Enaminone-Based Synthesis of (*S*)-3-(Pyrazolyl)alanines from L-Aspartic Acid

Uroš Uršič, David Bevk, Samo Pirc, Lidija Pezdirc, Branko Stanovnik,* Jurij Svete*

Faculty of Chemistry and Chemical Technology, University of Ljubljana, Aškerčeva 5, 1000 Ljubljana, Slovenia
Fax +386(1)2419220; E-mail: branko.stanovnik@fkkt.uni-lj.si; E-mail: jurij.svete@fkkt.uni-lj.si

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Dedicated to Professor Miha Tišler, Professor Emeritus of the University of Ljubljana, on the occasion of his 80th birthday

Abstract: Protected N(1′)-substituted (*S*)-3-(4-methoxycarbonyl-1*H*-pyrazol-5-yl)alanines **7a**–**h** were prepared in 34–94% yields by acid-catalysed cyclocondensations of chiral enaminone **5**, available from L-aspartic acid, with hydrazines **6a**–**h** hydrochlorides. Deprotection of **7a**,**b**,**e** by catalytic hydrogenation afforded the corresponding free pyrazoylalanines **8a**,**b**,**e**. On the other hand, 1-benzyl 6-methyl (*S*)-2-benzyloxycarbonylamino-4-oxohexanedioate (**4**), precursor of the enaminone **5**, reacted with hydrazines **6** in two different ways. In the reactions of **4** with (hetero)arylhydrazines **6b**,**e**,**i**, the five-membered ring was formed and the corresponding 3-pyrazolylalanine esters **10b**,**i** and **10′e** were obtained, whilst treatment of **4** with hydrazine hydrate (**6a**) and methylhydrazine (**6h**) led to the formation of the six-membered ring furnishing tetrahydropyridazinones **11a**,**h**.

Key words: amino acids, enaminones, hydrazines, cyclizations, pyrazoles

Non-proteinogenic α-amino acids represent an important group of compounds, not only due to their occurrence in nature and their pharmaceutical and biological applications, but also because of their utilisation in organic synthesis and in asymmetric transformations.[1] A group of such α-amino acids are 3-heteroarylalanines,[2,3] useful as the non-proteinogenic analogues of histidine and tryptophane. Several 3-heteroarylalanines, such as (*S*)-3-(1*H*-pyrazol-1-yl)alanine,[3] mimosine,[4] (*S*)-3-(4-carboxy-3-furyl)alanine,[5] and (*S*)-azatyrosine,[6] have been isolated from natural sources, mostly from plants (Figure 1).

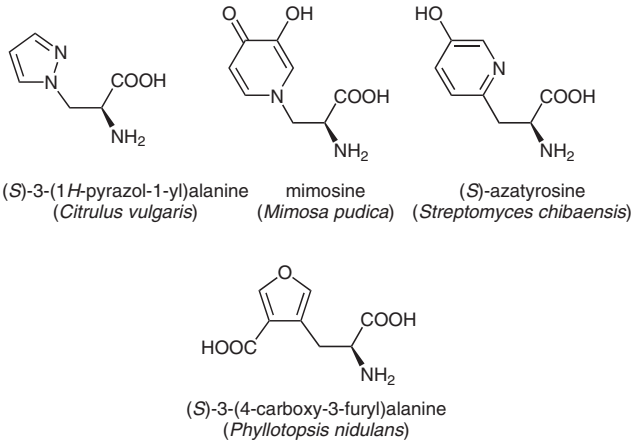

Figure 1 Some examples of naturally occurring 3-heteroarylalanines

An important synthetic approach towards non-racemic 3-heteroarylalanines is the chiron approach, where the heterocyclic ring is formed by heterocyclisation of alanine derivative with a suitable functional moiety at β-position, such as formyl group and α-halo ketone, ynone, and dicarbonyl moiety. For example, (*S*)-5-bromo-4-oxonorvaline derivatives were transformed with ambident nucleophiles into protected (thiazol-4-yl)-, 3-(indolizin-3-yl)-, and 3-(imidazo[1,2-*x*]azin-2-yl)alanines,[7,8] reactions of α-amino acid vicinal tricarbonyls with ambident nucleophiles gave 3-(quinoxalinyl)-, 3-(pyrazinyl)-, and 3-(1,2,4-triazinyl)alanines,[9a] while α-amino acid ynones were used in the synthesis of pyridinyl-, pyrazolyl-, isoxazolyl-, and (1,2,3-triazolyl)alanines.[9b] Similarly, (*S*)-3-formylalanines were used as the key intermediates in the synthesis of 3-([1,2,4]triazolo[4,3-*x*]azin-3-yl)alanines[8] and in three-component Hantzsch and Biginelli cyclocondensations leading to 3-(pyridinyl)alanines and 3-(pyrimidinyl)alanines.[10]

Recently, a series of alkyl 2-substituted 3-(dimethylamino)propenoates and their analogues have been prepared as versatile reagents for the preparation of various heterocyclic systems and in the synthesis of functionalised heterocycles, including 3-heteroarylalanine derivatives.[11] In this context, Young and co-workers have previously reported utilisation of α-(dimethylaminomethylidene)pyroglutamic acid esters in the 'ring switching' synthesis of 3-pyrazolyl, isoxazolyl, and pyrimidinyl substituted alanines via hydrolysis of the enamino group into the formyl group followed by treatment with ambident nucleophiles.[12] Later on, we reported an improved variation of Young's methodology,[13] which has been extended also on the preparation of 3-heteroaryl substituted alaninols,[14] lactic acids,[15] and propane-1,2-diols.[16] The same enaminones were also used as the key intermediates in a stereoselective α-amination of 5-substituted γ-lactams and γ-lactones, via nitrosation of the dimethylaminomethylidene group followed by catalytic hydrogenation of the intermediate oximes.[17] Recently, (+)-camphor derived enaminone, (1*R*,4*E*,5*S*)-4-[(dimethylamino)methylidene]-1,8,8-trimethyl-2-oxabicyclo[3.2.1]octan-3-one, was transformed via nitrosation into the corresponding 4-oximino analogue, which, upon treatment with alkylmagnesium halides, furnished (1*R*,4*S*,5*S*)-4-dialkylamino-1,8,8-trimethyl-2-oxabicyclo[3.2.1]octan-3-ones as novel non-proteinogenic amino acid derivatives containing a terpene moiety.[18]

