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Electrochemical generation of 4-amino-2-aryl-2-oxazolines

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Abstract—A convenient method for the synthesis of the title compounds has been established. Chloralbenzamides were efficiently converted to *N*-(1-amino-2,2-dichloroethyl)benzamides which were directly transformed to 4-amino-2-aryl-2-oxazolines in fair to good yields by electrochemical reduction in an aprotic medium under constant cathodic potential. The molecular structure of the electrolysis products has been corroborated by X-ray crystallographic analysis of 4-(1-benzyl-3-phenylureido)-2-phenyl-2-oxazoline.

1. Introduction

2-Oxazolines exhibit a wide range of properties and as such are considered to be a highly important class of compounds.[1] They are versatile synthetic intermediates.[1e–g] This in conjunction with their therapeutic potential[1c,2] and many other significant applications,[1c] has for many years led to intensive research activity on the chemistry of these heterocycles. Regarding the most general methodology to synthesize 2-oxazolines, simple members of the family can be directly prepared by high temperature dehydration of carboxylic acids with β-amino alcohols.[1g,3] Owing to the drastic experimental conditions required, this procedure has found a limited scope; however, it can be substantially improved by a number of modified reactions that can be promoted at room temperature.[1g] β-Amino alcohols react also with imidic esters,[4] ethyl thioacetate,[5] dimethylformamide derivatives,[6] and further reagents,[1] to yield 2-oxazolines. Treatment of hydroxyamides with thionyl chloride followed by cyclization in a strong basic medium is also a general preparative method,[7,8] but the results are frequently limited by the indiscriminate action of both thionyl chloride and the strong base. This method has been substantially improved by using specific reagents.[9] Certain intermediates such as eneamines, epoxides, aziridines, ylides and isocyanides have been found useful for particular preparations.[1g] There is a noteworthy renewed interest in the progress of the synthesis of 2-oxazolines.[10] However, the electrogeneration of 2-oxazolines has been scarcely investigated; solely the formation of some of these compounds by anodic oxidation of dienes or by reductive ring opening of *N*-acylaziridines has been previously reported.[11]

Chloral is an inexpensive multipurpose starting material for organic synthesis.[12] Direct reactions of chloral hydrate with carboxylic amides provide the corresponding choralamides **1** in almost quantitative yields.[13] As shown in Scheme 1, in this reaction we recognised the starting point of new synthetic routes for the synthesis of heterocyclic compounds of significant interest. Compounds **1** can be efficiently transformed to *N*-(1-amino-2,2-dichloroethyl)benzamides **4** according to well established procedures[14] that involve either intermediates **3** or **5**. As a result of our research project in electrochemical synthesis of heterocyclic compounds, we reported in a preliminary communication[15] the first synthesis of 4-amino-2-aryl-2-oxazolines **7**, which gave access to novel 2-imidazolidinones.[16] Intermediates **4** could efficiently be converted to the corresponding aminooxazolines **7** by electrochemical reduction in an aprotic medium at constant cathodic potential.[15] In this paper we describe full details of the previous communication, as well as new results obtained by exploring the scope of the reported electrochemical conversion. Spectral data of the new aminooxazoline compounds and a confirmatory X-ray crystallographic analysis of a ureido derivative are also reported.

2. Results and discussion

Intermediates **4** were prepared by direct addition reactions of alkylamines to *N*-(2,2-dichlorovinyl)amides[14] **3**. Amination

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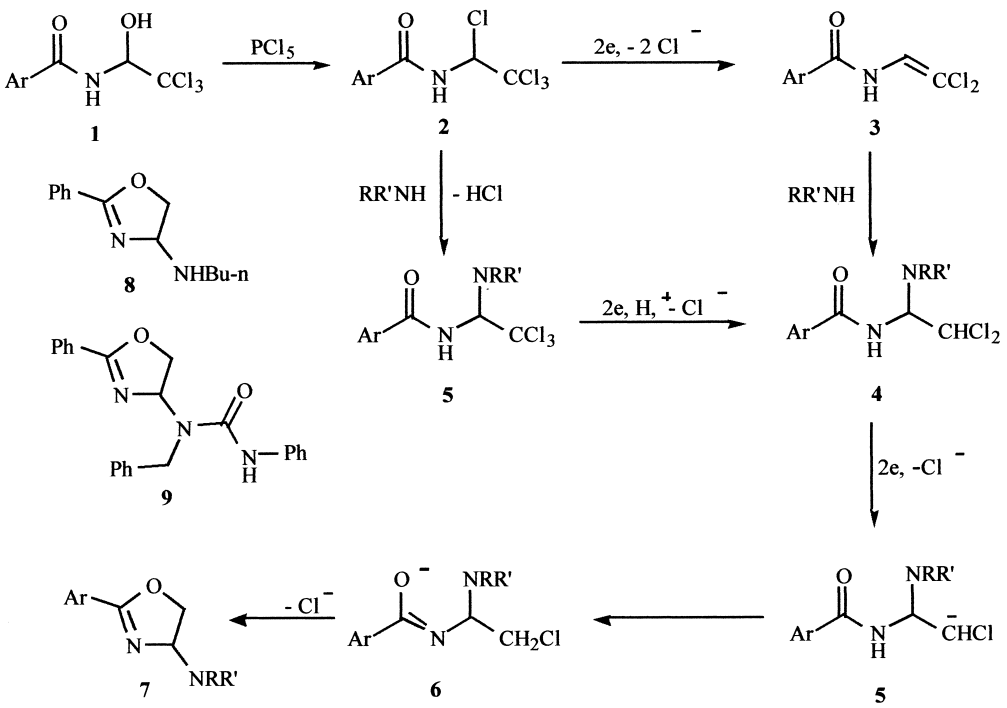

