Transformation of Amino Acids into Nonracemic 1-(Heteroaryl)ethanamines by the Enamino Ketone Methodology

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N-Protected L-phenylalanines **1a**,**b** were transformed, *via* the corresponding *Weinreb* amides **2** and ethynyl ketones **3**, into chiral enamino ketones **4** (*Scheme 1*). Similarly, L-threonine **6** was transformed in four steps into the enamino ketone **10**. Cyclocondensations of **4** and **10** with pyrazolamines **11**, benzenecarboximidamide (**12**), and hydrazine derivatives **18** afforded *N*-protected 1-heteroaryl-2-phenylethanamines **15a**–**e**, **16**, **17**, and **21a**–**k** and 1-heteroaryl-1-aminopropan-2-ols **23a**,**b** in good yields (*Schemes 2* and *3*). Finally, deprotection by catalytic hydrogenation furnished free amines **22a**–**g** and **24a**,**b** (*Scheme 3*).

Introduction. – Nonracemic amines and α-amino alcohols represent important groups of organic compounds, which found a widespread use in various applications, such as reagents in organic synthesis and resolving agents, chiral auxilliaries and ligands in asymmetric synthesis (for an illustration, see [1]). A typical example of a synthetic application of enantiomerically pure α-amino alcohols is their use as chiral catalysts in asymmetric reactions, such as additions of dialkylzinc to aldehydes (for an illustration, see [2]) and asymmetric reductions of ketones with borane complexes (for an illustration, see [3]). Such examples are (+)-methylbenzylamine, amphetamine, (+)-ephedrine, (1*S*,2*R*)-2-amino-1,2-diphenylethanol, and (*S*)-α,α-diphenylprolinol (*Fig. 1*).

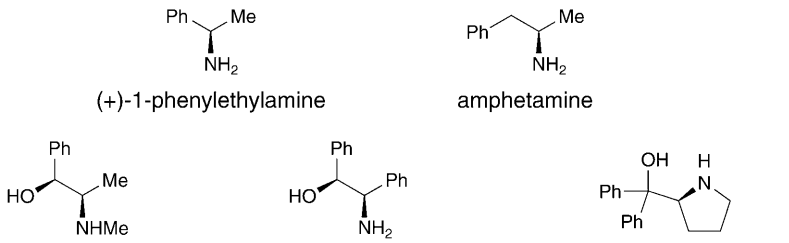


Fig. 1. *Some examples of important 2-phenylethanamines and α-amino alcohols*

Recently, a series of alkyl 2-substituted 3-(dimethylamino)prop-2-enoates and related enamino ketones have been prepared as versatile reagents for the preparation of various didehydroalanine derivatives, heterocyclic systems, and natural-product ana-

logs. In extention, chiral cyclic enamino lactams and lactones, derived from α-amino acids and (+)-camphor have been employed in the synthesis of functionalized heterocycles, such as (heteroaryl)alanines, (heteroaryl)alaninols, (heteroaryl)propanediols, 3-(heteroaryl)camphors, and heterocyclic compounds with an α-amino acid or dipeptide structural element incorporated into the ring system (for recent reviews, see [4]; for recent publications, see [5]). Recently, alkyl 2-substituted 3-(dimethylamino)prop-2-enoates and related enamino ketones have been employed in a combinatorial synthesis of heterocycles and *N*-acyldidehydroalanine esters [6] and in the synthesis of natural-product analogs, such as aplysinopsins [7] and meridianins [4a][8].

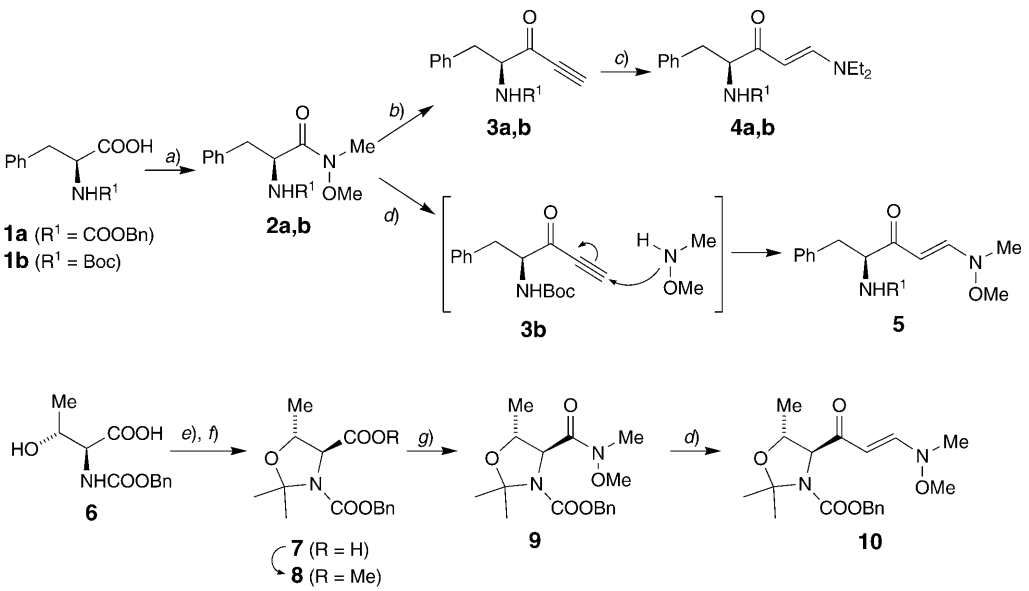
The 3-(dimethylamino)prop-2-enoates and their chiral analogs are usually prepared by treatment of a suitably functionalized methylene compound with formamide acetal, *e.g.*, with *N*,*N*-dimethylformamide dimethyl acetal or with *tert*-butoxy-*N*,*N*,*N*′,*N*′-tetramethylmethanediamine (*Bredereck*'s reagent) [4]. On the other hand, *Giacomelli* and co-workers reported the preparation of acyclic chiral enamino ketones from commercially available α-amino acids by treatment of a suitably protected *Weinreb* amide of an α-amino acid with (trimethylsilyl)magnesium bromide to give the corresponding silyl ynone, followed by reaction with Et_2NH to afford the enamino ketone. These enamino ketones were then used in reactions with various α-hydrazino acids and phenylhydrazine to afford pyrazole-containing peptidomimetics [9] and α-pyrazoylglycines [10].

Within this context and in continuation of our research in the field of chiral enamino ketones, we now report the preparation of chiral acyclic enamino ketones **4a**,**b** and **10** from α-amino acids and their utilization in a two-step synthesis of 1-(heteroaryl)-2-phenylethanamines **22** and 1-(heteroaryl)-1-aminopropan-2-ols **24**.

Results and Discussion. – First, *Weinreb* amides **2a**,**b** were prepared from *N*-protected L-phenylalanines **1a**,**b** according to a known procedure [11]. Treatment of **2a** and **2b** with ethynylmagnesium bromide followed by quenching excess *Grignard* reagent with aqueous $NaHSO_4$ solution afforded the ynones **3a** and **3b**. Upon reaction of **3a**,**b** with Et_2NH in CH_2Cl_2 at 0°, the desired enamino ketones **4a** and **4b** were obtained in 86% and 92% yield, respectively. However, *tert*-butyl {(1*S*,3*E*)-1-benzyl-4-[methoxy(methyl)amino]-2-oxobut-3-enyl}carbamate (**5**) was isolated instead of the expected ynone **3b**, when aqueous ammonium chloride was used for quenching of the reaction mixture obtained upon treatment of **2b** with ethynylmagnesium bromide. This could be explained by initial formation of **3b** as the intermediate and *N*,*O*-dimethylhydroxylamine as the by-product, which undergoes addition to the polarized triple bond of **3b** to give the enamino ketone **5**. Similarly, *N*-[(benzyloxy)carbonyl]-L-threonine (**6**) was transformed in three steps into the *Weinreb* amide **9** according to the literature procedure [12]. Reaction of **9** with ethynylmagnesium bromide followed by quenching with aqueous NH_4Cl afforded benzyl (4*S*,5*R*)-4-{(2*E*)-3-[methoxy(methyl)-amino]prop-2-enoyl}-2,2,5-trimethyloxazolidine-3-carboxylate (**10**) in 73% yield (*Scheme 1*, *Table*).

Cyclocondensations of enamino ketones **4a**,**b** and **10** with 1*H*-pyrazole-3-amine (**11a**), 5-methyl-1*H*-pyrazole-3-amine (**11b**), and 3-amino-1*H*-pyrazole-4-carbonitrile (**11c**) in EtOH at 20–80° in the presence of an equimolar amount of aqueous HCl solution afforded 1-(pyrazolo[1,5-*a*]pyrimidin-7-yl)-substituted [(1*S*)-2-phenylethyl]carbamates **15a**–**e** and [(1*R*,2*R*)-2-hydroxypropyl]carbamate **16** in 20–77% yields.

Scheme 1



a) ClCOOBu, *N*-methylmorpholine, AcOEt, 0°, then MeNHOMe, 0° → r.t. *b*) HC≡CMgBr, THF, −78° → r.t., then aq. $NaHSO_4$ soln. *c*) Et_2NH, CH_2Cl_2, 0° → r.t. *d*) HC≡CMgBr, THF, −78° → r.t., then aq. NH_4Cl soln. *e*) $Me_2C(OMe)_2$, $BF_3 \cdot Et_2O$, r.t. *f*) MeI, K_2CO_3, acetone, 0° → r.t. *g*) i-PrMgBr, MeNHOMe, THF, −78° → −20°, then aq. NH_4Cl soln.

Under these reaction conditions, **4b** did not react with benzenecarboximidamide hydrochloride (**12**). However, in the presence of K_2CO_3, cyclocondensation took place to afford *tert*-butyl [(1*S*)-2-phenyl-1-(2-phenylpyrimidin-4-yl)ethyl]carbamate (**17**) in 27% yield. According to the general reactivity of *N*,*N*-dimethyl(enamino) ketones [4], these cyclocondensations can be explained by initial substitution of the diethylamino group followed by condensation with the keto group (*Scheme 2*, *Table*).

Next, cyclocondensations of enamino ketones **4a**,**b** and **10** with the hydrazine derivatives hydrazine hydrochloride (**18a**·HCl), phenylhydrazine hydrochloride (**18b**·HCl), (4-nitrophenyl)hydrazine (**18c**), (4-methoxyphenyl)hydrazine (**18d**), (2-bromophenyl)-hydrazine hydrochloride (**18e**·HCl), 2-hydrazinopyridine (**18f**), 2-hydrazinopyrimidine (**18g**), 6-chloro-3-hydrazinopyridazine (**18h**), and 3-hydrazino-6-phenylpyridazine (**18i**) were studied. When **4a**,**b** were treated with **18a**–**i** in EtOH in the presence of 1 equiv. of aqueous HCl solution[1]), *N*-protected (1*S*)-2-phenyl-1-pyrazolyl-ethanamines **21a**–**k** were obtained in 54–98% yields. Also in this case, the reaction can be explained by substitution of the diethylamino group to give the enehydrazino ketone **19**, which cyclizes into the dihydropyrazole **20**, from which H_2O is eliminated to give the 2-phenyl-1-pyrazolylethanamine **21** [4][13]. Compounds **21a**,**b**, obtained from **4a**,**b** and $N_2H_4 \cdot HCl$ (**18a**), exist in solution as mixtures of 1*H*-pyrazol-5-yl and -3-yl isomers **21a**,**b** and

[1]) In the case of hydrazine hydrochlorides **18a**,**b**,**e**, no aqueous HCl solution was added.

