Synthesis of 2,5-Disubstituted Pyrroles and Pyrrolidines by Intramolecular Cyclization of 6-Amino-3-keto Sulfones

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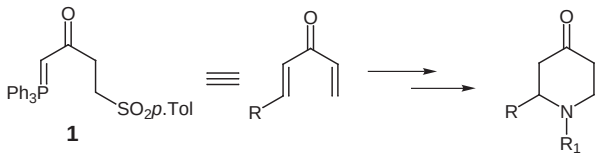
Abstract: Wittig reaction of 4-[(4-methylphenyl)sulfonyl]-1-(triphenylphosphoranylidene)butan-2-one (**1**) with *N*-protected α-amino aldehydes furnished *N*-protected γ-amino-α,β-unsaturated keto sulfones which have been conveniently utilized as precursors of both aromatic and non-aromatic 2,5-disubstituted five-membered heterocyclic compounds. While 2,5-disubstituted pyrroles are efficiently formed by cyclodehydration of the starting materials, 2,5-disubstituted pyrrolidines and pyrrolenines could be obtained by prior reduction of the conjugated double bond followed by acid- or base-mediated cyclization. The ready availability of the materials required for the whole sequence makes this methodology a convenient way to generate both aromatic and saturated 2,5-disubstituted five-membered heterocyclic compounds.

Key words: pyrroles, pyrrolidines, amino aldehydes, cyclodehydration, sulfones

The pyrrole subunit is a frequently found motif in many naturally occurring compounds as well as in substances with important biological activities. The importance of pyrrole derivatives in pharmaceutical and agricultural development, has created the need for efficient preparation of this nucleus, usually constructed through the classical Paal–Knorr synthesis starting from primary amines and 1,4-dicarbonyl compounds.[1] More recent approaches utilize conjugate addition of α-aminoalkylcuprates to alkynyl ketones[2] or aldol-type reactions between α-amino aldehydes and lithium enolates of various ketones[3] or intramolecular cyclodehydration of γ-substituted-α,β-unsaturated ketone derivatives.[4] We have recently introduced 4-[(4-methylphenyl)sulfonyl]-1-(triphenylphosphoranylidene)butan-2-one (**1**) as a versatile four-carbon building block for substituted divinyl ketones able to take part in a domino sequence initiated by a nitrogen-centered nucleophile, allowing the construction of a variety of six-membered heterocyclic ring systems (Scheme 1).[5]



Scheme 1

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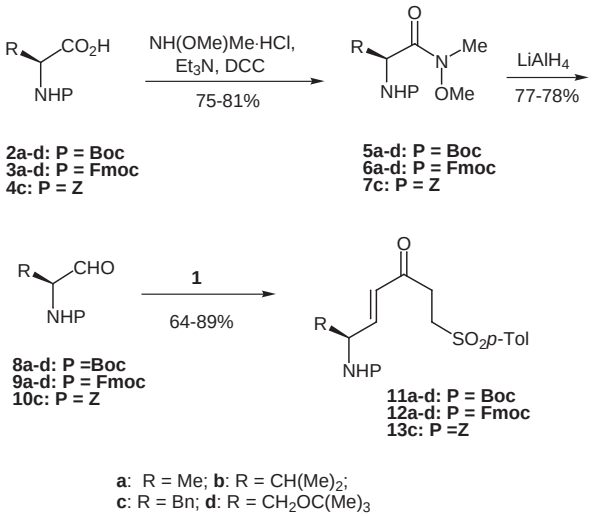
Since the two double bonds adjacent to the carbonyl group could be generated in separate steps, namely a Wittig reaction with a suitable aldehyde and a base-promoted β-elimination of the sulfone group, we anticipated that chiral non-racemic compounds like the γ-amino-α,β-unsaturated keto sulfones **11**–**13** could provide diastereomeric 2-substituted piperidine nuclei. To test this hypothesis, we have now prepared the derivatives **11**–**13**[6] through Wittig alkenylation of **1** with suitably *N*-protected amino aldehydes **8**–**10**,[7] in turn conveniently obtained by $LiAlH_4$ reduction of the corresponding *N*-methyl-*N*-methoxyamides **5**–**7** of suitably *N*-protected amino acids **2**–**4** such as alanine, valine, phenylalanine and serine (Scheme 2).



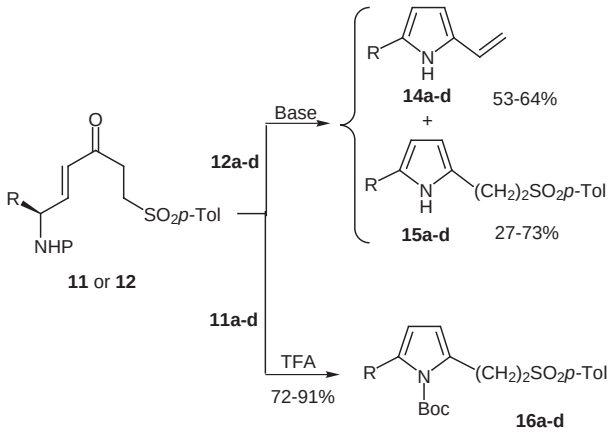
Scheme 2

An accurate inspection of the polifunctionalized intermediates **11**–**13** revealed that their γ-amino-α,β-unsaturated ketone moiety could take part in an intramolecular cyclodehydratation leading to five-membered heterocycles. The present paper deals with this useful synthetic strategy.

Different nitrogen protective groups were utilized considering that they can be cleaved under different experimental conditions (strongly acidic, basic or hydrogenolytically), thus offering more options to obtain aromatic and saturated 2,5-disubstituted five-membered

heterocyclic compounds with both free and protected nitrogen atom.

Thus, base induced deprotection of the amine function of **12a–d** led to the formation of a mixture of the interesting and quite rare vinyl pyrrole derivatives **14a–d** and the expected pyrrole sulfones **15a–d**. The ratio of the two compounds depends on the base used in the deprotection step, and piperidine, the classical base used for Fmoc removal,[8] gave higher yields of vinyl pyrrole derivatives **14a–d**. Otherwise, mild acid treatment of **11a–d** with trifluoroacetic acid (TFA) promoted a spontaneous intramolecular cyclodehydration giving *N*-Boc 2,5-disubstituted pyrrole sulfone derivatives **16a–d** bearing the intact sulfone moiety as an additional interesting functionality in the side chain (Scheme 3 and Table).



Scheme 3

It is likely that an acid- or base-induced *trans/cis* isomerization of the double bond geometry is required to allow the cyclodehydration, which, of course, occurr with loss of the chirality of the starting amino acid due to the formation of the aromatic heterocyclic compounds.

As a logical extension of our method, we next explored the possibility to obtain compounds in which the chirality information could be preserved and transferred to eventually created new chiral centers. To this end, we decided to anticipate the reduction of the double bond to the cyclization step, submitting the model compounds **11c** and **12c**

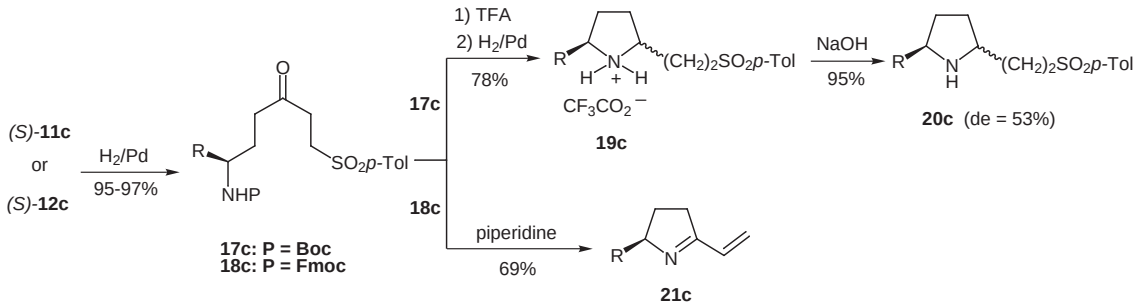
Table Synthesis of Vinylpyrroles **14** and Pyrrole Sulfones **15**, **16** from γ-Amino-α,β-unsaturated Keto Sulfones **11**–**12**

