Green Chemistry

Cite this: *Green Chem.*, 2012, **14**, 217

www.rsc.org/greenchem

PAPER

A simple direct phosgeneless route to N-heteroaryl unsymmetrical ureas

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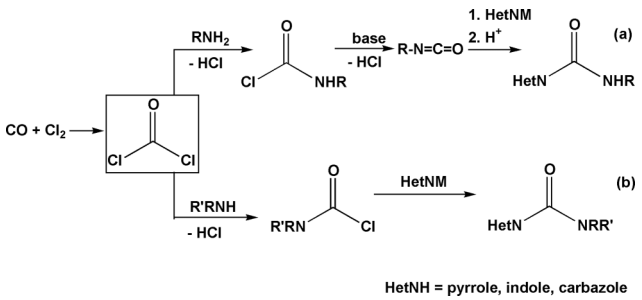
Received 9th August 2011, Accepted 11th October 2011
DOI: 10.1039/c1gc15984d

A new simple approach to the synthesis of unsymmetrical ureas HetNC(O)NRR′ (HetNH = pyrrole, indole, carbazole; R, R′ = H, alkyl, aryl) has been explored, which involves the direct reaction of the *N*-phenoxycarbonyl derivatives of pyrrole, indole and carbazole, $HetNCO_2Ph$, with amines. The aminolysis reaction can be catalyzed by the amidine base DBU (1,8-diazabicyclo[5.4.0]undec-7-ene) under usually very mild conditions and provides a straightforward convenient entry into the target products through a route which avoids the traditional protocols based on multistep procedures and toxic phosgene or phosgene-derivatives.

Introduction

The search for new direct eco-friendly synthetic routes is a major challenge for modern chemistry.[1] Despite the efforts currently devoted to redesign the synthesis of many classes of products according to strategies more sustainable from the environmental point of view, HetNC(O)NRR′ carboxamides of N-heteroarenes as pyrrole, indole and carbazole provide an example of chemicals which are still manufactured through traditional multistep methods based on risky and/or harmful starting materials. These particular unsymmetrical ureas,[2,3] wherein one of the ureidic N atoms is also part of a heteroaromatic ring,[4] are widely used as synthetic intermediates,[5,6] find practical application in several fields,[7] and usually exhibit biological activity or interesting pharmacological properties.[8,9]

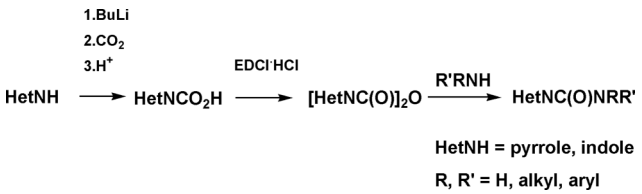
The classic methods of synthesis of these compounds start from derivatives of phosgene[4,10] or directly from $COCl_2$,[5,8] a toxic and harmful species, the utilization of which in chemical synthesis finds, nowadays, larger and larger constraints due to governmental policies for environmental protection.[11] The preliminary formation of a N-heteroaryl metal salt, HetNM, is often required. Usually, HetNC(O)NHR ureas are prepared by reaction of HetNM (M = Li, K, MgX) salts with isocyanates (Scheme 1(a)).[10a,b,d] *N*,*N*-Disubstituted ureas HetNC(O)NRR′[4,5,8] have been often obtained by reaction of HetNM salts with *N*,*N*-disubstituted carbamoyl chlorides (Scheme 1(b)).[4] A major additional problem of these approaches (Scheme 1) is also the regioselectivity of the electrophilic attack



Scheme 1 Classic phosgene-based synthetic routes to unsymmetrical ureas HetNC(O)NRR′.

to the heterocyclic salt HetNM, which may depend on the nature of cation M and, therefore, necessitate the empirical characterization of the experimental conditions privileging *N*- over *C*-functionalization.[12]

A relatively more recent method (Scheme 2) used CO_2 as the source of carbonyl group and was based on the activation of carboxylic acid $HetNCO_2H$ (HetNH = pyrrole, indole) to anhydride $[HetNC(O)]_2O$.[13] However, the activation step requires the use of a stoichiometric amount of a coupling reagent as EDCI·HCl (1-[3-(dimethylamino)propyl]-3-ethylcarbodiimide hydrochloride), usually manufactured from phosgene.[14] Moreover, the synthetic route is atomically uneconomical, as it implies a multistep procedure and needs 2 mol of HetNH (for preforming the anhydride) per mol of product.



Scheme 2 Synthesis of unsymmetrical ureas HetNC(O)NRR′ *via* $HetNCO_2H$ activation.

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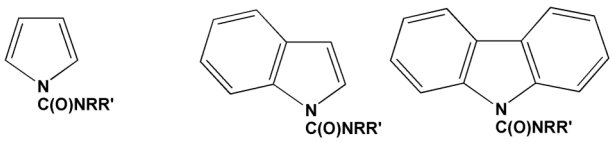
In the last few years many efforts have been addressed to develop a fully phosgene-free chemistry and the study of safe non-toxic active carbonyl species which can serve as substitutes for phosgene or phosgene-derivatives has been drawing growing attention.[15–18] In this regard, carbonic acid diesters have been shown to play an important role[15a,16–18] as these compounds are currently manufactured, even on the industrial scale, through phosgene-free routes.[19,20] As a part of our studies in this field,[16,17] we have recently reported on the direct carbonylation of N-heteroaromatics HetNH, such as pyrrole, indole and carbazole, with organic carbonates for the phosgeneless synthesis of carbonyl derivatives $HetNCO_2R$,[17b,d] usually obtained through phosgenation methods.[21] The carbonylation reaction can be catalyzed by superbases as DBU (1,8-diazabicyclo[5.4.0]undec-7-ene) or phosphazenes. Notably, the DBU-promoted reaction of HetNH (pyrrole, indole, carbazole) with diphenyl carbonate was shown to be an excellent new method for the selective high-yield synthesis of the *N*-phenoxycarbonyl derivatives $HetNCO_2Ph$ **1–3** [eqn (1)].[17d] Herein, with the intent of designing a fully phosgene-free green approach to the synthesis of unsymmetrical ureas HetNC(O)NRR′ (R, R′ = H, alkyl, aryl), we have explored the potential of compounds **1–3** as carbonylating agents of amines [eqn (2)]. Under usually mild conditions, the direct reaction of **1–3** with amines provided a straightforward phosgeneless access into N-heteroaryl unsymmetrical ureas HetNC(O)NRR′ (Fig. 1) through a convenient route which is an eco-friendly alternative to the classic methods described above.

$$\underset{}{HetNH} + (PhO)_2CO \xrightarrow{DBU} \underset{\mathbf{1–3}}{HetNCO_2Ph} + PhOH \quad (1)$$

HetNH = pyrrole (**1**), indole (**2**), carbazole (**3**)

$$\underset{\mathbf{1–3}}{HetNCO_2Ph} + RR'NH \rightarrow \underset{\mathbf{4–16}}{HetNC(O)NRR'} + PhOH \quad (2)$$

HetNH = pyrrole, indole, carbazole



4: R = H, R' = benzyl
5: R = H, R' = allyl
6: NRR' = $N(CH_2CH_2)_2O$
7: R = R' = benzyl
8: R = H, R' = Ph
9: R = Me, R' = Ph
10: R = H, R' = $CH(CO_2Me)CH_2CHMe_2$
11: R = H, R' = CH_2CH_2OH
12: R = H, R' = $CH_2CH(Ph)OH$
13: R = H, R' = allyl
14: NRR' = $N(CH_2CH_2)_2O$
15: R = H, R' = allyl
16: NRR' = $N(CH_2CH_2)_2O$

Fig. 1 Synthesized unsymmetrical ureas.