Table. *Yields of Enamino Ketones* **4a**,**b**, **5**, **10**, *1*H-*Pyrazolamines* **18a**–**c**, *Hydrazine Derivatives* **18a**–**i**, *2-Phenylethanamines* **15a**–**e**, **17**, **21a**–**k**, **22a**–**g**, *and* α*-Amino Alcohols* **16**, **22a**,**b**, *and* **24a**,**b**

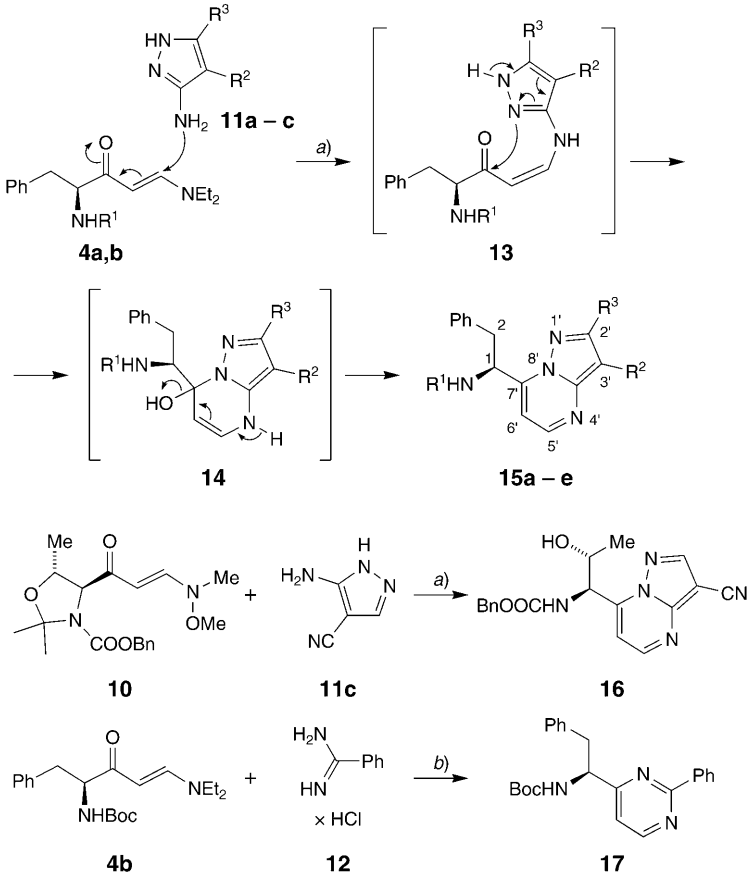
Reaction	R^1	R^2	R^3	Yield [%]
2a → **3a** → **4a**	COOBn			52[a])
2b → **3b** → **4b**	Boc			83[a])
2b → **5**				50
9 → **10**				73
4a+**11a** → **15a**	COOBn	H	H	76
4b+**11a** → **15b**	Boc	H	H	44
4a+**11b** → **15c**	COOBn	H	Me	32
4a+**11c** → **15d**	COOBn	CN	H	73
4b+**11c** → **15e**	Boc	CN	H	20
10+**11c** → **16**	COOBn	CN	H	77
4a+**12** → **17**	Boc			27
4a+**18a** → **21a/21′a**	COOBn	H		98
4b+**18a** → **21b/21′b**	Boc	H		86
4a+**18b** → **21c**	COOBn	Ph		95
4a+**18c** → **21d**	COOBn	4-nitrophenyl		80
4a+**18d** → **21e**	COOBn	4-methoxyphenyl		70
4b+**18e** → **21f**	Boc	2-bromophenyl		90
4a+**18f** → **21g**	COOBn	pyridin-2-yl		83
4a+**18g** → **21h**	COOBn	pyrimidin-2-yl		89
4a+**18h** → **21i**	COOBn	6-chloropyridazin-3-yl		91
4b+**18h** → **21j**	Boc	6-chloropyridazin-3-yl		54
4a+**18i** → **21k**	COOBn	6-phenylpyridazin-3-yl		78
10+**18b** → **23a**		Ph		92
10+**18i** → **23b**		6-phenylpyridazin-3-yl		63
21a/21′a → **22a**		H		92
21c → **22b**		Ph		82
21d → **22c**		4-aminophenyl		95
21e → **22d**		4-methoxyphenyl		98
21g → **22e**		pyridin-2-yl		85
21h → **22f**		pyrimidin-2-yl		69
21k → **22g**		6-phenylpyridazin-3-yl		70
23a → **24a**		Ph		83
23b → **24b**		6-phenylpyridazin-3-yl		64

[a]) Yield over two steps.

21′a,**b**, respectively. Deprotection of compounds **21c**–**e**,**g**,**h**,**k** by catalytic hydrogenation in the presence of 10% Pd/C afforded the free 2-phenyl-1-pyrazolyl-ethanamines **22a**–**g** in 70–98% yields. Similarly, 1-amino-1-pyrazolyl-propan-2-ols **24a**,**b** were prepared in two steps *via* **23a**,**b** from enamino ketone **10** (*Scheme 3*, *Table*).

All novel compounds were characterized by spectroscopic (IR, MS, HR-MS, ^{1}H- and ^{13}C-NMR) methods and elemental analyses for C, H, and N. Compounds **3a**,**b**, **4a**,**b**, **5**, **10**, **15c**,**d**, **21c**–**e**,**h**, **23a**, **22a**–**g**, and **24a**,**b** were not prepared in analytically pure form. The identities of these compounds were confirmed by HR-EI-MS and ^{13}C-NMR spectra or, in the case of **22a**, by FAB-MS and ^{13}C-NMR spectra. The structure of compound **15b** was determined by X-ray diffraction (*Fig. 2*).

Scheme 2[a])

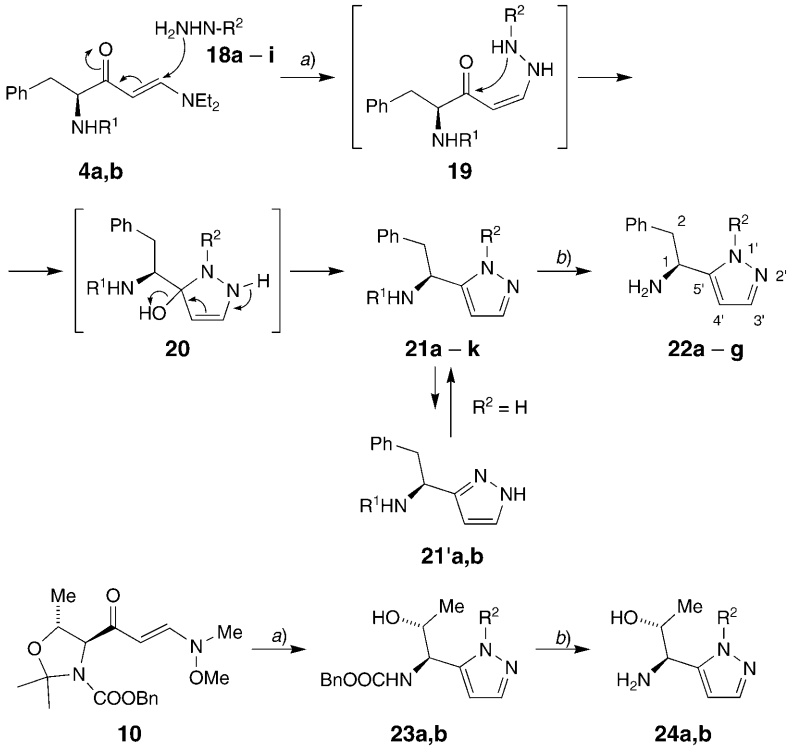


[a]) See *Table* for R^1 – R^3.

a) EtOH, 37% aq. HCl soln. (1 equiv.), r.t. → reflux. *b*) EtOH, K_2CO_3, reflux.

Conclusions. – Chiral enamino ketones **4a**,**b** and **10** are available in 3–4 steps from *N*-protected L-phenylalanines **1a**,**b** and L-threonine **6**, respectively. They were used efficiently as the key reagents in a two-step synthesis of 1-(heteroaryl)-2-phenylethanamines **22a**–**g** and 1-amino-1-(heteroaryl)propan-2-ols **24a**,**b**. Due to the wide applicability of 2-substituted alkyl 3-(dimethylamino)propenoates and related enamino ketones in heterocyclic synthesis and, since related enamino ketones could also be prepared from other commercially available α-amino acids *via* the corresponding *Weinreb* amides, this methodology could be extended also to the preparation of several other types of 1-(heteroaryl)alkanamines. In comparison with some known synthetic methods [14–16], especially with the ynone-mediated approach of *Knochel* and co-workers [14], the presented enamino ketone methodology is an additional and useful option for the efficient synthesis of chiral nonracemic 1-(heteroaryl)alkanamines.

Scheme 3[a])



[a]) See *Table* for R^1 and R^2.

a) EtOH, 37% aq. HCl soln. (1 equiv.), r.t. → reflux. *b*) H_2 (1 bar), EtOH and/or THF, 10% Pd/C, r.t.

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Experimental Part

1. *General*. *N*-[(Benzyloxy)carbonyl]-L-phenylalanine (**1a**), *N*-[(*tert*-butoxy)carbonyl]-L-phenylalanine (**1b**), *N*-[(benzyloxy)carbonyl]-L-threonine (**6**), 1*H*-pyrazolamines **11a**–**c**, and hydrazines **18a**–**f** are commercially available (*Fluka* AG and *Sigma-Aldrich*). *Weinreb* amides **2a**,**b** [11] and **9** [12], 2-hydrazinopyrimidine (**18g**) [17], 6-chloro-3-hydrazinopyridazine (**18h**) [18], and 3-hydrazino-6-phenylpyridazine (**18i**) [19] were prepared according to the published procedures. All starting materials were commercially available (in most cases from *Fluka*) and purified following the standard techniques. Column chromatography (CC): silica gel *60* (0.04–0.06 mm; *Fluka*). Medium-pressure liquid chromatography

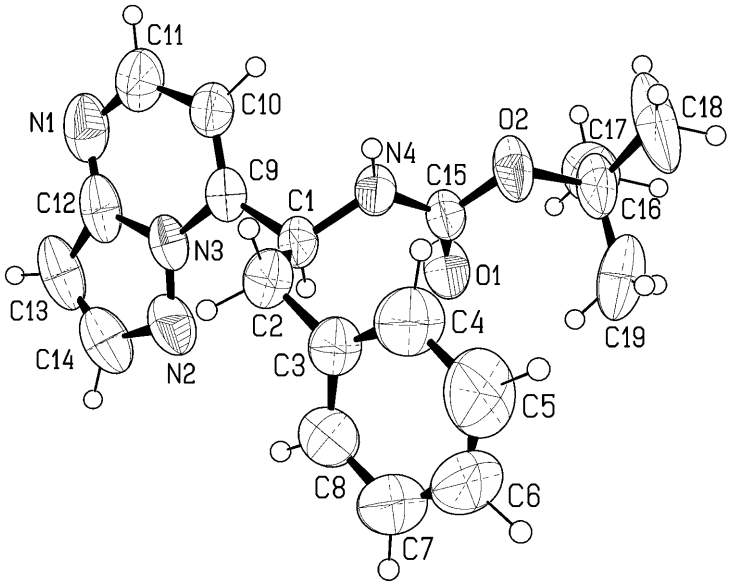

Fig. 2. *ORTEP View of the asymmetric unit of compound* **15b**. Arbitrary atom numbering. Ellipsoids at the 50% probability level.

(MPLC): *Büchi* isocratic system with detection[2]); silica gel *60* (0.015–0.035 mm; *Merck*); 15×460 mm column (dry filled); backpressure 10–15 bar; UV detection at 254 nm; 100–150 mg of sample per run. TLC: aluminium foils coated with silica gel *60 F 254* (0.2 mm; *Merck*). M.p.: *Kofler* micro hot stage. Optical rotations: *Perkin-Elmer-241-MC* polarimeter. IR: *Perkin-Elmer-Spectrum-BX-FTIR* spectophotometer; in cm^{-1}. ^{1}H-(300 MHz) and ^{13}C-NMR (75.5 MHz): *Bruker-Avance-DPX-300* spectrometer; δ in ppm rel. to Me_4Si as internal standard (=0 ppm), *J* in Hz. MS: *Autospeck-Q* (*VG-Analytical*) spectrometer; in *m*/*z*. Elemental analyses: *Perkin-Elmer-CHN-2400-II* analyzer.