Keto Sulfones **11**, **12**	R	Promoter	Time (h)	**14** Yield (%)	**15** Yield (%)	**16** Yield (%)
11a	Me	TFA	12	-	-	85
11b	$CH(Me)_2$	TFA	20	-	-	78
11c	Bn	TFA	16	-	-	91
11d	$CH_2OC(Me)_3$	TFA	16	-	-	72
12a	Me	piperidine	0.45	61	35	-
		Et_3N	2.5	20	73	-
12b	$CH(Me)_2$	piperidine	1	53	32	-
		$NaHCO_3$	24[a]	-	-	-
		IRA-420[b]	24[a]	-	35	-
		TMG	0.5	-	88	-
12c	Bn	piperidine	1.5	72	18	-
		Et_3N	2	60	27	-
12d	$CH_2OC(Me)_3$	piperidine	1	64	25	-
		Et_3N	1.5	39	53	-

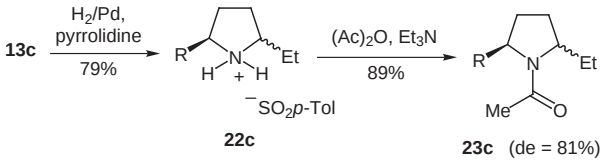
[a] At reflux.
[b] Fluka Amberlite basic anion exchange resin.

obtained as above described to catalytic hydrogenation in the presence of Pd/C. Thus, acid-promoted dehydration of the resulting saturated compound **17c** followed by hydrogenation of the crude reaction mixture led to the formation of the pyrrolidine sulfone **20c** with a modest 53% de, while double bond reduction of **12c** followed by base deprotection of the amine function of **18c** produced the optically active vinylpyrroline **21c** (Scheme 4).

A much better result in term of induced chirality transfer has been found when we applied the reduction/deprotection sequence to compound **13c**, the saturated pyrrolidine **23c** being formed in good chemical yield and satisfactory de (81%, Scheme 5).



Scheme 4



Scheme 5

On the basis of NMR spectra we could not specify the absolute configurations of the new chiral centers at C-5 of pyrrolidines **20c** and **23c** however, assuming facial selectivity in the *cis*-hydrogenation of pyrroline intermediates, we suppose the *cis*-diastereomers are predominant in the mixture.

In summary, the reaction of ylide **1** with easily available *N*-protected α-amino aldehydes opened a convenient access to *N*-protected γ-amino-α,β-unsaturated keto sulfone derivatives, which have been conveniently utilized as precursors of both aromatic and non-aromatic 2,5-disubstituted five-membered heterocyclic compounds. Moreover, an appropriate choice of nitrogen protecting group allows obtaining *N*-protected or free 2,5-disubstituted pyrroles as well as 2,5-disubstituted pyrrolidines and pyrrolenines simply by prior reduction of the conjugated double bond. Interestingly, the ready availability of the starting materials makes this methodology a convenient way to generate both aromatic and saturated 2,5-disubstituted five-membered heterocyclic compounds and could find applications in the synthesis of natural products.

Melting points were determined on a Reichert-Kofler apparatus and are uncorrected. NMR spectra were recorded on a Brucker AC-200 spectrometer. Chemical shifts are given in parts per million (δ) downfield from tetramethylsilane as an internal standard. IR spectra were recorded on a Perkin-Elmer FT-IR Paragon 500 spectrometer. Optical rotations [α] were determined using a Perkin-Elmer 241 polarimeter operating at 589 nm (sodium D line) at 20 °C. Organic solutions were dried over anhyd $MgSO_4$ and evaporated with a rotary evaporator. PE (light petroleum) refers to the fractions boiling in the range 40–60 °C. HPLC analysis was performed on a Gilson 119 variable wavelength detector. Chiral HPLC was run using two Astec column systems with the appropriate eluents mixture: Chirobiotic V (column system 1) and Cyclobond 2000 (column system 2). TLC was done with precoated plates of silica gel (Merk F-254) using the indicated solvent system. Flash chromatography was carried out with Merck silica gel (230–400 mesh). Elemental analyses were measured at the microanalytical laboratory of Dipartimento di Chimica, University of Ferrara.

Compounds (*S*)-5d and (*S*)-6d; General Procedure
DCC (1.135 g, 5.5 mmol) and the *N*-protected α-amino acid **2d** or **3d** (5 mmol) were successively added to a stirred suspension of *N*,*O*-dimethylhydroxylamine hydrochloride (537 mg, 5.5 mmol) and Et_3N (506 mg, 5.5 mmol) in anhyd CH_2Cl_2. After stirring at r.t. for 40 min, the mixture was filtered through Celite and the solid washed with CH_2Cl_2 (2 × 5 mL). Evaporation of the solvent and column chromatography of the residue yielded pure (*S*)-**5d** or (*S*)-**6d**.

[2-*tert*-Butoxy-(*S*)-1-(methoxymethylcarbamoyl)-1-ethyl]-carbamic Acid *tert*-Butyl Ester [(*S*)-5d]
Solid (81%); mp 125–126 °C; R_f 0.2 (EtOAc–hexane, 1:3); $[\alpha]_D^{20}$ +26.1 (*c* = 1.00, $CHCl_3$).

IR (KBr): 3318, 1720, 1232, 1190, 1089 cm^{-1}.

^1H NMR (200 MHz, $CDCl_3$): δ = 1.21 (s, 9 H, $CH_2OC_4H_9$-*t*), 1.35 (s, 9 H, $CO_2C_4H_9$-*t*), 3.31 (s, 3 H, OCH_3), 3.58 (t, 1 H, *J* = 7 Hz, CH), 3.81 (s, 3 H, OCH_3), 4.18–4.23 (m, 2 H, CH_2), 5.61 (d, 1 H, *J* = 7.9 Hz, NH).

^{13}C NMR (50 MHz, $CDCl_3$): δ = 27.2, 27.5, 45.4, 53.6, 61.2, 67.5, 73.7, 155.9, 169.5.

Anal. Calcd for $C_{14}H_{28}N_2O_5$ (304.4): C, 55.24; H, 9.27; N, 9.20. Found: 54.32; H, 9.01; N, 9.35.

[2-*tert*-Butoxy-(*S*)-1-(methoxymethylcarbamoyl)-1-ethyl]-carbamic Acid 9*H*-Fluoren-9-ylmethyl Ester [(*S*)-6d]
Solid (75%); mp 131–132 °C; R_f 0.2 (EtOAc–hexane, 1:2); $[\alpha]_D^{20}$ +14.5 (*c* = 1.00, $CHCl_3$).

IR (KBr): 3309, 1723, 1652, 1450, 1247, 1195, 1099, 760, 741 cm^{-1}.

^1H NMR (200 MHz, $CDCl_3$): δ = 1.17 (s, 9 H, CH_2Ot-C_4H_9), 3.35 (s, 3 H, OCH_3), 3.64 (t, 1 H, *J* = 7.1 Hz, HNC*H*), 3.79 (s, 3 H, OCH_3), 4.20–4.27 (m, 2 H, *t*-BuOCH_2), 4.37 (d, 2 H, *J* = 6.8 Hz, CO_2CH_2), 4.81–4.92 (m, 1 H, OCH_2CH), 5.70 (d, 1 H, *J* = 9 Hz, NH), 7.27–7.78 (m, 8 H_{arom}).

^{13}C NMR (50 MHz, $CDCl_3$): δ = 27.4, 47.2, 51.9, 61.5, 62.1, 67.1, 73.6, 120.0, 125.3, 127.1, 127.7, 141.3, 143.9, 144.1, 156.1, 170.7.

Anal. Calcd for $C_{24}H_{30}N_2O_5$ (426.5): C, 67.59; H, 7.09; N, 6.57. Found: C, 67.40; H, 7.00; N, 6.83.

Aldehydes (*S*)-8d and (*S*)-9d; General Procedure
To an ice-cooled solution of (*S*)-**5d** or (*S*)-**6d** (3 mmol) in anhyd Et_2O (10 mL) was added $LiAlH_4$ (125 mg, 3.3 mmol) in one portion and the stirring was continued for 10 min at the same temperature. The mixture was quenched with a few drops of aq 3% $KHSO_4$, filtered through Celite, washed with Et_2O (2 × 5 mL) and dried. After evaporation of the solvent, the crude residue was purified by column chromatography to give (*S*)-**8d** or (*S*)-**9d**.

