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The reaction of 4-amino-2-oxazolines with isocyanates and isothiocyanates. Synthesis and X-ray structures of polysubstituted 2-imidazolidinones, 1,3-oxazolidines and 1,3-thiazolidines

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Abstract—Reactions of 4-alkylamino-2-phenyl-2-oxazolines **1** with isocyanates and isothiocyanates provide unprecedented efficient and regioselective heterocycle–heterocycle transformations. Compounds **1** reacted rapidly with tosyl isocyanate yielding directly 3-alkyl-4-benzamido-1-tosyl-2-imidazolidinones **4** in almost quantitative yields. The corresponding ureido intermediates **2** were not isolable species. However, the reactions with non-sulfonylated isocyanates or isothiocyanates were slower, leading to the expected ureido and thioureido derivatives **5**, which were easily and efficiently transformed to either polysubstituted 2-imino-1,3-oxazolidine or 2-imino-1,3-thiazolidine hydrochlorides **7**, respectively, by treatment with hydrochloric acid. The possible reasons for this disparity in chemical behaviour are discussed. X-ray crystallographic structures for 4-benzamido-3-methyl-1-tosyl-2-imidazolidinone **4b**, 4-[1-isopropyl-3-(4-nitrophenyl)ureido]-2-phenyl-2-oxazoline **5e**, (*Z*)-3-benzyl-4-benzamido-2-phenylimino-1,3-oxazolidine hydrochloride **7a** and (*Z*)-3-benzyl-4-benzamido-2-phenylimino-1,3-thiazolidine hydrochloride **7b** have been determined.

1. Introduction

2-Oxazolines are remarkably versatile synthetic intermediates.[1–4] The vast number of transformations[1] reported over the last few years have led to a renewed interest in the chemistry of these compounds. However, only a few examples of transformations of 2-oxazolines into other heterocycles have been described; most work on this subject has been focused on either hydrogenation or dehydrogenation processes to give products retaining the original ring system.[1]

As a result of our research project on new methods for the synthesis of heterocyclic compounds, based on using chloral as a key starting material, we developed an efficient and general preparative procedure that provided novel 4-amino-2-aryl-2-oxazolines[5,6] **1** from chloralamides. Continuing this project, we focused the work on the reactions of these compounds with isocyanates and isothiocyanates. Given the peculiar structural arrangement of the expected ureido and thioureido derivatives, it was considered that these reactions could be the starting point for attractive approaches to novel heterocyclic compounds. In preliminary communication[7,8] we reported the successful application of this synthetic methodology for preparing novel 2-imidazolidinones, 1,3-oxazolidines and 1,3-thiazolidines. In this paper we describe full details of this work and new results of the preparative procedures, together with spectral and X-ray crystallographic data for the hitherto unknown classes of compounds newly accessed. Differences in chemical behaviour observed for ureido and thioureido intermediates may be attributed to crucial electronic effects associated with the presence or absence of the sulfonyl group.

2. Results and discussion

4-Alkylamino-2-aryl-2-oxazolines **1** were treated with *p*-toluenesulfonyl isocyanate in ether solution at room temperature (Scheme 1). The reactions occurred quickly under such mild experimental conditions. The instantaneous formation of a white solid precipitate was observed in all cases. The resulting voluminous crude solid products were isolated by filtration and identified by the usual analytical methods

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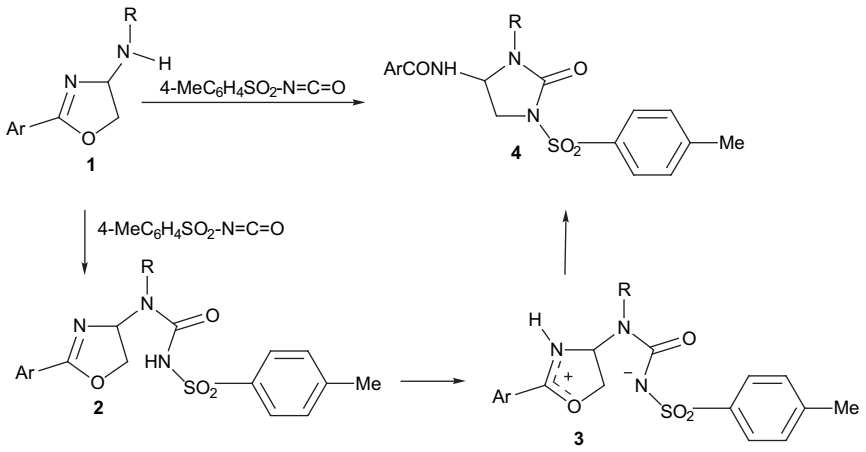


	Ar	R
a	C_6H_5	$C_6H_5CH_2$
b	C_6H_5	CH_3
c	C_6H_5	$(CH_3)_2CH$
d	3-ClC_6H_4	$C_6H_5CH_2$
e	3,4,5-$(CH_3O)_3C_6H_2$	$C_6H_5CH_2$

Scheme 1.

as highly pure 3-alkyl-4-benzamido-1-tosyl-2-imidazolidinones **4**. Yields were nearly quantitative. IR and NMR spectra for crude and recrystallized products showed negligible differences.

The structural assignment of these compounds was corroborated by X-ray crystallographic analysis of 4-benzamido-3-methyl-1-tosyl-2-imidazolidinone **4b**. The molecular structure is illustrated in Figure 1. Selected intramolecular distances (crystallographic numbering of atoms) and selected bond angles are given in Table 1. Suitable single crystals for this analysis were obtained from hexane/chloroform and contained one molecule of chloroform per molecule of **4b**. A thermogravimetric analysis of this compound showed a sharp peak at 106.2 °C, corresponding to quantitative loss of chloroform. The crystallographic analysis showed the crystal packing to be determined by N–H···O and Cl···O interactions.

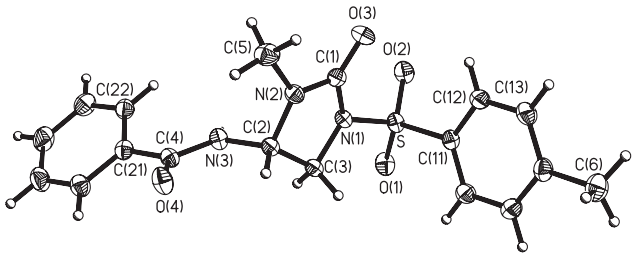


Figure 1. Molecular structure of product **4b**, showing the crystallographic numbering system used.

A particularly facile rearrangement of the ureido intermediates **2** to imidazolidinones **4** appears as a key step in this transformation (Scheme 1). However, ureido derivatives are, in general, stable crystalline compounds that can be used for the separation and characterization of amines. In contrast, 2-oxazolines are characterized by a high reluctance to undergo alteration of the ring system by nucleophilic attacks, and are indeed commonly used as protecting or activating groups in strongly nucleophilic media.[9] Therefore, the pronounced lability evidenced by intermediates **2** indicates the existence of some special factors that promote a remarkable enhancement of electrophilic activity at C-5. A reasonable explanation for this might be a protonic autoactivation induced by the sulfonyl group, which would generate an internal acidic centre. In conjunction with the cogeneration of a benzamido group, this would strongly facilitate an

Table 1. Selected bond lengths and bond angles in crystal structure of **4b**

Lengths (Å)

O(3)–C(1)	1.213(2)	O(4)–C(4)	1.229(2)
N(1)–C(1)	1.418(2)	N(1)–C(3)	1.474(2)
N(2)–C(1)	1.349(2)	N(2)–C(5)	1.453(2)
N(2)–C(2)	1.458(2)	N(3)–C(4)	1.351(2)
N(3)–C(2)	1.449(2)	C(2)–C(3)	1.537(2)

Angles (°)

