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Chiral diamides as efficient catalytic precursors for the borane-mediated asymmetric reduction of prochiral ketones

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Abstract—Chiral diamides [(2*S*)-5-oxo-2-(arylamino)carbonylpyrrolidines] derived from the abundantly available (*S*)-glutamic/(*S*)-pyroglutamic acids were successfully utilized as effective chiral catalytic precursors in the borane-mediated asymmetric reduction of prochiral ketones in refluxing toluene, to provide the corresponding secondary alcohols with up to 91% enantiomeric purities.

1. Introduction

We have recently reported[1] a simple and convenient methodology for the borane-mediated asymmetric reduction of prochiral ketones employing the chiral diamine,[2] (2*S*)-2-anilinomethylpyrrolidine **1**, as an efficient chiral catalytic source in refluxing toluene thus providing the secondary alcohols with high enantiomeric purities. In continuation of our interest in finding suitable chiral catalysts for the borane-mediated asymmetric reduction of prochiral ketones,[1,3–8] we herein report chiral diamides, (2*S*)-5-oxo-2-(arylamino)carbonylpyrrolidines **2a–i** derived from abundantly available (*S*)-glutamic/(*S*)-pyroglutamic acids (Fig. 1), as possible catalytic sources for the asymmetric

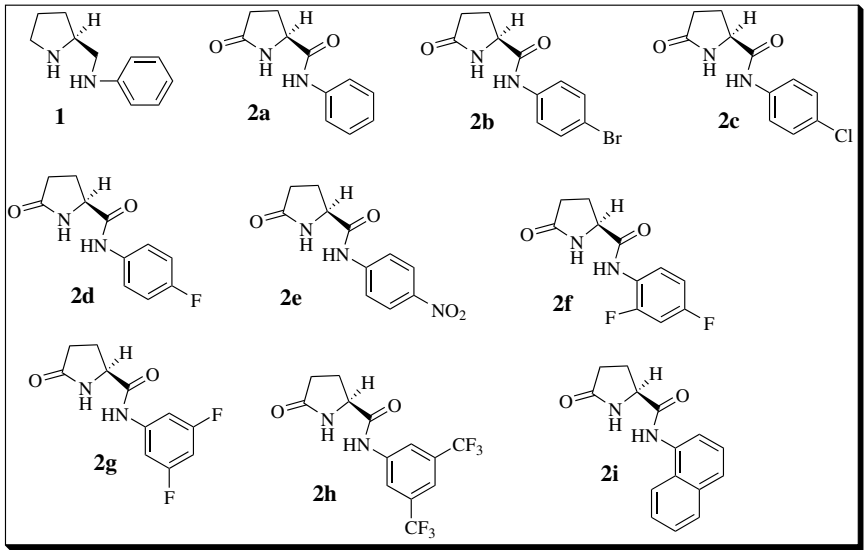

Figure 1.

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reduction of representative prochiral ketones, thus leading to the synthesis of secondary alcohols in up to 91% enantiomeric purities.

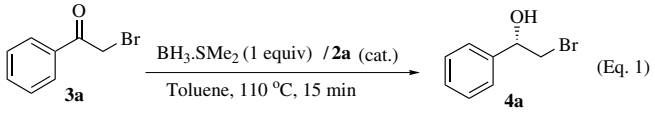
2. Results and discussion

The reduction of amides using $BH_3{\cdot}SMe_2$ (THF) to provide the corresponding amines is a well documented and useful synthetic reaction in organic synthesis.[9]

It therefore occurred to us that the diamide, (2*S*)-5-oxo-2-anilinocarbonylpyrrolidine **2a**, could in principle be reduced in situ by $BH_3{\cdot}SMe_2$ to the corresponding diamine, (2*S*)-2-anilinomethylpyrrolidine **1**, which could then be as such used, without isolation, as a chiral catalytic precursor for the reduction of prochiral ketones to produce the corresponding, enantiomerically enriched secondary alcohols. This would mean that the diamide, (2*S*)-5-oxo-2-anilinocarbonylpyrrolidine **2a**, can itself directly act as the catalytic precursor for the borane-mediated reduction of prochiral ketones to provide the desired enantiomerically enriched secondary alcohols in a one-pot process.

Accordingly we have synthesized (2*S*)-5-oxo-2-anilinocarbonylpyrrolidine **2a**, via the reaction of (*S*)-glutamic acid with aniline according to the literature procedure.[10] We have examined the potential of this diamide **2a**, as a possible chiral catalytic precursor for the borane-mediated reduction of prochiral ketones, first selecting phenacyl bromide **3a** as a substrate. The borane-mediated reduction was performed with varying catalytic amounts of (2*S*)-5-oxo-2-anilinocarbonylpyrrolidine **2a** (2, 5, 7, 10 mol %) in order to determine the minimum amount of catalyst required to obtain the maximum selectivity (Eq. 1) and the enantioselectivities are shown in Table 1. From these results it is clear that enantioselectivities are similar in all the cases.