Entry	Ar	RR'N
a	C_6H_5	$C_6H_5CH_2NH$
b	C_6H_5	CH_3NH
c	C_6H_5	$CH_3CH_2CH_2NH$
d	C_6H_5	$(CH_3)_2CHNH$
e	C_6H_5	$(CH_3CH_2)_2N$
f	C_6H_5	Cy-$C_6H_{11}NH$
g	2-ClC_6H_4	$C_6H_5CH_2NH$
h	3-ClC_6H_4	$C_6H_5CH_2NH$
i	4-ClC_6H_4	$CH_3(CH_2)_2CH_2NH$
j	4-$O_2NC_6H_4$	$C_6H_5CH_2NH$
k	3-BrC_6H_4	$C_6H_5CH_2NH$
l	4-BrC_6H_4	$C_6H_5CH_2NH$
m	3,4,5-$(CH_3O)_3C_6H_2$	$C_6H_5CH_2NH$
n	2-$CH_3C_6H_4$	$(CH_3)_2N$
o	4-$CH_3C_6H_4$	$(CH_3)_2CHCH_2CH_2NH$
p	C_6H_5	C_6H_5NH
q	C_6H_5	4-$CH_3OC_6H_4NH$
r	C_6H_5	H_2N

Scheme 1.

of intermediates **3** with amines of lower nucleophilicity than alkylamines, such as arylamines and ammonia, could be accomplished following an alternative preparative procedure involving intermediates **5**, which were efficiently transformed to products **4** by electrochemical reduction in a protic medium.[14] In general, the cathodic reductions of compounds **4** were carried out in an aprotic medium (acetonitrile–tetrabutylammonium perchlorate) at a relatively high negative potential (range −1.90 to −2.20 V vs. SCE). These processes afforded coulometric measurements corresponding to an electricity consumption of 2 F/mol. The electrolysis products were easily isolated in high purity by removing the solvent in vacuo and by shaking the residue with ether. The solvent was then removed and the isolated products were purified by column chromatography, providing viscous oils that were subjected to IR, EI MS, FAB MS, NMR spectroscopy and microanalyses which afforded analytical data which were fully in agreement with those expected for 4-amino-2-aryl-2-oxazolines **7**. GC/MS analyses with capillary column showed a single peak for each compound **7**. Yields ranged from fair to high.

Given the oily nature of products **7**, a crystalline ureido derivative was prepared in order to corroborate the results of

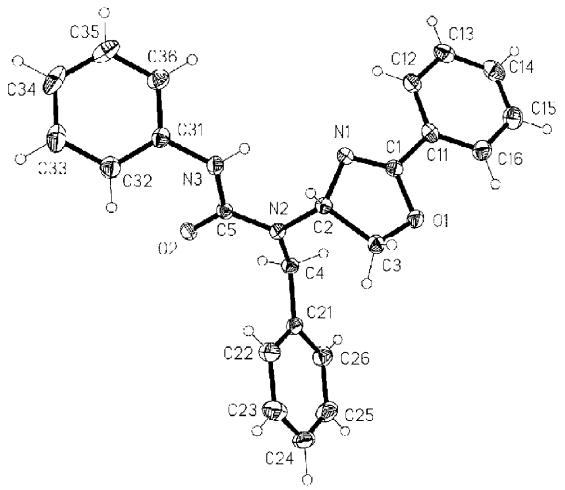

Figure 1. Molecular structure of **9**, showing the crystallographic numbering system used. Ellipsoids represent 50% probability levels.

the spectroscopic structural assignments. Thus, 4-(1-benzyl-3-phenylureido)-2-phenyl-2-oxazoline **9** was prepared by reaction of **7a** with phenylisocyanate, and single crystals were analysed by X-ray crystallography. The molecular structure is illustrated in Fig. 1. Selected intramolecular distances (crystallographic numbering and selected bond angles are given in Table 1.