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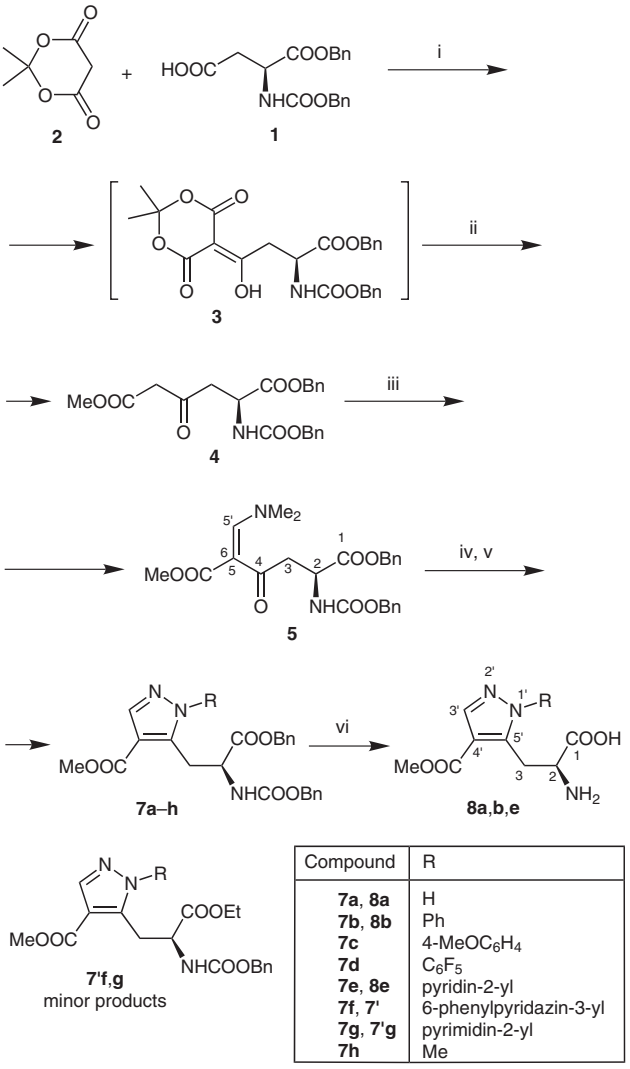
In continuation of our work in this field, we now report another enaminone-based methodology for the preparation of 3-pyrazolylalanines **8** via transformation of (*S*)-*N*-(benzyloxycarbonyl)aspartic acid 1-benzyl ester (**1**) into 1-benzyl 6-methyl (5*E*,2*S*)-5-[(dimethylamino)methylidene]-2-benzyloxycarbonylamino-4-oxohexanedioate (**5**), followed by treatment with hydrazine derivatives **6** and hydrogenolytic deprotection.

The key intermediate, 1-benzyl 6-methyl (5*E*,2*S*)-5-[(dimethylamino)methylidene]-2-benzyloxycarbonylamino-4-oxohexanedioate (**5**), was prepared in three steps from 1-benzyl (*S*)-*N*-(benzyloxycarbonylamino)aspartate (**1**), available in three steps from L-aspartic acid according to the literature procedures.[19] Following closely related examples from the literature,[20] the acid **1** was first coupled with Meldrum's acid (**2**) to give the intermediate **3**, which was then heated in anhydrous methanol to afford 1-benzyl 6-methyl (*S*)-2-benzyloxycarbonylamino-4-oxohexanedioate (**4**) in 66% yield over two steps. Further treatment of **4** with *N*,*N*-dimethylformamide dimethyl acetal (DMF-DMA) gave the desired enaminone **5** in almost quantitative yield. Cyclocondensations of **5** with hydrazines **6a–e**,**h** hydrochlorides in methanol at room temperature or in ethanol under reflux afforded the corresponding fully protected 3-pyrazolylalanines **7a–e**,**h** in 57–94% yields. Further deprotection of compounds **7a**,**b**,**e** by catalytic hydrogenation in the presence of Pd–C furnished the free amino acids **8a**,**b**,**e** in 75–82% yields. On the other hand, acid-catalysed cyclocondensations of **5** with the less reactive 3-hydrazino-6-phenylpyridazine (**6f**) and 2-hydrazinopyrimidine (**6g**) in refluxing ethanol were accompanied by partial transesterification. Consequently, mixtures of the major benzyl esters **7f**,**g** and the minor ethyl esters **7′f**,**g** were formed. Chromatographic separation afforded pure compounds **7f**, **7g**, **7′f**, and **7g** (Scheme 1).

Due to the β-keto ester moiety, which is included along positions 4–6 in 1-benzyl 6-methyl (*S*)-2-benzyloxycarbonylamino-4-oxohexanedioate (**4**), this compound is also a suitable precursor for the synthesis of 3-pyrazolylalanines. Consequently, **4** was treated with hydrazines **6a**,**b**,**e**,**h**,**i**. Surprisingly, two types of products were obtained. Reactions of **4** with phenylhydrazine (**6b**), and 4-nitrophenylhydrazine (**6i**) gave (*S*)-3-(1-aryl-5-oxo-4,5-dihydro-1*H*-pyrazol-3-yl)-*N*-(benzyloxycarbonyl)alanine benzyl esters **10b** and **10i**. Similarly, treatment of **4** with 2-hydrazinopyridine (**6e**) led to the protected (*S*)-3-[3-oxo-1-(pyridin-2-yl)-1,2-dihydro-3*H*-pyrazol-5-yl]alanine **10e**. On the other hand, reactions of **4** with hydrazine hydrate (**6a**) and methylhydrazine (**6h**) led to the formation of the six-membered ring to afford the corresponding tetrahydropyridazinones **11a**,**h**. The reaction mechanism could be explained by initial formation of the intermediate hydrazone **9**. Further cyclisation of the hydrazone **9** can take place, either to the methoxycarbonyl group leading to pyrazolylalanine **10** (Path A), or to the benzyloxycarbonyl group leading to the pyridazinone **11** (Path B). Unfortunately, we do not have a firm explanation for this selectivity, which, on the other hand, might be



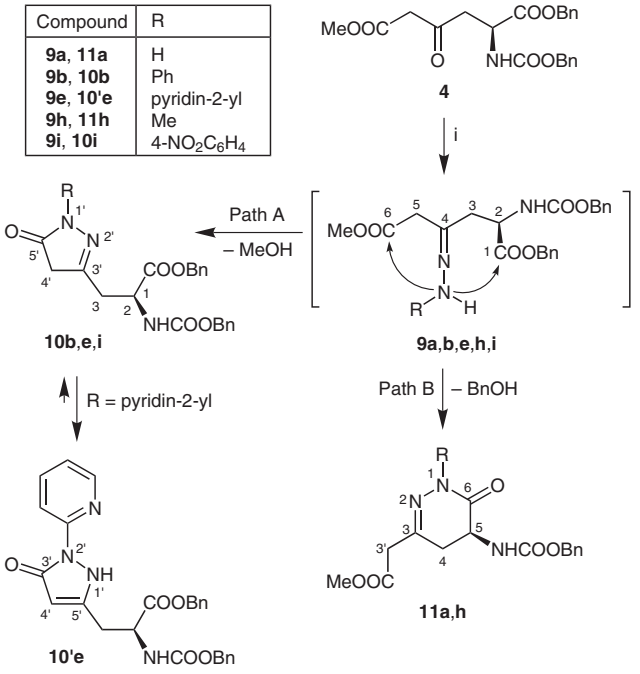
Compound	R
7a, **8a**	H
7b, **8b**	Ph
7c	4-MeOC$_6$H$_4$
7d	C$_6$F$_5$
7e, **8e**	pyridin-2-yl
7f, **7'**	6-phenylpyridazin-3-yl
7g, **7'g**	pyrimidin-2-yl
7h	Me

Scheme 1 *Reagents and conditions*: (i) DCC, DMAP, CH_2Cl_2, –5 °C; (ii) MeOH, reflux; (iii) DMFDMA, CH_2Cl_2, r.t.; (iv) $RNHNH_2$ (**6a–h**)·HCl, MeOH or EtOH, r.t. or reflux; (v) chromatographic separation (column chromatography followed by MPLC); (vi) H_2 (1 bar); 10% Pd–C, MeOH, r.t.

attributed to steric and/or electronic factors. Apparently, cyclisation of less nucleophilic and sterically more demanding *N*-arylhydrazones **9b**,**e**,**i** takes place preferentially to the position 6, while in the case of more nucleophilic and sterically less demanding hydrazones **9a**,**h** cyclisation to the position 1 is favoured (Scheme 2).