Table 1. Asymmetric reduction of phenacyl bromide **3a** with varying catalytic amounts of **2a**[a,b]



(Eq. 1)

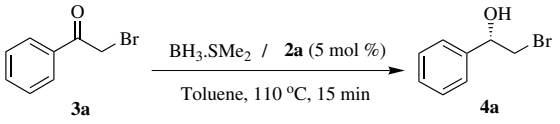
Entry	Catalyst **2a** (mol %)	Yield[c] (%) **4a**	Enantiomeric purity[d] (%) **4a**
1	2	86	87[e]
2	**5**	**88**	**89**
3	7	83	87
4	10	85	88

[a] All reactions were carried out on 1 mM scale of phenacyl bromide **3a** with $BH_3{\cdot}SMe_2$ (1 mM) in the presence of **2a** in refluxing toluene for 15 min.
[b] The absolute configuration was assigned by comparison of the sign of the specific rotation with that of the reported molecule.[11]
[c] Isolated yields of alcohol after purification by column chromatography (silica gel, 5% ethyl acetate in hexanes).
[d] Determined by HPLC analyses using the chiral column, Chiralcel-OD-H.
[e] This reaction was carried out on 2 mM scale of phenacyl bromide **3a** with $BH_3{\cdot}SMe_2$ (2 mM) in the presence of **2a** in refluxing toluene for 15 min.

However, we decided upon using 5 mol % catalyst for further studies as this provide slightly better selectivity (Table 1, entry 2).

With a view to examine the influence of amount of $BH_3{\cdot}SMe_2$ on the enantioselectivity and also to understand the appropriate amount of $BH_3{\cdot}SMe_2$ required to obtain the maximum selectivity, we have carried out the asymmetric reduction of phenacyl bromide **3a** using 5 mol % (2*S*)-5-oxo-2-anilinocarbonylpyrrolidine **2a** with varying amounts (0.9–1.8 equiv with respect to prochiral ketone) of $BH_3{\cdot}SMe_2$. Although there is not much effect on the enantioselectivity with 1–1.8 equiv of $BH_3{\cdot}SMe_2$, 1.4 equiv of $BH_3{\cdot}SMe_2$ provides slightly better enantioselectivity (Eq. 2, Table 2, entry 4).

Table 2. Asymmetric reduction of phenacyl bromide **3a** with varying amounts of the $BH_3{\cdot}SMe_2$[a,b]

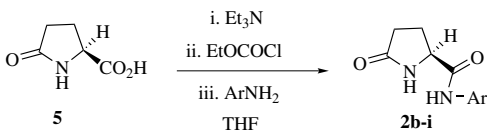


(Eq. 2)

Entry	$BH_3{\cdot}SMe_2$ (equiv)	Yield[c] (%) **4a**	Enantiomeric purity[d] (%) **4a**
1	0.9	84	81
2	1.0	88	89
3	1.2	84	88
4	**1.4**	**86**	**91**
5	1.6	87	89
6	1.8	85	89

[a] All reactions were carried out on 1 mM scale of phenacyl bromide **3a** with $BH_3{\cdot}SMe_2$ in the presence of 5 mol % **2a** in refluxing toluene for 15 min.
[b] The absolute configuration was assigned by comparison of the sign of the specific rotation with that of the reported molecule.[11]
[c] Isolated yields of alcohol after purification by column chromatography (silica gel, 5% ethyl acetate in hexanes).
[d] Determined by HPLC analyses using the chiral column, Chiralcel-OD-H.

Encouraged by these results and with a view for understanding the influence of different substitutions with various steric and electronic requirements on the aromatic (phenyl) ring of the diamide, (2*S*)-5-oxo-2-anilinocarbonylpyrrolidine **2a**, we selected eight diamides **2b–i** to study. The required diamides were conveniently prepared by the reaction of (*S*)-pyroglutamic acid **5** with the corresponding aryl amines according to Eq. 3 (no attempts were made to optimize the yields). The structures of **2b**, **2d**, and **2f** were also established by the single crystal X-ray data (Figs. 2–4).



