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Synthesis of spiropyrrolidines and spiropyrrolizidines by 1,3-dipolar cycloadditions of azomethine ylides to substituted α-methylene-γ-lactones

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Abstract—1,3-Dipolar cycloadditions of (*E*)- and (*Z*)-substituted α-methylene-γ-lactones with azomethine ylides derived from *N*-methyl glycine and L-proline gave the corresponding spiropyrrolidine and spiropyrrolizidine cycloadducts in good to moderate yields with various extent of stereoselectivity and regioselectivity. Cycloadditions of the azomethine ylide derived from L-proline exhibited *endo* selectivity especially in the case of (*Z*)-isomers of starting methylene lactones. Reactivity and regioselectivity were rationalized by a comparison with quantum chemical calculations (AM1). Structures of derivatives prepared were determined by NMR spectroscopy and by X-ray. © 2001 Elsevier Science Ltd. All rights reserved.

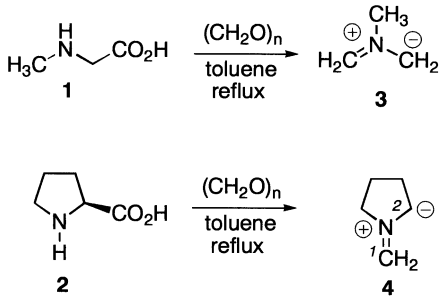
1. Introduction

α-Methylene-γ-lactone derivatives attract research chemists' attention not only as desired target molecules which offer various biological activities,[1] but also as a starting material of further possible synthetic utilization.[2] Recently, several reports on the reactivity of methylene lactones in 1,3-dipolar cycloadditions have been published dealing with additions of diazomethane,[3,4] nitrile oxides,[5–7] nitrile imines,[8,9] nitrones,[10] and nitrile ylides.[11,12] Among increasing number of studies, only two isolated examples of azomethine ylide cycloadditions to unsubstituted α-methylene-γ-butyrolactone could be found,[13,14] despite the fact that azomethine ylides represent one of the most reactive and versatile classes of 1,3-dipoles and react readily with a range of dipolarophiles forming substituted pyrrolidines.[15] Their role in pyrrolizidine and indolizidine synthesis has been reviewed recently.[16,17] Since we have been involved in α-methylene lactone chemistry for several years, we decided to look more closely at their reactivity in the 1,3-dipolar cycloaddition reactions with azomethine ylides. In this paper we report our investigation of the cycloadditions of two different azomethine ylides to (*E*)- and (*Z*)-isomers of substituted α-methylene-γ-lactones.

2. Results and discussion

Azomethine ylides can be prepared by a number of methods from more or less easy available starting materials. The 'decarboxylation route' generates them in situ by thermal decarboxylation of mixtures of α-amino acids and aldehydes.[18] Reactive azomethine ylides can then be trapped by various dipolarophiles. This convenient method was also adopted in our study using *N*-methylglycine (**1**) and L-proline (**2**) which were transformed into dipoles **3** and **4** by the reactions with paraformaldehyde in boiling toluene (Scheme 1).

A set of methylene lactone derivatives was on hand from our previous research.[19–21] Substitution at their exocyclic double bond covered a wide range of electronic effects offering a good opportunity of investigation of the reactivity towards the dipoles **3** and **4**. According to the general knowledge that electron rich dipolarophiles do not undergo



Scheme 1.

Keywords: cycloadditions; methylene lactones; azomethine ylides; regioselectivity; stereoselectivity.
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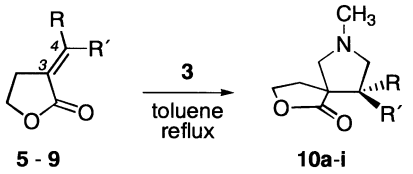


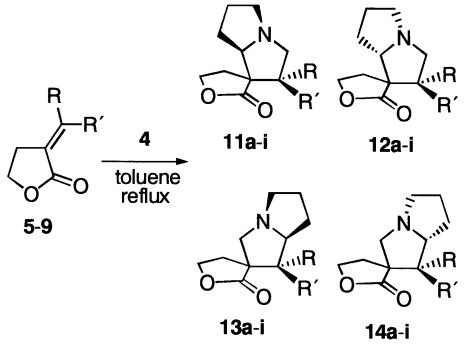
Scheme 2.

