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Diastereoselective cycloadditions of nitrilimines to enantiopure acrylamides

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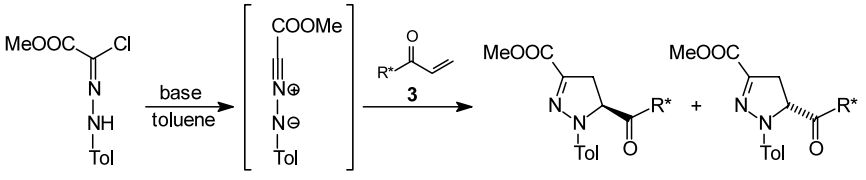
Abstract—The diastereoselective cycloaddition of the nitrilimine **2** with enantiopure acrylamides **3** was exploited to obtain enantiopure 4,5-dihydropyrazoles **4** and **5**. Basic hydrolysis of the cycloadducts gave the dicarboxy derivatives **6** and **7** or **8** and **9**, which are of potential interest as new chiral building blocks.

1. Introduction

The field of stereoselective 1,3-dipolar cycloadditions has grown in importance over the past decade, as is testified by a number of authoritative reviews[1] and books.[2] In particular, the cycloaddition reactions of nitrile oxides[3] and nitrones[4] have gained popularity among organic chemists due to the array of latent functionalities presented by the cycloadducts.[5] Despite the utility of enantiopure pyrazolines in organic synthesis[6] and some interesting applications of related products,[7] the cycloadditions of nitrilimines has not been applied for pyrazoline synthesis since, as recently stated in the Gothelf and Jørgensen review, ''only very few studies have been performed in the field of asymmetric 1,3-dipolar cycloadditions involving nitrile imines'' (sic).[1a]

2. Results and discussion

To gain better insights about this methodology, we decided to investigate the behaviour of *N*-(4-methyl)phenyl-*C*-methoxycarbonyl nitrilimine **2** towards a series of enantiopure acrylamides **3** (Scheme 1). The latter, which were synthesised from the appropriate chiral auxiliary according to literature procedures,[8] were submitted to cycloadditions with hydrazonoyl chloride **1**[9] in dry toluene and in the



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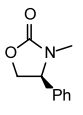
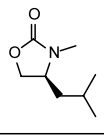
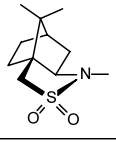
R*					

Scheme 1.

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presence of a suitable base. The reaction times and bases, as well as yields and diastereoisomeric ratio data, are collected in Table 1. All reactions were completely regioselective, giving only the 5-aminocarbonyl-4,5-dihydropyrazoles **4** and **5**, whose spectroscopic data (^{1}H and ^{13}C NMR) are in full agreement with those of structurally similar 5-substituted-4,5-dihydropyrazoles.[10]

The absolute configuration of the newly formed stereocentre of the major diastereoisomers **4a**[11] and **4c** (Fig. 1) was unequivocally determined by means of X-ray diffraction analyses; both cycloadducts had the (5*S*)-configuration at the 4,5-dihydropyrazole ring. Chemical correlation experiments allowed us to assign the (5*S*)-absolute configuration to all major cycloadducts **4** and the (5*R*)-configuration to the minor products **5** (Scheme 2). Basic hydrolysis of **4a** and **4b** gave the same dicarboxy derivative **6**, while hydrolysis of **5a** and **5b** gave diastereoisomers **7**. Similar treatment of compounds **4c**–**e** led to cleavage of the auxiliary, giving the 3,5-dicarboxy-4,5-dihydropyrazole (*S*)-(+)-**8** and allowing the recovery of the chiral auxiliary (see Section 3). Enantiomer (*R*)-(−)-**9** was obtained by treatment of compounds **5c**–**e** with base. As far as diastereoselectivity of the cycloaddition is concerned, it can be seen from Table 1 that the diastereomeric ratio ranges between 58:42 and 83:17 and depends upon the chiral auxiliary connected to the α,β-unsaturated dipolarophile. The best results, obtained with acrylamides **3c** (R* = (4*S*)-(+)-phenyl-2-oxazolidinone) and **3e** (R* = (1*S*,2*R*)-(−)-2,10-camphorsultam), possibly reflect the lower conformational flexibility of the latter two substrates compared to **3a**, **3b** and **3d**. Finally, the base (chiral or achiral) and the presence of salts such as LiCl and $(AcO)_2Mg$, which were investigated as potential complexing additives, exerted little or no influence on the diastereoselectivity of the cycloaddition.