2. *Ethynyl Ketones* **3a**,**b**: *General Procedure.* At −78°, 0.5M (HC≡CMgBr in THF 80 ml, 40 mmol) was added slowly to the stirred soln. of **2** (10 mmol) in anh. THF (20 ml) under Ar, and the resulting mixture was stirred at −78° for 1 h and at r.t. for 12 h. The mixture was poured into cold (0°) 1M aq. $NaHSO_4$ (150 ml) and stirred for 1 h. THF was evaporated at 35–40° and the aq. residue extracted with Et_2O (2×150 ml). The combined org. phase was washed successively with 1M aq. $NaHSO_4$ (150 ml), sat. aq. $NaHCO_3$ soln. (150 ml), and brine (150 ml), dried (Na_2SO_4), and evaporated and the residue purified by CC (AcOEt/hexanes): **3a**,**b**.

Benzyl [(1S)-1-Benzyl-2-oxobut-3-ynyl]carbamate (**3a**). From **2a** (3.2 g, 9.3 mmol), after CC (AcOEt/hexanes 1:3): 1.74 g (61%) of **3a**. Oil. $[\alpha]_D^{23}=+1.27$ ($c=1.05$, $CHCl_3$). IR (NaCl): 3404, 3270, 3031, 2093 (C≡C), 1687 (C=O), 1497, 1455, 1254, 1045, 697. ^{1}H-NMR ($CDCl_3$): 3.20 (*dd*, *J*=6.0, 14.3, 1 H of PhCH_2); 3.29 (*dd*, *J*=5.7, 14.3, 1 H of PhCH_2); 3.39 (*s*, H–C(1)); 4.71–4.80 (*m*, H–C(4)); 5.09 (*s*, PhCH_2O); 5.22 (*d*, *J*=7.2, NH); 7.09–7.15 (*m*, 2 H of Ph); 7.22–7.40 (*m*, 8 H of Ph). ^{13}C-NMR ($CDCl_3$): 37.1; 62.8; 67.5; 80.1; 83.1; 127.7; 128.5; 128.7; 128.9; 129.1; 129.8; 135.5; 136.6; 156.1; 185.4. EI-MS: 307 (M^+). EI-HR-MS: 307.12060 ($C_{19}H_{17}N_1O_3^+$, M^+; calc. 307.120844).

tert-*Butyl [(1S)-1-Benzyl-2-oxobut-3-ynyl]carbamate* (**3b**). From **2b** (2.5 g, 8.1 mmol), after CC (AcOEt/hexanes 1:5): 2.0 g (90%) of **3b**. Oil. $[\alpha]_D^{22}=+8.66$ ($c=1.73$, $CHCl_3$). IR (NaCl): 3354, 3268, 2979, 2093 (C≡C), 1711 (C=O), 1688 (C=O), 1497, 1456, 1367, 1252, 1165, 1048, 700. ^{1}H-NMR ($CDCl_3$): 1.41 (*s*, *t*-BuO); 3.16 (*dd*, *J*=5.7, 14.3, H_a–C(5)); 3.27 (*dd*, *J*=5.7, 14.3, H_b–C(5)); 3.39 (*s*,

[2]) Donation of the *Alexander von Humboldt Foundation*, Germany.

H–C(1)); 4.62–4.73 (*m*, H–C(4)); 4.97 (*d*, *J* = 6.8, NH); 7.13–7.19 (*m*, 2 H of Ph); 7.21–7.39 (*m*, 3 H of Ph). ^{13}C-NMR ($CDCl_3$): 28.7; 37.2; 62.4; 80.3; 80.6; 82.6; 127.6; 129.0; 129.8; 135.7; 155.4; 186.0. FAB-MS: 274 ($[M+H]^+$).

3. *Alkyl [(1S,3E)-1-Benzyl-4-(diethylamino)-2-oxobut-3-enyl]carbamates* **4a**,**b**: *General Procedure* Et_2NH (0.73 ml, 5.2 mmol) was added to a cooled (0°) soln. of **3a**,**b** (5 mmol) in CH_2Cl_2 (35 ml), and the soln. was stirred at r.t. for 12 h. Volatile components were evaporated, and the residue was purified by CC (AcOEt/hexanes 2:1): **4a**,**b**.

Benzyl [(1S,3E)-1-Benzyl-4-(diethylamino)-2-oxobut-3-enyl]carbamate (**4a**). From **3a** (1.2 g, 3.9 mmol) and Et_2NH (0.55 ml): 1.28 g (86%) of **4a**. Oil. $[\alpha]_D^{21} = +34.4$ (*c* = 1.13, $CHCl_3$). IR (NaCl): 3397, 3292, 2976, 1717 (C=O), 1649, 1565, 1497, 1365, 1281, 1045, 699. ^{1}H-NMR ($CDCl_3$): 1.03, 1.18 (2 *m*, 1:1, 2 $MeCH_2$); 2.92–3.16 (*m*, $MeCH_2$, H_a–C(5), H_b–C(5)); 3.21 (br. *s*, $MeCH_2$); 4.49–4.62 (*m*, H–C(4)); 4.85 (*d*, *J* = 12.4, H–C(2)); 5.09 (*s*, $PhCH_2O$); 5.80 (br. *d*, *J* = 6.8, NH); 7.09–7.24 (*m*, Ph); 7.28–7.39 (*m*, Ph); 7.49 (br. *s*, H–C(1)). ^{13}C-NMR ($CDCl_3$): 11.8; 15.0; 40.4; 43.0; 50.9; 66.8; 126.8; 128.28; 128.30, 128.6; 128.8; 130.0; 137.2; 137.9; 151.8; 156.1; 193.5. EI-MS: 380 (M^+). EI-HR-MS: 380.210870 ($C_{23}H_{28}N_2O_3^+$, M^+; calc. 380.209993).

tert-*Butyl [(1S,3E)-1-Benzyl-4-(diethylamino)-2-oxobut-3-enyl]carbamate* (**4b**). From **3b** (1.7 g, 6.2 mmol) and Et_2NH (0.9 ml): 1.98 g (92%) of **4b**. Oil. $[\alpha]_D^{21} = +32.3$ (*c* = 0.75, $CHCl_3$). IR(NaCl): 3412, 2976, 2932, 1709 (C=O), 1649, 1568, 1468, 1366, 1283, 1170, 1047, 776, 701. ^{1}H-NMR ($CDCl_3$): 1.04, 1.17 (2*m*, 1:1, 2 *Me*CH_2); 1.41 (*s*, *t*-Bu); 2.91–3.14 (*m*, $MeCH_2$, $PhCH_2$); 3.21 (br. *s*, $MeCH_2$); 4.45–4.56 (*m*, H–C(4)); 4.85 (*d*, *J* = 12.8, H–C(2)); 5.53 (br. *d*, *J* = 7.2, NH); 7.12–7.26 (*m*, Ph); 7.48 (br. *s*, H–C(1)). ^{13}C-NMR ($CDCl_3$): 11.8; 15.0; 28.8; 40.6; 42.9; 50.9; 79.4; 126.7; 128.5; 130.0; 138.2; 151.7; 155.7; 194.1. EI-MS: 346 (M^+). EI-HR-MS: 346.225013 ($C_{20}H_{30}N_2O_3^+$, M^+; calc. 346.225643).

4. N-*Methoxy*-N-*methyl(enamino) Ketones* **5** *and* **10**: *General Procedure.* At −78°, 0.5M (HC≡CMgBr in THF 80 ml, 40 mmol) was added slowly to a stirred soln. of **2b** or **9** (10 mmol) in anh. THF (20 ml) under Ar, and the mixture was stirred at −78° for 1 h and at r.t for 12 h. The mixture was poured into cold (0°) sat. aq. NH_4Cl soln. (100 ml) and stirred at r.t. for 1 h. THF was then evaporated at *ca.* 30°, and the aq. residue was extracted with Et_2O (2 × 150 ml). The combined org. phase was washed successively with 1M aq. $NaHSO_4$ (150 ml), sat. aq. $NaHCO_3$ soln. (150 ml), and brine (150 ml), dried (Na_2SO_4), and evaporated and the residue purified by CC (AcOEt/hexanes 1:1): **5** or **10**.

tert-*Butyl {(1S,3E)-4-[Methoxy(methyl)amino]-2-oxobut-3-enyl}carbamate* (**5**). From **2b** (2.5 g, 8.1 mmol): 1.35 g (50%) of **5**. Oil. $[\alpha]_D^{21} = +100.8$ (*c* = 0.52, $CHCl_3$). IR (NaCl): 3414, 3323, 2975, 1709 (C=O), 1657, 1578, 1493, 1366, 1170, 1046, 1012, 701. ^{1}H-NMR ($CDCl_3$): 1.41 (*s*, *t*-BuO); 3.00–3.06 (*m*, $PhCH_2$); 3.10 (*s*, MeN); 3.58 (*s*, MeO); 4.51–4.59 (*m*, H–C(4)); 5.26 (*d*, *J* = 12.8, H–C(2)); 5.42 (*d*, *J* = 7.5, NH); 7.15–7.29 (*m*, Ph); 7.35 (*d*, *J* = 12.4, H–C(1)). ^{13}C-NMR ($CDCl_3$): 28.8; 39.8; 39.9; 59.2; 60.1; 79.6; 95.1; 126.8; 128.6; 130.0; 137.7; 148.4; 155.6; 195.2. EI-MS: 335 ($[M+H]^+$). FAB-MS: 335 ($[M+H]^+$). EI-HR-MS: 335.198060 ($C_{18}H_{27}N_2O_4^+$, $[M+H]^+$; calc. 335.197083).

Benzyl (4S,5R)-4-{(2E)-3-[Methoxy(methyl)amino]prop-2-enoyl}-2,2,5-trimethyloxazolidine-3-carboxylate (**10**). From **9** (4.77 g, 14.2 mmol): 3.73 g (73%) of **10**. Oil. $[\alpha]_D^{25} = -35.7$ (*c* = 1.00, $CHCl_3$). IR (NaCl): 2982, 1708 (C=O), 1663, 1579, 1410, 1350, 1123, 1072, 988, 696. ^{1}H-NMR ((D_6)DMSO, 80°): 1.30 (*d*, *J* = 6.0, Me–C(5)); 1.52, 1.55 (2*s*, 1:1, 2 Me–C(2)); 3.17 (*s*, MeN); 3.58 (*s*, MeO); 3.89–3.99 (*m*, H–C(5)); 4.07 (*d*, *J* = 7.5, H–C(4)); 4.98 (*s*, $PhCH_2O$); 5.30 (*d*, *J* = 12.4, C*H*=CHNMe); 7.21–7.36 (*m*, Ph); 7.48 (*d*, *J* = 12.4, CH=C*H*NMe). ^{13}C-NMR ((D_6)DMSO, 80°): 19.9; 25.4; 27.7; 39.9; 60.0; 66.8; 71.1; 75.3; 93.7; 95.0; 128.3; 128.4; 129.0; 137.4; 149.0; 152.5; 192.6. EI-MS: 363 ($[M+H]^+$). EI-HR-MS: 363.193002 ($C_{19}H_{27}N_2O_5^+$, $[M+H]^+$; calc. 363.191997).

5. *Compounds* **15a**–**e**, **21a**–**k**, *and* **23a**,**b**. *General Procedure A (G.P. A).* A mixture of **4a**,**b** or **10** (0.5 mmol), hydrazine derivative **18** (0.5 mmol), EtOH (4 ml), and 37% aq. HCl soln.[1]) (2 drops, *ca.* 0.6 mmol) was slowly heated up and then refluxed for 1.5–6 h. After cooling the precipitate was collected by filtration and washed with cold (0°) EtOH and Et_2O. Compounds **21g**,**i**–**k** and **23b** were prepared in this manner.