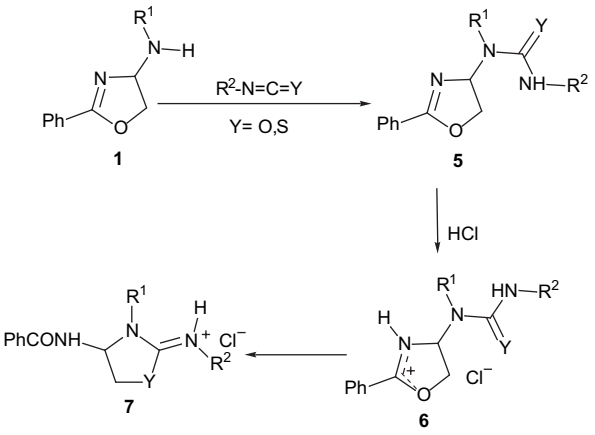
C(1)–N(1)–C(3) 110.l9(13)	C(3)–N(1)–S 120.49(11)	C(1)–N(2)–C(2) 113.88(13)
C(4)–N(3)–C(2) 122.79(14)	O(3)–C(1)–N(2) 127.28(16)	N(3)–C(2)–N(2) 112.19(13)
N(2)–C(2)–C(3) 102.29(12)	C(1)–N(1)–S 122.86(11)	C(1)–N(2)–C(5) 121.19(14)
C(5)–N(2)–C(2) 123.46(14)	O(3)–C(1)–N(2) 127.3(2)	N(2)–C(1)–N(1) 106.57(13)
N(3)–C(2)–C(3) 112.11(13)	N(1)–C(3)–C(2) 102.25(13)	

intramolecular attack at that site. Therefore, a rearrangement process involving a ring opening of the oxazolinic intermediates **3** with simultaneous ring closure to form the corresponding imidazolidinones **4** could take place easily in this way. This type of rearrangement is as yet unknown in the literature. A paper containing a remotely related process reported the conversion of 5-aryl(or benzyl)-3-(2-bromoethyl)1,3,4-oxadiazol-2(3*H*)ones to 1-acylamino-3-alkylimidazolin-2-ones by treatment with primary alkylamines.[10c]

The isolation of the presumably labile sulfonylureido intermediates **2** was attempted by carrying out the reactions at subambient temperature. Thus, oxazolines **1d**,**e** reacted with tosyl isocyanate at 0 °C yielding the targeted ureido derivatives **2d**,**e** instead of imidazolines **4d**,**e**. These products demonstrated a great tendency towards the postulated rearrangement to give the corresponding imidazolidinones **4d**,**e**. In agreement with this discussion, compounds **2d**,**e** showed mass spectra and melting points fully coincident with those of **4d**,**e**. However, they were clearly distinguishable by analyzing the samples with non-aggressive low-temperature analytical techniques such as IR and NMR spectroscopy.

2-Imidazolidinones[11] are compounds of great interest. As far as we know, direct conversion of 2-oxazolines into 2-imidazolidinones has not yet been reported. The wide variety of 2-oxazolines **1** available[5,6] confers a high versatility on this new approach to specifically polysubstituted 2-imidazolidinones. The most extended methodology for preparing 2-imidazolidinones involves carbonylation of diamines with various reagents[12] and reactions of diols,[12a] aminols[12a] and 1,2-dicarbonyl compounds[13] with urea. In general, the limitations found for these procedures are caused by lack of mildness in the required experimental conditions or a deficient regiocontrol in the formation of more complex products. It should be noted that the synthesis of specifically substituted 2-imidazolidinones has received significant attention.[10] It is also worth considering that certain polysubstituted 2-imidazolidinones exhibit a wide range of therapeutic[14] and other important properties and applications.[15,16] Of special importance is the anticancer activity[14c,17] found in several *N*-arylsulfonyl-4-phenyl-2-imidazolidinones whose structure is closely related to that of the products **4** described here.

The above results strongly favoured the study of the behaviour of the oxazolines **1** in reactions with simple aryl isocyanates instead of tosyl isocyanate, since the role as activator agent presumed for the sulfonyl group of ureides **2** would be evidenced by these experiments. Thus, aminooxazolines **1** were treated with aryl isocyanates in dry ether at room temperature (Scheme 2). In contrast to the reactions with *p*-toluenesulfonyl isocyanate, which occurred almost instantaneously, a longer reaction time was necessary, although solid precipitates were also formed. These were easily isolated by filtration, and were identified as highly pure 4-[1-alkyl-3-arylureido]-2-phenyl-2-oxazolines **5** rather than products analogous to compounds **4**. IR and NMR spectra for crude and crystallized products showed negligible differences. Yields were almost quantitative. The molecular structure of one of these novel compounds, 4-[1-isopropyl-3-(4-nitrophenyl)ureido]-2-phenyl-2-oxazoline **5e**, was determined by X-ray crystallography. The molecular structure is illustrated in Figure 2. Selected intramolecular distances (crystallographic numbering of atoms) and selected bond angles are given in Table 2.



entry	Y	R^2	R^1
a	O	C_6H_5	$C_6H_5CH_2$
b	S	C_6H_5	$C_6H_5CH_2$
c	S	$4\text{-}CH_3OC_6H_5$	$C_6H_5CH_2$
d	O	$4\text{-}ClC_6H_4$	$C_6H_5CH_2$
e	O	$4\text{-}NO_2C_6H_4$	$(CH_3)_2CH$
f	O	$C_6H_5CH_2$	$C_6H_5CH_2$
g	O	$(CH_3)_2CH$	$C_6H_5CH_2$
h	O	$C_6H_5CH_2$	$(CH_3)_2CH$
i	O	$CH_3CH_2CH_2$	$C_6H_5CH_2$

Scheme 2.

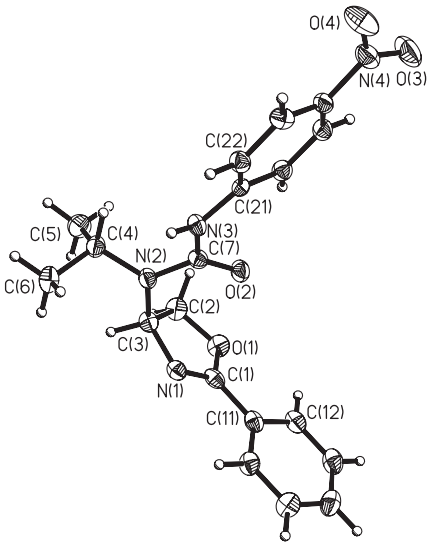


Figure 2. Molecular structure of product **5e**, showing the crystallographic numbering system used.

Compounds **5** were much more stable than the tosylated intermediates **2**. In contrast to the lability exhibited by compounds **2d**,**e**, the non-sulfonylated ureido derivatives **5** were stable enough to be handled in solution and to permit prolonged storage without need of any special care. Given the absence of the sulfonyl group, this relative stability appears to be attributable to the lack of the protonic autoactivation postulated above. In order to seek a firm support to this

Table 2. Selected bond lengths and bond angles in crystal structure of **5e**

Lengths (Å)			
O(1)–C(1)	1.3515(18)	N(1)–C(3)	1.4697(19)
N(2)–C(3)	1.4608(18)	C(2)–C(3)	1.541(2)
O(1)–C(2)	1.4485(19)	N(1)–C(1)	1.2796(19)

Angles (°)		
C(1)–O(1)–C(2) 106.00(11)	N(1)–C(1)–C(11) 125.60(14)	O(1)–C(2)–C(3) 104.31(12)
C(1)–N(1)–C(3) 106.96(13)	N(1)–C(1)–O(1) 118.39(14)	O(1)–C(1)–C(11) 116.01(13)
N(2)–C(3)–N(1) 111.33(12)	N(1)–C(3)–C(2) 104.10(12)	

hypothesis, it was considered that the treatment of ureides **5** with a mineral acid would circumvent the non-presence of the sulfonyl group. Consequently, solutions of compounds **5** in ether were treated with concentrated hydrochloric acid resulting in almost instantaneous reactions with formation of solid precipitates. The products were crystallized and characterized as the corresponding 2-arylimino-1,3-oxazolidine or 2-arylimino-1,3-thiazolidine hydrochlorides **7**. Crude and crystallized products showed negligible spectroscopic differences. Yields were almost quantitative. The molecular structure of one of these compounds, (*Z*)-3-benzyl-4-benzamido-2-phenylimino-1,3-oxazolidine hydrochloride **7a**, was corroborated by X-ray crystallography. The structure is illustrated in Figure 3. Selected intramolecular distances (crystallographic numbering of atoms) and selected bond angles are given in Table 3. It is of significant interest that similar treatment of ureides **2d**,**e** with hydrochloric acid provided the corresponding imidazolidinones **4d**,**e** instead of oxazolidine hydrochloride products.

Analogous reactions of aminooxazolines **1** with isothiocyanates instead of isocyanates were carried out, providing parallel results. Highly pure 4-[1-alkyl-3-arylthioureido]-2-phenyl-2-oxazolines **5** were isolated in high yields. Such compounds are also indefinitely stable, but were quickly and quantitatively convertible to (*Z*)-3-alkyl-4-benzamido-2-phenylimino-1,3-thiazolidine hydrochlorides **7** by treatment with hydrochloric acid. The molecular structure of one of these compounds, (*Z*)-3-benzyl-4-benzamido-2-phenylimino-1,3-thiazolidine hydrochloride **7b**, was determined by X-ray crystallography. The structure is illustrated in Figure 4. Selected intramolecular distances (crystallographic numbering of atoms) and selected bond angles are given in Table 4.