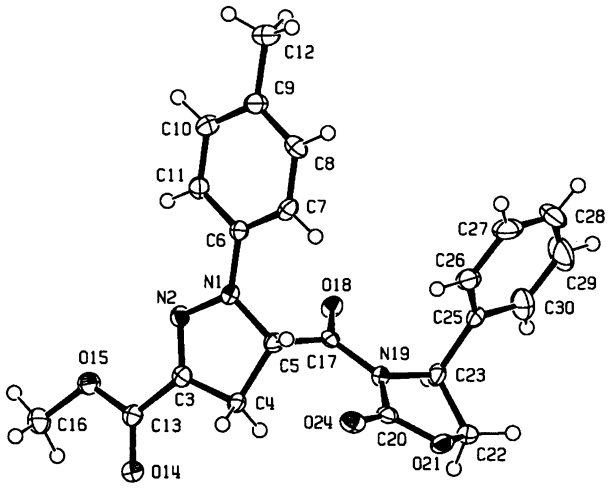
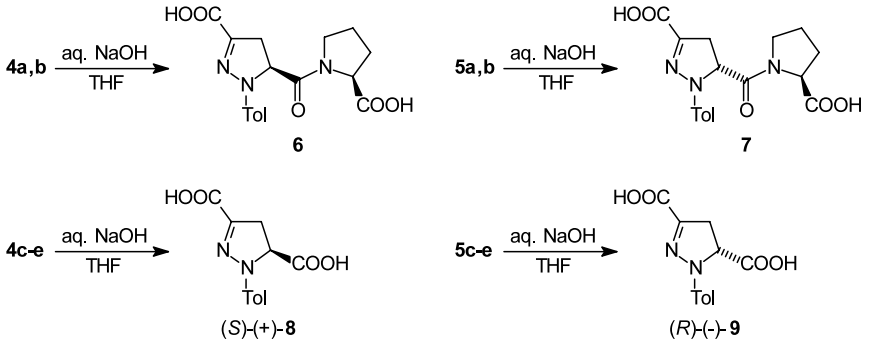


Figure 1. ORTEP*III* plot of **4c** at 90 K with the crystallographic numbering scheme. Ellipsoids at 50% probability level. H atoms not to scale.

Table 1. Cycloadditions between nitrilimine **2** and enantiopure acrylamides **3** in toluene[a]

Entry	Acrylamide	Time (h)	Base (equiv.)	Additive (equiv.)	**4**+**5** (%)[b]	**4**:**5**[c]
1	**3a**	48	Et_3N (5)	—	50	67:33
2	**3a**	45	Et_3N (2)	LiCl (2.5)	55	65:35
3	**3a**	45	Et_3N (1)	$(AcO)_2Mg$ (2)	49	67:33
4	**3a**	23	AcOAg (2)	—	70	67:33
5	**3a**	72	(−)-Sparteine (1.5)	—	25	68:32
6	**3b**	42	Et_3N (5)	—	82	68:32
7	**3b**	47	Et_3N (2)	LiCl (2.5)	71	64:36
8	**3b**	70	Et_3N (1)	$(AcO)_2Mg$ (2)	62	63:37
9	**3b**	24	AcOAg (2)	—	85	67:33
10	**3b**	72	(−)-Sparteine (1.5)	—	32	63:37
11	**3c**	27	Et_3N (5)	—	58	80:20
12	**3c**	48	Et_3N (2)	LiCl (2.5)	54	80:20
13	**3c**	72	Et_3N (1)	$(AcO)_2Mg$ (2)	57	75:25
14	**3c**	16	AcOAg (2)	—	64	80:20
15	**3c**	72	(−)-Sparteine (1.5)	—	45	80:20
16	**3d**	48	Et_3N (5)	—	66	61:39
17	**3d**	72	Et_3N (2)	LiCl (2.5)	36	62.38
18	**3d**	72	Et_3N (1)	$(AcO)_2Mg$ (2)	31	60:40
19	**3d**	22	AcOAg (2)	—	60	58:42
20	**3d**	48	(−)-Sparteine (1.5)	—	28	58:42
21	**3e**	30	Et_3N (5)	—	80	80:20
22	**3e**	43	Et_3N (2)	LiCl (2.5)	72	68:32
23	**3e**	72	Et_3N (1)	$(AcO)_2Mg$ (2)	54	75:25
24	**3e**	20	AcOAg (2)	—	62	83:17
25	**3e**	67	(−)-Sparteine (1.5)	—	41	78:22

