Pergamon

Tetrahedron, Vol. 53, No. 30, pp. 10603-10614, 1997

0040-4020/97 $17.00 + 0.00

PII: S0040-4020(97)00671-6

Ruthenium-Catalyzed Enyne Metathesis in Stereoselective Preparation of Cyclic 1-Amino-1-Carboxylic Acids.

Kristin Hammer and Kjell Undheim*

Department of Chemistry, University of Oslo, N-0315 Oslo, Norway.

Abstract: Stereoselective syntheses of α-amino acids are described. The α-carbon of the amino acid is incorporated into a five- or six-membered ring which is a conjugated diene with one exocyclic double bond. Enynes were intermediates for the metathesis cyclization reaction effected by ruthenium(II)-catalysis. The enyne substrates were available in stereochemically pure form by stepwise alkylations of the chiral auxiliary (*R*)-2,5-dihydro-3,6-dimethoxy-2-isopropylpyrazine with bromo-alkenes and -alkynes.
© 1997 Elsevier Science Ltd.

Rigidified α-carbosubstituted α-amino acids play an important role in drug design and development involving small peptides and peptidomimetics.[1] We have recently described stereoselective syntheses of rigidified α-amino acids where the α-carbon of the amino acid was incorporated into an unsaturated five-, six- or seven-membered carbocycle (Fig. 1; **A**, R = H),[2] and most recently the stereoselective preparation of β-hydroxy derivatives which can be regarded as rigidified analogues of serine or threonine (Fig. 1; **A**, R = OH).[3] The cyclic amino acids were isolated as pure stereoisomers. The cyclic amino acids **A** are functionalized by an endocyclic double bond (Fig. 1). The target molecules of the present work were to be conjugated diene homologues having an exocyclic double bond with general structure **B** (Fig. 1).

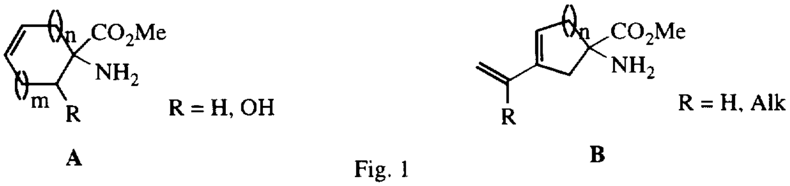
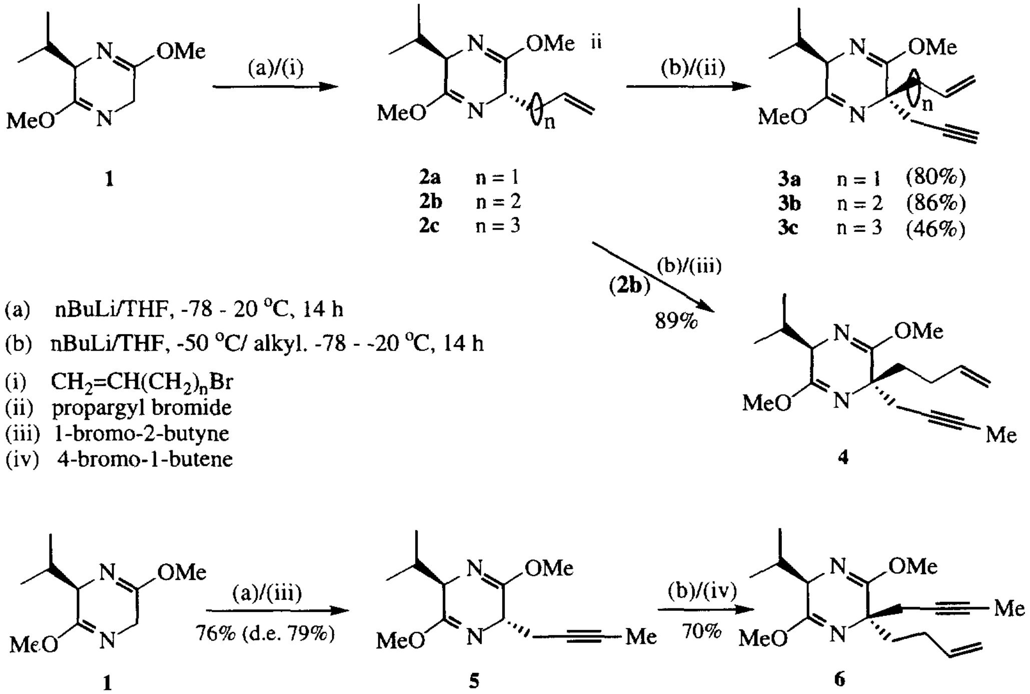


Fig. 1

The key step in our previous preparation of the cycloalkenyl derivatives **A** was a ring closing metathesis (RCM) reaction effected on bisalkenyl substrates with predetermined stereochemistry. Bis(tricyclohexylphosphine)benzylidene ruthenium dichloride was the catalyst system used.[4] The target structures **B** (Fig. 1) were expected to become available by enyne metathesis.

Several recent reports describe metal-catalyzed formation of 1-vinylcycloalkenes from enyne substrates by intramolecular reactions, in particular the five-membered ring compound. Catalytic systems include a tungsten carbene complex,[5] a Fischer chromium carbene complex in stoichiometric reactions,[6] palladium and platinum systems,[7] the ruthenium system $[RuCl_2(CO)_3 \cdot [CO]$,[8] and bis(tricyclohexylphosphine)alkylidene ruthenium dichloride systems.[9] The latter have been successfully applied for the formation of azaheterocycles,[9] and for ring-closing metathesis of dienynes leading to fused bicyclic ring structures.[10] In this report we describe the use of the bis(tricyclohexylphosphine)benzylidene ruthenium dichloride catalyst system in metathesis rearrangement of enynes to precursors for the cyclic amino acids **B** (Fig. 1). The choice of the Ru(II)-catalyst was based on our experience with the Ru(II)-catalyst in RCM reactions furnishing the cycloalkenes **A** (Fig. 1). This catalyst also appears to be highly versatile for intramolecular metathesis reactions of enynes. Mechanistically these reactions differ. In the RCM reactions of bisalkenes the terminal methylenes are expelled as ethylene during the ring closure. In the enyne reactions the terminal alkylidene moiety of the alkene is transferred onto the alkyne carbon in the formation of the cyclic diene (Scheme 4).[9]



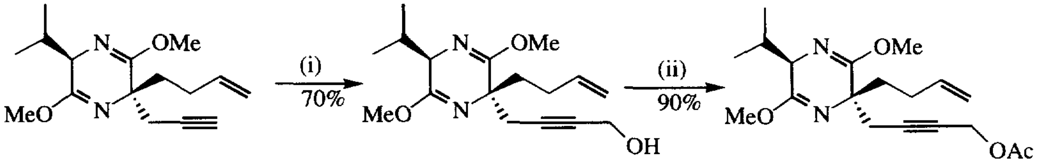
(a) nBuLi/THF, -78 - 20 °C, 14 h
(b) nBuLi/THF, -50 °C/ alkyl. -78 - -20 °C, 14 h
(i) $CH_2=CH(CH_2)_nBr$
(ii) propargyl bromide
(iii) 1-bromo-2-butyne
(iv) 4-bromo-1-butene

Scheme 1

The enyne substrates for the RCM reactions were prepared in a stereoselective manner by alkylation reactions of the Schöllkopf chiral auxiliary, the bislactim ether **1**.[11] The alkylating agent was either an alkenyl or an alkynyl halide. The diastereomeric excess (d.e.) in the first alkylation step was variable.[1] The stereochemical yield in this step, however, is of little importance in this context since the stereochemistry at C-5 in the initial products **2** or **5** is lost when the monoalkylated species are metalated again for the second alkylation. The d.e. in the second alkylation was invariably very high using propargyl bromide for the formation of the enyne **3**. This parallels previous findings in dialkylation with ω-bromo-1-alkenes.[2] Only the isomer with the propargyl group in a *trans*-relationship to the isopropyl group was seen (GLC, TLC, NMR). The pentenyl derivative **2c** was formed in significantly lower yield (46%) than the lower alkenyl derivatives **2a** and **2b** which we attribute to higher steric interference in **2c**. When the rate of alkylation is decreased, competitive metal-hydrogen exchange between the lithiated bislactim ether **2** and acetylenic hydrogen in the propargyl reagent becomes more important.