(Eq. 3)

Ar = 4-Bromophenyl **2b**; 4-Chlorophenyl **2c**; 4-Fluorophenyl **2d**; 4-Nitrophenyl **2e**; 2,4-Difluorophenyl **2f**; 3,5-Difluorophenyl **2g**; 3,5-Bis(trifluoromethyl)phenyl **2h**; 1-Naphthyl **2i**

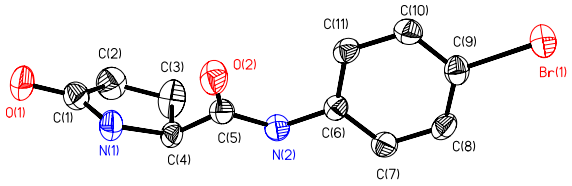


Figure 2. ORTEP diagram of **2b** (hydrogen atoms were omitted for clarity).

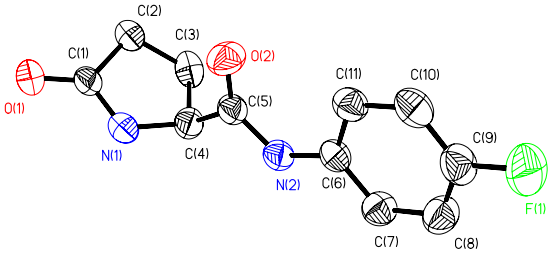


Figure 3. ORTEP diagram of **2d** (hydrogen atoms were omitted for clarity).

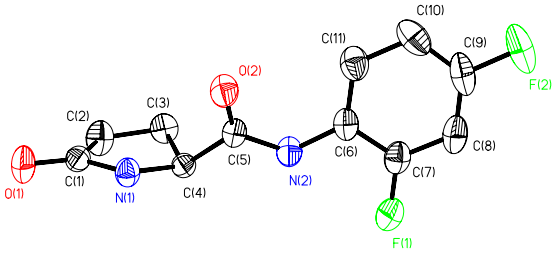


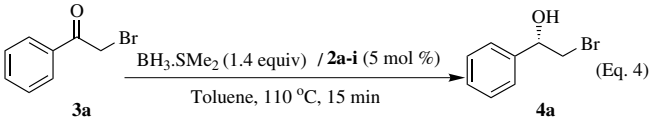
Figure 4. ORTEP diagram of **2f** (hydrogen atoms were omitted for clarity).

With a view to examining the chiral catalytic potential of these diamides, we selected three representative prochiral ketones, phenacyl bromide **3a**, phenacyl chloride **3b**, and acetophenone **3c**, as substrates in the borane-mediated asymmetric reduction. Thus we first carried out the asymmetric reduction of phenacyl bromide **3a** in the presence of 5 mol % chiral diamide **2b–i** with $BH_3{\cdot}SMe_2$ (1.4 equiv) in refluxing toluene for 15 min. The corresponding secondary alcohol, (*S*)-2-bromo-1-phenylethanol **4a** was obtained with 68–91% enantiomeric purities (Eq. 4, Table 3, entries 2–9).

Similar borane-mediated reductions of phenacyl chloride **3b** and acetophenone **3c** using chiral diamides, **2a–i**, as chiral catalytic sources provided (*S*)-2-chloro-1-phenylethanol **4b** and (*R*)-1-phenylethanol **4c** in 67–89% (Eq. 5, Table 4, entries 1–9) and 53–83% (Eq. 6, Table 5, entries 1–9) enantiomeric excesses, respectively.

These results to some extent suggest that the substitution on the phenyl group [of (2*S*)-5-oxo-2-anilinocarbonylpyrrolidine **2a**] does not play any significant role with regards to the chiral induction. However, the chiral diamide (2*S*)-5-oxo-2-(1-naphthylamino)carbonylpyrrolidine **2i** with a 1-naphthyl moiety provides inferior selectivities in all these cases in comparison with other diamides **2a–h**. The lower

Table 3. Asymmetric reduction of phenacyl bromide **3a** using the chiral diamides **2a–i** as chiral catalytic sources[a,b]

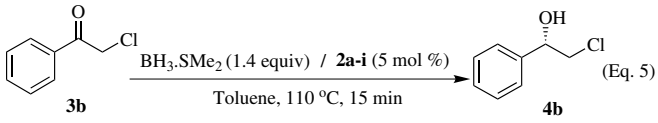


3a 4a

Entry	Chiral diamide	Yield[c] (%) **4a**	Enantiomeric purity[d] (%) **4a**
1	**2a**	86	91
2	**2b**	87	90
3	**2c**	86	91
4	**2d**	82	90
5	**2e**	88	88
6	**2f**	83	89
7	**2g**	84	88
8	**2h**	83	90
9	**2i**	84	68

[a] All reactions were carried out on 1 mM scale of phenacyl bromide **3a** with $BH_3{\cdot}SMe_2$ (1.4 mM) in the presence of 5 mol % **2a–i** in refluxing toluene for 15 min.
[b] The absolute configuration was assigned by comparison of the sign of the specific rotation with that of the reported molecule.[11]
[c] Isolated yields of alcohol after purification by column chromatography (silica gel, 5% ethyl acetate in hexanes).
[d] Determined by HPLC analyses using the chiral column, Chiralcel-OD-H.