[a] At room temperature.
[b] Isolated yields.
[c] Deduced from ^{1}H NMR analysis of crude reaction product.



Scheme 2.

3. Experimental

Melting points were determined with a Büchi apparatus in open tubes and are uncorrected. IR spectra were recorded with a Perkin–Elmer 1725 X spectrophotometer. Mass spectra were determined with a VG-70EQ apparatus. ^{1}H NMR spectra were taken with a Bruker AC 300 or a Bruker AMX 300 instrument (in $CDCl_3$ solutions at room temperature). Chemical shifts are given as ppm from tetramethylsilane and J values are given in Hz. Optical rotations, $[\alpha]_D^{25}$, were recorded on a Perkin–Elmer Model 241 polarimeter at the sodium D line.

3.1. General procedure for the cycloaddition between hydrazonoyl chloride 1 and enantiopure acrylamides 3

A solution of **1** (1.70 g, 7.5 mmol) and **3** (8.0 mmol) in dry toluene (100 mL) was treated with the base and additive (see Table 1) under stirring at room temperature. After the time indicated in Table 1, the undissolved material was filtered off and the solvent was evaporated under reduced pressure. The residue was chromatographed on a silica gel column with 2:1 ethyl acetate–hexane. First fractions contained the major cycloadducts **4**, further elution gave minor cycloadducts **5**. Subsequent crystallisation with diisopropyl ether gave analytically pure **4** and **5**.

Compound **4a**: mp 95°C; $[\alpha]_D^{25}=-180.0$ ($CHCl_3$, $c=0.25$); IR: (Nujol) 1740, 1695 (cm^{-1}); ^{1}H NMR δ: ($CDCl_3$) 1.80–2.20 (4H, m), 2.32 (3H, s), 3.23 (1H, dd, J 18.0, 7.0), 3.45–3.60 (3H, m), 3.70 (3H, s), 3.84 (3H, s), 4.50 (1H, dd, J 8.2, 4.8), 4.96 (1H, dd, J 13.7, 7.0), 6.90–7.10 (4H, m); ^{13}C NMR δ: ($CDCl_3$) 20.6 (q), 24.7 (t), 28.5 (t), 36.5 (t), 46.4 (t), 52.2 (q), 52.3 (q), 59.6 (d), 63.2 (d), 114.2 (d), 129.3 (d), 131.4 (s), 137.0 (s), 140.2 (s), 162.6 (s), 168.2 (s), 172.0 (s); MS: m/z 373 (M$^+$). Anal. calcd for $C_{19}H_{23}N_3O_5$: C, 61.11; H, 6.21; N, 11.25. Found: C, 61.07; H, 6.17; N, 11.30%.