When the alkenylation-alkynylation sequence of the bislactiom ether is changed, the enynes formed have the opposite stereochemistry at C-5 allowing for the synthesis of enantiomeric target compounds without changing the configuration of the chiral auxiliary used in the reaction.

For the subsequent study of substituent effects on the metathesis reaction, a methyl group was introduced indirectly on the acetylenic carbon by using 1-bromo-2-butyne for the alkynylation of **2b**, the product being the enyne **4**. Its isomer **6** with the opposite strereochemistry at C-5, was available by initial alkynylation of the bislactim ether **1** with 1-bromo-2-butyne to give intermediate **5** in high yield, but the d.e. was low (79%). The stereochemistry at C-5, however, is lost on lithiation. After the subsequent alkylation with 4-bromo-1-butene only the stereoisomer **6** was obtained (70% yield).

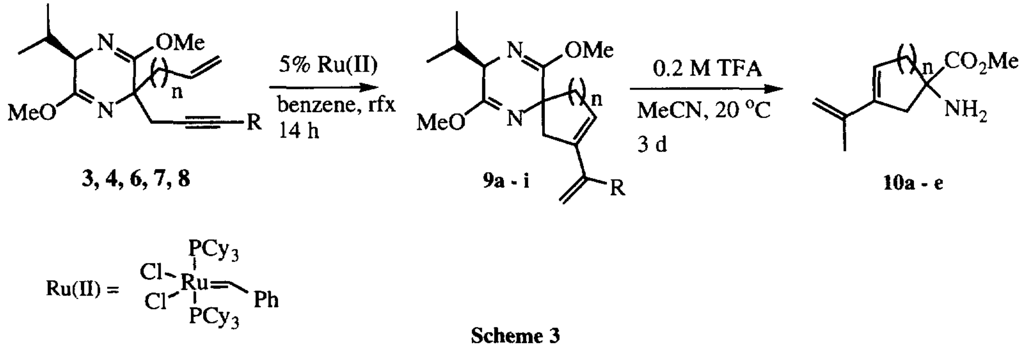


3b **7** **8**

(i) BuLi, -78 - 20 °C/$(CH_2O)_n$, 14 h
(ii) Ac_2O, DMAP, CH_2Cl_2, 20 °C, 30 min

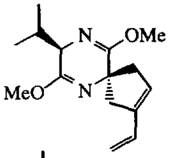
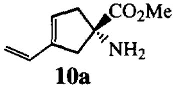
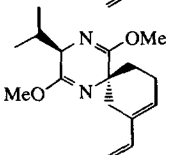
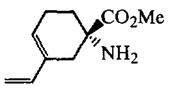
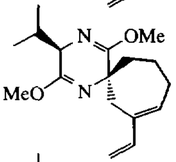
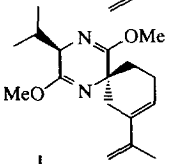
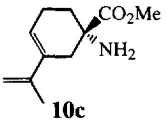
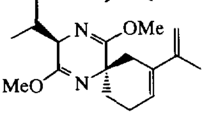
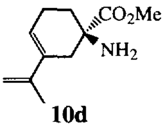
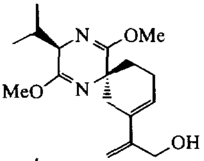
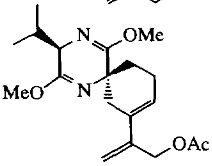
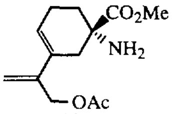
Scheme 2

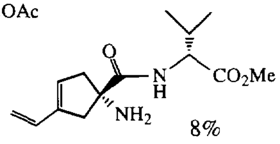
In the enynes **3**, an acidic and readily removable proton is situated on the terminal acetylenic carbon. Hence substitution on terminal alkyne carbon in the enyne **3** can be effected by lithiation and treatment with an electrophile; formaldehyde from paraformaldehyde was the reagent used for hydroxymethylation of the lithiated species of **3b** with formation of the alcohol **7**. The hydroxyl group in **7** was protected as the acetyl derivative **8** before the subsequent metathesis rearrangement.



Scheme 3

Table 1. Products from the Metathesis Reaction and Subsequent Hydrolysis.

Substrate	Product	Yield	Amino acid ester	[α]$_D$	Yield
3a	 **9a**	73%	 **10a**	-36.9°	42%*
3b	 **9b**	81%	 **10b**	+3.6°	83%
3c	 **9c**	0%			
4	 **9d**	51%	 **10c**	+5.1°	80%
6	 **9e**	86%	 **10d**	-5.0°	73%
7	 **9f**	0%			
8	 **9g**	71%	 **10e**	+3.9°	65%

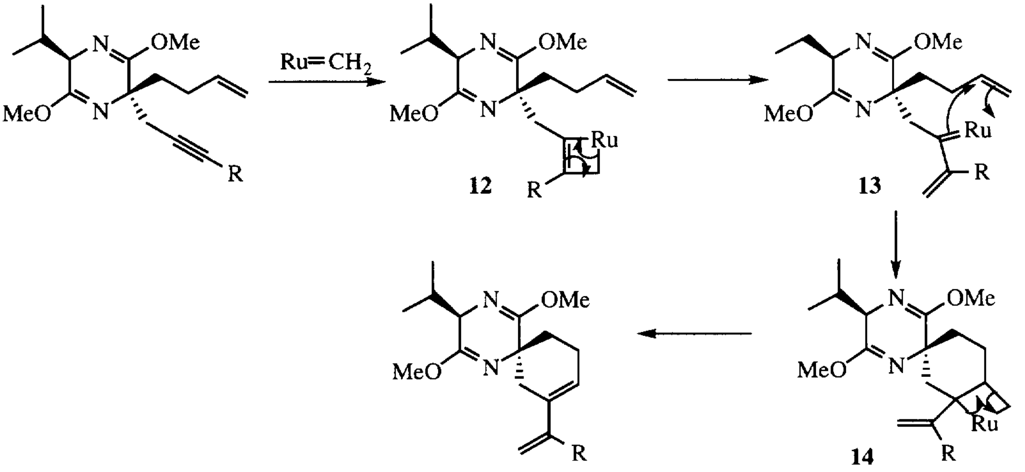


11 8%

The metathesis reactions of the enyne substrates were effected in refluxing dry and deoxygenated benzene solution with 5% of the ruthenium carbene catalyst. Benzene was a better choice than 1,2-dichloroethane and toluene (reflux) as solvent. In this manner the 1-vinylcyclohexenyl derivative **9b** was formed in 81% yield (Table 1) and the five-membered ring derivative **9a** in 73% yield. The ready formation of the cyclopentenyl derivative **9a** contrasts the results from studies on RCM reactions of dienes where formation of five-membered spirane rings was difficult to effect.[2,3] Another difference was the ease of formation of seven-membered spirane rings in the diene RCM reaction,[2,3] whereas the enyne metathesis rearrangement using the same ruthenium catalyst failed to yield the seven-membered ring product **9c**. Azacycloheptene formation under similar conditions, however, has been reported.[9] The difference in behaviour of the ruthenium catalyst indicates two mechanistically different pathways (*vide supra*).