General Procedure B (G.P. B). A mixture of **4a**,**b** or **10** (0.5 mmol), 1*H*-pyrazolamine **11** or hydrazine derivative **18a**–**i** (0.5 mmol), EtOH (4 ml), and 37% aq. HCl[1]) soln. (2 drops, *ca.* 0.6 mmol) was stirred at 20–80° for 2–48 h. Volatile components were evaporated, and the residue was purified by CC. Compounds **15a**–**e**, **21a**–**f**,**h**, and **23a** were prepared in this manner.

*Benzyl [(1S)-2-Phenyl-1-(pyrazolo[1,5-*a*]pyrimidin-7-yl)ethyl]carbamate* (**15a**). From **4a** (0.190 g, 0.5 mmol) and **11a** (0.042 g, 0.5 mmol) by *G.P. B* (stirring at 80° for 5 h). CC (AcOEt/hexanes 1:2) gave 0.142 g (76%) of **15a**. M.p. 155–157° (from EtOH). $[\alpha]_D^{22} = +64.7$ ($c = 0.44$, $CHCl_3$). IR (KBr): 3311, 1683 (C=O), 1615, 1537, 1454, 1272, 1089, 1057, 1022, 745, 703. ^{1}H-NMR ($CDCl_3$): 3.37 (*dd*, $J = 7.1$, 13.3, H_a–C(2)); 3.53 (*dd*, $J = 8.1$, 13.3, H_b–C(2)); 5.01, 5.09 (2*d*, $J = 12.1$, PhCH_2O); 5.40–5.51 (*m*, H–C(1)); 6.42 (*d*, $J = 4.1$, H–C(6′)); 6.57 (br. *d*, $J = 9.0$, NH); 6.76 (*d*, $J = 2.3$, H–C(3′)); 6.90–6.99 (*m*, 2 H of Ph); 7.15–7.22 (*m*, 3 H of Ph); 7.26–7.37 (*m*, Ph); 8.18 (*d*, $J = 2.3$, H–C(2′)); 8.29 (*d*, $J = 4.1$, H–C(5′)). ^{13}C-NMR ($CDCl_3$): 38.1; 54.8; 67.1; 97.0; 106.4; 127.0; 128.1; 128.2; 128.5; 128.6; 129.0; 136.1; 136.4; 144.5; 145.9; 149.0; 149.3; 155.6. EI-MS: 372 (M^+). EI-HR-MS: 372.159560 ($C_{22}H_{20}N_4O_2^+$, M^+; calc. 372.158626). Anal. calc. for $C_{22}H_{20}N_4O_2$ (372.42): C 70.95, H 5.41, N 15.04; found: C 70.80, H 5.47, N 15.08.

tert-*Butyl [(1S)-2-Phenyl-1-(pyrazolo[1,5-*a*]pyrimidin-7-yl)ethyl]carbamate* (**15b**). From **4b** (0.173 g, 0.5 mmol) and **11a** (0.042 g, 0.5 mmol) by *G.P. B* (stirring at 20° for 48 h). CC (AcOEt/hexanes 1:2) gave 0.074 g (44%) of **15b**. M.p. 141–144°. $[\alpha]_D^{24} = +54.6$ ($c = 0.50$, $CHCl_3$). IR (KBr): 3346, 1686 (C=O), 1616, 1526, 1456, 1274, 1169, 820, 704. ^{1}H-NMR ($CDCl_3$): 1.38 (*s*, *t*-BuO); 3.32 (*dd*, $J = 6.8$, 13.2, H_a–C(2)); 3.51 (*dd*, $J = 7.9$, 13.2, H_b–C(2)); 5.37–5.47 (*m*, H–C(1)); 6.22 (br. *d*, $J = 6.4$, NH); 6.43 (br. *d*, $J = 3.0$, H–C(6′)); 6.76 (*d*, $J = 2.3$, H–C(3′)); 6.92–7.00 (*m*, 2 H of Ph); 7.16–7.22 (*m*, 3 H of Ph); 8.20 (*d*, $J = 2.3$, H–C(2′)); 8.30 (br. *d*, $J = 3.0$, H–C(5′)). ^{13}C-NMR ($CDCl_3$): 28.3; 38.2; 54.1; 80.2; 96.9; 106.3; 126.9; 128.5; 129.0; 136.6; 144.5; 146.5; 149.0; 149.3; 154.9. Anal. calc. for $C_{19}H_{22}N_4O_2$ (338.40): C 67.44, H 6.55, N 16.56; found: C 67.71, H 6.77, N 16.52.

*Benzyl [(1S)-1-(2-Methylpyrazolo[1,5-*a*]pyrimidin-7-yl)-2-phenylethyl]carbamate* (**15c**). From **4a** and (0.190 g, 0.5 mmol) and **11b** (0.049 g, 0.5 mmol) by *G.P. B* (stirring at 20° for 48 h). CC (AcOEt/hexanes 2:3) gave 0.060 g (32%) of **15c**. M.p. 169–173°. $[\alpha]_D^{25} = +49.9$ ($c = 0.40$, $CHCl_3$). IR(KBr): 3458, 3309, 1685, 1613, 1536, 1268, 740, 696. ^{1}H-NMR ($CDCl_3$): 2.56 (*s*, Me–C(2′)); 3.36 (*dd*, $J = 7.0$, 13.2, H_a–C(2)); 3.52 (*dd*, $J = 7.9$, 13.2, H_b–C(2)); 5.02, 5.10 (2*d*, $J = 12.1$, PhCH_2O); 5.34–5.45 (*m*, H–C(1)); 6.31 (*d*, $J = 4.1$, H–C(6′)); 6.51 (*s*, H–C(3′)); 6.64 (br. *d*, $J = 8.7$, NH); 6.90–7.00 (*m*, 2 H of Ph); 7.14–7.22 (*m*, 3 H of Ph); 7.27–7.40 (*m*, Ph); 8.20 (*d*, $J = 4.1$, H–C(5′)). ^{13}C-NMR ($CDCl_3$): 15.2; 38.6; 55.3; 67.5; 77.3; 96.6; 106.0; 127.4; 128.6; 129.0; 129.5; 136.6; 136.9; 137.2; 145.6; 149.1; 150.5; 155.4; 156.1. EI-MS: 386 (M^+). EI-HR-MS: 386.175060 ($C_{23}H_{22}N_4O_2$, M^+; calc. 386.174276).

*Benzyl [(1S)-1-(3-Cyanopyrazolo[1,5-*a*]pyrimidin-7-yl)-2-phenylethyl]carbamate* (**15d**). From **4a** (0.190 g, 0.5 mmol) and **11c** (0.054 g, 0.5 mmol) by *G.P. B* (stirring at 80° for 4 h). CC ($CHCl_3$/MeOH 60:1) gave 0.145 g (73%) of **15d**. M.p. 85–89°. $[\alpha]_D^{21} = +55.46$ ($c = 0.61$, $CHCl_3$). IR (KBr): 3343, 2230 (C≡N), 1696 (C=O), 1620, 1552, 1527, 1264, 1217, 1057, 737, 698. ^{1}H-NMR ($CDCl_3$): 3.31 (*dd*, $J = 7.3$, 13.4, H_a–C(2)); 3.48 (*dd*, $J = 7.4$, 13.7, H_b–C(2)); 4.97–5.10 (*m*, PhCH_2O); 5.51–5.61 (*m*, H–C(1)); 6.06 (br. *d*, $J = 8.6$, NH); 6.73 (*d*, $J = 4.5$, H–C(6′)); 6.91–6.97 (*m*, 2 H of Ph); 7.20–7.25 (*m*, 3 H of Ph); 7.26–7.39 (*m*, Ph); 8.46 (*s*, H–C(2′)); 8.55 (*d*, $J = 4.5$, H–C(5′)). ^{13}C-NMR ($CDCl_3$): 38.4; 54.4; 67.8; 83.9; 109.3; 112.9; 127.9; 128.6; 128.8; 129.0; 129.25; 129.29; 135.9; 136.2; 147.5; 149.1; 151.1; 153.1; 155.9. EI-MS: 397 (M^+). FAB-MS: 398 ($[M+H]^+$). EI-HR-MS: 397.154250 ($C_{23}H_{19}N_5O_2^+$, M^+; calc. 397.153875).

tert-*Butyl [(1S)-1-(3-Cyanopyrazolo[1,5-*a*]pyrimidin-7-yl)-2-phenylethyl]carbamate* (**15e**). From **4b** (0.173 g, 0.5 mmol) and **11c** (0.054 g, 0.5 mmol) by *G.P. B* (stirring at 20° for 24 h). CC (AcOEt/hexanes 1:2) gave 0.036 g (20%) of **15e**. M.p. 149–152°. $[\alpha]_D^{24} = +55.7$ ($c = 0.50$, $CHCl_3$). IR (KBr): 3362, 2231 (C≡N), 1712 (C=O), 1620, 1553, 1518, 1368, 1250, 1168, 701. ^{1}H-NMR ($CDCl_3$): 1.38 (*s*, *t*-BuO); 3.20–3.32 (*m*, H_a–C(2)); 3.46 (*dd*, $J = 7.2$, 13.6, H_b–C(2)); 5.49–5.58 (*m*, H–C(1)); 5.73 (br. *s*, NH); 6.75 (br. *d*, $J = 3.8$, H–C(6′)); 6.92–7.01 (*m*, 2 H of Ph); 7.18–7.25 (*m*, 3 H of Ph); 8.47 (*s*, H–C(2′)); 8.57 (br. *d*, $J = 3.8$, H–C(5′)). ^{13}C-NMR ($CDCl_3$): 28.7; 38.6; 53.9; 81.3; 83.9; 109.1; 113.0; 127.9; 129.3; 192.4; 136.1; 147.6; 149.9; 151.2; 153.1; 155.2. Anal. calc. for $C_{20}H_{21}N_5O_2$ (363.41): C 66.10, H 5.82, N 19.27; found: C 66.04, H 6.08, N 18.98.