There are no precedents for compounds of type **7**. As far as we know, this is the first time that direct conversions of 2-oxazoline rings to either 1,3-oxazolidine or 1,3-thiazolidine ring systems have been reported. The high versatility of the reactions[5,6] involved in preparing the starting materials **1** implies a concomitantly wide versatility for these synthetic approaches. The described preparative procedures in separate steps could also be carried out in a one-pot process, which allows quick and highly efficient preparations of the same compounds. It should be noted that the synthesis of either 2-iminooxazolidines or 2-iminothiazolidines has

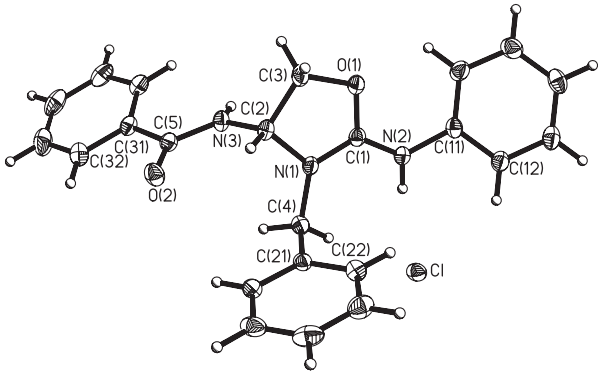


Figure 3. Molecular structure of product **7a**, showing the crystallographic numbering system used.

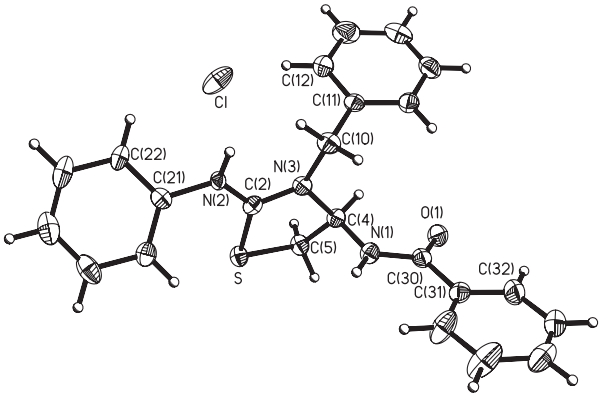


Figure 4. Molecular structure of product **7b**, showing the crystallographic numbering system used.

Table 3. Selected bond lengths and bond angles in crystal structure of **7a**

Lengths (Å)			
C(1)–O(1)	1.3182(14)	C(1)–N(1)	1.3204(14)
C(1)–N(2)	1.3241(15)	C(2)–N(3)	1.4350(14)
C(2)–N(1)	1.4776(14)	C(2)–C(3)	1.5331(17)
C(3)–O(1)	1.4632(14)		

Angles (°)		
N(1)–C(2)–C(3) 100.70(9)	O(1)–C(3)–C(2) 105.66(9)	C(1)–N(1)–C(4) 128.23(10)
C(1)–N(1)–C(2) 110.87(9)	C(4)–N(1)–C(2) 120.73(9)	C(1)–N(2)–C(11) 126.77(10)
C(1)–O(1)–C(3) 108.24(9)	C(5)–N(3)–C(2) 122.28(9)	O(1)–C(1)–N(1) 113.88(10)
O(1)–C(1)–N(2) 120.03(10)	N(1)–C(1)–N(2) 126.08(10)	N(3)–C(2)–N(1) 111.29(9)
N(3)–C(2)–C(3) 113.76(9)		

Table 4. Selected bond lengths and bond angles in crystal structure of **7b**

Lengths (Å)

S–C(2)	1.7448(13)	S–C(5)	1.8135(12)
C(2)–N(2')	1.323(7)	C(2)–N(3)	1.3338(16)
N(3)–C(4)	1.4635(15)	N(3)–C(10)	1.4802(16)
C(4)–N(1)	1.4518(16)	C(4)–C(5)	1.5226(17)
C(10)–C(11)	1.5047(19)	N(2')–C(21')	1.427(7)
C(30)–O(1)	1.2331(16)	C(30)–N(1)	1.3557(16)
C(30)–C(31)	1.4988(19)		

Angles (°)

C(2)–S–C(5)	90.45(6)	N(2')–C(2)–N(3)	129.5(3)	N(2')–C(2)–S	116.7(3)
N(3)–C(2)–S	113.75(9)	C(2)–N(3)–C(4)	114.62(10)	C(2)–N(3)–C(10)	125.97(10)
C(4)–N(3)–C(10)	117.41(10)	N(1)–C(4)–N(3)	109.57(9)	N(1)–C(4)–C(5)	115.03(11)
N(3)–C(4)–C(5)	105.64(10)	C(4)–C(5)–S	106.30(8)	N(3)–C(10)–C(11)	110.64(10)
C(2)–N(2')–C(21')	127.7(6)	O(1)–C(30)–N(1)	120.70(13)	O(1)–C(30)–C(31)	120.88(12)
N(1)–C(30)–C(31)	118.42(12)				

special interest because certain members of these types of compound exhibit important therapeutic and biological activities.[18]

2-Imino-1,3-oxazolidines have usually been prepared by either dehydration of *N*-(β-hydroxyethyl)-*N*,*N*′-diarylureas[19] or reaction of oxiranes with carbodiimides,[20] whereas syntheses of 2-iminothiazolidines are based on reactions of 1,2-dihaloalkanes with thioureas,[21] treatment of 2-haloamines or γ-halocrotonic acid derivatives with isothiocyanates,[22] cycloaddition between aziridines and isothiocyanates[23] and treatment of α-haloketone imines with potassium thiocyanate.[24]

With regard to the relatively high electrophilic activity of the oxazoline moieties (Schemes 1 and 2), the evidence described above clearly shows that both protonation and generation of a benzamido group would be the main factors operating to facilitate the unusual nucleophilic attacks occurring at C-5. Consequently, in each type of rearrangement, analogous activated intermediates (**3** or **6**) would be involved. However, this primary assumption needs to be considered in conjunction with the participation of either nitrogen or oxygen and sulfur as nucleophilic active centres. From this perspective it can be concluded that nucleophilicities of the ureido moieties are crucially influenced by electronic differences substantial enough to cause a total disparity in the results. The different reaction modalities may thus be explained taking into consideration that ureas and thioureas are attacked[25] by electrophilic agents, preferentially at the oxygen or sulfur atoms, respectively; this seems mainly attributable to a relatively high electron density at such heteroatoms. This is the case for the formation of products **7** via intermediates **6**. The formation of products **4** via intermediates **3**, however, would be a consequence of the strong electron withdrawing effect of the sulfonyl group, which would substantially decrease the nucleophilicity at the oxygen.

In conclusion, the first direct conversions of 2-oxazolines into either 2-imidazolidinones or 1,3-oxazolidines **7** (Y=O) or 1,3-thiazolidines **7** (Y=S) derivatives are reported. The formation of these products involves hitherto unknown rearrangement processes. The preparative methods described here are of significant synthetic utility, providing directly polysubstituted heterocyclic products of potential biological interest with a full control of the substitution pattern. Versatility, good yields, easy availability of starting materials, mildness and simple experimental procedure are noteworthy advantages of these approaches, which provide potential access to previously unattainable compounds. It seems feasible to extend the described synthetic methodology to prepare a wide variety of heterocyclic compounds.

3. Experimental

3.1. General

NMR spectra were determined on Bruker AC-200 or Varian Unity 300 Unity instruments with tetramethylsilane as internal reference. Electron-impact mass spectra were obtained on Hewlett–Packard 5995 and Autospect 5000 VG spectrometers under an ionizing voltage of 70 eV. IR spectra (Nujol emulsions) were recorded on a Nicolet Impact 400 spectrophotometer. Microanalyses were performed on a Carlo Erba EA-1108 analyzer. Melting points were determined on a Kofler hot-plate melting point apparatus, and are uncorrected.

X-ray crystallographic data were collected using Mo Kα radiation (λ=0.71073 Å). For compounds **4b** and **5e** a Siemens P4 diffractometer was used (ω-scans, $2\theta_{max}$ 55° and 50°, respectively); for **7a** and **7b** a Bruker SMART 1000 CCD (ω- and ø-scans, $2\theta_{max}$ 60°). Structures were refined anisotropically on F^2 using the program SHELXL-97 (G.M. Sheldrick, University of Göttingen). Hydrogen atoms were included using rigid methyl groups or a riding model, except for compound **4b** C-5 methyl group which is disordered over two sites. Crystal data are given below for each compound individually.

3.2. Preparation of 4-benzamido-3-alkyl-1-tosyl-2-imidazolidinones (4) and 4-(1-alkyl-3-tosylureido)-2-aryl-2-oxazolines (2)

A solution of *p*-toluenesulfonyl isocyanate (1 mmol) in dry ether (3 mL) was added dropwise at room temperature to a stirred solution of the appropriate aminooxazoline **1** (1 mmol) in dry ether (5 mL). A white precipitate formed almost instantaneously. The solid products **4** were filtered off, washed with cold ether and crystallized from a mixture of hexane/chloroform or hexane/dichloromethane. The reactions carried out at 0 °C yielded the ureido intermediates **2** instead of the final products **4**.