Results and discussion

A preliminary study concerned the reaction of a primary aliphatic amine such as benzylamine with 1-phenoxycarbonyl pyrrole (**1**), which was selected as the reference substrate (Table 1). At 293 K, in the absence of any catalyst, **1** reacted promptly with an excess of benzylamine, used both as reactant and solvent, to afford 1-benzylaminocarbonyl pyrrole (**4**) and phenol: under the used solventless conditions (entry 1, Table 1), **1** was quantitatively converted into **4** within a short time (1 h). The formation of **4** was very selective (>99%). The attack of the amine to the substrate caused the selective expulsion of phenoxy group with formation of **4**, which, under the working conditions, did not react further with the amine to generate the symmetrical urea $(RNH)_2CO$ (R = benzyl). Accordingly, the IR spectrum of the reaction mixture in the range 1800–1600 cm^{-1} showed one only absorption at 1701 cm^{-1} due to **4**.

Depending on the solvent properties and/or expensiveness of amine reactant, the use of solventless conditions, or a large excess of amine, may be poorly attractive from the synthetic point of view or not practicable at all. Therefore, the aminolysis reaction was studied also in ethereal solvents (diethyl ether or THF),[22] using a modest excess of amine. In diethyl ether, at ambient temperature, the reaction of **1** with a slight excess (≈10 mol%) of $PhCH_2NH_2$ afforded **4** in practically quantitative yield (Entry 2, Table 1). However, under the used conditions, the conversion rate, while being satisfactory soon after mixing the reactants, became excessively slow in the long run (entry 2, Table 1) and the full conversion of the substrate required a markedly longer time.

The above behavior may reflect the fact that aminolysis of carbamates is usually catalyzed by amine itself, since a second molecule of amine can act as a catalyst of the process.[23] We have, therefore, investigated the effect of a base organo-catalyst and focused the attention on the strong amidine superbase DBU. Under experimental conditions otherwise analogous to those used in entry 2 (Table 1), the presence of 1 equivalent of the amidine superbase enhanced markedly the conversion rate (entry 3, Table 1). The aminolysis reaction was promoted also by markedly lower loadings of DBU, but less effectively, unless the working temperature was increased. Accordingly, at 338 K, in the presence of 10 mol% of DBU, **1** converted quantitatively to **4** within only 2 h (entry 4, Table 1).

Table 2 summarizes the results obtained with a few other amines. Like benzylamine, at ambient temperature also allylamine reacted easily with **1** (RNH_2/**1** ≈ 1.14 mol/mol), in THF and in the presence of 1 equivalent of DBU, to afford 1-allylaminocarbonyl pyrrole (**5**) (entry 1, Table 2).

The behavior of a few representative secondary aliphatic amines was also studied. In ethereal solvents (diethyl ether, THF) the DBU-promoted aminolysis of **1** with a cyclic secondary amine such as morpholine proceeded smoothly under very mild conditions and produced the relevant unsymmetrical urea **6** selectively (≥99%) with quantitative yield (entries 2 and 3, Table 2). In comparison, a sterically encumbered secondary acyclic amine, such as dibenzylamine, was, by far, much less reactive. For instance, under conditions similar to those used for morpholine in entry 3 (Table 2), dibenzylamine exhibited very poor reactivity towards **1** (entry 4, Table 1). Even at 393 K, the DBU-assisted aminolysis of **1** with a very modest excess of $(PhCH_2)_2NH$ (≈10 mol% *vs.* **1**), in THF, required prohibitively long reaction times (entries 5 and 6, Table 2). Much higher conversion rates, which depended on the used catalyst load (10–100 mol%), were observed at higher temperature (423 K) under solventless conditions, using the amine in larger excess with respect to the substrate (entry 7 and entry 8, Table 2). In the range 393–423 K (entries 5–8, Table 2) the selectivity towards 1-dibenzylaminocarbonyl pyrrole (**7**) was moderate (≈75–85%)

Table 1 Aminolysis of $C_4H_4NCO_2Ph$ (**1**) with $PhCH_2NH_2$, under different experimental conditions. The catalytic role of DBU

Entry	$PhCH_2NH_2$ (mmol)	**1** (mmol)	DBU (mol%)[a]	Solvent	T/K	t/h	Conversion[b] [%]	**4** [%][c]
1	5.95	1.07	—	—	293	1	100	86
2	0.66	0.59	—	Diethyl ether[d]	293	36[e]	≈100	>99[f]
3	1.24	1.10	100	Diethyl ether[g]	293	2	≈100	87
4	1.11	1.08	9.9	THF[d]	338	2	≈100	90

[a] Relative to **1**. [b] Of **1** (by GC). [c] Isolated yield (based on **1**), unless otherwise specified. [d] 1 mL. [e] See also main text. [f] Selectivity to **4**. [g] 2 mL.

Table 2 Aminolysis of $C_4H_4NCO_2Ph$ (**1**) to $C_4H_4NC(O)NRR'$ (R, R′ = H, alkyl, aryl) ureas by aliphatic or aromatic amines

Entry	amine (mmol)	**1** (mmol)	DBU (mol%)[a]	Solvent[b]	T/K	t/h	Conversion[c] [%]	Urea: [%][d]
1	$CH_2{=}CHCH_2NH_2$ (0.94)	0.82	101	THF	293	2	100	**5**: 87
2	$O(CH_2CH_2)_2NH$ (0.63)	0.55	103	diethyl ether	293	2	100	**6**: >99[e]
3	$O(CH_2CH_2)_2NH$ (1.20)	1.08	9.9	THF	338	2	100	**6**: 93
4	$(PhCH_2)_2NH$ (1.20)	1.09	9.8	THF	338	6	≈ 0	**7**: [f]
5	$(PhCH_2)_2NH$ (1.20)	1.09	9.8	THF	393	285	100[g]	**7**: [h]
6	$(PhCH_2)_2NH$ (0.62)	0.57	99.4	THF	393	166	99[i]	**7**: [h]
7	$(PhCH_2)_2NH$ (2.47)	0.82	10.0	—	423	18	99	**7**: [h]
8	$(PhCH_2)_2NH$ (2.47)	0.82	102	—	423	5	100	**7**: [h]
9	$(PhCH_2)_2NH$ (2.34)	0.74	202	—	293	60	100[j]	**7**: 81
10	$PhNH_2$ (5.49)	0.55	—	—	293	18	≈0	**8**: [f]
11	$PhNH_2$ (5.49)	0.55	104	diethyl ether	293	48	99	**8**: 81
12	$PhNH_2$ (2.47)	0.82	103	—	293	12	≈100	**8**: 83
13	PhNMeH (2.40)	0.81	108	—	293	38	≈100	**9**: 89
14	PhNMeH (2.49)	0.83	102	—	338	8	100	**9**: 88
15	PhNMeH (2.77)	0.85	10.2	—	373	48	99	**9**: 97[e]

