

# Ruthenium catalysed *N,N'*-Diarylurea Synthesis from *N*-Aryl substituted Formamides and Aminoarenes

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*N*-Aryl substituted formamides react smoothly with aminoarenes in the presence of a catalytic amount of dichlorotris(triphenylphosphine)ruthenium to afford various *N,N'*-diarylureas in good yields.

Urea and its derivatives are important compounds not only to agriculture but also to medicine and industry. Examples of syntheses of urea derivatives are limited to the reaction of isocyanates with amines,<sup>1</sup> and transition metal complex catalysed carbonylation of amines and/or nitro compounds.<sup>2</sup>

In recent years, much attention has been paid to more straightforward and efficient synthesis of urea derivatives without using poisonous and dangerous phosgene or carbon monoxide. In the course of our study on ruthenium catalysis, we have already found that ruthenium complexes show high catalytic activities both in hydrogen transfer reactions leading to *N*-alkylation and *N*-heterocyclisation<sup>3</sup> and in the activation of formyl C–H bonds.<sup>4</sup> In this communication, we report a ruthenium complex catalysed novel synthesis of urea derivatives from *N*-aryl substituted formamides and aminoarenes [equation (1)]. In the present reaction, we use formamide

derivatives as a carbonyl source and neither carbon monoxide pressure nor atmosphere is required.

In the presence of a catalytic amount of RuCl<sub>2</sub>(PPh<sub>3</sub>)<sub>3</sub>, formanilide reacted smoothly with aniline to give *N,N'*-diphenylurea in 92% yield (Table 1, run 1). Furthermore, a stoichiometric amount of hydrogen (3.6 mmol in run 1) was evolved spontaneously into the gas phase, thus it is not necessary to add any hydrogen acceptors to the present catalytic system. Other ruthenium complexes and group 8 metal complexes showed nothing more than low catalytic activities (runs 2–8). Among the solvents employed, mesitylene (b.p. 164.7 °C) was most effective (run 1).

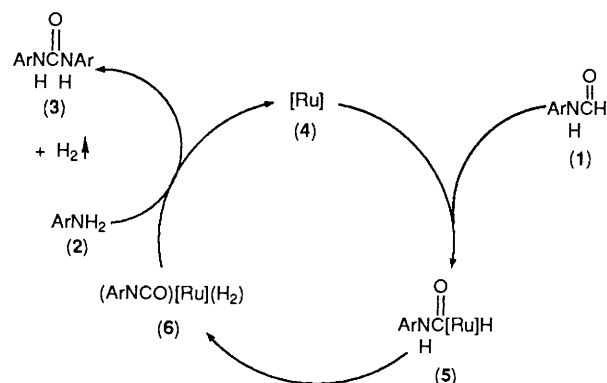
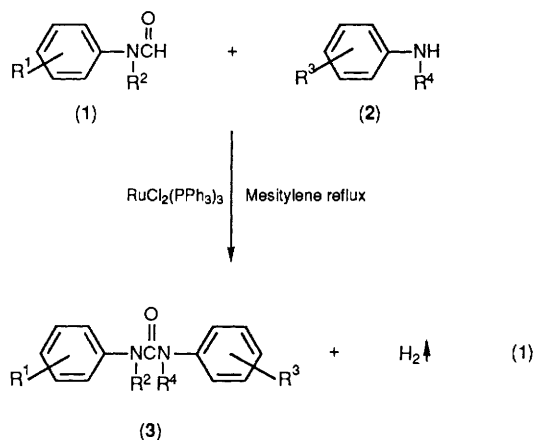
As shown in Table 2, various symmetrically *N,N'*-disubstituted ureas, including sterically hindered *N,N'*-bis(2,6-dimethylphenyl)urea, were obtained in good to excellent yields. On the contrary, asymmetrically disubstituted *N*-phenyl-*N'*-*p*-tolylurea could not be obtained selectively from the reaction of formanilide with *p*-toluidine, which afforded a mixture of three ureas instead (run 6). Heck *et al.* have reported that *N*-phenyl-*N'*-*p*-tolylurea did not react with *p*-toluidine at 90 °C,<sup>2b</sup> nevertheless, thermal dissociation of ureas to the corresponding isocyanates and amines is well known.<sup>5</sup> Our control experiment, refluxing of only *N*-phenyl-*N'*-*p*-tolylurea in mesitylene also afforded the same 1:2:1 mixture of three ureas as shown in run 6. Thus, we now speculate that *N*-phenyl-*N'*-*p*-tolylurea generated initially underwent thermal disproportionation to *N,N'*-diphenylurea and *N,N'*-di-*p*-tolylurea. It is noteworthy that an *N,N'*-disubstituted formamide such as *N*-methylformanilide did not react with amines under the present reaction conditions (runs 7, 8).