[2-*tert*-Butoxy-(*S*)-1-formylethyl]carbamic Acid *tert*-Butyl Ester [(*S*)-8d]
Yellowish oil (78%); R_f 0.3 (EtOAc–hexane, 1:2); $[\alpha]_D^{20}$ +37.8 (*c* = 1.00, $CHCl_3$).

IR (neat): 3442, 3310, 1728, 1710, 1237, 1081 cm^{-1}.

^1H NMR (200 MHz, $CDCl_3$): δ = 1.20 (s, 9 H, CH_2Ot-C_4H_9), 1.39 (s, 9 H, CO_2t-C_4H_9), 4.29 (t, 1 H, *J* = 7.0, HNC*H*), 4.32–4.41 (m, 2 H, OCH_2), 5.64 (d, 1 H, *J* = 7.8 Hz, NH), 9.64 (s, 1 H, COH).

^{13}C NMR (50 MHz, $CDCl_3$): δ = 26.9, 29.2, 48.1, 61.4, 66.3, 72.5, 158.4, 200.1.

Anal. Calcd for $C_{12}H_{23}NO_4$ (245.3): C, 58.75; H, 9.45; N, 5.71. Found: C, 58.48; H, 9.32; N, 5.70.

[2-*tert*-Butoxy-(*S*)-1-formylethyl]carbamic acid, 9*H*-Fluoren-9-ylmethyl Ester [(*S*)-9d]
Oil (77%); R_f 0.37 (EtOAc–hexane, 1:2); $[\alpha]_D^{20}$ +31.4 (*c* = 1.00, $CHCl_3$).

IR (neat): 3440, 3318, 1725, 1695, 1506, 1450, 1364, 1247, 1088, 759, 741 cm^{-1}.

^1H NMR (200 MHz, $CDCl_3$): δ = 1.16 (s, 9 H, CH_2Ot-C_4H_9), 4.34 (t, 1 H, *J* = 7.0, HNC*H*), 4.38–4.95 (m, 5 H, *t*-BuOCH_2, CO_2CH_2 and OCH_2CH), 5.66 (d, 1 H, *J* = 8 Hz, NH), 7.25–7.78 (m, 8 H, fluorene), 9.62 (s, 1 H, CHO).

^{13}C NMR (50 MHz, $CDCl_3$): δ = 27.3, 47.2, 60.1, 60.6, 67.2, 73.9, 120.0, 125.2, 127.2, 127.8, 141.4, 143.9, 156.3, 199.2.

Anal. Calcd for $C_{22}H_{25}NO_4$ (367.5): C, 71.91; H, 6.86; N, 3.81. Found: C, 72.43; H, 6.91; N, 3.74.

Alkenes 11–13; General Procedure

A mixture of the appropriate aldehyde **8**–**10** (1 mmol) and **1** (487 mg, 1 mmol) in anhyd toluene was refluxed until the reaction was completed (TLC monitoring). After evaporation of the solvent the crude residue was purified by column chromatography.

[(*S*)-1-Methyl-4-oxo-6-(toluene-4-sulfonyl)hex-2-enyl]carbamic Acid *tert*-Butyl Ester [(*S*)-11a]

Solid (76%); R_f 0.2 (EtOAc–hexane, 1:1); mp 104–106 °C; $[\alpha]_D^{20}$ –37.1 (*c* = 1.00, $CHCl_3$).

IR (KBr): 3320, 1695, 1560, 1308, 1156 cm^{-1}.

^1H NMR (200 MHz, $CDCl_3$): δ = 1.26 (d, 3 H, *J* = 7.1 Hz, $NCCH_3$), 1.38 (s, 9 H, *t*-C_4H_9), 2.43 (s, 3 H, $C_6H_4CH_3$), 2.98 (t, 2 H, *J* = 7.4 Hz, $COCH_2$), 3.42 (t, 2 H, *J* = 7.4 Hz, CH_2S), 4.35−4.42 (m, 1 H, HCN), 4.80 (d, 1 H, *J* = 8 Hz, NH), 6.06 (d, 1 H, *J* = 15.2 Hz, OC-CH=), 6.68 (dd, 1 H, *J* = 15.2, 5 Hz, NCCH=), 7.27–7.60 (m, 4 H_{arom}).

^{13}C NMR (50 MHz, $CDCl_3$): δ = 20.3, 21.9, 28.6, 34.2, 50.9, 52.5, 80.0, 126.4, 128.6, 130.2, 135.8, 142.3, 145.2, 156.2, 197.4.

Anal. Calcd for $C_{19}H_{27}NO_5S$ (381.5): C, 59.82; H, 7.13; N, 3.67; S, 8.41. Found: C, 59.72; H, 7.18; N, 3.58; S, 8.50.

[(*S*)-1-Methyl-4-oxo-6-(toluene-4-sulfonyl)hex-2-enyl]carbamic Acid 9*H*-Fluoren-9-ylmethyl Ester [(*S*)-12a]

Solid (81%); mp 121–123 °C; R_f 0.12 (EtOAc–hexane, 1:1.5); $[\alpha]_D^{20}$ –32.9 (*c* = 1.00, $CHCl_3$).

IR (KBr): 3323, 1690, 1684, 1534, 1315, 1264, 1145 cm^{-1}.

^1H NMR (200 MHz, $CDCl_3$): δ = 1.28 (d, 3 H, *J* = 7 Hz, $NCCH_3$), 2.43 (s, 3 H, $C_6H_4CH_3$), 3.03 (t, 2 H, *J* = 7.8 Hz, $COCH_2$), 3.39 (t, 2 H, *J* = 7.8 Hz, CH_2S), 4.17–4.23 (m, 1 H, $CHCH_3$), 4.37–4.45 (m, 3 H, OCH_2 and OCH_2CH), 4.88 (br d, 1 H, *J* = 8 Hz, NH), 6.10 (d, 1 H, *J* = 16 Hz, OCCH=), 6.74 (dd, 1 H, *J* = 16, 5.9 Hz, NCCH=), 7.26–7.80 (m, 12 H, fluorene and C_6H_4).

^{13}C NMR: δ = 20.1, 21.6, 33.1, 47.2, 50.7, 66.7, 120.0, 124.9, 127.1, 127.4, 127.8, 128.0, 130.0, 135.9, 141.4, 143.8, 143.9, 145.1, 148.3, 155.4, 195.2.

Anal. Calcd for $C_{29}H_{29}NO_5S$ (503.6): C, 69.16; H, 5.80; N, 2.78; S, 6.37. Found: C, 69.45; H, 5.91; N, 2.82; S, 6.21.

[(*S*)-1-Isopropyl-4-oxo-6-(toluene-4-sulfonyl)hex-2-enyl]-carbamic Acid *tert*-Butyl Ester [(*S*)-11b]

Solid (74%); mp 104–106 °C; R_f 0.3 (EtOAc–hexane, 1:1.5); $[\alpha]_D^{20}$ –37.1 (*c* = 1.00, $CHCl_3$).

IR (KBr): 3329, 1695, 1305, 1148 cm^{-1}.

^1H NMR (200 MHz, $CDCl_3$): δ = 0.87 (d, 3 H, *J* = 6.8 Hz, CH_3CH), 0.92 (d, 3 H, *J* = 6.6 Hz, CH_3CH), 1.36 (s, 9 H, *t*-C_4H_9), 1.80–1.93 (m, 1 H, CH), 2.44 (s, 3 H, $C_6H_4CH_3$), 2.65–2.73 (m, 1 H, *H*CNH), 2.95 (t, 2 H, *J* = 7.1 Hz, $COCH_2$), 3.35 (t, 2 H, *J* = 7.1 Hz, CH_2S), 5.18 (d, 1 H, *J* = 8.3 Hz, NH), 6.16 (d, 1 H, *J* = 15.9 Hz, OCCH=), 6.74 (dd, 1 H, *J* = 15.9, 6.1 Hz, NCCH=), 7.35 (d, 2 H, *J* = 8 Hz, C_6H_5), 7.80 (d, 2 H, *J* = 8 Hz, C_6H_5).

^{13}C NMR (50 MHz, $CDCl_3$): δ = 17.5, 20.8, 28.9, 32.9, 33.4, 47.9, 60.2, 68.9, 126.2, 127.8, 129.3, 135.2, 143.0, 143.3, 158.1, 198.7.