[a] Relative to **1**. [b] 1 mL, when solvent (diethyl ether, THF) was used. [c] Of **1** (by GC). [d] Isolated yield (based on **1**) of $C_4H_4NC(O)NRR'$, unless otherwise specified. [e] Selectivity. [f] The product formed in trace amounts. [g] After 8 days the conversion of **1** was close to 80%. [h] Not isolated. [i] After 4 days the conversion of **1** was close to 75%. [j] After 1 day the conversion of **1** was close to 70%.

because of side-formation of other species, such as, for instance, phenyl *N*,*N*-dibenzylcarbamate (the major by-product)[24] and very minor amounts of 1,1′-carbonyldipyrrole.[17d] The formation of significant amounts of $(PhCH_2)_2NCO_2Ph$ demonstrates that, at these temperatures, the substitution of pyrryl moiety can seriously compete with that of phenoxy group. Higher selectivity to the target product **7** may be favored by markedly lower reaction temperatures. To overcome the consequent drawback due to the lower conversion rate a higher catalyst load was used. Accordingly, at 293 K, under solventless conditions, urea **7** was obtained selectively (≈99%) and quantitatively within a still reasonable reaction time (60 h) by reacting **1** with $(PhCH_2)_2NH$ (amine/**1** ≈ 3 mol/mol) in the presence 2 equivalent of DBU (entry 9, Table 2).

Under those conditions wherein benzylamine reacted readily with **1** in the absence of DBU (entry 1, Table 1), a primary aromatic amine such as aniline was practically inert towards **1** (entry 10, Table 2). The presence of DBU (1 equivalent *vs.* **1**) in the reaction mixture promoted the aminolysis of **1** with formation of 1-phenylaminocarbonyl pyrrole (**8**) even at ambient temperature (entries 11 and 12, Table 2). Under solventless conditions (entry 12, Table 2) the conversion rate was more satisfactory than in diethyl ether (entry 11, Table 2). The aminolysis reaction was promoted also by catalytic amounts of DBU, but, in this case, the quantitative conversion of **1** required a longer reaction time at ambient temperature. At 393 K (DBU = 10 mol% *vs.* **1**; $PhNH_2$/**1** = 3 mol/mol), the conversion was faster, but less selective because of major formation of *N*,*N*′-diphenylurea, which, under the working conditions, formed by further reaction of **8** with aniline.[10a] The analysis of the reaction mixture showed also the side-formation of trace amounts of 1,1′-carbonyldipyrrole.[17d]

The synthetic protocol followed for aniline was extended also to *N*-methyl aniline (entries 13–15, Table 2) for the synthesis of 1-(*N*-methyl-*N*-phenylaminocarbonyl) pyrrole (**9**). The aminolysis reaction was selective (>96%) and, for instance, even at the highest temperature investigated (373 K; entry 15, Table 2), the side-formation of $MePhNCO_2Ph$ was modest.

We have also explored the compatibility of the synthetic approach with the presence of a few functional groups in the molecule of amine and studied the ureidization of functionalized amines, such as the methyl ester of L-leucine, which we have used in the form of chlorohydrate salt, and a few amino alcohols (Table 3).

At 293 K, the salt L-$Me_2CHCH_2CH(CO_2Me)NH_3Cl$ (L-RNH_3Cl) was poorly reactive towards **1** (entry 1, Table 3) because of poor nucleophilicity of quaternary N atom. A negligible conversion to urea **10** was observed also when the substrate and the salt were reacted at ambient temperature in the presence of 1 equivalent (*vs* the salt) of the amidine base (entry 2, Table 3), which, under the working conditions, acted mainly as a proton scavenger [eqn (3)][25] rather than as the catalyst. The aminolysis of **1** by the chlorohydrate salt required a larger amount of the amidine base and, under very mild temperature conditions (293–333 K), was achieved more

Table 3 Aminolysis of $C_4H_4NCO_2Ph$ (**1**) with functionalized amines

Entry	amine reactant[a] (mmol)	**1** (mmol)	DBU (mol%)[b]	THF (mL)	T/K	t/h	Conversion[c][%]	Urea: [%][d]
1	L-RNH_3Cl (0.65)	0.49	—	1	293	46	[e]	**10**: [e]
2	L-RNH_3Cl (0.65)	0.49	131[f]	3	293	24	<10	**10**: [g]
3	L-RNH_3Cl (0.68)	0.55	246[h]	3	293	44	≈100	**10**: 84
4	L-RNH_3Cl (0.76)	0.60	229[i]	3	333	16	≈100	**10**: 87
5	$H_2NCH_2CH_2OH$ (16.6)	0.75	—	—	293	1	100	**11**: ≈100[j]
6	$H_2NCH_2CH_2OH$ (0.89)	0.56	—	1	293	2	≈100	**11**: ≈100[j]
7	$H_2NCH_2CH_2OH$ (0.63)	0.58	—	1	293	36	[k]	**11**: 85
8	$H_2NCH_2CH_2OH$ (0.64)	0.56	11.8	1	293	1	100	**11**: 81
9	$H_2NCH_2CH(Ph)OH$ (0.99)	0.60	—	1	293	2	100	**12**: 91
10	$H_2NCH_2CH(Ph)OH$ (0.79)	0.64	10.4	1	293	2	≈100	**12**: 80
11	$H_2NCH_2CH(Ph)OH$ (0.67)	0.58	100.5	1	293	0.25	100	**12**: 78

[a] R is $Me_2CHCH_2CH(CO_2Me)$. [b] Relative to **1**. [c] Of **1** (by GC). [d] Isolated yield (based on **1**), unless otherwise specified. [e] No reaction was observed. [f] Corresponding to 1 equivalent of DBU with respect to the chlorohydrate salt. [g] Not isolated. [h] Corresponding to 1.97 equivalents of DBU with respect to the chlorohydrate salt. [i] Corresponding to 1.81 equivalents of DBU with respect to the chlorohydrate salt. [j] Selectivity to **11**. [k] After 36 h the conversion was nearly quantitative and addition of more AE (0.011 mL, 0.20 mmol) caused the fast conversion of the residual amounts of **1**.

effectively by working in the presence of ≈2 equivalents of DBU (*vs* the salt; entry 3 and entry 4, Table 3).[28]

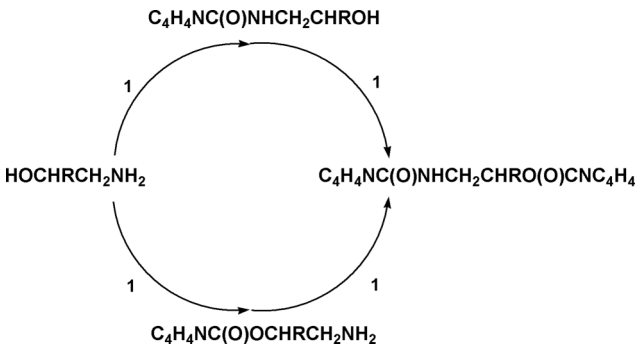
$$Me_2CHCH_2CH(CO_2Me)NH_3Cl + DBU \rightleftarrows DBU{\cdot}HCl + Me_2CHCH_2CH(CO_2Me)NH_2 \quad (3)$$