Reactivity of the dipolarophiles **5**–**9** towards **3** decreased in the following order of substituents: tosyloxy>ethynyl> 2-thienyl. The (*Z*)-isomers were less reactive than the corresponding (*E*)-isomers. Except for the thienyl derivatives, the lactones used were more reactive than the unsubstituted methylene lactone **9** (entry 9). Reaction times ranged from 2.5 h for tosylates (*E*)-**5** and (*Z*)-**5**, having the most electron

Table 1. 1,3-Dipolar cycloadditions of dipole **3** with lactones **5**–**9**

Entry	Lactone	R	R′	R. time (h)	Product	Yield (%)
1	(*E*)-**5**	Tosyloxy	H	2.5	**10a**	63
2	(*Z*)-**5**	H	Tosyloxy	4.0	**10b**	65
3	(*E*)-**6**	2-Thienyl	H	10.0	**10c**	75
4	(*Z*)-**6**	H	2-Thienyl	48	**10d**	65
5	(*E*)-**7**	C≡CPh	H	4.0	**10e**	66
6	(*Z*)-**7**	H	C≡CPh	6.0	**10f**	64
7	(*E*)-**8**	C≡CTMS	H	4.5	**10g**	68
8	(*Z*)-**8**	H	C≡CTMS	6.5	**10h**	66
9	**9**	H	H	8.0	**10i**	62

cycloaddition reactions with azomethine ylides,[22] lactones substituted with electron-donor groups such as amino, alkoxy, alkyl, and aryl were indeed found to be unreactive. On the other hand, the thermal 1,3-dipolar cycloaddition of **3** with methylene lactones **5**–**8** bearing sufficiently electron withdrawing substituents (tosyloxy, 2-thienyl, and alkynyl, respectively) on the double bond, as well as the unsubstituted methylene lactone **9**, gave corresponding cycloadducts, racemic spiropyrrolidines **10**, in good yield (Scheme 2, Table 1).



Scheme 3.

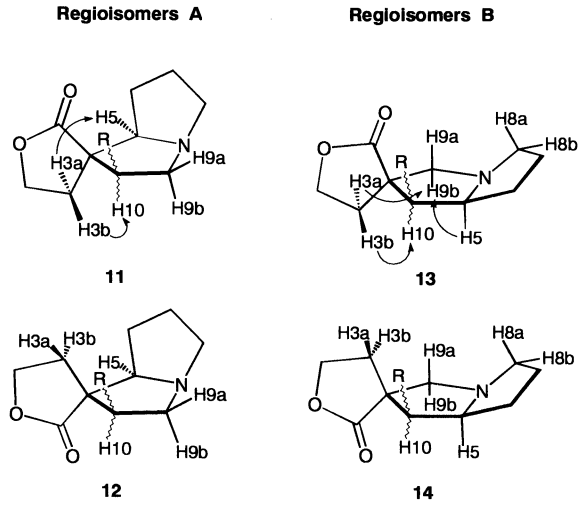
deficient double bond (entries 1 and 2), to two days for thienyl derivative (*Z*)-**6** (entry 4). Interestingly, 2-furyl derivatives, which have been tested as well, were found to be unreactive. In the reactions of propynylidene lactones ((*E*)-**7**, (*E*)-**8**, (*Z*)-**7**, and (*Z*)-**8**), the dipole **3** selectively added to the exocyclic double bond ignoring the triple bond; alkynyl substituted spiropyrrolidines **10e**–**h** were thus exclusively obtained (entries 5–8). Formation of different diastereomers in the reactions of corresponding geometric isomers of the lactones **5**–**8** indicated that the stereochemistry of the exocyclic double bond has been retained during the cycloaddition of the dipole **3**.