Anal. Calcd for $C_{21}H_{31}NO_5S$ (409.6): C, 61.59; H, 7.63; N, 3.42; S, 7.83. Found: C, 61.59; H, 7.61; N, 3.45; S, 7.86.

[(*S*)-1-Isopropyl-4-oxo-6-(toluene-4-sulfonyl)hex-2-enyl]-carbamic Acid 9*H*-Fluoren-9-ylmethyl Ester [(*S*)-12b]

Solid (85%); mp 113–115 °C; R_f 0.2 (EtOAc–hexane, 1:1.5); $[\alpha]_D^{20}$ –40.5 (*c* = 1.00, $CHCl_3$).

IR (KBr): 3326, 1689, 1539, 1302, 1143 cm^{-1}.

^1H NMR (200 MHz, $CDCl_3$): δ = 0.88 (d, 3 H, *J* = 7.1 Hz, CH_3CH), 0.91 (d, 3 H, *J* = 7.2 Hz, CH_3CH), 1.85–1.95 (m, 1 H, CH), 2.43 (s, 3 H, $C_6H_4CH_3$), 3.02 (t, 2 H, *J* = 7.8 Hz, $COCH_2$), 3.35–3.50 (m, 3 H, CH_2S and *H*CNH), 4.19 (t, 1 H, *J* = 6.9 Hz, OCH_2CH), 4.44 (d, 2 H, *J* = 6.9 Hz, OCH_2), 5.02 (br d, 1 H, *J* = 7.9 Hz, NH), 6.11 (d, 1 H, *J* = 15.9 Hz, OCCH=), 6.75 (dd, 1 H, *J* = 15.9, 6.2 Hz, NCCH=), 7.15–7.80 (m, 12 H, C_6H_4 and fluorene).

^{13}C NMR (50 MHz, $CDCl_3$): δ = 16.9, 20.2, 30.3, 33.3, 47.1, 59.5, 66.9, 119.6, 124.8, 125.1, 127.3, 127.9, 128.2, 128.8, 130.0, 135.9, 140.1, 141.8, 142.1, 143.7, 155.5, 199.9.

Anal. Calcd for $C_{31}H_{33}NO_5S$ (531.7): C, 70.03; H, 6.26; N, 2.63; S, 6.03. Found: C, 69.26; H, 6.02; N, 2.99; S, 6.41.

[(*S*)-1-Benzyl-4-oxo-6-(toluene-4-sulfonyl)hex-2-enyl]carbamic Acid *tert*-Butyl Ester [(*S*)-11c]

Solid (69%); mp 121–124 °C; R_f 0.32 (EtOAc–hexane, 1:2); $[\alpha]_D^{20}$ –5.1 (*c* = 1.00, $CHCl_3$). HPLC with chiral column (system 1): isocratic elution (MeCN–MeOH–Et_3N–AcOH = 85:15:0.01:0.01); t_1 = 3.45; ee = 96%.

IR (KBr): 3351, 1690, 1683, 1525, 1313, 1171, 1144 cm^{-1}.

^1H NMR (200 MHz, $CDCl_3$): δ = 1.40 (s, 9 H, *t*-C_4H_9), 2.46 (s, 3 H, $CH_2C_6H_5$), 2.89 (d, 2 H, *J* = 6.9 Hz, $CH_2C_6H_4$), 2.99 (t, 2 H, *J* = 8.2 Hz, CH_2CO), 3.38 (t, 2 H, *J* = 8.2 Hz, CH_2S), 4.58 (br s, 2 H, NH and NCH), 6.08 (d, 1 H, *J* = 15.9 Hz, OCCH=), 6.82 (dd, 1 H, *J* = 15.9, 4.8 Hz, NCCH=), 7.13–7.80 (m, 9 H, C_6H_5 and C_6H_4).

^{13}C NMR (50 MHz, $CDCl_3$): δ = 21.7, 27.0, 28.3, 33.1, 40.7, 50.7, 52.5, 80.1, 127.1, 128.0, 128.1, 128.7, 129.3, 130.1, 136.0, 136.1, 145.0, 147.3, 155.0, 195.0.

Anal. Calcd for $C_{25}H_{31}NO_5S$ (457.6): C, 65.62; H, 6.83; N, 3.06; S, 7.01. Found: C, 65.49; H, 6.79; N, 3.09; S, 7.11.

[(*R*,*S*)-1-Benzyl-4-oxo-6-(toluene-4-sulfonyl)hex-2-enyl]-carbamic Acid *tert*-Butyl Ester [(*R*,*S*)-11c]

Solid (75%); mp 114–116 °C; R_f 0.32 (EtOAc–hexane, 1:2). HPLC with chiral column (system 1): isocratic elution (MeCN–MeOH–Et_3N–AcOH = 85:15:0.01:0.01); t_1 = 3.45; t_2 = 4.94.

[(*S*)-1-Benzyl-4-oxo-6-(toluene-4-sulfonyl)-hex-2-enyl]-carbamic Acid 9*H*-Fluoren-9-ylmethyl Ester [(*S*)-12c]

Solid (89%) mp 150–152 °C; R_f 0.4 (EtOAc–hexane, 1:1.5); $[\alpha]_D^{20}$ –10.2 (*c* = 1.00, $CHCl_3$).

IR (KBr): 3326, 1690, 1534, 1315, 1258, 1146 cm^{-1}.

^1H NMR (200 MHz, $CDCl_3$): δ = 2.46 (s, 3 H, $CH_3C_6H_4$), 2.91 (d, 2 H, *J* = 6.4 Hz, $CH_2C_6H_5$), 2.99 (t, 2 H, *J* = 8 Hz, CH_2CO), 3.38 (t, 2 H, *J* = 8 Hz, CH_2S), 4.18 (t, 1 H, *J* = 6.6 Hz, HCCN), 4.38–4.47 (m, 2 H, CH_2O), 4.50–4.52 (m, 1 H, $HCCH_2O$), 4.81 (br d, 1 H, NH), 6.08 (d, 1 H, *J* = 16 Hz, OCCH=), 6.71 (dd, 1 H, *J* = 16, 5 Hz, NCCH=), 7.10–7.80 (m, 17 H, fluorene, C_6H_4, C_6H_5).

^{13}C NMR (50 MHz, $CDCl_3$): δ = 20.3, 33.9, 46.9, 48.3, 50.8, 66.8, 121.1, 122.1, 124.5, 125.3, 126.9, 127.2, 127.7, 128.1, 128.3, 131.2, 136.0, 141.0, 141.3, 143.7, 143.9, 148.6, 155.9, 194.8.

Anal. Calcd for $C_{35}H_{33}NO_5S$ (579.7): C, 72.52; H, 5.74; N, 2.42; S, 5.53. Found: C, 72.49; H, 5.70; N, 2.42; S, 5.65.

[(*S*)-1-Benzyl-4-oxo-6-(toluene-4-sulfonyl)hex-2-enyl]carbamic Acid Benzyl Ester [(*S*)-13c]

Solid (70%); mp 106–108 °C; R_f 0.3 (EtOAc–hexane, 1:2); $[\alpha]_D^{20}$ –19.9 (c = 1.00, $CHCl_3$).

IR (KBr): 3328, 1690, 1684, 1535, 1315, 1261, 1143 cm^{-1}.

^1H NMR (200 MHz, $CDCl_3$): δ = 2.46 (s, 3 H, $CH_3C_6H_4$), 2.85 (d, 2 H, *J* = 7 Hz, $CH_2C_6H_5$), 2.93 (t, 2 H, *J* = 8.1 Hz, CH_2CO), 3.38 (t, 2 H, *J* = 8.1 Hz, CH_2S), 4.62–4.70 (m, 1 H, CH), 4.86 (d, 1 H, *J* = 8 Hz, NH), 5.05–5.07 (m, 2 H, OCH_2), 6.08 (d, 1 H, *J* = 15.8, OC-

CH=), 6.79 (dd, 1 H, *J* = 15.8, 5 Hz, NCCH=), 7.12–7.80 (m, 14 H, 2 C_6H_5, C_6H_4).

^{13}C NMR (50 MHz, $CDCl_3$): δ = 19.9, 30.0, 41.2, 47.7, 54.3, 71.5, 123.6, 124.5, 127.2, 127.4, 127.8, 128.6, 128.8, 130.5, 130.7, 137.6, 138.5, 140.0, 145.3, 155.8, 198.2.