In principle, the reaction of **1** with aminoalcohols H_2N-R-OH may effect not only the functionalization of H_2N-moiety but also that of OH group with formation of carbamate $C_4H_4NC(O)O$-R-NH_2. Elsewhere, in fact, we have reported that **1** can react with alcohols through a transesterification reaction.[17d] Methanol reacted easily with **1**, even at ambient temperature, to give 1-methoxycarbonyl pyrrole, $C_4H_4NCO_2Me$, but more sterically crowded alcohols, as $PhCH_2OH$ or *t*-BuOH, required the use of higher temperatures and/or a catalyst as DBU. In the presence of DBU the transesterification process was less selective, as the amidine base can also cause the defunctionalization of the heteroaromatic ring with formation of pyrrole and carbonic acid diesters ($ROC(O)OPh$, $(RO)_2CO$).[17b,d]

We have found that, in THF, in the presence of DBU (10-100 mol% *vs.* **1**), **1** reacted smoothly with aminoalcohols H_2N-R-OH (H_2N-R-OH/**1** = 1.14–1.20 mol/mol) such as 2-aminoethanol (AE) or (±)-2-amino-1-phenylethanol (Ph-AE) to give, under very mild conditions (293 K), the corresponding ureas **11** and **12** with high yield (entries 8, 10 and 11, Table 3). However, variable amounts of $C_4H_4NC(O)NHCH_2CHRO(O)CNC_4H_4$ (**17**: R = H; **18**: R = Ph) also formed under the working conditions (see also Experimental).

Scheme 3 shows two possible routes for the formation of $C_4H_4NC(O)NHCH_2CHRO(O)CNC_4H_4$, both of which, in principle, may be operative. However, we note that in no case we detected (by GC, GC-MS) the presence of $C_4H_4NCO_2CHRCH_2NH_2$ (R = H, Ph) in the reaction mixture. This fact suggests that $C_4H_4NCO_2CHRCH_2NH_2$, if it really formed, did not accumulate in the reaction mixture, but reacted fast to give $C_4H_4NC(O)NHCH_2CHRO(O)CNC_4H_4$.

The selectivity towards the target products can be controlled more easily by working in the absence of the amidine base and suitably varying the H_2N-R-OH/**1** molar ratio. For instance, only minor amounts of $C_4H_4NC(O)NHCH_2CH_2O(O)CNC_4H_4$ were detected in the reaction mixture when **1** was reacted with a slight excess of AE (AE/**1** = 1.09 mol/mol; entry 7, Table 3), at



Scheme 3 Possible routes to $C_4H_4NC(O)NHCH_2CHRO(O)CNC_4H_4$.

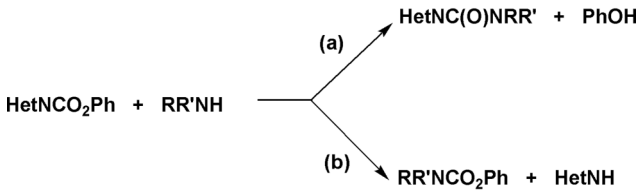
293 K, in THF. Under the above conditions most of substrate (≈90%) reacted within the first 4–5 h, but the conversion of the residual amounts of **1** required a longer time. The use of a higher H_2N-R-OH/**1** molar ratio (60–65 mol%; entry 6 and 9 in Table 3) or of solventless conditions (entry 5, Table 3) allowed to overcome the above drawback and to conjugate high selectivity (≈100%) towards **11** or **12** with more satisfactory conversion rate.

Table 4 shows a few examples of aminolysis of 1-phenoxycarbonyl indole (**2**) and 9-phenoxycarbonyl carbazole (**3**). Under the working conditions (Table 4), the aminolysis of **3** with morpholine proceeded more sluggishly. Moreover, substrate **3** reacted with the investigated amines (allylamine, morpholine) with moderate selectivity (≈70%) mainly because of competitive defunctionalization of **3** and formation of carbazole

Table 4 DBU-promoted aminolysis of $HetNCO_2Ph$ (**2**, **3**) to HetNC(O)NRR′[a]

Entry	Amine (mmol)	$HetNCO_2Ph$ (mmol)	Urea: [%][b]
1	$CH_2{=}CHCH_2NH_2$ (0.96)	**2** (0.86)	**13**: 92
2	$CH_2{=}CHCH_2NH_2$ (0.96)	**3** (0.86)	**14**: 64
3	$O(CH_2CH_2)_2NH$ (0.80)	**2** (0.71)	**15**: 92
4	$O(CH_2CH_2)_2NH$ (0.80)	**3** (0.71)	**16**: 61

[a] Solvent: THF (1 mL); DBU: ≈100 mol% *vs.* **2** or **3**; temperature: 293 K; reaction time: 3 h, except in entry 4 (10 h). Under the working conditions, the substrate (**2** or **3**) converted quantitatively or, if any, was detected in trace amounts. [b] Isolated yield (based on $HetNCO_2Ph$) of HetNC(O)NRR′.



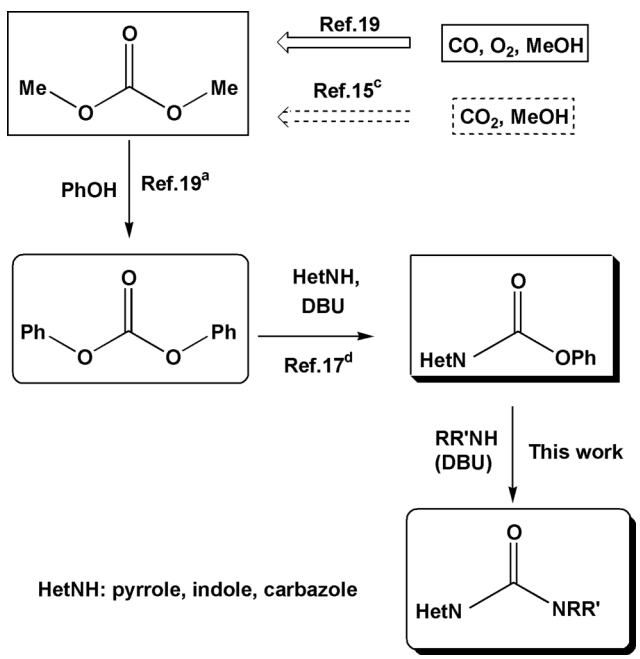
Scheme 4 Aminolysis of $HetNCO_2Ph$.

(Scheme 4, route (b)). In comparison, the analogous reactions of **1** (see also Table 2) and **2** with the same amines were more selective and only in the aminolysis of **2** with morpholine (entry 3, Table 4) minor amounts of HetNH (indole) and $O(CH_2CH_2)_2NCO_2Ph$ were found in the reaction mixture. The above features may reflect the importance of steric factors (bulkiness of both the attacking amine and HetN group in the substrate) in controlling not only the rate of the aminolysis process, but also the direction of the substitution reaction.

Conclusion

The reaction of the *N*-phenoxycarbonyl derivatives of pyrrole, indole and carbazole, $HetNCO_2Ph$, with amines has been shown to be a convenient method of synthesis of unsymmetrical ureas HetNC(O)NRR′ (HetNH = pyrrole, indole, carbazole). The aminolysis reaction can be catalyzed by the amidine base DBU under usually mild conditions and proceeded with good to excellent selectivity depending on the working conditions (substrate, amine, temperature). The protocol has been successfully extended also to functionalized amines, such as amino esters and amino alcohols.

The synthetic approach is simple, direct, efficient and allows to gain access to the target products through a phosgene- and halogen-free synthetic pathway (Scheme 5; as a comparison, see also Scheme 1), which is safe and obviates the large co-generation of wastes (salts, *etc.*) typical of phosgenation methods. It provides a new solution for the synthesis of unsymmetrical ureas HetNC(O)NRR′ through a green route alternative to the current conventional procedures.



