Pergamon

Tetrahedron: *Asymmetry* 12 (2001) 1851–1863

TETRAHEDRON: *ASYMMETRY*

Synthesis of novel optically pure quinolyl-β-amino alcohol derivatives from 2-amino thiophenol and chiral α-acetylenic ketones and their IBX-mediated oxidative cleavage to *N*-Boc quinolyl carboxamides†

Gemma Cabarrocas,[a] Montserrat Ventura,[a] Miguel Maestro,[b] José Mahía[b] and José M. Villalgordo[a,*]

[a]*Departament de Química, Facultat de Ciències, Universitat de Girona, Campus de Montilivi, E-17071 Girona, Spain*
[b]*Servicios Xerais de Apoio a Investigación, Universidade da Coruña, Campus da Zapateira s/n, E-15071 A Coruña, Spain*

Received 8 June 2001; accepted 2 July 2001

Abstract—A methodology directed toward the stereoselective synthesis of novel quinolyl glycines is presented. This strategy is based on the cyclocondensation reaction between 2-amino thiophenol **4** and chiral acetylenic ketones of the type **3** containing a latent α-amino acid functionality. The initially formed benzo[*b*][1,4]thiazepine derivatives **5**, readily undergo sulphur extrusion in refluxing toluene to yield the corresponding 2,4-disubstituted quinolines **6**. Subsequent oxazolidine ring opening followed by in situ re-protection of the amino group afforded the corresponding quinolyl-β-amino alcohols **8a**–**8f** in enantiomerically pure form and good overall yields. The derivatives **8** are in principle suitable precursors for the synthesis of novel optically pure quinolyl glycines through oxidation of the alcohol side chain. However, these amino alcohol derivatives **8**, did not afford the expected quinolyl glycines **10** using numerous oxidising agents and reaction conditions. Instead, by reacting **8** with the mild oxidising reagent IBX **11**, an oxidative C–C cleavage leading to the *N*-Boc quinolyl carboxamides **12** took place. © 2001 Published by Elsevier Science Ltd.

1. Introduction

The non-coded amino acids are a diverse range of compounds whose synthesis in enantiomerically pure form has attracted considerable attention in the last few years.[1,2] Interest in the development of synthetic methods toward the preparation of non-proteinogenic amino acids has arisen due to the biological and toxicological properties displayed by many of these compounds.[3–5] In addition, non-standard amino acids are valuable tools for the creation of peptide or non-peptide based combinatorial libraries[6] and incorporation of 'unusual' amino acids into peptides or peptidomimetics often provides biostability to the degradation by peptidases. The synthesis of these types of substrates is therefore of interest in the design of potential novel therapeutic agents.[7–9] An important class of such non-proteinogenic amino acids are the arylglycines.[10] This type of α-amino acid is present in many biologically active compounds such as cephalosporins,[11] penicillins, nocardicins[12] and glycopeptidic antibiotics of the vancomycin group.[13] Although several approaches have been reported for the asymmetric synthesis of a number of arylglycines,[10,14] their application for the preparation of heterocyclic analogues has been extended generally with limited success in terms of efficiency and/or optical purities. Recently, a remarkably successful approach regarding the stereoselective synthesis of isoxazolyl α-amino acids has been reported.[15]

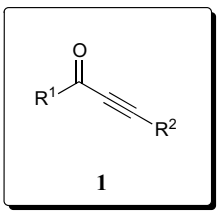
α-Acetylenic ketones of the type **1** have been shown to be highly versatile building blocks. These conjugated ynones have proven to be very suitable substrates for the synthesis of a wide range of heterocyclic systems,[16–25] including for instance the synthesis of the natural product L-lathyrine and related analogues.[26] In addition, when properly functionalised, these types of compounds **1** have also proven to be very valuable

* Corresponding author. Fax: +34 972 418 150; e-mail: jose.villalgordo@udg.es

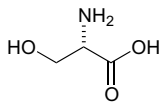
† Taken in part from the Ph.D. Thesis of G.C., Universitat de Girona, 1999.

0957-4166/01/$ - see front matter © 2001 Published by Elsevier Science Ltd.
PII: S0957-4166(01)00308-1

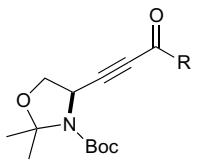
substrates for the preparation of highly structurally diverse 2,4,6-trisubstituted pyrimidines by combinatorial and parallel synthesis methods.[27,28] In view of the great synthetic potential offered by these conjugated ynones and in connection with our ongoing studies dealing with the synthesis of non-proteinogenic aromatic and heteroaromatic α-amino acids in optically active form, we recently described an efficient synthesis of novel chiral α-acetylenic ketones **1** from naturally occurring serine **2**[29] (Scheme 1). Compounds **3**, bearing a latent α-amino acid moiety as a special structural feature, were designed to readily incorporate a masked amino acid functionality into a variety of relevant heterocycles. Subsequent oxazolidine ring opening and oxidation of the primary alcohol side chain should lead to novel heteroarylglycines in optically active form. In this context, we focussed our attention on the quinoline nucleus and now report the full details of our studies regarding the use of chiral α-acetylenic ketones **3** as potential precursors of novel quinolyl glycines.



1



2



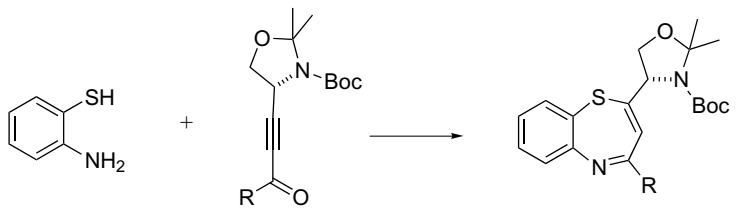
3

Scheme 1.

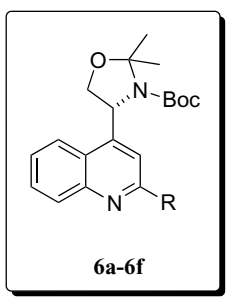
2. Results and discussion

When 2-amino thiophenol **4** was allowed to react in anhydrous THF at −78°C with chiral α-alkynyl ketones of the type **3** for a period of 3–12 h, followed by acid-catalysed cyclisation at 0°C, the corresponding seven-membered benzo[*b*][1,4]thiazepine derivatives **5a**–**5f** were isolated in excellent yields. In the single case of **5f**, containing an aliphatic substituent, addition of PPTS (as acidic catalyst) to effect cyclocondensation was not necessary. These transformations leading to **5a**–**5f** took place in a very efficient and clean manner. Derivatives **5a**–**5f** were stable enough to be subjected to a rapid chromatographic filtration over a small plug of silica to afford pure **5a**–**5f** as yellow oils or foams, allowing for structural determination and characterisation by standard spectroscopic techniques. However, on standing for more than 24 h at rt, **5a**–**5f** spontaneously underwent partial sulphur extrusion to yield quinolines **6**. In view of these results, in a second set of experiments we moved directly onto **6a**–**6f** by evaporating the THF solution containing derivatives of type **5**, adding dry toluene, and heating under reflux for several hours. By using this procedure, quinolines **6** were obtained exclusively in very good yields (72–95% overall yields for two steps) (Scheme 2, Tables 1 and 2).

At this stage, due to the known configurational stability of the stereogenic centre of the oxazolidine ring in **3**, the synthetic sequence above described was expected to be stereospecific. We checked the optical purity of the isolated quinolines **6**, and these were indeed found to be enantiomerically pure ($\geq$95%) as determined by ^{1}H NMR analysis (200 MHz) in the presence of varying amounts of Eu(hfc)$_3$. In addition, we were able to obtain crystals of **6c** that were suitable for X-ray crystallographic structure determination which confirmed both the proposed structure and additionally that the



4 **3a-3f** **5a-5f**



6a-6f

Scheme 2.

Table 1. Benzo[*b*][1,4]thiazepine derivatives **5a–5f**

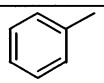
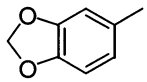
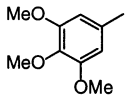
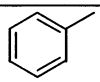
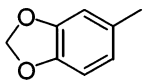
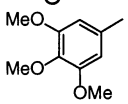
Entry	R	Product	Yield (%)	$[\alpha]_D^{25}$ in MeOH
i		**5a**	95	-46.9 (c = 0.64)
ii		**5b**	96	-21.5 (c = 0.72)
iii		**5c**	96	-83.0 (c = 0.97)
iv		**5d**	57	-90.4 (c =1.34)
v		**5e**	94	-157.2 (c = 1.03)
vi	n-C_6H_{13}	**5f**	76	-79.1 (c = 1.11)

Table 2. Chiral quinolyl oxazolidine derivatives **6a–6f**

Product	R	Yield (%)[a]	M.p., (°C)	$[\alpha]_D^{25}$ in MeOH
6a		92	132-133	-182.0 (c=0.81)
6b		85	164-165	-139.7 (c=1.03)
6c		86	204-205	-199.8 (c=0.84)
6d		71	161-162	-127.4 (c = 0.94)
6e		89	114-115	-139.2 (c = 0.75)
6f	n-C_6H_{13}	72	Colourless oil	-88.3 (c = 0.89)

[a] Yields for the one-pot, two-step procedure.

crystals were enantiomerically pure. It was then assumed that they had the expected absolute configuration. This assumption was extended to the complete series of synthesised compounds **6a–6f** (Fig. 1).

After sulphur extrusion, we then proceeded to selectively cleave the oxazolidine ring in **6** without affecting the *N*-protecting group. After trying a number of different conditions, **8** was obtained by treatment of **6** with *p*-toluenesulphonic acid in dry MeOH at rt; however, the yields were very low (~10%). Alternatively, treatment of **6a–6f** with TFA in MeOH at 0°C afforded the corresponding amino alcohols **7a–7f** which were not isolated but were re-protected in situ to afford *N*-Boc-protected chiral β-amino alcohols **8a–8f** in very good overall yields. For the particular case **8b**, we did prepare the corresponding Mosher's ester derivative **9** from the crude reaction mixture. The enantiomeric excess of this derivative **9** was assessed by ^{1}H NMR and found to be diastereoisomerically pure (Scheme 3, Table 3).

In addition, we were able to grow crystals of **8f** of adequate quality for an X-ray crystallographic structure determination that confirmed the proposed structure and showed that **8f** was enantiomerically pure. It was then assumed that they had the expected absolute configuration. This assumption was extended to the complete series of synthesised *N*-Boc-β-amino alcohol derivatives **8a–8f** (Fig. 2).

