Optically Active 5-(Hydroxyalkyl)- and 5-(Aminoalkyl)pyrazolidin-3-ones by Ring-Chain Transformation of α,β-Unsaturated Lactones or Lactams with Hydrazines☆

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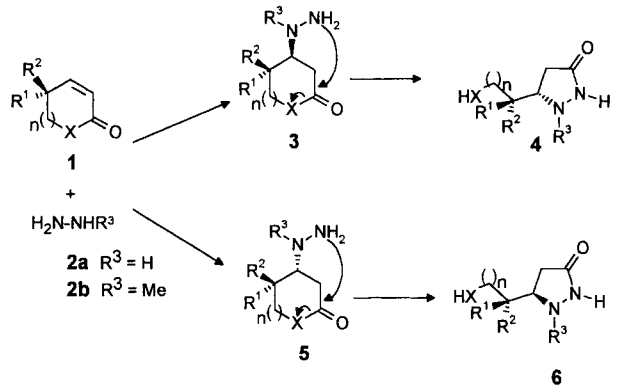
α,β-Unsaturated lactones or lactams **1** react with hydrazines **2** via Michael-like addition and subsequent ring transformation by nucleophilic attack of the hitherto unchanged hydrazine nitrogen atom at the carbonyl carbon atom. The addition is highly trans-stereoselective, thus affording optically active hydroxylalkyl- or aminoalkylpyrazolidin-3-ones **4** and **6**. These pyrazolidin-3-ones are further transformed to tosylated, acetylated or silylated derivatives **9** or react with benzaldehyde to give the azomethine imine **10**.

Chiral saturated 6-membered and 7-membered heterocycles with a lactam moiety and an aminoalkyl have attracted interest as peptidomimetics[1]. In this paper we report on efforts to synthesize structurally related compounds in the 5-membered series using a synthetic approach recently developed in our laboratory[2]. In the preliminary report the ring transformation of butenolides **1** (X = O, *n* = 0) with hydrazines **2** (R^3 = H, Me) affording novel optically active 5-(α-hydroxyalkyl)pyrazolidin-3-ones **4** (X = O, *n* = 0) was described[2]. This reaction starts with a stereoselective (*trans* attack with respect to a substituent R^1 or R^2) Michael-like addition of the hydrazines **2a**, **b** to the butenolides **1d**, **f** giving β-hydrazinolactones **3** (X = O). The latter subsequently open the original lactone ring while the pyrazolidine ring is formed by attack of the secon nucleophilic site of the hydrazine at the carbonyl carbon atom. Within this ring transformation both major fragments of the products **4**, i.e. the hydroxyalkyl substituent and the pyrazolidinone ring, are formed. Phenylhydrazine (R^3 = Ph) also adds to the butenolide **1f** but the resulting β-hydrazinobutyrolactone **7** resists further ring transformation. Very recently, extensions of the aforementioned ring transformation to 6-membered sugar lactones **8**[3,4] as well as to achiral 2-ethylpentenolide[5] with hydrazine or benzylhydrazine were reported affording 5-(β-hydroxyalkyl)pyrazolidin-3-ones in a stereoselective manner. In these cases of the 6-membered series the hydrazines enter the α,β-unsaturated lactones **8** *anti* with respect to an $AcOCH_2$ substituent at C-6 of the dihydro-2-pyrone ring regardless of the configuration at C-5 which is adjacent to the site of nucleophilic attack.

In the present paper full experimental details of our preliminary results[2] are reported as well as the extension of the ring transformation (Scheme 1) to α,β-unsaturated lactams **1a**, **b**, to the butenolide **1e**, to the bicyclic lactam **1c** and to chiral pentenolides **1g**, **h** which are not derived from sugars. Furthermore, the preparation of some derivatives of the resulting pyrazolin-3-ones **4** is included. α,β-Unsaturated lactones **1** (X = O) react with hydrazine or methylhydrazine **2** (R^3 = H, Me) to give the corresponding 5-(hydroxy-alkyl)pyrazolidin-3-ones **4c–f** or **6a** (Methods B, C). Intermediate 3-hydrazinolactones **3** or **5** (X = O) could not be isolated in pure form but some compounds **3** were detected by NMR spectroscopy as mixtures with the corresponding pyrazolidinones **4** after short reaction times ac-

Scheme 1



1	a	b	c	d	e	f	g	h
R^1	H	$CH_2OTBDMS$	Me	CH_2OH	$CH_2OTBDMS$	Me/H	H	H
R^2	H	H	O, N	H	H	H/Me	H	NBoc
X	NBoc	NBoc		O	O	O	O	O
n	0	0	0	0	0	0	1	1

[a] For substituents R of compounds **3**, **4**, and **6** see Table 1.