The electrochemical reductions of dichlorides **4** led to the corresponding oxazolines **7**. The scope of the reaction is somewhat limited due to the high reduction potential of the dihalides **4**. Thus, an anomalous reaction was found in the electrolysis of **4j** which gave a complex mixture of products that could not be identified. Since nitro compounds easily undergo electrochemical reduction, the failure of this electrolysis can be reasonably attributed to ill-defined processes promoted by initial electron transfer to the nitro group. On the other hand, the reductions of compounds **4g** and **4i** gave the corresponding dechlorinated oxazolines **7a** and **8**, respectively. Given the formation of the non-dechlorinated oxazoline **7h** in the reduction of **4h** which has the chlorine atom at *m*-position, it seems likely that the conjugative electron-withdrawing effect of the oxazoline system would be the main factor favouring dechlorination of those chlorine atoms supported by the most activated carbon atoms. The reductions of compounds **4k** and **4l** also gave the same dehalogenated oxazoline **7a**.

The formation of oxazolines **7** can be reasonably explained on the basis of a two-electron cleavage of one of the carbon–chlorine bonds of **4** with generation of the chlorocarbanionic intermediates **5**, which would generate the amide anions **6**. Therefore, the heterocyclization would be promoted by nucleophilic displacement of the remaining chlorine atom on **6**. Electroreduction of *gem*-polyhalogenated derivatives with generation of carbanionic intermediates has been studied from various points of view.[17] In this work an especially useful reaction has been found, namely the generation of an anionic centre starting from molecules with a particular arrangement in which the negative charge can be transferred to a heteroatom. The presence of two suitably placed centres of opposite activity in the newly formed transient intermediate makes the heterocyclization process feasible.

Table 1. Selected bond lengths and bond angles in crystal structure of **9**

Bond lengths (Å)			
C(1)–N(1)	1.276(2)	C(2)–N(1)	1.4833(19)
C(1)–O(1)	1.3663(19)	C(2)–C(3)	1.541(2)
C(1)–C(11)	1.472(2)	C(3)–O(1)	1.4493(17)
C(2)–N(2)	1.453(2)		
Bond angles (°)			
N(1)–C(1)–O(1)	118.57(13)	N(1)–C(2)–C(3)	103.85(12)
N(1)–C(1)–C(11)	126.32(14)	O(1)–C(3)–C(2)	104.06(12)
O(1)–C(1)–C(11)	115.11(13)	C(1)–N(1)–C(2)	106.35(12)
N(2)–C(2)–N(1)	112.00(13)	C(2)–N(2)–C(4)	118.59(12)
N(2)–C(2)–C(3)	115.08(13)	C(1)–O(1)–C(3)	105.15(11)

In conclusion, a simple and effective procedure for the synthesis of previously unattainable 4-amino-2-aryl-2-oxazolines is reported. The availability of starting materials, the mildness of the reaction conditions and the reaction efficiency are notable advantages of the method. In contrast to other procedures involving halogenoamides, many synthetic problems associated with the lack of selectivity of halogenating reagents can be avoided since chlorination is unnecessary. Moreover, the cyclization of halogenoamides commonly requires strongly basic media. However, the oxazoline precursor used contains a probase[18] centre which is activated upon electron transfer, and internally neutralized. Therefore, the reaction medium remains close to neutrality.

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 ionising 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 analyser. Melting points were determined on a Kofler hot-plate melting point apparatus and are uncorrected. Electrochemical experiments were performed with an Amel 557 potentiostat coupled to an Amel 558 integrator. *N*-(1-amino-2,2-dichloroethyl)benzamides **4** were prepared as previously described.[14]