Cycloaddition reactions of the azomethine ylide **4** were studied with the same set of lactone dipolarophiles. As in the above case, the lactones substituted by electron-donor groups were found to be unreactive. The lactones **5**–**9**, however, reacted smoothly yielding a set of four different racemic spiropyrrolizidine cycloadducts in each reaction. The products obtained in the reactions of (*E*)-isomers differed from those prepared from the corresponding (*Z*)-isomers. This fact, caused by a lower symmetry of the dipole **4**, is apparent from Scheme 3 where **4** adds to methylene lactones with retention of starting configuration of the dipolarophile double bond. Different mutual orientations of

Table 2. 1,3-Dipolar cycloadditions of dipole **4** with lactones **5**–**9**

Entry	Lactone	R	R′	R. time (h)	Yield[a] (%)	Isomer ratio[b] (%)			
						11	**12**	**13**	**14**
a	(*E*)-**5**	Tosyloxy	H	2.0	60	57	8[c]	29	6[c]
b	(*Z*)-**5**	H	Tosyloxy	3.0	62	72	3[c]	20	5[c]
c	(*E*)-**6**	2-Thienyl	H	6.0	68	54	(4/3)	39	(4/3)
d	(*Z*)-**6**	H	2-Thienyl	15.0	66	75	(5/4)	16	(5/4)
e	(*E*)-**7**	C≡CPh	H	4.0	62	47	(6/4)	43	(6/4)
f	(*Z*)-**7**	H	C≡CPh	5.0	65	51	(4/3)	43	(4/3)
g	(*E*)-**8**	C≡CTMS	H	3.5	70	43	9	39	9
b	(*Z*)-**8**	H	C≡CTMS	4.5	67	45	(5/3)	47	(5/3)
i	**9**	H	H	9.0	60	63	(4/2)	31	(4/2)

[a] Overall isolated yields.
[b] Detected in crude reaction mixtures; values in parentheses show the ratios of peaks of the minor isomers detected by GC-MS without assignment them to the structures **12** and **14**.
[c] Determined by ^{1}H NMR.



Scheme 4.

the dipole and the lactone resulted in formation of two diastereomers of each possible regioisomer. Compounds **11** and **12** are formed by an *endo* and *exo* approach of the dipole **4** oriented by its exocyclic methylene to exocyclic methylene of the lactone, respectively. The prefixes *endo* and *exo* refer to the lactone carbonyl group. The *endo* and *exo* approaches of **4** oriented by its exocyclic methylene towards the annular carbon of the lactone double bond lead then to cycloadducts **13** and **14**, respectively (Scheme 3).

The ratios of the cycloadducts in the reaction mixtures have been determined by ^{1}H NMR spectroscopy (Table 2, entries a and b) or by GC (entries c–i). The major isomers **11a–i** and **13a–i** have successfully been isolated by column chromatography on alumina and fully characterized. Our attempts to isolate the minor isomers **12** and **14** were unsuccessful; therefore, all information about their structures has been obtained by analyses of the corresponding reaction mixtures. Since the presence of tosyloxy group in compounds **12a**,**b** and **14a**,**b** shifted the signals of hydrogen atoms H10 downfield (for numbering cf. Scheme 4), ^{1}H NMR spectra have been used to analyze the reaction mixtures in those cases. Four signals of different H10 protons have been found in the NMR spectra of each mixture. Different shapes of the signals (dd for structures **11** and **12** vs d for **13** and **14**) helped to assign them to the

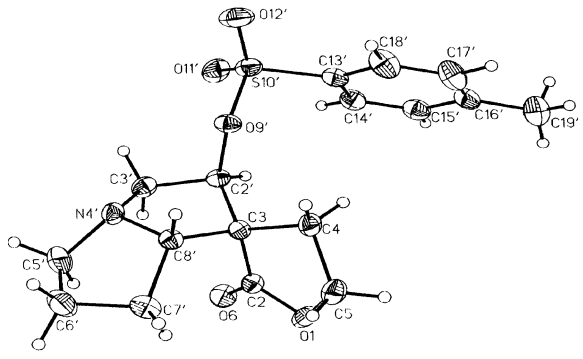


Figure 1. ORTEP representation of **11a**.

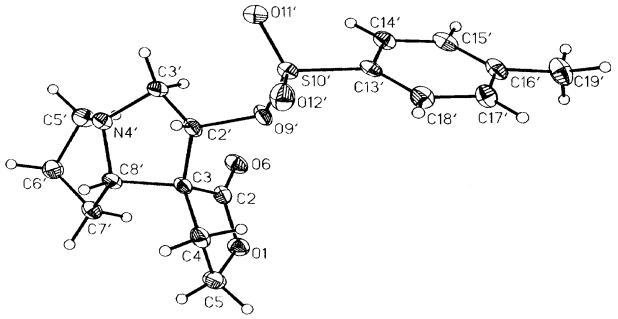


Figure 2. ORTEP representation of **11b**.

corresponding regioisomers and to determine the product ratio.