Compound **4b**: mp 75°C; $[\alpha]_D^{25}=-248.0$ ($CHCl_3$, $c=0.24$); IR: (Nujol) 1740, 1660 (cm^{-1}); ^{1}H NMR δ: ($CDCl_3$) 1.90–2.00 (4H, m), 2.26 (3H, s), 3.20 (1H, dd, J 17.8, 6.7), 3.50–3.60 (3H, m), 3.85 (3H, s), 4.56 (1H, dd, J 8.1, 4.7), 4.92 (1H, dd, J 12.9, 6.7), 5.08 (1H, d, J 16.7), 5.14 (1H, d, J 16.7), 6.90–7.30 (9H, m); ^{13}C NMR δ: ($CDCl_3$) 20.4 (q), 24.3 (t), 29.2 (t), 36.8 (t), 47.3 (t), 52.6 (q), 53.2 (q), 60.2 (d), 63.2 (d), 72.1 (t), 114.3 (d), 128.0–129.3, 132.1 (s), 134.7 (s), 136.8 (s), 140.9 (s), 161.2 (s), 168.9 (s), 170.0 (s); MS: m/z 449 (M$^+$). Anal. calcd for $C_{25}H_{27}N_3O_5$: C, 66.80; H, 6.05; N, 9.35. Found: C, 66.84; H, 6.08; N, 9.39%.

Compound **4c**: mp 87°C; $[\alpha]_D^{25}=+221.4$ ($CHCl_3$, $c=0.11$); IR: (Nujol) 1780, 1700 (cm^{-1}); ^{1}H NMR δ: ($CDCl_3$) 2.32 (3H, s), 2.96 (1H, dd, J 18.3, 6.3), 3.62 (1H, dd, J 18.3, 14.0), 3.79 (3H, s), 4.32 (1H, dd, J 9.1, 3.7), 4.68 (1H, dd, J 9.1, 8.7), 5.38 (1H, dd, J 8.7, 3.7), 6.13 (1H, dd, J 14.0, 6.3), 6.90–7.30 (9H, m); ^{13}C NMR δ: ($CDCl_3$) 20.6 (q), 37.0 (t), 52.2 (d), 57.5 (d), 62.1 (q), 70.6 (t), 114.2 (d), 125.7–129.9, 131.4 (s), 136.7 (s), 138.0 (s), 140.0 (s), 153.6 (s), 162.5 (s), 167.9 (s); MS: m/z 407 (M$^+$). Anal. calcd for $C_{22}H_{21}N_3O_5$: C, 64.86; H, 5.20; N, 10.31. Found: C, 64.90; H, 5.24; N, 10.35%.

Compound **4d**: mp 127°C; $[\alpha]_D^{25}=+356.0$ ($CHCl_3$, $c=0.19$); IR: (Nujol) 1788, 1700 (cm^{-1}); ^{1}H NMR δ: ($CDCl_3$) 0.88 (3H, d, J 7.0), 0.93 (3H, d, J 7.0), 1.30–1.60 (3H, m), 2.24 (3H, s), 3.08 (1H, dd, J 18.4, 5.9), 3.62 (1H, dd, J 18.4, 13.9), 3.83 (3H, s), 4.04–4.38 (3H, m), 6.03 (1H, dd, J 13.9, 5.9), 6.90–7.10 (4H, m); ^{13}C NMR δ: ($CDCl_3$) 20.6 (q), 21.8 (q), 23.6 (q), 25 1 (d), 36.7 (t), 41.3 (t), 52.2 (d), 53.9 (d), 62.2 (d), 69.2 (t), 114.2 (d), 129.8 (d), 131.3 (s), 136.9 (s), 139.3 (s), 154.1 (s), 162.7 (s), 168.9 (s); MS: m/z 387 (M$^+$). Anal. calcd for $C_{20}H_{25}N_3O_5$: C, 62.00; H, 6.50; N, 10.85. Found: C, 62.05; H, 6.54; N, 10.92%.