The enyne with a terminal methyl group on the acetylenic carbon (*S*)-**4** gave the cyclic product (5*S*)-**9d** in only 50% yield. In the analogous (*R*)-series the yield of the cyclic product was significantly higher, *viz*. 86%, presumably due to differences in the non-bonded interactions in the formation of the two diastereomers **9d** and **9e**. If desirable, a more efficient process for the generation of **9d** can be effected by changing the stereochemistry of the chiral bislactim auxiliary which is used for generating the enyne substrate.

The hydroxymethyl enyne **7** failed to undergo skeletal rearrangement metathesis. In contrast, allylic alcohols were compatible in the diene RCM reaction using the same catalyst.[2,3] After protection of the hydroxyl group as an acetyl derivative, however, 71% yield of the ring-closed product **9g** was obtained.



Scheme 4

Adaption of the reaction mechanism proposed by Mori,[9b] suggests a reaction path as in Scheme 4. The catalytic cycle starts by adduct formation between the triple bond and the ruthenium carbene as indicated by structure **12**. A ruthenium methylene carbene is initially generated and is the operator in the catalytic cycle.

The spirane metathesis products **9** were all cleaved to the desired amino acid methyl esters **10** under mild acid conditions (Scheme 3). 0.2 M trifluoroacetic acid in acetonitrile effected the hydrolysis. The five-membered ring derivative **9a** was most difficult to hydrolyze; the yield of the amino acid ester **10a** was 42% (Table 1). An additional product (8% yield) from this reaction was identified as the partially hydrolyzed dipeptidic valine derivative **11**. The difficulties observed in the hydrolysis of **9a** paralellels previous observations in other five-membered ring analogues.[2,3] Hydrolysis of the acetyl derivative **9g** gave the amino acid ester **10e** in 65% yield. In accordance with the enatiomeric assignments the stereoisomers **9d** and **9e** showed approximately the same figures for the optical rotations which were of opposite sign (Table 1).

In conclusion, we have established a ruthenium(II)-catalyzed pathway to cyclic amino acids from enyne substrates. The latter are available by highly stereoselective alkylation reactions from bislactim ether chiral auxiliaries, either from **1** or its enantiomer. The configuration at the new stereogenic center in the cyclic amino acids is controlled either by the configuration of the chiral auxiliary or by the order of alkylation used in the preparation of the intermediate enyne substrates.

EXPERIMENTAL

^1H NMR spectra were recorded in $CDCl_3$ at 300 MHz or 200 MHz with Bruker DPX 300 or DPX 200. The ^{13}C spectra were recorded in $CDCl_3$ at 75 MHz or 50 MHz. Chemical shifts are reported in ppm using residual $CHCl_3$ (7.24 ppm) and $CDCl_3$ (77.00 ppm) as references. The mass spectra under electron impact conditions (EI) were recorded at 70 eV ionizing potential. The spectra are presented as *m/z* (% rel. int.). Dry THF and benzene were distilled from sodium and benzophenone. Benzene was degassed by bubbling argon through the solvent. Bis(tricyclohexylphosphine)benzylidene ruthenium dichloride was purchased from Strem Chemicals Inc., 7 Mulliken Way, Newburyport, MA.

(2*R*,5*S*)-5-Allyl-2,5-dihydro-3,6-dimethoxy-2-isopropylpyrazine (**2a**,[12] (2*R*,5*S*)-5-(3-butenyl)-2,5-dihydro-3,6-dimethoxy-2-isopropylpyrazine (**2b**,[1] (2*R*,5*S*)-2,5-dihydro-3,6-dimethoxy-2-isopropyl-5-(4-pentenyl)-pyrazine (**2c**,[1] were prepared as described.

General procedure for the preparation of (2*R*,5*S*)-5-alkenyl-2,5-dihydro-3,6-dimethoxy-2-isopropyl-5-(2-propynyl)pyrazine (**3**). nBuLi (4.40 mmol, 2.2 M in hexane) was added to a solution of (2*R*,5*S*)-5-alkenyl-2,5-dihydro-3,6-dimethoxy-2-isopropylpyrazine (4.00 mmol) in dry THF (15 ml) under argon at -50 °C. The mixture was stirred for 45 min and cooled to -78 °C. Propargyl bromide (6.00 mmol, 80% in toluene) in THF (2 ml) was added dropwise, the mixture left to slowly reach ambient temperaure overnight, 0.1 M phosphate buffer (pH 7, 10 ml) added and the aqueous layer extracted with dichloromethane (3 x 20 ml). The combined organic extracts were dried ($MgSO_4$) and evaporated. The crude product was purified by flash chromatography using 2% diethyl ether in hexane as eluent

(2*R*,5*S*)-5-Allyl-2,5-dihydro-3,6-dimethoxy-2-isopropyl-5-(2-propynyl)pyrazine (**3a**) was obtained from (2*R*,5*S*)-5-allyl-2,5-dihydro-3,6-dimethoxy-2-isopropylpyrazine in 80% yield as a colourless oil. Found: C, 68.84; H, 8.40. Calc. for $C_{15}H_{22}N_2O_2$: C, 68.67; H, 8.45%. $[\alpha]_D = -32.5^o$ (c = 1.23, $CHCl_3$). ^1H NMR (300 MHz): δ 0.62 (d, *J* 7 Hz, 3H, CH_3), 1.05 (d, *J* 7 Hz, 3H, CH_3), 1.83 (t, *J* 3 Hz, 1H, CH), 2.26--2.62 (m, 5H, 2 x CH_2, CH), 3.66 (s, 3H, CH_3O), 3.67 (s, 3H, CH_3O), 3.98 (d, *J* 3 Hz, 1H, H-2), 4.97 (m, 2H, CH_2=), 5.63 (m, 1H, CH=). ^{13}C NMR (75 MHz): δ 17.09 (CH_3), 19.52 (CH_3), 30.51 (CH), 31.07 (CH_2), 44.01 (CH_2), 52.29 (CH_3O), 52.41 (CH_3O), 60.82 (C-2), 61.47 (C-5), 70.09 (CH), 80.42 (C), 117.92 (CH_2=), 133.94 (CH=), 162.33 (C), 163.70 (C). MS(EI): 262 (0.7, M^+), 223 (54), 222 (11), 221 (42), 219 (25), 181 (100), 179 (72), 164 (22), 149 (46). MS(EI): *M* 262.1676. Calc. for $C_{15}H_{22}N_2O_2$: 262.1681.

(2*R*,5*S*)-5-(3-Butenyl)-2,5-dihydro-3,6-dimethoxy-2-isopropyl-5-(2-propynyl)pyrazine (**3b**) was obtained from (2*R*,5*S*)-5-(3-butenyl)-2,5-dihydro-3,6-dimethoxy-2-isopropylpyrazine in 85% yield as a colourless oil. Found: C, 69.13; H, 8.70. Calc. for $C_{16}H_{24}N_2O_2$: C, 69.53; H, 8.75%. $[\alpha]_D$= -20.4^o (c = 1.11, $CHCl_3$).

