Regioselective Preparation of Pyridin-2-yl Ureas from 2-Chloropyridines Catalyzed by Pd(0)

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Abstract: The palladium-catalyzed ureidation reaction of 2-chloropyridines can be regioselectively performed in good yield, with both aryl and aliphatic ureas, using xantphos as the ligand, $Pd(OAc)_2$ as the source of palladium, NaO*t*-Bu/H_2O or NaOH/H_2O as the base, and dioxane as the solvent

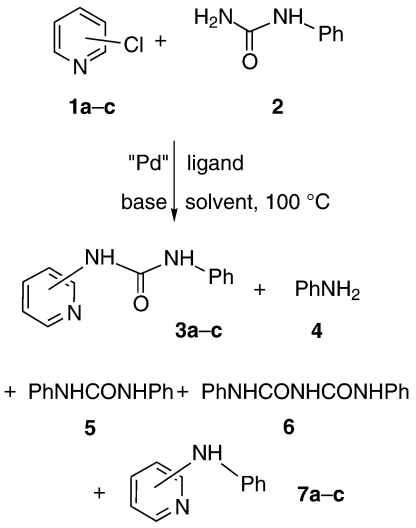
Key words: palladium, catalysis, cross-coupling, pyridines, ureidation

The pyridinyl ureido moiety constitutes a structural motif common to several classes of ureas of great interest in the pharmacologic, agronomic and new material fields.[1] Much interest has been recently paid to pyridin-2-yl ureas, which due to the particular disposition of their ureido and pyridine groups are able to participate in specific hydrogen bonding patterns that control their physical and biological properties. Recent examples include pyridin-2-yl ureas with anticancer properties, a new class of potent Cdk4 inhibitors,[2] strong receptors for cytosine, with potential use as DNA binders,[3] a new type of low molecular-weight gelators, with great potential for functional materials,[4] and pyridin-2-yl-based photodegradable polymers, potentially useful in the field of micro/nanolithography.[5]

In general, conventional procedures for the preparation of pyridinyl ureas involve the use of toxic and troublesome reagents such as isocyanates, phosgene or CO_2.[2–5,6] In spite of the large amount of research work that has been done on the palladium-catalyzed C–N bond forming reactions of aryl/heteroaryl systems (e.g. amine,[7] amide,[8] imine,[9] carbamate,[10] lactam,[11] sulphonamide,[8] and sulfoximines[12] arylations have been described), only a few examples of palladium-catalyzed arylation of ureas have been reported recently. These include the cross-coupling of urea and phenylurea with activated[13] and unactivated[14] aryl bromides and iodides, the coupling of an aryl bromide with cyclic ureas,[8] and some intramolecular palladium-catalyzed arylation of ureas.[15] To the best of our knowledge, the analogous cross-coupling reaction of heteroaryl halides, and in particular of the generally less reactive chlorides, has not been explored.[16]

In relation to our interest in the preparation of pyridinyl ureas,[17] we have investigated the viability of the palladium-catalyzed coupling of readily available chloropyridines with several types of ureas. We show that 2-chloropyridines can react efficiently with both aryl and alkyl ureas, allowing the preparation of both *N*-phenyl- and *N*-alkyl-*N*′-pyridin-2-yl ureas in good to excellent yields.[18]

Initially, we examined the cross-coupling of 2-chloropyridine (**1a**) with phenylurea (**2**) under the conditions previously described by Beletskaya[13,14] for the related coupling of aryl bromides with the same urea (Table 1, entry 1). Under these conditions the reaction took place smoothly, to give a 90% of conversion after 3 hours, affording the expected *N*-phenyl-*N*′-(pyridin-2-yl)urea (**3a**) in relatively good isolated yield (78%). Trace amounts of aniline (**4**), *N*,*N*′-diphenylurea (**5**), 1,5-diphenylbiuret (**6**)[19] and *N*-phenyl-*N*′-(pyridin-2-yl)amine (**7a**)[20] were observed as side-products (Scheme 1), the amounts of which strongly depended on the reaction times. Increasing the reaction times in order to achieve a complete conversion of the reactants did not lead to a higher yield of isolated **3a**, but resulted in a significant increase of all of the side-products formed in the reaction.[21]



a, **b** and **c**: substitution at 2-, 3-, and 4-positions, respectively, of the pyridine ring

Scheme 1

Control experiments showed that the first three compounds, **4**–**6**, result from disproportionation of phenylurea under the reaction conditions used, while the formation of

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Table 1 Palladium-Catalyzed Cross-Coupling Ureidation of Chloropyridines

Entry	Chloropyridine[a]	Urea[a]	Reaction conditions[b]	Reaction time[c]	Main reaction products[d]
1	**1a** (1)	**2** (1)	**A**[e]	3 h	**3a** (78%)
2	**1a** (1)	**2** (1)	**B**[e]	2 h	**3a** (75%)
3	**1a** (1)	**2** (1)	**C**[f]	2 h	**3a** (72%); **7a** (18%)
4	**1a** (1)	**2** (1)	**D**[f]	2.5 h	**3a** (93%)
5	**1a** (1)	**2** (1)	**E**[f]	3 h	**3a** (89%)
6	**1c** (1)	**2** (1)	**D**[f]	2 h	**3c** (8%); **7c** (2%)
7	**1a** (1)	**8a** (1)	**D**[f]	2 h	**9a** (98%)
8	**1a** (1)	**8b** (0.5)	**D**[e]	3 h	**10b** (93%)
9	**1a** (1)	**8c** (0.5)	**D**[e]	6 h	**10c** (95%)
10	**11a** (1)	**2** (1)	**D**[f]	2 h	**12a** (75%); **13a** (23%)
11	**11b** (1)	**2** (1)	**D**[f]	3.5 h	**12b** (80%); **15**[g] (6%)
12	**11c** (1)	**2** (1)	**D**[f]	3.5 h	**12c** (94%)
13	**11d** (1)	**2** (1)	**D**[f]	1 h	**12d** (90%); **14d** (3%); **16** (3%)
14	**11e** (1)	**2** (1–2)	**A–D**[f]	up to12 h	No cross-coupling urea formed
15	**11a** (1)	**8b** (0.33)	**A**[e]	5 h	**17a** (11%); **18a** (65%)
16	**11b** (1)	**8b** (0.5)	**D**[f]	1 h	**17b** (70%)
17	**11c** (1)	**8b** (0.5)	**D**[f]	1.5 h	**17c** (80%)
18	**11d** (1)	**8b** (0.33)	**A**[h]	1.5 h	**17d** (75%)

[a] Equivalents within parentheses.
[b] All reactions were carried out in dioxane at 100 ºC; **A**: $Pd_2dba_3{\cdot}CHCl_3$ (2 mol%), Xantphos (6 mol%), Cs_2CO_3 (1.4 equiv); **B**: $Pd_2dba_3{\cdot}CHCl_3$ (2 mol%), Xantphos (6 mol%), NaO*t*-Bu (1.4 equiv); **C**: $Pd(OAc)_2$ (3 mol%), Xantphos (6 mol%), NaO*t*-Bu (1.4 equiv); **D**: $Pd(OAc)_2$ (3 mol%), Xantphos (6 mol%), NaO*t*-Bu (1.4 equiv), H_2O (1.4 equiv); **E**: $Pd(OAc)_2$ (3 mol%), Xantphos (6 mol%), NaOH (1.4 equiv), H_2O (1.4 equiv).
[c] For complete reaction of starting material.
[d] Yields of pure isolated compounds are given within parentheses.
[e] 0.2 M in chloropyridine.
[f] 0.4 M in chloropyridine.
[g] Compound **15**: *N*-(2-chloro-pyridin-4-yl)-*N*′-phenyl urea (see text).
[h] 0.6 M in chloropyridine.