Structures of compounds **4**, **5**, **7**, **8**, **10**, and **11** were determined by spectroscopic (IR, ^{1}H and ^{13}C NMR, MS, HRMS) methods and by elemental analyses for C, H, and N. Compounds **4**, **5**, **7′f**,**g**, **8a**,**b**,**e**, **10i**, and **11a**,**h** were not isolated in analytically pure form. Their identities were confirmed by ^{13}C NMR and HRMS spectroscopy.

The configuration around the C(5)=C(5′) bond in compound **5** was determined by HMBC spectroscopy on the basis of long-range coupling constants ($^3J_{C-H}$) between the methylidene proton [HC(5′)] and the carbonyl carbon atoms [O=C(4) and O=C(6)], measured from the antiphase splitting of cross peaks in the HMBC spectrum. General-



Scheme 2 *Reagents and conditions*: (i) $RNHNH_2$ (**6a**,**b**,**e**,**h**,**i**), MeOH, r.t.

ly, the magnitude of the coupling constant $^3J_{C-H}$ for nuclei with *cis*-configuration around the C=C bond is smaller (2–6 Hz) than that for *trans*-oriented nuclei (8–12 Hz).[11b,c,f,21–23] In compound **5**, the magnitudes of coupling constants, $^3J_{C(4)-H(5')} = 6.6$ Hz (*trans*) and $^3J_{C(6)-H(5')} = 4.8$ Hz (*cis*) showed the (*E*)-configuration around the C(5)=C(5′) bond (Figure 2).

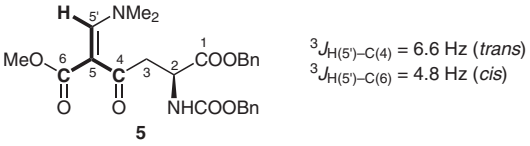


Figure 2 Determination of configuration around the C(5)=C(5′) bond in enaminone **5** by HMBC spectroscopy

Like other pyrazolones,[24] the 3-pyrazoylalanine derivatives **10** can also exist in three tautomeric forms, **10** and/or **10′**, and/or **10″**. Differentiation between these three tautomeric forms is possible by IR and NMR. In our case, compounds **10b**,**i** were isolated as the 5-oxo-4,5-dihydro-1*H*-pyrazole tautomers, while compound **10′e** was isolated as the 3-oxo-1,2-dihydro-3*H*-pyrazole tautomer. All compounds, **10b**,**i** and **10′e**, exhibited C=O absorption bands at 1719–1733 cm^{-1}, corresponding to the COOBn groups and the ring C=O group of the pyrazolone tautometic form **10**. Compound **10′e** also exhibited another C=O absorption band at 1688 cm^{-1}, which is in agreement with typical literature vibrations for 3-oxo-1,2-dihydro-3*H*-pyrazoles.[24,25] On the other hand, the appearance of the 4′-CH_2 group as two doublets at ca 3.3 and 3.5 ppm in the ^{1}H NMR spectra of **10b**,**i** clearly supported the 5-oxo-4,5-dihydro-1*H*-pyrazole tautomeric forms. In the case of compound **10′e**, HC(4′) appeared as a singlet at 5.31 ppm and was in agreement with the proposed tautomeric form **10′**. Higher stability of the 3-oxo-1,2-dihydro-3*H*-pyrazole tautomeric form **10′** in the case of compound **10′e** could be due to intramolecular N·····H hydrogen bond between the HN(1′) and the pyridine ring nitrogen atom N(1″) (Figure 3).

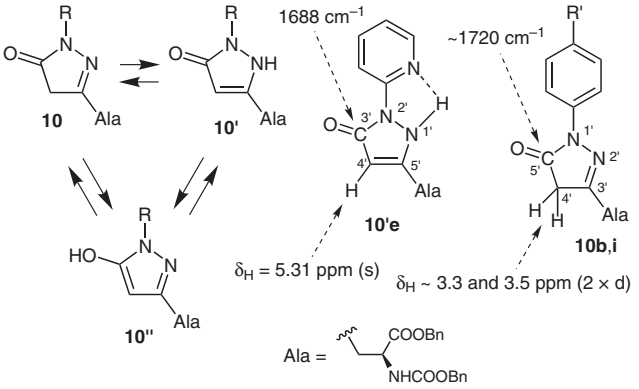


Figure 3

Finally, we tried to establish possible (partial) racemisation, which might accompany cyclisations of **4** and **5** with hydrazine derivatives **6**. First, ^{1}H NMR spectra of 10 mg of compound **7a** in the presence of 10 mg, 20 mg, and 30 mg of tris[3-(heptafluoropropylhydroxymethylene)-D-camphorato]europium were taken. Unfortunately, these spectra were not very informative, due to strong broadening of characteristic signals. On the other hand, ^{1}H NMR spectrum of the free amino acid **8b** in the presence of equimolar amount of (+)-camphor-10-sulfonic acid exhibited a single set of signals. Similarly, the Mosher amide, prepared by acylation of **8b** with (*R*)-α-methoxy-α-trifluoromethylphenylacetic acid [(*R*)-Mosher acid], was found to be isomerically pure according to ^{1}H NMR. Finally, HPLC analysis of compounds **7a**,**e**,**h** and **11a**,**h** on a chiral stationary phase resulted in elution of single peaks, which supported enantiomeric purity of these compounds. Despite the fact that the results of this study were not completely unambigous, they indicated that cyclisations of **4** and **5** with hydrazine derivatives **6** probably proceed racemisation-free.

In conclusion, N(1′)-substituted (*S*)-3-(4-methoxycarbonyl-1*H*-pyrazol-5-yl)alanines were prepared from chiral enaminone **5**, available in six steps from L-aspartic acid, via acid-catalysed cyclocondensations with hydrazines **6** followed by deprotection. In addition to the previously published 'ring switching' approach,[12–16] this methodology represents an alternative route towards 3-heteroarylalanines via L-aspartic acid derived acyclic enaminone **5**.

Melting points were determined on a Kofler micro hot stage. The ^{1}H NMR spectra were obtained on a Bruker Avance DPX 300 spectrometer at 300 MHz for ^{1}H NMR and 75.5 MHz for ^{13}C NMR, using DMSO-d_6 and $CDCl_3$ as solvents and tetramethylsilane as the internal standard. Mass spectra were recorded on an AutoSpecQ

spectrometer. IR spectra were obtained on a Perkin–Elmer Spectrum BX FTIR spectrophotometer. Microanalyses were performed on a Perkin-Elmer CHN Analyser 2400 II. Column chromatography was performed on silica gel (Fluka, silica gel 60, 0.04–0.06 mm). Medium pressure liquid chromatography (MPLC) was performed with Büchi isocratic system with detection on silica gel (Merck, Lichrospher® 60, 0.012 mm); column dimensions: 15 × 450 mm (wet filled); UV detection (254 nm); sample amount: 150 mg per each run. HPLC analyses of compounds **7a**,**e**,**h** and **11a**,**h** were performed on a Hewlett–Packard Liquid Chromatograph 1050; column: Supelcosil (*S*)-DNBPG (250 × 4.6 mm); mobile phase: EtOAc–*n*-hexane (50:50 or 75:25); flow: 2 mL/min; UV detector (254 nm).