^{1}H NMR (200 MHz): δ 0.63 (d, *J* 7 Hz, 3H, CH_3), 1.07 (d, *J* 7 Hz, 3H, CH_3), 1.62--2.64 (m, 8H, 3 x CH_2, 2 x CH), 3.67 (s, 6H, 2 x CH_3O), 3.99 (d, *J* 3 Hz, 1H, H-2), 4.90 (m, 2H, CH_2=), 5.75 (m, 1H, CH=). ^{13}C NMR (50 MHz): δ 16.88 (CH_3), 19.51 (CH_3), 29.09 (CH_2), 30.47 (CH), 31.65 (CH_2), 38.54 (CH_2), 52.31 (CH_3O), 52.39 (CH_3O), 60.90 (CH), 61.32 (C), 70.01 (CH), 80.35 (C), 114.30 (CH_2=), 138.31 (CH=), 162.46 (C), 164.01 (C). MS(EI): 276 (2, *M*$^+$). 261 (14), 237 (76), 233 (43), 196 (12), 195 (100), 179 (23), 153 (35).

(2*R*,5*S*)-2,5-Dihydro-3,6-dimethoxy-2-isopropyl-5-(4-pentenyl)-5-(2-propynyl)pyrazine (**3c**) was obtained from (2*R*,5*S*)-2,5-dihydro-3,6-dimethoxy-2-isopropyl-5-(4-pentenyl)pyrazine in 46% yield as a colourless oil. Found: C, 69.88; H, 8.89. Calc. for $C_{17}H_{26}N_2O_2$: C, 70.31; H, 9.02%. $[\alpha]_D$ = -21.1^o (c = 0.95, $CHCl_3$). ^{1}H NMR (300 MHz): δ 0.64 (d, *J* 7 Hz, 3H, CH_3), 1.07 (d, *J* 7 Hz, 3H, CH_3), 1.03--2.61 (m, 10H, 4 x CH_2, 2 x CH), 3.65 (s, 3H, CH_3O), 3.68 (s, 3H, CH_3O), 3.99 (d, *J* 3 Hz, 1H, H-2), 4.91 (m, 2H, CH_2=), 5.76 (m, 1H, CH=). ^{13}C NMR (75 MHz): δ 16.93 (CH_3), 19.54 (CH_3), 23.92 (CH_2), 30.56 (CH), 31.71 (CH_2), 33.56 (CH_2), 38.83 (CH_2), 52.32 (CH_3O), 52.39 (CH_3O), 60.92 (C-2), 61.59 (C-5), 69.93 (CH), 80.51 (C), 114.29 (CH_2=), 138.60 (CH=), 162.66 (C), 163.84 (C). MS(EI): 290 (6, *M*$^+$), 252 (16), 251 (89), 247 (41), 219 (18), 209 (69). MS(EI): *M* 290.1985. Calc. for $C_{17}H_{26}N_2O_2$: 290.1994.

(2*R*,5*S*)-5-(3-Butenyl)-5-(2-butynyl)-2,5-dihydro-3,6-dimethoxy-2-isopropylpyrazine (**4**). nBuLi (1.62 ml, 3.73 mmol, 2.3 M in heptane) was added to a solution of (2*R*,5*R*/*S*)-5-(3-butenyl)-2,5-dihydro-3,6-dimethoxy-2-isopropylpyrazine (807 mg, 3.37 mmol) in dry THF (15 ml) under argon at -50 ^{o}C. The solution was cooled to -78 ^{o}C after 45 min and 1-bromo-2-butyne[13] (585 mg, 4.40 mmol) in THF (0.5 ml) added dropwise. The solution was allowed to reach ambient temperature overnight, 0.1 M phosphate buffer (10 ml, pH 7) added, the aqueous phase extracted with dichloromethane (3 x 30 ml) and the combined organic phases dried ($MgSO_4$) and evaporated. The pure product was flash chromatographed using 3% diethyl ether in hexane as eluent; yield 877 mg (89%) of a colourless oil. Found: C, 70.28; H, 9.08. Calc. for $C_{17}H_{26}N_2O_2$: C, 70.31; H, 9.02%. $[\alpha]_D$ = -16.5^o (c = 1.56, $CHCl_3$). ^{1}H NMR (300 MHz): δ 0.64 (d, *J* 7 Hz, 3H, CH_3), 1.08 (d, *J* 7 Hz, 3H, CH_3), 1.61--2.55 (m, 10 H, 3 x CH_2, CH_3, CH), 3.66 (s, 3H, CH_3O), 3.68 (s, 3H, CH_3O), 3.93 (d, *J* 3 Hz, 1H, H-2), 4.90 (m, 2H, CH_2=), 5.77 (m, 1H, CH=). ^{13}C NMR (75 MHz): δ 3.53 (CH_3), 16.90 (CH_3), 19.53 (CH_3), 29.23 (CH_2), 30.54 (CH), 32.12 (CH_2), 38.44 (CH_2), 52.30 (CH_3O), 52.40 (CH_3O), 60.84 (C-2), 61.59 (C-5), 74.92 (C), 77.24 (C), 114.19 (CH_2=), 138.56 (CH=), 162.85 (C), 163.69 (C). MS(EI): 290 (2, *M*$^+$), 275 (6), 247 (7), 238 (10), 237 (63), 196 (12), 195 (100), 153 (29).

(2*R*,5*S*)-5-(2-Butynyl)-2,5-dihydro-3,6-dimethoxy-2-isopropylpyrazine (**5**) and (2*R*,5*R*)-5-(2-butynyl)-2,5-dihydro-3,6-dimethoxy-2-isopropylpyrazine. nBuLi (2.00 ml, 2.30 mmol, 2.3 M in heptane) was added dropwise to a solution of (*R*)-2,5-dihydro-3,6-dimethoxy-2-isopropylpyrazine (764 mg, 4.15 mmol) in dry THF (15 ml) at -78 ^{o}C under argon. 1-Bromo-2-butyne[13] (716 mg, 5.39 mmol) in THF (0.5 ml) was added dropwise after 15 min, the mixture allowed to reach ambient temperature overnight, the reaction quenched by addition of 0.1 M phosphate buffer (10 ml, pH 10), the aqueous layer extracted with dichloromethane (3 x 30 ml) and the combined organic layers dried ($MgSO_4$) and evaporated. The crude product was purified by flash chromatography using hexane/diethyl ether 9:1 as eluent; yield 744 mg (76%, d.e. 79%) of a colourless oil. Found: C, 65.66; H, 8.35. Calc. for $C_{13}H_{20}N_2O_2$: C, 66.07, H, 8.53%. $[\alpha]_D$ = +16.5^o (c = 0.60, $CHCl_3$).

^1H NMR (300 MHz): δ 0.62 (d, *J* 7 Hz, 3H, CH_3), 1.00 (d, *J* 7 Hz, 3H, CH_3), 1.65 (t, *J* 2.5 Hz, 3H, CH_3), 2.22 (m, 1H, CH), 2.57 (m, 2H, CH_2), 3.65 (s, 6H, 2 x CH_3O), 3.92--4.03 (m, 2H, H-2, H-5). ^{13}C NMR (75 MHz): δ 3.45 (CH_3), 16.40 (CH_3), 19.02 (CH_3), 25.28 (CH_2), 31.45 (CH), 52.35 (CH_3O), 52.41 (CH_3O), 54.73 (C-5), 60.73 (C-2), 74.84 (C), 77.23 (C), 162.00 (C), 164.44 (C). MS(EI): 236 (5, M^+), 221 (6), 183 (52), 141 (100). MS(EI): *M* 236.1522. Calc. for $C_{13}H_{20}N_2O_2$: 236.1525.