the amine **7a** can be attributed to the cross-coupling reaction of chloropyridine **1a** with the aniline generated in the reaction medium. This type of disproportionation reaction has been previously observed in the arylation of phenylurea with aryl halides, particularly with the less reactive ones.[13]

After these preliminary results, and in order to get the higher yield of urea **3a**, extensive research was performed on the optimization of the reaction conditions. Evaluation of the influence of different bases, palladium sources, ligands, solvents and reaction times was carried out, and a summary of the main results is as follows. Replacement of Cs_2CO_3 by bases such as K_2CO_3, K_3PO_4, in all cases in the presence of a small amount of water (1–5 equiv),[22] led to rather slower coupling reactions that required longer reaction times for a high degree of conversion. Significant amounts of side-products were originated, particularly aniline and 2-aminopyridines (e.g. K_2CO_3, 20 h, 65% of **3a**; K_3PO_4, 26 h, 50% of **3a**,). The use of NaO*t*-Bu afforded similar results to those obtained with Cs_2CO_3, although a slight shortening of the coupling reaction time was observed (Table 1, entry 2). The change of the palladium precatalyst from $Pd_2dba_3{\cdot}CHCl_3$ to $Pd(OAc)_2$ did not have a detrimental effect on the yield of **3a**, although substantial amounts of the amine **7a**[20] were formed (Table 1, entry 3). A decrease in the amount of the catalyst used or a reduction in the reaction temperature led to a decrease in the conversion. The employment of other ligands successfully used in palladium-catalyzed amination of aryl halides, e.g. BINAP,[23] P*t*-Bu_3,[24] $P[N(i\text{-}Bu)CH_2CH_2]_3N$[16b] or 1,3-bis(2,4,6-diisopropylphenyl)imidazol-2-ylidene (IPr·HCl)[16i] did not improve the results described above,

giving no cross-coupling product or leading to low yields of the urea **3a**. It is worth noting that with some of these ligands a rapid disproportionation of phenylurea (**2**) took place, as in the case of P*t*-Bu_3, which basically led to unreacted chloropyridine **1a** and aniline after 3 hours [$Pd(OAc)_2$ (5% mol), P*t*-Bu_3 (5% mol), NaO*t*-Bu (1.4 equiv), dioxane, 100 °C].

It was found, after additional optimization of the reaction conditions, that a higher yield of the urea **3a** could be obtained by conducting the cross-coupling reaction in the presence of an equimolar amount of water with respect to NaO*t*-Bu (Table 1, entry 4). Substitution of the NaO*t*-Bu/H_2O base system by NaOH/H_2O led to comparable results (Table 1, entry 5). Control experiments showed that the disproportionation of the phenylurea is drastically reduced under these conditions. A nearly quantitative yield of urea **3a** was obtained using an excess of phenylurea (ca. 1.5–2 equiv). However, the use of an equimolar amount of phenylurea with respect to the chloropyridine counterpart greatly aided in the isolation and purification of the cross-coupling urea. With both NaO*t*-Bu/H_2O and NaOH/H_2O base systems the coupling reaction of **1a** and **2** takes place very cleanly, resulting in the higher yields of the coupling urea, and without formation of appreciable amounts of side-products, and therefore these conditions were employed for the remainder of the study.

That the palladium was necessary for these reactions was established by means of appropriate control experiments run under the above-mentioned conditions differing only in that the palladium source was omitted. No formation of urea **3a** was observed after 20 hours. This result seems to exclude the possibility that the observed coupling proceeds via a standard nucleophilic aromatic substitution mechanism.

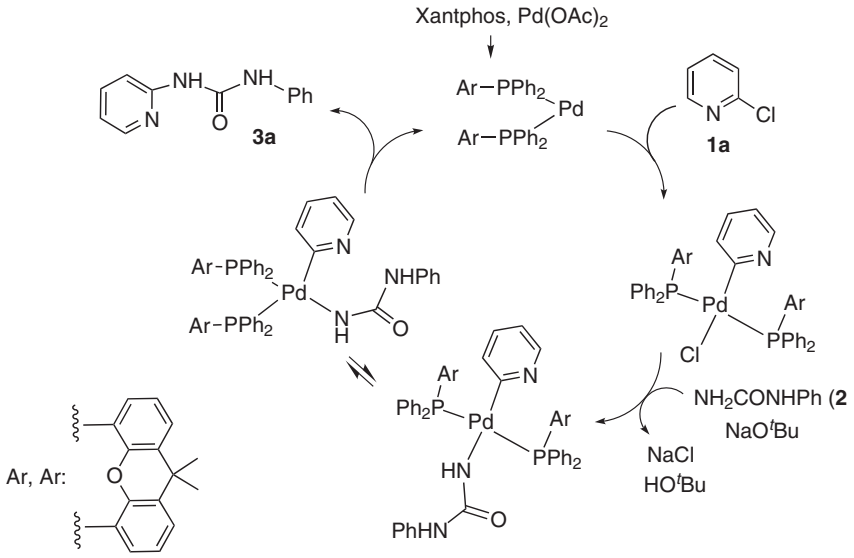
In parallel to the above coupling of **1a** and phenylurea (**2**), we also examined the cross-coupling reaction of regioisomeric 3- and 4-chloropyridines, **1b** and **1c** respectively, with **2**. Despite some effort, we were unable to develop useful conditions for the coupling of 3-chloropyridine (**1b**) and phenylurea. Only the products originating from the disproportion of phenylurea and small amounts of *N*-phenyl-*N*′-(pyridin-3-yl)amine (**7b**)[20] were observed under several different reaction conditions, including those discussed above for 2-chloropyridine (**1a**). In these reactions, none of the urea **3b** could be detected even after prolonged reaction times in the presence of an excess of phenylurea. The contrast between the absence of reactivity of **1b** in this cross-coupling reaction and the efficient amination that it experiences with primary and secondary amines under relatively similar conditions is quite remarkable.[16b,25]

On the other hand, the coupling reaction of 4-chloropyridine (**1c**) with phenylurea did take place, though very slowly, under several of the conditions described above for **1a**, always affording very low yields of the coupled urea. Thus, only 8% of urea **3c** was obtained after two hours under the standardized conditions used for **1a** (Table 1, entry 6). Longer reaction times led to still lower yields of the coupling urea; for example, only 4% of urea **3c** was obtained after seven hours and none of the coupling ureas was observed after 12 hours of reaction. Apparently, the coupling reaction of **1c** with phenylurea occurs so sluggishly under the different reaction conditions assayed, that the decomposition of the *N*-phenyl-*N*′-(pyridin-4-yl)urea formed takes place at relatively comparable rate to the cross-coupling reaction itself.[26]