Unfortunately, similar NMR analyses of the other reaction mixtures (entries c–i) were impossible because H10 signals in the spectra overlapped with another signals of CH_2 groups. However, as proven by GC-MS analyses, in each reaction mixture, as expected, there were four different compounds present with molecular weights equal to 1:1 adducts of **4** and the corresponding lactones. Of course, this information was not sufficient to assign the minor peaks to the structures **12** and **14**. Therefore, only peak ratios are listed in the Table 2 at corresponding columns (cf. note b of Table 2).

3. Assignment of configurations by means of ^{1}H NMR spectroscopic data

1D and 2D NMR experiments have been the main tools of elucidation of the major cycloadduct structures. The basic differences identifying the both types of regioisomers (**A** vs **B**, Scheme 4), the multiplicity of H10 NMR signals, have already been mentioned. Splitting of H5 signals was an additional feature characterizing the regioisomers. These signals were triplets due to coupling with H6a and H6b in the compounds of the type **A**, whereas an additional coupling with H10 resulted in appearance of more complex multiplets observed in **B** type regioisomers. Supporting evidence for the **B** type isomers is the presence of AB systems of H9a and H9b protons, which gave, on the other hand, more complicated multiplets in the spectra of the regioisomers **A**.

Stereochemistry of the isolated cycloadducts was studied by NOESY experiments. All major regioisomers of the type **A** were found to have structure **11**. Our assignment was mainly based on positive NOE between hydrogens H5 and H3a (for numbering cf. Scheme 4) detected in NOESY spectra of these diastereomers. No interactions, which would support the structure **12**, were observed. The NMR based structure assignments were also confirmed by X-ray analyses of the tosyloxy substituted spiropyrrolizidines **11a** and **11b**. (Figs. 1 and 2, respectively)

Structures of the **B** type major regioisomers were assigned by means of NOE between H3a and H9b, and between H5 and H9b protons. Positive NOE detected these protons to be located on the same side of the pyrrolizidine ring system,

Table 3. Dihedral angles Φ(H5–C5–C10–H10) calculated by AM1 and a comparison of the vicinal coupling constants ^3J(H5–H10) determined by NMR ($^3J_{exp}$) and calculated from the Karplus equation ($^3J_{calcd}$) in **13a–h**

Cycloadduct	$^3J_{exp}$ (Hz)	Φ (°) (AM1)	$^3J_{calcd}$ (Hz)
13a	7.3	150.9	7.4
13b	4.7	36.3	5.2
13c	9.9	169.7	8.9
13d	8.7	25.2	6.6
13e	9.6	172.4	9.1
13f	7.1	25.5	6.6
13g	9.9	171.6	9.0
13h	7.0	24.5	6.7

which corresponded to the structure of the diastereomer **13** (Scheme 4).

The relative configuration of proton H10 in the major isomers has also been obvious from NOESY spectra. Significant H10–H3b NOE interactions have been found in all the derivatives prepared from (*Z*)-substituted dipolarophiles, while H10–H6a NOEs were detected in the cycloadducts isolated from the reactions of (*E*)-substituted lactones. Different geometry of starting lactone could also be traced with the help of vicinal spin–spin coupling constants of protons H5 and H10 in the adducts **13a–h**. The (*Z*)-isomer adducts gave lower coupling constants than the (*E*)-isomer. The constants are in good agreement with those calculated from the Karplus equation[23] using dihedral angles obtained from AM1 optimized models[24] of **13** (Table 3).