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Table 1. β-Hydrazinolactams **3** (X = N), β-hydrazinolactones **3** (X = O), and pyrazolidinones **4** and **6a**

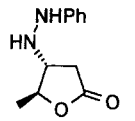
	R^1	R^2	X	*n*	R^3	Yield (%)/ method	Ratio of diastereomers	Starting material 1
3a	H	H	NBoc	0	Me	80	[a]	ref. [6]
3b	$CH_2OTBDMS$	H	NBoc	0	Me	77	>95:5	ref. [7]
3c	Me			0	Me	64	>95:5	ref. [8]
3d	Me			0	H	30	>95:5	ref. [8]
4a	H	H	NBoc	0	Me	56/A	[a]	ref. [6]
4b	$CH_2OTBDMS$	H	NBoc	0	Me	31/A	>95:5	ref. [7]
4c	CH_2OH	H	O	0	H	72/B	>95:5	[b]
4d	$CH_2OTBDMS$	H	O	0	H	26/C	>95:5	ref. [9]
4e	Me/H	H/Me	O	0	H	63/B	88:12 [a]	[b]
4f	Me/H	H/Me	O	0	Me	61/B	84:16 [a]	[b]
4g	H	H	O	1	H	81/D	[a]	[b]
6a	H	NHBoc	O	1	H	73/C	>95:5	ref. [10]

[a] Racemic mixtures. – [b] Commercially available.

cording to Method B. In contrast, the reaction of α,β-unsaturated lactams **1** (X = NR) with hydrazines **2** stopped at the stage of the adducts **3** at room temperature. The ability to undergo further ring transformation to 5-(aminoalkyl) pyrazolidin-3-ones **4** (X = NR) is affected by the nature of the substituent attached to the ring nitrogen atom. In the case of the electron-withdrawing Boc group (X = *N*–Boc) the lactams **3** could be transformed to the corresponding pyrazolidinones **4a** and **4b** by heating in aqueous methanolic NaOH (Method A). In contrast, the bicyclic lactams **3c** and **3d** lacking an electron-withdrawing substituent at the ring nitrogen atom did not undergo further ring transformation.

The stereoselectivity of the Michael-like addition of the hydrazines **2** to lactones or lactams **1** is generally high. Unless X is an oxygen atom and R^1 and R^2 are Me or H, respectively (i.e. formation of **4e** and **4f**) only one stereoisomer could be detected by NMR spectroscopy. It is worth mentioning that the reaction of 6-membered pentenolide **1h** (R^2 = NHBoc) with **2a** proceeded with complete stereoselectivity to afford **6a**. Whereas in the known reaction[3,4] of the sugar lactones **8** the substituent ($AcOCH_2$) governs the stereoselectivity (*anti* attack), the stereochemical outcome of the aforementioned reaction of the 5-unsubstituted pentenolides **1h** is efficiently directed by the substituent R^2 at C-4 effecting also *trans* addition. Hence there is no difference in stereocontrol in reactions of pentenolides **1h** (X = O, *n* = 1) on the one hand and 5-membered butenolides **1d**–**f** (X = O, *n* = 0) on the other hand.

The hydrazinolactams and lactones **3** and pyrazolidin-3-ones **4** and **6** are colorless oils or resins. Due to their high hygroscopy it was difficult to isolate pure compounds in some cases. The constitution and the configuration of products **3**, **4** and **6** could be determined by spectroscopic data (see Experimental). In contrast to the adducts **3** ring transformation products **4** and **6** exhibit an amide-NH ^{1}H-NMR signal at δ = 8–9 and two ^{15}N-NMR signals at δ ≈ 80 and 140. The regioselectivity of the reaction of methylhydrazine **2b**, i.e. the primary nucleophilic attack of the MeNH group rather than of the NH_2 group, was proved by showing the proximity of the methyl group and the substituent R^1 in the case of the ring transformation product **4d** (R^1 = $CH_2OTBDMS$) by NOE difference NMR techniques. Furthermore, X-ray crystal analysis[2] of the tosylated pyrazolidinone **9a** revealed the constitution and configuration of the ring transformation product **4e**, thus proving the *anti* addition of the hydrazines **2** to lactones **1**. This fact is in line with the stereoselectivity of known additions of simple amines to butenolides[11,12].



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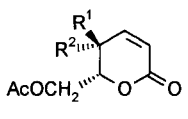

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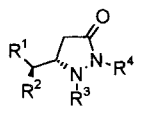

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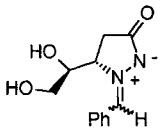

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9	**a**	**b**	**c**	**d**
R^1	OH	OAc	OTBDMS	OTBDMS
R^2	Me	Me	Me	$CH_2OTBDMS$
R^3	Tos	Me	Me	H
R^4	H	Ac	H	H