*Benzyl [(1S)-2-Phenyl-1-(1*H*-pyrazol-5-yl)ethyl]carbamate* (**21a**) *and Benzyl [(1S)-2-Phenyl 1-(1*H*-pyrazol-3-yl)ethyl]carbamate* (**21′a**). From **4a** (0.190 g, 0.5 mmol) and **18a** (0.035 g, 0.5 mmol) by *G.P. B* (stirring at 80° for 6 h). CC ($CHCl_3$/MeOH 30:1) gave 0.158 g (98%) of **21a**/**21′a** 72:28. M.p. 122–138° (CH_2Cl_2/hexane). $[\alpha]_D^{22} = -21.7$ ($c = 0.62$, $CHCl_3$). IR (KBr): 3356, 1693 (C=O), 1537, 1455, 1249, 1040, 744, 701. ^{1}H-NMR ($CDCl_3$): 3.18 (*d*, $J = 6.0$, H–C(2)); 4.97–5.21 (*m*, H–C(1)); 5.08 (*s*,

PhCH_2O); 5.60 (br. *s*, NH); 6.05 (*s*, H–C(4′)); 6.75 (br. *s*, H–N(1′)); 7.00–7.14 (*m*, 2 H of Ph); 7.15–7.24 (*m*, 3 H of Ph); 7.27–7.47 (*m*, Ph, H–C(3′)). ^{1}H-NMR ((D$_6$)DMSO): 2.95 (*dd*, *J* = 9.8, 13.6, H$_a$–C(2)); 3.03–3.16 (*m*, H$_b$–C(2)); 4.82–5.01 (*m*, PhCH_2O, H–C(1)); 6.18 (*s*, H–C(4′)); 7.14–7.38 (*m*, 2 Ph); 7.61 (*s*, H–C(3′)); 7.43 (br. *s*, NH (**21′a**)); 7.64 (br. *s*, NH (**21a**)); 12.52 (br. *s*, H–N(1′) (**21a**)); 12.65 (br. *s*, H–N(1′) (**21′a**)). EI-MS: 322 ([*M* + H]$^+$). EI-HR-MS: 322.156050 ($C_{19}H_{20}N_3O_2^+$, ([*M* + H]$^+$); calc. 322.155552). Anal. calc. for $C_{19}H_{19}N_3O_2$ (321.37): C 71.07, H 5.96, N 13.08; found: C 70.95, H 6.04, N, 13.08.

tert-*Butyl [(1*S*)-2-Phenyl-1-(1*H*-pyrazol-5-yl)ethyl]carbamate* (**21b**) *and* tert-*Butyl [(1*S*)-2-Phenyl-1-(1*H*-pyrazol-3-yl)ethyl]carbamate* (**21′b**). From **4b** (0.173 g, 0.5 mmol) and **18a** (0.034 g, 0.5 mmol) by *G.P. B* (stirring at 80° for 6 h). CC ($CHCl_3$/MeOH 40:1) gave 0.124 g (86%) of **21b**/**21′b** 87:13. M.p. 113–115°. $[\alpha]_D^{21} = -28.7$ (*c* = 0.65, $CHCl_3$). IR (KBr): 3379, 2978, 1690 (C=O), 1518, 1366, 1247, 1171, 1023, 800, 700. ^{1}H-NMR ($CDCl_3$): 1.40 (*s*, *t*-BuO); 3.16 (*d*, *J* = 5.7, H–C(2)); 5.06 (br. *d*, *J* = 5.7, H–C(1)); 5.20 (br. *s*, NH); 6.05 (*s*, H–C(4′)); 6.40 (br. *s*, H–N(1′)); 7.08–7.14 (*m*, 2 H of Ph); 7.15–7.28 (*m*, 3 H of Ph); 7.45 (*d*, *J* = 1.9, H–C(3′)). ^{1}H-NMR ((D$_6$)DMSO): 1.19 (*s*, *t*-BuO (**21′b**)); 1.29 (*s*, *t*-BuO (**21b**)); 2.92 (*dd*, *J* = 9.4, 13.2, H$_a$–C(2)); 3.05 (*dd*, *J* = 5.3, 13.2, H$_b$–C(2)); 4.82 (br. *s*, H–C(1)); 6.16 (*s*, H–C(4′) (**21b**)); 6.67 (br. *s*, H–C(4′) (**21′b**)); 7.02–7.37 (*m*, Ph, H–C(3′)); 7.59 (*s*, NH); 12.48 (br. *s*, H–N(1′) (**21b**)); 12.56 (br. *s*, H–N(1′) (**21′b**)). ^{13}C-NMR ($CDCl_3$): 28.3; 41.7 (**21b**); 44.4 (**21′b**); 49.8 (**21b**); 52.1 (**21′b**); 79.7; 103.2; 126.4; 128.2; 129.5; 131.8; 137.5; 150.3 (**21b**); 151.1 (**21′b**); 155.5 (**21′b**); 156.1 (**21b**). Anal. calc. for $C_{16}H_{21}N_3O_2$ (287.36): C 66.88, H 7.37, N 14.62; found: C 67.18, H 7.61, N 14.61.

*Benzyl [(1*S*)-2-Phenyl-1-(1-phenyl-1*H*-pyrazol-5-yl)ethyl]carbamate* (**21c**). From **4a** (0.190 g, 0.5 mmol) and **18b** (0.073 g, 0.5 mmol) by *G.P. B* (stirring at 80° for 6 h). CC (AcOEt/hexanes 1:2) gave 0.189 g (95%) of **21c**. Oil. $[\alpha]_D^{21} = +12.2$ (*c* = 1.50, $CHCl_3$). IR (NaCl): 3310, 3063, 3031, 1713 (C=O), 1599, 1530, 1503, 1454, 1399, 1250, 1028, 697. ^{1}H-NMR ($CDCl_3$): 2.90 (*dd*, *J* = 7.5, 13.3, H$_a$–C(2)); 3.00 (*dd*, *J* = 5.8, 13.2, H$_b$–C(2)); 4.95–5.20 (*m*, H–C(1), NH, PhCH_2O); 6.31 (*d*, *J* = 1.9, H–C(4′)); 6.83–6.89 (*m*, 2 H of Ph); 7.11–7.23 (*m*, 5 H of Ph); 7.26–7.40 (*m*, 8 H of Ph); 7.60 (*d*, *J* = 1.9, H–C(3′)). ^{13}C-NMR ($CDCl_3$): 42.7; 49.4; 67.4; 104.9; 126.3; 127.3; 128.5; 128.6; 128.81; 128.84; 129.0; 129.5; 129.7; 136.4; 136.6; 139.6; 140.3; 144.3; 155.6. EI-MS: 398 ([*M* + H]$^+$). FAB-MS: 398 ([*M* + H]$^+$). EI-HR-MS: 398.187950 ($C_{25}H_{24}N_3O_2^+$, [*M* + H]$^+$; calc. 398.186852).

*Benzyl {(1*S*)-1-[1-(4-Nitrophenyl)-1*H*-pyrazol-5-yl]-2-phenylethyl}carbamate* (**21d**). From **4a** (0.190 g, 0.5 mmol), **18c** (0.077 g, 0.5 mmol), and 37% aq. HCl soln. (2 drops, *ca.* 0.6 mmol) by *G.P. B* (stirring at 80° for 1.5 h). CC (AcOEt/hexanes 1:2) gave 0.177 g (80%) of **21d**. Oil. $[\alpha]_D^{24} = +71.2$ (*c* = 0.612, $CHCl_3$). IR (KBr): 3317, 3031, 1711 (C=O), 1598, 1522, 1503, 1342, 1246, 1111, 1026, 855, 698. ^{1}H-NMR ($CDCl_3$): 2.89 (*dd*, *J* = 8.7, 12.8, H$_a$–C(2)); 3.10 (*dd*, *J* = 4.9, 13.2, H$_b$–C(2)); 5.06 (*s*, PhCH_2O); 5.08–5.20 (*m*, H–C(1), NH); 6.45 (*d*, *J* = 1.9, H–C(4′)); 6.79–6.84 (*m*, 2 H of C_6H_4); 7.08–7.21 (*m*, 4 H of Ph); 7.27–7.41 (*m*, 6 H of Ph); 7.67 (*d*, *J* = 1.9, H–C(3′)); 8.10–8.23 (*m*, 2 H of C_6H_4). ^{13}C-NMR ($CDCl_3$): 43.3; 49.6; 67.5; 106.2; 124.8; 126.5; 127.6; 128.5; 128.8; 128.95, 129.05, 129.5; 136.1; 136.5; 141.6; 144.6; 145.2; 147.1; 155.9. EI-MS: 443 ([*M* + H]$^+$). EI-HR-MS: 443.172680 ($C_{25}H_{23}N_4O_4^+$, [*M* + H]$^+$; calc. 443.171931).

*Benzyl {(1*S*)-1-[1-(4-Methoxyphenyl)-1*H*-pyrazol-5-yl]-2-phenylethyl}carbamate* (**21e**). From **4a** (0.190 g, 0.5 mmol) and **18d** (0.087 g, 0.5 mmol) by *G.P. B* (stirring at 80° for 3 h). CC (AcOEt/hexanes 1:2) gave 0.150 g (70%) of **21e**. Oil. $[\alpha]_D^{21} = +11.6$ (*c* = 1.74, $CHCl_3$). IR (NaCl): 3312, 3031, 2936, 1716 (C=O), 1518, 1455, 1251, 1028, 837, 699. ^{1}H-NMR ($CDCl_3$): 2.91 (*dd*, *J* = 7.5, 13.2, H$_a$–C(2)); 2.96–3.06 (*m*, H$_b$–C(2)); 3.82 (*s*, MeO); 5.03 (*m*, H–C(1), NH, PhCH_2O); 6.28 (*d*, *J* = 1.9, H–C(4′)); 6.80–6.91 (*m*, 2 H of C_6H_4); 7.00–7.11 (*m*, 2 H of Ph); 7.13–7.21 (*m*, 2 H of C_6H_4); 7.26–7.40 (*m*, Ph); 7.57 (*d*, *J* = 1.9, H–C(3′)). ^{13}C-NMR ($CDCl_3$): 42.7; 49.4; 55.9; 67.3; 104.4; 114.6; 127.3; 127.8; 128.5; 128.6; 128.8; 128.9; 129.7; 132.6; 136.5; 136.6; 139.9; 144.3; 155.6; 159.9. EI-MS: 428 ([*M* + H]$^+$). HR-MS: 428.198300 ($C_{26}H_{26}N_3O_3^+$, [*M* + H]$^+$; calc. 428.197417).

tert-*Butyl {(1*S*)-1-[1-(2-Bromophenyl)-1*H*-pyrazol-5-yl]-2-phenylethyl}carbamate* (**21f**). From **4b** (0.173 g, 0.5 mmol) and **18e** (0.112 g, 0.5 mmol) by *G.P. B* (stirring at 80° for 2 h). CC (AcOEt/hexanes 1:2) gave 0.199 g (90%) of **21f**. M.p. 39–45°. $[\alpha]_D^{21} = -57.4$ (*c* = 0.53, $CHCl_3$). IR (KBr): 3273, 2976, 1703 (C=O), 1494, 1455, 1366, 1248, 1169, 1019, 928, 763, 698. ^{1}H-NMR ((D$_6$)DMSO, 80°): 1.16 (*s*, *t*-BuO); 2.93 (br. *d*, *J* = 8.3, CH_2(2)); 4.53–4.63 (*m*, H–C(1)); 6.51 (*d*, *J* = 1.5, H–C(4′)); 6.88 (br. *s*, NH); 6.94–7.02 (*m*,

2 H of Ph); 7.10–7.24 (*m*, 3 H of Ph, 1 H of C_6H_4); 7.41–7.52 (*m*, 2 H of C_6H_4); 7.58 (*d*, *J* = 1.5, H–C(3′)); 7.76–7.82 (*m*, 1 H of C_6H_4). Anal. calc. for $C_{22}H_{24}BrN_3O_2$ (442.35): C 59.73; H 5.47; N 9.50; found: C 59.66, H 5.60, N 9.46.

*Benzyl {(1*S*)-2-Phenyl-1-[1-(pyridin-2-yl)-1*H*-pyrazol-5-yl]ethyl}carbamate* (**21g**). From **4a** (0.190 g, 0.5 mmol), **18f** (0.054 g, 0.5 mmol), and 37% aq. HCl soln. (2 drops, *ca.* 0.6 mmol) by *G.P. A* (reflux for 3 h): 0.165 g (83%) of **21g**. M.p. 165–166°. $[\alpha]_D^{24} = +20.3$ (*c* = 0.80, $CHCl_3$). IR (KBr): 3334, 1687 (C=O), 1594, 1543, 1475, 1436, 1387, 1261, 1028, 801, 779, 743, 699. ^{1}H-NMR ($CDCl_3$): 3.08 (*dd*, *J* = 7.9, 13.7, H_a–C(2)); 3.17 (*dd*, *J* = 7.4, 13.7, H_b–C(2)); 5.04 (*s*, PhCH_2O); 5.74–5.85 (*m*, H–C(1)); 6.21 (*d*, *J* = 1.5, H–C(4′)); 6.63 (br. *d*, *J* = 7.2, NH); 6.99–7.06 (*m*, 2 H of Ph); 7.13–7.22 (*m*, 3 H of Ph); 7.25 (*ddd*, *J* = 1.0, 5.0, 8.3, H–C(5″)); 7.26–7.37 (*m*, 5 H of Ph); 7.55 (*d*, *J* = 1.5, H–C(3′)); 7.86 (‘*dt*’, *J* = 1.8, 8.2, H–C(4″)); 7.99 (br. *d*, *J* = 8.1, H–C(3″)); 8.49 (br. *d*, *J* = 4.5, H–C(3″)). ^{13}C-NMR ($CDCl_3$): 41.3; 50.6; 67.0; 109.6; 116.8; 122.1; 127.0; 128.4; 128.7; 128.9; 129.6; 137.0; 137.9; 139.4; 141.1; 144.7; 147.6; 153.7; 156.1. EI-MS: 398 (M^+). EI-HR-MS: 398.175250 ($C_{24}H_{22}N_4O_2^+$, M^+; calc. 398.174276). Anal. calc. for $C_{24}H_{22}N_4O_2$ (398.46): C 72.34, H 5.75, N 14.06; found: C 72.61, H 5.63, N 13.72.