3.2.1. 4-(1-Benzyl-3-tosylureido)-2-(3-chlorophenyl)-2-oxazoline (2d). Yield 88%; crystallization from petroleum ether/dichloromethane gave white powder; mp 222–223 °C; ^{1}H NMR ($CDCl_3$, 300 MHz) δ (ppm): 2.43 (s, 3H), 4.20 (dd, 1H, J=10.0 Hz, J=6.3 Hz), 4.28 (d, 1H, J=17.1 Hz), 4.39 (d, 1H, J=17.1 Hz), 4.49 (t, 1H, J=10.0 Hz), 6.35–6.37 (m, 1H), 7.26–7.49 (m, 11H), 7.75–7.87 (m, 3H); ^{13}C NMR ($CDCl_3$, 75.4 MHz) δ (ppm): 21.73 (CH_3), 46.49 (CH_2), 71.66 (CH_2), 77.83 (CH), 126.87 (CH), 126.99 (CH), 128.22 (C), 128.34 (CH), 128.44 (CH), 128.84 (CH), 129.41 (CH), 129.50 (CH), 129.93 (CH), 132.50 (CH), 134.71 (C), 136.14 (C), 136.28 (C), 144.63 (C), 151.99 (CO), 166.30 (C=N); MS (EI, 70 eV) m/z (rel intensity, %): 483 [M$^+$] (1), 392 (23), 328 (94), 173 (66), 155 (15), 139 (86), 131 (43), 111 (44), 106 (48), 91 (100), 77 (9), 65 (31); IR (Nujol) ν_{max}/cm^{-1} 3321, 1678, 1647, 1462, 1349, 1246, 1165, 1088, 1069, 967, 713, 664; Anal. Calcd for $C_{24}H_{22}ClN_3O_4S$ (483.97): C, 59.56; H, 4.58; N, 8.68; S, 6.63. Found: C, 59.43; H, 4.61; N, 8.72; S, 6.51.

3.2.2. 4-(1-Benzyl-3-tosylureido)-2-(3,4,5-trimethoxyphenyl)-2-oxazoline (2e). Yield 96%; crystallization from petroleum ether/dichloromethane gave white powder; mp 247–250 °C; ^{1}H NMR ($CDCl_3$, 300 MHz) δ (ppm): 2.43 (s, 3H), 3.85 (s, 6H), 3.88 (s, 3H), 4.20 (dd, 1H, J=10.0 Hz, J=6.0 Hz), 4.29 (d, 1H, J=15.9 Hz), 4.39 (d, 1H, J=16.0 Hz), 4.45 (t, 1H, J=10.0 Hz), 6.29–6.32 (m, 1H), 7.15 (s, 2H), 7.24–7.36 (m, 7H), 7.78 (d, 2H, J=8.0 Hz); ^{13}C NMR ($CDCl_3$, 75.4 MHz) δ (ppm): 21.69 (CH_3), 46.67 (CH_2), 56.32 (CH_3O), 60.99 (CH_3O), 71.66 (CH_2), 77.88 (CH), 106.08 (CH), 121.33 (CH), 127.02 (CH), 128.17 (CH), 128.40 (CH), 129.24 (CH), 129.44 (CH), 136.30 (C), 136.45 (C), 141.92 (C), 144.51 (C), 152.07 (C), 153.18 (C), 167.34 (C=N); MS (EI, 70 eV) m/z (rel intensity, %): 539 [M$^+$] (7), 384 (2), 328 (51), 211 (26), 195 (69), 173 (38), 106 (5), 91 (100), 77 (4), 65 (9); IR (Nujol) ν_{max}/cm^{-1} 1692, 1630, 1586, 1467, 1382, 1345, 1228, 1165, 1129, 1084, 1013, 819, 724, 681; Anal. Calcd for $C_{27}H_{29}N_3O_7S$ (539.60): C, 60.10; H, 5.42; N, 7.79; S, 5.94. Found: C, 59.98; H, 5.46; N, 9.84; S, 5.89.

3.2.3. 3-Benzyl-4-benzamido-1-tosyl-2-imidazolidinone (4a). Yield 95%; crystallization from petroleum ether/chloroform gave white needles; mp 215–216 °C; ^{1}H NMR ($CDCl_3$, 300 MHz) δ (ppm): 2.47 (s, 3H), 3.90–3.98 (m, 2H), 4.23 (d, 1H, J=15.0 Hz), 4.53 (d, 1H, J=15.3 Hz), 5.80 (m, 1H), 7.18–7.53 (m, 11H), 7.77 (d, 2H, J=7.8 Hz), 7.88 (d, 2H, J=8.1 Hz); ^{13}C NMR ($CDCl_3$, 75.4 MHz) δ (ppm): 21.80 (CH_3), 45.48 (CH_2), 49.53 (CH_2), 58.69 (CH), 127.49 (CH), 127.95 (CH), 128.15 (CH), 128.48 (CH), 128.59 (CH), 128.82 (CH), 129.89 (CH), 132.22 (CH), 133.15 (C), 134.55 (C), 136.24 (C), 145.23 (C), 153.49 (CO), 167.59 (CO); MS (EI, 70 eV) m/z (rel intensity, %): 449 [M$^+$] (2), 358 (6), 328 (55), 294 (11), 173 (37), 155 (5), 131 (27), 105 (95), 91 (100), 77 (40); IR (Nujol) ν_{max}/cm^{-1} 3311, 1743, 1640, 1523, 1464, 1377, 1166, 1123, 1098 cm^{-1}; Anal. Calcd for $C_{24}H_{23}N_3O_4S$ (449.52): C, 64.13; H, 5.16; N, 9.35; S, 7.13. Found: C, 64.23; H, 5.20; N, 9.39; S, 7.09.

3.2.4. 4-Benzamido-3-methyl-1-tosyl-2-imidazolidinone (4b). Yield 97%; crystallization from hexane/chloroform gave colourless prisms; mp 216–218 °C; ^{1}H NMR ($CDCl_3$, 300 MHz) δ (ppm): 2.45 (s, 3H), 2.79 (s, 3H), 3.90 (dd, 1H, J=10.2 Hz, J=8.4 Hz), 4.05 (dd, 1H, J=10.3 Hz, J=2.4 Hz), 5.87 (td, 1H, J=8.4 Hz, J=2.4 Hz), 7.29 (d, 2H, J=8.1 Hz), 7.42 (t, 2H, J=7.8 Hz), 7.55 (t, 1H, J=5.1 Hz), 7.83 (d, 2H, J=8.4 Hz), 7.97–8.03 (m, 3H); ^{13}C NMR ($CDCl_3$, 75.4 MHz) δ (ppm): 21.68 (CH_3), 28.00 (CH_3), 48.72 (CH_2), 59.69 (CH), 127.68 (CH), 127.92 (CH), 128.50 (CH), 129.82 (CH), 132.05 (CH), 133.31 (C), 134.50 (C), 145.04 (C), 153.41 (CO), 168.00 (CO); MS (EI, 70 eV) m/z (rel intensity, %): 373 [M$^+$] (1), 252 (19), 218 (20), 155 (13), 105 (100), 91 (47), 77 (41); IR (Nujol) ν_{max}/cm^{-1} 3310, 1732, 1667, 1537, 1464, 1366, 1265, 1171, 1134, 857, 814, 760, 666; Anal. Calcd for $C_{19}H_{20}Cl_3N_3O_4S \equiv C_{18}H_{19}N_3O_4S(CHCl_3)$ (492.80): C, 46.31; H, 4.09; N, 8.53; S, 6.51. Found: C, 46.24; H, 4.11; N, 8.49; S, 6.58.

Crystallographic data for **4b**. $CHCl_3$: $C_{19}H_{20}Cl_3N_3O_4S$, triclinic, space group $P(-1)$, a=5.9314(6), b=13.013(2), c=15.650(2) Å, α=109.983(8), β=99.405(10), γ=96.709(10)°, V=1100.4 Å^3, Z=2. A colourless prism 0.60×0.38×0.28 mm was used to measure 5540 reflections at T=173 K, of which 4945 were unique (R_{int}=0.010). Refinement proceeded to wR_2=0.0948 (all data), R_1=0.0351 and GOF=1.07 [$I>2\sigma(I)$]. Maximum residual electron density was 0.82 eÅ^{-3}.