In order to obtain less hygroscopic compounds which were easier to purify some 5-(α-hydroxyalkyl)pyrazolidinones (X = O, *n* = 0), i.e. **4c**, **4e** and **4f** were transformed to derivatives such as the *N*-tosylate **9a**, the diacetyl derivative **9b** and silyl ethers **9c** and **9d**. We further approached the synthesis of chiral azomethinimines by reaction of the pyrazolidinones **4** with aldehydes or ketones. Benzaldehyde gave a clean reaction with the pyrazolidinone **4c** to afford the corresponding betaine **10** as a diastereomeric mixture (66:34) of unknown *E*/*Z* geometry. Other aldehydes or ketones reacted very sluggishly giving only traces of the expected products sometimes as mixtures with the corresponding isomeric pyrazolidino[3,4-*b*]oxazolidines. Although azomethinimines derived from simple achiral pyrazolidinones and aldehydes or ketones are known to undergo smooth 1,3-dipolar cycloadditions[13], the reaction of betaine **10** with dihydrofuran or styrene gave only traces of cycloadducts even at high pressure (10 kbar, **10** was mainly recovered).

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Experimental

NMR spectra were recorded in [D_6]DMSO with a Bruker AC 300. In the case of diastereomeric mixtures the spectral data refer to the major diastereomer. – Mass spectra (70 eV) were recorded with HP 5995 A (Hewlett-Packard). – Melting points were determined with a Boëtius hot-stage apparatus and are uncorrected. – Optical rotations were measured with a Perkin-Elmer 241 polarimeter by using a 1-ml cell. – Silica gel 60 from Merck was used for column chromatography. – No satisfactory microanalyses could be

obtained from **3c**, **3d**, **4b**, **4c**, **4e**, **4f**, **4g**, and **6a** because the compounds contained traces of water which could not be removed from these hygroscopic materials. Some of these compounds were converted to less polar derivatives **9** of analytical purity.

General Procedure for the Preparation of the Hydrazinolactams **3** (X = NR): 2.5 mmol of hydrazine hydrate (80% aqueous solution) was added dropwise to a solution of 2.5 mmol of unsaturated lactam **1** (X = N) in water/methanol (1:3, 6 ml). After stirring for 3 h at room temperature the solvent was evaporated under vacuum and the remainder was purified by column chromatography on silica gel (**3a**, **3d**: $CHCl_3$/MeOH, 60:40; **3b**: $CHCl_3$/MeOH, 85:15; **3c**: *n*-hexane/AcOEt, 1:1).

1-(tert-Butoxycarbonyl)-4-(1-methylhydrazino)pyrrolidin-2-one (**3a**, racemic mixture): Oil. – ^{1}H NMR: δ = 1.45 (s, 9H, *t*-Bu), 2.47 (s, 3H, NCH_3), 2.56 (d, 2H, *J* = 8 Hz, CH_2CO), 2.89 (br, 2H, NH_2), 3.03 (m, 1H, CHN), 3.64 (dd, 1H, *J* = 11, 6 Hz, CH_2NCO), 3.85 (dd, 1H, *J* = 11, 8 Hz, CH_2NCO). – ^{13}C NMR: δ = 28.0 [$(CH_3)_3C$], 37.4 (CH_2CO), 48.3 (CH_3N), 50.0 (CH_2NCO), 59.1 (CHN), 82.9 [$(CH_3)_3C$], 149.9 (CO_{Boc}), 172.6 (CO). – MS, *m/z* (%): 172 (M^+ – 57, 8), 99 (100), 57 (36). – $C_{10}H_{19}N_3O_3$ (229.3): Calcd. C 52.39, H 8.35, N 18.32; found C 52.71, H 7.93, N 17.86.

(4S,5S)-1-(tert-Butoxycarbonyl)-5-(tert-butyldimethylsilyloxymethyl)4-(1-methylhydrazino)pyrrolidin-2-one (**3b**): Oil. – ^{1}H NMR: δ = 0.00 (s, 3H, CH_3Si), 0.02 (s, 3H, CH_3Si), 0.84 [s, 9H, $(CH_3)_3CSi$], 1.51 [s, 9H, $(CH_3)_3CO$], 2.49 (s, 3H, CH_3N), 2.50 (dd, 1H, *J* = 18, 1.5 Hz, CH_2CO), 2.71 (dd, 1H, *J* = 18, 8 Hz, CH_2CO), 3.08 (m, 1H, C*H*NCH_3), 3.70 (dd, 1H, *J* = 10.5, 2 Hz, CH_2O), 3.91 (dd, 1H, *J* = 10.5, 4 Hz, CH_2O), 4.24 (m, 1H, CHNCO). – ^{13}C NMR: δ = –5.6 (CH_3Si), –5.5 (CH_3Si), 18.1 [$(CH_3)_3CSi$], 25.8 [$(CH_3)_3CSi$], 28.1 [$(CH_3)_3CO$], 36.1 (CH_2CO), 47.1 (NCH_3), 61.5 (*C*HNCH_3), 61.7 (*C*HNCO), 63.5 (CH_2O), 82.7 [$(CH_3)_3CO$], 150.0 (CO_{Boc}), 173.8 (CO). – MS, *m/z* (%): 316 (M^+ – 57, 11), 99 (24), 57 (100). – $[\alpha]_{546}^{20}$ = –37.3 (*c* = 2.2, MeOH). – $C_{17}H_{35}N_3O_4Si$ (373.6): Calcd. C 54.64, H 9.46, N 11.25; found C 54.58, H 9.46, N 11.46.