Table 4. Asymmetric reduction of phenacyl chloride (**3b**) using the chiral diamides **2a–i** as chiral catalytic sources[a,b]



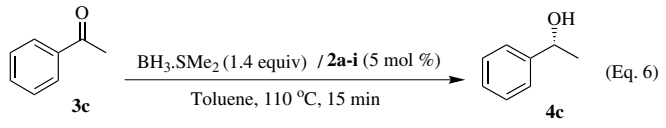
3b 4b

Entry	Chiral diamide	Yield[c] (%) **4b**	Enantiomeric purity[d] (%) **4b**
1	**2a**	83	88
2	**2b**	82	87
3	**2c**	84	89
4	**2d**	80	88
5	**2e**	85	86
6	**2f**	82	87
7	**2g**	83	87
8	**2h**	87	89
9	**2i**	81	67

[a] All reactions were carried out on 1 mM scale of phenacyl chloride **3b** with $BH_3{\cdot}SMe_2$ (1.4 mM) in the presence of 5 mol % **2a–i** in refluxing toluene for 15 min.
[b] The absolute configuration was assigned by comparison of the sign of the specific rotation with that of the reported molecule.[11]
[c] Isolated yields of alcohol after purification by column chromatography (silica gel, 5% ethyl acetate in hexanes).
[d] Determined by HPLC analyses using the chiral column, Chiralcel-OD-H.

enantioselectivity in the case of **2i** might be attributed to the competitive non-catalytic reduction of prochiral ketone with $BH_3{\cdot}SMe_2$ as the sterically bulky 1-naphthyl moiety may to some extent disfavor the effective coordination of prochiral ketone with the boron of the diazaborolidine (which might be forming in situ) (Scheme 1).

Table 5. Asymmetric reduction of acetophenone **3c** using the chiral diamides **2a–i** as chiral catalytic sources[a,b]



Entry	Chiral diamide	Yield[c] (%) **4c**	Enantiomeric purity[d] (%) **4c**
1	**2a**	76	82
2	**2b**	74	81
3	**2c**	72	83
4	**2d**	74	79
5	**2e**	76	77
6	**2f**	74	78
7	**2g**	75	82
8	**2h**	73	81
9	**2i**	77	53

[a] All reactions were carried out on 1 mM scale of acetophenone **3c** with $BH_3{\cdot}SMe_2$ (1.4 mM) in the presence of 5 mol % **2a–i** in refluxing toluene for 15 min.

[b] The absolute configuration was assigned by comparison of the sign of the specific rotation with that of the reported molecule.[12]

[c] Isolated yields of alcohol after purification by column chromatography (silica gel, 5% ethyl acetate in hexanes).

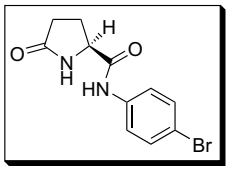
[d] Determined by HPLC analyses using the chiral column, Chiralcel-OD-H.

3. Conclusion

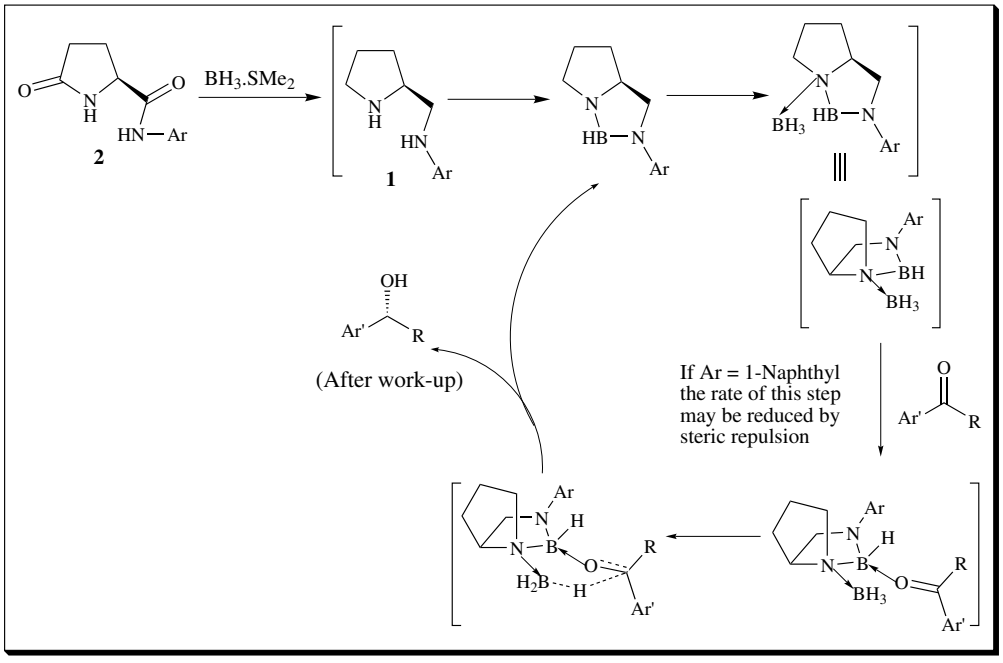
We have successfully demonstrated the potential of the chiral diamides, (2*S*)-5-oxo-2-(arylamino)carbonylpyrrolidines **2a–i**, derived from the abundantly available (*S*)-glutamic/(*S*)-pyroglutamic acids, as possible catalytic sources in the borane-mediated asymmetric reduction of prochiral ketones.