A slower moving component during flash chromatography was was identified as (2*R*,5*R*)-5-(2-butynyl)-2,5-dihydro-3,6-dimethoxy-2-isopropyl-pyrazine: Colourless oil. ^1H NMR (300 MHz): δ 0.73 (d, *J* 7 Hz, 3H, CH_3), 1.03 (d, *J* 7 Hz, 3H, CH_3), 1.67 (t, *J* 3 Hz, 3H, CH_3), 2.24 (m, 1H, CH), 2.63 (m, 2H, CH_2), 3.66 (s, 3H, CH_3O), 3.67 (s, 3H, CH_3O), 3.88, 4.05 (2 x m, 2H, H-2 and H-5). ^{13}C NMR (75 MHz): δ 3.58 (CH_3), 17.31 (CH_3), 19.61 (CH_3), 25.10 (CH_2), 31.08 (CH), 52.32 (CH_3O), 52.53 (CH_3O), 54.82 (C-5), 60.77 (C-2), 75.68 (C), 77.41 (C), 161.64 (C), 163.77 (C).

(2*R*,5*R*)-5-(3-Butenyl)-5-(2-butynyl)-2,5-dihydro-3,6-dimethoxy-2-isopropylpyrazine (**6**). nBuLi (1.33 ml, 3.08 mmol, 2.3 M in heptane) was added to a solution of (2*R*,5*S*)-5-(2-butynyl)-2,5-dihydro-3,6-dimethoxy-2-isopropylpyrazine (661 mg, 2.80 mmol) in dry THF (10 ml) under argon at -50 °C. The solution was cooled to -78 °C after 45 min and 4-bromo-1-butene (0.35 ml, 3.36 mmol) in THF (0.5 ml) was added dropwise. The mixture was left to slowly reach ambient temperature overnight. A 0.1 M phosphate buffer solution (10 ml, pH 7) was addded and the aqueous phase was extracted with dichloromethane (3 x 20 ml). The combined organic layers were dried ($MgSO_4$) and evaporated. The residue was purified by flash chromatography using 3% diethyl ether in hexane as eluent; yield 568 mg (70%) of a colourless oily material. Found: C, 70.09; H, 9.15. Calc. for $C_{17}H_{26}N_2O_2$: C, 70.31; H, 9.02%. $[\alpha]_D$ = -35.3° (c = 1.13, $CHCl_3$). ^1H NMR (300 MHz): δ 0.72 (d, *J* 7 Hz, 3H, CH_3), 1.08 (d, *J* 7 Hz, 3H, CH_3), 1.63 (t, *J* 3 Hz, 3H, CH_3), 1.61--2.68 (m, 7H, 3 x CH_3, CH), 3.66 (s, 3H, CH_3O), 3.67 (s, 3H, CH_3O), 3.85 (d, *J* 3 Hz, 1H, H-2), 4.88 (m, 2H, CH_2=), 5.70 (m, 1H, CH=). ^{13}C NMR (75 MHz): δ 3.60 (CH_3), 16.99 (CH_3), 19.61 (CH_3), 28.58 (CH_2), 30.58 (CH), 31.39 (CH_2), 39.48 (CH_2), 52.38 (2 x CH_3O), 60.91 (C-2), 61.58 (C-5), 75.82 (C), 77.28 (C), 114.29 (CH_2=), 138.08 (CH=), 162.92 (C), 163.09 (C). MS(EI): 290 (3, M^+), 247 (20), 237 (34), 196 (12), 195 (100), 193 (13), 153 (22). MS(EI): *M* 290.2022. Calc. for $C_{17}H_{26}N_2O_2$: 290.1994.

(2*R*,5*S*)-5-(3-Butenyl)-2,5-dihydro-3,6-dimethoxy-5-(4-hydroxy-2-butynyl)-2-isopropylpyrazine (**7**). nBuLi (2.00 ml, 4.60 mmol, 2.3 M in heptane) was added to a solution of (2*R*,5*S*)-5-(3-butenyl)-2,5-dihydro-3,6-dimethoxy-2-isopropyl-5-(2-propynyl)pyrazine (1.16 g, 4.18 mmol) in dry THF (10 ml) at -78 °C under argon. The solution was transfered after 30 min via a teflon tubing to a suspension of paraformaldehyde (188 mg, corresponding to 6.27 mmol of monomer) in THF (5 ml). The mixture was allowed to slowly reach ambient temperature over night, 0.1 M phosphate buffer solution (pH 7, 10 ml) added and the aqueous layer extracted with dichloromethane (3 x 15 ml). The combined organic layers were dried ($MgSO_4$), evaporated and flash chromatographed using hexane/ethyl acetate 4:1 as eluent; yield 964 mg (74%) of a white waxy material melting at 48 °C. Found: C, 67.19; H, 8.43. Calc. for $C_{17}H_{26}N_2O_3$: C, 66.64; H, 8.55%. $[\alpha]_D$ = -10.3° (c = 1.94, $CHCl_3$). ^1H NMR (200 MHz): δ 0.63 (d, *J* 7 Hz, 3H, CH_3), 1.07 (d, *J* 7 Hz, 3H, CH_3), 1.63--2.67 (m, 8H, 3 x CH_2, CH, OH), 3.67 (s, 6H, 2 x CH_3O), 3.97 (d, *J* 3 Hz, 1H, H-2), 4.11 (s, 2H, CH_2O), 4.92 (m, 2H, CH_2=), 5.77 (m, 1H, CH=). ^{13}C NMR (50 MHz): δ 16.87 (CH_3), 19.48 (CH_3), 29.13 (CH_2), 30.54 (CH), 32.12 (CH_2), 38.40 (CH_2), 50.98 (CH_2O), 52.45 (2 x CH_3O), 60.80 (C-2), 61.51 (C-5), 80.32 (C), 82.04 (C), 114.33 (CH_2=), 138.32 (CH=), 162.91 (C), 163.87 (C). MS(EI): 306 (0.6, M^+), 289 (22), 237 (65), 195 (100), 153 (27). MS(EI): *M* 306.1922. Calc. for $C_{17}H_{26}N_2O_3$: 306.1943.

(2*R*,5*S*)-5-(4-Acetoxy-2-butynyl)-5-(3-butenyl)-2,5-dihydro-3,6-dimethoxy--2-isopropylpyrazine (**8**). Acetic anhydride (0.10 ml, 1.02 mmol) was added dropwise to a solution of (2*R*,5*S*)-5-(3-butenyl)-2,5-dihydro-3,6-dimethoxy-5-(4-hydroxy-2-butynyl)-2-isopropylpyrazine (285 mg, 0.93 mmol) and 4-dimethylaminopyridine (125 mg, 1.02 mmol) in dichloromethane (10 ml) at ambient temperature under argon. The solvent was evaporated after 30 min and the product isolated by flash chromatography using hexane/ethyl acetate (4:1) as eluent; yield 299 mg (92%) of a colourless oily material. Found: C, 66.31; H, 8.16. Calc. for $C_{19}H_{28}N_2O_4$: C, 65.49; H, 8.10. $[\alpha]_D$ = -13.4° (c = 1.03, $CHCl_3$). ^1H NMR (300 MHz): δ 0.63 (d, *J* 7 Hz, 3H, CH_3), 1.07 (d, *J* 7 Hz, 3H, CH_3), 1.62--1.90 (m, 4H, 2 x CH_2), 2.04 (s, 3H, $CH_3C{=}O$), 2.30--2.65 (m, 3H, CH_2, CH), 3.66 (s, 3H, CH_3O), 3.67 (s, 3H, CH_3O), 3.97 (d, *J* 3 Hz, 1H, H-2), 4.54 (t, *J* 2 Hz, 2H, CH_2O), 4.95 (m, 2H, CH_2=), 5.75 (m, 1H, CH=). ^{13}C NMR (75 MHz): 16.88 (CH_3), 19.54 (CH_3), 20.68 (CH_3), 29.13 (CH_2), 30.46 (CH), 32.03 (CH_2), 38.46 (CH_2), 52.39 (2 x CH_3O), 52.53 (CH_2O), 60.77 (C-2), 61.31 (C-5), 75.75 (C), 83.43 (C), 114.34 (CH_2=), 138.34 (CH=), 162.29 (C), 164.05 (C), 170.21 (C=O). MS(EI): 348 (0.6, M^+), 305 (10), 289 (42), 237 (77), 195 (100), 153 (18). MS(EI): *M* 348.2059. Calc. for $C_{19}H_{28}N_2O_4$: 348.2049.