Compound **4e**: mp 85°C; $[\alpha]_D^{25}=-8.6$ ($CHCl_3$, $c=1.85$); IR: (Nujol) 1730, 1695 (cm^{-1}); ^{1}H NMR δ: ($CDCl_3$) 0.94 (3H, s), 1.42 (3H, s), 1.43–1.95 (7H, m), 2.43 (3H, s), 3.50 (1H, dd, J 18.4, 6.9), 3.56 (1H, d, J 13.9), 3.58 (1H, dd, J 18.4, 13.2), 3.62 (1H, d, J 13.9), 3.87 (3H, s), 3.92 (1H, dd, J 6.7, 6.3), 5.65 (1H, dd, J 13.2, 6.9), 6.95–7.05 (4H, m); ^{13}C NMR δ: ($CDCl_3$) 19.8 (q), 20.6 (q), 21.0 (q), 26.3 (t), 29.6 (s), 32.8 (t), 33.0 (s), 38.1 (t), 44.7 (d), 52.2 (q), 53.1 (t), 62.3 (d), 65.0 (d), 70.4 (t), 114.2 (d), 129.8 (d), 131.1 (s), 136.5 (s), 139.8 (s), 162.7 (s), 167.5 (s); MS: m/z 459 (M$^+$). Anal. calcd for $C_{23}H_{29}N_3O_5S$: C, 60.11; H, 6.36; N, 9.14. Found: C, 60.06; H, 6.40; N, 9.18%.

Compound **5a**: mp 74°C; $[\alpha]_D^{25}=+80.4$ ($CHCl_3$, $c=0.20$); IR: (Nujol) 1740, 1690 (cm^{-1}); ^{1}H NMR δ: ($CDCl_3$) 1.80–2.20 (4H, m), 2.34 (3H, s), 3.20 (1H, dd,

J 17.9, 6.8), 3.45–3.60 (3H, m), 3.76 (3H, s), 3.88 (3H, s), 4.41 (1H, dd, *J* 8.2, 4.8), 4.88 (1H, dd, *J* 13.1, 6.8), 6.90–7.10 (4H, m); ^{13}C NMR δ: ($CDCl_3$) 20.5 (q), 24.3 (t), 28.7 (t), 37.0 (t), 44.6 (t), 52.2 (q), 52.3 (q), 59.8 (d), 62.9 (d), 113.8 (d), 129.2 (d), 131.8 (s), 136.2 (s), 140.4 (s), 162.1 (s), 168.4 (s), 172.1 (s); MS: *m*/*z* 373 (M^+). Anal. calcd for $C_{19}H_{23}N_3O_5$: C, 61.11; H, 6.21; N, 11.25. Found: C, 61.06; H, 6.23; N, 11.32%.

Compound **5b**: mp 68°C; $[\alpha]_D^{25}=+76.3$ ($CHCl_3$, *c*= 0.19); IR: (Nujol) 1740, 1665 (cm^{-1}); ^{1}H NMR δ: ($CDCl_3$) 1.80–2.00 (4H, m), 2.28 (3H, s), 3.21 (1H, dd, *J* 17.6, 6.8), 3.50–3.65 (3H, m), 3.85 (3H, s), 4.56 (1H, dd, *J* 8.2, 3.1), 4.94 (1H, dd, *J* 13.8, 6.8), 5.10 (2H, s), 7.00–7.40 (9H, m); ^{13}C NMR δ: ($CDCl_3$) 19.5 (q), 23.9 (t), 29.7 (t), 38.2 (t), 46.4 (t), 52.6 (q), 55.0 (q), 62.1 (d), 65.4 (d), 70.2 (t), 114.3 (d), 128.5–129.7, 132.2 (s), 134.6 (s), 137.1 (s), 140.2 (s), 160.6 (s), 167.2 (s), 172.1 (s); MS: *m*/*z* 449 (M^+). Anal. calcd for $C_{25}H_{27}N_3O_5$: C, 66.80; H, 6.05; N, 9.35. Found: C, 66.76; H, 6.07; N, 9.40%.