(3R,7S,7aS)-3-Ethyl-7-(1-methylhydrazino)hexahydropyrrolo-[1,2-a]oxazol-5-one (**3c**): Oil. – ^{1}H NMR: δ = 0.84 (t, 3H, *J* = 7 Hz, CH_3CH_2), 1.41 (s, 3H, CH_3), 1.62 (m, 2H, CH_3CH_2), 2.43 (dd, 1H, *J* = 17, 1 Hz, CH_2CO), 2.63 (s, 3H, NCH_3), 2.81 (dd, 1H, *J* = 17, 8 Hz, CH_2CO), 3.21 (m, 1H, C*H*NCH_3), 3.84 (m, 2H, CH_2O, CHN), 4.33 (dd, 1H, *J* = 8, 7 Hz, CH_2O). – ^{13}C NMR: δ = 10.7 (*C*H_3CH_2), 26.4 (CH_3), 28.3 (CH_3CH_2), 38.7 (CH_2CO), 47.5 (NCH_3), 55.1 (*C*HNCH_3), 69.2 (CHN), 72.6 (CH_2O), 102.0 (OCN), 176.5 (CO). – MS, *m/z* (%): 213 (M^+, 1), 114 (100), 84 (48), 72 (46). – $[\alpha]_{546}^{20}$ = +28.2 (*c* = 1.2, MeOH).

(3R,7S,7aS)-3-Ethyl-7-hydrazino-hexahydropyrrolo[1,2-a]oxazol-5-one (**3d**): Oil. – ^{1}H NMR: δ = 0.89 (t, 3H, *J* = 7 Hz, CH_3CH_2), 1.43 (s, 3H, CH_3), 1.56 (m, 2H, CH_3CH_2), 2.26 (d, 1H, *J* = 17 Hz, CH_2CO), 2.82 (dd, 1H, *J* = 17, 6 Hz, CH_2CO), 3.21 (m, 4H, NH, NH_2, C*H*NCH_3), 3.82 (dd, 1H, *J* = 8, 4 Hz, CH_2O), 3.92 (m, 1H, CHN), 4.12 (dd, 1H, *J* = 8, 7 Hz, CH_2O). – ^{13}C NMR: δ = 10.7 (*C*H_3CH_2), 25.8 (CH_3), 27.6 (CH_3CH_2), 39.1 (*C*H_2CO), 55.9 (*C*HNH), 67.2 (CHN), 73.2 (CH_2O), 100.3 (OCN), 176.0 (CO).

General Procedures for the Preparation of Pyrazolidinones **4** *and* **6a**. – *Method A:* 0.7 ml of 0.25 M aqueous NaOH (0.175 mmol) was added dropwise to a solution of the hydrazinolactam **3** (1 mmol) in 6 ml of MeOH. After heating at reflux for 12 h the solvent was removed. The remaining product was purified by column chromatography on silica gel (**4a**: $CHCl_3$/MeOH, 60:40, **4b**: *n*-hexane/AcOEt/EtOH, 45:45:10.

Method B: 5 mmol of hydrazine hydrate (0.313 g of 80% aqueous solution) was added to a solution of 5 mmol of α,β-unsaturated lactone **1** in 5 ml of water (**4c**, **4e**, **4f**) or 5 ml of water/MeOH (1:1) (**4d**, **6a**). After heating at 80°C (**4c**, **4e**: 15 min, **4f**: 40 min, **4d**, **6a**: 45 min) the solvent was removed and the remainder was purified by column chromatography on silica gel (**4c**, **4e**: $CHCl_3$/MeOH, 60:40, **4d**: $CHCl_3$/MeOH, 96:4, **4f**: $CHCl_3$/MeOH, 80:20, **6a**: $CHCl_3$/MeOH, 90:10).