Meldrum's acid (**1**), 4-dimethylaminopyridine (DMAP), *N*,*N*′-dicyclohexylcarbodiimide (DCC), *N*,*N*-dimethylformamide dimethyl acetal (DMFDMA), hydrazines **6a–e**,**h**,**i**, tris[3-(heptafluoropropylhydroxymethylene)-D-camphorato]europium, (*R*)-α-methoxy-α-(trifluoromethyl)phenylacetic acid [(*R*)-Mosher acid], and (+)-camphor-10-sulfonic acid are commercially available (Sigma–Aldrich). (*S*)-*N*-(Benzyloxycarbonyl)aspartic acid 1-benzyl ester (**1**),[19] 3-hydrazino-6-phenylpyridazine (**6f**),[26] and 2-hydrazinopyrimidine (**6g**)[27] were prepared according to the literature procedures.

1-Benzyl 6-Methyl (2*S*)-2-Benzyloxycarbonylamino-4-oxohexanedioate (4)

This compound was prepared according to a slightly modified procedure described previously for closely related compounds.[20] A solution of DCC (5.674 g, 27.5 mmol) in anhyd CH_2Cl_2 (25 mL) was slowly added to a solution of Meldrum's acid **2** (3.603 g, 25 mmol), compound **1** (8.934 g, 25 mmol), and DMAP (3.360 g, 27.5 mmol) in anhyd CH_2Cl_2 (55 mL) at –5 °C. The reaction mixture was stirred at –5 °C for 2.5 h and was then allowed to warm slowly to r.t. (ca 1 h), filtered, and the precipitate was washed with anhyd CH_2Cl_2 (25 mL). The filtrate was washed with 1 M aq $NaHSO_4$ (2 × 170 mL) and brine (2 × 170 mL), dried over anhyd Na_2SO_4, filtered, and the filtrate was evaporated in vacuo. The residue was dissolved in anhyd MeOH (150 mL) and heated under reflux for 5 h. Volatile components were evaporated in vacuo and the residue was cyrstallised from cyclohexane to give **4**. Experimental, analytical, and spectral data for compound **4** are given in Tables 1– 4.

6-Benzyl 1-Methyl (2*E*,5*S*)-2-[(Dimethylamino)methylidene]-5-benzyloxycarbonylamino-3-oxohexanedioate (5)

DMFDMA (0.75 mL, 5.2 mmol) was added to a solution of **4** (2.065 g, 5 mmol) in anhyd CH_2Cl_2 and the mixture was stirred at r.t. for 3.5 h and then evaporated in vacuo. The residue was purified by column chromatography. Fractions containing the product were combined and evaporated in vacuo to give **5**. Experimental, analytical, and spectral data for compound **5** are given in Tables 1– 4.

Acid-Catalysed Cyclocondensations of 5 with Hydrazine Hydrochlorides 6a–h; General Procedures for the Preparation of Protected (*S*)-3-(1*H*-pyrazol-5-yl)alanines 7a–h and 7′f,g

Method A: A mixture of **5** (0.468 g, 1 mmol), MeOH (10 mL), and hydrazine hydrochloride **6a** (0.068 g, 1 mmol) was stirred at r.t. for 16 h. Volatile components were evaporated in vacuo and the residue was purified by column chromatography followed by MPLC. Fractions containing the product were combined and evaporated in vacuo to give **7a**. Experimental, analytical, and spectral data for compound **7a** are given in Tables 1– 4.

Method B: A mixture of **5** (0.468 g, 1 mmol), EtOH (10 mL), and hydrazine hydrochloride **6b**,**c** (1 mmol) or hydrazine **6d–g** (1 mmol) and 37% aq HCl (3 drops, ca 1 mmol) was refluxed for 1–16 h. Volatile components were evaporated in vacuo and the residue was purified by column chromatography followed by MPLC. Fractions containing the product were combined and evaporated in vacuo to give compounds **7b–g** and **7′f**,**g**. Compounds **7b**,**c** were obtained in pure form upon column chromatography purification. Experimental, analytical, and spectral data for compound **7b–g** and **7′f**,**g** are given in Tables 1– 4.

Method C: A mixture of **5** (0.468 g, 1 mmol), MeOH (10 mL), methylhydrazine (**6h**; 0.046 g, 1 mmol), and 37% aq HCl (3 drops, ca 1 mmol) was stirred at r.t. for 18 h. The reaction mixture was evaporated in vacuo to one-third of the initial volume (ca 3 mL). Water was added dropwise until a slight turbidity appeared, and the mixture was left in a refrigerator (+4 °C) for several hours. The precipitate was collected by filtration to give **7h**. Experimental, analytical, and spectral data for compound **7h** are given in Tables 1– 4.

Preparation of Free (*S*)-3-(1*H*-Pyrazol-5-yl)alanines 8a,b,e; General Procedure

A mixture of **7** (1 mmol), MeOH (25 ml), and 10% Pd–C (0.1 g) was hydrogenated (1 bar H_2, r.t.) for 24 h. The catalyst was removed by filtration through a short pad of Celite® and washed with MeOH (ca 50 mL). The filtrate was evaporated in vacuo to give **8a**,**b**,**e**. Experimental, analytical, and spectral data for compounds **8a**,**b**,**e** are given in Tables 1– 4.

Cyclocondensations of 4 with Free Hydrazines 6a,b,e,h,i; General Procedures for the Preparation of Protected (*S*)-3-(1*H*-pyrazol-3-yl)alanines 10b,e,i and Tetrahydropyridazinones 11a,h

Method A: A mixture of **4** (0.310 g, 0.75 mmol), MeOH (10 mL), and hydrazine **6** (0.75 mmol) was stirred at r.t. for 5–96 h and then evaporated in vacuo. The residue was purified by column chromatography followed by MPLC. Fractions containing product were combined and evaporated in vacuo to give compounds **10b,i** and **11a**,**h**. Compound **11a** was obtained in pure form upon column chromatography purification. Experimental, analytical, and spectral data for compound **10b**,**i** and **11a**,**h** are given in Tables 1– 4.

Method B: A mixture of **4** (0.310 g, 0.75 mmol), MeOH (10 mL), and 2-hydrazinopyridine (**6e**; 0.082 g, 0.75 mmol) was stirred at r.t. for 22 h. The reaction mixture was evaporated in vacuo to one-third of the initial volume (ca 3 mL). Water was added dropwise until a slight turbidity appeared, and the mixture was left in a refrigerator (+4 °C) for several hours. The precipitate was collected by filtration to give **10e**. Experimental, analytical, and spectral data for compound **10e** are given in Tables 1– 4.

Table 1 Experimental and Physical Data for Compounds **4**, **5**, **7**, **7′**, **8**, **10**, and **11**

Compound	R	Method	Time (h)	Column chromatography, MPLC[a]	Yield (%)	Mp (°C), crystallisation solvent
4	–	–	–	–	66	88–94 (cyclohexane)
5	–	–		Column chromatography: A (2:1)	98	212–216 ($CHCl_3$)
7a	H	A	16	Column chromatography: A (2:1) MPLC: A (1:1)	57	86–90 (toluene)

Table 1 Experimental and Physical Data for Compounds **4**, **5**, **7**, **7′**, **8**, **10**, and **11** (continued)