Anal. Calcd for $C_{28}H_{29}NO_5S$ (491.6): C, 68.41; H, 5.95; N, 2.85; S, 6.52. Found: C, 68.11; H, 5.81; N, 2.84; S, 6.58.

[(*S*)-1-*tert*-Butoxymethyl-4-oxo-6-(toluene-4-sulfonyl)hex-2-enyl]carbamic Acid *tert*-Butyl Ester [(*S*)-11d]
Solid (64%); mp 102–103 °C; R_f 1.4 (EtOAc–hexane, 1:2.5); $[\alpha]_D^{20}$ –51.3 (*c* = 1.00, $CHCl_3$).

IR (KBr): 3320, 1692, 1652, 1314, 1274, 1236, 1143 cm^{-1}.

^{1}H NMR (200 MHz, $CDCl_3$): δ = 1.18 (s, 9 H, O*t*-C_4H_9), 1.35 (s, 9 H, $CO_2C_4H_9$-*t*), 2.35 (s, 3 H, C*H*$_3C_6H_4$), 3.12 (t, 2 H, *J* = 7.2 Hz, CH_2CO), 3.43 (t, 2 H, *J* = 7.2 Hz, CH_2S), 3.51 (d, 2 H, *J* = 6.9 Hz, OCH_2), 4.01–4.20 (m, 1 H, HCCN), 5.31 (d, 1 H, *J* = 8.4 Hz, NH), 6.23 (d, 1 H, *J* = 15.8 Hz, OCCH=), 6.83 (dd, 1 H, *J* = 15.8, 5.3 Hz, NCCH=), 7.40 (d, 2 H, *J* = 8.1 Hz, C_6H_4), 7.78 (d, 2 H, *J* = 8.1 Hz, C_6H_4).

^{13}C NMR (50 MHz, $CDCl_3$): δ = 21.2, 27.9, 31.0, 32.9, 46.9, 52.7, 67.7, 69.8, 71.1, 122.5, 128.7, 131.3, 138.0, 141.2, 156.9, 198.2.

Anal. Calcd for $C_{23}H_{35}NO_6S$ (453.6): C, 60.90; H, 7.78; N, 3.09; S, 7.07. Found: C, 61.26; H, 7.93; N, 3.45; S, 6.86.

[(*S*)-1-*tert*-Butoxymethyl-4-oxo-6-(toluene-4-sulfonyl)hex-2-enyl]carbamic Acid 9*H*-Fluoren-9-ylmethyl Ester [(*S*)-12d]
Solid (68%); mp 87–89 °C; R_f 1.2 (EtOAc–hexane, 1:2.5); $[\alpha]_D^{20}$ –61.8 (*c* = 1.00, $CHCl_3$).

IR (KBr): 3317, 1695, 1648, 1337, 1274, 1258, 1153 cm^{-1}.

^{1}H NMR (200 MHz, $CDCl_3$): δ = 1.17 (s, 9 H, O*t*-C_4H_9); 2.45 (s, 3 H, C*H*$_3C_6H_4$), 3.05 (t, 2 H, *J* = 7 Hz, CH_2CO), 3.40 (t, 2 H, *J* = 7 Hz, CH_2S), 3.44–3.53 (m, 1 H, CH), 4.28 (t, 1 H, *J* = 7.2 Hz, HCCN), 4.39–4.48 (m, 4 H, 2 OCH_2), 5.30 (br d, 1 H, NH), 6.2 (d, 1 H, *J* = 14.2 Hz), 6.83 (dd, 1 H, *J* = 14.2, 6.9 Hz, NCCH=), 7.32–7.81 (m, 8 H).

^{13}C NMR (50 MHz, $CDCl_3$): δ = 21.6, 27.3, 33.0, 47.2, 50.7, 52.3, 63.0, 66.9, 120.0, 124.9, 127.1, 127.7, 128.0, 128.9, 130.0, 135.7, 141.3, 143.7, 145.0, 145.8, 156.2, 194.9.

Anal. Calcd for $C_{33}H_{37}NO_6S$ (575.7): C, 68.85; H, 6.48; N, 2.43; S, 5.57. Found: C, 68.09; H, 6.30; N, 2.39; S, 5.29.

Vinylpyrroles 14a–d and Pyrrole Sulfones 15a–d; General Procedure
A solution of **12** (1 mmol) in CH_2Cl_2 (10 mL) was treated with piperidine (170 mg, 2 mmol) and stirring was continued until consumption of the starting material (TLC monitoring). The solvent was evaporated under reduced pressure and the residue purified by column chromatography.

2-Methyl-5-vinyl-1*H*-pyrrole (14a)
Oil (61%); R_f 0.11 (EtOAc–hexane, 1:2).

IR (neat): 3401, 1632, 1601, 1487, 987 cm^{-1}.

^{1}H NMR (200 MHz, $CDCl_3$): δ = 2.06 (s, 3 H, CH_3), 5.58–5.52 (m, 1 H, =CH, pyrrole), 5.57–5.62 (m, 1 H, =CH pyrrole), 7.24 (dd, 1 H, *J* = 15.6, 8.1 Hz, =CH), 7.75–7.81 (m, 2 H, $=CH_2$), 10.1 (br s, 1 H, NH).

^{13}C NMR (50 MHz, $CDCl_3$): δ = 14.1, 106.9, 107.8, 115.0, 116.2, 129.9, 136.9.

Anal. Calcd for C_7H_9N (107.2): C, 78.46; H, 8.47; N, 13.07. Found: C, 78.58; H, 8.57; N, 12,94.

2-Isopropyl-5-vinyl-1*H*-pyrrole (14b)
Oil (53%); R_f 0.13 (EtOAc–hexane, 1:4).

IR (neat): 3423, 1635, 1631, 1476, 980 cm^{-1}.

^{1}H NMR (200 MHz, $CDCl_3$): δ = 1.27 (d, 6 H, *J* = 7 Hz, 2 CH_3), 2.92 (sept, 1 H, *J* = 7 Hz, CH), 5.74–5.79 (m, 2 H, 2 =CH pyrrole), 7.24 (dd, 1 H, *J* = 15.6, 8.1 Hz, =CH), 7.75–7.81 (m, 2 H, $=CH_2$), 10.15 (br s, 1 H, NH).

^{13}C NMR (50 MHz, $CDCl_3$): δ = 24.9, 34.8, 106.8, 107.0, 114.9, 118.0, 127.1, 136.8.

Anal. Calcd for $C_9H_{13}N$ (135.2): C, 79.95; H, 9.69; N, 10.36. Found: C, 79.95; H, 9.78; N, 10.21.

2-Benzyl-5-vinyl-1*H*-pyrrole (14c)
Oil (72%), R_f 0.2 (EtOAc–hexane, 1:4).

IR (neat): 3416, 1589, 1579, 1455, 987, 964 cm^{-1}.

^{1}H NMR (200 MHz, $CDCl_3$): δ = 3.92 (s, 2 H, CH_2), 5.72–5.75 (m, 2 H, 2 =CH pyrrole), 7.21–7.98 (m, 8 H, C_6H_5, $CH=CH_2$), 10.04 (br s, 1 H, NH).

^{13}C NMR (50 MHz, $CDCl_3$): δ = 35.4, 105.6, 107.8, 117.1, 119.1, 125.5, 125.9, 128.9, 130.0, 137.7, 138.9.

Anal. Calcd for $C_{13}H_{13}N$ (183.3): C, 85.21; H, 7.15; N, 7.64. Found: C, 85.61; H, 7.02; N, 7.55.

2-*tert*-Butoxymethyl-5-vinyl-1*H*-pyrrole (14d)
Oil (64%); R_f 0.1 (EtOAc–hexane, 1:4).

IR (neat): 3415, 1631, 1605, 1487, 1286, 1127, 987 cm^{-1}.

^{1}H NMR (200 MHz, $CDCl_3$): δ = 1.19 (s, 9 H, *t*-C_4H_9), 4.72 (s, 2 H, OCH_2), 5.66–5.69 (m, 1 H, =CH pyrrole), 5.81–5.86 (m, 1 H, =CH pyrrole), 7.19 (dd, 1 H, *J* = 15.3, 8.0 Hz, =CH), 7.81–7.89 (m, 2 H, $=CH_2$), 9.92 (br s, 1 H, NH).