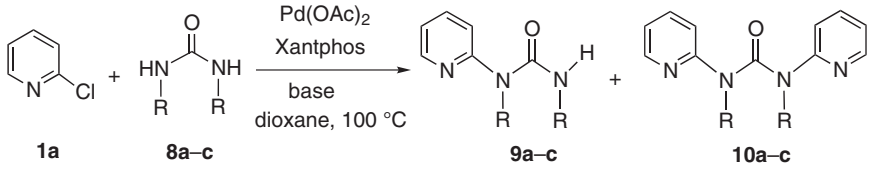
In principle, the different reactivity of 2-, 3-, and 4-chloropyridines in the coupling reaction with phenylurea parallels the known relative reactivity of these positions observed in nucleophilic aromatic substitutions (2 > 4 >> 3). It does not seem that the unreactivity of the 3-chloropyridine in the coupling reaction with phenylurea can be attributed to the difficulty with which the oxidative addition at this position takes place. As mentioned above, this chloropyridine undergoes a smooth Pd-catalyzed amination with aniline under similar conditions to those used in the coupling with phenylurea, a reaction that must, in principle, take places via the same oxidative addition step involved in the ureidation process. It is reasonable to suppose, as previously suggested,[14] that the reductive elimination is the rate-determining step of this ureidation reaction. Probably, both the low nucleophilicity of the ureido group and diminishing electrophilicity of the 3-pyridinyl position contribute to the key reductive elimination step being particularly unfavorable for the reaction of **1b**.[27] In principle, the Pd-catalyzed ureidation reaction of aryl systems is a less favorable process than the amination reaction, a circumstance that is well correlated with the relative nucleophilicity of the ureido and amino moieties, and which determines the rate at which the C-N bond is formed in the reductive elimination process. In congruence with this argument, competitive control experiments proved that the coupling reaction of 4-bromocianobenzene with aniline is three times faster than the reaction rate with phenylurea. We observed, however, that 2-chloropyridine (**1a**) does not follow this trend and reacts faster with phenylurea than with aniline (by a factor of 1.5). We speculate about the possibility that the observed higher rate of the ureidation reaction of 2-chloropyridine might be related with some form of intramolecular assistance of the azomethine nitrogen atom in the reductive elimination step, which probably occurs from a 16-electron four-coordinated intermediate, after *trans* to *cis* isomerization (Scheme 2).[7a,8]

We also explored the Pd(0)-catalyzed ureidation of 2-chloropyridine (**1a**) with aliphatic ureas. An efficient coupling reaction took place with *N*,*N*′-dimethylurea (**8a**) under the above standardized conditions (Scheme 3), to give exclusively the mono-coupling urea **9a** in nearly quantitative yield (Table 1, entry 7). Formation of the di-coupling urea **10a** was not observed even when longer reaction times and an excess of 2-chloropyridine were used.

On the other hand, a slightly slower but also efficient coupling reaction took place between 2-chloropyridine (**1a**) and both the six- and five-membered cyclic ureas, **8b** and



Scheme 2 Potential mechanism for the Pd-catalyzed cross-coupling reaction of 2-chloropyridine (**1a**) with phenylurea (**2**).



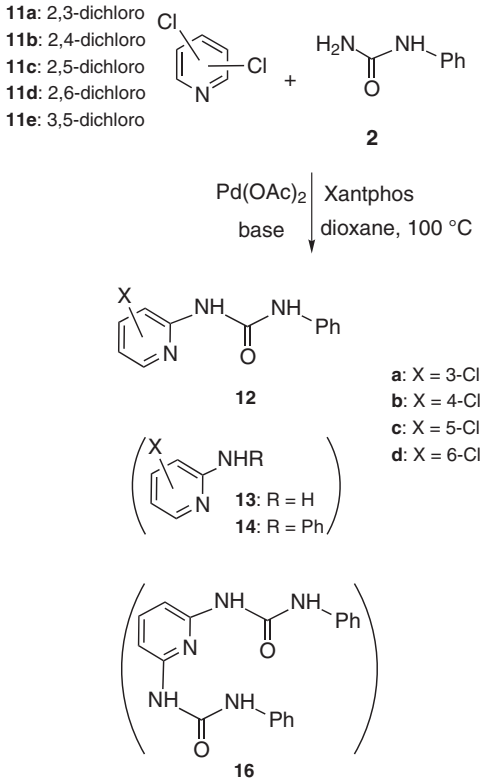
a: R = CH_3; **b**: R,R = CH_2-CH_2-CH_2; **c**: R,R = CH_2-CH_2

Scheme 3

8c respectively, to give primarily the corresponding di-coupling ureas (Scheme 3). Thus, coupling of **1a** with **8b**, using an equimolar ratio of the reactants, afforded a 19% yield of the mono-coupling urea **9b** and a 52% yield of the di-coupling urea **10b** after three hours. The latter was the only coupling product isolated when an appropriate proportion of reactants was used (Table 1, entry 8). The coupling of **1a** with the five-membered cyclic urea **8c** took also place very efficiently to give a very high yield of the corresponding di-coupling urea **10c** (Table 1, entry 9). It must be noted that for successful coupling of **1a** with the cyclic ureas, **8b** and **8c**, it was necessary to run these reactions at lower concentration (0.2 M in the urea), probably due to their lower solubility in the reaction medium.

To complete our study on the palladium-catalyzed ureidation of chloropyridines, we have also examined the coupling reaction of several regioisomeric dichloropyridines with phenylurea (**2**) (Scheme 4).[28] The most interesting results are shown in the Table 1 (entries 10–14). As expected, in view of the previous results shown above, the ureidation reaction occurs regioselectively at the 2-position; however, not all the dichloropyridines behave identically under the reaction conditions used. Thus, 2,3-dichloropyridine (**11a**) readily reacts under the standardized conditions to give a good yield of the corresponding *N*-(3-chloro-pyridin-2-yl)-*N*′-phenylurea (**12a**), together with substantial amounts, up to 23%, of 3-chloro-pyridin-2-ylamine (**13a**),[29] easily separated from the former by column chromatography (Table 1, entry 10). The formation of this amine, which must originate from urea **12a**, could not be suppressed by changing the reaction conditions or reducing the reaction time. For example, 10% of this amine was already formed after just one hour of reaction, corresponding to approximately 70% of the dichloropyridine conversion. This was the only case in which this type of amine was observed. Formation of appreciable amounts of analogue chloro-pyridin-2-ylamines **13** was not detected with any of the other dichloropyridines.

The coupling reaction of 2,4- and 2,5-dichloropyridines, **11b** and **11c**, respectively, was somewhat slower requiring from 3–4 hours for completion. Coupling of **11b** and phenylurea gave a good yield of *N*-(4-chloro-pyridin-2-yl)-*N*′-phenyl-urea (**12b**), together with traces of the urea resulting from the coupling at the 4-position, *N*-(2-chloro-pyridin-4-yl)-*N*′-phenyl-urea (**15**), a commercial plant grown regulator known as CPPU (Table 1, entry 11). The reaction of **11c** was very clean, affording regioselectively an excellent yield of the coupling urea **12c** (Table 1, entry 12). As previously observed for the coupling reaction of **1a** with phenylurea, the use of water in these reactions was essential to drastically reduce or completely avoid the formation of *N*-(pyridin-2-yl)-*N*′-phenylamines **14**. For example, the reaction of **11c** with phenylurea in the absence of water (reaction conditions **C** in Tables 1, 7 h)

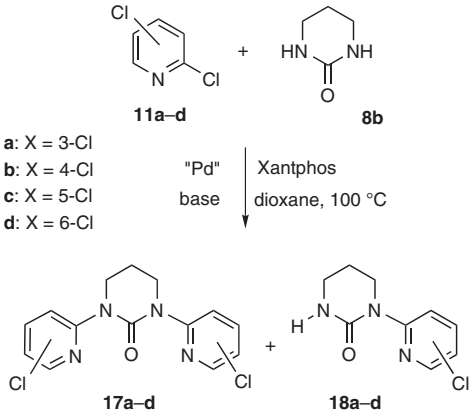


Scheme 4

gave a 74% yield of the urea **12c** and a 20% yield of *N*-(5-chloropyridin-2-yl)-*N*′-phenyl-amine (**14c**). The coupling reaction of 2,6-dichloropyridine (**11d**) with phenylurea was particularly rapid, giving a 90% yield of the coupling urea **12d** in just one hour of reaction (Table 1, entry 13). This was the only case in which the diurea formed by substitution of both chlorine atoms, the *N*-phenyl-*N*′-[6-(3-phenylureido)pyridin-2-yl]urea (**16**), was isolated, albeit in a very low yield (3%). In this case, a small amount (3–4%) of *N*-(6-chloropyridin-2-yl)-*N*′-phenylamine (**14d**) was also obtained.