Scheme 5 Phosgeneless route to unsymmetrical ureas HetNC(O)-NRR′.

Experimental

General methods

All solvents were dried according to conventional methods (P_2O_5; Na/benzophenone)[29] and stored under N_2. The carbonyl derivatives **1–3** were obtained as previously reported.[17d] DBU and the amines were commercial products (Fluka or Aldrich) and were stored and manipulated under N_2 to prevent any significant contamination by atmospheric CO_2 and moisture. Ph-AE was purified by column chromatography (silica gel; MeOH as eluent) and recrystallized from EtOH(minimum amount)/diethyl ether/n-hexane before use. GC analyses were performed with a HP 5890 Series II gas-chromatograph (capillary column: Heliflex AT-5, 30 m × 0.25 mm, 0.25 μm film thickness). GC-MS analyses were carried out with a Shimadzu GC-17A linked to a Shimadzu GC-MS QP5050 selective mass detector (capillary column: Supelco MDN-5S, 30 m × 0.25 mm, 0.25 μm film thickness). IR spectra were taken on a Shimadzu FT-IR Prestige 21 spectrophotometer or recorded with a Perkin Elmer FT-IR 1710 instrument. Polarimetric measurements were carried out with a Perkin Elmer 343 Polarimeter. NMR spectra were run with a Varian Inova 400 spectrometer or a Bruker AM 500 instrument. Chemical shift are in δ (ppm) *vs.* Me_4Si. Coupling constants are in Hz.

Synthesis and characterization of unsymmetrical ureas HetNC(O)NRR′ (4–16)

The reactions were preferably conducted under N_2 and carried out in a ≈20 mL glass reactor equipped with a Sovirel cap and a Thorion stopcock.

1-Benzylaminocarbonyl pyrrole (*N*-benzyl-1*H*-pyrrole-1-carboxamide) 4. To the solution of **1** (0.2021 g, 1.08 mmol) in THF (1 mL), DBU (0.016 mL, 0.107 mmol) and the amine (0.130 mL, 1.11 mmol) were added (entry 4, Table 1). The reaction solution was stirred at 338 K for 2 h and, then, cooled to room temperature. Product **4** was isolated by column chromatography (silica gel; petroleum ether/diethyl ether (2 : 1 v/v)). Yield of **4**: 194 mg, 90%. Found: C, 71.94; H, 6.09; N, 14.00. Calc. for $C_{12}H_{12}N_2O$: C, 71.98; H, 6.04; N, 13.98%; ν_{max}(Nujol)/cm^{-1} 3321 s (NH), 1684vs (C═O); δ_H (400 MHz; $CDCl_3$; 293 K) 4.57 (2 H, d, J = 5.9, CH_2), 5.78 (1 H, br, NH), 6.25 (2 H, t, J = 2.2, H_β), 7.18 (2 H, t, J = 2.2, H_α), 7.26–7.38 (5 H, m, Ph); δ_C (100 MHz; $CDCl_3$; 293 K) 44.91 (CH_2), 111.99 (C_β), 118.38 (C_α), 127.88 (C_{ortho}), 127.91 (C_{para}), 128.87 (C_{meta}), 137.49 (C_{ipso}), 150.87 (C═O); m/z (EI) 200 (M^+), 133 (M – C_4H_4NH), 104, 91, 67, 51, 39.

1-Allylaminocarbonyl pyrrole (*N*-(prop-2-en-1-yl)-1*H*-pyrrole-1-carboxamide) 5. The reaction mixture, prepared by adding DBU (0.125 mL, 0.84 mmol) and the amine (0.070 mL, 0.94 mmol) to the solution of **1** (0.1540 g, 0.82 mmol) in THF (1 mL), was stirred at 293 K for 2 h. Product **5** was isolated by column chromatography (silica gel; petroleum ether/diethyl

ether (2 : 1 v/v)). Yield of **5**: 107 mg, 87%. Found: C, 64.10; H, 6.73; N, 18.59. Calc. for $C_8H_{10}N_2O$: C, 63.99; H, 6.71; N, 18.65%; ν_{max}(Nujol)/cm^{-1} 3333 s (NH), 1682vs (C═O); δ_H (500 MHz; $CDCl_3$; 293 K) 4.00 (2 H, tt, $^3J_{HCNH} \approx {}^3J_{HCCH} = 5.8$, $^4J = 1.5$, CH_2), 5.18 (1 H, dq, $^3J_{cis} = 10.3$, $^4J \approx {}^2J = 1.4$, H_{cis}), 5.24 (1 H, dq, $^3J_{trans} = 17.2$, $^4J \approx {}^2J = 1.4$, H_{trans}), 5.76 (1 H, br, NH), 5.89 (1 H, m, $HC{=}CH_2$), 6.25 (2 H, t, $J = 2.3$, H_β), 7.19 (2 H, t, $J = 2.3$, H_α); δ_C (125 MHz; $CDCl_3$; 293 K) 43.21 (CH_2), 111.89 (C_β), 117.05 (CH = CH_2) 118.35 (C_α), 133.62 (HC = CH_2),150.84 (C═O); *m*/*z* (EI) 150 (M^+), 135, 106, 94, 80, 67, 54, 41, 39.

1-Morpholinocarbonyl pyrrole (morpholin-4-yl(1*H*-pyrrol-1-yl)methanone) 6. To the solution of **1** (0.2012 g, 1.08 mmol) in THF (1 mL), DBU (0.016 mL, 0.107 mmol) and the amine (0.105 mL, 1.20 mmol) were added. The reaction solution was stirred at 338 K for 2 h, and, then, cooled to room temperature. Product **6** was isolated by column chromatography (silica gel; petroleum ether/diethyl ether (1 : 1 v/v)). Yield of **6**: 180 mg, 93%. Found: C, 60.07; H, 6.80; N, 15.56. Calc. for $C_9H_{12}N_2O_2$: C, 59.99; H, 6.71; N, 15.54%; ν_{max}(Nujol)/cm^{-1} 1682vs (C═O); δ_H (500 MHz; $CDCl_3$; 293 K) 3.60 (4 H, t, $J = 4.8$, NCH_2), 3.72 (4 H, t, OCH_2), 6.22 (2 H, t, $J = 2.2$, H_β), 6.98 (2 H, t, $J = 2.3$ Hz, H_α); δ_C (125 MHz; $CDCl_3$; 293 K) 46.98 (NCH_2), 66.56 (OCH_2), 110.98 (C_β), 120.33 (C_α), 153.88 (C═O); *m*/*z* (EI) 180 (M^+), 149, 135, 122, 114 (M – C_4H_4N), 94, 80, 70, 66, 56, 42.