*Benzyl {(1*S*)-2-Phenyl-1-[1-(pyrimidin-2-yl)-1*H*-pyrazol-5-yl]ethyl}carbamate* (**21h**). From **4a** (0.190 g, 0.5 mmol), **18g** (0.055 g, 0.5 mmol), and 37% (aq. HCl soln. 2 drops, *ca.* 0.6 mmol) by *G.P. B* (stirring at 80° for 3 h). CC (AcOEt) gave 0.177 g (89%) of **21h**. M.p. 139–142°. $[\alpha]_D^{21} = +23.9$ (*c* = 1.00, $CHCl_3$). IR (KBr): 3442, 3329, 1696 (C=O), 1573, 1541, 1422, 1258, 1027, 921, 737, 696. ^{1}H-NMR ($CDCl_3$): 2.98–3.13 (*m*, H_a–C(2)); 3.22 (*dd*, *J* = 6.0, 13.9, H_b–C(2)); 5.03 (*s*, PhCH_2O); 5.82 (br. *d*, *J* = 7.1, NH); 5.98–6.07 (*m*, H–C(1)); 6.28 (*d*, *J* = 1.5, H–C(4′)); 7.03–7.11 (*m*, 2 H of Ph); 7.17–7.37 (*m*, 8 H of Ph, H–C(5″)); 7.68 (*d*, *J* = 1.5, H–C(3′)); 8.81 (*d*, *J* = 4.5, H–C(4″), H–C(6″)). ^{13}C-NMR ($CDCl_3$): 41.1; 50.1; 66.7; 109.4; 118.6; 126.7; 128.0; 128.37, 128.41, 129.2; 136.4; 136.8; 142.0; 146.1; 155.5; 157.2; 158.6. EI-MS: 399 (M^+). EI-HR-MS: 399.170620 ($C_{23}H_{21}N_5O_2^+$, M^+; calc. 399.169525).

*Benzyl {(1*S*)-1-[1-(6-Chloropyridazin-3-yl)-1*H*-pyrazol-5-yl]-2-phenylethyl}carbamate* (**21i**). From **4a** (0.190 g, 0.5 mmol), **18h** (0.073 mg, 0.5 mmol), and 37% aq. HCl soln. (2 drops, *ca.* 0.6 mmol) by *G.P. A* (reflux for 3 h): 0.197 g (91%) of **21i**. M.p. 181–184° (EtOH). $[\alpha]_D^{24} = +22.5$ (*c* = 1.00, $CHCl_3$). IR (KBr): 3338, 1694 (C=O), 1539, 1467, 1425, 1256, 1027, 921, 698. ^{1}H-NMR ($CDCl_3$): 3.11–3.22 (*m*, H_a–C(2)); 3.30 (*dd*, *J* = 6.4, 13.9, H_b–C(2)); 5.00 (*s*, PhCH_2O); 5.75–5.86 (*m*, H–C(1)); 6.11 (br. *d*, *J* = 7.9, NH); 6.33 (*d*, *J* = 1.5, H–C(4′)); 7.07–7.13 (*m*, 2 H of Ph); 7.18–7.36 (*m*, 8 H of Ph); 7.63 (br. *d*, *J* = 8.7, H–C(5″)); 7.64 (*d*, *J* = 1.5, H–C(3′)); 8.23 (*d*, *J* = 8.7, H–C(4″)). ^{13}C-NMR ($CDCl_3$): 41.0; 50.8; 67.1; 110.7; 123.7; 127.2; 128.4; 128.85, 128.88, 129.7; 131.2; 136.8; 137.4; 142.8; 146.3; 155.0; 156.0; 156.1. EI-MS: 433 (M^+). Anal. calc. for $C_{23}H_{20}ClN_5O_2$ (433.89): C 63.67, H 4.65, N 16.14; found: C 63.56, H 4.72, N 16.23.

tert-*Butyl {(1*S*)-1-[1-(6-Chloropyridazin-3-yl)-1*H*-pyrazol-5-yl]-2-phenylethyl}carbamate* (**21j**). From **4b** (0.173 g, 0.5 mmol), **18h** (0.072 g, 0.5 mmol), and 37% aq. HCl soln. (2 drops, *ca.* 0.6 mmol) by *G.P. A* (reflux for 6 h): 0.108 g (54%) of **21j**. M.p. 198–201° (EtOH). $[\alpha]_D^{26} = +36.6$ (*c* = 0.32, CH_2Cl_2). IR (KBr): 3366, 1689 (C=O), 1525, 1429, 1422, 1251, 1169, 1021, 922, 838. ^{1}H-NMR ($CDCl_3$): 1.34 (*s*, *t*-BuO); 3.02–3.16 (*m*, H_a–C(2)); 3.27 (*dd*, *J* = 5.7, 13.6, H_b–C(2)); 5.77 (br. *s*, H–C(1), NH); 6.33 (*s*, H–C(4′)); 7.07–7.16 (*m*, 2 H of Ph); 7.17–7.28 (*m*, 3 H of Ph); 7.63 (*d*, *J* = 9.4, H–C(5″)); 7.64 (*s*, H–C(3′)); 8.21 (br. *d*, *J* = 9.4, H–C(4″)). ^{13}C-NMR ($CDCl_3$): 28.3; 40.8; 49.9; 79.7; 110.1; 123.2; 126.7; 128.4; 129.3; 130.6; 137.1; 142.3; 146.5; 154.5; 155.0; 155.8. Anal. calc. for $C_{20}H_{22}ClN_5O_2$ (399.87): C 60.07, H 5.55, N 17.51; found: C 60.05, H 5.64, N, 17.55.

*Benzyl {(1*S*)-2-Phenyl-1-[1-(6-phenylpyridazin-3-yl)-1*H*-pyrazol-5-yl]ethyl}carbamate* (**21k**). From **4a** (0.190 g, 0.5 mmol), **18i** (0.093 g, 0.5 mmol), and 37% aq. HCl soln. (2 drops, *ca.* 0.6 mmol) by *G.P. A* (reflux for 1.5 h): 0.185 g (78%) of **21k**. M.p. 203–206°. $[\alpha]_D^{24} = +20.7$ (*c* = 0.50, $CHCl_3$). IR (KBr): 3337, 1694 (C=O), 1538, 1427, 1396, 1264, 1051, 924, 802, 745, 688. ^{1}H-NMR ($CDCl_3$): 3.24–3.38 (*m*, H–C(2)); 5.04 (*s*, PhCH_2O); 5.79–5.89 (*m*, H–C(1)); 6.32 (*d*, *J* = 1.5, H–C(4′)); 6.50 (br. *d*, *J* = 6.4, NH); 7.05–7.13 (*m*, 2 H of Ph); 7.16–7.24 (*m*, 3 H of Ph); 7.27–7.40 (*m*, 5 H of Ph); 7.51–7.61 (*m*, 3 H of Ph); 7.64 (*d*, *J* = 1.5, H–C(3′)); 8.01 (*d*, *J* = 9.0, H–C(5″)); 8.06–8.14 (*m*, 2 H of Ph); 8.28 (*d*, *J* = 9.0, H–C(4″)). ^{1}H-NMR ((D$_6$)DMSO): 2.86 (*dd*, *J* = 10.2, 13.2, H_a–C(2)); 3.23 (*dd*, *J* = 3.8, 13.6, H_b–C(2)); 4.92 (*s*, PhCH_2O); 5.97–6.07 (*m*, H–C(1)); 6.65 (*d*, *J* = 1.5, H–C(4′)); 6.86 (br. *s*, NH); 7.16–7.42 (*m*, 9 H of Ph); 7.56–7.66 (*m*, 3 H of Ph); 7.85 (*d*, *J* = 1.5, H–C(3′)); 8.08–8.14 (*m*, 1 H of

Ph); 8.20 (*d*, *J* = 9.2, H–C(5″)); 8.22–8.26 (*m*, 2 H of Ph); 8.45 (*d*, *J* = 9.2, H–C(4″)). ^{13}C-NMR ((D$_6$)DMSO): 41.8; 51.6; 66.1; 108.6; 122.1; 127.2; 127.8; 128.27; 128.35; 128.5; 128.9; 129.1; 130.01; 130.02; 131.1; 136.2; 137.9; 139.2; 142.9; 149.1; 156.3; 156.5; 158.3. EI-MS: 475 (M^+). EI-HR-MS: 476.207780 ($C_{29}H_{26}N_5O_2^+$, $[M+H]^+$; calc. 476.208650). Anal. calc. for $C_{29}H_{25}N_5O_2$ (475.54): C 73.25, H 5.30, N 14.73; found: C 72.92, H 5.38, N 14.34.

*Benzyl {(1*R*,2*R*)-2-Hydroxy-1-(1-phenyl-1*H*-pyrazol-5-yl)propy}lcarbamate* (**23a**). From **10** (181 mg, 0.5 mmol) and **18b** (0.072 g, 0.5 mmol) by *G.P. B* (stirring at 80° for 6 h). CC (AcOEt/hexanes 1:1) gave 0.161 g (92%) of **23a**. Oil. $[\alpha]_D^{24} = +37.05$ (*c* = 1.88, $CHCl_3$). IR (NaCl): 3311, 1709 (C=O), 2598, 1503, 1455, 1399, 1272, 1063, 928, 766, 697. ^{1}H-NMR ($CDCl_3$): 1.08 (*d*, *J* = 6.4, Me(3)); 1.85 (*s*, OH); 3.76–3.86 (*m*, H–C(2)); 4.77–4.93 (*m*, H–C(1)); 5.09 (*s*, PhCH_2O); 5.44 (*d*, *J* = 6.4, NH); 6.38 (*d*, *J* = 1.9, H–C(4′)); 7.28–7.55 (*m*, 2 Ph); 7.63 (*dd*, *J* = 0.5, 1.9, H–C(3′)). ^{13}C-NMR ($CDCl_3$): 20.5; 53.7; 67.5; 69.4; 105.7; 126.5; 128.5; 128.7; 128.97; 129.02; 129.7; 136.6; 139.7; 140.3; 143.4; 156.7. EI-MS: 352 ($[M+H]^+$). FAB-MS: 352 ($[M+H]^+$). EI-HR-MS: 352.167200 ($C_{20}H_{22}N_3O_3^+$, calc. $[M+H]^+$; 352.166117).