With a good and reliable procedure in our hands to efficiently prepare optically active quinolyl-β-amino alcohols of type **8**, we proceeded to further study the critical oxidation step of the lateral chain containing the primary alcohol moiety. This transformation should afford the initially targeted novel optically active quinolyl glycines. To achieve this transformation we

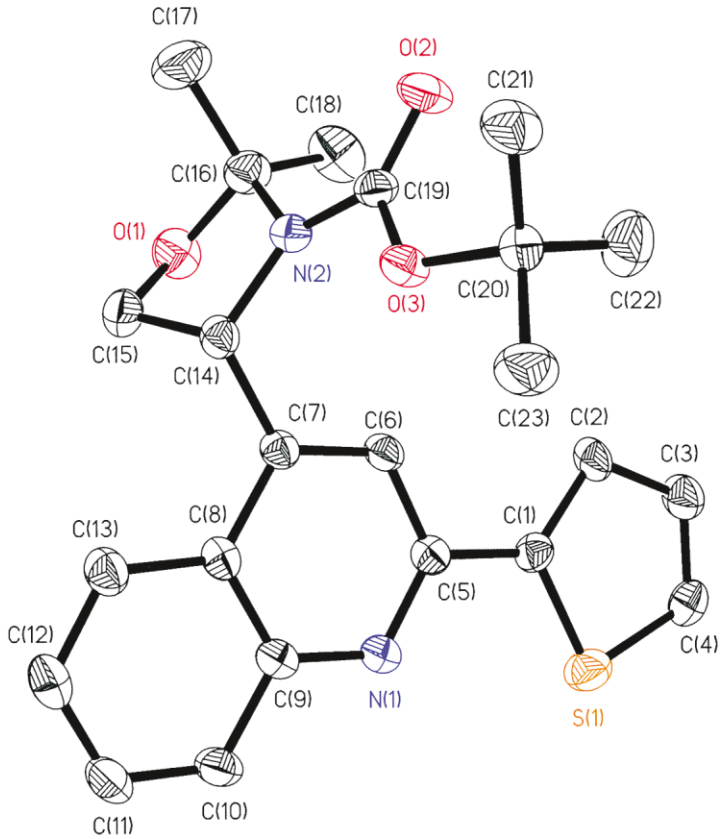


Figure 1. ORTEP plot of the molecular structure of **6c** with 30% probability ellipsoids[42] (Table 5).

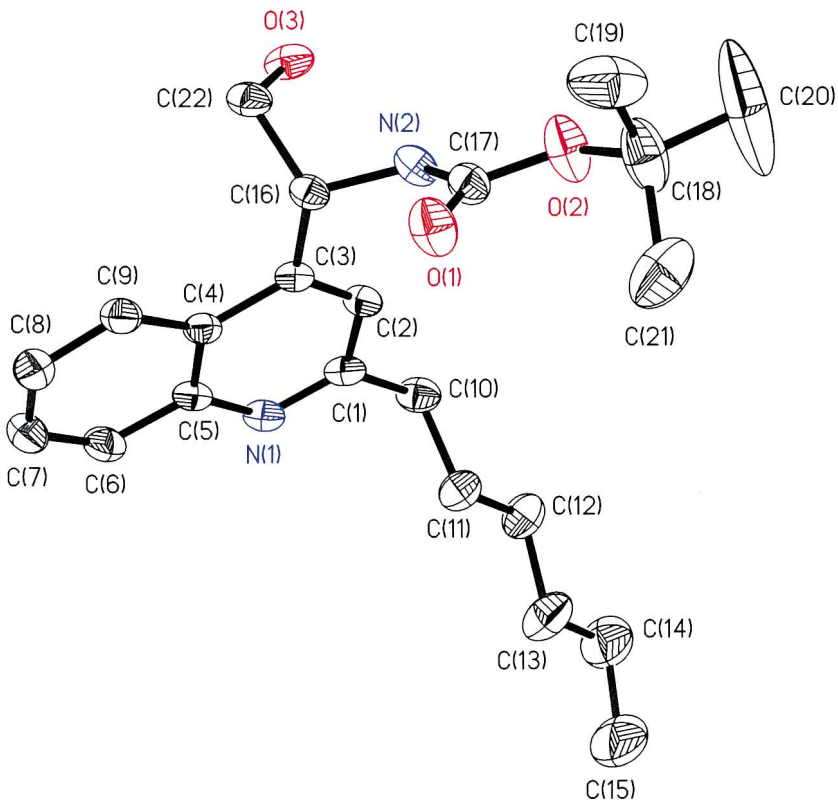
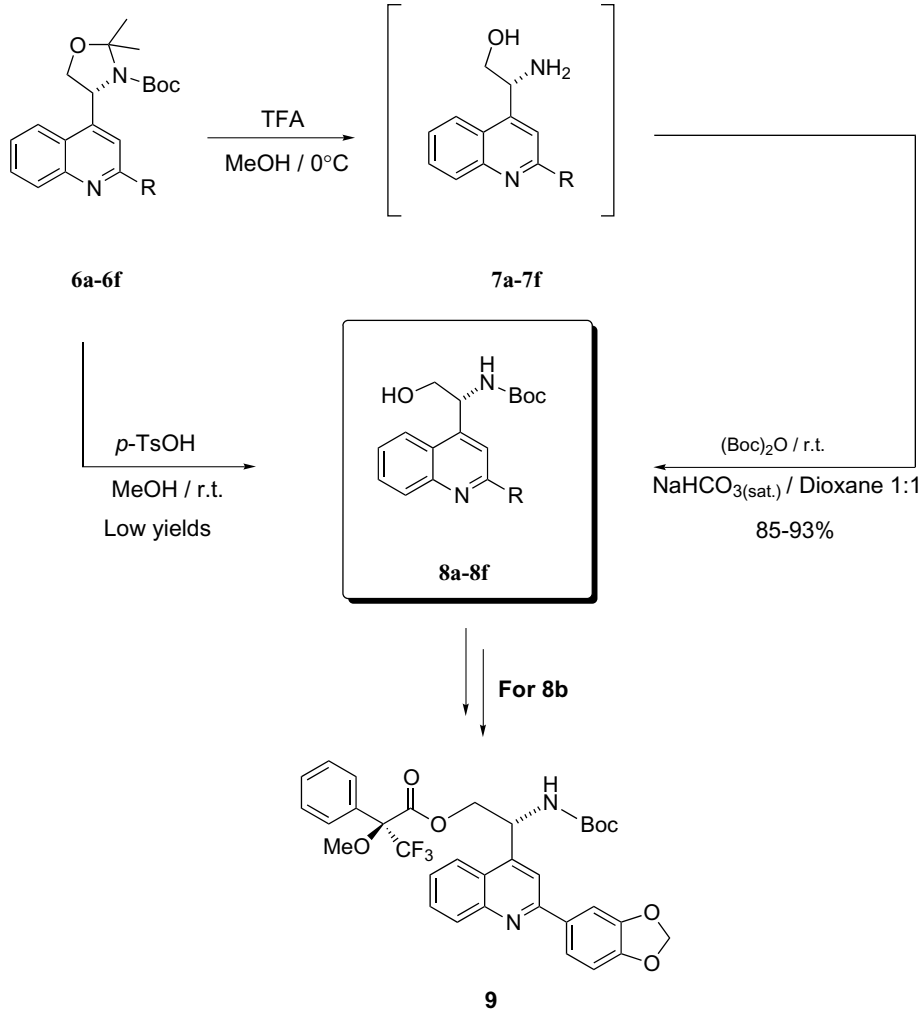
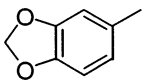
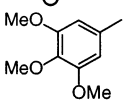


Figure 2. ORTEP plot of the molecular structure of **8f** with 30% probability ellipsoids[42] (Table 5).



Scheme 3.

Table 3. Chiral *N*-Boc-protected quinolyl-β-amino alcohol derivatives **8a**–**8f**

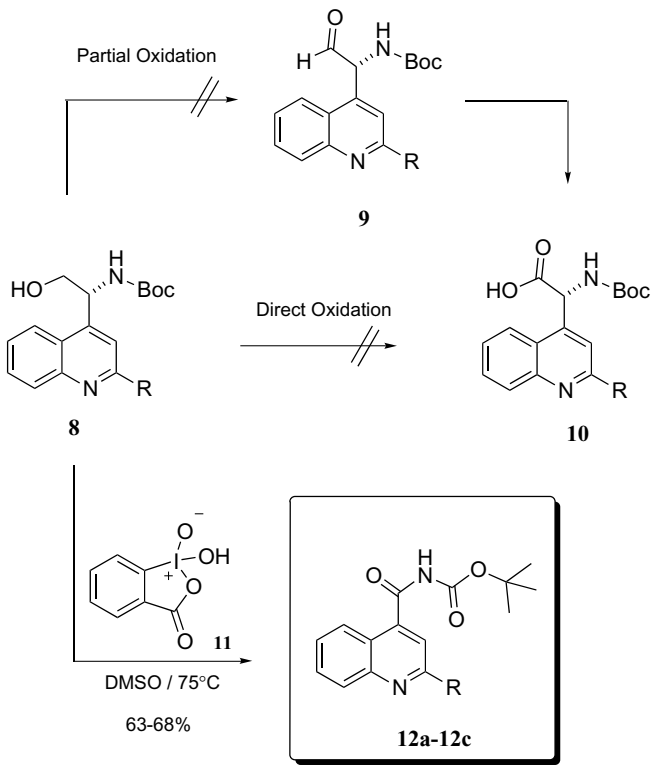
Entry	R	Product	Yield (%)	M.p. (°C)	$[\alpha]_D^{25}$ in MeOH
i		**8a**	93	164-165	-71.4 (c = 0.82)
ii		**8b**	90	180-181	-85.3 (c = 0.99)
iii		**8c**	91	183-184	-81.8 (c = 0.80)
iv		**8d**	74	170-171	-63.4 (c = 0.84)
v		**8e**	91	159-160	-80.6 (c = 0.94)
vi	n-C_6H_{13}	**8f**	85	132-133	-33.4 (c = 0.99)

initially attempted a direct oxidative strategy to the corresponding carboxylic acid. From the large amount of available data reported in the literature regarding the direct oxidation of primary alcohols to carboxylic acids[30] we selected several different methods to carry out this transformation. Thus, when chiral β-amino alcohol derivatives of the type **8** were allowed to react with either dilute aqueous $KMnO_4$,[31,32] TEMPO/

$NaClO$[33] or with $RuCl_3/NaIO_4$ (Sharpless oxidation)[34–36] very complex mixtures of products were obtained. Only in the case of using TEMPO/NaClO, the presence of carboxylic acids of type **10** could be detected but only in trace amounts. In view of these discouraging results, we decided to use a milder oxidative method that could account for the partial oxidation of **8** to the corresponding aldehydes **9** that in turn would be further oxidised to the corresponding α-amino acids **10** under stronger oxidising conditions. However, when we attempted the partial oxidation of chiral β-amino alcohol derivatives **8** to the corresponding aldehydes **9** under Swern oxidation conditions,[37–39] complex reaction mixtures were also obtained. Finally, we found that when the *N*-Boc-protected amino alcohol derivatives **8a**, **8c**, **8e** were allowed to react with 2 equiv. of 1-hydroxy-1-oxo-benzo[*d*][1,2]iodoxol-3-one[40] **11** (IBX) at 75°C in DMSO, a clean transformation leading to the formation of *N*-Boc quinolyl carboxamides of type **12** took place instead of the formation of the aldehydes **9** or the acids **10** (Scheme 4, Table 4).

A plausible mechanism that could account for the formation of quinolyl carboxamides of type **12** is depicted in Scheme 5.

