of palladium-catalyzed reactions with urea, see: (a) Artamkina, G. A.; Sergeev, A. G.; Beletskaya, I. P. *Tetrahedron Lett.* **2001**, *42*, 4381. (b) Sergeev, A. G.; Artamkina, G. A.; Beletskaya, I. P. *Tetrahedron Lett.* **2003**, *44*, 4719. For examples of copper-catalyzed reactions with urea, see: (c) Buchwald, S. L.; Klapars, A.; Antilla, J. C.; Job, G. E.; Wolter, M.; Kwong, F. Y.; Nordmann, G.; Hennessy, E. J. PCT Int. Appl. WO 02085838, **2002**; *Chem. Abstr.* **2002**, *137*, 352492. (d) Nandakumar, M. V. *Tetrahedron Lett.* **2004**, *45*, 1989. (e) Trost, B. M.; Styles, D. T. *Org. Lett.* **2005**, *7*, 2117. For examples with benzimidazolinones, see: (f) Ward, R. E.; Meyer, T. Y. *Macromolecules* **2003**, *36*, 4368.

(10) Yang, G. X.; Chang, L. L.; Truong, Q.; Doherty, G. A.; Magriotis, P. A.; de Laszlo, S. E.; Li, B.; MacCoss, M.; Kidambi, U.; Egger, L. A.; McCauley, E.; Van Riper, G.; Mumford, R. A.; Schmidt, J. A.; Hagmann, W. K. *Bioorg. Med. Chem. Lett.* **2002**, *12*, 1497.

(11) (a) Mann, G.; Hartwig, J. F.; Driver, M. S.; Fernández-Rivas, C. *J. Am. Chem. Soc.* **1998**, *120*, 827. (b) Grasa, G. A.; Viciu, M. S.; Huang, J.; Nolan, S. P. *J. Org. Chem.* **2001**, *66*, 7729. (c) Vargas, V. C.; Rubio, R. J.; Hollis, T. K.; Salcido, M. E. *Org. Lett.* **2003**, *5*, 4847. (d) Klapars, A.; Antilla, J. C.; Huang, X.; Buchwald, S. L. *J. Am. Chem. Soc.* **2001**, *123*, 7727. (e) Antilla, J. C.; Baskin, J. M.; Barder, T. E.; Buchwald, S. L. *J. Org. Chem.* **2004**, *69*, 5578.

(12) Kiyomori, A.; Marcoux, J.-F.; Buchwald, S. L. *Tetrahedron Lett.* **1999**, *40*, 2657.
(13) For reviews, see: (a) Nilsson, P.; Olofsson, K.; Larhed, M. *Top. Curr. Chem.* **2006**, *266*, 103. (b) Wan, Y.; Alterman, M.; Hallberg, A. *Synthesis* **2002**, 1597. (c) Yadav, L. D. S.; Yadav, B. S.; Rai, V. K. *Synthesis* **2006**, 1868. (d) Lange, J. H. M.; Hofmeyer, L. J. F.; Hout, F. A. S.; Osnabrug, S. J. M.; Verveer, P. C.; Kruse, C. G.; Feenstra, R. W. *Tetrahedron Lett.* **2002**, *43*, 1101. (e) For a review involving urea, see: Wannberg, J.; Dallinger, D.; Kappe, C. O.; Larhed, M. *J. Comb. Chem.* **2005**, *7*, 574.
(14) Forrest, T. P.; Dauphinee, G. A.; Chen, F. M. F. *Can. J. Chem.* **1974**, *52*, 2725.
(15) Leadbeater has shown that when the Powermax cooling function is used, the standard IR sensor does not give accurate temperature measurements. In DMSO at a nominal temperature of 100 °C, the actual temperature was 20 °C higher, whereas in hexane, the actual temperature was 20 °C lower. We have used dioxane so the respective effects could level out, however the real temperature could vary by about ±20 °C from the given value in the case of the experiments reported in Table 3.
(16) Marckwald, W. *Ber. Dtsch. Chem. Ges.* **1892**, *25*, 2354.
(17) Duchinsky, R.; Dolan, L. A. *J. Am. Chem. Soc.* **1946**, *68*, 2351.
(18) Golovko, V. V.; Statsenskaya, A. I.; Baskakov, Y. A.; Putsykin, Y. G. *Chem. Heterocycl. Compd.* **1986**, *22*, 1084.
(19) Cortes, S.; Liao, Z.-K.; Watson, D.; Kohn, H. *J. Med. Chem.* **1985**, *28*, 601.