1-Dibenzylaminocarbonyl pyrrole (*N*,*N*-dibenzyl-1*H*-pyrrole-1-carboxamide) 7. To the mixture of **1** (0.139 g, 0.74 mmol) and the amine (0.450 mL, 2.34 mmol), DBU (0.225 mL, 1.51 mmol) was added (entry 9, Table 2). The reaction solution was stirred at 293 K for 60 h and, then, dissolved in diethyl ether (25 mL). The ethereal solution was washed with H_2O (2 × 25 mL), HCl 0.13 M (2 × 25 mL), again with H_2O, dried over $MgSO_4$ and evaporated *in vacuo*. Yield of **7**: 174 mg, 81%. Product **7** can be recrystallized at 253 K from diethyl ether/n-hexane. Found: C, 78.63; H, 6.28; N, 9.61. Calc. for $C_{19}H_{18}N_2O$: C, 78.59; H, 6.25; N, 9.64%; ν_{max}(Nujol)/cm^{-1} 1674vs (C═O); δ_H (400 MHz; $CDCl_3$; 293 K) 4.58 (4 H, s, CH_2), 6.21 (2 H, t, $J = 2.2$, H_β), 7.11 (2 H, t, $J = 2.2$, H_α), 7.23 (4 H, dm, H_{ortho}), 7.31 (2 H, m, H_{para}), 7.37 (4 H, m, H_{meta}); δ_C (100 MHz; $CDCl_3$; 293 K) 50.76 (CH_2), 111.02 (C_β), 120.59 (C_α), 127.73, 127.80, 128.88, 135.94 (C_{ipso}) 155.14 (C═O); *m*/*z* (EI) 290 (M^+), 224 (M – C_4H_4N), 199 (M-PhCH_2), 156, 132, 104, 91, 77, 65, 51, 39.

1-Phenylaminocarbonyl pyrrole (*N*-phenyl-1*H*-pyrrole-1-carboxamide) 8. To the substrate **1** (0.1525 g, 0.82 mmol), DBU (0.125 mL, 0.837 mmol) and the amine (0.225 mL, 2.47 mmol) were added (entry 12, Table 2). The reaction mixture was stirred at 293 K for 12 h and, then, dissolved in diethyl ether (25 mL). The resulting solution was extracted with H_2O (2 × 20 mL) and the organic solvent was evaporated. The solid residue was washed with small volumes of H_2O and dried *in vacuo*. Yield of **8**: 126 mg, 83%. Found: C, 70.93; H, 5.45; N, 15.01. Calc. for $C_{11}H_{10}N_2O$: C, 70.96; H, 5.41; N, 15.04%; ν_{max}(Nujol)/cm^{-1} 3335 s (NH), 1690vs (C═O); δ_H (400 MHz; $CDCl_3$; 293 K) 6.31 (2 H, t, $J = 2.2$, H_β), 7.15 (1 H, m, H_{para}), 7.26 (1 H, br, NH), 7.28 (2 H, t, $J = 2.2$, H_α), 7.35 (2 H, m, H_{meta}), 7.48 (2 H, dm, H_{ortho}); δ_C (100 MHz; $CDCl_3$; 293 K) 112.51 (C_β), 118.53 (C_α), 120.41 (C_{ortho}), 124.91, (C_{para}), 129.22 (C_{meta}), 136.76 (C_{ipso}), 148.34 (C═O); *m*/*z* (EI) 186 (M^+), 119 (M – C_4H_4NH), 91, 67, 51, 39.

1-(*N*-Methyl-*N*-phenylaminocarbonyl) pyrrole (*N*-methyl-*N*-phenyl-1*H*-pyrrole-1-carboxyamide) 9. To the substrate **1** (0.1509 g, 0.81 mmol), DBU (0.130 mL, 0.870 mmol) and the amine (0.260 mL, 2.40 mmol) were added (entry 13, Table 2). The reaction mixture was stirred at 293 K for 38 h and, then, dissolved in diethyl ether (10 mL). The resulting solution was washed with H_2O (20 mL), HCl 0.17 M (35 mL), NaOH 1 M (10 mL) and, again, with H_2O. The organic phase was dried on $MgSO_4$ and evaporated *in vacuo*. Yield of **9**: 144 mg, 89%. Found: C, 71.93; H, 6.10; N, 13.97. Calc. for $C_{12}H_{12}N_2O$: C, 71.98; H, 6.04; N, 13.99%; ν_{max}(neat)/cm^{-1} 1697vs and 1682vs (poorly resolved, C═O); δ_H (400 MHz; $CDCl_3$; 293 K) 3.44 (3 H, s, CH_3), 5.97 (2 H, t, $J = 2.2$, H_β), 6.74 (2 H, t, $J = 2$, H_α), 7.06 (2 H, dm, H_{ortho}), 7.21 (1 H, m, H_{para}), 7.31 (2 H, m, H_{meta}); δ_C (100 MHz; $CDCl_3$; 293 K) 40.11 (Me), 110.46 (C_β), 121.14 (C_α), 125.45 (C_{ortho}), 126.83 (C_{para}), 129.81 (C_{meta}), 144.48 (C_{ipso}), 152.97 (C═O); *m*/*z* (EI) 200 (M^+), 134 (M – C_4H_4N), 119, 106, 77, 51, 39.

Methyl 4-methyl-2-[(1*H*-pyrrol-1-ylcarbonyl)amino]pentanoate 10. To the mixture of **1** (0.1122 g, 0.60 mmol) and L-leucine methylester hydrochloride (0.1377 g, 0.76 mmol), the solvent (THF, 3 mL) and DBU (0.295 mL, 1.37 mmol) were added (entry 4, Table 3). The resulting suspension was stirred at 333 K for 16 h, cooled to room temperature and filtered to remove the precipitate (mainly DBU·HCl). The solvent was evaporated and the residue fractionated by flash chromatography on a silica gel column with a petroleum ether/diethyl ether mixture (4 : 1 and, then, 2 : 1 (v/v)). Yield of **10**: 124 mg, 87%. The product can be recrystallized at 253 K from diethyl ether/n-hexane. Found: C, 60.61; H, 7.70; N, 11.68. Calc. for $C_{12}H_{18}N_2O_3$: C, 60.49; H, 7.61; N, 11.75%; ν_{max}(Nujol)/cm^{-1} 3325 s (NH), 1744vs (CO_2Me), 1667vs (C═O); δ_H (400 MHz; $CDCl_3$; 293 K) 0.95 (3 H, d, $^3J = 8$, CH_3), 0.97 (3 H, d, $^3J = 8$, CH_3), 1.58–1.80 (3 H, overlapped multiplets, CH_2 and $CHMe_2$), 3.76 (3 H, s, OMe), 4.68 (1 H, td, $^3J_{HCCH} = 5$, $^3J_{HCCH} \approx {}^3J_{HCNH} = 8$, $CHCO_2Me$), 5.79 (1 H, br d, $^3J_{HCNH} = 8$, NH), 6.25 (2 H, t, $J = 2$, H_β), 7.19 (2 H, t, $J = 2$, H_α); δ_C (100 MHz; $CDCl_3$; 293 K) 21.91 (Me), 22.78 (Me), 24.83 ($CHMe_2$), 41.79 (CH_2), 51.99 ($CHCO_2Me$), 52.57 (OMe), 112.11 (C_β), 118.42 (C_α), 150.43 (C═O), 173.38 (CO_2Me); *m*/*z* (EI) 238 (M^+), 179 (M – CO_2Me), 163, 138, 112, 88, 67, 55, 41.