Thus, IBX **11** would initially oxidise amino alcohol derivatives **8** to the corresponding aldehydes **9**. These aldehydes **9**, through their enol form **13**, would react with another molecule of **11** to give spicrocyclic intermediate **14**, which would undergo C–C bond cleavage affording carboxamides **12** in addition to *o*-iodosobenzoic acid **16** and formic acid **15**. This mechanism has been proposed in analogy to those suggested for chromium(VI)-based reagents where C–C bond cleavage is known to occur frequently in the case of readily enolisable aldehydes.[41] To the best of our knowledge, however, this is the first time that IBX is reported to promote such oxidative C–C cleavage of readily enolisable aldehydes.

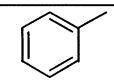
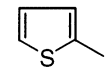
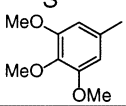


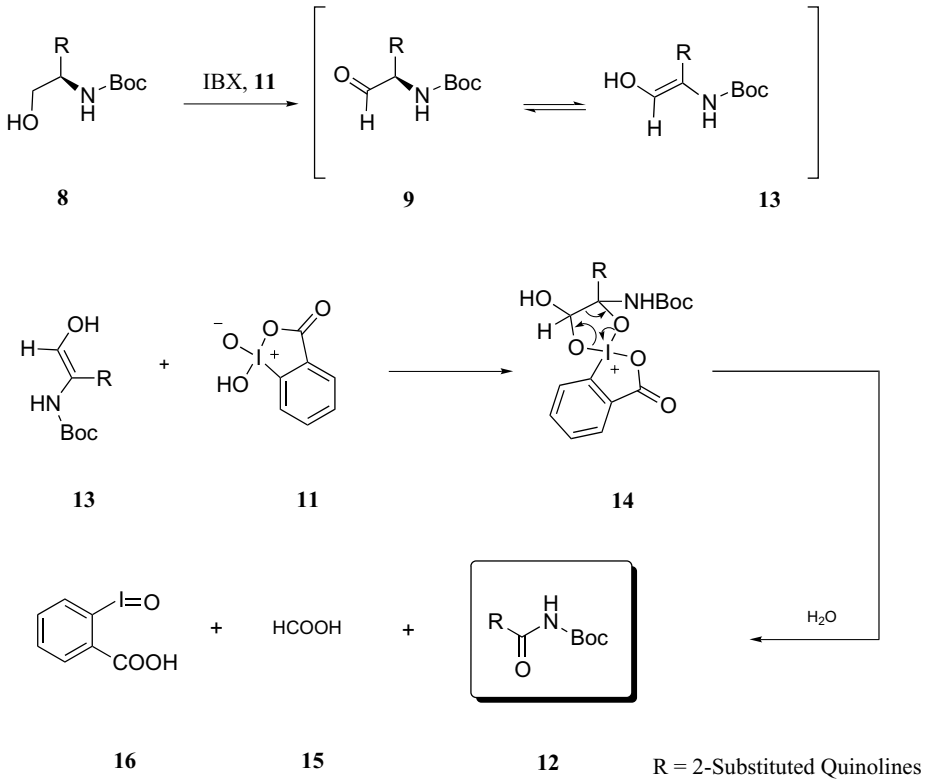
Scheme 4.

3. Conclusion

In summary, we have shown that chiral α-acetylenic ketones of the type **3**, containing a masked α-amino acid group can serve as valuable synthetic intermediates to incorporate this structural motif into heterocycles such as quinolines. In consequence, an efficient and straightforward synthesis of novel optically active quinolyl-β-amino alcohols of the type **8** has been developed. These derivatives are of particular interest, since they can serve as novel building blocks for biologically active molecules or they can be used as chiral ligands for asymmetric transformations. In addition, compounds **8** could be in principle adequate precursors for the synthesis of novel chiral quinolyl glycines **10**. However, under a variety of reaction conditions using different oxidising reagents we were unable obtain our initially targeted α-amino acids of type **10**. In the best case, we discovered that substrates of the type **8** underwent oxidative C–C bond cleavage with mild oxidising agent **11**, presumably through the enol form of the corresponding aldehyde **9**. A mechanism to explain such a transformation has been proposed. Nevertheless, the idea of incorporating latent α-amino acid functionalities into relevant core structures such as quinolines through acetylenic ketones of type **3** proved successful. At present, new acetylenic ketones incorporating other masked α-amino acid functionalities into their structure that could avoid the critical oxidation step are being studied intensively in our laboratories and the results will be reported in due course.

Table 4. *N*-Boc quinolyl carboxamide derivatives **12a**–**12c** prepared

Entry	R	Product	Yield (%)	M.p. (°C)
i		**12a**	67	147-148
ii		**12b**	63	144-145
ii		**12c**	68	150-151



Scheme 5.

4. Experimental

4.1. General methods

All commercially available chemicals were used as purchased, except THF and Toluene that were distilled over Na/benzophenone prior to use. Melting points (capillary tube) were measured with a Gallenkamp apparatus and are uncorrected. IR spectra were recorded on a Mattson-Galaxy Satellite FT-IR. ^{1}H and $^{13}CNMR$ spectra were recorded at 200 and 50 MHz, respectively, on a Bruker DPX200 Advance instrument with TMS as internal standard. MS spectra were recorded on a VG Quattro instrument in the positive-ionisation FAB mode, using 3-NBA or 1-thioglycerol as the matrix or in a Hewlett–Packard 5989A instrument for electron-impact (70 eV) mode. Elemental analyses were performed on an apparatus from Thermo instruments, model EA1110-CHNS. Optical rotation measurements were performed on a Perkin–Elmer 241 polarimeter. Analytical TLC was performed on precoated TLC plates, silica gel 60 F_{254} (Merck). Flash chromatography purifications were performed on silica gel 60 (230–400 mesh, Merck). X-Ray data were collected on a Bruker SMART CCD area-detector diffractometer with graphite-monochromated Mo Kα radiation ($\lambda = 0.71073$ Å) operating at rt, using the phi–omega scan method. Absorption corrections were applied using SADABS.[43] The structures were solved by the direct method using SHELXS-97[44] and were refined by the least-squares method on F^2. All non-hydrogen atoms were refined anisotropically. Hydrogen atoms were included in geometrically calculated positions and refined using a riding model. Crystal data and details on the data collection and refinement are summarised in Table 5.

Table 5. Crystallographic data for **6c** and **8f**

Data/compound	**6c** (Fig. 1)	**8f** (Fig. 2)
Empirical formula	$C_{23}H_{26}N_2O_2S$	$C_{22}H_{32}N_2O_2$
Formula weight	410.52	372.5
Space group	$P2_1$	$P2(1)2(1)2(1)$
Crystal system	Monoclinic	Orthorhombic
Z	2	4
a (Å)	9.351(2)	5.069(1)
b (Å)	10.561(4)	15.743(1)
c (Å)	11.992(3)	27.667(1)
β (°)	112.863(13)	90
V (Å^3)	1091.4(6)	2208.7(1)
ρ(calcd) (g/cm^3)	1.294	1.121
μ_{calcd} (mm^{-1})	0.174	0.074
F (000)	436	808
Radiation (Mo Kα) (Å)	0.70173	0.70173
T (K)	298(2)	298(2)
Crystal size (mm)	$0.45 \times 0.40 \times 0.25$	$0.50 \times 0.15 \times 0.05$
Crystal colour	Colourless	Pale brown
Reflections measured	4627	9389
Independent reflections	3197 ($R_{int} = 0.0170$)	3887 ($R_{int} = 0.0409$)
Max./min. transmission coefficients	0.958/0.926	0.996/0.964
Data/restrains/parameters	3197/1/263	3887/0/245
θ Range for data collection	1.8–25.0	1.5–25.0
Goodness-of-fit	1.061	1.119
Final R_1, wR_2 indices[a] $[I > 2\sigma(I)]$	0.0413, 0.1079	0.0534, 0.1247

[a] $R_1 = \Sigma||F_o|-|F_c||/\Sigma|F_o|$ and $wR_2 = \{\Sigma[w(F_o^2-F_c^2)^2]/\Sigma[w(F_o^2)^2]\}^{1/2}$.

Crystallographic data (excluding structure factors) for the structures reported in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication no. CCDC 161478 (for **6c**) and CCDC 161479 (for **8f**). Copies of the data can be obtained free of charge on application to: CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (fax: (+44)1223-336-033; e-mail: deposit@ccdc.cam.ac.uk).

4.2. Synthesis of benzo[*b*][1,4]thiazepine derivatives 5a–5f and quinoline derivatives 6a–6f. General procedure

Into a cooled (−78°C) solution of **3** in anhydrous THF (2.1 mL/mmol), another solution of 2-amino thiophenol **4** (1.2 equiv.) in THF (1 mL/mmol), was added dropwise. The reaction mixture was stirred at −78°C until total consumption of **3** (3–12 h, monitored by TLC). The reaction was slowly warmed to 0°C, and 20 mol% of pyridinium *p*-toluenesulphonate (PPTS) was added (except for **3f**). After stirring at 0°C for 8–15 h (monitored by TLC), the mixture was partitioned between 0.1 M phosphate buffer (pH 7.1) and AcOEt. The organic layer was separated, dried over $MgSO_4$ (anhyd.), the solvent eliminated under reduced pressure (T <35°C), and the resulting residue purified through a short silica-gel column (hexanes/AcOEt as eluent) to afford pure **5a**–**5f**. These compounds **5a**–**5f** were dissolved in dry toluene (3 ml/mmol) and refluxed for 12–15 h. Evaporation of the solvent and flash chromatography of the resulting residue (*n*-hexane/AcOEt as eluent) afforded pure **6a**–**6f**.

Alternatively, after cyclocondensation has been effected, THF was removed under reduced pressure (T <35°C), dry toluene (3 ml/mmol) added to the residue, and the mixture refluxed for 12–15 h. Work-up identical as above afforded pure **6a**–**6f** (Tables 1 and 2).

4.2.1. Benzo[*b*][1,4]thiazepine 5a. According to the general procedure described above, reaction between **3a** (200 mg, 0.60 mmol), **4** (121.6 mg, 0.973 mmol) and PPTS (30.5 mg, 0.12 mmol) afforded **5a** as a yellow foam (251 mg, 95%); $[\alpha]_D^{20}$ −46.9 (*c* 0.64, MeOH); IR (KBr, ν, cm^{-1}): 3060w, 2979m, 2931m, 2875w, 1701s, 1626w, 1570w, 1455m, 1370s, 1296w, 1259m, 1210w, 1168m, 1101m, 1060m, 851m, 762m, 694m; ^1H NMR (DMSO-d_6, T=60°C): δ 8.1–7.3 (m, 9H, $CH_{arom.}$), 6.76 (s, 1H), 4.80–4.75 (m, 1H), 4.31 (dd, 1H, J=9.2 Hz, J'=7 Hz, AB sys., CH_2O), 3.94 (dd, 1H, J=9.2 Hz, J'=7 Hz, AB sys., CH_2O), 1.78 (s, 3H, $C(CH_3)_2$), 1.60 (s, 3H, $C(CH_3)_2$), 1.40 (s, br., 9H, $C(CH_3)_3$); ^{13}C NMR (DMSO-d_6, T=60°C): δ 164.2 (s, C=N), 151.2, 150.8, 149.2, 138.3 (4s, $C_{arom.}$+NCO), 131.6, 130.5, 129.0, 128.1 (4d, $CH_{arom.}$), 127.1 (s, $C_{arom.}$), 126.9, 126.4, 125.6, 124.4 (4d, $CH_{arom.}$), 94.0 (s, $C(CH_3)_2$), 79.4 (s, $C(CH_3)_3$), 66.9 (t, CH_2O), 62.4 (d, CH), 27.5 (q, $C(CH_3)_3$), 25.7, 23.7 (2q, $C(CH_3)_2$); MS (EI, 70 eV) m/e: 436 (M^+, 5), 289 (20), 262 (13), 261 (30), 57 (100).