4. Experimental

4.1. Representative procedure[13a] for synthesis of (2*S*)-5-oxo-2-(4-bromoanilino)carbonylpyrrolidine 2b[13b]



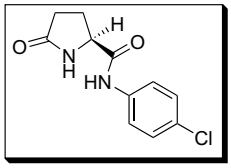
To a stirred mixture of (*S*)-pyroglutamic acid (5 mM, 0.6455 g) in THF (10 mL) was added a solution of Et_3N (5 mM, 0.7 mL) in THF (5 mL) at −15 °C. After stirring for 15 min, a solution of ethyl chloroformate (5.5 mM, 0.53 mL) in THF (5 mL) was added slowly at −15 °C and the reaction mixture was stirred for 15 min. A solution of 4-bromoaniline (5 mM, 0.86 g) in THF (5 mL) was then added at the same temperature to the above reaction mixture and stirred at 0 °C for 1 h followed by 14 h at room temperature. The solvent was removed under reduced pressure and the residue, thus obtained, was diluted with EtOAc (150 mL) and saturated aqueous $NaHCO_3$ (30 mL). Organic layer was separated and washed with saturated aqueous $NaHCO_3$ (3 × 30 mL) and dried over anhydrous Na_2SO_4. Solvent was removed under reduced pressure and the residue, thus obtained, was purified by column chromatography (silica gel, EtOAc) to provide the desired (2*S*)-5-oxo-2-(4-bromoanilino)carbonylpyrrolidine **2b** as a white solid (0.75 g) in 53% yield. Mp: 212–214 °C (lit.[13b] 225–227 °C); $[\alpha]_D^{25} = +13.0$ (*c* 1.09, MeOH); IR (KBr): *ν* 3500–3000 (multiple bands), 1693, 1668 cm^{-1}; ^1H NMR [400 MHz ($CDCl_3$–DMSO-d_6 = 4:1)]: *δ* 2.06–2.49 (m, 4H), 4.21–4.30 (m, 1H), 7.39 (d, 2H, *J* = 8.8 Hz), 7.59 (d, 2H, *J* = 8.8 Hz), 7.84 (s, 1H), 9.95



Scheme 1.

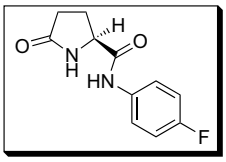
(s, 1H); ^{13}C NMR [50 MHz ($CDCl_3$–DMSO-d_6 = 4:1)]: δ 24.51, 28.70, 56.31, 115.25, 120.78, 130.65, 136.94, 170.24, 177.47; LC–MS (m/z): 283 $(M+H)^+$, 285 $(M+2+H)^+$; Anal. Calcd for $C_{11}H_{11}BrN_2O_2$: C, 46.66; H, 3.92; N, 9.89. Found: C, 46.68; H, 3.92; N, 9.98.

4.2. (2*S*)-5-Oxo-2-(4-chloroanilino)carbonylpyrrolidine 2c



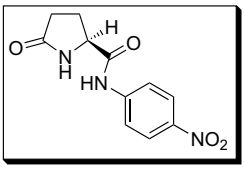
Time:[14] 14 h; yield: 50%; mp: 194–196 °C; $[\alpha]_D^{25} = +14.1$ (c 1.04, MeOH); IR (KBr): ν 3400–3000 (multiple bands), 1701, 1660 cm^{-1}; ^{1}H NMR [400 MHz ($CDCl_3$–DMSO-d_6 = 4:1)]: δ 2.08–2.49 (m, 4H), 4.23–4.34 (m, 1H), 7.25 (d, 2H, J = 8.6 Hz), 7.64 (d, 2H, J = 8.6 Hz), 7.84 (s, 1H), 9.93 (s, 1H); ^{13}C NMR [50 MHz ($CDCl_3$–DMSO-d_6 = 4:1)]: δ 24.24, 28.37, 55.93, 120.12, 127.06, 127.37, 136.28, 170.00, 177.00; LC–MS (m/z): 239 $(M+H)^+$, 241 $(M+2+H)^+$; Anal. Calcd for $C_{11}H_{11}ClN_2O_2$: C, 55.36; H, 4.65; N, 11.74. Found: C, 55.17; H, 4.64; N, 11.76.