A tentative catalytic cycle is illustrated in Scheme 1. Oxidative addition of the formyl C–H bond to the active ruthenium centre (4) would afford a hydride carbamoyl ruthenium intermediate (5),<sup>6</sup> followed by β-hydride elimination to give an isocyanate co-ordinated dihydride or hydrogen ruthenium intermediate (6).<sup>7</sup> Nucleophilic attack of amines (2) on the isocyanate moiety of (6) gives the corresponding

**Table 1.** RuCl<sub>2</sub>(PPh<sub>3</sub>)<sub>3</sub> catalysed *N,N'*-diphenylurea synthesis from formanilide and aniline.<sup>a</sup>

Run	Catalyst	Solvent	Yield <sup>b</sup> /%
1	RuCl <sub>2</sub> (PPh <sub>3</sub> ) <sub>3</sub>	Mesitylene	92 (90)
2	RuHCl(PPh <sub>3</sub> ) <sub>3</sub>	"	18
3	RuH <sub>2</sub> (PPh <sub>3</sub> ) <sub>4</sub>	"	34
4	Ru <sub>3</sub> (CO) <sub>12</sub> + PPh <sub>3</sub> <sup>c</sup>	"	26
5	PdCl <sub>2</sub> (PPh <sub>3</sub> ) <sub>2</sub>	"	~0
6	RhCl(PPh <sub>3</sub> ) <sub>3</sub>	"	0
7	CoCl <sub>2</sub> (PPh <sub>3</sub> ) <sub>2</sub>	"	0
8	PtCl <sub>2</sub> (PPh <sub>3</sub> ) <sub>2</sub>	"	0
9 <sup>d</sup>	RuCl <sub>2</sub> (PPh <sub>3</sub> ) <sub>3</sub>	Decane	80
10 <sup>d</sup>	"	Diglyme	42
11 <sup>d</sup>	"	DMSO <sup>e</sup>	0
12 <sup>d</sup>	"	<i>m</i> -Xylene	14

<sup>a</sup> Formanilide (4 mmol), aniline (4 mmol), catalyst (0.2 mmol), and solvent (5 ml) under reflux for 12 h. <sup>b</sup> Determined by HPLC. Figure in parentheses shows an isolated yield. <sup>c</sup> Ru<sub>3</sub>(CO)<sub>12</sub> (0.07 mmol), PPh<sub>3</sub> (0.6 mmol). <sup>d</sup> Formanilide (2 mmol), aniline (2 mmol), catalyst (0.1 mmol), and solvent (5 ml) under reflux for 6 h. <sup>e</sup> Dimethyl sulphoxide.



**Scheme 1**

**Table 2.** Synthesis of various *N,N'*-diarylureas.<sup>a</sup>

Run	R <sup>1</sup>	(1) R <sup>2</sup>	R <sup>3</sup>	(2) R <sup>4</sup>	Yield <sup>b</sup> /%
1	4-Cl	H	4-Cl	H	85
2	4-MeO	H	4-MeO	H	78
3	4-Me	H	4-Me	H	76
4	2-Me	H	2-Me	H	93
5	2,6-di-Me	H	2,6-di-Me	H	88
6	H	H	4-Me	H	<sup>c</sup>
7	H	Me	H	H	0
8	H	Me	H	Me	0

<sup>a</sup> (1) (4 mmol), (2) (4 mmol), RuCl<sub>2</sub>(PPh<sub>3</sub>)<sub>3</sub> (0.2 mmol), and mesitylene (5 ml) under reflux for 12 h. <sup>b</sup> Isolated yields. <sup>c</sup> *N,N'*-Diphenylurea, 19%; *N*-phenyl-*N'*-*p*-tolylurea, 38%; *N,N'*-di-*p*-tolylurea, 21%; by HPLC.

urea derivatives (3) together with the evolution of hydrogen. This mechanism, involving the formation of an isocyanate intermediate, is consistent with the results reported.

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