Method C: 5 mmol of hydrazine hydrate (0.313 g of 80% aqueous solution) was added to a solution of 5 mmol of α,β-unsaturated lactone **1** in 5 ml of water. After stirring at room temperature for 2 h the solvent was removed and the product was subjected to column chromatography at silica gel ($CHCl_3$/MeOH, 60:40).

rac-5-[(tert-Butoxycarbonyl)aminomethyl]-1-methylpyrazolidin-3-one (**4a**): Oil. – ^{1}H NMR: δ = 1.38 [s, 9H, $(CH_3)_3C$], 2.07 (dd, 1H, *J* = 17, 4, CH_2CO), 2.56 (s, 3H, NCH_3), 3.22 (dd, 1H, *J* = 17, 8, CH_2CO), 3.07–3.13 (m, 3H, CH_2NH, C*H*NCH_3), 5.82 (br, 1H, NH_{Boc}), 8.88 (br, 1H, NHCO). – ^{13}C NMR: δ = 28.3 [$(CH_3)_3C$], 32.4 (CH_2CO), 42.5 (CH_2NH), 47.0 (NCH_3), 64.2 (CHN), 79.5 [$(CH_3)_3C$], 156.1 (CO_{Boc}), 173.6 (CO). – MS, *m/z* (%): 172 (M^+ – 57, 1), 99 (27), 57 (100), 46 (43). – $C_{10}H_{19}N_3O_3$ (229.3): Calcd. C 52.39, H 8.35, N 18.32, found C 51.86, H 8.65, N 17.75.

(5S,αS)-5-[1-(tert-Butoxycarbonylamino)-2-(tert-butyldimethylsilyloxy)ethyl]-1-methylpyrazolidin-3-one (**4b**): Oil. – ^{1}H NMR: δ = –0.01 (s, 3H, CH_3Si), 0.00 (s, 3H, CH_3Si), 0.83 [s, 9H, $(CH_3)_3CSi$], 1.38 (s, 9H, $(CH_3)_3CO$], 2.31 (dd, 1H, *J* = 16, 7 Hz, CH_2CO), 2.55 (s, 3H, NCH_3), 2.81 (dd, 1H, *J* = 16, 9 Hz, CH_2CO), 3.23 (m, 1H, C*H*NCH_3), 3.54 (d, 2H, *J* = 7 Hz, CH_2O), 3.64 (m, 1H, CHNCO), 3.89 (d, 1H, *J* = 7 Hz, CH_2O), 4.75 (d, 1H, *J* = 9 Hz, NH_{Boc}), 7.84 (br, 1H, NHCO). – ^{13}C NMR: δ = –5.5 (2 CH_3Si), 18.2 ($C_{qu}Si$), 25.8 [$(CH_3)_3CSi$], 28.3 [$(CH_3)_3CO$], 33.0 (CH_2CO), 47.6 (NCH_3), 61.9 (CHN), 62.3 (CHN), 81.5 ($C_{qu}O$), 155.8 (CO_{Boc}), 173.9 (CO). – $[\alpha]_{546}^{20}$ = +12.2 (*c* = 1.7, MeOH).

(5S,αS)-5-(1,2-Dihydroxyethyl)pyrazolidin-3-one (**4c**): Oil. – ^{1}H NMR: δ = 2.19 (dd, 1H, *J* = 16, 7 Hz, CH_2CO), 2.32 (dd, 1H, *J* = 16, 7 Hz, CH_2CO), 3.36 (m, 4H, CHN, CHO, CH_2O), 4.59 (br, 1H, OH), 4.90 (br, 1H, OH), 8.94 (br, 1H, NHCO). – ^{13}C NMR: δ = 32.8 (CH_2CO), 58.8 (CHN), 62.8 (CH_2O), 70.6 (CHO), 175.6 (CO). – MS, *m/z* (%): 146 (M^+, 3), 85 (100), 57 (39), 43 (33). – $[\alpha]_{546}^{20}$ = +4.9 (*c* = 1, H_2O).

(5S,αS)-5-(2-tert-Butyldimethylsilyloxy-1-hydroxyethyl)pyrazolidin-3-one (**4d**): M.p. 118–120°C. – ^{1}H NMR (CD_3OD): δ = 0.08 (s, 6H, CH_3Si), 0.91 [s, 9H, $(CH_3)_3CSi$], 2.42 (dd, 1H, *J* = 16, 8 Hz, CH_2CO), 2.61 (dd, 1H, *J* = 16, 7 Hz, CH_2CO), 3.65 (m, 4H, CH_2O, CHO, CHN). – ^{13}C NMR (CD_3OD): δ = –5.3 (CH_3Si), 19.2 [$(CH_3)_3C$], 26.4 [$(CH_3)C$], 33.4 (CH_2CO), 60.1 (CHN), 66.2 (CH_2O), 71.9 (CHO), 178.5 (CO). – MS, *m/z* (%): 260 (M^+, 5), 203 (64), 85 (100), 75 (93). – $[\alpha]_{546}^{20}$ = –0.55 (*c* = 0.9, $CHCl_3$). – $C_{11}H_{24}N_2O_3Si$ (260.5): Calcd. C 50.72, H 9.31, N 10.76; found C 50.38, H 9.11, N 10.68.