4.3. (2*S*)-5-Oxo-2-(4-fluoroanilino)carbonylpyrrolidine 2d



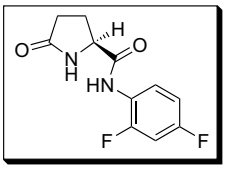
Time:[14] 24 h; yield: 45%; mp: 178–180 °C; $[\alpha]_D^{25} = +14.0$ (c 1.08, MeOH); IR (KBr): ν 3450–3150 (multiple bands), 1693, 1666 cm^{-1}; ^{1}H NMR [400 MHz ($CDCl_3$–DMSO-d_6 = 4:1)]: δ 2.18–2.52 (m, 4H), 4.22–4.34 (m, 1H), 6.93–7.04 (m, 2H), 7.55–7.71 (m, 3H), 9.65 (s, 1H); ^{13}C NMR [100 MHz ($CDCl_3$–DMSO-d_6 = 4:1)]: δ 24.63, 28.80, 56.37, 114.40 (d, J = 21.8 Hz), 120.86 (d, J = 8.0 Hz), 133.82 (d, J = 2.9 Hz), 158.09 (d, J = 241.5 Hz), 170.11, 177.65; LC–MS (m/z): 223 $(M+H)^+$; Anal. Calcd for $C_{11}H_{11}FN_2O_2$: C, 59.45; H, 4.99; N, 12.61. Found: C, 59.52; H, 5.01; N, 12.52.

4.4. (2*S*)-5-Oxo-2-(4-nitroanilino)carbonylpyrrolidine 2e



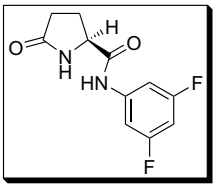
Time:[14] 24 h; yield: 38%; mp: 214–216 °C; $[\alpha]_D^{25} = +21.0$ (c 0.60, MeOH); IR (KBr): ν 3400–3000 (multiple bands), 1707, 1682 cm^{-1}; ^{1}H NMR [400 MHz ($CDCl_3$–DMSO-d_6 = 4:1)]: δ 2.16–2.54 (m, 4H), 4.31–4.37 (m, 1H), 7.79 (s, 1H), 7.88 (d, 2H, J = 9.2 Hz), 8.15 (d, 2H, J = 9.2 Hz), 10.37 (s, 1H); ^{13}C NMR [50 MHz ($CDCl_3$–DMSO-d_6 = 4:1)]: δ 24.34, 28.43, 56.11, 118.27, 123.55, 141.83, 143.83, 170.88, 177.22; LC–MS (m/z): 248 $(M-H)^+$; Anal. Calcd for $C_{11}H_{11}N_3O_4$: C, 53.01; H, 4.45; N, 16.86. Found: C, 53.15; H, 4.44; N, 16.80.

4.5. (2*S*)-5-Oxo-2-(2,4-difluoroanilino)carbonylpyrrolidine 2f



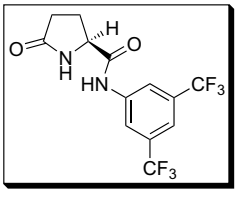
Time:[14] 24 h; yield: 44%; mp: 138–140 °C; $[\alpha]_D^{25} = +12.9$ (c 1.02, MeOH); IR (KBr): ν 3450–3100 (multiple bands), 1695, 1655 cm^{-1}; ^{1}H NMR [400 MHz ($CDCl_3$–DMSO-d_6 = 4:1)]: δ 2.18–2.55 (m, 4H), 4.34–4.43 (m, 1H), 6.82–6.96 (m, 2H), 7.72 (s, 1H), 7.89–8.00 (m, 1H), 9.36 (s, 1H); ^{13}C NMR [100 MHz ($CDCl_3$–DMSO-d_6 = 4:1)]: δ 24.19, 28.11, 55.14, 102.48 (dd, J = 24.0 and 25.8 Hz), 109.54 (dd, J = 3.6 and 21.1 Hz), 120.93 (dd, J = 3.2 and 11.3 Hz), 124.02 (dd, J = 2.2 and 9.0 Hz), 152.80 (dd, J = 12.4 and 247.3 Hz), 157.57 (dd, J = 10.9 and 244.0 Hz), 170.35, 176.84; LC–MS (m/z): 239 $(M-H)^+$; Anal. Calcd for $C_{11}H_{10}F_2N_2O_2$: C, 55.00; H, 4.20; N, 11.66. Found: C, 55.06; H, 4.21; N, 11.73.