3.2. Preparation of 4-amino-2-aryl-2-oxazolines (7, 8)

Preparative electrolyses were carried out under a constant cathodic potential in a concentric cylindrical cell with two compartments separated by a circular glass frit (medium) diaphragm. A mercury pool (diameter 5 cm; Luggin-capillary situated to the side of the pool) was used as the cathode and a platinum plate as the anode. The catholyte was magnetically stirred. The temperature was kept at approximately 18°C by external cooling. The reductions were performed in anhydrous MeCN–Bu_4NClO_4, 0.4 M of which 35 and 15 mL, approximately, were placed respectively

in the cathodic and the anodic compartments. Anhydrous sodium carbonate (3 g) was placed in the anode compartment to prevent accumulation of electrogenerated acid. Solutions of compounds **4** (5 mmol) were electrolysed under the following cathodic potentials: −2.10 V vs SCE (entries m, o); −2.05 V vs SCE (entries a–f); −2.00 V vs SCE (entries n, r); −1.90 V (entries g–i, k, l, p, q). The average current intensity was 200 mA at the beginning, and 15 mA at the end. The cell voltage values remained below 8 V in all cases. All electrolysis products were isolated by removing the solvent in vacuo. The residue was then shaken with ether (3×50 mL) over a period of 30 min. The ethereal solutions were combined and concentrated leaving oily crude products in high purity state,[19] which were purified by column chromatography on silica gel (ethyl acetate or ethyl acetate–hexane 1:1). The isolated products were viscous yellow oils that gave satisfactory elemental and spectroscopic analyses.

3.2.1. 4-Benzylamino-2-phenyl-2-oxazoline (7a). (72%), pale yellow oil. (Found: C 75.98; H 6.44; N 11.14; $C_{16}H_{16}N_2O$ requires C 76.16; H 6.39; N 11.10); ^{1}H NMR δ ($CDCl_3$, 300 MHz): 2.79 (br s, 1H), 3.91 (d, 1H, J=13.2 Hz), 4.03–4.08 (m, 2H), 4.45 (t, 1H, J=9.0 Hz), 5.22 (dd, 1H, J=8.7, 6.6 Hz), 7.22–7.47 (m, 8H), 7.98 (dd, 2H, J=8.4, 1.5 Hz); ^{13}C NMR δ ($CDCl_3$, 75.4 MHz): 49.19 (CH_2), 71.93 (CH_2), 80.85 (CH), 126.89 (CH), 127.60 (CH), 128.14 (CH), 128.24 (CH), 128.28 (CH), 128.31 (CH), 131.47 (C), 139.90 (C), 164.56 (C=N); MS, *m/z* (%): 251 (M^+−H, 28), 131 (72), 118 (44), 104 (63), 91 (100), 77 (31); FAB$^+$: 253 (M+1, 100); IR (film): 3268, 1643, 1452, 1372, 1249, 1139, 1088, 1025, 956, 744, 694 cm^{-1}.

3.2.2. 2-Phenyl-4-methylamino-2-oxazoline (7b). (92%), pale yellow oil. (Found: C 68.38; H 6.91; N 15.96; $C_{10}H_{12}N_2O$ requires: C 68.16; H 6.86; N 15.90); ^{1}H NMR δ (DMSO-d_6, 300 MHz): 2.36 (br s, 4H), 3.96 (dd, 1H, J=9.0, 7.2 Hz), 4.43 (t, 1H, J=9.3 Hz), 5.03 (dd, 1H, J=9.3, 7.2 Hz), 7.43–7.57 (m, 3H), 7.92 (dd, 2H, J=8.8, 1.8 Hz); ^{13}C NMR δ (DMSO-d_6, 75.4 MHz): 31.04 (CH_3), 70.96 (CH_2), 82.25 (CH), 127.80 (CH), 127.88 (CH), 128.52 (CH), 131.45 (C), 162.45 (C=N); MS, *m/z* (%): 176 (M^+, 66), 175 (100), 146 (78), 105 (72), 104 (88), 91 (57), 77 (86); IR (film): 3287, 2949, 1647, 1578, 1451, 1355, 1310, 1246, 1140, 1085, 1067, 1027, 960, 698 cm^{-1}.

3.2.3. 2-Phenyl-4-propylamino-2-oxazoline (7c). (65%), pale yellow oil. (Found: C 70.71; H 7.87; N 13.68; $C_{12}H_{16}N_2O$ requires: C 70.56; H 7.90; N 13.71); ^{1}H NMR δ ($CDCl_3$, 200 MHz): 0.93 (t, 3H, J=7.4 Hz), 1.43–1.58 (m, 3H), 2.58–2.71 (m, 1H), 2.79–2.92 (m, 1H), 4.04 (dd, 1H, J=9.2, 6.6 Hz), 4.47 (t, 1H, J=9.2 Hz), 5.18 (dd, 1H, J=8.9, 6.6 Hz), 7.29–7.48 (m, 3H), 7.97 (dd, 2H, J=7.0, 1.5 Hz); ^{13}C NMR δ ($CDCl_3$, 50.4 MHz): 11.80 (CH_3), 23.57 (CH_2), 46.89 (CH_2), 71.96 (CH_2), 81.34 (CH), 127.72 (CH), 128.32 (CH), 128.46 (CH), 131.49 (C), 164.36 (C=N); MS, *m/z* (%): 204 (M^+, 50), 203 (75), 146 (100), 118 (53), 105 (89), 91 (92), 77 (88); IR (film): 3289, 2961, 1649, 1579, 1450, 1355, 1242, 1136, 1086, 1025, 965, 698 cm^{-1}.