^{13}C NMR (50 MHz, $CDCl_3$): δ = 28.7, 69.1, 70.0, 105.4, 107.3, 117.7, 119.0, 131.5, 132.6.

Anal. Calcd for $C_{11}H_{17}NO$ (179.3): C, 73.70; H, 9.56; N, 7.81. Found: C, 72.74; H, 9.40; N, 7.76.

2-Methyl-5-[2-(toluene-4-sulfonyl)ethyl]-1*H*-pyrrole (15a)
Oil (73%); R_f 0.2 (EtOAc–hexane, 1:4).

IR (neat): 3450, 1320, 1115 cm^{-1}.

^{1}H NMR (200 MHz, $CDCl_3$): δ = 2.23 (s, 3 H, CH_3), 2.47 (s, 3 H, C*H*$_3C_6H_4$), 3.02 (t, 2 H, *J* = 7.3 Hz, CH_2), 3.36 (t, 2 H, *J* = 7.3 Hz, CH_2S), 5.73–5.75 (m, 2 H, 2 =CH pyrrole), 7.38 (d, 2 H, *J* = 8.2 Hz, C_6H_4), 7.80 (d, 2 H, *J* = 8.2 Hz, C_6H_4), 8.22 (br, 1 H, NH).

^{13}C NMR (50 MHz, $CDCl_3$): δ = 14.2, 21.9, 25.8, 57.9, 108.8, 109.8, 126.4, 129.3, 129.8, 130.1, 136.5, 138.4.

Anal. Calcd for $C_{14}H_{17}NO_2S$ (263.4): C, 63.85; H, 6.51; N, 5.32; S, 11.00. Found: C, 63.75; H, 6.25; N, 5.39; S, 12.29.

2-Isopropyl-5-[2-(toluene-4-sulfonyl)ethyl]-1*H*-pyrrole (15b)
Oil (88%); R_f 0.28 (EtOAc–hexane, 1:4).

IR (neat): 3351, 1316, 1146 cm^{-1}.

^{1}H NMR (200 MHz, $CDCl_3$): δ = 1.23 (d, 6 H, *J* = 6.8 Hz, 2 CH_3), 2.47 (s, 3 H, C*H*$_3C_6H_4$), 2.88 (sept, 1 H, CH), 3.06 (t, 2 H, *J* = 7.4 Hz, CH_2), 3.40 (t, 2 H, *J* = 7.4 Hz, CH_2S), 5.76–5.78 (m, 2 H, 2 =CH pyrrole), 7.38 (d, 2 H, *J* = 8 Hz, C_6H_4), 7.83 (d, 2 H, *J* = 8 Hz, C_6H_4), 8.43 (br, 1 H, NH).

^{13}C NMR (50 MHz, $CDCl_3$): δ = 21.2, 21.9, 22.6, 27.1, 56.4, 102.8, 105.9, 125.9, 128.1, 130.0, 135.9, 139.1, 145.0.

Anal. Calcd for $C_{16}H_{21}NO_2S$ (291.4): C, 65.95; H, 7.26; N, 4.81; S, 11.00. Found: C, 65.83; H, 7.20; N, 4.79; S, 11.21.

2-Benzyl-5-[2-(toluene-4-sulfonyl)ethyl]-1*H*-pyrrole (15c)
Oil (27%); R_f 0.32 (EtOAc–hexane, 1:4).

IR (neat): 3365, 1652, 1324, 1144 cm^{-1}.

^1H NMR (200 MHz, $CDCl_3$): δ = 2.46 (s, 3 H, C*H*$_3$C$_6$H$_4$), 3.16 (t, 2 H, CH_2), 3.24 (t, 2 H, CH_2S), 3.62 (s, 2 H, C*H*$_2$C$_6$H$_5$), 5.45–5.47 (m, 1 H, =CH pyrrole), 5.83–5.85 (m, 1 H, =CH pyrrole), 7.25 (s, 5 H, C_6H_5); 7.33 (d, 2 H, *J* = 8 Hz, C_6H_4), 7.80 (d, 2 H, *J* = 8 Hz, C_6H_4), 8.41 (br, 1 H, NH).

^{13}C NMR (50 MHz, $CDCl_3$): δ = 21.7, 21.9, 35.9, 56.7, 102.6, 104.9, 124.8, 125.7, 128.7, 129.0, 129.5, 129.8, 130.5, 131.8.

Anal. Calcd for $C_{20}H_{21}NO_2S$ (339.5): C, 70.77; H, 6.24; N, 4.13; S, 9.45. Found: C, 70.84; H, 6.37; N, 4.15; S, 9.45.

2-*tert*-Butoxymethyl-5-[2-(toluene-4-sulfonyl)-ethyl]-1*H*-pyrrole (15d)
Oil (53%); R_f 0.48 (EtOAc–hexane, 1:2).

IR (neat): 3359, 1318, 1246, 1195, 1140 cm^{-1}.

^1H NMR (200 MHz, $CDCl_3$): δ = 1.27 (s, 9 H, *t*-C_4H_9), 2.47 (s, 3 H, C*H*$_3$C$_6$H$_4$), 2.87–2.96 (m, 2 H, CH_2), 3.13–3.21 (m, 2 H, CH_2S), 4.36 (s, 2 H, OCH_2), 5.66–5.68 (m, 1 H, =CH pyrrole), 5.79–5.82 (m, 1 H, =CH pyrrole), 7.37 (d, 2 H, *J* = 8 Hz, C_6H_4), 7.79 (d, 2 H, *J* = 8 Hz, C_6H_4), 8.83 (br, 1 H, NH).

^{13}C NMR (50 MHz, $CDCl_3$): δ = 21.04, 21.6, 27.6, 31.2, 56.0, 57.3, 73.6, 106.3, 106.7, 127.6, 128.1, 129.2, 129.9, 135.9, 144.8.

Anal. Calcd for $C_{18}H_{25}NO_3S$ (335.5): C, 64.45; H, 7.51; N, 4.18; S, 9.56. Found: C, 65.03; H, 7.62; N, 4.06; S, 9.41.

***N*-Boc-pyrrole Sulfones 16a–d; General Procedure**
CF_3CO_2H (3 mmol) was added to a solution of **11** (1 mmol) in CH_2Cl_2 (10 mL) at r.t. and the mixture was kept at the same temperature until completion of the reaction (TLC monitoring). The solvent was evaporated under reduced pressure and the residue was subjected to column chromatography to give pure **16**.

2-Methyl-5-[2-(toluene-4-sulfonyl)ethyl]pyrrole-1-carboxylic Acid *tert*-Butyl Ester (16a)
Oil (85%); R_f 0.3 (EtOAc–hexane, 1:2).

IR (neat): 1737, 1319, 1110 cm^{-1}.

^1H NMR (200 MHz, $CDCl_3$): δ = 1.4 (s, 9 H, *t*-C_4H_9), 2.20 (s, 3 H, CH_3), 2.50 (s, 3 H, C*H*$_3$C$_6$H$_4$), 3.02 (t, 2 H, *J* = 7.4 Hz, CH_2), 3.35 (t, 2 H, *J* = 7.4 Hz, CH_2S), 5.69–5.72 (m, 2 H, 2 =CH pyrrole), 7.33 (d, 2 H, *J* = 8.2 Hz, C_6H_4), 7.83 (d, 2 H, *J* = 8.2 Hz, C_6H_4).

^{13}C NMR (50 MHz, $CDCl_3$): δ = 21.7, 25.8, 27.9, 36.6, 54.9, 83.7, 109.8, 111.1, 126.2, 128.3, 129.1, 129.8, 136.5, 145.2, 149.9.

Anal. Calcd for $C_{19}H_{25}NO_4S$ (363.5): C, 62.78; H, 6.93; N, 3.85; S, 8.82. Found: C, 62.88; H, 6.95; N, 3.83; S, 8.80.

2-Isopropyl-5-[2-(toluene-4-sulfonyl)ethyl]pyrrole-1-carboxylic Acid *tert*-Butyl Ester (16b)
Oil (78%); R_f 0.5 (EtOAc–hexane, 1:4).

IR (neat): 1735, 1598, 1316, 1086 cm^{-1}.