As was anticipated, the cross-coupling reaction of 3,5-dichloropyridine (**11e**) was particularly problematic due to the remarkable unreactivity of these positions of the pyridine ring for the ureidation reaction. No ureidation products were detected under any of the reaction conditions described above (Table 1, entry 14). Only the products formed by disproportionation of phenylurea and traces of the amination product, (5-chloro-pyridin-3-yl)-phenyl-amine, were observed after prolonged reaction times.

Finally, we briefly explored the reactivity of dichloropyridines with the cyclic urea **8b**, as a representative of their behavior in the coupling reaction with aliphatic ureas. The reaction of dichloropyridines **11b** and **11c** under similar conditions to those previously used with 2-chloropyridine (**1a**) afforded the corresponding 1,3-bis(chloropyridin-2-yl)tetrahydro-2-pyrimidinones **17b** and **17c**, respectively, in a relatively efficient way (Scheme 5; Table 1, entries 16 and 17). Under these conditions, only the formation of



Scheme 5

trace amounts of the mono-coupling products, **18b** or **18c**, was observed.

Initial attempts to react 2,6-dichloropyridine (**11d**), with **8b** under the same standardized coupling conditions led to very low yields of the urea **17d**, probably due to the formation of very polar polyurea-type compounds.[30] For this dichloropyridine, the best yield of the ureidation product **17d** was obtained by using Beletskaya reaction conditions and a large excess of dichloropyridine with respect to **8b** (Table 1, entry 18).[13] Approximately a 3–4% yield of compounds **19** (Figure 1) was isolated from this reaction, suggesting, in this case too, the more than probable formation of polymeric materials.

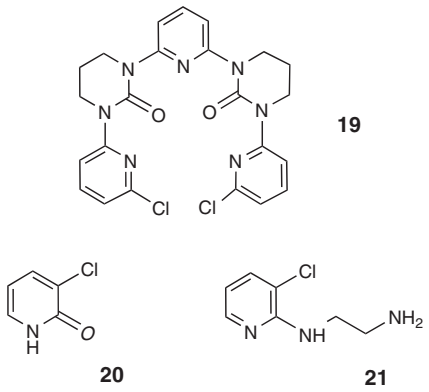


Figure 1

The behavior of the 2,3-dichloropyridine (**11a**), in the coupling reaction with **8b** was somewhat different. The reaction was initially carried out using Na*t*-OBu/H_2O as the base (reaction conditions **D**), which led, after four hours, to a complex product distribution and the isolation of about 30% of 3-chloropyridin-2(1*H*)-one (**20**, Figure 1),[31] very small amounts (3–5%) of 1- and 1,3-bis(3-chloropyridin-2-yl)tetrahydro-2-pyrimidinones, **18a** and **17a**, respectively, and approximately 10% of *N*-(2-aminoethyl)-3-chloropyridin-2-amine (**21**, Figure 1),[32] probably formed by hydrolysis of the latter. Control experiments showed that the formation of **20** in the above reaction

does not seem to take place via replacement of chlorine by OH, by direct nucleophilic substitution or through catalysis by Pd(0), since its formation was not observed in the absence of the urea **8b**. However, a detailed study of the origin of the formation of this unexpected product was not undertaken. Replacement of NaO*t*-Bu/H_2O by Cs_2CO_3 led to a much higher yield of the mono-ureidation product, **18a**, although a longer reaction time was required (Table 1, entry 15). Under these reaction conditions, only a small amount of the dicoupling product **17a** was obtained, in spite of the large excess of dichloropyridine used, and only traces of **20** were detected.

In summary, we have shown that the palladium-catalyzed ureidation of most of the 2-chloropyridines can be regioselectively performed in high yield with both aryl and aliphatic ureas, using xantphos as the ligand, $Pd(OAc)_2$ as the source of palladium, NaO*t*-Bu/H_2O or NaOH/H_2O as base, and dioxane as the solvent. It has been shown that the 2-position of the pyridine ring is particularly reactive in the ureidation reaction, and in contrast to that observed with aryl halides, this reaction occurs at this position faster than the related amination reaction.

All reagents were purchased from Aldrich and were used without further purification. Xantphos was prepared according to literature procedures.[33] NaO*t*-Bu, $Pd_2dba_3{\cdot}CHCl_3$ and phosphine ligands were kept in a dry box. Dioxane was distilled from sodium–benzophenone ketyl immediately before use. The palladium-catalyzed reactions were run under N_2 using standard Schlenk and vacuum line techniques. Flash column chromatography was performed on Merck silica gel 60 (230–400 mesh) using the eluent specified under medium pressure. TLC was carried out using TLC plates of silica gel 60 with fluorescent indicator (Merck 60 F_{254}). The eluent used for the R_f (retention factor) determination is indicated in each case. IR spectra were measured using a Nicolet Avatar 320 spectrometer. HRMS data were recorded with a VG AutoSpec spectrometer using the EI method (70 eV). Elemental analyses were performed by 'servicio de semimicroanálisis' of Alicante University (Spain). NMR spectra were recorded on a Bruker AC-300 spectrometer. Chemical shifts are reported in ppm relative to the residual CHD_2SOCD_3 in DMSO-d_6, set at δ = 2.46 ppm for ^{1}H NMR and δ = 39.500 ppm for ^{13}C NMR.

Reaction of Ureas with Chloropyridines (Method D); General Procedure

A Schlenk-type flask was charged under N_2 with $Pd(OAc)_2$ (7.3 mg, 0.032 mmol), xantphos (38 mg, 0.065 mmol) and dioxane (2.7 mL), and the mixture was degassed through several freeze-thaw cycles. The chloropyridine (1.09 mmol), urea (1.08 mmol), NaO*t*-Bu (151 mg, 1.57 mmol) and previously degassed water (28 μL, 1.55 mmol) were successively added to the flask. The reaction mixture was heated at 100 °C while stirring until TLC analysis showed the absence of starting reactants (the time reported in Table 1). After cooling at r.t., the solvent was evaporated to dryness using a rotatory evaporator (60–70 °C), the solid residue was mixed with $CHCl_3$ (ca. 5–6 mL) and the mixture absorbed on a small amount of silica gel. Evaporation of the solvent afforded a solid residue, which was deposited on the top of a column of silica gel and eluted, first with $CHCl_3$ and then with a mixture of $CHCl_3$–EtOAc (9:1; or the indicated eluent). Evaporation of the solvent afforded the pure coupled ureas.

***N*-Phenyl-*N*′-(pyridin-2-yl)urea (3a)**

Mp 191–191.3 °C (Dioxane–hexane) (Lit.[34] 190–191 °C); R_f 0.43 ($CHCl_3$–EtOAC, 6:4).

IR (KBr): 3059, 3001, 2920, 1691, 1599, 1581, 1564, 1479, 1417, 1321, 1301, 754 cm^{-1}.

^{1}H NMR (300 MHz, DMSO-d_6): δ = 10.47 (s, 1 H, NH), 9.40 (s, 1 H, N′-H), 8.24 [ddd, *J* = 5.1, 1.9, 0.8 Hz, 1 H, H-6 (Py)], 7.71 [ddd, *J* = 8.5, 1.9, 0.8 Hz, 1 H, H-4 (Py)], 7.47 [m, 3 H, H-3 (Py), H-3 (Ph), H-5 (Ph)], 7.27 [m, 2 H, H-3, H-5 (Ph)], 6.98 [m, 2 H, H-5 (Py), H-4 (Ph)].