4.6. (2*S*)-5-Oxo-2-(3,5-difluoroanilino)carbonylpyrrolidine 2g



Time:[14] 24 h; yield: 35%; mp: 198–200 °C; $[\alpha]_D^{25} = +13.4$ (c 1.08, MeOH); IR (KBr): ν 3400–3170 (multiple bands), 1697, 1676 cm^{-1}; ^{1}H NMR [400 MHz ($CDCl_3$–DMSO-d_6 = 4:1)]: δ 2.16–2.53 (m, 4H), 4.23–4.32 (m, 1H), 6.49–6.59 (m, 1H), 7.27–7.37 (m, 2H), 7.65 (s, 1H), 10.00 (s, 1H); ^{13}C NMR [100 MHz ($CDCl_3$–DMSO-d_6 = 4:1)]: δ 24.40, 28.54, 56.18, 97.72 (t, J = 25.5 Hz), 101.73 (dd, J = 8.7 and 20.7 Hz), 140.09 (t, J = 13.1 Hz), 161.81 (dd, J = 14.5 and 243.7 Hz), 170.60, 177.29; LC–MS (m/z): 241 $(M+H)^+$; Anal. Calcd for $C_{11}H_{10}F_2N_2O_2$: C, 55.00; H, 4.20; N, 11.66. Found: C, 55.03; H, 4.18; N, 11.76.

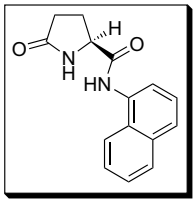
4.7. (2*S*)-5-Oxo-2-[3,5-bis(trifluoromethyl)anilino]carbonylpyrrolidine 2h



Time:[14] 24 h; yield: 45%; mp: 182–184 °C; $[\alpha]_D^{25} = +4.9$ (c 2.09, MeOH); IR (KBr): ν 3400–3000 (multiple bands), 1716, 1674 cm^{-1}; ^{1}H NMR [400 MHz ($CDCl_3$–DMSO-

$d_6 = 4{:}1$)]: δ 2.20–2.61 (m, 4H), 4.27–4.33 (m, 1H), 7.54 (s, 1H), 7.61 (s, 1H), 8.27 (s, 2H), 10.26 (s, 1H); ^{13}C NMR [100 MHz ($CDCl_3$–DMSO-$d_6 = 4{:}1$)]: δ 24.67, 28.73, 56.58, 115.85 (sept, $J = 3.6$ Hz), 118.87 (unresolved quartet), 122.49 (q, $J = 270.6$ Hz), 130.89 (q, $J = 32.7$ Hz), 139.64, 171.20, 177.65; LC–MS (m/z): 341 $(M+H)^+$; Anal. Calcd for $C_{13}H_{10}F_6N_2O_2$: C, 45.89; H, 2.96; N, 8.23. Found: C, 45.71; H, 2.98; N, 8.22.

4.8. (2*S*)-5-Oxo-2-(1-naphthylamino)carbonylpyrrolidine 2i



Time:[14] 24 h; yield: 36%; mp: 198–200 °C; $[\alpha]_D^{25} = +15.0$ (c 1.09, MeOH); IR (KBr): ν 3400–3150 (multiple bands), 1722, 1670 cm^{-1}; ^{1}H NMR [400 MHz ($CDCl_3$–DMSO-$d_6 = 4{:}1$)]: δ 2.21–2.61 (m, 4H), 4.42–4.54 (m, 1H), 7.42–7.55 (m, 3H), 7.71 (d, 2H, $J = 7.8$ Hz), 7.83–7.92 (m, 2H), 8.01–8.07 (m, 1H), 9.75 (s, 1H); ^{13}C NMR [50 MHz ($CDCl_3$–DMSO-$d_6 = 4{:}1$)]: δ 24.65, 28.70, 56.04, 121.00, 121.44, 124.52, 124.93, 125.05, 127.28, 131.82, 133.03, 170.85, 177.33; LC–MS (m/z): 253 $(M-H)^+$. Anal. Calcd for $C_{15}H_{14}N_2O_2$: C, 70.85; H, 5.55; N, 11.02. Found: C, 70.66; H, 5.55; N, 11.05.