3.2.5. 4-Benzamido-3-isopropyl-1-tosyl-2-imidazolidinone (4c). Yield 96%; crystallization from petroleum ether/chloroform gave white micro needles; mp 222–224 °C; ^{1}H NMR ($CDCl_3$, 300 MHz) δ (ppm): 1.22 (m, 6H), 2.45 (s, 3H), 3.84–4.03 (m, 3H), 5.98 (t, 1H, J=8.4 Hz), 7.26–7.56 (m, 6H), 7.84–7.90 (m, 4H); ^{13}C NMR ($CDCl_3$, 75.4 MHz) δ (ppm): 19.23 (CH_3), 21.34 (CH_3), 21.78 (CH_3), 45.47 (CH), 50.40 (CH_2), 57.05 (CH), 127.39 (CH), 128.24 (CH), 128.80 (CH), 129.84 (CH), 132.31 (CH), 133.33 (C), 134.60 (C), 145.09 (C), 152.78 (CO), 166.93 (CO); MS (EI, 70 eV) m/z (rel intensity, %): 401 [M$^+$] (1), 358 (31), 280 (75), 265 (24), 216 (8), 155 (6), 125 (87), 105 (100), 91 (90), 83 (70), 77 (61); IR (Nujol) ν_{max}/cm^{-1} 3405, 1723, 1667, 1526, 1464, 1351, 1240, 1225, 1171, 1138, 1108, 716, 669; Anal. Calcd for $C_{20}H_{23}N_3O_4S$ (401.48): C, 59.83; H, 5.77; N, 10.47; S, 7.99. Found: C, 59.90; H, 5.81; N, 10.41; S, 8.05.

3.2.6. 3-Benzyl-4-(3-chlorobenzamido)-1-tosyl-2-imidazolidinone (4d). Yield 98%; crystallization from petroleum ether/dichloromethane gave white needles; mp 220–221 °C; ^{1}H NMR ($CDCl_3$, 300 MHz) δ (ppm): 2.47 (s, 3H), 3.85 (dd, 1H, J=10.5 Hz, J=8.1 Hz), 3.99 (dd, 1H, J=10.0 Hz, J=2.1 Hz), 4.23 (d, 1H, J=15.0 Hz), 4.56 (d, 1H, J=15.0 Hz), 5.78 (td, 1H, J=8.7 Hz, J=2.1 Hz), 7.16–7.36 (m, 8H), 7.50 (d, 1H, J=8.1 Hz), 7.70–7.88 (m, 5H); ^{13}C NMR ($CDCl_3$, 75.4 MHz) δ (ppm): 21.79 (CH_3), 45.44 (CH_2), 49.37 (CH_2), 58.56 (CH), 125.92 (CH), 127.80 (CH), 128.09 (CH), 128.49 (CH), 128.85 (CH), 129.88 (CH), 132.17 (CH), 134.29 (C), 134.75 (C), 135.09 (C), 136.13 (C), 145.34 (C), 153.68 (CO), 166.39 (CO); MS (EI, 70 eV) m/z (rel intensity, %): 483 [M$^+$] (1), 328 (34), 173 (30), 155 (6), 139 (68), 106 (20), 91 (100), 77 (5); IR (Nujol) ν_{max}/cm^{-1} 3297, 1745, 1639, 1529, 1466, 1365, 1254, 1165, 1106, 810, 747, 703; Anal. Calcd for $C_{24}H_{22}ClN_3O_4S$ (483.97): C, 59.56; H, 4.58; N, 8.68; S, 6.63. Found: C, 59.38; H, 4.63; N, 8.61; S, 6.61.

3.2.7. 3-Benzyl-4-(3,4,5-trimethoxybenzamido)-1-tosyl-2-imidazolidinone (4e). Yield 94%; crystallization from hexane/dichloromethane gave white needles; mp 250 °C; ^{1}H NMR (DMSO-d_6, 300 MHz) δ (ppm): 2.44 (s, 3H), 3.71 (s, 3H), 3.82 (m, 7H), 4.17 (d, 1H, J=15.3 Hz), 4.22 (t, 1H, J=9.3 Hz), 4.38 (d, 1H, J=15.0 Hz), 5.69 (td, 1H, J=8.5 Hz, J=3.3 Hz), 7.09–7.12 (m, 4H), 7.22–7.24 (m, 3H), 7.48 (d, 2H, J=8.0 Hz), 7.90 (d, 2H, J=8.0 Hz), 9.10 (d, 1H, J=8.5 Hz); ^{13}C NMR (DMSO-d_6, 75.4 MHz) δ (ppm): 21.11 (CH_3), 44.33 (CH_2), 48.10 (CH_2), 56.15 (CH_3O), 58.49 (CH), 60.13 (CH_3O), 105.28 (CH), 127.31 (CH), 127.54 (CH), 127.78 (CH), 128.34 (CH), 128.40 (C), 129.74 (CH), 134.90 (C), 136.56 (C), 140.64 (C), 144.76 (C), 152.57 (C), 152.72 (C), 166.24 (CO); MS (EI, 70 eV) m/z (rel intensity, %): 539 [M$^+$] (8), 384 (3), 328 (66), 211 (34), 195 (84), 173 (53), 155 (7), 131 (25), 106 (8), 91 (100), 77 (6), 65 (13); IR (Nujol) ν_{max}/cm^{-1} 3304, 1744, 1637, 1584, 1525, 1501, 1465, 1378, 1331, 1239, 1174, 1130, 1002, 844, 813, 740, 670; Anal. Calcd for $C_{27}H_{29}N_3O_7S$ (539.60): C, 60.10; H, 5.42; N, 7.79; S, 5.94. Found: C, 60.02; H, 5.37; N, 8.85; S, 6.01.

3.3. Preparation of 4-[1-alkyl-3-arylureido]-2-phenyl-2-oxazolines and 4-[1-alkyl-3-arylthioureido]-2-phenyl-2-oxazolines (5)

A solution of the appropriate isocyanate or isothiocyanate (1.8 mmol) in dry ether (9 mL) was added dropwise at room temperature to a stirred solution of the corresponding aminooxazoline **1** (1.2 mmol) in dry ether (9 mL). After 1 h the solid precipitate was filtered off and crystallized from a suitable solvent.

3.3.1. 4-(1-Benzyl-3-phenylureido)-2-phenyl-2-oxazoline (5a). Yield 81%; crystallization from petroleum ether/dichloromethane gave white needles; mp 122–125 °C; ^{1}H NMR ($CDCl_3$, 200 MHz) δ (ppm): 4.30 (dd, 1H, J=10.1 Hz, J=6.3 Hz), 4.40 (d, 1H, J=17.4 Hz), 4.52 (d, 1H, J=17.4 Hz), 4.63 (t, 1H, J=9.8 Hz), 6.61 (br s, 1H), 6.67 (dd, 1H, J=9.3 Hz, J=6.3 Hz), 6.95–7.53 (m, 13H), 7.99 (d, 2H, J=7.5 Hz); ^{13}C NMR ($CDCl_3$, 50.4 MHz) δ (ppm): 46.86 (CH_2), 71.72 (CH_2), 77.96 (CH), 119.84 (CH), 123.30 (CH), 126.94 (C), 127.07 (CH), 128.14 (CH), 128.57 (CH), 128.77 (CH), 128.90 (CH), 129.35 (CH), 132.24 (CH), 137.67 (C), 138.68 (C), 155.71 (CO), 166.87 (C=N); MS (EI, 70 eV) m/z (rel intensity, %): 371 [M$^+$] (1), 250 (5), 146 (15), 131 (19), 119 (19), 105 (25), 91 (100), 77 (28); IR (Nujol) ν_{max}/cm^{-1} 3295, 1632, 1532, 1446, 1377, 1315, 1173, 965, 756, 700; Anal. Calcd for $C_{23}H_{21}N_3O_2$ (371.43): C, 74.37; H, 5.70; N, 11.31. Found: C, 74.28; H, 5.71; N, 11.21.

3.3.2. 4-(1-Benzyl-3-phenylthioureido)-2-phenyl-2-oxazoline (5b). Yield 92%; crystallization from hexane/dichloromethane gave white needles; mp 99–102 °C; ^{1}H NMR ($CDCl_3$, 200 MHz) δ (ppm): 4.38 (dd, 1H, J=10.3 Hz, J=6.3 Hz), 4.62 (d, 1H, J=17.0 Hz), 4.79 (d, 1H, J=17.0 Hz), 4.85 (t, 1H, J=10.0 Hz), 7.13–7.52 (m, 15H), 7.98 (d, 2H, J=7.0 Hz); ^{13}C NMR ($CDCl_3$, 50.4 MHz) δ (ppm): 49.10 (CH_2), 72.98 (CH_2), 82.16 (CH), 125.28 (CH), 126.01 (CH), 126.90 (CH), 128.34 (CH), 128.54 (CH), 128.72 (CH), 128.80 (CH), 129.45 (CH), 132.29 (CH), 136.25 (C), 139.23 (C), 167.40 (C=N), 182.94 (C=S); MS (EI, 70 eV) m/z (rel intensity, %): 387 [M$^+$] (16), 266 (43), 240 (58), 207 (8), 182 (26), 175 (32), 167 (70), 148 (32), 137 (23), 121 (24), 105 (69), 91 (100), 77 (70), 65 (22); IR (Nujol) ν_{max}/cm^{-1} 3313, 1637, 1524, 1463, 1378, 1347, 1321, 1144, 1094, 1051, 967, 697; Anal. Calcd for $C_{23}H_{21}N_3OS$ (387.50): C, 71.29; H, 5.46; N, 10.84; S, 8.28. Found: C, 71.33; H, 5.49; N, 10.95; S, 8.25.