3.2.4. 4-Isopropylamino-2-phenyl-2-oxazoline (7d). (68%), pale yellow oil. (Found: C 70.48; H 7.95; N 13.67; $C_{12}H_{16}N_2O$ requires: C 70.56; H 7.90; N 13.71); ^{1}H NMR δ ($CDCl_3$, 200 MHz): 1.12 (d, 6H, J=6.3 Hz), 1.86 (br s, 1H), 3.36 (sept, 1H, J=6.3 Hz), 3.97 (dd, 1H, J=9.3, 6.9 Hz), 4.52 (t, 1H, J=9.1 Hz), 5.22 (t, 1H, J=8.7 Hz), 7.36–7.52 (m, 3H), 7.96 (dd, 2H, J=8.8, 1.7 Hz); ^{13}C NMR δ ($CDCl_3$, 75.4 MHz): 22.43 (CH_3), 24.39 (CH_3), 45.45 (CH), 73.17 (CH_2), 79.33 (CH), 127.90 (CH), 128.30 (CH), 128.35 (CH), 131.46 (C), 164.26 (C=N); FAB$^+$: 205 (M^++1, 100); IR (film): 3295, 1648, 1578, 1448, 1350, 1174, 1086, 1026, 987, 948, 698 cm^{-1}.

3.2.5. 4-Dietilamino-2-phenyl-2-oxazoline (7e). (73%), pale yellow oil. (Found: C 71.71; H 8.34; N 12.80; $C_{13}H_{18}N_2O$ requires: C 71.53; H 8.31; N 12.83); ^{1}H NMR δ ($CDCl_3$, 300 MHz): 1.13 (t, 6H, J=7.2 Hz), 2.64 (c, 4H, J=7.2 Hz), 4.19 (dd, 1H, J=9.5, 5.7 Hz), 4.36 (t, 1H, J=9.5 Hz), 5.35 (dd, 1H, J=9.5, 5.7 Hz), 7.37–7.47 (m, 3H), 7.97 (dd, 2H, J=8.2, 1.5 Hz); ^{13}C NMR δ ($CDCl_3$, 75.4 MHz): 13.83 (CH_3), 42.86 (CH_2), 70.17 (CH_2), 84.08 (CH), 127.76 (CH), 128.28 (CH), 128.40 (CH), 131.39 (C), 164.21 (C=N); MS, *m/z* (%): 218 (M^+, 11), 217 (23), 146 (69), 145 (100), 117 (60), 105 (37), 90 (76), 89 (39), 77 (39), 58 (76), 57 (40); IR (film): 3327, 2975, 1648, 1525, 1456, 1386, 1349, 1306, 1216, 1070, 967 cm^{-1}.

3.2.6. 4-Cyclohexylamino-2-phenyl-2-oxazoline (7f). (60%), pale yellow oil. (Found: C 73.63; H 8.19; N 11.43; $C_{15}H_{20}N_2O$ requires: C 73.74; H 8.25; N 11.46); ^{1}H NMR δ ($CDCl_3$, 200 MHz): 0.91–2.35 (m, 12H), 3.96 (dd, 1H, J=9.2, 6.9 Hz), 4.51 (t, 1H, J=9.1 Hz), 5.25 (dd, 1H, J=8.6, 6.9 Hz), 7.31–7.48 (m, 3H), 7.96 (dd, 2H, J=8.2, 1.8 Hz); ^{13}C NMR δ ($CDCl_3$, 50.4 MHz): 24.79 (CH_2), 25.10 (CH_2), 26.09 (CH_2), 33.29 (CH_2), 34.87 (CH_2), 53.39 (CH), 73.23 (CH_2), 78.91 (CH), 127.92 (CH), 128.31 (CH), 128.37 (CH), 131.47 (C), 164.29 (C=N); MS, *m/z* (%): 244 (M^+, 6), 243 (19), 146 (100), 123 (55), 91 (44), 77 (47), 56 (53); IR (film): 3251, 1645, 1455, 1377, 1354, 1246, 1160, 1092, 1026, 956, 696 cm^{-1}.