4.9. Crystal data: (2*S*)-5-oxo-2-(4-bromoanilino)carbonylpyrrolidine 2b

Empirical formula, $C_{11}H_{11}BrN_2O_2$; formula weight, 283.13; colorless, needle crystal; crystal dimensions, $0.18 \times 0.10 \times 0.10$ mm^3; monoclinic, lattice type, primitive; $a = 5.1189(6)$ Å, $b = 7.6470(9)$ Å, $c = 14.2151(16)$ Å; $\alpha = 90.00$; $\beta = 97.717(2)$; $\gamma = 90.00$; $V = 551.40(11)$ $Å^3$; space group, $P2_1$ (International Table No. 4); $Z = 2$; $D_{calcd} = 1.705$ g/cm^3; $F_{000} = 284$; λ(Mo K_α) = 0.71073 Å; R ($I \geqslant 2\sigma_1$) = 0.0360; $wR^2 = 0.0656$. Detailed X-ray crystallographic data are available from the Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK (CCDC No. 636930).

4.10. (2*S*)-5-Oxo-2-(4-fluoroanilino)carbonylpyrrolidine 2d

Empirical formula, $C_{11}H_{11}FN_2O_2$; formula weight, 222.22; colorless, block crystal; crystal dimensions, $0.38 \times 0.26 \times 0.26$ mm^3; monoclinic, lattice type, primitive; $a = 4.9456(8)$ Å, $b = 9.8911(15)$ Å, $c = 10.4695(16)$ Å; $\alpha = 90.00$; $\beta = 92.151(2)$; $\gamma = 90.00$; $V = 511.78(14)$ $Å^3$; space group, $P2_1$ (International Table No. 4); $Z = 2$; $D_{calcd} = 1.442$ g/cm^3; $F_{000} = 232$; λ(Mo K_α) = 0.71073 Å; R ($I \geqslant 2\sigma_1$) = 0.0373; $wR^2 = 0.0906$. Detailed X-ray crystallographic data are available from the Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK (CCDC No. 636931).

4.11. (2*S*)-5-Oxo-2-(2,4-difluoroanilino)carbonylpyrrolidine 2f

Empirical formula, $C_{11}H_{10}F_2N_2O_2$; formula weight, 240.21; colorless, block crystal; crystal dimensions, $0.42 \times 0.32 \times 0.18$ mm^3; orthorhombic, lattice type, primitive; $a = 4.8924(6)$ Å, $b = 8.9735(11)$ Å, $c = 23.921(3)$ Å; $\alpha = 90.00$; $\beta = 90.00$; $\gamma = 90.00$; $V = 1050.2(2)$ $Å^3$; space group, $P2_12_12_1$ (International Table No. 19); $Z = 4$; $D_{calcd} = 1.519$ g/cm^3; $F_{000} = 496$; λ(Mo K_α) = 0.71073 Å; R ($I \geqslant 2\sigma_1$) = 0.0670; $wR^2 = 0.1429$. Detailed X-ray crystallographic data are available from the Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK (CCDC No. 636932).

4.12. Asymmetric reduction of phenacyl bromide 3a: synthesis of (*S*)-2-bromo-1-phenylethanol 4a: representative procedure

To a stirred mixture of (2*S*)-5-oxo-2-anilinocarbonylpyrrolidine **2a** (0.05 mM, 10.2 mg) in toluene (5 mL) was added $BH_3{\cdot}SMe_2$ (1.4 mM, 1.4 mL, 1 M solution in toluene) at room temperature and the reaction mixture was heated under reflux for 15 min. A solution of phenacyl bromide **3a** (1 mM, 199 mg) in toluene (2 mL) was added slowly dropwise and heating was continued under reflux for further 15 min. The reaction mixture was then cooled to room temperature and quenched with MeOH. Solvent was removed under reduced pressure and the residue thus obtained was purified by column chromatography (silica gel, 5% ethyl acetate in hexanes) to provide the desired (*S*)-2-bromo-1-phenylethanol **4a** in 86% (173 mg) yield as a colorless oil.

All alcohols **4a**–**c** are already known in the literature.[11,12] In fact, we have also prepared alcohols **4a**–**c** and reported their spectral data.[6,8] The present spectral data (IR, ^{1}H and ^{13}C NMR) of **4a**–**c** are in agreement with the earlier data.

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13. (a) The chiral diamides **2b–i** were synthesized following a similar literature procedure for the preparation of 1-(*tert*-butoxycarbonyl)indoline-2-carboxamides with some modification;[2b] (b) The compound **2b** was known and the spectral data were reported.[15] Our spectral data are in agreement with the reported data.
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