^{13}C NMR (75 MHz, DMSO-d_6): δ = 152.9 (C), 152.2 (C), 146.9 (CH), 139.0 (C), 138.6 (CH), 128.9 (2 × CH), 122.5 (CH), 118.8 (2 × CH), 117.5 (CH), 111.9 (CH).

MS (EI): *m*/*z* (%) = 213 (18) [M$^+$], 170 (7), 120 (19), 94 (100).

HRMS (EI): *m*/*z* [M] calcd for $C_{12}H_{11}N_3O$: 213.0902; found: 213.0894.

***N*-Phenyl-*N*′-(pyridin-4-yl)urea (3c)**

Mp 240–242 °C (at 182–184 °C prism-like crystals were transformed into needle-like crystals) (MeOH) (Lit.[35] 180–182 °C, MeOH); R_f 0.21 (EtOAc); eluted in column chromatography with EtOAc.

IR (KBr): 3388, 2956, 1721, 1599, 1584, 1490, 1194, 755 cm^{-1}.

^{1}H NMR (300 MHz, DMSO-d_6): δ = 9.06 (1 H, N′H), 8.82 (1 H, NH), 8.32 [dd, *J* = 4.9, 1.5 Hz, 2 H, H-2 (Py), H-6 (Py)], 7.45–7.37 [m, 4 H, H-2 (Ph), H-6 (Ph), H-3 (Py), H-5 (Py)], 7.26 [m, 2 H, H-3 (Ph), H-5 (Ph)], 6.97 [tt, *J* = 7.4, 1.1 Hz, 1 H, H-4 (Ph)].

^{13}C NMR (75 MHz, DMSO-d_6): δ = 152.1 (C), 150.1 (2 × CH), 146.5 (C), 139.1 (C), 128.8 (2 × CH), 122.4 (CH), 118.5 (2 × CH), 112.2 (2 × CH).

MS (EI): *m*/*z* (%) = 213 (61) [M$^+$], 120 (9), 119 (13), 94 (40), 93 (100).

HRMS (EI): *m*/*z* [M] calcd for $C_{12}H_{11}N_3O$: 213.0902; found: 213.0892.

***N*,*N*′-Dimethyl-*N*-(pyridin-2-yl)urea (9a)**

Yellowish oil; R_f 0.34 ($CHCl_3$–EtOAc, 6:4).

IR (KBr): 3489, 3201, 1667, 1595, 1573, 1544, 1474, 1436, 1321 cm^{-1}.

^{1}H NMR (300 MHz, DMSO-d_6): δ = 9.08 (br s, 1 H, NH), 8.26 (dd, *J* = 4.9, 2.0 Hz, 1 H, H-6), 7.75 (ddd, *J* = 8.5, 7.3, 2.0 Hz, 1 H, H-4), 7.23 (dd, *J* = 8.5, 0.8 Hz, 1 H, H-3), 7.01 (ddd, *J* = 7.3, 4.9, 0.8 Hz, 1 H, H-5), 3.25 (s, 3 H, CH_3N), 2.70 (d, *J* = 4.5 Hz, 3 H, $CH_3N'H$).

^{13}C NMR (75 MHz, DMSO-d_6): δ = 156.5 (C), 155.5(C), 146.2 (CH), 138.5 (CH), 117.4 (CH), 113.4 (CH), 32.6 (CH_3), 26.9 (CH_3).

MS (EI): *m*/*z* (%) = 165 (8) [M$^+$], 135 (3), 108 (100), 79 (58).

HRMS (EI): *m*/*z* [M] calcd for $C_8H_{11}N_3O$: 165.0902; found: 165.0900.

Tetrahydro-1-(pyridin-2-yl)pyrimidin-2(1*H*)-one (9b)

Mp 138–142 °C ($CHCl_3$) (Lit.[36] 143–144 °C, EtOAc); R_f 0.10 ($CHCl_3$–EtOAc, 6:4).

IR (KBr): 3319, 3231, 3079, 1666, 1467, 1418, 1298, 789 cm^{-1}.

^{1}H NMR (300 MHz, DMSO-d_6): δ = 8.27 (ddd, *J* = 4.9, 1.9, 1.0 Hz, 1 H, H-6), 7.79 (ddd, *J* = 8.5, 1.0, 0.9 Hz, 1 H, H-3), 7.61 (ddd, *J* = 8.5, 7.2, 1.9 Hz, 1 H, H-4), 6.97 (ddd, *J* = 7.2, 4.9, 0.9 Hz, 1 H, H-5), 6.83 (br s, 1 H, NH), 3.82 [m, *J* = 5.8 Hz, 2 H, H-4 (pyrimidine)], 3.17 [td, *J* = 5.8, 2.5 Hz, 2 H, H-6 (pyrimidine)], 1.88 [q, *J* = 5.8 Hz, 2 H, H-5 (pyrimidine)].

^{13}C NMR (75 MHz, DMSO-d_6): δ = 154.7 (C), 154.3 (C), 146.9 (CH), 136.4 (CH) 118.6 (CH), 118.2 (CH), 44.3 (CH_2), 39.7 (CH_2), 21.9 (CH_2).

MS (EI): *m*/*z* (%) = 177 (100) [M$^+$], 133 (10), 119 (57), 78 (34).

HRMS (EI): *m*/*z* [M] calcd for $C_9H_{11}N_3O$: 177.0902; found: 177.0899.

1-(Pyridin-2-yl)imidazolidin-2-one (9c)
Mp 159–162 °C (DMSO–H_2O) (Lit.[37] 165–167 °C, EtOH); R_f 0.15 ($CHCl_3$–EtOAc, 6:4).

IR (KBr): 3233, 3106, 1706, 1589, 1472, 1402, 1272, 777 cm^{-1}.

^{1}H NMR (300 MHz, DMSO-d_6): δ = 8.23 (ddd, *J* = 5.1, 2, 0.9 Hz, 1 H, H-6), 8.12 (ddd, *J* = 8.5, 0.9, 0.9 Hz, 1 H, H-3), 7.64 (ddd, *J* = 8.5, 7.2, 2 Hz, 1 H, H-4), 7.12 (br s, 1 H, NH), 6.02 (ddd, *J* = 7.2, 5.1, 0.9 Hz, 2 H, H-5), 3.94 (br t, *J* = 8 Hz, 2 H, NCH_2CH$_2$NH), 3.35 (br t, *J* = 8 Hz, 2 H, NCH$_2$CH_2NH).

MS (EI): *m*/*z* (%) 163 (100) [M$^+$], 162 (60), 119 (97), 78 (50).

HRMS (EI): *m*/*z* [M] calcd for $C_8H_9N_3O$: 168.0746; found: 163.0715.

1,3-Di-(pyridin-2-yl)-tetrahydro-pyrimidin-2(1*H*)-one (10b)
Mp 79–83 °C ($CHCl_3$); R_f 0.27 ($CHCl_3$–EtOAc, 6:4); eluted in column chromatography with $CHCl_3$–EtOAc (8:2).

IR (KBr): 1666, 1586, 1460, 1402, 1285, 1192, 786, 739 cm^{-1}.

^{1}H NMR (300 MHz, DMSO-d_6): δ = 8.36 (ddd, *J* = 4.9, 1.7, 1.0 Hz, 2 H, H-6), 7.69 (m, 4 H, H-3, H-4), 7.10 (ddd, *J* = 7.2, 4.9, 0.9 Hz, 2 H, H-5), 3.94 [t, *J* = 5.9 Hz, 4 H, H-4, H-6 (pyrimidine)], 2.11 [quint, *J* = 5.9 Hz, 2 H, H-5 (pyrimidine)].