General procedure for the preparation of (2*R*,5*S*/*R*)-2,5-dihydro-3,6-dimethoxy-2-isopropylpyrazine-5-spiro(3-alkenyl-3-cycloalkenes) (**9**). Bis(tricyclohexylphosphine)benzylidene ruthenium dichloride (0.036 mmol) in dry degassed benzene (3 ml) was added to a solution of (2*R*,5*S*/*R*)-5-alkenyl-5-alkynyl-2,5-dihydro-3,6-dimethoxy-2-isopropylpyrazine (0.72 mmol) in dry degassed benzene (10 ml) and the mixture refluxed under argon for 14 h. The solvent was then evaporated, and the residue purified by flash chromatography using 2% diethyl ether in hexane as eluent.

(2*R*,5*S*)-2,5-Dihydro-3,6-dimethoxy-2-isopropylpyrazine-5-spiro(3-vinyl-3-cyclopentene) (**9a**) was obtained from (2*R*,5*S*)-5-allyl-2,5-dihydro-3,6-dimethoxy-2-isopropyl-5-(2-propynyl)pyrazine in 73% yield as a colourless oily material. Found: C, 68.65; H, 8.23. Calc. for $C_{15}H_{22}N_2O_2$: C, 68.67; H, 8.45%. $[\alpha]_D$ = +13.1° (c = 1.35, $CHCl_3$). ^1H NMR (300 MHz): δ 0.66 (d, *J* 7 Hz, 3H, CH_3), 1.03 (d, *J* 7 Hz, 3H, CH_3), 2.21 (m, 1H, CH), 2.42 (m, 2H, CH_2), 3.03 (m, 2H, CH_2), 3.61 (s, 3H, CH_3O), 3.67 (s, 3H, CH_3O), 3.98 (d, *J* 3 Hz, 1H, H-2), 5.03 (m, 2H, CH_2), 5.62 (bs, 1H, CH=), 6.51, 6.56 (dd, *J* 10 Hz, 1H, CH=) . ^{13}C NMR (75 MHz): δ 16.75 (CH_3), 19.24 (CH_3), 31.14 (CH), 47.08 (CH_2), 49.13 (CH_2), 52.22 (CH_3O), 52.44 (CH_3O), 61.03 (C-2), 62.47 (C-5), 114.29 (CH_2=), 127.45 (CH=), 133.24 (CH=), 140.48 (C=), 161.32 (C), 165.72 (C). MS(EI): 262 (9, M^+), 220 (15), 219 (100), 153 (20), 149 (12). MS(EI): *M* 262.1666. Calc. for $C_{15}H_{22}N_2O_2$: 262.1681.

(2*R*,5*S*)-2,5-Dihydro-3,6-dimethoxy-2-isopropylpyrazine-5-spiro(3-vinyl-3-cyclohexene) (**9b**) was obtained from (2*R*,5*S*)-5-(3-butenyl)-2,5-dihydro-3,6-dimethoxy-2-isopropyl-5-(2-propynyl)pyrazine in 81% yield as a white solid material, m.p. 68 °C. Found: C, 69.00; H, 8.74. Calc. for $C_{16}H_{24}N_2O_2$: C, 69.53; H, 8.75%. $[\alpha]_D$ = +7.7° (c = 0.87, $CHCl_3$). ^1H NMR (300 MHz): δ 0.66 (d, *J* 7 Hz, 3H, CH_3), 1.06 (d, *J* 7 Hz, 3H, CH_3), 1.23--2.70 (m, 7H, 3 x CH_2, CH), 3.56 (s, 3H, CH_3O), 3.66 (s , 3H, CH_3O), 3.95 (d , *J* 3 Hz, 1H, H-2), 4.90 (m, 2H, CH_2=), 5.81 (bs, 1H, CH=), 6.35, 6.41 (dd, *J* 11 Hz, 1H, CH=). ^{13}C NMR (75 MHz): δ 16.88 (CH_3), 19.36 (CH_3), 22.19 (CH_2), 30.84 (CH), 32.69 (CH_2), 35.55 (CH_2), 52.05 (CH_3O), 52.37 (CH_3O), 55.90 (C-5), 60.53 (C-2), 109.38 (CH_2=), 128.67 (CH=), 132.90 (C=), 140.07 (CH=), 161.01 (C), 166.04 (C). MS(EI): 276 (74, M^+), 250 (12), 233 (98), 153 (93), 149 (95). MS(EI) *M* 276.1843. Calc. for $C_{16}H_{24}N_2O_2$: 276.1838.

(2*R*,5*S*)-2,5-Dihydro-3,6-dimethoxy-2-isopropylpyrazine-5-spiro(3-isopropenyl-3-cyclohexene) (**9d**) was obtained from (2*R*,5*S*)-5-(3-butenyl)-5-(2-butynyl)-2,5-dihydro-3,6-dimethoxy-2-isopropylpyrazine in 51% yield as a colourless oil. $[\alpha]_D$ = -11.4° (c = 0.51, $CHCl_3$). ^1H NMR (300 MHz): δ 0.67 (d, *J* 7 Hz, 3H, CH_3), 1.07 (d, *J* 7 Hz, 3H, CH_3), 1.41--2.77 (m, 7H, 3 x CH_2, CH), 1.91 (s, 3H, CH_3), 3.56 (s, 3H, CH_3O), 3.66 (s, 3H, CH_3O), 3.95 (d, *J* 3 Hz, 1H, H-2), 4.80 (d, *J* 12 Hz, 2H, CH_2=), 5.94 (m, 1H, CH=). ^{13}C NMR (75 MHz): δ 16.88 (CH_3), 19.38 (CH_3), 20.78 (CH_3), 22.27 (CH_2), 30.84 (CH), 32.21 (CH_2), 37.12 (CH_2), 52.07 (CH_3O), 52.39 (CH_3O), 56.31 (C-5), 60.50 (C-2), 109.27 (CH_2=), 123.94 (CH=), 133.29 (C=), 143.69 (C=), 160.89 (C), 166.23 (C). MS(EI): 290 (53, M^+), 249 (14), 247 (69), 195 (30), 153 (100). MS(EI): *M* 290.1981. Calc. for $C_{17}H_{26}N_2O_2$: 290.1994.