Compound **5c**: mp 183°C; $[\alpha]_D^{25}=-183.2$ ($CHCl_3$, *c*= 0.13); IR: (Nujol) 1775, 1700 (cm^{-1}); ^{1}H NMR δ: ($CDCl_3$) 2.20 (3H, s), 3.21 (1H, dd, *J* 18.3, 6.7), 3.70 (1H, dd, *J* 18.3, 13.7), 3.88 (3H, s), 4.40 (1H, dd, *J* 9.1, 3.9), 4.79 (1H, dd, *J* 9.1, 8.7), 5.38 (1H, dd, *J* 8.7, 3.7), 5.96 (1H, dd, *J* 13.7, 6.7), 6.70–7.30 (9H, m); ^{13}C NMR δ: ($CDCl_3$) 20.6 (q), 37.3 (t), 52.9 (d), 57.2 (d), 61.3 (q), 69.6 (t), 114.2 (d), 125.5–129.5, 131.7 (s), 137.0 (s), 138.5 (s), 139.7 (s), 153.1 (s), 163.2 (s), 169.9 (s); MS: *m*/*z* 407 (M^+). Anal. calcd for $C_{22}H_{21}N_3O_5$: C, 64.86; H, 5.20; N, 10.31. Found: C, 64.89; H, 5.20; N, 10.37%.

Compound **5d**: mp 138°C; $[\alpha]_D^{25}=+300.0$ ($CHCl_3$, *c*= 0.22); IR: (Nujol) 1780, 1700 (cm^{-1}); ^{1}H NMR δ: ($CDCl_3$) 0.88 (3H, d, *J* 6.7), 0.90 (3H, d, *J* 6.7), 1.40–1.70 (3H, m), 2.28 (3H, s), 3.32 (1H, dd, *J* 18.3, 6.0), 3.63 (1H, dd, *J* 18.3, 13.7), 3.86 (3H, s), 4.20–4.43 (3H, m), 6.08 (1H, dd, *J* 13.7, 6.0), 6.90–7.10 (4H, m); ^{13}C NMR δ: ($CDCl_3$) 20.6 (q), 21.4 (q), 23.9 (q), 24.7 (d), 37.4 (t), 41.1 (t), 52.1 (d), 53.5 (d), 62.2 (d), 68.4 (t), 114.2 (d), 129.8 (d), 131.2 (s), 136.9 (s), 139.9 (s), 153.5 (s), 162.6 (s), 168.8 (s); MS: *m*/*z* 387 (M^+). Anal. calcd for $C_{20}H_{25}N_3O_5$: C, 62.00; H, 6.50; N, 10.85. Found: C, 62.03; H, 6.48; N, 10.90%.

Compound **5e**: mp 104°C; $[\alpha]_D^{25}=-7.9$ ($CHCl_3$, *c*= 0.35); IR: (Nujol) 1740, 1695 (cm^{-1}); ^{1}H NMR δ: ($CDCl_3$) 0.94 (3H, s), 1.44 (3H, s), 1.40–2.00 (7H, m), 2.48 (3H, s), 3.17 (1H, dd, *J* 18.4, 6.0), 3.48 (1H, d, *J* 14.1), 3.64 (1H, dd, *J* 18.4, 14.0), 3.60 (1H, d, *J* 14.1), 3.88 (3H, s), 3.96 (1H, dd, *J* 6.5, 6.3), 5.70 (1H, dd, *J* 14.0, 6.0), 6.95–7.05 (4H, m); ^{13}C NMR δ: ($CDCl_3$) 19.9 (q), 20.7 (q), 21.2 (q), 26.2 (t), 30.2 (s), 32.1 (t), 33.0 (s), 38.8 (t), 45.3 (d), 52.0 (q), 54.1 (t), 62.3 (d), 65.9 (d), 68.9 (t), 114.4 (d), 129.9 (d), 131.6 (s), 134.5 (s), 140.1 (s), 161.6 (s), 168.3 (s); MS: *m*/*z* 459 (M^+). Anal. calcd for $C_{23}H_{29}N_3O_5S$: C, 60.11; H, 6.36; N, 9.14. Found: C, 60.13; H, 6.38; N, 9.20%.