3.3.3. 4-[1-Benzyl-3-(4-methoxyphenyl)thioureido]-2-phenyl-2-oxazoline (5c). Yield 86%; crystallization from hexane/dichloromethane gave white needles; mp 118–120 °C; ^{1}H NMR ($CDCl_3$, 300 MHz) δ (ppm): 3.76 (s, 3H), 4.37 (dd, 1H, J=10.2 Hz, J=6.3 Hz), 4.63 (d, 1H, J=17.1 Hz), 4.77 (d, 1H, J=17.1 Hz), 4.84 (t, 1H, J=9.9 Hz), 6.81 (d, 2H, J=8.7 Hz), 7.03 (d, 2H, J=9.0 Hz), 7.25–7.53 (m, 10H), 7.97 (d, 2H, J=7.2 Hz); ^{13}C NMR ($CDCl_3$, 75.4 MHz) δ (ppm): 48.87 (CH_2), 55.48 (CH_3O), 72.94 (CH_2), 82.28 (CH), 114.01 (CH), 126.80 (CH), 127.09 (C), 127.46 (CH), 128.25 (CH), 128.52 (CH), 128.80 (CH), 129.39 (CH), 132.24 (CH), 136.30 (C), 157.96 (C), 167.32 (C=N), 183.49 (C=S); MS (EI, 70 eV) m/z (rel intensity, %): 417 [M$^+$] (30), 296 (85), 270 (230), 237 (36), 212 (58), 197 (69), 165 (75), 148 (27), 121 (28), 105 (73), 91 (100), 77 (68), 65 (21); IR (Nujol) ν_{max}/cm^{-1} 3314, 1639, 1519, 1467, 1346, 1280, 1093, 1052, 967, 826, 727, 703, 670; Anal. Calcd for $C_{24}H_{23}N_3O_2S$ (417.52): C, 69.04; H, 5.55; N, 10.06; S, 7.68. Found: C, 68.97; H, 5.47; N, 9.98; S, 7.74.

3.3.4. 4-[1-Benzyl-3-(4-chlorophenyl)ureido]-2-phenyl-2-oxazoline (5d). Yield 90%; crystallization from THF/hexane gave white powder; mp 169–172 °C; ^{1}H NMR ($CDCl_3$, 200 MHz) δ (ppm): 4.29 (dd, 1H, J=10.0 Hz, J=6.3 Hz), 4.39 (d, 1H, J=16.7 Hz), 4.51 (d, 1H, J=16.7 Hz), 4.61 (t, 1H, J=10.0 Hz), 6.62 (dd, 1H, J=9.2 Hz, J=6.4 Hz), 6.68 (s, 1H), 6.58–7.53 (m, 12H), 7.98 (d, 2H, J=6.8 Hz); ^{13}C NMR δ ($CDCl_3$, 50.4 MHz) δ (ppm): 46.93 (CH_2), 71.61 (CH_2), 78.07 (CH), 121.03 (CH), 126.87 (C), 127.05 (CH), 128.22 (CH), 128.59 (CH), 128.78 (CH), 128.87 (CH), 129.39 (CH), 132.32 (CH), 137.36 (C), 137.53 (C), 155.58 (CO), 166.97 (C=N); MS (EI, 70 eV) m/z (rel intensity, %): 405 [M$^+$] (6), 284 (53), 258 (11), 251 (16), 161 (8), 153 (46), 146 (37), 131 (53), 118 (39), 105 (48), 91 (100), 77 (38); IR (Nujol) ν_{max}/cm^{-1} 3378, 1676, 1633, 1593, 1526, 1494, 1455, 1374, 1337, 1226, 1106, 1011, 828, 706; Anal. Calcd for $C_{23}H_{20}ClN_3O_2$ (405.88): C, 68.06; H, 4.97; N, 10.35. Found: C, 67.94; H, 4.99; N, 10.42.

3.3.5. 4-[1-Isopropyl-3-(4-nitrophenyl)ureido]-2-phenyl-2-oxazoline (5e). Yield 89%; crystallization from petroleum ether/chloroform gave yellow prisms; mp 160–164 °C; ^{1}H NMR ($CDCl_3$, 300 MHz) δ (ppm): 1.28 (d, 3H, J=6.6 Hz), 1.36 (d, 3H, J=6.6 Hz), 4.29 (t, 1H, J=9.6 Hz), 4.47 (sept., 1H, J=6.6 Hz), 4.64 (t, 1H, J=9.6 Hz), 5.82 (t, 1H, J=9.6 Hz), 7.28 (d, 2H, J=9.3 Hz), 7.51 (t, 2H, J=7.8 Hz), 7.62 (t, 1H, J=7.8 Hz), 7.68 (br s, 1H), 8.03–8.07 (m, 4H); ^{13}C NMR ($CDCl_3$, 75.4 MHz) δ (ppm): 21.09 (CH_3), 21.89 (CH_3), 46.58 (CH), 71.81 (CH_2), 76.57 (CH), 118.14 (CH), 125.11 (CH), 126.24 (C), 128.70 (CH), 128.90 (CH), 132.97 (CH), 142.38 (C), 145.15 (C), 154.73 (CO), 167.51 (C=N); MS (EI, 70 eV) m/z (rel

intensity, %): 368 [M$^+$] (5), 247 (25), 217 (14), 203 (51), 189 (18), 175 (11), 164 (45), 146 (100), 134 (51), 118 (43), 105 (94), 90 (60), 83 (53), 77 (57); IR (Nujol) ν_{max}/cm^{-1} 3235, 3281, 3131, 1680, 1635, 1598, 1545, 1505, 1463, 1371, 1307, 1113, 1079, 1028, 848, 704; Anal. Calcd for $C_{19}H_{20}N_4O_4$ (368.39): C, 61.95; H, 5.47; N, 15.21. Found: C, 62.02; H, 5.56; N, 15.15.

Crystallographic data for **5e**: $C_{19}H_{20}N_4O_4$, monoclinic, space group $P2_1/n$, a=12.3880(12), b=11.5752(12) Å, c=13.6715(12) Å, β=110.444(4)°, V=1836.9(3) Å^3, Z=4. A colourless prism 0.42×0.22×0.20 mm was used to measure 3736 reflections at T=173 K, of which 3234 were unique (R_{int}=0.013). Refinement proceeded to wR_2=0.0803 (all data), R_1=0.0344 and GOF=0.901 [$I>2\sigma(I)$]. Maximum residual electron density was 0.12 eÅ^{-3}.

3.4. One-pot synthesis of (*Z*)-3-alkyl-4-benzamido-2-arylimino-1,3-oxazolidine and (*Z*)-3-alkyl-4-benzamido-2-arylimino-1,3-thiazolidine hydrochlorides (7)

To a well-stirred solution of aminooxazoline **1** (1 mmol) in dry ether (10 mL) a solution of the corresponding isocyanate or isothiocyanate (1 mmol) in dry ether (10 mL) was added dropwise, and the reaction mixture was stirred at room temperature for 1 h. Then, hydrochloric acid (0.15 mL; 35%) was added and the solid product was filtered off and crystallized from the appropriate solvent.