4.2.2. Benzo[*b*][1,4]thiazepine 5b. According to the general procedure described above, reaction between **3b** (600 mg, 1.61 mmol), **4** (246 mg, 1.93 mmol) and PPTS (83 mg, 0.32 mmol) afforded **5b** as a yellow foam (741 mg, 96%); $[\alpha]_D^{20}$ −21.5 (*c* 0.72, MeOH); IR (KBr, ν, cm^{-1}): 2976m, 2926m, 2856m, 1699s, 1626w, 1591w, 1571w, 1487m, 1443m, 1370s, 1296m, 1249s, 1210w, 1168m, 1100m, 1038m, 937w, 850w, 810w, 761m; ^1H NMR ($CDCl_3$): δ 7.65–7.10 (m, 6H, $CH_{arom.}$), 6.87 (d, J=8 Hz, 1H, $CH_{arom.}$), 6.49 (s, 1H), 6.05 (s, 2H, OCH_2O), 4.6 (s, br., 1H, C*H*), 4.21 (dd, J=9.1 Hz, J'=6.9 Hz, 1H, CH_2O), 3.99 (s, br., 1H, CH_2O), 1.80–1.25 (m, br., 15H); ^{13}C NMR ($CDCl_3$, doubling of some signals observed): δ 164.3+163.6 (s, C=N), 151.6, 150.6, 150.0, 149.7 (4s, $C_{arom.}$+NCO), 148.2, 133.5 (2s, $C_{arom.}$), 132.0, 130.9, 129.2, 128.8 (4d, $CH_{arom.}$), 128.2+127.5 (s, $C_{arom.}$), 126.4+126.2, 124.7+124.0, 123.4+123.0, 107.8+107.4 (4d, $CH_{arom.}$), 101.9+101.5 (t, OCH_2O), 95.2+94.6 (s, $C(CH_3)_2$), 80.8+80.4 (s, $C(CH_3)_3$), 67.5+67.2 (t, CH_2O), 63.2 (d, CH), 28.3+28.0 (q, $C(CH_3)_3$), 26.9+26.1 (q, $C(CH_3)_2$), 24.6+23.4 (q, $C(CH_3)_2$); MS (EI, 70 eV) m/e: 480 (M^+, 5), 448 (25), 334 (14), 333 (53), 317 (10), 304 (23), 83 (10), 71 (10), 69 (13), 57 (100).

4.2.3. Benzo[*b*][1,4]thiazepine 5c. According to the general procedure described above, reaction between **3c** (850 mg, 2.54 mmol), **4** (382 mg, 3.05 mmol) and PPTS (127 mg, 0.50 mmol) afforded **5c** as a yellow foam (1.07 g, 96%); $[\alpha]_D^{20}$ −83.0 (*c* 0.97, MeOH); IR (film, ν, cm^{-1}): 3294w, 3260w, 3069w, 2977m, 2932, 2875m, 1699s, 1624w, 1567m, 1456m, 1422m, 1371s, 1301d, 1245m, 1205w, 1168m, 1097m, 1057m, 939w, 849m, 807w, 761m, 713m, 676w; ^1H NMR (DMSO-d_6, T=60°C): δ 7.85 (dd, J=5.1 Hz, J'=1 Hz, 1H, $CH_{arom.}$), 7.61 (dd, J=3.6 Hz, J'=1 Hz, 1H, $CH_{arom.}$), 7.50–7.25 (m, 5H, $CH_{arom.}$), 6.85 (s, 1H), 4.74 (dd, J=7.0 Hz, J'=3.8 Hz, 1H, CH), 4.29 (dd, J=9.2 Hz, J'=7.0 Hz, 1H, AB sys., CH_2O), 3.91 (dd, J=9.2 Hz, J'=3.8 Hz, 1H, AB sys., CH_2O), 1.81 (s, 3H, $C(CH_3)_2$), 1.60 (s, 3H, $C(CH_3)_2$), 1.38 (s, br., 9H, $C(CH_3)_3$); ^{13}C NMR (DMSO-d_6, T=60°C): δ 159.2 (s, C=N), 151.4, 150.8, 148.9, 145.0 (4s, $C_{arom.}$+NCO), 131.7, 130.9, 129.1, 128.9, 127.6 (5d, $CH_{arom.}$), 126.7 (s, $C_{arom.}$), 126.6, 125.8, 123.5 (3s, $CH_{arom.}$), 94.0 (s, $C(CH_3)_2$), 79.3 (s, $C(CH_3)_3$), 66.9 (t, CH_2O), 62.4 (d, CH), 27.5 (q, $C(CH_3)_2$), 25.6 (q, $C(CH_3)_2$), 23.8 (q, $C(CH_3)_3$); MS (FAB^+) m/e: 444 ($[M+2]^+$, 28), 443 ($[M+1]^+$, 100), 442 ($[M]^+$, 23), 387 (33), 329 (21), 268 (32), 267 (51), 218 (22).

4.2.4. Benzo[*b*][1,4]thiazepine 5d. According to the general procedure described above, reaction between **3d** (150 mg, 0.47 mmol), **4** (70.63 mg, 0.56 mmol) and PPTS (24.5mg, 0.097 mmol) afforded **5d** as a yellow oil (0.114 g, 57%); $[\alpha]_D^{20}$ −90.4 (*c* 1.34, MeOH); IR (film, ν, cm^{-1}): 3131w, 3058w, 2980w, 2932m, 2877w, 1737w, 1700s, 1626w, 1592w, 1562w, 1477m, 1456m, 1370s, 1303w, 1251m, 1207w, 1166m, 1093m, 1053m, 1012w, 944w, 919w, 809w, 850m, 758m, 676w; ^1H NMR (DMSO-d_6, T=60°C): δ 7.96 (dd, J=1.8 Hz, J'=0.8 Hz, 1H, $CH_{arom.}$), 7.55–7.30 (m, 4H, $CH_{arom.}$), 7.16 (dd, J=3.4 Hz, J'=0.8 Hz, 1H, $CH_{arom.}$), 6.77 (dd, J=3.4 Hz, J'=1.8 Hz, 1H, $CH_{arom.}$), 6.75 (s, 1H, $CH_{arom.}$), 4.71 (dd, J=7.0 Hz, J'=3.6 Hz, 1H, CH), 4.27 (dd,

$J=9.2$ Hz, $J'=7.0$ Hz, 1H, AB sys., CH_2O), 3.88 (dd, $J=9.2$ Hz, $J'=3.6$ Hz, 1H, AB sys., CH_2O), 1.80 (s, 3H, $C(CH_3)_2$), 1.59 (s, 3H, $C(CH_3)_2$), 1.36 (s, br., 9H, $C(CH_3)_3$); ^{1}H NMR (DMSO-d_6, $T=60$°C): δ 154.9 (s, C=N), 152.5, 151.7, 150.8, 149.1 (4s, $C_{arom.}$+NCO), 145.5, 131.8, 129.2, 126.7 (4d, $CH_{arom.}$), 125.9 (s, $C_{arom.}$), 125.8, 123.0, 113.1, 112.0 (4d, $CH_{arom.}$), 94.1 (s, $C(CH_3)_2$), 79.4 (s, $C(CH_3)_3$), 66.8 (t, CH_2O), 62.5 (d, CH), 27.5 (q, $C(CH_3)_2$), 25.6 (q, $C(CH_3)_2$), 23.8 (q, $C(CH_3)_3$); MS (EI, 70 eV) m/e: 428 ([M+2]$^+$, 1), 427 ([M+1]$^+$, 3), 426 ([M]$^+$, 10), 293 (10), 279 (27), 252 (18), 251 (55), 57 (100).

4.2.5. Benzo[*b*][1,4]thiazepine 5e. According to the general procedure described above, reaction between **3e** (775 mg, 1.85 mmol), **4** (279 mg, 2.22 mmol) and PPTS (93 mg, 0.37 mmol) afforded **5e** as a yellow foam (0.914 g, 94%); $[\alpha]_D^{20}$ −157.6 (*c* 1.03, MeOH); IR (film, ν, cm^{-1}): 3057w, 2973m, 2934m, 2876m, 1698s, 1626w, 1573m, 1503m, 1457m, 1411w, 1372s, 1339m, 1256m, 1206w, 1170m, 1126m, 1064w, 1006w, 849m, 762m, 699w; ^{1}H NMR (DMSO-d_6, $T=60$°C): δ 7.55–7.30 (m, 6H, $CH_{arom.}$), 6.76 (s, 1H, $CH_{arom.}$), 4.77 (dd, $J=6.9$ Hz, $J'=3.3$ Hz, 1H, CH), 4.35–4.10 (m, 2H, CH_2O), 3.98 (s, 6H, 2×CH_3O), 3.89 (s, 3H, CH_3O), 1.80 (s, 3H, $C(CH_3)_2$), 1.60 (s, 3H, $C(CH_3)_2$), 1.37 (s, br., 9H, $C(CH_3)_3$); ^{13}C NMR (DMSO-d_6, $T=60$°C): δ 163.3 (s, C=N), 153.1, 150.9, 150.6, 149.1 (4s, $C_{arom.}$+NCO), 140.9, 133.5 (2s, $C_{arom.}$), 131.6, 128.9 (2d, $CH_{arom.}$), 127.1 (s, $C_{arom.}$), 126.2, 125.6, 122.6, 105.8 (4s, $CH_{arom.}$), 93.9 (s, $C(CH_3)_2$), 79.3 (s, $C(CH_3)_3$), 66.8 (t, CH_2O), 62.6 (d, CH), 59.8, 56.1 (2q, 3xCH_3O), 27.4 (q, $C(CH_3)_2$), 25.8 (q, $C(CH_3)_2$), 24.1 (q, $C(CH_3)_3$); MS (FAB$^+$) m/e: 528 ([M+2]$^+$, 31), 527 ([M+1]$^+$, 100), 526 ([M]$^+$, 14), 471 (28), 391 (18), 327 (12), 326 (46), 279 (15).