3.2.7. 4-Benzylamino-2-(3-chlorophenyl)-2-oxazoline (7h). (58%), pale yellow oil. (Found: C 66.95; H 5.22; N 9.69; $C_{16}H_{15}ClN_2O$ requires: C 67.02; H 5.27; N 9.77); ^{1}H NMR δ ($CDCl_3$, 200 MHz): 1.95 (br s, 1H), 3.89–4.13 (m, 3H), 4.49 (t, 1H, J=9.3 Hz), 5.23 (dd, 1H, J=8.8, 6.8 Hz), 7.24–7.49 (m, 7H), 7.86 (dt, 1H, J=7.7, 1.4 Hz), 7.98 (t, 1H, J=1.8 Hz); ^{13}C NMR δ ($CDCl_3$, 50.4 MHz): 49.51 (CH_2), 72.33 (CH_2), 81.16 (CH), 126.54 (CH), 127.12 (CH), 128.31 (CH), 128.48 (CH), 128.57 (CH), 129.60 (C), 129.72 (CH), 131.63 (CH), 134.50 (C), 139.98 (C), 163.46 (C=N); MS, *m/z* (%): 286 (M^+, 1), 195 (3), 180 (5), 152 (5), 138 (19), 131 (65), 118 (28), 104 (31), 91 (100), 75 (15); IR (film): 3282, 3066, 3029, 2900, 1737, 1647, 1574, 1470, 1355, 1246, 1145, 1119, 1079, 969 cm^{-1}.

3.2.8. 4-Benzylamino-2-(3,4,5-trimethoxyphenyl)-2-oxazoline (7m). (55%), pale yellow powder; mp 100–103°C. (Found: C 66.55; H 6.50; N 8.23; $C_{19}H_{22}N_2O_4$ requires: C 66.65; H 6.48; N 8.18); ^{1}H NMR δ ($CDCl_3$, 200 MHz): 1.91 (s, 1H), 3.89 (s, 3H), 3.92 (s, 6H), 3.95–4.05 (m, 2H), 4.10 (dd, 1H, J=6.2, 3.5 Hz), 4.49 (t, 1H, J=8.9 Hz), 5.25 (dd, 1H, J=8.8, 6.5 Hz), 7.23 (s, 2H), 7.26–7.41 (m, 5H); ^{13}C NMR δ ($CDCl_3$, 50.4 MHz): 49.34 (CH_2), 56.27 (CH_3O), 60.97 (CH_3O), 72.22 (CH_2), 81.18 (CH), 105.60 (CH), 122.93 (C), 127.07 (CH), 128.25 (CH), 128.46 (CH), 140.11

(C), 141.02 (C), 153.08 (C), 164.41 (C=N); MS, *m/z* (%): 342 (M^+, 1), 236 (6), 211 (26), 194 (10), 177 (8), 150 (5), 118 (15), 91 (100), 77 (10); IR (Nujol): 3291, 1647, 1591, 1463, 1362, 1231, 1136, 1001, 850, 739 cm^{-1}.

3.2.9. 4-Dimethylamino-2-(2-methylphenyl)-2-oxazoline (7n). (66%), pale yellow oil. (Found: C 70.68; H 7.92; N 13.67; $C_{12}H_{16}N_2O$ requires: C 70.56; H 7.90; N 13.71); ^1H NMR δ ($CDCl_3$, 200 MHz): 2.37 (s, 6H), 2.61 (s, 3H), 4.16–4.35 (m, 2H), 5.16 (dd, 1H, *J*=8.9, 5.5 Hz), 7.18–7.39 (m, 3H), 7.79 (d, 1H, *J*=7.9 Hz); ^{13}C NMR δ ($CDCl_3$, 50.4 MHz): 21.81 (CH_3), 39.72 (CH_3), 68.87 (CH_2), 87.24 (CH), 125.62 (CH), 130.04 (CH), 130.75 (CH), 131.26 (CH), 138.96 (C), 165.26 (C=N); MS, *m/z* (%): 204 (M^+, 13), 189 (8), 160 (75), 146 (7), 132 (36), 117 (21), 105 (50), 91 (40), 77 (20); 57 (100); IR (film): 2941, 2869, 2839, 2796, 1644, 1456, 1345, 1311, 1276, 1235, 1061, 966, 932, 889, 766 cm^{-1}.