3.2. Hydrolysis of cycloadducts 4a,b and 5a,b

A solution of **4a**,**b** (or **5a**,**b**) (0.7 mmol) in tetrahydrofuran (5 mL) and 2 M aqueous sodium hydroxide (5 mL) was stirred at room temperature for 2 h. Aqueous hydrochloric acid (1 M) was added to pH 3 and the mixture was extracted with ethyl acetate (3×50 mL). The organic layer was washed with water (50 mL), dried over sodium sulfate and evaporated. Crystallisation from diisopropylether–isopropanol gave pure **6** or **7**.

Compound **6**: (from **4a**: 0.18 g, 75%; from **4b**: 0.17 g, 70%): mp 118°C; $[\alpha]_D^{25}=-227.0$ ($CHCl_3$, *c*=0.28); IR: (Nujol) 3240, 1670 (cm^{-1}); ^{1}H NMR δ: ($CDCl_3$) 1.80–2.10 (4H, m), 2.20 (3H, m), 3.14 (1H, dd, *J* 17.8, 6.9), 3.58 (1H, dd, *J* 17.8, 14.0), 3.67–3.85 (2H, m), 4.33 (1H, dd, *J* 8.0, 3.7), 5.25 (1H, dd, *J* 14.0, 6.9), 6.90–7.20 (4H, m); ^{13}C NMR δ: [$(CD_3)_2CO$] 20.2 (q), 22.8 (t), 25.6 (t), 37.0 (t), 47.4 (t), 59.7 (d), 62.9 (d), 114.6 (d), 130.1 (d), 130.8 (s), 138.1 (s), 141.8 (s), 163.4 (s), 168.5 (s), 173.1 (s); MS: *m*/*z* 345 (M^+). Anal. calcd for $C_{17}H_{19}N_3O_5$: C, 59.12; H, 5.55; N, 12.17. Found: C, 59.07; H, 5.58; N, 12.21%.

Compound **7**: (from **5a**: 0.20 g, 81%; from **5b**: 0.21 g, 85%): mp 62°C; $[\alpha]_D^{25}=+109.0$ ($CHCl_3$, *c*=0.10); IR: (Nujol) 3240, 1670 (cm^{-1}); ^{1}H NMR δ: ($CDCl_3$) 1.80–2.10 (4H, m), 2.21 (3H, m), 2.98 (1H, dd, *J* 17.8, 6.7), 3.61 (1H, dd, *J* 17.8, 13.9), 3.65–3.87 (2H, m), 4.71 (1H, dd, *J* 8.0, 3.9), 5.00 (1H, dd, *J* 13.9, 6.7), 6.90–7.25 (4H, m); ^{13}C NMR δ: [$(CD_3)_2CO$] 20.5 (q), 23.2 (t), 26.0 (t), 37.4 (t), 47.8 (t), 59.4 (d), 62.9 (d), 114.4 (d), 130.2 (d), 130.3 (s), 138.9 (s), 141.0 (s), 163.3 (s), 167.8 (s), 177.1 (s); MS: *m*/*z* 345 (M^+). Anal. calcd for $C_{17}H_{19}N_3O_5$: C, 59.12; H, 5.55; N, 12.17. Found: C, 59.16; H, 5.52; N, 12.22%.

3.3. Hydrolysis of cycloadducts 4c–e and 5c–e

A solution of **4c**–**e** (or **5c**–**e**) (0.5 mmol) in tetrahydrofuran (6 mL) and 2 M aqueous sodium hydroxide (6 mL) was stirred at room temperature for 3 h. Aqueous hydrochloric acid (1 M) was added to pH 3, and the mixture was extracted with ethyl acetate (3×50 mL). The organic layer was washed with water (40 mL), dried over sodium sulfate and evaporated. Crystallisation from isopropanol–dichloromethane gave pure **8** or **9**.