^{13}C NMR (75 MHz, DMSO-d_6): δ = 154.7 (C), 153.7 (2 × C), 147.3 (2 × CH), 136.7 (2 × CH), 119.9 (2 × CH), 119.6 (2 × CH), 45.3 (2 × CH_2), 22.2 (CH_2).

MS (EI): *m*/*z* (%) = 254 (100) [M$^+$], 160 (29), 133 (44), 119 (48), 78 (35).

HRMS (EI): *m*/*z* [M] calcd for $C_{14}H_{14}N_4O$: 254.1168; found: 254.1154.

Anal. Calcd for $C_{14}H_{14}N_4O$: C, 66.13; H, 5.55; N, 22.03. Found: C, 65.72; H, 5.49; N, 22.20.

1,3-Di-(pyridin-2-yl)imidazolidin-2-one (10c)
Mp 182–184 °C (DMSO–H_2O); R_f 0.37 ($CHCl_3$–EtOAc, 6:4).

IR (KBr): 1711, 1588, 1465, 1433, 1389, 1298, 1238, 1141, 773, 739 cm^{-1}.

^{1}H NMR (300 MHz, DMSO-d_6): δ = 8.33 (ddd, *J* = 4.9, 1.9, 0.9 Hz, 2 H, H-6), 8.20 (ddd, *J* = 8.6, 1.0, 0.9 Hz, 2 H, H-3), 7.76 (ddd, *J* = 8.6, 7.2, 1.9 Hz, 2 H, H-4), 7.05 (ddd, *J* = 7.2, 4.9, 0.9 Hz, 2 H, H-5), 4.05 (s, 4 H, NCH_2CH_2N).

^{13}C NMR (75 MHz, DMSO-d_6): δ = 153.7 (C), 151.7 (2 × C), 147.6 (2 × CH), 137.5 (2 × CH), 118.3 (2 × CH), 112.5 (2 × CH), 40.4 (2 × CH_2).

MS (EI): *m*/*z* (%) = 240 (68) [M$^+$], 162 (6), 119 (100), 78 (30).

HRMS (EI): *m*/*z* [M] calcd for $C_{13}H_{12}N_4O$: 240.1011; found: 240.0998.

Anal. Calcd for $C_{13}H_{12}N_4O$: C, 64.99; H, 5.03; N, 23.32. Found: C, 64.64; H, 4.98; N, 23.13.

***N*-(3-Chloropyridin-2-yl)-*N*′-phenylurea (12a)**
Mp 135–137 °C ($CHCl_3$–hexane); R_f 0.70 ($CHCl_3$–EtOAc, 6:4); eluted in column chromatography with $CHCl_3$.

IR (KBr): 3241, 3025, 1686, 1594, 1561, 1486, 1446, 1280, 750 cm^{-1}.

^{1}H NMR (300 MHz, DMSO-d_6): δ = 10.99 (1 H, NH), 8.62 (1 H, N′H), 8.32 [dd, *J* = 4.9, 1.7 Hz, 1 H, H-6 (Py)], 7.95 [dd, *J* = 7.9, 1.7 Hz, 1 H, H-4 (Py)], 7.53 [dd, *J* = 8.5, 1 Hz, 2 H, H-2 (Ph), H-6 (Ph)], 7.29 [m, 2 H, H-3 (Ph), H-5 (Ph)], 7.11 [dd, *J* = 7.9, 4.9 Hz, 1 H, H-5 (Py)], 7.01 [tt, *J* = 7.5, 1 Hz, 1 H, H-4 (Ph)].

^{13}C NMR (75 MHz, DMSO-d_6): δ = 151.3 (C), 148.6 (C), 145.2 (CH), 139.0 (CH), 138.6 (C), 128.9 (2 × CH), 122.9 (CH), 119.3 (2 × CH), 119.2 (CH), 118.5 (C).

MS (EI): *m*/*z* (%) = 249 (9.5) [M$^+$ + 2], 247 (30) [M$^+$], 130 (30), 128 (100), 93 (26), 73 (99).

HRMS (EI): *m*/*z* [M] calcd for $C_{12}H_{10}{}^{35}ClN_3O$: 247.0512; found: 247.0503.

Anal. Calcd for $C_{12}H_{10}ClN_3O$: C, 58.19; H, 4.07; N, 16.97. Found: C, 57.83; H, 4.05; N, 16.97.

***N*-(4-Chloropyridin-2-yl)-*N*′-phenylurea (12b)**
Mp 198–202 °C ($CHCl_3$–hexane); R_f 0.57 ($CHCl_3$–EtOAc, 6:4).

IR (KBr): 3041, 2998, 1695, 1595, 1566, 1449, 1378, 753 cm^{-1}.

^{1}H NMR (300 MHz, DMSO-d_6): δ = 9.89 (1 H, NH), 9.49 (1 H, N′H), 8.22 [d, *J* = 5.5 Hz, 1 H, H-6 (Py)], 7.70 [d, *J* = 1.7 Hz, 1 H, H-3 (Py)], 7.46 [dd, *J* = 8.3, 1.1 Hz, 2 H, H-2 (Ph), H-6 (Ph)], 7.28 [m, 2 H, H-3 (Ph), H-5 (Ph)], 7.10 [dd, *J* = 5.5, 1.7 Hz, 1 H, H-5 (Py)], 6.99 [tt, *J* = 7.4, 1.1 Hz, 1 H, H-4 (Ph)].

^{13}C NMR (75 MHz, DMSO-d_6): δ = 153.9 (C), 151.8 (C), 148.9 (CH), 144.1 (C), 138.7 (C), 128.9 (2 × CH), 122.7 (CH), 118.7 (2 × CH), 117.7 (CH), 111.1 (CH).

MS (EI): *m*/z (%) = 249 (0.17) [M$^+$ + 2], 247 (5) [M$^+$], 128 (49), 93 (47), 73 (100).

HRMS (EI): *m*/*z* [M] calcd for $C_{12}H_{10}{}^{35}ClN_3O$: 247.0512; found: 247.0516.

***N*-(5-Chloropyridin-2-yl)-*N*′-phenylurea (12c)**
Mp 203–204 °C (dioxane–hexane) (Lit.[5a] 200–203 °C); R_f 0.5 ($CHCl_3$–EtOAc, 6:4).

IR (KBr): 3046, 2985, 1693, 1596, 1562, 1479, 1369, 1315, 1225, 833, 757 cm^{-1}.

^{1}H NMR (300 MHz, DMSO-d_6): δ = 9.75 (1 H, NH), 9.42 (1 H, N′H), 8.28 [dd, *J* = 2.5, 0.4 Hz, 1 H, H-6 (Py)], 7.82 [dd, *J* = 8.9, 2.5 Hz, 1 H, H-4 (Py)], 7.67 [dd, *J* = 8.9, 0.4 Hz, 1 H, H-3 (Py)], 7.45 [dd, *J* = 8.5, 1.1 Hz, 2 H, H-2 (Ph), H-6 (Ph)], 7.27 [m, 2 H, H-3 (Ph), H-5 (Ph)], 6.98 [tt, *J* = 7.5, 1.1 Hz, 1 H, H-4 (Ph)].

^{13}C NMR (75 MHz, DMSO-d_6): δ = 151.8 (C), 151.5 (C), 145.6 (CH), 138.9 (C), 138.1 (CH), 128.9 (2 × CH), 123.4 (C), 122.6 (CH), 118.7 (2 × CH), 113.0 (CH).