(2*R*,5*R*)-2,5-Dihydro-3,6-dimethoxy-2-isopropylpyrazine-5-spiro(3-isopropenyl-3-cyclohexene) (**9e**) was obtained from (2*R*,5*R*)-5-(3-butenyl)-5-(2-butynyl)-2,5-dihydro-3,6-dimethoxy-2-isopropylpyrazine in 86% yield as a colourless oil. Found: C, 70.21; H, 9.10. Calc. for $C_{17}H_{26}N_2O_2$: C, 70.31; H, 9.02%. $[\alpha]_D$ = -74.3° (c = 1.81, $CHCl_3$). ^1H NMR (300 MHz): δ 0.71 (d, *J* 7 Hz, 3H, CH_3), 1.06 (d, *J* 7 Hz, 3H, CH_3), 1.40--2.81 (m, 7H, 3 x CH_2, CH), 1.91 (s, 3H, CH_3), 3.57 (s, 3H, CH_3O), 3.66 (s, 3H, CH_3O), 3.94 (d, *J* 3 Hz, 1H, H-2), 4.80 (d, *J* 9 Hz, 2H, CH_2=), 5.94 (m, 1H, CH=). ^{13}C NMR (75 MHz): δ 17.00 (CH_3), 19.36 (CH_3), 20.76 (CH_3), 21.98 (CH_2), 31.08 (CH), 32.30 (CH_2), 36.84 (CH_2), 52.06 (CH_3O), 52.39 (CH_3O), 56.23 (C-5), 60.55 (C-2), 109.20 (CH_2=), 124.08 (CH=), 133.24 (C=), 143.63 (C=), 161.00 (C), 166.29 (C). MS(EI): 290 (100, M^+), 247 (100), 153 (83). MS(EI): *M* 290.1985. Calc. for $C_{17}H_{26}N_2O_2$: 290.1994.

(2*R*,5*S*)-2,5-Dihydro-3,6-dimethoxy-2-isopropylpyrazine-5-spiro[3-(3-acetoxy-1-propen-2-yl)-3-cyclohexene] (**9g**) was obtained from (2*R*,5*S*)-5-(4-acetoxy-2-butynyl)-5-(3-butenyl)-2,5-dihydro-3,6-dimethoxy-2-isopropylpyrazine in 71% yield as a colourless oil. Found: C, 64.43; H, 8.04. Calc. for $C_{19}H_{28}N_2O_4$: C, 65.49; H, 8.10. $[\alpha]_D$ = -19.2° (c = 0.65, $CHCl_3$). ^1H NMR (300 MHz): δ 0.65 (d, *J* 7 Hz, 3H, CH_3), 1.05 (d, *J* 7 Hz, 3H, CH_3), 1.04--2.76 (m, 7H, 3 x CH_2, CH), 2.04 (s, 3H, CH_3),3.54 (s, 3H, CH_3O), 3.65 (s, 3H, CH_3O), 3.94 (d, *J* 3 Hz, 1H, H-2), 4.77 (s, 2H, CH_2-OAc), 5.04 (s, 2H, CH_2=), 5.90 (m, 1H, CH=). ^{13}C NMR (75 MHz): δ 16.84 (CH_3), 19.31 (CH_3), 20.98 (CH_3), 22.20 (CH_2), 30.79 (CH), 32.08 (CH_2), 37.23 (CH_2), 52.01 (CH_3O), 52.41 (CH_3O), 56.09 (C-5), 60.46 (C-2), 65.14 (CH_2O), 111.45 (CH_2=), 124.46 (CH=), 130.63 (C=), 142.29 (C=), 161.00 (C), 165.88 (C), 170.71 (C=O). MS(EI): 348 (100, M^+), 305 (48), 263 (12), 245 (78), 153 (61). MS(EI): *M* 348.2057. Calc. for $C_{19}H_{28}N_2O_4$: 348.2049.

General procedure for the preparation of methyl (*S/R*)-3-alkenyl-1-amino-3-cycloalkene-1-carboxylate (**10**). The (2*R*,5*S/R*)-2,5-dihydro-3,6-dimethoxy-2-isopropylpyrazine-5-spiro(3-alkenyl-3-cycloalkene) (0.50 mmol) was added to a solution of TFA (25 ml, 5.00 mmol, 0.2 M) and MeCN (25 ml) and the mixture stirred for 3 d at ambient temperature. The acetonitrile was then evaporated off and the aqueous residue made alkaline by addition of conc. ammonia (pH 10). The resultant suspension was extracted with dichloromethane (3 x 20 ml), the combined dichloromethane layers dried ($MgSO_4$) and evaporated. The title compound was isolated by flash chromatography using 2% methanol in dichloromethane as eluent.

Methyl (*S*)-1-amino-3-vinyl-3-cyclopentene-1-carboxylate (**10a**) was obtained from (2*R*,5*S*)-2,5-dihydro-3,6-dimethoxy-2-isopropylpyrazine-5-spiro(3-vinyl-3-cyclopentene) in 42% yield as a colourless oily material. $[\alpha]_D = -36.9^o$ (c = 0.90, $CHCl_3$). ^1H NMR(300 MHz): δ 1.78 (bs, 2H, NH_2), 2.38 (m, 2H, CH_2), 3.02 (d, *J* 15 Hz, 2H, CH_2), 3.70 (s, 3H, CH_3O), 5.02 (m, 2H, CH_2=), 5.60 (bs, 1H, CH=), 6.46, 6.51 (dd, 11 Hz, 1H, CH=). ^{13}C NMR (75 MHz): δ 45.04 (CH_2), 46.93 (CH_2), 52.36 (CH_3O), 63.26 (C-1), 114.68 (CH_2=), 126.92 (CH=), 132.86 (CH=), 140.04 (C=), 177.50 (C=O). MS(EI): 135 (8, *M-CH_3OH*), 119 (15), 118 (15), 108 (100).

Methyl (*S*)-1-amino-3-vinyl-3-cyclohexene-1-carboxylate (**10b**) was obtained from (2*R*,5*S*)-2,5-dihydro-3,6-dimethoxy-2-isopropylpyrazine-5-spiro(3-vinyl-3-cyclohexene) in 83% yield as a colourless oily material. $[\alpha]_D = +3.6^o$ (c = 0.80, $CHCl_3$). ^1H NMR (300 MHz): δ 1.72--2.68 (m, 8H, 3 x CH_2, NH_2), 3.72 (s, 3H, CH_3O), 4.90 (d, *J* 11 Hz, 1H, 1/2 CH_2=), 5.04 (d, *J* 18 Hz, 1H, 1/2 CH_2=), 5.74 (bs, 1H, CH=), 6.32, 6.38 (dd, *J* 10 Hz, 1H, CH=). ^{13}C NMR (75 MHz): δ 22.70 (CH_2), 31.50 (CH_2), 34.52 (CH_2), 52.75 (CH_3O), 56.43 (C), 110.98 (CH_2), 128.04 (CH=), 133.37 (C=), 139.71 (CH=), 177.49 (C=O). MS(EI): 181 (25, M^+), 164 (9), 122 (100), 105 (75), 101 (29). MS(EI): *M* 181.1116. Calc. for $C_{10}H_{15}NO_2$: 181.1103.

Methyl (*S*)-1-amino-3-isopropenyl-3-cyclohexene-1-carboxylate (**10c**) was obtained from (2*R*,5*S*)-2,5-dihydro-3,6-dimethoxy-2-isopropylpyrazine-5-spiro(3-isopropenyl-3-cyclohexene) in 80% as a colourless oil. $[\alpha]_D = +5.1^o$ (c = 0.85, $CHCl_3$). ^1H NMR (200 MHz): δ 1.64--2.75 (m, 8H, 3 x CH_2, NH_2), 1.87 (s, 3H, CH_3), 3.71 (s, 3H, CH_3O), 4.86 (d, *J* 16 Hz, 2H, CH_2), 5.86 (bs, 1H, CH=). ^{13}C NMR (50 MHz): δ 20.66 (CH_3), 22.34 (CH_2), 30.54 (CH_2), 35.62 (CH_2), 52.30 (CH_3O), 56.31 (C-1), 110.19 (CH_2=), 122.99 (CH=), 133.48 (C=), 143.00 (C=), 177.20 (C). MS(EI): 195 (20, M^+), 178 (9), 136 (68), 119 (52), 101 (39). MS(EI): *M* 195.1241. Calc. for $C_{11}H_{17}NO_2$: 195.1259.