3.2.10. 4-Isopentylamino-2-(4-methylphenyl)-2-oxazoline (7o). (68%), pale yellow oil. (Found: C 72.98; H 8.99; N 11.43; $C_{15}H_{22}N_2O$ requires: C 73.13; H 9.00; N 11.37); ^1H NMR δ ($CDCl_3$, 200 MHz): 0.82 (d, 6H, *J*=6.6 Hz), 1.30 (q, 2H, *J*=7.1 Hz), 1.50–1.64 (m, 2H), 2.30 (s, 3H), 2.54–2.67 (m, 1H), 2.79–2.92 (m, 1H), 3.94 (dd, 1H, *J*=9.3, 6.4 Hz), 4.38 (t, 1H, *J*=9.1 Hz), 5.09 (dd, 1H, *J*=8.8, 6.6 Hz), 7.13 (d, 2H, *J*=8.1 Hz), 7.77 (d, 2H, *J*=8.1 Hz); ^{13}C NMR δ ($CDCl_3$, 50.4 MHz): 21.57 (CH_3), 22.57 (CH_3), 22.77 (CH_3), 26.12 (CH), 39.54 (CH_2), 43.40 (CH_2), 71.97 (CH_2), 81.52 (CH), 124.98 (C), 128.34 (CH), 129.06 (CH), 141.89 (C), 164.50 (C=N); MS, *m/z* (%): 246 (M^+, 2), 228 (3), 171 (26), 159 (100), 144 (14), 131 (51), 119 (37), 104 (49), 77 (40); IR (film): 3277, 1739, 1646, 1511, 1467, 1349, 1244, 1131, 1082, 1021, 966, 825, 729 cm^{-1}.

3.2.11. 2-Phenyl-4-phenylamino-2-oxazoline (7p). (52%), pale yellow oil. (Found: C 75.70; H 5.92; N 11.69; $C_{15}H_{14}N_2O$ requires: C 75.61; H 5.92; N 11.76); ^1H NMR δ ($CDCl_3$, 300 MHz): 4.10 (br s, 1H), 4.17 (dd, 1H, *J*=9.3, 6.3 Hz), 4.62 (t, 1H, *J*=8.4 Hz), 5.80 (dd, 1H, *J*=8.4, 6.3 Hz), 6.67–6.82 (m, 3H), 7.14–7.23 (m, 2H), 7.37–7.51 (m, 3H), 7.97–7.99 (m, 2H); ^{13}C NMR δ ($CDCl_3$, 75.4 MHz): 73.23 (CH_2), 77.07 (CH), 114.19 (CH), 118.92 (CH), 127.41 (CH), 128.43 (CH), 128.63 (CH), 129.45 (CH), 131.88 (C), 145.82 (C), 165.90 (C=N); MS, *m/z* (%): 145 ($M^+-C_6H_5NH_2$, 62), 117 (48), 105 (5), 93 (100), 90 (67), 77 (34); IR (film): 3358, 1633, 1606, 1521, 1454, 1368, 1308, 1246, 1149, 1090, 1028, 968, 750 cm^{-1}.

3.2.12. 4-(4-Methoxyphenylamino)-2-phenyl-2-oxazoline (7q). (50%), pale yellow oil. (Found: C 71.58; H 5.97; N 10.43; $C_{16}H_{16}N_2O_2$ requires: C 71.62; H 6.01; N 10.44); ^1H NMR δ ($CDCl_3$, 200 MHz): 3.74 (s, 3H), 3.76 (br s, 1H), 4.16 (dd, 1H, *J*=9.5, 6.5 Hz), 4.63 (t, 1H, *J*=9.2 Hz), 5.74 (dd, 1H, *J*=8.1, 6.5 Hz), 6.71–6.84 (m, 4H), 7.35–7.49 (m, 3H), 7.95–8.00 (m, 2H); ^{13}C NMR δ ($CDCl_3$, 50.4 MHz): 55.80 (CH_3O), 73.08 (CH_2), 78.21 (CH), 115.02 (CH), 116.10 (CH), 127.54 (C), 128.41 (CH), 128.62 (CH), 131.82 (CH), 139.83 (C), 153.33 (C), 165.63 (C=N); FAB$^+$: 269 (M^++1, 100); IR (film): 3363, 1644, 1521, 1366, 1288, 1237, 1088, 1029, 978, 826, 702 cm^{-1}.