Compound	R	Method	Time (h)	Column chromatography, MPLC[a]	Yield (%)	Mp (°C), crystallisation solvent
7b	Ph	B	1	Column chromatography: A (1:2)	94	Oil
7c	4-Methoxyphenyl	B	4.5	Column chromatography: A (1:2)	82	Oil
7d	Pentafluorophenyl	B	5	Column chromatography: A (1:2) MPLC: A (1:5)	73	Oil
7e	Pyridin-2-yl	B	2	Column chromatography: A (1:1)	85	89–93
7f	6-Phenylpyridazin-3-yl	B	1.5	Column chromatography: A (1:2) MPLC: A (2:3)	53	49–52
7′f	6-Phenylpyridazin-3-yl	B	1.5	Column chromatography: A (1:2) MPLC: A (2:3)	27	45–48
7g	Pyrimidin-2-yl	B	5	Column chromatography: B (20:1) MPLC: A (100:0)	34	Oil
7′g	Pyrimidin-2-yl	B	5	Column chromatography: B (20:1) MPLC: A (100:0)	22	Oil
7h	Me	C	18	–	62	102–104 (MeOH–H_2O)
8a	H	–	18	–	82	210–213
8b	Ph	–	22.5	–	75	173–176 (CH_2Cl_2)
8e	Pyridin-2-yl	–	21.5	–	82	183–186 (DMSO–Et_2O)
10b	Ph	A	20	Column chromatography: A (2:1) MPLC: A (1:1)	44	Oil
10e	Pyridin-2-yl	B	22	–	96	110–112 (MeOH–H_2O)
10i	4-Nitrophenyl	A	96	Column chromatography: A (2:1) MPLC: A (1:1)	69	Oil
11a	H	A	5	Column chromatography: A (2:1)	37	101–105
11h	Me	A	24	Column chromatography: A (2:1) MPLC: A: (2:1)	39	96–98 (MeOH–H_2O)

[a] A: EtOAc–hexanes, B: $CHCl_3$–MeOH.

Table 2 Analytical, MS, and IR Data for Compounds **4**, **5**, **7**, **7′**, **8**, **10**, and **11**

Compound	Molecular formula analysis	EI–MS (*m*/*z*) EI–HRMS (*m*/*z*)	IR (cm^{-1})	$[\alpha]_D^{20}$
4	Anal. Calcd for $C_{22}H_{23}NO_7$ (413.42): C, 63.91; H, 5.61; N, 3.39. Found: C, 64.71; H, 5.82; N, 3.76.	278 [M^+ – COOBn] FAB: 414 [MH^+]	3308, 3034, 2941, 1748, 1740, 1714, 1689, 1533, 1298, 1260, 1139, 1079, 1022, 735, 696	+17.2 (*c* = 0.37, $CHCl_3$)
5	Anal. Calcd for $C_{25}H_{28}N_2O_7$ (468.50): C, 64.09; H, 6.02; N, 5.98. Found: C, 63.69; H, 6.34; N, 6.16.	468 [M^+] Calcd: 468.189652. Found: 468.190880.	3327, 2932, 1722, 1639, 1578, 1499, 1423, 1381, 1283, 1210, 1111, 1057, 740, 698	+26.3 (*c* = 0.31, $CHCl_3$)
7a	Anal. Calcd for $C_{23}H_{23}N_3O_6$ (437.45): C, 63.15; H, 5.30; N, 9.61. Found: C, 63.35; H, 5.41; N, 9.44.		3327, 2950, 1743, 1719, 1693, 1539, 1500, 1336, 1275, 1214, 1093, 735, 697	+0.52 (*c* = 0.11, $CHCl_3$)
7b	Anal. Calcd for $C_{29}H_{27}N_3O_6$ (513.54): C, 67.83; H, 5.30; N, 8.18. Found: C, 67.83; H, 5.40; N, 7.95.		3338, 2950, 1732, 1710, 1687, 1556, 1526, 1502, 1290, 1255, 1224, 1098, 1055, 770, 753, 697	+3.2 (*c* = 0.31, $CHCl_3$)
7c	Anal. Calcd for $C_{30}H_{29}N_3O_7$ (543.57): C, 66.29; H, 5.38; N, 7.73. Found: C, 66.18; H, 5.63; N, 7.69.		3354, 2951, 1717, 1555, 1518, 1251, 1215, 1096, 1052, 1027, 837, 738, 697	–7.5 (*c* = 0.27, $CHCl_3$)

Table 2 Analytical, MS, and IR Data for Compounds **4**, **5**, **7**, **7′**, **8**, **10**, and **11** (continued)