Methyl (*R*)-1-amino-3-isopropenyl-3-cyclohexene-1-carboxylate (**10d**) was obtained from (2*R*,5*R*)-2,5-dihydro-3,6-dimethoxy-2-isopropylpyrazine-5-spiro(3-isopropenyl-3-cyclohexene) in 73% yield as a colourless oil. ^1H NMR (300 MHz): δ 1.64--2.73 (m, 8H, 3 x CH_2, NH_2), 1.87 (s, 3H, CH_3), 3.71 (s, 3H, CH_3O), 4.86 (d, *J* 16 Hz, 2H, CH_2=), 5.86 (bs, 1H, CH=). ^{13}C NMR (75 MHz): δ 20.66 (CH_3), 22.33 (CH_2), 30.53 (CH_2), 35.63 (CH_2), 52.29 (CH_3O), 56.23 (C-1), 110.17 (CH_2=), 122.98 (CH=), 133.44 (C=), 142.96 (C=), 177.32 (C=O). MS(EI): 195 (16, M^+), 136 (51), 119 (22), 101 (26). MS(EI): *M* 195.1249. Calc. for $C_{11}H_{17}NO_2$: 195.1259.

Methyl (*S*)-1-amino-3-(3-acetoxy-1-propen-2-yl)-3-cyclohexen-1-carboxylate (**10e**) was obtained from (2*R*,5*S*)-2,5-dihydro-3,6-dimethoxy-2-isopropylpyrazine-5-spiro[3-(3-acetoxy-1-propen-2-yl)-3-cyclohexene] in 65% yield as a colourless oily material. $[\alpha]_D = +3.9^o$ (c = 0.70, $CHCl_3$). ^1H NMR (300 MHz): δ 1.65--

2.72 (8 H, m, 3 x CH_2, NH_2), 2.06 (s, 3H, CH_3), 3.71 (s, 3H, CH_3O), 4.73 (s, CH_2O), 5.13 (d, *J* 9 Hz, 2H, CH_2=), 5.84 (bs, 1H, CH=). ^{13}C (75 MHz): δ 21.00 (CH_3), 22.31 (CH_2), 30.49 (CH_2), 35.71 (CH_2), 52.34 (CH_2O), 56.12 (C-1), 65.03 (CH_2O), 112.61 (CH_2=), 123.68 (CH=), 130.90 (C=), 141.67 (C=), 170.72 (C=O), 176.98 (C=O). MS(EI): 253 (26, M^+), 195 (13), 194 (100), 176 (26), 134 (73), 117 (33). MS(EI): *M* 253.1301. Calc. for $C_{13}H_{19}NO_4$: 253.1314.

Methyl (*S*)-*N*-(1-amino-3-vinyl-3-cyclopentene-1-carbonyl)-(*R*)-valinate (**11**). A second product from the reaction mixture which gave **10a**, was the dipeptide **11**. It was eluated before **10a** during flash cromatography (*vide supra*); yield 12 mg (8%). ^1H NMR (300 MHz): δ 0.89 (d, *J* 7 Hz, 3H, CH_3), 0.92 (d, *J* 7 Hz, 3H, CH_3), 2.18 (m, 1H, CH), 2.30 (m, 4H, CH_2, NH_2), 3.13, 3.22 (dd, *J* 16 Hz, 2H, CH_2), 3.72 (s, 3H, CH_3O), 4.47, 4.50 (dd, *J* 5 Hz, 1H, $C\underline{H}$-NH), 5.03 (d, *J* 11 Hz, 1H, 1/2 CH_2=), 5.08 (d, *J* 4 Hz, 1H, 1/2 CH_2), 5.61 (bs, 1H, CH=), 6.48, 6.54 (dd, *J* 11 Hz, 1H, CH=), 7.98 (d, *J* 9 Hz, 1H, NH). ^{13}C NMR (75 MHz): δ 17.77 (CH_3), 19.08 (CH_3), 31.31 (CH), 45.75 (CH_2), 47.84 (CH_2), 52.05 (CH_3O), 57.18 (CH), 64.21 (C), 115.11 (CH_2=), 125.73 (CH=), 132.90 (CH=), 140.59 (C=), 172.52 (C=O), 175.96 (C=O).

REFERENCES.

1. (a) Goodman, M.; Shao, H. *Pure Appl. Chem.* **1996**, *68*, 1303-1308 and references therein; (b) Degrado, W. F. *Adv. Protein Chem.* **1988**, *39*, 51-124 and references therein.
2. Hammer, K.; Undheim, K. *Tetrahedron* **1997**, *53*, 2309-2322.
3. Hammer, K.; Undheim, K. *Tetrahedron* **1997**, *53*, 5925-5936.
4. (a) Schwab, P.; Grubbs, R. H.; Ziller, J. W. *J. Am. Chem. Soc.* **1996**, *118*, 100-110; (b) Grubbs, R. H.; Miller, S. J.; Fu, G. C. *Acc. Chem. Res.* **1995**, *28*, 446-452
5. (a) Katz, T. J.; Sivavec, T. M. *J. Am. Chem. Soc.* **1985**, 107, 737-738; (b) Sivavec T. M.; Katz, T. J.; Chiang, M. Y.; Yang, G. Xu-G. *Organometallics* **1989**, *8*, 1620-1625.
6. (a) Watanuki, S.; Mori, M. *Organometallics* **1995**, *14*, 5054-5061; (b) Watanuki, S.; Ochifuji, N.; Mori, M. *Organometallics* **1995**, *14*, 5062-5067.
7. (a) Trost, B. M.; Chang, V. K. *Synthesis* **1993**, 824-832; (b) Trost, B. M.; Yanai, M.; Hoogsteen, K. *J. Am. Chem. Soc.* **1993**, *115*, 5294-5295; (c) Trost, B. M.; Trost, M. K. *J. Am. Chem. Soc.* **1991**, *113*, 1850-1852.
8. Chatani, N.; Morimoto, T.; Muto, T.; Murai, S. *J. Am. Chem. Soc.* **1994**, *116*, 6049-6050.
9. (a) Kinoshita, A.; Mori, M. *J. Org. Chem.* **1996**, *61*, 8356-8357; (b) Kinoshita, A.; Mori, M. SYNLETT **1994**, 1020-1021.
10. (a) Kim, S.-H.; Bowden, N.; Grubbs, R.H. *J. Am. Chem. Soc.* **1994**, *116*, 10801-10802; (b) Zuercher, W. J.; Hashimoto, M.; Grubbs, R. H. *J. Am. Chem. Soc.* **1996**, *118*, 6634-6640.
11. Schöllkopf, U. *Tetrahedron* **1983**, *39*, 2085-2091.
12. Rose, J. E.; Leeson, P. D.; Gani, D. *J. Chem. Soc. Perkin Trans. 1* **1995**, 157-165.
13. Marson, C. M.; Grabowska, U.; Walsgrove, T.; Eggelston, D. S.; Baures, P. W. *J. Org. Chem.* **1994**, *59*, 284-290.

(*Received in UK* 28 *April* 1997; *revised* 30 *May* 1997; *accepted* 5 *June* 1997)