(5R,αS)- and (5S,αR)-5-(1-Hydroxyethyl)pyrazolidin-3-one (**4e**, racemate of the major diastereomer): Oil. – ^{1}H NMR: δ = 1.03 (d, 3H, *J* = 6 Hz, CH_3), 2.21 (dd, 1H, *J* = 16, 7 Hz, CH_2CO), 2.30 (dd, 1H, *J* = 16, 7 Hz, CH_2CO), 3.20 (q, 1H, *J* = 7 Hz, CHN), 3.51 (quint, 1H, *J* = 6 Hz, CHO), 8.91 (br, 1H, NHCO). – ^{13}C NMR: δ = 20.8 (CH_3), 33.2 (CH_2CO), 63.0 (CHN), 66.0 (CHO), 175.6 (CO). – ^{15}N NMR: δ = 78.9 (NHCH), 140.0 (NHCO). – MS, *m/z* (%): 130 (M^+ + 1, 23), 85 (100), 57 (83), 42 (56).

(5R,αS)- and (5S,αR)-5-(1-Hydroxyethyl)-1-methylpyrazolidin-3-one (**4f**, racemate of the major diastereomer): Oil. – ^{1}H NMR: δ = 1.11 (d, 3H, *J* = 6 Hz, CH_3), 2.61 (s, 3H, NCH_3), 2.58 (m, 2H, CH_2CO), 2.95 (m, 1H, CHN), 3.90 (m, 1H, CHO), 8.75 (br, 1H, NHCO). – ^{13}C NMR: δ = 20.3 (CH_3), 30.5 (CH_2CO), 47.3 (NCH_3), 66.2 (CHN), 70.0 (CHO), 172.3 (CO). – MS, *m/z* (%): 144 (M^+, 8), 99 (90), 72 (93), 56 (100), 42 (67).

rac-5-(2-Hydroxyethyl)pyrazolidin-3-one (**4g**): Oil. – ^{1}H NMR: δ = 1.55 (m, 2H, CH_2CH_2CH), 1.95 (dd, 1H, *J* = 16, 8 Hz, CH_2O), 2.33 (dd, 1H, *J* = 16, 7 Hz, CH_2CO), 3.50 (m, 3H, CH_2OH, CHNH), 8.93 (br, 1H, NHCO). – ^{13}C NMR: δ = 36.1 (CH_2), 38.0 (CH_2), 55.1 (CHNH), 58.1 (CH_2OH), 176.1 (CO). – MS; *m/z* (%): 130 (M^+, 15), 85 (100), 57 (58), 41 (60).

(5R,αS)-5-[1-(tert-Butoxycarbonylamino)-2-hydroxyethyl]-1-methylpyrazolidin-3-one (**6a**): m.p. 44–48 °C. – ^{1}H NMR (CD_3OD): δ = 1.44 [s, 9H, $(CH_3)_3C$], 2.38 (dd, 1H, *J* = 17, 7 Hz, CH_2CO), 2.63 (dd, 1H, *J* = 17, 8 Hz, CH_2CO), 3.50–3.80 (m, 4H, CH_2OH, CHN, CHN_{Boc}), 7.90 (s, 1H, NHCO). – ^{13}C NMR (CD_3OD): δ = 28.7 [$(CH_3)_3C$], 35.8 (CH_2CO), 56.1 (CHN), 58.6 (CHN), 62.8 (CH_2O), 80.5 ($C_{qu}O$), 158.5 (CO_{Boc}), 178.1 (CO). – $[\alpha]_{546}^{20}$ = –24.9 (*c* = 0.75, $CHCl_3$).

(4R,5S)- and (4S,5R)-4-Methyl-3-(2-phenylhydrazino)-tetrahydrofuran-2-one (**7**, racemic mixture): 0.54 g (5 mmol) of phenylhydrazine was added to a solution of 0.49 g (5 mmol) of β-angelica lactone in 2 ml of water. The mixture was stirred and heated at 80 °C for 10 min. After evaporation of water under vacuum the remainder was extracted three times with 10 ml of Et_2O. The product **7** slowly crystallized from the mother liquor as a yellowish solid, which was filtered off and dried under vacuum. Yield: 0.155 g (15%), m.p. 112–114 °C, d.e. >90%. – ^{1}H NMR: δ = 1.25 (d, 3H, *J* = 7 Hz, CH_3), 2.30 (dd, 1H, *J* = 18, 3 Hz, CH_2CO), 2.82 (dd, 1H, *J* = 18, 7 Hz, CH_2CO), 3.37 (m, 1H, CHN), 4.45 (qd, 1H, *J* = 7, 2 Hz, CHO), 4.82 (br, 1H, NH), 6.90 (m, 5H, Ph), 7.62 (br, 1H, NHPh). – ^{13}C NMR: δ = 19.0 (CH_3), 32.6 (CH_2CO), 60.9 (CHN), 79.6 (CHO), 111.8 (CH_{arom}), 117.2 (CH_{arom}), 128.7 (CH_{arom}), 150.5 (C_{arom}), 176.1 (CO). – MS, *m/z* (%): 206 (M^+, 26), 161 (86), 77 (100). – $C_{11}H_{14}N_2O_2$ (206.3): calcd. C 64.05, H 6.86, N 13.58; found C 64.26, H 6.92, N 13.78.