4.2.6. Benzo[*b*][1,4]thiazepine 5f. According to the general procedure described above, reaction between **3f** (500 mg, 1.48 mmol) and **4** (258 mg, 2.07 mmol) (no addition of PPTS) afforded **5f** as a yellow oil (0.497 g, 76%); $[\alpha]_D^{20}$ −79.1 (*c* 1.11, MeOH); IR (film, ν, cm^{-1}): 3059w, 2957m, 2930m, 2859m, 1704s, 1631m, 1607w, 1581w, 1459m, 1371s, 1261m, 1170m, 1205w, 1095m, 1063m, 944w, 850m, 806w, 762m, 678w, 590w; ^{1}H NMR (DMSO-d_6, $T=60$°C): δ 7.50–7.10 (m, 4H, $CH_{arom.}$), 6.29 (s, 1H), 4.70–4.55 (m, 1H, CH), 4.23 (dd, $J=9.2$ Hz, $J'=7.0$ Hz, 1H, AB sys., CH_2O), 3.82 (dd, $J=9.2$ Hz, $J'=3.4$ Hz, 1H, AB sys., CH_2O), 2.65–2.55 (m, 2H), 1.85–1.35 (m, 23H), 0.98 (t, $J=6.8$ Hz, 3H); ^{13}C NMR (DMSO-d_6, $T=60$°C): δ 161.4 (s, C=N), 150.7, 149.5, 149.2 (3s, $C_{arom.}$+NCO), 131.6, 128.9 (2d, $CH_{arom.}$), 127.3 (s, $C_{arom.}$), 126.2, 125.9, 125.4 (3d, $CH_{arom.}$), 93.9 (s, $C(CH_3)_2$), 79.2 (s, $C(CH_3)_3$), 66.9 (t, CH_2O), 62.2 (d, CH), 40.2, 37.7, 30.7, 28.4 (4t, CH_2), 27.5, 25.9 (2q, $C(CH_3)_2$), 24.2 (q, $C(CH_3)_3$), 21.6 (t, CH_2), 13.4 (q, CH_3); MS (EI, 70 eV) m/e: 446 ([M+2]$^+$, 1), 445 ([M+1]$^+$, 3), 57 (100).

4.2.7. Quinolyl oxazolidine 6a. By following the general procedure described above, **6a** was isolated in 92% yield as a colourless solid; mp 132–133°C; $[\alpha]_D^{20}$ −182.0 (*c* 0.81, MeOH); IR (KBr, ν, cm^{-1}): 3063w, 2981m, 2932m, 2890w, 2863w, 1698s, 1685s, 1602m, 1550w, 1496w, 1475w, 1452w, 1386s, 1365m, 1264m, 1243m, 1205w, 1167m, 1097m, 1053m, 1031w, 945w, 885w, 853m, 809w, 771m, 692m, 619w; ^{1}H NMR (DMSO-d_6, $T=60$°C): δ 8.30–8.25 (m, 4H, $CH_{arom.}$), 7.95–7.60 (m, 6H, $CH_{arom.}$), 5.95–5.90 (m, 1H, CH), 4.75–4.65 (m, 1H, CH_2O), 3.94 (d, $J=9$ Hz, 1H, CH_2O), 1.96 (s, 3H, $C(CH_3)_2$), 1.76 (s, 3H, $C(CH_3)_2$), 1.30 (s, br., 9H, $C(CH_3)_3$); ^{13}C NMR (DMSO-d_6, $T=60$°C): δ 153.3, 151.1 (2s, $C_{arom.}$), 148.3 (s, NCO), 147.7, 138.7 (2s, $C_{arom.}$), 129.7, 129.2, 129.1, 128.6, 126.4, 126.2 (6d, $CH_{arom.}$), 124.3 (s, $C_{arom.}$), 122.7, 113.7 (d, $CH_{arom.}$), 93.8 (s, $C(CH_3)_2$), 79.3 (s, $C(CH_3)_3$), 68.8 (t, CH_2O), 56.7 (d, CH), 27.4 (q, $C(CH_3)_3$), 26.1, 23.4 (2q, $C(CH_3)_2$); MS (EI, 70 eV) m/e: 405 ([M+1]$^+$, 10), 404 ([M]$^+$, 4), 333 (11), 289 (42), 57 (100). Anal. calcd for $C_{25}H_{28}N_2O_3$ (404.50): C, 74.23; H, 6.98; N, 6.93. Found: C, 73.95; H, 7.20; N, 7.14%.

4.2.8. Quinolyl oxazolidine 6b. By following the general procedure described above, **6b** was isolated in 85% yield as a colourless solid; mp 164–165°C; $[\alpha]_D^{20}$ −139.7 (*c* 1.03, MeOH); IR (KBr, ν, cm^{-1}): 3082w, 2983m, 2904w, 2876w, 1693s, 1601m, 1552w, 1500m, 1449m, 1383s, 1307w, 1247m, 1165m, 1095m, 1042m, 939w, 878w, 847m, 814m, 762m, 696w; ^{1}H NMR (DMSO-d_6, $T=60$°C): δ 8.20–8.15 (m, 2H, $CH_{arom.}$), 7.90–7.65 (m, 5H, $CH_{arom.}$), 7.18 (d, $J=8.2$ Hz, 1H, $CH_{arom.}$), 6.21 (s, 2H, OCH_2O), 5.90–5.85 (m, 1H, CH), 4.75–4.65 (m, 1H, CH_2O), 3.95–3.90 (m, 1H, CH_2O), 1.95 (s, 3H, $C(CH_3)_3$), 1.74 (s, 3H, $C(CH_3)_3$), 1.30 (s, br. 9H, $C(CH_3)_3$); ^{13}C NMR (DMSO-d_6, $T=60$°C): δ 154.7, 151.2 (2s, $C_{arom.}$), 148.6, 148.2, 148.0, 147.7 (4s, $C_{arom.}$+NCO), 133.1 (s, $C_{arom.}$), 129.6, 129.3, 126.0 (3d, $CH_{arom.}$), 124.2 (s, $C_{arom.}$), 122.7, 120.7, 113.4, 108.4, 106.4 (5d, $CH_{arom.}$), 101.2 (t, OCH_2O), 93.8 (s, $C(CH_3)_2$), 79.3 (s, $C(CH_3)_3$), 68.8 (t, CH_2O), 56.8 (d, CH), 27.5 (q, $C(CH_3)_3$), 26.1 (q, $C(CH_3)_2$), 23.5 (q, $C(CH_3)_2$); MS (EI, 70 eV) m/e: 449 ([M+1]$^+$, 11), 448 ([M]$^+$, 38), 377 (14), 334 (21), 333 (85), 317 (14), 303 (15), 291 (13), 289 (12), 274 (14), 57 (100). Anal. calcd for $C_{26}H_{28}N_2O_5$ (448.51): C, 69.63; H, 6.29; N, 6.25. Found: C, 69.36; H, 6.47; N, 6.03%.

4.2.9. Quinolyl oxazolidine 6c. By following the general procedure described above, **6c** was isolated in 86% yield as a colourless solid; mp 204–205°C; $[\alpha]_D^{20}$ −199.8 (*c* 0.84, MeOH); IR (KBr, ν, cm^{-1}): 3074w, 2979m, 2930w, 2879w, 1685s, 1605m, 1551w, 1454w, 1428m, 1392s, 1364m, 1262m, 1239m, 1168m, 1096m, 1072w, 1052m, 875w, 831w, 809w, 767m, 730m, 690w; ^{1}H NMR (C_6D_6, $T=60$°C): δ 8.36 (d, $J=8.5$ Hz, 1H, $CH_{arom.}$), 8.09 (s, 1H, $CH_{arom.}$), 7.90 (d, $J=3.8$ Hz, 1H, $CH_{arom.}$), 7.62 (d, $J=8.5$ Hz, 1H, $CH_{arom.}$), 7.55–7.45 (m, 1H, $CH_{arom.}$), 7.35–7.25 (m, 1H, $CH_{arom.}$), 7.16 (d, $J=5$ Hz, 1H, $CH_{arom.}$), 6.95 (dd, $J=5$ Hz, $J'=3.8$ Hz, 1H, $CH_{arom.}$), 5.56 (dd, $J=7.4$ Hz, $J'=3.2$ Hz, 1H, CH), 4.21 (dd, $J=8.8$ Hz, $J'=7.4$ Hz, 1H, AB sys., CH_2O), 3.74 (dd, $J=8.8$ Hz, $J'=3.2$ Hz, 1H, AB sys., CH_2O), 2.11 (s, 3H, $C(CH_3)_2$), 1.81 (s, 3H, $C(CH_3)_2$), 1.26 (s, br., 9H $C(CH_3)_3$); ^{13}C NMR (C_6D_6, $T=60$°C): δ 153.4,

152.8, 150.1, 149.2, 147.2 (5s, $C_{arom.}$+NCO), 131.8, 130.1, 129.3, 129.0, 126.7, 126.6 (6d, $CH_{arom.}$), 126.2 (s, $C_{arom.}$), 123.1, 115.0 (2d, $CH_{arom.}$), 95.8 (s, $C(CH_3)_2$), 80.8 (s, $C(CH_3)_3$), 70.2 (t, CH_2O), 58.6 (d, CH), 28.9 (q, $C(CH_3)_3$), 27.4, 24.8 (2q, $C(CH_3)_2$); MS (FAB$^+$) m/e: 412 ([M+2]$^+$, 26), 411 ([M+1]$^+$, 100), 410 ([M]$^+$, 15), 355 (42), 295 (41), 281 (16), 279 (12), 253 (17), 252 (17), 251 (13), 238 (20), 237 (16), 236 (34), 225 (18), 212 (27). Anal. calcd for $C_{23}H_{26}N_2O_3S$ (410.53): C, 67.29; H, 6.38; N, 6.82; S, 7.81 Found: C, 67.52; H, 6.09; N, 6.96; S, 8.11%.

4.2.10. Quinolyl oxazolidine 6d. By following the general procedure described above, **6d** was isolated in 71% yield as a pale yellow solid; mp 161–162°C; $[\alpha]_D^{20}$ −127.4 (c 0.94, MeOH); IR (KBr, ν, cm^{-1}): 2981w, 2932w, 2900w, 1691s, 1604m, 1552w, 1500w, 1454w, 1390s, 1261m, 1166m, 1094m, 1051w, 1012w, 855w, 814w, 752m, 599w; ^{1}H NMR (DMSO-d_6, T=60°C): δ 8.20–7.65 (m, 6H, $CH_{arom.}$), 7.34 (d, J=3.2 Hz, 1H, $CH_{arom.}$), 6.80–6.75 (m, 1H, $CH_{arom.}$), 5.90–5.85 (m, 1H, CH), 4.75–4.65 (m, 1H, CH_2O), 3.91 (dd, J=9 Hz, J'=2.6 Hz, 1H, CH_2O), 1.95 (s, 3H, $C(CH_3)_2$), 1.74 (s, 3H, $C(CH_3)_2$), 1.31 (s, br., 9H, $C(CH_3)_3$); ^{13}C NMR (DMSO-d_6, T=60°C): δ 153.2, 151.1 (2s, $C_{arom.}$), 148.4 (s, NCO), 147.8, 147.7 (2s, $C_{arom.}$), 144.6, 129.5, 129.3, 126.1 (4d, $CH_{arom.}$), 124.3 (s, $C_{arom.}$), 122.8, 112.4, 112.2, 109.6 (4d, $CH_{arom.}$), 93.8 (s, $C(CH_3)_2$), 79.3 (s, $C(CH_3)_3$), 68.7 (t, CH_2O), 56.7 (d, CH), 27.5 (q, $C(CH_3)_3$), 26.0, 23.4 (2q, $C(CH_3)_2$); MS (EI, 70 eV) m/e: 395 ([M+1]$^+$, 1), 394 ([M]$^+$, 4), 279 (22), 57 (100). Anal. calcd for $C_{23}H_{26}N_2O_4$ (394.46): C, 70.03; H, 6.64; N, 7.10. Found: C, 70.22; H, 6.39; N, 7.36%.