3.2.13. 4-Amino-2-phenyl-2-oxazoline (7r). (66%), pale yellow oil. (Found: C 66.70; H 6.18; N 17.14; $C_9H_{10}N_2O$ requires: C 66.65; H 6.21; N 17.27); ^1H NMR δ ($CDCl_3$, 200 MHz): 1.90 (br s, 2H), 3.98 (dd, 1H, *J*=9.4, 6.7 Hz), 4.53 (t, 1H, *J*=9.3 Hz), 5.24 (dd, 1H, *J*=8.7, 6.7 Hz), 7.37–7.49 (m, 3H), 7.95 (d, 2H, *J*=6.6 Hz); ^{13}C NMR δ ($CDCl_3$, 50.4 MHz): 73.70 (CH_2), 76.33 (CH), 127.61 (CH), 128.26 (CH), 128.33 (CH), 131.55 (C), 164.06 (C=N); FAB$^+$: 163 (M^++1, 100); IR (film): 3330, 1636, 1455, 1358, 1249, 1070, 961, 699 cm^{-1}.

3.2.14. 4-Butylamino-2-phenyl-2-oxazoline (8). (61%), pale yellow oil. (Found: C 71.67; H 8.29; N 12.89; $C_{13}H_{18}N_2O$ requires: C 71.53; H 8.31; N 12.83); ^1H NMR δ ($CDCl_3$, 300 MHz): 0.92 (t, 3H, *J*=7.1 Hz), 1.25–1.55 (m, 4H), 1.74 (br s, 1H), 2.65–2.73 (m, 1H), 2.87–2.95 (m, 1H), 4.05 (dd, 1H, *J*=9.3, 6.3 Hz), 4.48 (t, 1H, *J*=9.0 Hz), 5.20 (dd, 1H, *J*=8.9, 6.6 Hz), 7.38–7.51 (m, 3H), 7.96 (d, 2H, *J*=6.9 Hz); ^{13}C NMR δ ($CDCl_3$, 75.4 MHz): 14.03 (CH_3), 20.50 (CH_2), 32.65 (CH_2), 44.95 (CH_2), 72.10 (CH_2), 81.58 (CH), 127.85 (C), 128.39 (CH), 128.43 (CH), 131.57 (CH), 164.47 (C=N); MS, *m/z* (%): 218 (M^+, 4), 217 (13), 146 (100), 134 (12), 118 (31), 104 (31), 91 (75), 84 (41), 77 (61); IR (film): 3281, 2958, 2928, 2861, 1651, 1579, 1466, 1351, 1133, 1086, 1067, 1026, 969, 782 cm^{-1}.

3.2.15. Preparation of 4-(1-benzyl-3-phenylureido)-2-phenyl-2-oxazoline (9). To a solution of 4-benzylamino-2-phenyl-2-oxazoline **7a** (1.2 mmol) in dry ether (9 mL) a solution of phenylisocyanate (1.8 mmol) in dry ether (9 mL) was added dropwise and the reaction mixture was stirred at room temperature for 1.5 h. The white solid precipitated was filtered off and was crystallized from petroleum ether–dichloromethane.

(81%), white needles mp 122–125°C. (Found: C 74.43; H 5.72; N 11.28; $C_{23}H_{21}N_3O_2$ requires: C 74.37; H 5.70; N 11.31); (81%) white needles, mp 122–125°C; ^1H NMR δ ($CDCl_3$, 200 MHz): 4.30 (dd, 1H, *J*=10.1, 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, 6.3 Hz), 6.95–7.53 (m, 13H), 7.99 (d, 2H, *J*=7.5 Hz); ^{13}C NMR δ ($CDCl_3$, 50.4 MHz): 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, *m/z* (%): 371 (M^+, 1), 250 (5), 146 (15), 131 (19), 119 (19), 105 (25), 91 (100), 77 (28); IR (Nujol): 3295, 1632, 1532, 1446, 1377, 1315, 1173, 965, 756, 700 cm^{-1}.

3.3. X-Ray crystallographic analysis of 4-(1-benzyl-3-phenylureido)-2-phenyl-2-oxazoline (9)

Crystal data. Monoclinic, space group *Cc*, *a*=21.2412(16), *b*=11.4944(8), *c*=8.2049(6) Å, β=111.582(3)°, *U*=1862.8 Å^3, *Z*=4, *T*=−130°C. *Data collection*. A crystal ca. 0.4×0.13×0.08 mm^3 was used to record 12578 intensities on a Bruker SMART 1000 CCD diffractometer (Mo Kα radiation, $2\theta_{max}$ 56.6°). *Structure refinement*. The structure was refined anisotropically on F^2 (program SHELXL-97, Sheldrick, G. M. University of Göttingen) to *wR*2 0.077, *R*1 0.030 for 257 parameters and 2313 unique

reflections (Friedel opposites were merged). The NH hydrogen was refined freely, others using a riding model.

Complete crystallographic data (excluding structure factors) have been deposited at the Cambridge Crystallographic Data Centre under the reference number CCDC 188232. 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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