(5R,αS)- and (5S,αR)-5-(1-Hydroxyethyl)-1-tosylpyrazolidin-3-one (**9a**, racemic mixture): A mixture of 0.800 g (5 mmol) of 1-substituted pyrazolidin-3-one **4e** and about 20 mg of 4-dimethylaminopyridine was stirred under argon at –15 °C. 0.95 g (5 mmol) of TsCl was added in portions. After the color of the mixture had turned red stirring and cooling were continued for 2 h. After the mixture had been allowed to warm to room temperature it was poured onto ice. The product gradually crystallized. It was filtered by suction and recrystallized from *i*-PrOH. Yield: 1.066 g (75%), m.p. 206–208 °C. – ^{1}H NMR (CD_3OD): δ = 1.11 (d, 3H, *J* = 6 Hz, CH_3), 1.22 (dd, 1H, *J* = 17, 9 Hz, CH_2CO), 1.99 (d, 1H, *J* = 17 Hz, CH_2CO), 2.42 (s, 3H, $PhCH_3$), 3.54 (m, 1H, CHO), 3.78 (t, 1H, *J* = 7 Hz, CHN), 5.07 (d, 1H, OH), 7.48 (d, 2H, *J* = 8 Hz, CH_{arom}), 7.74 (d, 2H, *J* = 8 Hz, CH_{arom}), 10.73 (s, 1H, NH). – ^{13}C NMR (CD_3OD): δ = 20.1 (CH_3), 21.2 (CH_3), 29.7 (CH_2CO), 64.7 (CHN), 67.1 (CHO), 129.0 (CH_{arom}), 130.2 (CH_{arom}), 130.2 (C_{arom}), 145.4 (C_{arom}), 174.3 (CO). – $C_{12}H_{16}N_2O_4S$ (284.4): calcd. C 50.68, H 5.68, N 9.85, S 11.27; found C 50.00, H 5.88, N 10.49, S 11.30.

(5R,αS)- and (5S,αR)-5-(1-Acetoxyethyl)-2-acetyl-1-methylpyrazolidin-3-one (**9b**, racemic mixture): 2.0 g (20 mmol) of acetic anhydride was added dropwise to a solution of 0.286 g (2 mmol) of pyrazolidin-3-one **4f** (diastereomeric mixture 84:16) in 2 ml of dry pyridine under ice cooling. After the mixture had been stirred for 5 h at room temperature it was poured into 10 ml of water. After extraction with 3 portions of 10 ml of CH_2Cl_2 the combined organic layer were dried with Na_2SO_4 and the solvent was evaporated under vacuum. The remainder was purified by chromatography on silica gel (AcOEt/*n*-hexane 1:1). Yield: 0.269 g (59%), m.p. 60–63 °C. – ^{1}H NMR ($CDCl_3$): δ = 1.20 (d, 3H, *J* = 6, CH_3), 1.94 [s, 3H, $CH_3C(O)O$], 2.38 [s, 3H, $CH_3C(O)N$], 2.49 (d, 1H, *J* = 16 Hz, CH_2CO), 2.72 (s, 3H, CH_3N), 3.08 (m, 2H, CH_2CO, CHN), 4.83 (m, 1H, CHO). – ^{13}C NMR ($CDCl_3$): δ = 16.6 (CH_3), 21.0 [$CH_3C(O)O$], 24.4 [$CH_3C(O)O$], 32.0 (CH_2CO), 45.6 (CH_3N), 63.9 (CHN), 71.7 (CHO), 166.4 (CO), 170.0 (CO), 172.4 (CO). – MS, *m/z* (%): 228 (M^+, 0.2), 186 (11), 89 (100). – $C_{10}H_{16}N_2O_4$ (228.3): calcd. C 52.61, H 7.08, N 12.27; found C 52.51, H 7.12, N 12.16.