^1H NMR (200 MHz, $CDCl_3$): δ = 1.24 (d, 6 H, *J* = 7 Hz, 2 CH_3), 1.44 (s, 9 H, *t*-C_4H_9), 2.47 (s, 3 H, C*H*$_3$C$_6$H$_4$), 2.81–2.94 (m, 1 H, CH), 3.05–3.12 (m, 2 H, CH_2), 3.35–3.45 (m, 2 H, CH_2S), 5.75–5.78 (m, 2 H, 2 =CH pyrrole), 7.38 (d, 2 H, *J* = 7.2 Hz, C_6H_4), 7.81 (d, 2 H, *J* = 7.2 Hz, C_6H_4).

^{13}C NMR (50 MHz, $CDCl_3$): δ = 21.3, 21.9, 22.2, 22.9, 27.8, 57.0, 83.9, 102.6, 106.2, 125.4, 128.6, 130.2, 136.2, 140.3, 145.5, 150.2.

Anal. Calcd for $C_{21}H_{29}NO_4S$ (391.5): C, 64.42; H, 7.47; N, 3.58; S, 8.19. Found: C, 64.45; H, 7.54; N, 3.50; S, 8.27.

2-Benzyl-5-[2-(toluene-4-sulfonyl)ethyl]pyrrole-1-carboxylic Acid *tert*-Butyl Ester (16c)
Oil (91%); R_f 0.6 (EtOAc–hexane, 1:1.5).

IR (neat): 1729, 1598, 1322, 1150, 1111 cm^{-1}.

^1H NMR (200 MHz, $CDCl_3$): δ = 1.40 (s, 9 H, *t*-C_4H_9), 2.46 (s, 3 H, C*H*$_3$C$_6$H$_4$), 3.18 (t, 2 H, *J* = 8.2 Hz, CH_2), 3.41 (t, 2 H, *J* = 8.2 Hz, CH_2S), 4.10 (s, 2 H, C*H*$_2$C$_6$H$_5$), 5.66 (d, 1 H, *J* = 3.3 Hz, =CH pyrrole), 5.83 (d, 1 H, *J* = 3.3 Hz, =CH pyrrole), 7.03–7.83 (m, 9 H, C_6H_5 and C_6H_4).

^{13}C NMR (50 MHz, $CDCl_3$): δ = 21.7, 23.6, 27.0, 27.8, 35.7, 55.9, 84.4, 110.8, 112.0, 126.1, 128.2, 128.3, 128.5, 129.9, 131.5, 134.6, 136.2, 139.9, 144.6, 149.8.

Anal. Calcd for $C_{25}H_{29}NO_4S$ (439.6): C, 68.31; H, 6.65; N, 3.19; S, 7.29. Found: C, 68.30; H, 6.67; N, 3.11; S, 7.22.

2-*tert*-Butoxymethyl-5-[2-(toluene-4-sulfonyl)ethyl]pyrrole-1-carboxylic Acid *tert*-Butyl Ester (16d)
Oil (72%); R_f 0.49 (EtOAc–hexane, 1:2).

IR (neat): 1725, 1315, 1283, 1143 cm^{-1}.

^1H NMR (200 MHz, $CDCl_3$): δ = 1.27 (s, 9 H, *t*-C_4H_9), 1.38 (s, 9 H, *t*-C_4H_9), 2.46 (s, 3 H, C*H*$_3$C$_6$H$_4$), 2.80–2.87 (m, 2 H, CH_2), 3.19–3.24 (m, 2 H, CH_2S), 4.34 (s, 2 H, OCH_2), 5.71 (d, 1 H, *J* = 2.8 Hz, =CH pyrrole), 5.85 (d, 1 H, *J* = 2.8 Hz, =CH pyrrole), 7.30 (d, 2 H, *J* = 8 Hz, C_6H_4), 7.81 (d, 2 H, *J* = 8 Hz, C_6H_4).

^{13}C NMR (50 MHz, $CDCl_3$): δ = 21.14, 27.5, 29.2, 31.5, 55.1, 57.6, 73.0, 79.3, 106.5, 107.2, 127.4, 128.8, 129.0, 130.8, 136.4, 145.8, 150.0.

Anal. Calcd for $C_{23}H_{33}NO_6S$ (435.6): C, 63.42; H, 7.64; N, 3.22; S, 7.19. Found: C, 63.58; H, 7.80; N, 3.28; S, 7.19.

Compounds 17c and 18c; General Procedure
A solution of **11c** or **12c** (1 mmol) in EtOAc (10 mL) was hydrogenated during 5 h in a Parr apparatus at 75 psi in the presence of 10% Pd/C as the catalyst. Filtration through Celite and evaporation of the solvent gave **17c** and **18c**, respectively.

[1-Benzyl-4-oxo-6-(toluene-4-sulfonyl)hexyl]carbamic Acid *tert*-Butyl Ester (17c)
White solid (97%); mp 158–160 °C; R_f 0.3 (Et_2O–PE, 3:1); $[\alpha]_D^{20}$ –48.9 (*c* = 1.00, $CHCl_3$).

IR (KBr): 3367, 1710, 1680, 1522, 1315, 1150 cm^{-1}.

^1H NMR (200 MHz, $CDCl_3$): δ = 1.36 (s, 9 H, *t*-C_4H_9), 1.43–1.60 (m, 1 H), 1.78–1.90 (m, 1 H), 2.43 (s, 3 H, C*H*$_3$C$_6$H$_4$), 2.48 (d, 2 H, *J* = 7 Hz), 2.68–2.80 (m, 2 H), 2.81 (t, 2 H, *J* = 7.9 Hz, CH_2CO), 3.34 (t, 2 H, *J* = 7.9 Hz, CH_2S), 3.78 (m, 1 H), 4.34 (br s, 1 H, NH), 7.12–7.77 (m, 9 H, C_6H_5 and C_6H_4).

^{13}C NMR (50 MHz, $CDCl_3$): δ = 21.6, 28.1, 28.3, 35.3, 39.4, 41.9, 50.6, 51.0, 79.8, 126.4, 127.9, 128.4, 129.3, 130.0, 135.9, 137.6, 144.9, 155.6, 205.8.

Anal. Calcd for $C_{25}H_{33}NO_5S$ (495.6): C, 65.33; H, 7.24; N, 3.05; S, 6.98. Found: C, 65.99; H, 7.48; N, 3.00; S, 6.80.

[1-Benzyl-4-oxo-6-(toluene-4-sulfonyl)hexyl]carbamic Acid 9*H*-Fluoren-9-ylmethyl Ester (18c)
Solid (95%); mp 128–130 °C; R_f 0.3 (Et_2O–PE, 5:1); $[\alpha]_D^{20}$ –58.3 (*c* = 1.00, $CHCl_3$).

IR (KBr): 3381, 1712, 1600, 1453, 1318, 1141 cm^{-1}.

^1H NMR (200 MHz, $CDCl_3$): δ = 1.52–1.93 (m, 2 H), 2.40 (s, 3 H, C*H*$_3$C$_6$H$_4$), 2.46 (d, 2 H, *J* = 7.1 Hz), 2.72–2.85 (m, 4 H), 3.31 (t, 2 H, *J* = 7.6 Hz), 3.60–3.80 (m, 1 H), 4.13 (t, 1 H, *J* = 6.5 Hz), 4.20–4.45 (m, 2 H), 4.60 (br d, 1 H, NH), 7.10–7.81 (m, 17 H).

^{13}C NMR (50 MHz, $CDCl_3$): δ = 21.1, 30.0, 32.1, 34.9, 36.5, 42.8, 48.9, 52.8, 72.0, 123.1, 123.9, 124.6, 126.8, 127.1, 128.5, 128.7, 129.9, 134.6, 136.6, 139.8, 143.5, 143.7, 155.2, 205.5.

Anal. Calcd for $C_{35}H_{35}NO_5S$ (581.7): C, 72.26; H, 6.06; N, 2.41; S, 5.51. Found: C, 72.29; H, 6.12; N, 2.52; S, 5.43.