Compound (*S*)-(+)-**8**: (from **4c**: 0.10 g, 80%; from **4d**: 0.11 g, 87%, from **4e**: 0.11 g, 87%): mp 185°C; $[\alpha]_D^{25}=+$ 5.5 (DMSO, *c*=0.40); IR: (Nujol) 3230, 1750 (cm^{-1}); ^{1}H NMR δ: ($CDCl_3$) 2.36 (3H, s), 3.27 (1H, dd, *J* 17.5, 6.5), 3.62 (1H, dd, *J* 17.7, 13.4), 5.08 (1H, dd, *J* 13.4, 6.5), 7.05–7.15 (4H, m); ^{13}C NMR δ: ($CDCl_3$) 19.3 (q), 36.7 (t), 63.3 (d), 112.9 (d), 129.2 (d), 138.2 (s), 139.0 (s), 139.8 (s), 162.4 (s), 168.9 (s); MS: *m*/*z* 248 (M^+). Anal. calcd for $C_{12}H_{12}N_2O_4$: C, 58.06; H, 4.87; N, 11.29. Found: C, 58.11; H, 4.90; N, 11.33%.

Compound (*R*)-(−)-**9**: (from **5c**: 0.10 g, 84%; from **5d**: 0.11 g, 88%, from **5e**: 0.11 g, 87%): $[\alpha]_D^{25}=-5.8$ (DMSO,

$c=0.42$). Anal. calcd for $C_{12}H_{12}N_2O_4$: C, 58.06; H, 4.87; N, 11.29. Found: C, 58.09; H, 4.92; N, 11.35%.

Vacuum evaporation of the mother liquor gave the starting chiral auxiliary: (4*S*)-(+)-phenyl-2-oxazolidinone was recovered from **4c** (60 mg, 75%) and **5c** (65 mg, 80%); (4*S*)-(+)-isobutyl-2-oxazolidinone was recovered from **4d** (52 mg, 73%) and **5d** (56 mg, 78%); (1*S*, 2*R*)-(−)-2,10-camphorsultam was recovered from **4e** (90 mg, 83%) and **5e** (85 mg, 80%).

3.4. Crystal data for compound 4c

$C_{22}H_{21}N_3O_5$, Fw = 407.42, orthorhombic, space group $P2_12_12_1$, $T=90$ K, $a=4.9093(10)$, $b=18.902(3)$, $c=22.213(4)$ Å, $V=2061.3(6)$ Å^3, $Z=2$, $D_x=1.313$ Mg m^{-3}, μ (Mo-Kα) = 0.095 mm^{-1}; crystal dimensions 0.36×0.16×0.12 mm^3, $\lambda=0.71073$ Å (Mo-Kα radiation, graphite monochromator, Bruker SMART-APEX CCD diffractometer, equipped with KRIO-FLEX low temperature device). Data collection: ω and φ scan mode, $2\theta<55.00°$; 30937 collected reflections, 2775 unique [2482 with $I_o>2\sigma(I_o)$], merging $R=0.0380$. The structure was solved by SIR92[12] and refined by SHELXL-97[13] by full-matrix least-squares based on F_o^2, with weights $w=1/[\sigma^2(F_o)^2+(0.0301P)^2]$, where $P=(F_o^2+2F_c^2)/3$. H atoms were refined isotropically. The final consistency index were $R=0.0616$ and $Rw=0.0933$ (0.0530 and 0.0901, respectively, for observed reflections), goodness-of-fit = 1.082. The final map ranges between −0.25 and 0.26 e Å^{-3}. The absolute configuration was determined on the base of the known C23 stereochemistry (see Fig. 1). Data were firstly collected and solved at room temperature, but data were of poor quality and quantity because of the very high atomic displacement parameters (ADPs) of the benzyl and tolyl moieties. In spite of the freezing at 90 K, ADPs of the benzene ring (C(25)–C(30)) are quite high. This feature is probably connected with a large channel along the *a* axis. Detailed crystallographic data were deposited as CCDC 185238 with the Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK.

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