(5R,αS)- and (5S,αR)-5-(1-tert-Butyldimethylsilyloxyethyl)-1-methylpyrazolidin-3-one (**9c**, racemic mixture): A solution of 0.432 g (3 mmol) of pyrazolidin-3-one **4f** (diastereomeric mixture 84:16), 0.542 g (3.6 mmol) of TBDMSCl and 0.51 g (7.5 mmol) of imidazole in 10 ml of dry DMF was stirred at room temperature until all **4f** had disappeared (TLC, about 4 d). The solvent was removed under vacuum and the remainder was purified by column chromatography on silica gel ($CHCl_3$/MeOH, 96:4). Yield: 0.325 g (42%), m.p. 60–66 °C. – ^{1}H NMR ($CDCl_3$): δ = 0.05 [s, 6H, $Si(CH_3)_2$], 0.86 (s, 9H, *t*Bu), 1.14 (d, 3H, *J* = 6 Hz, CH_3), 2.44 (dd, 1H, *J* = 16, 4 Hz, CH_2CO), 2.59 (s, 3H, CH_3N), 2.75 (dd, 1H, 16, 9 Hz, CH_2CO), 2.78 (m, 1H, CHN), 3.76 (quint, 1H, *J* = 6 Hz, CHO), 8.81 (br. s, 1H, NH). – ^{13}C NMR ($CDCl_3$): δ = –4.9 (CH_3Si), –4.6 (CH_3Si), 17.8 [$(CH_3)_3C$], 20.6 (CH_3), 25.6 [$(CH_3)_3C$], 30.6 (CH_2CO), 47.5 (CH_3N), 68.8 (CHN), 70.7 (CHO), 173.5 (CO). – $C_{12}H_{26}N_2O_2Si$ (258.5): calcd. C 55.75, H 10.16, N 10.84; found C 55.28, H 10.45, N 10.65.

(5S,αS)-5-[1,2-Bis(tert-butyldimethylsilyloxy)ethyl]pyrazolidin-3-one (**9d**): A solution of 0.146 g (1 mmol) of pyrazolidin-3-one **4c**, 0.768 g (5.1 mmol) of TBDMSCl, and 0.694 g (10.2 mmol) of imidazole in 4 ml of dry DMF was treated according to the procedure for the synthesis of **9c**. Yield: 0.359 g (96%), m.p. 115–120 °C. – ^{1}H NMR ($CDCl_3$): δ = 0.00 [s, 12H, $Si(CH_3)_2$], 0.82 (s, 18H, *t*-Bu), 2.77 (d, 2H, *J* = 7 Hz, CH_2CO), 3.41 (dd, 1H, *J* = 10, 8 Hz, CH_2O), 3.54 (dd, 1H, *J* = 10, 4 Hz, CH_2O), 3.80 (m, 1H, CHN), 4.53 (m, 1H, CHO), 8.45 (br s, 1H, NH). – ^{13}C NMR ($CDCl_3$): δ = –5.6, –5.1, –4.6, –3.6 ($SiCH_3$), 17.8, 18.2 [$(CH_3)_3C$], 25.6, 25.8 [$(CH_3)_3C$], 30.8 (CH_2CO), 57.2 (CHN), 63.4 (CH_2O), 74.6 (CHO), 169.3 (CO). – $[\alpha]_{546}^{20}$ = –76.0 (*c* = 1, $CHCl_3$). – $C_{17}H_{38}N_2O_3Si_2$ (374.8): calcd. C 54.48, H 10.24; found C 54.02, H 10.21.

(5S,αS)-1-Benzylidene-5-(1,2-dihydroxyethyl)pyrazolidin-3-one Ylide (**10**): 0.293 g (2 mmol) of pyrazolidin-3-one **4c** was dissolved in 2 ml of water by applying ultrasound. After the addition of 20 ml of benzene, 0.212 g (2 mmol) of benzaldehyde (freshly distilled) and about 30 mg of TsOH, the mixture was vigorously stirred and refluxed in a water separator for 2 h. After evaporation of the solvent under vacuum the remaining oil was crystallized by the addition of a few drops of methanol and scratching. The solid was filtered off by suction and recrystallized from dry MeOH (keeping in a refrigerator). Yield: 0.299 g (64%), m.p. 203–205 °C. – ^{1}H NMR: δ = 2.51 (m, 2H, CH_2CO), 3.32 (dd, 1H, *J* = 11, 7 Hz, CH_2OH), 3.42 (dd, 1H, *J* = 11, 7 Hz, CH_2OH), 4.12 (m, 1H, CHN), 4.83 (t, 1H, *J* = 7 Hz, CHO), 4.96 (t, 1H, *J* = 6 Hz, OH), 5.36 (d, 1H, *J* = 7 Hz, OH), 7.50 (m, 3H, CH_{arom}), 7.70 (s, 1H, $CH{=}N^+$), 8.31 (m, 2H, CH_{arom}). – ^{13}C NMR: δ = 29.2 (CH_2CO), 62.7 (CH_2OH), 71.7 (CH), 72.4 (CH), 128.6 (CH_{arom}), 130.3

(C_{arom}), 130.7 (CH=N^+), 130.9 (CH_{arom}), 131.1 (CH_{arom}), 183.6 (CO). – MS, *m/z* (%): 234 (M^+, 14), 128 (13), 107 (100), 91 (24), 43 (51). – $[\alpha]_{546}^{20} = -307.0$ (*c* = 1, CH_3OH). – $C_{12}H_{14}N_2O_3$ (234.3): calcd. C 61.52, H 6.04, N 11.96; found C 61.29, H 5.95, N 12.54.

☆ Dedicated to Professor Dr. *Siegfried Hünig* on the occasion of his 75th birthday.

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