3.4.1. (*Z*)-3-Benzyl-4-benzamido-2-phenylimino-1,3-oxazolidine hydrochloride (7a). Yield 92%; crystallization from ethanol gave colourless prisms; mp 164–165 °C; ^{1}H NMR (DMSO-d_6, 200 MHz) δ (ppm): 4.63 (d, 1H, J=16.1 Hz), 4.84 (dd, 1H, J=9.6 Hz, J=3.6 Hz), 5.10 (t, 1H, J=9.3 Hz), 5.52 (d, 1H, J=16.0 Hz), 6.00 (td, 1H, J=9.4 Hz, J=3.3 Hz), 7.23–7.60 (m, 13H), 7.90 (d, 2H, J=7.0 Hz), 9.82 (d, 1H, J=8.1 Hz); ^{13}C NMR (DMSO-d_6, 50.4 MHz) δ (ppm): 45.46 (CH_2), 64.87 (CH), 74.02 (CH_2), 119.58 (CH), 124.07 (CH), 126.51 (C), 126.95 (CH), 127.68 (CH), 128.10 (CH), 128.47 (CH), 128.68 (CH), 129.23 (CH), 132.26 (CH), 132.87 (C), 134.07 (C), 158.71 (C=N), 166.90 (CO); MS (EI, 70 eV) *m*/*z* (rel intensity, %): 371 [M$^+$−36] (1), 250 (1), 226 (2), 181 (2), 145 (77), 117 (63), 105 (43), 90 (100), 77 (61); IR (Nujol) ν_{max}/cm^{-1} 3212, 3185, 1682, 1665, 1596, 1531, 1462, 1378, 1278, 1153, 1070, 997, 944, 839, 767; Anal. Calcd for $C_{23}H_{22}ClN_3O_2$ (407.89): C, 67.73; H, 5.44; N, 10.30. Found: C, 67.46; H, 5.31; N, 10.24.

Crystallographic data for **7a**: $C_{23}H_{22}ClN_3O_2$, triclinic, space group $P(-1)$, a=9.7195(8), b=9.9757(8), c=11.2373(10) Å, α=90.287(3), β=112.816(3), γ=98.369(3)°, V=991.35 Å^3, Z=2. A colourless prism 0.35×0.18×0.15 mm was used to measure 15 487 reflections at T=143 K, of which 5751 were unique (R_{int}=0.047). Refinement proceeded to wR_2=0.0992 (all data), R_1=0.0373 and GOF=1.05 [$I>2\sigma(I)$]. Maximum residual electron density was 0.39 eÅ^{-3}.

3.4.2. (*Z*)-3-Benzyl-4-benzamido-2-phenylimino-1,3-thiazolidine hydrochloride (7b). Yield 88%; crystallization from acetonitrile gave colourless prisms; mp 172–174 °C; ^{1}H NMR (DMSO-d_6, 200 MHz) δ (ppm): 3.46 (dd, 1H, J=11.9 Hz, J=2.8 Hz), 3.91 (dd, 1H, J=11.9 Hz, J=7.8 Hz), 4.71 (d, 1H, J=15.9 Hz), 5.49 (d, 1H, J=15.9 Hz), 6.17 (td, 1H, J=8.0 Hz, J=2.8 Hz), 7.33–7.63 (m, 14H), 7.91 (d, 2H, J=7.1 Hz), 9.75 (d, 1H, J=8.0 Hz); ^{13}C NMR (DMSO-d_6 50.4 MHz) δ (ppm): 33.85 (CH_2), 48.81 (CH_2), 70.35 (CH), 125.33 (CH), 127.86 (CH), 127.99 (CH), 128.37 (CH), 128.78 (CH), 129.64 (CH), 132.10 (CH), 133.09 (C), 134.64 (C), 166.74 (CO); MS (EI, 70 eV) *m*/*z* (rel intensity, %): 387 [M$^+$−36] (11), 266 (44), 240 (45), 182 (20), 167 (76), 148 (24), 121 (27), 105 (63), 91 (100), 77 (68), 65 (22); IR (Nujol) ν_{max}/cm^{-1} 3146, 2692, 1650, 1626, 1587, 1519, 1487, 1463, 1378, 1181, 766, 700; Anal. Calcd for $C_{23}H_{22}ClN_3OS$ (423.96): C, 65.16; H, 5.23; N, 9.91; S, 7.56. Found: C, 65.23; H, 5.19; N, 9.87; S, 7.60.

Crystallographic data for **7b**: $C_{23}H_{22}ClN_3OS$, orthorhombic, space group *Pbca*, a=16.8839(16), b=10.7096(10), c=23.290(2) Å, V=4211.2 Å^3, Z=8. A colourless prism 0.38×0.21×0.21 mm was used to measure 33 360 reflections at T=143 K, of which 6161 were unique (R_{int}=0.058). The phenyl group at N2 is disordered over two positions. Refinement proceeded to wR_2=0.0928 (all data), R_1=0.0357 and GOF=1.03 [$I>2\sigma(I)$]. Maximum residual electron density was 0.32 eÅ^{-3}.

3.4.3. (*Z*)-3-Benzyl-4-benzamido-2-(4-methoxyphenyl)-imino-1,3-thiazolidine hydrochloride (7c). Yield 90%; crystallization from ethanol gave white powder; mp 173–182 °C dec; ^{1}H NMR (DMSO-d_6, 200 MHz) δ (ppm): 3.48 (dd, 1H, J=8.0 Hz, J=2.7 Hz), 3.80 (s, 3H), 3.92 (dd, 1H, J=7.9 Hz, J=7.8 Hz), 4.68 (d, 1H, J=16.0 Hz), 5.50 (d, 1H, J=16.0 Hz), 6.19 (td, 1H, J=8.0 Hz, J=2.7 Hz), 7.05 (d, 2H, J=8.7 Hz), 7.36–7.59 (m, 11H), 7.92 (d, 2H, J=7.9 Hz), 9.82 (d, 1H, J=8.0 Hz); ^{13}C NMR (DMSO-d_6, 50.4 MHz) δ (ppm): 33.88 (CH_2), 48.88 (CH_2), 55.56 (CH_3O), 70.84 (CH), 114.76 (CH), 127.20 (CH), 127.87 (CH), 127.99 (CH), 128.04 (CH), 128.35 (CH), 128.78 (CH), 131.43 (C), 132.10 (CH), 133.03 (C), 134.32 (C), 159.10 (C), 166.72 (CO); FAB$^+$, 418 (100); IR (Nujol) ν_{max}/cm^{-1} 3198, 2732, 2650, 1626, 1519, 1459, 1376, 1247, 1177, 1032, 828, 710; Anal. Calcd for $C_{24}H_{24}ClN_3O_2S$ (453.99): C, 63.49; H, 5.33; N, 9.26; S, 7.06. Found: C, 63.73; H, 5.47; N, 9.16; S, 7.03.

3.4.4. (*Z*)-3-Benzyl-4-benzamido-2-(4-chlorophenyl)-imino-1,3-oxazolidine hydrochloride (7d). Yield 94%; crystallization from methanol gave white powder; mp 167 °C; ^{1}H NMR (DMSO-d_6, 200 MHz) δ (ppm): 4.60 (d, 1H, J=16.1 Hz), 4.81 (dd, 1H, J=8.0 Hz, J=3.4 Hz), 5.07 (t, 1H, J=8.1 Hz), 5.44 (d, 1H, J=16.1 Hz), 5.98 (td, 1H, J=8.2 Hz, J=3.3 Hz), 7.12–7.65 (m, 12 H), 7.87 (d, 2H, J=6.9 Hz), 9.70 (d, 1H, J=8.1 Hz); ^{13}C NMR δ (DMSO-d_6, 50.4 MHz) δ (ppm): 45.53 (CH_2), 64.64 (CH), 73.68 (CH_2), 121.13 (CH), 125.59 (CH), 127.61 (CH), 128.03 (CH), 128.48 (CH), 128.67 (CH), 129.17 (CH), 132.23 (CH), 132.97 (C), 134.35 (C), 139.13 (C), 139.26 (C), 154.88 (C=N), 166.95 (CO); FAB$^+$, 406 (100); IR (Nujol) ν_{max}/cm^{-1} 3166, 2670, 1684, 1660, 1531, 1490, 1464, 1377, 1284, 1152, 1095, 1004, 959, 837, 809, 705; Anal. Calcd for $C_{23}H_{21}Cl_2N_3O_2$ (442.34): C, 62.45; H, 4.79; N, 9.50. Found: C, 62.13; H, 4.88; N, 9.43.

3.4.5. (*Z*)-4-Benzamido-3-isopropyl-2-(4-nitrophenyl)-imino-1,3-oxazolidine hydrochloride (7e). Yield 97%;

crystallization from ethanol/pentane gave white needles; mp 119–121 °C; ^{1}H NMR (DMSO-d_6, 200 MHz) δ (ppm): 1.23 (d, 3H, J=6.2 Hz), 1.43 (d, 3H, J=6.2 Hz), 4.36–4.39 (m, 1H), 4.97–5.07 (m, 2H), 6.17–6.19 (m, 1H), 7.62–7.82 (m, 5H), 8.11 (d, 2H, J=9.1 Hz), 8.28 (d, 2H, J=7.4 Hz), 9.69 (s, 1H); ^{13}C NMR δ (DMSO-d_6, 50.4 MHz) δ (ppm): 21.57 (CH_3), 47.98 (CH), 69.49 (CH), 74.14 (CH_2), 119.35 (CH), 124.52 (CH), 129.47 (CH), 129.92 (CH), 135.71 (CH), 141.34 (C), 146.77 (C), 153.78 (C=N), 170.02 (CO); MS (EI, 70 eV) *m*/*z* (rel intensity, %): 247 (2), 223 (4), 203 (5), 164 (18), 145 (80), 138 (69), 117 (76), 108 (62), 90 (100), 77 (26); IR (Nujol) ν_{max}/cm^{-1} 3258, 2576, 1677, 1613, 1502, 1464, 1376, 1312, 1244, 1077, 855, 703; Anal. Calcd for $C_{19}H_{21}ClN_4O_4$ (404.85): C, 56.37; H, 5.23; N, 13.84. Found: C, 56.14; H, 5.57; N, 13.86.