*Benzyl {(1*R*,2*R*)-2-Hydroxy-1-[1-(6-phenylpyridazin-3-yl)-1*H*-pyrazol-5-yl]propyl}carbamate* (**23b**). From **10** (181 mg, 0.5 mmol), **18i** (0.093 g, 0.5 mmol), and 37% aq. HCl soln. (2 drops, *ca.* 0.6 mmol) by *G.P. A* (reflux for 2 h): 0.114 g (63%) of **23b**. M.p. 210–211°. $[\alpha]_D^{25} = +30.0$ (*c* = 0.5, $CHCl_3$). IR (KBr): 3510, 1696 (C=O), 1528, 1464, 1435, 1394, 1269, 1231, 1062, 920, 689. ^{1}H-NMR ($CDCl_3$): 1.33 (*d*, *J* = 6.0, Me(3)); 2.54 (*s*, OH); 4.40–4.51 (*m*, H–C(2)); 5.08 (*s*, PhCH_2O); 5.65 (*dd*, *J* = 3.0, 8.7, H–C(1)); 6.31 (*d*, *J* = 8.8, NH); 6.52 (*d*, *J* = 1.6, H–C(4′)); 7.27–7.41 (*m*, Ph); 7.49–7.60 (*m*, 3 H of Ph); 7.72 (*d*, *J* = 1.7, H–C(3′)); 7.99 (*d*, *J* = 8.9, H–C(5″)); 8.02–8.08 (*m*, 2 H of Ph); 8.25 (*d*, *J* = 9.5, H–C(4″)). ^{1}H-NMR ((D$_6$)DMSO): 1.10 (*d*, *J* = 6.0, Me(3)); 3.94–4.05 (*m*, H–C(2)); 4.79 (*d*, *J* = 5.7, OH); 4.99, 5.04 (2*d*, 1:1, *J* = 12.8, PhCH_2O); 5.82 (*dd*, *J* = 4.1, 9.3, H–C(1)); 6.66 (*d*, *J* = 1.5, H–C(4′)); 7.27–7.39 (*m*, 4 H of Ph); 7.53 (*d*, *J* = 9.8, H–C(5″)); 7.55–7.64 (*m*, 3 H of Ph); 7.81 (*d*, *J* = 1.5, H–C(3′)); 8.16–8.25 (*m*, 3 H of Ph); 8.46 (*d*, *J* = 9.4, H–C(4″)). ^{13}C-NMR ($CDCl_3$): 21.1; 54.5; 66.4; 68.6; 109.9; 122.7; 127.7; 128.2; 128.5; 128.6; 129.2; 130.0; 131.1; 136.1; 137.9; 142.7; 146.7; 156.6; 157.0; 158.2. EI-MS: 411 ($[M-H_2O]^+$). EI-HR-MS: 411.170300 ($C_{24}H_{21}N_5O_2^+$, calc. $[M-H_2O]^+$; 411.169525). Anal. calc. for $C_{24}H_{23}N_5O_3$ (429.47): C 67.12, H 5.40, N 16.31; found: C 67.00, H 5.51, N 16.15.

6. *Benzyl [(1*R*,2*R*)1-(3-Cyanopyrazolo[1,5-*a*]pyrimidin-7-yl)-2-hydroxypropyl]carbamate* (**16**). A mixture of **10** (0.181 g, 0.5 mmol), **11c** (54 mg, 0.5 mmol), EtOH (4 ml), and 37% aq. HCl soln. (3 drops, *ca.* 1 mmol) was heated under reflux for 6 h. After cooling, the precipitate was collected by filtration and washed with EtOH and Et_2O to give the first portion of **16**. The filtrate was evaporated and the residue purified by CC (AcOEt/hexanes 1:1) to give a second portion of **16** which was crystallized from $CHCl_3$. Combined yield: 0.135 g (77%) of **16**. M.p. 168–174°. $[\alpha]_D^{25} = -35.2$ (*c* = 0.5, $CHCl_3$). IR (KBr): 3402, 2228 (C≡N), 1695 (C=O), 1622, 1551, 1511, 1322, 1261, 1215, 1097, 691. ^{1}H-NMR ($CDCl_3$): 1.42 (*d*, *J* = 6.4, Me(3)); 2.37 (*d*, *J* = 2.6, OH); 4.46–4.59 (*m*, H–C(1)); 5.12 (*s*, PhCH_2O); 5.40 (*dd*, *J* = 1.9, 8.7, H–C(2)); 6.07 (*d*, *J* = 8.7, NH); 7.06 (*d*, *J* = 4.1, H–C(6′)); 7.29–7.43 (*m*, Ph); 8.37 (*s*, H–C(2′)); 8.69 (*d*, *J* = 4.1, H–C(5′)). ^{13}C-NMR ($CDCl_3$): 20.9; 56.6; 65.8; 66.8; 82.1; 110.0; 114.2; 128.5; 128.7; 129.2; 137.7; 148.2; 150.9; 151.8; 154.5; 157.2. EI-MS: 352 ($[M+H]^+$). Anal. calc. for $C_{18}H_{17}N_5O_3$ (351.36): C 61.53, H 4.88, N 19.93; found: C 61.59, H 4.95, N 19.96.

7. tert-*Butyl [(1*S*)-2-Phenyl-1-(2-phenylpyrimidin-4-yl)ethyl]carbamate* (**17**). A mixture of **4b** (0.173 g, 0.5 mmol), **12** (0.117 g, 0.75 mmol), K_2CO_3 (0.070 g, 0.5 mmol), and EtOH (4 ml) was heated under reflux for 6 h. The mixture was cooled and evaporated, and the residue purified by CC (AcOEt/hexanes 1:2): 0.050 g (27%) of **17**. M.p. 114–116°. $[\alpha]_D^{24} = -2.57$ (*c* = 0.50, $CHCl_3$). IR(KBr): 3383, 2978, 1690 (C=O), 1568, 1559, 1514, 1389, 1169, 1018, 694. ^{1}H-NMR ($CDCl_3$): 1.44 (*s*, *t*-BuO); 3.13 (*dd*, *J* = 7.9, 13.2, H_a–C(2)); 3.28 (*dd*, *J* = 5.3, 13.2, H_b–C(2)); 4.93–5.11 (*m*, H–C(1)); 5.62 (br. *d*, *J* = 6.8, NH); 6.76 (*d*, *J* = 4.9, H–C(5′)); 6.98–7.09 (*m*, 2 H of Ph); 7.13–7.24 (*m*, 3 H of Ph); 7.46–7.56 (*m*, 3 H of Ph); 8.41–8.51 (*m*, 2 H of Ph); 8.60 (*d*, *J* = 4.9, H–C(6′)). ^{13}C-NMR ($CDCl_3$): 28.8; 42.5; 56.9; 80.27; 117.6; 127.1; 128.7; 128.8; 129.0; 129.9; 131.2; 137.2; 137.9; 155.6; 157.6; 164.8; 168.5. EI-MS: 375 (M^+). EI-HR-MS: 375.194777 ($C_{23}H_{25}N_3O_2^+$, M^+; calc. 375.194677). Anal. calc. for $C_{23}H_{25}N_3O_2$ (375.46): C 73.57, H 6.71, N 11.19; found: C 73.82, H 6.98, N 11.05.

8. *Compounds* **22a**–**g** *and* **24a**,**b**: *General Procedure.* A mixture of *N*-[(benzyloxy)carbonyl]-protected amine **21a**,**c**–**e**,**g**,**h**,**k** or **23a**,**b** (0.5 mmol) in EtOH, THF, or EtOH/THF (10 ml) and 10% Pd/C

(40 mg) was hydrogenated (1 bar) at r.t. for 24 h. The mixture was filtered through a short pad of *Celite*® and washed thoroughly with MeOH. The filtrate was evaporated when necessary, the product was purified by CC. Compounds **22a**–**g** and **24a**,**b** were prepared in this manner.

(1S)-2-Phenyl-1-(1H-pyrazol-5-yl)ethanamine (**22a**). From a mixture **21a**/**21′a** (0.161 g, 0.5 mmol) in EtOH, CC ($CHCl_3$/MeOH 10:1) gave 0.086 g (92%) of **22a**. Oil. $[\alpha]_D^{24} = -9.00$ ($c = 1.54$, $CHCl_3$). IR (NaCl): 3177, 2922, 1602, 1584, 1495, 1454, 1380, 927, 768, 700. ^{1}H-NMR ($CDCl_3$): 2.86 (*dd*, $J = 8.7$, 13.6, H_a–C(2)); 3.17 (*dd*, $J = 4.9$, 13.6, H_b–C(2)); 4.00 (br. *s*, NH_2); 4.35 (*dd*, $J = 4.9$, 8.7, H–C(1)); 6.19 (*d*, $J = 1.9$, H–C(4′)); 7.16–7.40 (*m*, Ph, H–N(1′)); 7.51 (*d*, $J = 2.3$, H–C(3′)). ^{1}H-NMR ((D_6)DMSO): 2.04 (br. *s*, NH_2); 2.81 (*dd*, $J = 7.9$, 13.2, H_a–C(2)); 3.00 (*dd*, $J = 6.0$, 13.2, H_b–C(2)); 4.11 (*dd*, $J = 6.0$, 7.9, H–C(1)); 6.11 (*s*, H–C(4′)); 7.13–7.28 (*m*, Ph); 7.45 (br. *s*, H–C(3′)); 12.45 (br. *s*, H–N(1′)). ^{13}C-NMR ($CDCl_3$): 45.2; 51.1; 102.6; 127.0; 128.9; 129.8; 133.9; 138.8; 152.2. FAB-MS: 188 ($[M+H]^+$).

(1S)-2-Phenyl-1-(1-phenyl-1H-pyrazol-5-yl)ethanamine (**22b**). From **21c** (0.199 g, 0.5 mmol) in EtOH: 0.108 g (82%) of **22b**. Oil. $[\alpha]_D^{21} = -12.1$ ($c = 1.97$, $CHCl_3$). IR (NaCl): 3365, 3062, 3028, 2922, 1599, 1503, 1454, 1398, 1199, 1072, 924, 697. ^{1}H-NMR ($CDCl_3$): 1.62 (br. *s*, NH_2); 2.81 (*dd*, $J = 8.3$, 13.4, H_a–C(2)); 3.01 (*dd*, $J = 5.7$, 13.5, H_b–C(2)); 4.26 (*dd*, $J = 5.7$, 8.1, H–C(1)); 6.45 (*d*, $J = 1.5$, H–C(4′)); 6.94–7.03 (*m*, 2 H of Ph); 7.14–7.24 (*m*, 3 H of Ph); 7.28–7.35 (*m*, 2 H of Ph); 7.37–7.48 (*m*, 3 H of Ph); 7.63 (*d*, $J = 1.5$, H–C(3′)). ^{1}H-NMR ((D_6)DMSO): 2.04 (br. *s*, NH_2); 2.82 (*dd*, $J = 7.2$, 13.2, H_a–C(2)); 2.87 (*dd*, $J = 6.8$, 13.2, H_b–C(2)); 4.05 (*dd*, $J = 6.8$, 7.2, H–C(1)); 6.53 (*d*, $J = 1.9$, H–C(4′)); 6.90–6.95 (*m*, 2 H of Ph); 7.09–7.20 (*m*, 3 H of Ph); 7.29–7.34 (*m*, 2 H of Ph); 7.38–7.50 (*m*, 3 H of Ph); 7.57 (*d*, $J = 1.9$, H–C(4′)). ^{13}C-NMR ($CDCl_3$): 45.3; 49.7; 104.3; 126.3; 127.1; 128.7; 128.9; 129.5; 129.6; 138.2; 140.1; 140.3. EI-MS: 264 ($[M+H]^+$). EI-HR-MS: 264.150460 ($C_{17}H_{18}N_3^+$, $[M+H]^+$; calc. 264.150073).