4.2.11. Quinolyl oxazolidine 6e. By following the general procedure described above, **6e** was isolated in 89% yield as a yellowish solid; mp 114–115°C; $[\alpha]_D^{20}$ −139.2 (c 0.75, MeOH); IR (KBr, ν, cm^{-1}): 2977m, 2932m, 1700s, 1600m, 1551w, 1504m, 1461m, 1423w, 1367s, 1244m, 1170m, 1128m, 1098m, 1051w, 1005w, 851w, 765m; ^{1}H NMR (DMSO-d_6, T=60°C): δ 8.30–8.15 (m, 2H, $CH_{arom.}$), 7.95–7.80 (m, 2H, $CH_{arom.}$), 7.75–7.65 (m, 1H, $CH_{arom.}$), 7.55 (s, 2H, $CH_{arom.}$), 5.89 (dd, J=7.0 Hz, J'=2.6 Hz, 1H, CH), 4.71 (dd, J=8.9 Hz, J'=7 Hz, 1H, CH_2O), 4.02 (s, 6H, 2×CH_3O), 4.00–3.95 (m, 1H, CH_2O), 3.91 (s, 3H, CH_3O), 1.96 (s, 3H, $C(CH_3)_2$), 1.75 (s, 3H, $C(CH_3)_2$), 1.32 (s, br., 9H, $C(CH_3)_3$); ^{13}C NMR (DMSO-d_6, T=60°C): δ 155.6, 153.8, 151.8 (3s, $C_{arom.}$), 148.9 (s, NCO), 148.4, 140.3, 134.7 (3s, $C_{arom.}$), 130.4, 130.0, 126.9 (3d, $CH_{arom.}$), 124.9 (s, $C_{arom.}$), 123.4, 114.4, 105.4 (3d, $CH_{arom.}$), 94.5 (s, $C(CH_3)_2$), 80.0 (s, $C(CH_3)_3$), 69.5 (t, CH_2O), 60.6 (q, CH_3O), 57.56 (d, CH), 56.6 (q, 2×CH_3O), 28.2 (q, $C(CH_3)_3$), 26.6, 24.2 (2q, $C(CH_3)_2$); MS (FAB$^+$) m/e: 495 ([M+1]$^+$, 100), 494 ([M]$^+$, 59), 440 (17), 439 (64), 438 (10), 379 (21), 365 (24), 363 (10), 296 (10). Anal. calcd for $C_{28}H_{34}N_2O_6$ (494.58): C, 68.00; H, 6.93; N, 5.66. Found: C, 68.26; H, 6.64; N, 5.83%.

4.2.12. Quinolyl oxazolidine 6f. By following the general procedure described above, **6f** was isolated in 72% yield as a yellowish oil; $[\alpha]_D^{20}$ −88.3 (c 0.89, MeOH); IR (film, ν, cm^{-1}): 3065w, 2957m, 2929m, 2858m, 1702s, 1605m, 1561w, 1509w, 1457m, 1376s, 1365f, 1254m, 1205w, 1171m, 1096m, 1053m, 949w, 857m, 810w, 760m; ^{1}H NMR (DMSO-d_6, T=60°C): δ 8.15–8.05 (m, 2H, $CH_{arom.}$), 7.85–7.60 (m, 2H, $CH_{arom.}$), 7.30 (s, 1H, $CH_{arom.}$), 5.81 (dd, J=7.2 Hz, J'=2.6 Hz, 1H, CH), 4.66 (dd, J=9 Hz, J'=7.2 Hz, 1H, AB sys., CH_2O), 3.85 (dd, J=9 Hz, J'=2.6 Hz, 1H, AB sys., CH_2O), 3.01 (t, J=7.3 Hz, 2H), 1.89 (s, br., 4H), 1.72 (s, 3H, $C(CH_3)_2$), 1.50–1.30 (m, 16H), 0.95 (t, J=7 Hz, 3H); ^{13}C NMR (DMSO-d_6, T=60°C): δ 161.5, 151.1, 147.5, 147.2 (4s, $C_{arom.}$+NCO), 129.0, 128.6, 125.4 (3d, $CH_{arom.}$), 123.8 (s, $C_{arom.}$), 122.6, 116.5 (2d, $CH_{arom.}$), 93.7 (s, $C(CH_3)_2$), 79.1 (s, $C(CH_3)_3$), 68.8 (t, CH_2O), 56.6 (d, CH), 38.1, 30.7, 28.4, 28.0 (4t, CH_2), 27.5 (q, $C(CH_3)_3$), 25.9, 23.5 (2q, $C(CH_3)_2$), 21.5 (t, CH_2), 13.4 (q, CH_3); MS (EI, 70 eV) m/e: 413 ([M+1]$^+$, 1), 412 ([M]$^+$, 1), 342 (10), 286 (12), 57 (100). Anal. calcd for $C_{25}H_{36}N_2O_3$ (412.57): C, 72.78; H, 8.80; N, 6.79. Found: C, 72.49; H, 8.96; N, 7.04%.

4.3. Synthesis of quinolyl-β-amino alcohol derivatives 8a–8f. General procedure

To a cooled (0°C) solution of **6a**–**6f** in MeOH (0.7 mL/mmol), TFA (3 mL/mmol) was added dropwise. After stirring for 2 h at 0°C and overnight at rt, TFA was removed under a gentle stream of argon. The resulting residue was re-dissolved in a 1:1 mixture dioxane/$NaHCO_3$ (satd), (12 mL/mmol), cooled at 0°C and $(Boc)_2O$ (3.3 equiv.) added in one portion. The reaction mixture was stirred at 0°C for 4 h and overnight at rt. The mixture was partitioned between H_2O and AcOEt, the organic layer separated and dried over $MgSO_4$ (anhyd.). Removal of the solvent and purification of the resulting residue by flash chromatography (hexanes/AcOEt as eluent) afforded pure **8a**–**8f** (Table 3).

4.3.1. Quinolyl β-amino alcohol 8a. By following the general procedure described above, **8a** was isolated in 93% yield as a colourless solid; mp 164–165°C; $[\alpha]_D^{20}$ −71.4 (c 0.82, MeOH); IR (KBr, ν, cm^{-1}): 3400br., 3354m, 3230m, 3070w, 2972w, 2934w, 2875w, 1684s, 1609m, 1537m, 1447w, 1392w, 1367m, 1283m, 1252m, 1171m, 1065m, 1031w, 884w, 861w, 757m, 692m, 646w; ^{1}H NMR ($CDCl_3$): δ 8.20–7.35 (m, 10H, $CH_{arom.}$), 5.80 (s, br., 1H, NH), 5.56 (s, br., CH), 4.10–3.80 (m, 2H, CH_2O), 3.24 (s, br., 1H, OH), 1.47 (s, br., 9H, $C(CH_3)_3$); ^{13}C NMR ($CDCl_3$): δ 156.7, 155.8, 148.1, 146.3 (4s, $C_{arom.}$+NCO), 139.0 (s, $C_{arom.}$), 130.1, 129.6, 129.4, 128.7, 127.5, 126.7 (6d, $CH_{arom.}$), 124.8 (s, $C_{arom.}$), 122.4, 116.2 (2d, $CH_{arom.}$), 80.4 (s, $C(CH_3)_3$), 64.8 (t, CH_2O), 52.5 (d, CH), 28.3 (q, $C(CH_3)_3$); MS (EI, 70 eV) m/e: 365 ([M+1]$^+$, 1), 364 ([M]$^+$, 1), 233 (13), 57 (100). Anal. calcd for $C_{22}H_{24}N_2O_3$ (364.44): C, 72.50; H, 6.64; N, 7.69. Found: C, 72.73; H, 6.82; N, 7.42%.

4.3.2. Quinolyl β-amino alcohol 8b. By following the general procedure described above, **8b** was isolated in 90% yield as a colourless solid; mp 180–181°C; $[\alpha]_D^{20}$ −85.3 (c 0.99, MeOH); IR (KBr, ν, cm^{-1}): 3400br., 3074w, 2979w, 2927w, 2888w, 1679s, 1604m, 1505s, 1451m, 1366m, 1249s, 1167m, 1104w, 1040m, 934w,

873w, 759m, 635w; ^{1}H NMR ($CDCl_3$): δ 8.10 (d, $J=8.2$ Hz, 1H, $CH_{arom.}$), 7.90 (d, $J=8.2$ Hz, 1H, $CH_{arom.}$), 7.75–7.45 (m, 5H, $CH_{arom.}$), 6.90 (d, $J=8.6$ Hz, 1H, $CH_{arom.}$), 6.06 (s, 2H, OCH_2O), 5.83 (d, $J=6.8$ Hz, 1H, NH), 5.51 (s, br., 1H, CH), 4.05–3.80 (m, 2H, CH_2O), 3.75–2.80 (s, br., 1H, OH), 1.47 (s, br., 9H, $C(CH_3)_3$); ^{13}C NMR ($CDCl_3$): δ 156.0, 155.7, 148.9, 148.2, 148.0 (5s, $C_{arom.}$), 146.0 (s, NCO), 133.4 (s, $C_{arom.}$), 129.9, 129.6, 126.4 (3d, $CH_{arom.}$), 124.6 (s, $C_{arom.}$), 122.3, 121.8, 115.8, 108.4, 107.7 (5d, $CH_{arom.}$), 101.4 (t, OCH_2O), 80.3 (s, $C(CH_3)_3$), 64.8 (t, CH_2O), 52.6 (d, CH), 28.3 (q, $C(CH_3)_3$); MS (EI, 70 eV) m/e: 409 ([M+1]$^+$, 4), 408 ([M]$^+$, 14), 334 (17), 322 (11), 321 (21), 278 (10), 277 (49), 190 (10), 57 (100). Anal. calcd for $C_{23}H_{24}N_2O_5$ (408.45): C, 67.63; H, 5.92; N, 6.86. Found: C, 67.41; H, 6.18; N, 6.67%.