1-(2-Hydroxyethyl)aminocarbonyl pyrrole (*N*-(2-hydroxyethyl)-1*H*-pyrrole-1-carboxamide) 11. To the solution of **1** (0.1053 g, 0.56 mmol) in THF (1 mL), DBU (0.010 mL, 0.067 mmol) and the amino alcohol (0.036 mL, 0.64 mmol) were added (entry 8, Table 3). The reaction mixture was stirred at 293 K for about 1 h and, after evaporating the solvent *in vacuo*, was fractionated on a silica gel column using diethyl ether as the eluent. Yield of **11**: 70 mg, 81%.[30] The product can be recrystallized at 253 K from diethyl ether/n-hexane. Found: C, 54.61; H, 6.60; N, 18.10. Calc. for $C_7H_{10}N_2O_2$: C, 54.54; H, 6.54; N, 18.16%; ν_{max}(Nujol)/cm^{-1} 3395 s and 3310 s, 1682vs (C═O), 1551vs; δ_H (400 MHz; $CDCl_3$; 293 K) 2.67 (1 H, br s, OH), 3.52 (2 H, q, $^3J = 5$, NCH_2), 3.77 (2 H, t, $^3J = 5$, CH_2O), 6.23 (2 H, t, $J = 2$, H_β), 6.26 (1 H, br, NH), 7.18 (2 H, t, $J = 2.2$, H_α); δ_C (100 MHz; $CDCl_3$; 293 K) 43.12 (NCH_2), 61.65

(CH_2OH), 112.00 (C_β), 118.39 (C_α), 151.73 (C═O); *m/z* (EI) 154 (M^+), 136 (M – H_2O), 122 (M – MeOH), 106, 94, 80, 67, 56, 41.

1-(2-Hydroxy-2-phenylethyl)aminocarbonyl pyrrole (*N*-(2-hydroxy-2-phenylethyl)-1*H*-pyrrole-1-carboxamide) 12. To the solution of **1** (0.1205 g, 0.64 mmol) and Ph-AE (0.1053 g, 0.79 mmol) in THF (1 mL), DBU (0.010 mL, 0.067 mmol) was added (entry 10, Table 2). The reaction mixture was stirred at 293 K for 2 h and, after evaporating the solvent *in vacuo*, was fractionated on a silica gel column using a petroleum ether/diethyl ether (1 : 1 v/v) mixture as the eluent. Yield of **12**: 118.5 mg, 80%.[31] The product can be recrystallized (colorless plates) at 253 K from diethyl ether/n-hexane. Found: C, 67.90; H, 6.20; N, 12.09. Calc. for $C_{13}H_{14}N_2O_2$: C, 67.81; H, 6.13; N, 12.16%; ν_{max}(Nujol)/cm^{-1} 3294 s, 1674vs (C═O), 1558 ms; δ_H (400 MHz; $CDCl_3$; 293 K) 2.4 (1 H, very broad, OH), 3.42 (1 H, ddd, ^2J = 13.9, $^3J_{HCCH}$ = 8.4, $^3J_{HCNH}$ = 4.4, CH_2), 3.82 (1 H, ddd, ^2J = 13.9, $^3J_{HCCH}$ = 3.5, $^3J_{HCNH}$ = 7.3, CH_2), 4.92 (1 H, dd, $^3J_{HCCH}$ = 3.5, $^3J_{HCCH}$ = 8.3, CH), 5.99 (1 H, br, NH), 6.25 (2 H, t, J = 2, H_β), 7.16 (2 H, t, J = 2, H_α), 7.26–7.40 (5 H, m, Ph); δ_C (100 MHz; $CDCl_3$; 293 K) 48.02 (NCH_2), 73.27 (CHOH), 112.05 (C_β), 118.39 (C_α), 125.78, 128.24, 128.71, 141.20 (C_{ipso}), 151.49 (C═O); *m/z* (EI) 230 (M^+), 213 (M – OH), 181, 156, 144, 124, 107, 94, 80, 67, 51, 39.

1-Allylaminocarbonyl indole (*N*-(prop-2-en-1-yl)-1*H*-indole-1-carboxamide) 13. To the solution of **2** (0.2042 g, 0.86 mmol) in THF (1 mL), DBU (0.130 mL, 0.870 mmol) and the amine (0.072 mL, 0.96 mmol) were added. The reaction mixture was stirred at 293 K for 3 h and, then, evaporated *in vacuo*. The residue was dissolved in diethyl ether and the solution extracted with H_2O. After drying over $MgSO_4$, the ethereal solution was evaporated *in vacuo* and the residue was fractionated on a silica gel column using a petroleum ether/diethyl ether (3 : 1 v/v) mixture as the eluent. Yield of **13**: 158.6 mg, 92%. Product **13** can be recrystallized at 253 K from diethyl ether(minimum amount)/n-hexane. Found: C, 71.90; H, 6.10; N, 13.90. Calc. for $C_{12}H_{12}N_2O$: C, 71.98; H, 6.04; N, 13.98%; ν_{max}(Nujol)/cm^{-1} 3356 ms (NH), 1682vs and 1666vs (poorly resolved, C═O), 1535vs; δ_H (400 MHz; $CDCl_3$; 293 K) 4.09 (2 H, tt, $^3J_{HCCH} \approx {}^3J_{HCNH}$ = 5.5, ^4J = 1.5, CH_2), 5.21 (1 H, dq, J_{cis} = 10.2, $^2J \approx {}^4J$ = 1.5, H_{cis}), 5.30 (1 H, dq, J_{trans} = 17.2, $^2J \approx {}^4J$ = 1.5 Hz, H_{trans}), 5.65 (1 H, br, NH), 5.96 (1 H, m, CH), 6.61 (1 H, dd, ^3J = 3.7, ^4J = 1.1, 3-H), 7.21 (1 H, m, $^3J_{5,4}$ = 7.7, $^3J_{5,6}$ = 7.3, $^4J_{5,7}$ = 1.1, 5-H), 7.30 (1 H, m, $^3J_{6,5}$ = 7.3, $^3J_{6,7}$ = 8.1, $^4J_{6,4}$ = 1.5, 6-H), 7.44 (1 H, d, ^3J = 3.7, 2-H), 7.58 (1 H, dt, $^3J_{4,5}$ = 7.7, $^4J_{4,6} \approx {}^4J_{4,3}$ = 1.5, 4-H), 8.06 (1 H, dm, $^3J_{7,6}$ = 8, 7-H); δ_C (100 MHz; $CDCl_3$; 293 K) 43.28 (CH_2), 107.13, 114.01, 117.15, 121.22, 122.29, 123.96, 124.22, 130.17, 133.77, 135.03, 151.90 (C═O); *m/z* (EI) 200 (M^+), 130, 117, 89, 65, 63, 41, 39.