Compound	Molecular formula analysis	EI–MS (*m/z*) EI–HRMS (*m/z*)	IR (cm^{-1})	$[\alpha]_D^{20}$
7d	Anal. Calcd for $C_{29}H_{22}F_5N_3O_6$ (603.49): C, 57.72; H, 3.67; N, 6.96. Found: C, 57.99; H, 3.88; N, 6.79.	604 [MH^+] 694 [M – CH_2Ph^+] FAB: 604 [MH^+] Calcd: 604.150702. Found: 604.151890.	3360, 2954, 1718, 1533, 1520, 1266, 1213, 1096, 996, 850, 697	+1.7 (*c* = 0.30, $CHCl_3$)
7e	Anal. Calcd for $C_{28}H_{26}N_4O_6$ (514.53): C, 65.36; H, 5.09; N, 10.89. Found: C, 65.58; H, 5.34; N, 10.62.		3355, 2952, 1720, 1560, 1522, 1475, 1439, 1265, 1207, 1097, 1059, 785, 737, 698	–21.4 (*c* = 0.37, $CHCl_3$)
7f	Anal. Calcd for $C_{33}H_{29}N_5O_6$ (591.61): C, 67.00; H, 4.94; N, 11.84. Found: C, 67.02; H, 5.05; N, 11.92.		3380, 2952, 1720, 1547, 1452, 1431, 1262, 1207, 1094, 1060, 785, 746, 696	–3.0 (*c* = 0.29, $CHCl_3$)
7′f	Anal. Calcd for $C_{28}H_{27}N_5O_6$ (529.54): C, 63.51; H, 5.14; N, 13.23. Found: C, 64.15; H, 5.65; N, 12.88.	529 [M^+] Calcd: 529.196134. Found: 529.198050.	3330, 2929, 2851, 1721, 1627, 1547, 1453, 1432, 1381, 1261, 1210, 1093, 1028, 783, 748, 695	–7.9 (*c* = 0.11, $CHCl_3$)
7g	Anal. Calcd for $C_{27}H_{25}N_5O_6$ (515.52): C, 62.91; H, 4.89; N, 13.59. Found: C, 62.29; H, 5.12; N, 13.13.	515 [M^+] 606 [M – CH_2Ph^+] Calcd: 515.180484. Found: 515.181850.	3337, 2952, 1717, 1580, 1563, 1524, 1423, 1380, 1262, 1213, 1198, 1083, 737, 698	–7.9 (*c* = 0.22, $CHCl_3$)
7′g	Anal. Calcd for $C_{22}H_{23}N_5O_6$ (453.45): C, 58.27; H, 5.11; N, 15.44. Found: C, 58.38; H, 5.32; N, 15.22.		3346, 2953, 1719, 1580, 1562, 1524, 1424, 1380, 1262, 1211, 1199, 1026, 737, 699	–17.0 (*c* = 0.23, $CHCl_3$)
7h	Anal. Calcd for $C_{24}H_{25}N_3O_6$ (451.47): C, 63.85; H, 5.58; N, 9.31. Found: C, 64.03; H, 5.72; N, 9.41.		3311, 3035, 2951, 1735, 1705, 1682, 1557, 1530, 1500, 1452, 1374, 1299, 1282, 1263, 1241, 1198, 1059, 1040, 730, 694	+0.82 (*c* = 0.38, $CHCl_3$)
8a	Anal. Calcd for $C_8H_{11}N_3O_4$ (213.19): C, 45.07; H, 5.20; N, 19.71. Found: C, 42.30; H, 5.46; N, 17.94.	214 [MH^+] Calcd: 214.082781. Found: 214.083520.	3423, 3047, 2959, 1732, 1715, 1662, 1602, 1530, 1443, 1344, 1240, 1143, 1102, 966, 932, 538	–58.4 (*c* = 0.07, DMSO)
8b	Anal. Calcd for $C_{14}H_{15}N_3O_4$ (289.29): C, 58.13; H, 5.23; N, 14.53. Found: C, 57.99; H, 5.45; N, 13.72.	290 [MH^+] Calcd: 290.114081. Found: 290.115050.	3421, 3062, 2951, 2849, 1712, 1623, 1561, 1502, 1411, 1384, 1269, 1253, 1200, 1099, 986, 772, 696, 538, 507	+57.1 (*c* = 0.15, MeOH)
8e	Anal. Calcd for $C_{13}H_{14}N_4O_4$ (290.28): C, 53.79; H, 4.86; N, 19.30. Found: C, 53.36; H, 5.04; N, 18.45.	290 [M^+] FAB: 291 [MH^+] Calcd: 290.101505. Found: 290.102620.	3434, 3017, 2951, 1717, 1617, 1594, 1580, 1564, 1475, 1439, 1406, 1310, 1258, 1199, 1091, 1001, 932, 783, 721, 537	–24.8 (*c* = 0.07, DMSO)
10b	Anal. Calcd for $C_{27}H_{25}N_3O_5$ (471.51): C, 68.78; H, 5.34; N, 8.91. Found: C, 68.83; H, 5.68; N, 8.68.		3340, 3034, 2929, 1719, 1595, 1561, 1526, 1499, 1454, 1411, 1347, 1265, 1215, 1194, 1058, 755, 695	+7.1 (*c* = 0.31, $CHCl_3$)
10e	Anal. Calcd for $C_{26}H_{24}N_4O_5$ (470.52): C, 66.09; H, 5.12; N, 11.86. Found: C, 66.35; H, 5.20; N, 11.90.		3318, 3034, 2957, 1733, 1688, 1595, 1539, 1498, 1445, 1341, 1288, 1263, 1184, 1147, 1049, 781, 750, 698	–23.6 (*c* = 0.29, $CHCl_3$)
10i	Anal. Calcd for $C_{27}H_{24}N_4O_7$ (516.50): C, 62.79; H, 4.68; N, 10.85. Found: C, 62.32; H, 4.95; N, 10.15.	516 [M^+] 607 [M – CH_2Ph^+] Calcd: 516.164499. Found: 516.166100.	3407, 3341, 3034, 2955, 1727, 1596, 1516, 1499, 1454, 1329, 1273, 1214, 1111, 1057, 854, 752, 698	+14.8 (*c* = 0.23, $CHCl_3$)
11a	Anal. Calcd for $C_{15}H_{17}N_3O_5$ (319.31): C, 56.42; H, 5.37; N, 13.16. Found: C, 56.92; H, 5.62; N, 12.77.	319 [M^+] Calcd: 319.116821. Found: 319.117950.	3321, 2959, 1723, 1689, 1536, 1440, 1404, 1385, 1359, 1335, 1258, 1234, 1167, 1111, 1053, 984, 750, 699	–95.8 (*c* = 0.20, $CHCl_3$)
11h	Anal. Calcd for $C_{16}H_{19}N_3O_5$ (333.34): C, 57.65; H, 5.75; N, 12.61. Found: C, 58.50; H, 6.18; N, 12.17.	333 [M^+] Calcd: 333.132471. Found: 333.133150.	3296, 3060, 2951, 2929, 1720, 1656, 1542, 1435, 1353, 1330, 1272, 1216, 1179, 1153, 1104, 1024, 947, 735, 696	–133.7 (*c* = 0.11, $CHCl_3$)

Table 3 ^{1}H NMR Data for Compounds **4**, **5**, **7**, **7′**, **8**, **10**, and **11**