3.4.6. (*Z*)-3-Benzyl-2-benzylimino-4-benzamido-1,3-oxazolidine hydrochloride (7f). Yield 90%; crystallization from ethanol/hexane gave colourless prisms; mp 164 °C; ^{1}H NMR (DMSO-d_6, 200 MHz) δ (ppm): 4.53 (d, 1H, J=11.5 Hz), 4.58 (s, 2H), 4.83 (dd, 1H, J=9.3 Hz, J=3.7 Hz), 5.06 (t, 1H, J=8.8 Hz), 5.14 (d, 1H, J=11.5 Hz), 5.97 (td, 1H, J=8.0 Hz, J=3.6 Hz), 7.28–7.63 (m, 13H), 7.88 (d, 2H, J=7.1 Hz), 9.82 (d, 1H, J=7.9 Hz), 11.34 (t, 1H, J=5.9 Hz); ^{13}C NMR (DMSO-d_6, 50.4 MHz) δ (ppm): 45.06 (CH_2), 45.43 (CH_2), 65.10 (CH), 73.66 (CH_2), 127.71 (CH), 127.72 (CH), 127.83 (CH), 128.07 (CH), 128.16 (CH), 128.26 (CH), 128.45 (CH), 128.65 (CH), 132.24 (CH), 132.91 (C), 134.18 (C), 136.71 (C), 159.79 (C=N), 167.01 (CO); MS (EI, 70 eV) *m*/*z* (rel intensity, %): 264 (17), 240 (75), 145 (43), 117 (22), 106 (100), 91 (90), 77 (47); IR (Nujol) ν_{max}/cm^{-1} 3168, 1689, 1658, 1536, 1466, 1378, 1276, 1125, 1020, 952, 714; Anal. Calcd for $C_{24}H_{24}ClN_3O_2$ (421.92): C, 68.32; H, 5.73; N, 9.96. Found: C, 67.03; H, 5.88; N, 9.84.

3.4.7. (*Z*)-3-Benzyl-4-benzamido-2-isopropylimino-1,3-oxazolidine hydrochloride (7g). Yield 89%; crystallization from THF gave colourless prisms; mp 171 °C; ^{1}H NMR (DMSO-d_6, 200 MHz) δ (ppm): 1.30 (t, 6H, J=6.7 Hz), 3.99 (sept., 1H, J=6.6 Hz), 4.46 (d, 1H, J=16.3 Hz), 4.79 (dd, 1H, J=8.0 Hz, J=3.6 Hz), 5.04 (t, 1H, J=8.8 Hz), 5.09 (d, 1H, J=16.3 Hz), 5.89 (td, 1H, J=8.0 Hz, J=3.5 Hz), 7.29–7.58 (m, 8H), 7.83 (d, 2H, J=7.0 Hz), 9.62 (d, 1H, J=7.9 Hz), 10.10 (d, 1H, J=7.4 Hz); ^{13}C NMR δ (DMSO-d_6, 50.4 MHz) δ (ppm): 19.31 (CH_3), 19.62 (CH_3), 42.16 (CH_2), 43.75 (CH), 62.15 (CH), 70.82 (CH_2), 124.89 (CH), 125.11 (CH), 125.29 (CH), 125.73 (CH), 125.98 (CH), 129.50 (CH), 130.23 (C), 131.55 (C), 156.26 (C=N), 164.26 (CO); MS (EI, 70 eV) *m*/*z* (rel intensity, %): 337 (6), 322 (12), 252 (61), 216 (16), 201 (24), 191 (51), 146 (55), 131 (29), 106 (85), 91 (100), 77 (45); IR (Nujol) ν_{max}/cm^{-1} 3130, 1695, 1657, 1531, 1460, 1379, 1287, 1157, 1101, 1081, 716; Anal. Calcd for $C_{20}H_{24}ClN_3O_2$ (373.88): C, 64.25; H, 6.47; N, 11.24. Found: C, 63.79; H, 6.51; N, 11.05.

3.4.8. (*Z*)-2-Benzylimino-4-benzamido-3-isopropyl-1,3-oxazolidine hydrochloride (7h). Yield 95%; crystallization from THF/pentane gave white needles; mp 171 °C; ^{1}H NMR (DMSO-d_6, 200 MHz) δ (ppm): 1.15 (d, 3H, J=6.6 Hz), 1.39 (d, 3H, J=6.6 Hz), 4.22 (sept., 1H, J=6.6 Hz), 4.54 (s, 2H), 4.65 (dd, 1H, J=8.5 Hz, J=3.0 Hz), 4.89 (t, 1H, J=8.5 Hz), 6.06 (td, 1H, J=8.0 Hz, J=3.1 Hz), 7.30–7.65 (m, 8H), 7.91 (d, 2H, J=6.8 Hz), 9.76 (d, 1H, J=7.8 Hz), 10.71 (s, 1H); ^{13}C NMR (DMSO-d_6, 50.4 MHz) δ (ppm): 18.83 (CH_3), 20.90 (CH_3), 45.71 (CH_2), 46.51 (CH), 63.04 (CH), 73.80 (CH_2), 127.51 (CH), 127.59 (CH), 127.71 (CH), 128.66 (CH), 132.27 (CH), 133.27 (C), 137.09 (C), 158.09 (C=N), 166.48 (CO); MS (EI, 70 eV) *m*/*z* (rel intensity, %): 337 (1), 252 (7), 216 (39), 192 (45), 191 (43), 174 (19), 146 (37), 145 (38), 121 (19), 105 (79), 91 (100), 77 (61); IR (Nujol) ν_{max}/cm^{-1} 3175, 1683, 1539, 1456, 1364, 1298, 1281, 1215, 1081, 1038, 710; Anal. Calcd for $C_{20}H_{24}ClN_3O_2$ (373.88): C, 64.25; H, 6.47; N, 11.24. Found: C, 64.13; H, 6.49; N, 11.06.

3.4.9. (*Z*)-3-Benzyl-4-benzamido-2-propylimino-1,3-oxazolidine hydrochloride (7i). Yield 92%; crystallization from ethanol/pentane gave colourless prisms; mp 170 °C; ^{1}H NMR (DMSO-d_6, 300 MHz) δ (ppm): 0.93 (t, 3H, J=7.5 Hz), 1.58–1.70 (m, 2H), 3.32 (m, 2H), 4.48 (d, 1H, J=16.2 Hz), 4.80 (dd, 1H, J=8.7 Hz, J=3.9 Hz), 5.05 (t, 1H, J=8.7 Hz), 5.13 (d, 1H, J=16.2 Hz), 5.91 (td, 1H, J=8.1 Hz, J=3.3 Hz), 7.30–7.61 (m, 8H), 7.86 (d, 2H, J=8.1 Hz), 9.70 (d, 1H, J=8.0 Hz), 10.59 (s, 1H); ^{13}C NMR (DMSO-d_6, 75.4 MHz) δ (ppm): 11.00 (CH_3), 22.08 (CH_2), 44.01 (CH_2), 44.87 (CH_2), 64.90 (CH), 73.42 (CH_2), 127.58 (CH), 127.95 (CH), 128.37 (CH), 128.59 (CH), 132.13 (CH), 132.89 (C), 134.19 (C), 159.62 (C=N), 166.94 (CO); MS (EI, 70 eV) *m*/*z* (rel intensity, %): 337 (3), 252 (64), 192 (36), 146 (49), 106 (53), 90 (100), 77 (68); IR (Nujol) ν_{max}/cm^{-1} 3217, 3185, 1695, 1666, 1537, 1465, 1275, 1113, 996, 807, 712; Anal. Calcd for $C_{20}H_{24}ClN_3O_2$ (373.88): C, 64.25; H, 6.47; N, 11.24. Found: C, 63.86; H, 7.12; N, 11.37.

Crystallographic data (excluding structure factors) for the structures in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication numbers CCDC-299402 (**4b**), CCDC-298631 (**5e**), CCDC-243016 (**7a**) and CCDC-243018 (**7b**). Copies of the data can be obtained, free of charge, on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK [fax: +44 1223 336033 or e-mail: deposit@ccdc.cam.ac.uk].

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