MS (EI): *m*/*z* (%) = 249 (11) [M$^+$ + 2], 247 (35) [M$^+$], 130 (30), 128 (100), 93 (43).

HRMS (EI): *m*/*z* [M] calcd for $C_{12}H_{10}{}^{35}ClN_3O$: 247.0512; found: 247.0500.

***N*-(6-Chloropyridin-2-yl)-*N*′-phenylurea (12d)**
Mp 197.7–198.0 °C (dioxane-hexane); R_f 0.48 ($CHCl_3$–EtOAc, 6:4).

IR (KBr): 3201, 3092, 3040, 2979, 1696, 1596, 1568, 1457, 1396, 1258, 1164, 785, 755 cm^{-1}.

^{1}H NMR (300 MHz, DMSO-d_6): δ = 9.50 (1 H, NH), 9.29 (1 H, N′H), 7.76, 7.71 [m, AB portion of the ABX system, J_{AB} = 8.29 Hz, J_{AX} = 7.68 Hz, J_{BX} = 0.6 Hz, 2 H, H-3 (Py), H-4 (Py)],[38] 7.42 [dd, *J* = 8.5, 1.9 Hz, 2 H, H-2 (Ph), H-6 (Ph)], 7.28 [m, 2 H, H-3 (Ph), H-5 (Ph)], 7.06 [m, X part of the ABX system, J_{AX} = 7.68 Hz, J_{BX} = 0.6 Hz, 1 H, H-5 (Py)], 6.99 [tt, *J* = 7.5, 1.1 Hz, 1 H, H-4 (Ph)].

^{13}C NMR (75 MHz, DMSO-d_6): δ = 152.8 (C), 151.6 (C), 147.5 (C), 141.6 (CH), 138.8 (C), 128.9 (2 × CH), 122.7 (CH), 118.5 (2 × CH), 117.2 (CH), 110.3 (CH).

MS (EI): *m*/*z* (%) = 249 (9.9) [M$^+$ + 2], 247 (31) [M$^+$], 130 (32), 128 (100), 93 (54).

HRMS (EI): *m*/*z* [M] calcd for $C_{12}H_{10}{}^{35}ClN_3O$: 247.0512; found: 247.0502.

Anal. Calcd for $C_{12}H_{10}ClN_3O$: C, 58.19; H, 4.07; N, 16.97. Found: C, 58.47; H, 4.09; N, 16.87.

_N_-Phenyl-_N′_-[6-(3-phenyl-ureido)-pyridin-2-yl]urea (16)
Mp > 350 °C (the compound was crystallized by slow evaporation from EtOAc solution) (Lit.[30] > 370 °C); R_f 0.32 ($CHCl_3$–EtOAc, 6:4).

IR (KBr): 3300, 3027, 2924, 1696, 1657, 1599, 1554, 1454, 1282, 1231, 754 cm^{-1}.

^{1}H NMR (300 MHz, DMSO-d_6): δ = 9.80 (1 H, NH), 9.18 (1 H, N′H), 7.62 [t, *J* = 8.1 Hz, 1 H, H-4 (Py)], 7.54 [dd, *J* = 8.5, 1.1 Hz, 4 H, H-2, H-6 (Ph)], 7.28 [dd, *J* = 8.5, 7.5 Hz, 4 H, H-3, H-5 (Ph)], 7.1 [d, *J* = 8.1 Hz, 2 H, H-3, H-5 (Py)], 6.99 [tt, *J* = 7.5, 1.1 Hz, 2 H, H-4 (Ph)].

^{13}C NMR (DMSO-d_6, 75 MHz): δ = 151.9 (2 × C), 150.8 (2 × C), 140.4 (CH), 139.1 (2 × C), 128.8 (4 × CH), 122.5 (2 × CH), 119.1 (4 × CH), 104.9 (2 × CH).

MS (EI): *m*/*z* (%) = 347 (2) [M$^+$], 254 (12), 93 (100).

HRMS (EI): *m*/*z* [M] calcd for $C_{19}H_{17}N_5O_2$: 347.1382; found: 347.1400.

1,3-Bis(3-chloropyridin-2-yl)-tetrahydropyrimidin-2(1*H*)-one (17a)
Mp 164–166 °C ($CHCl_3$–hexane); R_f 0.16 (EtOAc).

IR (KBr): 1660, 1570, 1485, 1422, 1304, 1201, 798 cm^{-1}.

^{1}H NMR (300 MHz, DMSO-d_6): δ = 8.37 (ddd, *J* = 4.7, 1.5, 0.25 Hz, 2 H, H-6), 7.93 (dd, *J* = 8.0, 1.5 Hz, 2 H, H-4), 7.34 (ddd, *J* = 8.0, 4.7, 0.25 Hz, 2 H, H-5), 3.85, 3.50 (2 × m, 4 H, NC*H*$_2$CH$_2$C*H*$_2$N), 2.15 (m, 2 H, NCH$_2$C*H*$_2$CH$_2$N).

^{13}C NMR (75 MHz, DMSO-d_6): δ = 152.1 (2 × C), 151.5 (C), 147.1 (2 × CH), 138.7 (2 × CH), 123.9 (2 × CH), 47.0 (2 × CH_2), 22.8 (CH_2).

MS (EI): *m*/*z* (%) = 289 (33) [M$^+$ – 35 + 2], 287 (100) [M$^+$ – 35], 167 (8), 153 (12), 112 (35).

HRMS (FAB): *m*/*z* [M + 1] calcd for $C_{14}H_{13}{}^{35}Cl_2N_4O$: 323.0466; found: 323.0452.

1,3-Bis(4-chloropyridin-2-yl)-tetrahydropyrimidin-2(1*H*)-one (17b)
Mp 98–101 °C (DMSO–H_2O); R_f 0.61 ($CHCl_3$–EtOAc, 6:4).

IR (KBr): 1669, 1575, 1556, 1479, 1452, 1416, 1353, 1304, 1272, 1188, 1096, 829 cm^{-1}.

^{1}H NMR (300 MHz, DMSO-d_6): δ = 8.35 (d, *J* = 5.4 Hz, 2 H, H-6), 7.87 (d, *J* = 1.9 Hz, 2 H, H-3), 7.25 (dd, *J* = 5.4, 1.9 Hz, 2 H, H-5), 3.95 (t, *J* = 6.0 Hz, 4 H, NC*H*$_2$CH$_2$C*H*$_2$N), 2.11 (quint, *J* = 6.0 Hz, 2 H, NCH$_2$C*H*$_2$CH$_2$N).

^{13}C NMR (75 MHz, DMSO-d_6): δ = 155.5 (C), 153.5 (2 × C), 148.5 (2 × CH), 142.6 (2 × C), 119.7 (2 × CH), 119.2 (2 × CH), 45.3 (2 × CH_2), 21.9 (CH_2).

MS (EI): *m*/*z* (%) = 326 (10.5) [M$^+$ + 4], 324 (63) [M$^+$ + 2], 322 (100) [M$^+$], 279 (8), 167 (46), 153 (52), 113 (16).

HRMS (EI): *m*/*z* [M] calcd for $C_{14}H_{12}{}^{35}Cl_2N_4O$: 322.0388; found: 322.0402.

Anal. Calcd for $C_{14}H_{12}Cl_2N_4O$: C, 52.03; H, 3.74; N, 17.34. Found: C, 51.95; H, 3.69; N, 17.30.

1,3-Bis(5-chloropyridin-2-yl)-tetrahydropyrimidin-2(1*H*)-one (17c)
Mp 149–151 °C (DMSO–H_2O); R_f 0.75 ($CHCl_3$–EtOAc, 6:4).