Compound	Solvent	^{1}H NMR [δ (ppm)][a]
4	$CDCl_3$	3.13 [dd, *J* = 4.2, 18.5 Hz, 1 H, HaC(3)], 3.30 [dd, *J* = 4.5, 18.1 Hz, 1 H, HbC(3)], 3.41 (s, 2 H, 5-CH_2), 3.69 (s, 3 H, OMe), 4.63 [deg br dt, *J* = 4.3, 8.3 Hz, 1 H, HC(2)], 5.10, 5.16 [2 × s, 4 H, 2 × PhCH_2], 5.73 (d, *J* = 7.9 Hz, 1 H, NH), 7.25–7.41 (m, 10 H, 2 × Ph)
5	$CDCl_3$	2.78, 3.18 (2 × br s, 6 H, NMe_2), 3.25 [dd, *J* = 3.8, 17.7 Hz, 1 H, HaC(3)], 3.51 [dd, *J* = 4.9, 17.7 Hz, 1 H, HbC(3)], 3.72 (s, 3 H, OMe), 4.65 [deg br dt, *J* = 4.5, 8.8 Hz, 1 H, HC(2)], 5.10 (s, 2 H, PhCH_2), 5.12, 5.18 (2 × d, *J* = 12.8 Hz, 2 H, PhCH_2), 5.95 (d, *J* = 9.0 Hz, 1 H, NH), 7.26–7.36 (m, 10 H, 2 × Ph), 7.71 [s, 1 H, HC(5′)]
7a	$CDCl_3$	3.48 [br d, *J* = 5.9 Hz, 2 H, $H_2C(3)$], 3.78 (s, 3 H, OMe), 4.80 [deg br dt, *J* = 6.2, 7.9 Hz, 1 H, HC(2)], 5.06, 5.14 (2 × s, 4 H, 2 × PhCH_2), 6.03 (d, *J* = 8.3 Hz, 1 H, N*H*COOBn), 7.25–7.34 (m, 10 H, 2 × Ph), 7.91 [s, 1 H, HC(3′)]; HN(1′) exchanged
7b	$CDCl_3$	3.37 [dd, *J* = 4.9, 14.3 Hz, 1 H, HaC(3)], 3.50 [dd, *J* = 10.6, 14.3 Hz, 1 H, HbC(3)], 3.81 (s, 3 H, OMe), 4.54 [br ddd, *J* = 4.5, 8.7, 10.2 Hz, 1 H, HC(2)], 4.95, 5.03 (2 × d, *J* = 12.4 Hz, 2 H, PhCH_2), 5.07 (s, 2 H, PhCH_2), 5.72 (d, *J* = 8.7 Hz, 1 H, NH), 7.20–7.48 (m, 15 H, 3 × Ph), 7.98 [s, 1 H, HC(3′)]
7c	$CDCl_3$	3.31 [dd, *J* = 4.5, 14.3 Hz, 1 H, HaC(3)], 3.46 [dd, *J* = 10.9, 13.9 Hz, 1 H, HbC(3)], 3.80, 3.83 (2 × s, 6 H, 2 × OMe), 4.55 [deg ddd, *J* = 4.5, 8.7, 10.9 Hz, 1 H, HC(2)], 4.95, 5.03 (2 × d, *J* = 12.4 Hz, 2 H, PhCH_2), 5.07 (s, 2 H, PhCH_2), 5.75 (d, *J* = 8.3 Hz, 1 H, NH), 6.94 (d, *J* = 8.7 Hz, 2 H, C_6H_4), 7.20–7.37 (m, 12 H, 2 × Ph, 2 H of C_6H_4), 7.95 [s, 1 H, HC(3′)]
7d	$CDCl_3$	3.31 [dd, *J* = 8.7, 14.3 Hz, 1 H, HaC(3)], 3.46 [dd, *J* = 5.6, 14.7 Hz, 1 H, HbC(3)], 3.82 (s, 3 H, OMe), 4.47 [deg br dt, *J* = 6.5, 7.9 Hz, 1 H, HC(2)], 4.97 (s, 2 H, PhCH_2), 5.06, 5.11 (2 × d, *J* = 12.8 Hz, 2 H, PhCH_2), 5.50 (d, *J* = 7.9 Hz, 1 H, NH), 7.22–7.35 (m, 10 H, 2 × Ph), 8.07 [s, 1 H, HC(3′)]
7e	$CDCl_3$	3.73 [dd, *J* = 11.3, 13.6 Hz, 1 H, HaC(3)], 3.83 (s, 3 H, OMe), 3.98 [dd, *J* = 4.5, 13.6 Hz, 1 H, HbC(3)], 5.01 (s, 2 H, PhCH_2), 5.07 [br ddd, *J* = 4.6, 8.2, 11.5 Hz, 1 H, HC(2)], 5.19 (s, 2 H, PhCH_2), 6.95 (d, *J* = 7.9 Hz, 1 H, NH), 7.23–7.37 [m, 11 H, 2 × Ph, HC(5″)], 7.84–7.88 [m, 2 H, HC(3″), HC(4″)], 8.02 [s, 1 H, HC(3′)], 8.38 [dt, *J* = 1.4, 4.9 Hz, 1 H, HC(6″)]
7f	$CDCl_3$	3.85 (s, 3 H, OMe), 4.00 [dd, *J* = 11.3, 13.6 Hz, 1 H, HaC(3)], 4.21 [dd, *J* = 4.5, 13.6 Hz, 1 H, HbC(3)], 4.95, 5.00 (2 × d, *J* = 12.4 Hz, 2 H, PhCH_2), 5.08 [br ddd, *J* = 4.4, 9.0, 11.3 Hz, 1 H, HC(2)], 5.20 (s, 2 H, PhCH_2), 6.36 (d, *J* = 9.0 Hz, 1 H, NH), 7.20–7.39 (m, 10 H, 2 × Ph), 7.53–7.57 (m, 3 H, Ph), 7.99 [d, *J* = 9.4 Hz, 1 H, HC(5″)], 8.05–8.10 (m, 2 H, Ph), 8.08 [s, 1 H, HC(3′)], 8.11 [d, *J* = 8.3 Hz, 1 H, HC(4″)]
7′f	$CDCl_3$	1.27 (t, *J* = 7.2 Hz, 3 H, C$H_3$$CH_2$), 3.89 (s, 3 H, OMe), 4.02 [dd, *J* = 10.9, 13.6 Hz, 1 H, HaC(3)], 4.15–4.24 (m, 2 H, CH_3CH_2), 4.19 [dd, *J* = 3.0, 7.5 Hz, 1 H, HbC(3)], 4.95, 5.00 (2 × d, *J* = 12.4 Hz, 2 H, PhCH_2), 4.93–5.01 [m, 1 H, HC(2)], 6.28 (d, *J* = 8.3 Hz, 1 H, NH), 7.20–7.39 (m, 5 H, Ph), 7.53–7.58 (m, 3 H, Ph), 8.00 [d, *J* = 9.0 Hz, 1 H, HC(5″)], 8.07–8.12 (m, 2 H, OPh), 8.09 [s, 1 H, H–C(3′)], 8.13 [d, *J* = 9.8 Hz, 1 H, H–C(4″)]
7g	$CDCl_3$	3.83 [dd, *J* = 10.9, 13.2 Hz, 1 H, HaC(3)], 3.84 (s, 3 H, OMe), 4.00 [dd, *J* = 4.5, 13.2 Hz, 1 H, HbC(3)], 5.00, 5.18 (2 × s, 4 H, 2 × PhCH_2), 5.12 [br ddd, *J* = 4.9, 9.0, 10.9 Hz, 1 H, HC(2)], 6.33 (d, *J* = 8.3 Hz, 1 H, NH), 7.23–7.38 [m, 11 H, 2 × Ph, HC(5″)], 8.08 [s, 1 H, HC(3′)], 8.74 [d, *J* = 4.9 Hz, 2 H, HC(4″), HC(6″)]
7′g	$CDCl_3$	1.25 (t, *J* = 7.2 Hz, 3 H, C$H_3$$CH_2$), 3.84 [dd, *J* = 10.9, 13.2 Hz, 1 H, HaC(3)], 3.87 (s, 3 H, OMe), 3.99 [dd, *J* = 4.9, 13.2 Hz, 1 H, HbC(3)], 4.11–4.24 (m, 2 H, CH_3CH_2), 5.00 (s, 2 H, PhCH_2), 5.07 [br ddd, *J* = 5.3, 9.1, 10.9 Hz, 1 H, HC(2)], 6.26 (d, *J* = 8.7 Hz, 1 H, NH), 7.25–7.38 [m, 6 H, Ph, HC(5″)], 8.11 [s, 1 H, HC(3′)], 8.87 [d, *J* = 4.5 Hz, 2 H, HC(4″), HC(6″)]
7h	$CDCl_3$	3.37 [dd, *J* = 5.7, 14.3 Hz, 1 H, HaC(3)], 3.51 [dd, *J* = 9.0, 14.7 Hz, 1 H, HbC(3)], 3.77, 3.81 (2 × s, 6 H, NMe, OMe), 4.54–4.63 [m, 1 H, HC(2)], 5.03 (s, 2 H, PhCH_2), 5.12, 5.18 (2 × d, *J* = 12.4 Hz, 2 H, PhCH_2), 5.91 (d, *J* = 7.9 Hz, 1 H, NH), 7.26–7.40 (m, 10 H, 2 × Ph), 7.78 [s, 1 H, HC(3′)]
8a	DMSO-d_6	3.20 [dd, *J* = 7.9, 14.7 Hz, 1 H, HaC(3)], 3.34 (br s, 3 H, NH_3^+), 3.37 [dd, *J* = 5.3, 15.8 Hz, 1 H, HbC(3)], 3.67 [dd, *J* = 5.6, 7.9 Hz, 1 H, HC(2)], 3.73 (s, 3 H, OMe), 8.04 [s, 1 H, HC(3′)]
8b	DMSO-d_6	3.17 [d, *J* = 7.9 Hz, 2 H, $H_2C(3)$], 3.32 (br s, 3 H, NH_3^+), 3.52 [t, *J* = 7.9 Hz, 1 H, HC(2)], 3.79 (s, 3 H, OMe), 7.49–7.57 (m, 5 H, Ph), 8.00 [s, 1 H, HC(3′)]
8e	DMSO-d_6	3.32 (br s, 3 H, NH_3^+), 3.45 [dd, *J* = 9.4, 13.6 Hz, 1 H, HaC(3)], 3.59 [dd, *J* = 5.7, 9.0 Hz, 1 H, HbC(3)], 3.80 (s, 3 H, OMe), 3.91 [dd, *J* = 5.7, 13.6 Hz, 1 H, HC(2)], 7.51 [ddd, *J* = 1.1, 4.9, 7.5 Hz, 1 H, HC(5″)], 7.79 [ddd, *J* = 1.1, 7.5, 8.3 Hz, 1 H, HC(4″)], 8.08 [ddd, *J* = 0.8, 1.9, 8.3 Hz, 1 H, HC(3″)], 8.09 [s, 1 H, HC(3′)], 8.55 [ddd, *J* = 0.8, 1.9, 4.9 Hz, 1 H, HC(6″)]