4.3.3. Quinolyl β-amino alcohol 8c. By following the general procedure described above, **8c** was isolated in 91% yield as a colourless solid; mp 183–184°C; $[\alpha]_D^{20}$ −81.8 (*c* 0.80, MeOH); IR (KBr, ν, cm^{-1}): 3400br., 3348m, 3241m, 3070w, 2972w, 2931w, 2874w, 1682s, 1605m, 1536m, 1458w, 1427w, 1368m, 1283m, 1254m, 1169m, 1065m, 1032w, 878w, 836w, 757m, 706m, 644w; ^{1}H NMR (CD_3OD): δ 8.36 (d, $J=8.4$ Hz, 1H, $CH_{arom.}$), 8.24 (d, $J=8.4$ Hz, 1H, $CH_{arom.}$), 8.17 (s, 1H, $CH_{arom.}$), 8.05 (dd, $J=3.7$ Hz, $J'=1.1$ Hz, 1H, $CH_{arom.}$), 7.95–7.70 (m, 3H, $CH_{arom.}$), 7.37 (dd, $J=5.1$ Hz, $J'=3.7$ Hz, 1H, $CH_{arom.}$), 5.74 (s, br., 1H, CH), 4.14 (dd, $J=11.4$ Hz, $J'=4.6$ Hz, AB sys., 1H, CH_2O), 3.97 (dd, $J=11.4$ Hz, $J'=6.9$ Hz, AB sys., 1H, CH_2O), 1.63 (s, br., 9H, $C(CH_3)_3$); ^{13}C NMR (CD_3OD): δ 158.2, 153.9, 149.7, 149.2, 146.4 (5s, $C_{arom.}$+NCO), 131.2, 130.7, 130.2, 129.5, 127.9, 127.7 (6d, $CH_{arom.}$), 127.0 (s, $C_{arom.}$), 124.4, 116.7 (2d, $CH_{arom.}$), 81.0 (s, $C(CH_3)_3$), 65.6 (t, CH_2), 54.4 (d, CH), 29.0 (q, $C(CH_3)_3$); MS (FAB$^+$) m/e: 372 ([M+2]$^+$, 24), 371 ([M+1]$^+$, 100), 370 ([M]$^+$, 13), 315 (32), 297 (14), 284 (14), 283 (15), 254 (12), 239 (27), 236 (10), 212 (12). Anal. calcd for $C_{20}H_{22}N_2O_3S$ (370.47): C, 64.84; H, 5.99; N, 7.56; S, 8.66. Found: C, 64.61; H, 6.22; N, 7.33; S, 8.92%.

4.3.4. Quinolyl β-amino alcohol 8d. By following the general procedure described above, **8d** was isolated in 74% yield as a yellowish solid; mp 170–171°C; $[\alpha]_D^{20}$ −63.4 (*c* 0.84, MeOH); IR (KBr, ν, cm^{-1}): 3500br., 3376m, 3349m, 3081w, 3301m, 2980w, 2931w, 2875w, 1685s, 1608m, 1511m, 1461w, 1393w, 1366m, 1284m, 1247m, 1170m, 1091w, 1061m, 1019d, 883d, 759m, 618w; ^{1}H NMR ($CDCl_3$): δ 8.13 (d, $J=8.2$ Hz, 1H, $CH_{arom.}$), 8.02 (d, $J=8.2$ Hz, 1H, $CH_{arom.}$), 7.82 (s, 1H, $CH_{arom.}$), 7.75–7.50 (m, 3H, $CH_{arom.}$), 7.26 (d, $J=3.4$ Hz, 1H, CH), 6.63 (dd, $J=3.4$ Hz, $J'=1.6$ Hz, 1H, $CH_{arom.}$), 5.60 (s, br., 2H, CH+NH), 4.11 (s, br., 2H, CH_2O), 2.39 (s, br., 1H, OH), 1.49 (s, br., 9H, $C(CH_3)_3$); ^{13}C NMR ($CDCl_3$): δ 155.5, 152.8, 148.0, 147.4, 146.3 (5s, $C_{arom.}$, NCO), 143.9, 129.6, 129.1, 126.2 (4d, $CH_{arom.}$), 124.5 (s, $C_{arom.}$), 122.3, 114.5, 112.2, 110.5 (4d, $CH_{arom.}$), 80.2 (s, $C(CH_3)_3$), 64.7 (t, CH_2O), 52.5 (d, CH), 28.3 (q, $C(CH_3)_3$); MS (EI, 70 eV) m/e: 355 ([M+1]$^+$, 1), 354 ([M]$^+$, 2), 223 (15), 57 (100). Anal. calcd for $C_{20}H_{22}N_2O_4$ (354.40): C, 67.78; H, 6.26; N, 7.90. Found: C, 67.49; H, 6.49; N, 7.71%.

4.3.5. Quinolyl β-amino alcohol 8e. By following the general procedure described above, **8e** was isolated in 91% yield as a yellowish solid; mp 159–160°C; $[\alpha]_D^{20}$ −80.6 (*c* 0.94, MeOH); IR (KBr, ν, cm^{-1}): 3500br., 3490m, 3344m, 2971m, 2938m, 2866d, 2834w, 1681s, 1598m, 1534m, 1505m, 1459, 1425m, 1362s, 1276m, 1246m, 1170m, 1130s, 1096w, 1063m, 1005m, 859w, 759m, 647w; ^{1}H NMR ($CDCl_3$): δ 8.18 (d, $J=8.2$ Hz, 1H, $CH_{arom.}$), 7.99 (d, $J=8.2$ Hz, 1H, $CH_{arom.}$), 7.75–7.50 (m, 3H, $CH_{arom.}$), 7.31 (s, 2H, $CH_{arom.}$), 5.71 (d, $J=7$ Hz, 1H, NH), 5.59 (s, br., 1H, CH), 4.15–4.10 (m, 2H, CH_2O), 4.0 (s, 6H, 2×CH_3O), 3.95 (s, 3H, CH_3O), 2.98 (s, br., 1H, OH), 1.46 (s, br., 9H, $C(CH_3)_3$); ^{13}C NMR ($CDCl_3$): δ 156.5, 155.6, 153.5, 148.3, 146.0, 139.6, 135.0 (6s, $C_{arom.}$+NCO), 130.3, 129.6, 126.6 (3d, $CH_{arom.}$), 124.8 (s, $C_{arom.}$), 122.4, 116.0, 105.0 (3d, $CH_{arom.}$), 80.3 (s, $C(CH_3)_3$), 64.9 (t, CH_2O), 60.9 (q, CH_3O), 56.3 (q, 2×CH_3O), 52.8 (d, CH), 28.3 (q, $C(CH_3)_3$); MS (FAB$^+$) m/e: 455 ([M+1]$^+$, 100), 454 ([M]$^+$, 52), 399 (36), 381 (12), 323 (29). Anal. calcd for $C_{25}H_{30}N_2O_6$ (454.52): C, 66.06; H, 6.65; N, 6.16. Found: C, 66.24; H, 6.42; N, 5.95%.

4.3.6. Quinolyl β-amino alcohol 8f. By following the general procedure described above, **8f** was isolated in 85% yield as a colourless solid; mp 132–133°C; $[\alpha]_D^{20}$ −33.4 (*c* 0.99, MeOH); IR (KBr, ν, cm^{-1}): 3500br., 3353m, 3180m, 2957m, 2926m, 2857, 1689s, 1604w, 1525m, 1465w, 1367w, 1281w, 1246m, 1174m, 1086m, 1059m, 888w, 766m, 640w; ^{1}H NMR ($CDCl_3$): δ 7.89 (d, $J=7.9$ Hz, 1H, $CH_{arom.}$), 7.75 (d, $J=7.9$ Hz, 1H, CH), 7.55–7.20 (m, 3H, $CH_{arom.}$), 5.76 (d, $J=7.4$ Hz, 1H, NH), 5.53 (s, br., 1H, CH), 4.40–4.20 (s, br., 1H, OH), 4.12 (s, br., 2H, CH_2O), 2.85–2.75 (m, 2H), 1.75–1.30 (m, 17H), 0.90 (t, $J=6.2$ Hz, 3H, CH_3); ^{13}C NMR ($CDCl_3$): δ 162.6, 156.0, 147.8, 146.5 (4s, $C_{arom.}$+NCO), 129.6, 129.2, 126.3 (3d, $CH_{arom.}$), 124.6 (s, $C_{arom.}$), 122.7, 118.8 (2d, $CH_{arom.}$), 80.6 (s, $C(CH_3)_3$), 65.1 (t, CH_2O), 52.9 (d, CH), 39.4, 32.1, 30.4, 29.5 (4t, CH_2), 28.7 (q, $C(CH_3)_3$), 22.9 (t, CH_2), 14.5 (q, CH_3); MS (EI, 70 eV) m/e: 373 ([M+1]$^+$, 2), 372 ([M]$^+$, 1), 302 (45), 246 (25), 241 (34), 229 (17), 228 (100), 57 (83). Anal. calcd for $C_{22}H_{32}N_2O_3$ (372.50): C, 70.94; H, 8.66; N, 7.52. Found: C, 71.15; H, 8.44; N, 7.79%.

4.4. Synthesis of quinolyl carboxamide derivatives 12a–12c. General procedure

To a pre-heated (75°C) solution of the corresponding amino alcohol **8** in DMSO (3.8 mL/mmol), IBX **11** (2 equiv.) was added and the reaction mixture stirred at 75°C for 5 h. After cooling to rt, the mixture was partitioned between H_2O and ether. The layers were separated and the aqueous extracted further with ether. The combined organic layers were washed once with $NaHCO_3$ (satd) and the separated organic layer dried over $MgSO_4$ (anhyd.), and filtered. Removal of the solvent and purification of the resulting residue by flash chromatography (hexanes/AcOEt as eluent) afforded pure **12a**–**12c** (Table 4).

4.4.1. Quinolyl carboxamide 12a. According to the general procedure described above, reaction between **8a** (150 mg, 0.41 mmol) and IBX **11** (231 mg, 0.82 mmol) afforded 0.096 g (67%) of **12a** as a colourless solid; mp 147–148°C; IR (KBr, ν, cm^{-1}): 3450br., 3166w, 3065w, 2979w, 2982w, 2855w, 1767m, 1750s, 1682m, 1592m, 1519m, 1499m, 1459w, 1370m, 1344w, 1229m, 1141s, 1050w, 1032w, 935m, 847w, 769m, 692m, 653w; ^{1}H NMR ($(CD_3)_2CO$): δ 10.20 (s, br., 1H, NH), 8.55–7.70 (m, 10H, $CH_{arom.}$), 1.51 (s, 9H, $C(CH_3)_3$); ^{13}C NMR ($(CD_3)_2CO$): δ 169.7 (s, CO), 157.4, 151.0, 149.6, 143.9, 139.9 (5s, $C_{arom.}$+NCO), 131.3, 131.2, 131.0, 130.0, 128.6, 128.5, 126.0 (7d, $CH_{arom.}$), 124.5 (s, $C_{arom.}$), 117.6 (d, $CH_{arom.}$), 82.8 (s, $C(CH_3)_3$), 28.3 (q, $C(CH_3)_3$); MS (FAB$^+$) m/e: 349 ([M+1]$^+$, 54), 348 ([M]$^+$, 4), 293 (19), 275 (10), 250 (19), 249 (100), 248 (19), 205 (18), 204 (17). Anal. calcd for $C_{21}H_{20}N_2O_3$ (348.40): C, 72.40; H, 5.79; N, 8.04. Found: C, 72.66; H, 5.61; N, 8.28%.