IR (KBr): 1678, 1667, 1457, 1404, 1287, 1191, 1113, 836 cm^{-1}.

^{1}H NMR (300 MHz, DMSO-d_6): δ = 8.40 (dd, *J* = 2.6, 0.6 Hz, 2 H, H-6), 7.82 (dd, *J* = 8.9, 2.6, 2 H, H-4), 7.76 (dd, *J* = 8.9, 0.6 Hz, 2 H, H-5), 3.93 (t, *J* = 6.0 Hz, 4 H, NC*H*$_2$CH$_2$C*H*$_2$N), 2.11 (quint, *J* = 6.0 Hz, 2 H, NCH$_2$C*H*$_2$CH$_2$N).

^{13}C NMR (75 MHz, DMSO-d_6): δ = 153.5 (C), 153.1 (2 × C), 145.5 (2 × CH), 136.6 (2 × CH), 125.9 (2 × C), 121.0 (2 × CH), 45.4 (2 × CH_2), 21.9 (CH_2).

MS (EI): *m*/*z* (%) = 326 (9) [M$^+$ + 4], 324 (60) [M$^+$ + 2], 322 (93) [M$^+$], 287 (3), 279 (24), 167 (100), 154 (6).

HRMS (EI): *m*/*z* [M] calcd for $C_{14}H_{12}{}^{35}Cl_2N_4O$: 322.0388; found: 322.0396.

Anal. Calcd for $C_{14}H_{12}Cl_2N_4O$: C, 52.03; H, 3.74; N, 17.34. Found: C, 51.79; H, 3.68; N, 17.25.

1,3-Bis(6-chloropyridin-2-yl)-tetrahydropyrimidin-2(1*H*)-one (17d)
Mp 185–187 °C (DMSO–H_2O); R_f 0.77 ($CHCl_3$–EtOAc, 6:4).

IR (KBr): 1655, 1440, 1402, 1312, 1161, 791 cm^{-1}.

^{1}H NMR (300 MHz, DMSO-d_6): δ = 7.78, 7.73 [m, AB portion of the ABX system, J_{AB} = 8.10 Hz, J_{AX} = 0.64 Hz, J_{BX} = 7.82 Hz, 4 H, H-4, H-3 (Py)],[38] 7.217 [m, X part of the ABX system, J_{AX} = 0.64 Hz, J_{BX} = 7.82 Hz, 2 H, H-5 (Py)], 3.90 (br t, *J* = 6.0 Hz, 4 H, NC*H*$_2$CH$_2$C*H*$_2$N), 2.11 (quint, *J* = 6.0 Hz, 2 H, NCH$_2$C*H*$_2$CH$_2$N).

^{13}C NMR (DMSO-d_6, 75 MHz): δ = 154.4 (C), 153.3 (2 × C), 147.3 (2 × C), 140.2 (2 × CH), 119.5 (2 × CH), 118.4 (2 × CH), 45.3 (2 × CH_2), 21.8 (CH_2).

MS (EI): *m*/*z* (%) = 326 (0.7) [M$^+$ + 4], 324 (4.9) [M$^+$ + 2], 322 (7) [M$^+$], 210 (5), 167 (65), 153 (100).

HRMS (EI): *m*/*z* [M] calcd for $C_{14}H_{12}{}^{35}Cl_2N_4O$: 322.0388; found: 322.0402.

Anal. Calcd for $C_{14}H_{12}Cl_2N_4O$: C, 52.03; H, 3.74; N, 17.34. Found: C, 52.34; H, 3.70; N, 17.43.

1-(3-Chloropyridin-2-yl)-tetrahydropyrimidin-2(1*H*)-one (18a)
Mp 204–207 °C (at 189–192 °C flake-like crystals were transformed into needle like crystals) ($CHCl_3$–hexane); R_f 0.05 (EtOAc).

IR (KBr): 3222, 3071, 1672, 1501, 1437, 1422, 1312, 1181, 801 cm^{-1}.

^{1}H NMR (300 MHz, DMSO-d_6): δ = 8.36 (dd, *J* = 4.7, 1.7 Hz, 1 H, H-6), 7.91 (dd, *J* = 8.0, 1.7 Hz, 1 H, H-4), 7.29 (dd, *J* = 8.0, 4.7 Hz, 1 H, H-5), 6.70 (s, 1 H, NH), 3.70, 3.36 (2 × m, 2 H, NC*H*$_2$CH$_2$CH$_2$N), 3.21 (m, 2 H, NCH$_2$CH$_2$C*H*$_2$N), 1.92 (quint, *J* = 6.0 Hz, 2 H, NCH$_2$C*H*$_2$CH$_2$N).

^{13}C NMR (75 MHz, DMSO-d_6): δ = 153.4 (C), 152.8 (C), 146.9 (CH), 138.5 (CH), 129.1 (C), 123.3 (CH), 46.3 (CH_2), 39.7 (CH_2), 22.0 (CH_2).

MS (EI): *m*/*z* (%) = 176 (100) [M$^+$ – 35], 167 (1), 154 (2).

HRMS (FAB): *m*/*z* [M + 1] calcd for $C_9H_{11}{}^{35}ClN_3O$: 212.0590; found: 212.0598.

Compound 19
Mp 202–203 °C ($CHCl_3$–hexane); R_f 0.68 ($CHCl_3$–EtOAc, 6:4).

IR (KBr): 2982, 2956, 2891, 1668, 1582, 1558, 1485, 1397, 1330, 1222, 1195 1160, 1139, 789 cm^{-1}.

^1H NMR (300 MHz, DMSO-d_6): δ = 7.76, 7.74 [m, AB portion of the ABX system, J_{AB} = 8.29 Hz, J_{AX} = 1.91 Hz, J_{BX} = 7.32 Hz, 4 H, H-3, H-4 (both Cl-Py)],[38] 7.68 [m, X part of the ABX system, J_{AX} = 7.91 Hz, J_{BX} = 7.91 Hz, 1 H, H-4 (Py)], 7.45, 7.45 [m, AB portion of the ABX system, J_{AX} = 7.91 Hz, J_{BX} = 7.91 Hz, 2 H, H-3, H-5 (Py)], 7.18 [(m, X part of the ABX system, J_{AX} = 1.91 Hz, J_{BX} = 7.32 Hz, 2 H, H-5 (both Cl-Py)], 3.93 [m, 8 H, $NCH_2CH_2CH_2N$ (both pyrimidine moieties)], 2.11 [m, 4 H, $NCH_2CH_2CH_2N$ (both pyrimidine moieties)].

^{13}C NMR (DMSO-d_6, 75 MHz): δ = 154.5 (2 × C), 153.4 (2 × C), 152.4 (2 × C), 147.2 (2 × C), 140.0 (2 × CH), 137.8 (CH), 119.1 (2 × CH), 118.1 (2 × CH), 115.2 (2 × CH), 45.2 (4 × CH_2), 21.9 (2 × CH_2).

MS (EI): *m/z* (%) = 501 (10.8) [M^+ + 4], 499 (66.2) [M^+ + 2], 497 (100) [M^+], 462 (2), 369 (18), 329 (26).

HRMS (FAB): *m/z* [M + 1] calcd for $C_{23}H_{21}{}^{35}Cl_2N_7O_2$: 497.1134; found: 497.1045.

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(26) Appropriate experimental controls showed that nearly 70–80% of the urea **3c** was transformed into a mixture of disproportionated products, mainly aniline, diphenylurea and 4-aminopyridine, when treated under the coupling reaction conditions (as in entry 6 of Table 1, but omitting the phenylurea) for 17 h.

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