9-Allylaminocarbonyl carbazole (*N*-(prop-2-en-1-yl)-9*H*-carbazole-9-carboxamide) 14. To the solution of **3** (0.2465 g, 0.86 mmol) in THF (1 mL), DBU (0.130 mL, 0.870 mmol) and the amine (0.072 mL, 0.96 mmol) were added. The reaction mixture was stirred at 293 K for 3 h and, then, evaporated *in vacuo*. The residue was dissolved in diethyl ether and the solution extracted with H_2O. After drying over $MgSO_4$, the ethereal solution was evaporated *in vacuo* and the residue was fractionated on a silica gel column using a petroleum ether/diethyl ether (10 : 1 v/v) mixture as the eluent. Yield of **14**: 137.4 mg, 64%. The product can be recrystallized (colorless needles) at 253 K from diethyl ether(minimum amount)/n-hexane. Found: C, 76.85; H, 5.7; N, 11.09. Calc. for $C_{16}H_{14}N_2O$: C, 76.78; H, 5.64; N, 11.19%; ν_{max}(Nujol)/cm^{-1} 3271 ms (NH), 1667vs (C═O), 1528vs; δ_H (400 MHz; $CDCl_3$; 293 K) 4.18 (2 H, tt, $^3J_{HCCH} \approx {}^3J_{HCNH}$ = 6, ^4J = 1.5, CH_2), 5.25 (1 H, dq, J_{cis} = 10.3, $^2J \approx {}^4J$ = 1.5 Hz, H_{cis}), 5.34 (1 H, dq, J_{trans} = 17.2, $^2J \approx {}^4J$ = 1.5, H_{trans}), 5.77 (1 H, br, NH), 6.03 (1 H, m, CH), 7.33 (2 H, m), 7.47 (2 H, m), 8.02 (4 H, overlapped dm); δ_C (100 MHz; $CDCl_3$; 293 K) 43.45 (CH_2), 113.54, 117.43, 120.20, 122.29, 125.10, 126.95, 133.71, 138.27, 152.63 (C═O); *m/z* (EI) 250 (M^+), 167, 140, 115, 113, 83, 63, 56, 41.

1-Morpholinocarbonyl indole ((1*H*-indol-1-yl)(morpholin-4-yl)methanone) 15. To the solution of **2** (0.1673 g, 0.71 mmol) in THF (1 mL), DBU (0.105 mL, 0.703 mmol) and the amine (0.070 mL, 0.80 mmol) were added. The reaction mixture was stirred at 293 K for 3 h and, then, evaporated *in vacuo*. The residue was fractionated on a silica gel column using a petroleum ether/diethyl ether (1 : 1 v/v) mixture as the eluent. The fractions containing the product were collected and the solvent was evaporated. The product, which was contaminated by minor amounts of $O(CH_2CH_2)_2NCO_2Ph$, was recrystallized at 253 K from diethyl ether/n-hexane. Yield of **15**: 149.3 mg, 92%. Found: C, 67.90; H, 6.20; N, 12.10. Calc. for $C_{13}H_{14}N_2O_2$: C, 67.81; H, 6.13; N, 12.16%; ν_{max}(Nujol)/cm^{-1} 1682vs (C═O); δ_H (400 MHz; $CDCl_3$; 293 K) 3.59 (4 H, t, J = 4.7, NCH_2), 3.77 (4 H, t, J = 5 Hz, OCH_2), 6.60 (1 H, dd, ^3J = 3.7, ^4J = 1, 3-H), 7.19 (1 H, m, $^3J_{5,4}$ = 7.7, $^3J_{5,6}$ = 7.3, $^4J_{5,7}$ = 1.1, 5-H), 7.29 (1 H, m, $^3J_{6,5}$ = 7, $^3J_{6,7}$ = 8.4, $^4J_{6,4}$ = 1.1, 6-H), 7.29 (1 H, d, ^3J = 3.7, 2-H), 7.58 (1 H, dt, $^3J_{4,5}$ = 7.7, $^4J_{4,6} \approx {}^4J_{4,3}$ = 1, H-4), 7.67 (1 H, dm, $^3J_{7,6}$ = 8, 7-H); δ_C (100 MHz; $CDCl_3$; 293 K) 47.05 (NCH_2), 66.67 (OCH_2), 106.27, 113.17, 121.12, 122.05, 123.75, 126.10, 129.59, 135.15, 154.27 (C═O); *m/z* (EI) 230 (M^+), 200, 144 (M – $N(CH_2CH_2)_2O$), 130, 114 (M – C_8H_6N), 103, 89, 70, 63, 42.

9-Morpholinocarbonyl carbazole ((9*H*-carbazol-9-yl)(morpholin-4-yl)methanone) 16. To the solution of **3** (0.2028 g, 0.71 mmol) in THF (1 mL), DBU (0.105 mL, 0.703 mmol) and the amine (0.070 mL, 0.80 mmol) were added. The reaction mixture was reacted at 293 K for 10 h. After evaporating the solvent *in vacuo*, diethyl ether was added. The resulting solution was washed with H_2O, dried on $MgSO_4$ and fractionated on a silica gel column using a petroleum ether/diethyl ether (1 : 1 v/v) mixture as the eluent. The chromatographic separation allowed to recover pure carbazole and a mixture of $O(CH_2CH_2)_2NCO_2Ph$ and the target urea, from which **16** was isolated (120.2 mg, 61%) by recrystallyzation at 253 K from diethyl ether with n-hexane. Found: C, 72.90; H, 5.80; N, 9.95. Calc. for $C_{17}H_{16}N_2O_2$: C, 72.84; H, 5.75; N, 9.99%; ν_{max}(Nujol)/cm^{-1} 1666vs (C═O); δ_H (400 MHz; $CDCl_3$; 293 K) 3.60 (4 H, t, J = 4.8, NCH_2), 3.78 (4 H, t, J = 5, OCH_2), 7.31 (2 H, m), 7.46 (2 H, m), 7.65 (2 H, dm, J = 8.1), 8.02 (2 H, dm, J = 7.7); δ_C (100 MHz; $CDCl_3$; 293 K) 46.80 (NCH_2), 66.84 (OCH_2), 112.58, 120.24, 121.82, 124.48, 126.68, 138.44, 153.95 (C═O); *m/z* (EI) 280 (M^+), 194 (M – $N(CH_2CH_2)_2O$), 180, 166 (M – $OCN(CH_2CH_2)_2O$), 140, 114, 89, 70, 56, 42.

Acknowledgements

Università degli Studi di Bari (Fondi di Ateneo) and Ministero dell'Istruzione, dell'Università e della Ricerca (PRIN 2008A7P7YJ_002) are acknowledged for financial support. The Authors thank Dr C. Cardellicchio (ICCOM-CNR, Bari) for polarimetric analyses.

Notes and references

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(C═O); *m/z* (EI) 247 (M^+), 180 (M – C_4H_5N), 137, 111, 94, 80, 67, 42.

31 From the chromatographic separation we collected an impure fraction mainly containing the side-product **18** characterized as $C_4H_4NC(O)NHCH_2CH(Ph)O(O)CNC_4H_4$ on the basis of the NMR and mass spectra. δ_H (400 MHz; $CDCl_3$; 293 K) 3.90–3.96 (2 H, m, NCH_2), 5.95 (1 H, br unresolved t, NH), 6.07 (1 H, dd, J = 4, 8, OCH), 6.24 (2 H, t, J = 2 $H_{\beta,ureidic}$), 6.25 (2 H, t, J = 2, $H_{\beta,carbamic}$), 7.13 (2 H, t, J = 2, $H_{\alpha,ureidic}$), 7.28 (2 H, t, J = 2, $H_{\alpha,carbamic}$), 7.34–7.46 (5 H, m, Ph); δ_C (100 MHz; $CDCl_3$; 293 K) 45.98 (NCH_2), 77.88 (CH), 112.15 ($C_{\beta,ureidic}$), 113.01 ($C_{\beta,carbamic}$), 118.38 ($C_{\alpha,ureidic}$), 120.15 ($C_{\alpha,carbamic}$),126.36, 129.05, 129.18, 136.36 (C_{ipso}), 150.10 (C(O)O), 150.87 (C═O); *m/z* (EI) 323 (M^+), 281, 256, 213, 184, 170, 156, 146, 128, 104, 94, 77, 68, 51, 39.