4.4.2. Quinolyl carboxamide 12b. According to the general procedure described above, reaction between **8c** (80 mg, 0.22 mmol) and IBX **11** (123 mg, 0.44 mmol) afforded 0.049 g (63%) of **12b** as a yellowish solid; mp 144–145°C; IR (KBr, ν, cm^{-1}): 3460br., 3260br., 3169w, 2975w, 2928w, 1775s, 1701s, 1595m, 1549m, 1503m, 1461w, 1426m, 1370m, 1235m, 1217m, 1145s, 1058w, 931w, 837w, 762m, 715m; ^{1}H NMR ($CDCl_3$): δ 8.41 (s, br., 1H, NH), 8.08 (d, J=8.3 Hz, 1H, $CH_{arom.}$), 7.93 (d, J=8.3 Hz, 1H, $CH_{arom.}$), 7.75–7.45 (m, 5H, $CH_{arom.}$), 7.20–7.15 (m, 1H, $CH_{arom.}$), 1.50 (s, br., 9H, $C(CH_3)_3$); ^{13}C NMR ($CDCl_3$): δ 166.3 (s, CO), 151.6, 149.2, 148.1, 144.0, 141.3 (5s, $C_{arom.}$+NCO), 130.5, 129.3, 128.2, 127.3, 126.6, 124.4 (6d, $CH_{arom.}$), 122.6 (s, $C_{arom.}$), 115.0 (d, $CH_{arom.}$), 83.6 (s, $C(CH_3)_3$), 27.9 (q, $C(CH_3)_3$); MS (FAB$^+$) m/e: 356 ([M+2]$^+$, 4), 355 ([M+1]$^+$, 15), 354 ([M]$^+$, 5), 256 (24), 255 (100), 254 (23), 238 (15), 211 (23), 210 (23). Anal. calcd for $C_{19}H_{18}N_2O_3S$ (354.42): C, 64.39; H, 5.12; N, 7.90; S, 9.05. Found: C, 64.61; H, 4.93; N, 8.17; S, 9.31%.

4.4.3. Quinolyl carboxamide 12c. According to the general procedure described above, reaction between **8e** (80 mg, 0.17 mmol) and IBX **11** (98 mg, 0.34 mmol) afforded 0.051 g (68%) of **12c** as a yellowish solid; mp 150–151°C; IR (KBr, ν, cm^{-1}): 3260br., 3184w, 2969m, 2935m, 1775s, 1699m, 1594m, 1550w, 1507m, 1460m, 1423m, 1365m, 1327w, 1310w, 1228m, 1148s, 1131s, 1051w, 994w, 965w, 909w, 843w, 766m; ^{1}H NMR ($CDCl_3$): δ 8.26 (d, J=8.4 Hz, 1H, $CH_{arom.}$), 8.14 (s, br., 1H, NH), 8.09 (d, J=8.4 Hz, 1H, $CH_{arom.}$), 7.90–7.75 (m, 2H, $CH_{arom.}$), 7.65–7.55 (m, 1H, $CH_{arom.}$), 7.39 (s, 2H, $CH_{arom.}$), 4.02 (s, 6H, 2×CH_3O), 3.95 (s, 3H, CH_3O), 1.43 (s, 9H, $C(CH_3)_3$); ^{13}C NMR ($CDCl_3$): δ 166.8 (s, CO), 156.2, 153.6, 149.1, 148.1, 141.7, 139.9, 133.9 (7s, $C_{arom.}$+NCO), 130.4, 129.9, 127.5, 124.2 (4d, $CH_{arom.}$), 122.7 (s, $C_{arom.}$), 116.3, 104.9 (2d, $CH_{arom.}$), 83.7 (s, $C(CH_3)_3$), 60.9 (q, 2×CH_3O), 56.3 (q, CH_3O), 27.7 (q, $C(CH_3)_3$); MS (FAB$^+$) m/e: 439 ([M+1]$^+$, 22), 438 ([M]$^+$, 17), 361 (13), 340 (24), 339 (100), 338 (23), 337 (12), 323 (25), 309 (19), 307 (10), 295 (23), 294 (10), 293 (13), 277 (10), 265 (16), 263 (13). Anal. calcd for $C_{24}H_{26}N_2O_6$ (438.47): C, 65.74; H, 5.98; N, 6.39. Found: C, 66.02; H, 5.77; N, 6.65%.

Acknowledgements

Generous financial support from the Ministerio de Educación y Ciencia (Spain) through project PB98-0451, Universitat de Girona through project UdG98-452, Medichem SA (Barcelona) and Roviall Química SL (Murcia) is gratefully acknowledged. Thanks are also given to Dr. Llüisa Matas (Servei d'Anàlisi, Universitat de Girona) for recording the NMR spectra and microanalysis. One of us (G.C.) thanks the Ministerio de Educación y Ciencia (Spain) for a pre-doctoral fellowship.

References

1. Duthaler, R. O. *Tetrahedron* **1994**, *50*, 1539.
2. Hunt, S. *Chemistry and Biochemistry of the Amino Acids*; Chapman and Hall: New York, 1985; Vol. 4.
3. Rosenthal, G. A. *Plant Non-protein Amino and Imino Acids. Biological, Biochemical and Toxicological Properties*; Academic Press: New York, 1982.
4. Myers, A. G.; Gleason, J. L. *J. Org. Chem.* **1996**, *61*, 813.
5. Son, J.-E.; Ramalingan, K.; Woodward, R. W. *Synthesis* **1988**, 240.
6. Obrecht, D.; Villalgordo, J. M. *Solid-supported Combinatorial and Parallel Synthesis of Small-molecular-weight Compound Libraries*; Pergamon: Oxford, 1998; Vol. 17.
7. Müller, K.; Obrecht, D.; Knierzinger, A.; Stankovic, C.; Spiegler, C.; Bannwarth, W.; Trzeciak, A.; Englert, G.; Labhardt, A. M.; Schönholzer, P. *Perspectives in Medicinal Chemistry*; Verlag Helvetica Chimica Acta: Basel, 1993.
8. Villalgordo, J. M.; Heimgartner, H. *Tetrahedron* **1993**, *49*, 7215.
9. Walker, D. M.; Logusch, E. W. *Tetrahedron Lett.* **1989**, *30*, 1181.
10. Williams, R. M.; Hendrix, J. A. *Chem. Rev.* **1992**, *92*, 889.
11. Kukolja, S.; Draheim, S. E.; Pfeil, J. L.; Cooper, R. D. G.; Graves, B. J.; Holmes, R. E.; Neel, D. A.; Huffman, G. W.; Webber, J. A.; Kinnick, M. D.; Vasileff, R. T.; Foster, B. J. *J. Med. Chem.* **1985**, *28*, 1886.
12. Townsend, C. A.; Brown, A. M. *J. Am. Chem. Soc.* **1983**, *1983*, 913.
13. Williams, D. H.; Rajananda, D.; Williamson, M. P.; Bojeson, G. *Top. Antibiot. Chem.* **1980**, *5*, 119.
14. Medina, E.; Vidal-Ferran, A.; Moyano, A.; Pericàs, M. A.; Riera, A. *Tetrahedron: Asymmetry* **1997**, *8*, 1581.
15. Falorni, M.; Giacomelli, G.; Spanu, E. *Tetrahedron Lett.* **1998**, *39*, 9241.
16. Obrecht, D. *Helv. Chim. Acta* **1989**, *72*, 447.
17. Masquelin, T.; Obrecht, D. *Tetrahedron Lett.* **1994**, *35*, 9387.
18. Masquelin, T.; Obrecht, D. *Synthesis* **1995**, 276.
19. Utimoto, K.; Miwa, H.; Nozaki, H. *Tetrahedron Lett.* **1981**, *22*, 4277.
20. Masquelin, T.; Obrecht, D. *Tetrahedron* **1997**, *53*, 641.
21. Degl'Inocenti, A.; Scalfato, P.; Capperucci, A.; Bartoletti, L.; Mordini, A.; Reginato, G. *Tetrahedron Lett.* **1995**, *36*, 9031.

22. Garvey, D. S.; Wasicak, J. T.; Elliot, R. L.; Lebold, S. A.; Hettinger, A.-M.; Carrera, G. M.; Lin, N.-H.; He, Y.; Holladay, M. W.; Anderson, D. J.; Cadman, E. D.; Raszkiewicz, J. L.; Sullivan, J. P.; Arneric, S. P. *J. Med. Chem*. **1994**, *37*, 4455.
23. Falorni, M.; Giacomelli, G.; Spanedda, A. M. *Tetrahedron: Asymmetry* **1998**, *9*, 3039.
24. Cabarrocas, G.; Rafel, S.; Ventura, M.; Villalgordo, J. M. *Synlett* **2000**, 595.
25. Cabarrocas, G.; Ventura, M.; Maestro, M.; Mahía, J.; Villalgordo, J. M. *Tetrahedron: Asymmetry* **2000**, *11*, 2483.
26. Adlington, R. M.; Baldwin, J. E.; Catterick, D.; Pritchard, G. J. *J. Chem. Soc., Perkin Trans. 1* **1999**, 855.
27. Chucholowski, A.; Masquelin, T.; Obrecht, D.; Stadlwieser, J.; Villalgordo, J. M. *Chimia* **1996**, *50*, 525.
28. Obrecht, D.; Abrecht, C.; Grieder, A.; Villalgordo, J. M. *Helv. Chim. Acta* **1997**, *80*, 65.
29. Serrat, X.; Cabarrocas, G.; Rafel, S.; Ventura, M.; Linden, A.; Villalgordo, J. M. *Tetrahedron: Asymmetry* **1999**, *10*, 3417.
30. Burke, S. D.; Danheiser, R. L. *Handbook of Reagents for Organic Synthesis* (*Oxidizing and Reducing Agents*); Wiley: Chichester, UK, 1999.
31. Abiko, A.; Roberts, J. C.; Takemas, T.; Masamune, S. *Tetrahedron Lett*. **1986**, *27*, 4537.
32. Delcanale, E. *J. Org. Chem*. **1986**, *51*, 567.
33. Anelli, P. L.; Biffi, C.; Montanari, F.; Quici, S. *J. Org. Chem*. **1987**, *52*, 2559.
34. Behrens, C. H.; Sharpless, K. B. *J. Org. Chem*. **1985**, *50*, 5696.
35. Ermert, P.; Meyer, I.; Stucki, C.; Scheebeli, J.; Obrecht, J.-P. *Tetrahedron Lett*. **1988**, *29*, 1265.
36. Merino, P.; Lanaspa, A.; Merchan, F. L.; Tejero, T. *Tetrahedron: Asymmetry* **1998**, *9*, 629.
37. Dondoni, A.; Perrone, D. *Synthesis* **1997**, 527.
38. Wen, J. J.; Crews, C. N. *Tetrahedron: Asymmetry* **1998**, *9*, 1855.
39. Andrés, J. M.; Pedrosa, R. *Tetrahedron* **1998**, *54*, 5607.
40. Frigerio, M.; Santagostino, M.; Sputore, S.; Palmisano, G. *J. Org. Chem*. **1995**, *60*, 7272.
41. Meffre, P.; Gauzy, L.; Branquet, E.; Durand, P.; Goffic, F. L. *Tetrahedron* **1996**, *34*, 11215.
42. Johnson, C. K. Report ORNL-5138; Oak Ridge National Laboratory: Oak Ridge, TN, 1976.
43. Sheldrick, G. M. SADABS Program for Absorption Corrections using Bruker CCD Data; University of Göttingen: Germany 1996
44. Sheldrick, G. M. SHELXS-97; University of Göttingen: Germany 1997.