(1S)-1-[1-(4-Aminophenyl)-1H-pyrazol-5-yl]-2-phenylethanamine (**22c**). From **21d** (0.221 g, 0.5 mmol) in EtOH. CC ($CHCl_3$/MeOH 10:1) gave 0.132 g (95%) of **22c**. Oil. $[\alpha]_D^{24} = -14.2$ ($c = 1.38$, $CHCl_3$). IR (NaCl): 3343, 3217, 2923, 1627, 1609, 1522, 1400, 1294, 1172, 1078, 929, 834, 701. ^{1}H-NMR ($CDCl_3$): 1.81 (br. *s*, NH_2–C(1)); 2.78 (*dd*, $J = 8.3$, 13.2, H_a–C(2)); 2.99 (*dd*, $J = 5.7$, 13.6, H_b–C(2)); 3.80 (br. *s*, ArNH_2); 4.17 (*dd*, $J = 5.7$, 8.3, H–C(1)); 6.37 (*d*, $J = 1.9$, H–C(4′)); 6.59–6.68 (*m*, 2 H of C_6H_4); 6.94–7.06 (*m*, 2 H of Ph, 2 H of C_6H_4); 7.14–7.28 (*m*, 3 H of Ph); 7.57 (*d*, $J = 1.9$, H–C(3′)). ^{13}C-NMR ($CDCl_3$): 45.1; 49.6; 103.5; 115.4; 127.0; 127.7; 128.9; 129.7; 130.8; 138.4; 139.7; 147.3; 147.8. EI-MS: 278 (M^+). EI-HR-MS: 278.143500 ($C_{17}H_{18}N_4^+$, M^+; calc. 278.153147).

(1S)-1-[1-(4-Methoxyphenyl)-1H-pyrazol-5-yl]-2-phenylethanamine (**22d**). From **21e** (0.214 g, 0.5 mmol) in EtOH: 0.144 g (98%) of **22d**. Oil. $[\alpha]_D^{24} = -4.18$ ($c = 0.96$, $CHCl_3$). IR (NaCl): 3357, 2930, 2838, 1607, 1518, 1455, 1301, 1251, 1027, 837, 701. ^{1}H-NMR ($CDCl_3$): 2.96 (*dd*, $J = 7.2$, 13.2, H_a–C(2)); 3.06 (*dd*, $J = 6.8$, 13.2, H_b–C(2)); 3.51 (br. *s*, NH_2); 3.83 (*s*, MeO); 4.23 (*t*, $J = 7.2$, H–C(1)); 6.56 (*d*, $J = 1.9$, H–C(4′)); 6.86–6.92 (*m*, 2 H of C_6H_4); 6.93–6.99 (*m*, of C_6H_4); 7.04–7.11 (*m*, 2 H of Ph); 7.18–7.24 (*m*, 3 H of Ph); 7.59 (*d*, $J = 1.9$, H–C(3′)). ^{13}C-NMR ($CDCl_3$): 44.3; 49.6; 55.9; 104.5; 114.6; 127.3; 127.9; 129.0; 129.7; 132.6; 137.3; 140.1; 145.6; 160.0. EI-MS: 294 ($[M+H]^+$). EI-HR-MS 294.161030 ($C_{18}H_{20}N_3O^+$, $[M+H]^+$; calc. 294.160637).

(1S)-2-Phenyl-1-[1-(pyridin-2-yl)-1H-pyrazol-5-yl]ethanamine (**22e**). From **21g** (0.199 g, 0.5 mmol) in EtOH/THF 4:1. CC ($CHCl_3$/MeOH 10:1) gave 0.112 g (85%) of **22e**. Oil. $[\alpha]_D^{21} = -31.4$ ($c = 2.75$, $CHCl_3$). IR (NaCl): 3362, 3024, 2923, 1591, 1578, 1474, 1435, 1386, 1202, 1081, 922, 787, 699. ^{1}H-NMR ($CDCl_3$): 1.91 (br. *s*, NH_2); 2.91 (*dd*, $J = 9.0$, 13.6, H_a–C(2)); 3.29 (*dd*, $J = 4.9$, 13.6, H_b–C(2)); 5.02 (*dd*, $J = 4.9$, 9.0, H–C(1)); 6.45 (*d*, $J = 1.5$, H–C(4′)); 7.14–7.40 (*m*, Ph, H–C(5″)); 7.63 (*d*, $J = 1.5$, H–C(3′)); 7.79–7.86 (*m*, H–C(3″)); 7.88–7.94 (*m*, H–C(4″)); 8.45–8.49 (*m*, H–C(6″)). ^{13}C-NMR ($CDCl_3$): 43.7; 50.2; 106.5; 117.0; 121.9; 126.9; 128.8; 129.7; 139.1; 139.4; 141.1; 147.8; 150.0; 153.9. EI-MS: 264 (M^+). EI-HR-MS: 264.138220 ($C_{16}H_{16}N_4^+$, M^+; calc. 264.136159).

(1S)-2-Phenyl-1-[1-(pyrimidin-2-yl)-1H-pyrazol-5-yl]ethanamine (**22f**). From **21h** (0.200 g, 0.5 mmol) in EtOH. CC ($CHCl_3$/MeOH 10:1) gave 0.072 g (69%) of **22f**. Oil. $[\alpha]_D^{21} = -55.8$ ($c = 1.25$, $CHCl_3$). IR (NaCl): 3253, 2926, 1587, 1525, 1453, 1420, 799, 700. ^{1}H-NMR ($CDCl_3$): 2.01 (br. *s*, NH_2); 2.92 (*dd*, $J = 9.0$, 13.6, H_a–C(2)); 3.29 (*dd*, $J = 4.5$, 13.6, H_b–C(2)); 5.07 (*dd*, $J = 4.5$, 9.0, H–C(1)); 6.51 (*d*, $J = 1.5$, H–C(4′)); 7.18–7.41 (*m*, Ph, H–C(5″)); 7.73 (*d*, $J = 1.5$, H–C(3′)); 8.82 (*d*, $J = 4.9$, H–

C(4″), H–C(6″)). ^{13}C-NMR ($CDCl_3$): 43.7; 50.4; 107.6; 119.0; 127.0; 128.9; 129.7; 139.0; 142.5; 151.2; 158.4; 159.1. EI-MS: 265 (M^+), 264 ($[M-H]^+$). EI-HR-MS: 265.133070 ($C_{15}H_{15}N_5^+$, M^+; calc. 265.132746).

*(1*S*)-2-Phenyl-1-[1-(6-phenylpyridazin-3-yl)-1*H*-pyrazol-5-yl]ethanamine* (**22g**). From **21k** (0.238 g, 0.5 mmol) in THF. CC ($CHCl_3$/MeOH 20:1) and then MPLC ($CHCl_3$/MeOH 30:1) gave 0.120 g (70%) of **22g**. Oil. $[\alpha]_D^{24} = -36.9$ ($c = 1.78$, $CHCl_3$). IR (NaCl): 3360, 3061, 2924, 1535, 1464, 1453, 1431, 1396, 921, 747, 697. ^{1}H-NMR ($CDCl_3$): 2.12 (br. *s*, NH_2); 3.03 (*dd*, $J = 8.7$, 13.3, H_a–C(2)); 3.31 (*dd*, $J = 5.2$, 13.3, H_b–C(2)); 5.26 (*dd*, $J = 5.2$, 8.7, H–C(1)); 6.57 (*d*, $J = 1.8$, H–C(4′)); 7.15–7.30 (*m*, Ph); 7.49–7.59 (*m*, 3 H of Ph); 7.72 (*d*, $J = 1.8$, H–C(3′)); 7.98 (*d*, $J = 9.2$, H–C(5″)); 8.05–8.13 (*m*, 2 H of Ph); 8.18 (*d*, $J = 9.2$, H–C(4″)). ^{13}C-NMR ($CDCl_3$): 43.9; 50.3; 107.8; 121.8; 126.95; 126.96; 127.4; 128.8; 129.5; 129.9; 130.6; 136.1; 138.8; 142.4; 150.2; 156.1; 158.4. EI-MS: 341 (M^+). EI-HR-MS: 341.165120 ($C_{21}H_{19}N_5^+$, M^+; calc. 341.164046).

*(1*R*,2*R*)-1-Amino-1-(1-phenyl-1*H*-pyrazol-5-yl)propan-2-ol* (**24a**). From **23a** in EtOH. CC ($CHCl_3$/MeOH 10:1) gave 0.090 g (83%) of **24a**. Oil. $[\alpha]_D^{26} = +9.0$ ($c = 0.5$, $CHCl_3$). IR (NaCl): 3356, 1595, 1530, 1501, 1455, 1398, 1201, 1115, 1067, 1007, 928, 768. ^{1}H-NMR ($CDCl_3$): 0.99 (*d*, $J = 6.0$, Me(3)); 2.48 (*s*, OH, NH_2); 3.66 (*d*, $J = 7.9$, H–C(1)); 3.75 (*dq*, $J = 6.0$, 7.9, H–C(2)); 6.32 (*d*, $J = 1.9$, H–C(4′)); 7.39–7.52 (*m*, Ph); 7.61 (*dd*, $J = 0.5$, 1.9, H–C(3′)). ^{13}C-NMR ($CDCl_3$): 20.1; 54.0; 71.0; 104.0; 126.5; 129.0; 129.7; 139.8; 140.6; 146.1. EI-MS: 218 ($[M-H]^+$). FAB-MS: 218 ($[M-H]^+$). EI-HR-MS: 218.129900 ($C_{12}H_{16}N_3O^+$, $[M-H]^+$; calc. 218.129337).

*(1*R*,2*R*)-1-Amino-1-[1-(6-phenylpyridazin-3-yl)-1*H*-pyrazol-3-yl]propan-2-ol* (**24b**). From **23b** in EtOH/THF 3:7. CC ($CHCl_3$/MeOH 8:1) gave 0.094 g (64%) of **24b**. M.p. 113–118°. $[\alpha]_D^{26} = +2.0$ ($c = 0.5$, $CHCl_3$). IR (KBr): 3447, 1634, 1585, 1561, 1533, 1461, 1432, 1393, 1202, 1026, 937, 781, 743, 687. ^{1}H-NMR ($CDCl_3$): 1.21 (*d*, $J = 6.0$, Me(3)); 2.41 (br. *s*, OH, NH_2); 4.06 (*dq*, $J = 6.1$, 7.7, H–C(2)); 4.55 (*d*, $J = 7.7$, H–C(1)); 6.47 (*d*, $J = 1.7$, H–C(4′)); 7.49–7.61 (*m*, 3 H of Ph); 7.74 (*d*, $J = 1.7$, H–C(3′)); 8.03 (*d*, $J = 9.2$, H–C(5″)); 8.06–8.11 (*m*, 2 H of Ph); 8.26 (*d*, $J = 9.2$, H–C(4″)). ^{13}C-NMR ($CDCl_3$): 20.4; 54.6; 69.3; 107.7; 122.1; 127.2; 127.4; 129.6; 130.7; 135.9; 142.6; 148.2; 156.0; 158.6. EI-MS: 296 ($[M-H]^+$). FAB-MS: 296 ($[M-H]^+$). EI-HR-MS: 296.152001 ($C_{16}H_{18}N_5O^+$, $[M-H]^+$; calc. 296.151135).

9. *X-Ray Crystal-Structure Determination of* **15b**. A prismatic colorless crystal with dimensions $0.80 \times 0.35 \times 0.20$ mm was used for data collection at r.t. on a *Nonius-Kappa-CCD* diffractometer with graphite monochromated MoK_α radiation in the ω scan mode. The θ range was 2.55–26.02°. The data were processed with the DENZO [20] program. The number of integrated, symmetry-independent, and observed ($F^2 > 2.0\sigma F^2$) reflections were 26511, 2181, and 1589, respectively. The structure was solved by direct methods with SIR97 [21]. We employed full-matrix least-squares refinements on F magnitudes with anisotropic displacement factors for all non-H-atoms. The positions of H-atoms bonded to C(1), C(2), and N(4) were obtained from the difference *Fourier* map while the remaining were calculated. The parameters of H-atoms were not refined. In the final cycle of the refinement, we used 1949 reflections (included were those less-than reflections for which F_C was greater than F_O) and 226 parameters. The final R, R_w, and S were 0.061, 0.034, and 1.479, resp. The residual density in final difference map was max. 0.203 and min. -0.300 e/Å^3. The Xtal3.6 [22] system of crystallographic programs was used for the structure refinement and interpretation. ORTEPII [23] was used to produce molecular graphics.

CCDC-268823 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from the *Cambridge Crystallographic Data Centre via* www.ccdc.cam.ac.uk/data_request/cif.

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