Table 3 ^{1}H NMR Data for Compounds **4**, **5**, **7**, **7′**, **8**, **10**, and **11** (continued)

Compound	Solvent	^{1}H NMR [δ (ppm)][a]
10b	$CDCl_3$	3.02 [d, *J* = 5.5 Hz, 2 H, $H_2C(3)$], 3.26 [d, *J* = 23.4 Hz, 1 H, HaC(4′)], 3.41 [d, *J* = 23.6 Hz, 1 H, HbC(4′)], 4.78 [deg br dt, *J* = 5.5, 8.0 Hz, 1 H, HC(2)], 5.10 (s, 2 H, PhCH_2), 5.13, 5.26 (2 × d, *J* = 12.1 Hz, 2 H, PhCH_2), 5.71 (d, *J* = 8.2 Hz, 1 H, NH), 7.17 (tt, *J* = 1.9, 7.5 Hz, 1 H, Ph), 7.25–7.39 (m, 12 H, 2 × Ph, 2 H Ph), 7.75 (ddd, *J* = 2.3, 3.4, 8.7 Hz, 2 H, Ph)
10e	$CDCl_3$	3.07 [dd, *J* = 4.9, 15.5 Hz, 1 H, HaC(3)], 3.22 [dd, *J* = 5.3, 15.5 Hz, 1 H, HbC(3)], 4.76 [deg br dt, *J* = 5.0, 8.6, Hz, 1 H, HC(2)], 5.12, 5.13 (2 × s, 2 H, PhCH_2), 5.13, 5.20 (2 × d, *J* = 12.4 Hz, 2 H, PhCH_2), 5.31 [s, 1 H, HC(4′)], 5.87 [d, *J* = 8.7 Hz, 1 H, NHCO], 7.13 [ddd, *J* = 1.1, 5.3, 7.2 Hz, 1 H, HC(5″)], 7.23–7.38 (m, 10 H, 2 × Ph), 7.68 [d, *J* = 8.3 Hz, 1 H, HC(3″)], 7.79 [ddd, *J* = 1.5, 7.2, 8.7 Hz, 1 H, HC(4″)], 8.23 [ddd, *J* = 0.9, 1.7, 5.2 Hz, 1 H, HC(6″)]; HN(1′) exchanged
10i	$CDCl_3$	3.05 [d, *J* = 5.7 Hz, 2 H, $H_2C(3)$], 3.32 [d, *J* = 23.4 Hz, 1 H, HaC(4′)], 3.48 [d, *J* = 23.4 Hz, 1 H, HaC(4′)], 4.71–4.83 [m, 1 H, HC(2)], 5.10 (s, 2 H, PhCH_2), 5.13, 5.28 (2 × d, *J* = 12.1 Hz, 2 H, PhCH_2), 5.66 (d, *J* = 6.8 Hz, 1 H, NH), 7.23–7.33 (m, 10 H, 2 × Ph), 7.95, 8.21 (2 × br d, *J* = 9.4 Hz, 4 H, C_6H_4)
11a	$CDCl_3$	2.55 [dd, *J* = 14.7, 16.6 Hz, 1 H, HaC(4)], 3.23 [dd, *J* = 6.4, 16.2 Hz, 1 H, HbC(4)], 3.36, 3.43 (2 × d, *J* = 16.8 Hz, 2 H, CH_2COOMe), 3.75 (s, 3 H, OMe), 4.32 [ddd, *J* = 4.9, 6.8, 14.7 Hz, 1 H, HC(5)], 5.13 (s, 2 H, PhCH_2), 5.71 (br s, 1 H, NHCOOBn), 7.31–7.38 (m, 5 H, Ph), 8.44 [br s, 1 H, HN(1)]
11h	$CDCl_3$	2.49 [dd, *J* = 15.1, 16.2 Hz, 1 H, HaC(4)], 3.23 [dd, *J* = 6.4, 16.2 Hz, 1 H, HbC(4)], 3.35 (s, 3 H, NMe), 3.36, 3.40 (d, *J* = 16.6 Hz, 2 H, CH_2COOMe), 3.74 (s, 3 H, OMe), 4.23 [ddd, *J* = 4.5, 6.8, 15.6 Hz, 1 H, HC(5)], 5.12 (s, 2 H, PhCH_2), 5.79 (br s, 1 H, NH), 7.28–7.40 (m, 5 H, Ph)

[a] 'deg' = degenerate.

Table 4 ^{13}C NMR Data for Compounds **4**, **5**, **7f**,**g**, **7′f**,**g**, **8a**,**b**,**e**, and **11a**,**h**

Compound	Solvent	^{13}C NMR [δ (ppm)]
4	$CDCl_3$	45.0, 49.2, 50.4, 52.8, 67.5, 68.0, 128.5, 128.60, 128.64, 128.8, 128.9, 129.0, 135.6, 136.5, 156.4, 167.3, 170.9, 201.0
5	$CDCl_3$	25.4, 34.3, 43.5, 49.5, 51.4, 51.5, 67.2, 67.3, 128.37, 128.39, 128.5, 128.6, 128.8, 136.2, 136.9, 156.6, 159.1, 168.2, 172.3, 194.3
7f	$CDCl_3$	28.7, 52.1, 54.3, 67.0, 67.6, 116.5, 122.7, 127.0, 127.6, 128.2, 128.3, 128.4, 128.5, 128.8, 128.9, 129.6, 130.9, 135.7, 135.9, 136.9, 143.8, 145.0, 155.7, 156.5, 159.2, 164.1, 171.6
7′f	$CDCl_3$	14.5, 28.6, 52.1, 54.1, 62.0, 66.9, 116.5, 122.9, 127.1, 127.6, 128.2, 128.3, 128.8, 129.6, 130.9, 135.7, 136.9, 143.8, 145.1, 155.7, 156.4, 159.3, 164.1, 171.7
7g	$CDCl_3$	28.9, 52.1, 54.4, 67.1, 67.6, 116.5, 120.2, 128.3, 128.4, 128.6, 128.8, 128.8, 129.0, 135.9, 136.8, 143.5, 145.4, 156.5, 157.0, 159.3, 164.4, 171.8
7′g	$CDCl_3$	14.5, 29.0, 52.1, 54.2, 61.9, 67.0, 116.5, 120.2, 128.3, 128.4, 128.8, 136.9, 143.5, 145.6, 156.4, 157.1, 159.3, 164.4, 172.0
8a	D_2O	29.3, 35.9, 53.3, 53.3, 55.4, 112.9, 167.1, 174.5
8b	DMSO-d_6	28.2, 52.0, 53.1, 112.8, 127.6, 129.8, 130.0, 139.5, 142.0, 145.1, 164.3, 169.9
8e	DMSO-d_6, 80 °C	27.3, 48.9, 53.5, 115.1, 116.2, 122.8, 139.2, 139.8, 143.2, 148.4, 152.5, 162.7, 173.0
11a	$CDCl_3$	32.2, 42.4, 46.8, 52.9, 67.6, 128.5, 128.7, 129.0, 136.4, 151.1, 156.4, 166.3, 169.6
11h	$CDCl_3$	32.3, 36.9, 42.6, 47.1, 52.8, 67.5, 128.5, 128.6, 129.0, 136.5, 150.6, 156.4, 164.6, 169.6

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