2-Benzyl-5-{2-[(4-methylphenyl)sulfonyl]ethyl}pyrrolidinium Trifluoroacetate (19c)

A solution of **17c** (738 mg, 1.6 mmol) and CF_3CO_2H (0.37 mL, 4.8 mmol) in CH_2Cl_2 (10 mL) was stirred at r.t. for 24 h. The solvent was removed under reduced pressure and the crude residue was immediately dissolved in MeOH. The solution thus obtained was hydrogenated for 19 h in a Parr apparatus at 75 psi using 10% Pd/C as the catalyst. Filtration through Celite and evaporation of the solvent yielded a brown solid which was triturated with a mixture EtOAc–Et_2O (1:2) and filtered to give **19c** as a white solid (570 mg, 78%); mp 174–177 °C.

IR (KBr): 3360, 2495, 1603, 1456, 1385, 1010, 977 cm^{-1}.

^{1}H NMR (200 MHz, DMSO-d_6): δ = 1.50–1.62 (m, 2 H), 1.75–2.02 (m, 3 H), 2.42–2.50 (m, 4 H), 2.85 (dd, 1 H, *J* = 12, 7.8 Hz), 3.12 (dd, 1 H, *J* = 12, 7.8 Hz), 3.40–3.47 (m, 2 H), 3.57–3.78 (m, 2 H), 7.30 (s, 5 H, C_6H_5), 7.48 (d, 2 H, *J* = 7.8 Hz, C_6H_4), 7.79 (d, 2 H, *J* = 7.9 Hz, C_6H_4), 9.45 (br s, 2 H, NH_2).

^{13}C NMR (50 MHz, DMSO-d_6): δ = 21.1, 25.1, 29.4, 29.6, 37.3, 51.9, 57.2, 59.8, 126.7, 127.8, 128.5, 129.0, 130.0, 131.1 (q, CF_3, *J* = 259.3), 135.8, 137.2, 144.5.

Anal. Calcd for $C_{22}H_{26}F_3NO_4S$ (457.5): C, 57.76; H, 5.73; N, 3.06; S, 7.01. Found: C, 57.98; H, 6.00; N, 3.31; S, 7.29.

2-Benzyl-5-[2-(toluene-4-sulfonyl)ethyl]pyrrolidine (20c)

A solution of **19c** (100 mg, 0.29 mmol) in H_2O (3 mL) was treated with NaOH (23 mg, 0.4 mmol) and stirred at r.t. for 0.5 h. Additional H_2O (7 mL) was added and the mixture extracted with Et_2O (3 × 5 mL). The combined organic phases were dried and evaporated to give **20c** as a colourless oil (94 mg, 95%); R_f 0.65 (CH_2Cl_2–toluene–MeOH, 17:2:1); de = 53% as determined by chiral HPLC (system 1): isocratic elution (MeCN–MeOH–Et_3N–AcOH, 85:15:0.01:0.01); t_{R2} = 4.45, t_{R1} = 3.54.

IR (KBr): 3367, 1552, 1450, 1315, 1150 cm^{-1}.

^{1}H NMR (200 MHz, $CDCl_3$): δ (for the major isomer) = 1.20–1.50 (m, 2 H), 1.71–2.02 (m, 4 H), 2.43 (s, 3 H), 2.55–2.81 (m, 2 H), 3.07–3.49 (m, 5 H), 7.13–7.79 (m, 9 H, C_6H_5 and C_6H_4).

^{13}C NMR (50 MHz, $CDCl_3$): δ (for the major isomer) = 21.6, 29.8, 31.6, 31.8, 42.4, 54.3, 56.0, 58.4, 126.0, 126.2, 128.1, 128.3, 128.4, 129.0, 129.9, 136.3.

Anal. Calcd for $C_{20}H_{25}NO_2S$ (343.5): C, 69.93; H, 7.34; N, 4.08; S, 9.34. Found: C, 69.90; H, 7.29; N, 4.00; S, 9.48.

2-Benzyl-5-vinyl-3,4-dihydro-2*H*-pyrrole (21c)

A solution of **18c** (459 mg, 1 mmol) and piperidine (425 mg, 5 mmol) in CH_2Cl_2 (5 mL) was refluxed for 5 h, and then the solvent was evaporated. Purification of the crude oil by column chromatography afforded **21c** as an oil (128 mg, 69%); R_f 0.4 (EtOAc–hexane, 2:1 + 2% Et_3N); $[\alpha]_D^{20}$ +27.2 (*c* = 1.00, $CHCl_3$).

IR (KBr): 1645, 1598, 1465, 980 cm^{-1}.

^{1}H NMR (200 MHz, $CDCl_3$): δ = 1.45–1.69 (m, 2 H), 2.28–2.71 (m, 2 H), 2.48 (d, 2 H, *J* = 7.3 Hz), 4.31–4.48 (m, 1 H), 5.58–5.72 (m, 2 H, $=CH_2$), 6.71 (dd, 1 H, *J* = 17.2, 8.4 Hz, =CH), 7.22–7.30 (m, 5 H, C_6H_5).

^{13}C NMR (50 MHz, $CDCl_3$): δ = 20.0, 28.1, 42.3, 59.9, 121.6, 125.4, 126.1, 128.1, 128.5, 139.0, 168.9.

Anal. Calcd for $C_{13}H_{15}N$ (185.3): C, 84.28; H, 8.16; N, 7.56. Found: C, 83.75; H, 8.41; N, 7.42.

2-Benzyl-5-ethylpyrrolidine *p*-Toluenesulfonate (22c)

A solution of **13c** (491 mg, 1 mmol) and piperidine (425 mg, 5 mmol) in MeOH (10 mL) was hydrogenated for 5 h in a Parr apparatus (75 psi) in the presence of 10% Pd/C as the catalyst. The mixture was filtered through Celite and the solvent was evaporated. The residue was purified by column chromatography to give **22c** as a white solid (247 mg, 79%); mp 178–180 °C; R_f 0.35 (EtOAc–MeOH, 2:1).

IR (KBr): 3370, 2507, 1598, 1455, 1391, 1015, 962 cm^{-1}.

^{1}H NMR (200 MHz, DMSO-d_6): δ = 0.93 (t, 3 H, *J* = 7 Hz, CH_3), 1.25–2.15 (m, 4 H), 2.35 (s, 3 H, CH_3C$_6$H$_4$), 2.68–2.91 (m, 2 H), 3.15–3.70 (m, 4 H), 6.28 (br, 2 H, NH_2), 7.04–7.63 (m, 9 H, C_6H_5 and C_6H_4).

^{13}C NMR (50 MHz, DMSO-d_6): δ = 11.0, 21.4, 26.2, 29.8, 30.0, 60.0, 60.4, 124.4, 126.8, 128.6, 129.1, 137.3, 137.5, 139.3, 153.8.

Anal. Calcd for $C_{20}H_{27}NO_2S$ (313.5): C, 69.53; H, 7.88; N, 4.05; S, 9.28. Found: C, 69.24; H, 7.81; N, 3.89; S, 9.72.

1-(2-Benzyl-5-ethylpyrrolidin-1-yl)ethanone (23c)

Et_3N (0.2 mL, 1.45 mmol) and Ac_2O (0.06 mL, 0.6 mmol) were successively added to a stirred suspension of **22c** (100 mg, 0.29 mmol) in anhyd CH_2Cl_2 (5 mL). After stirring for 6 h, the mixture was evaporated and the oily residue subjected to column chromatography to yield **23c** as an oil (60 mg, 89%); R_f 0.2 (Et_2O–PE, 4:1); de 81% (by ^{1}H NMR spectroscopy).

IR (neat): 1684, 1605, 1555, 1463 cm^{-1}.

^{1}H NMR (200 MHz, $CDCl_3$): δ (for the major isomer) = 0.88 (t, 3 H, *J* = 7.1 Hz, CH_3CH$_2$), 1.32–2.04 (m, 4 H), 2.14 (s, 3 H, CH_3CO), 2.45–2.98 (m, 2 H), 3.26 (dd, 1 H, *J* = 12, 3 Hz), 3.52–3.69 (m, 1 H), 3.92–4.13 (m, 1 H), 4.25–4.39 (m, 1 H), 7.14–7.32 (m, 5 H, C_6H_5).

^{13}C NMR (50 MHz, $CDCl_3$): δ (for the major isomer) = 10.5, 15.8, 24.8, 25.5, 26.8, 40.2, 51.1, 52.7, 126.0, 128.0, 128.5, 138.4, 169.9.

Anal. Calcd for $C_{15}H_{21}NO$ (231.3): C, 77.88; H, 9.15; N, 6.05. Found: C, 77.85; H, 9.13; N, 6.11.

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