4. Comparison of quantum chemical results

We also compared our experimentally obtained results with predictions based on semiempirical quantum-chemical calculations (AM1).[24] It is a generally accepted estimation that 1,3-dipolar cycloaddition reactions of unstabilized azomethine ylides are controlled by HOMO(dipole)–LUMO(dipolarophile) interactions.[25] Our results (Table 4) confirmed this, too. The calculated HOMO energy of the ylide **4** is higher than that of **3** according to the higher reactivity of **4** in the cycloadditions. The order of the methylene lactone dipolarophile reactivities follows their LUMO energies: the lower LUMO energy the higher reactivity. An exception is the unsubstituted methylene lactone **9** that exhibits a slightly higher reactivity than that expected from its LUMO energy. The reason lies probably in the lower steric demand of its less substituted double bond.

Table 4. HOMO and LUMO energies (E_{HO} and E_{LU}, respectively) of the dipoles **3** and **4**, and the dipolarophiles **5–9**; absolute values of coefficients of the corresponding orbitals ($c^H{}_i$ and $c^L{}_i$) at interacting atoms *i*

Compound	E_{HO} (eV)	$c^H{}_1$	$c^H{}_2$	E_{LU} (eV)	$c^L{}_3$	$c^L{}_4$
3	−7.12	–	–	1.16	–	–
4	−6.88	0.39	0.42	1.06	–	–
(*E*)-**5**	−9.81	–	–	−1.42	0.27	0.19
(*Z*)-**5**	−9.94	–	–	−1.14	0.31	0.23
(*E*)-**6**	−9.31	–	–	−1.00	0.26	0.21
(*Z*)-**6**	−9.18	–	–	−0.91	0.39	0.31
(*E*)-**7**	−9.29	–	–	−1.02	0.18	0.14
(*Z*)-**7**	−9.01	–	–	−0.95	0.31	0.29
(*E*)-**8**	−10.06	–	–	−0.93	0.22	0.19
(*Z*)-**8**	−9.93	–	–	−0.89	0.55	0.51
9	−10.80	–	–	−0.88	0.14	0.09

For atom numbering see Schemes 1 and 3.

An examination of orbital coefficients c_i^H and c_i^L of interacting HOMO(dipole) and LUMO(dipolarophile), respectively, at the reacting atoms (*i*) predicts, according to second-order perturbation theory,[26] the regioselectivity of the dipole **4** cycloadditions in a good agreement with experiment. The prediction failed only with propynylidene lactone (*Z*)-**8** but the difference was in the range of experimental error.

Both regioisomeric approaches of the ylide **4** preferred remarkably the *endo* orientation, relatively to the lactone carbonyl, which resulted in the formation of the major diastereomers **11** and **13**. This *endo* selectivity could be explained by a repulsion of methylene hydrogens of ylide and hydrogens located in the β and γ-positions of the lactone ring in the *exo* transition state. The *endo* transition states yielding diastereomers **11** could, moreover, be stabilized by a weak hydrogen bond of ylide protons with lactone carbonyl oxygen.[27,28] No additional experiments or calculations were carried out to prove this presumption, however.

5. Conclusion

The results obtained in this study show that spiropyrrolidines and spiropyrrolizidines can be prepared in 1,3-dipolar cycloadditions of azomethine ylides to α-methylene-γ-lactones either unsubstituted, or substituted on the double bond with sufficiently electron withdrawing substituents. In these reactions, the configuration of the dipolarophile double bond is retained. The unsymmetrical azomethine ylide derived from L-proline remarkably prefers the *endo* access to the dipolarophile. This *endo* preference increases in the reactions of (*Z*)-isomers of the substituted methylene lactones. Regiochemistry of the cycloadditions is in good agreement with semiempirical quantum chemical calculations at the AM1 level.

6. Experimental

6.1. General

Melting points were obtained on a Kofler block and are uncorrected. ^{1}H and ^{13}C NMR spectra were obtained on an Avance Bruker DRX 500 (500 MHz) and Avance Bruker 300 (300 MHz) spectrometer in deuteriochloroform with tetramethylsilane as an internal standard. Ultraviolet spectra were recorded on an UV–VIS spectrophotometer UV-101 Shimadzu in ethanol. IR spectra were measured on a Genesis series FTIR, ATI Matson spectrometer in the KBr (pellets) or neat. Elemental analyses were performed by LACHEMA Brno. Toluene was dried by azeotropic distillation and stored over sodium. Literature procedures were used for the preparations of (*E*)- and (*Z*)-3-(tosyloxymethylene)tetrahydrofuran-2-ones.[21] Commercially available *N*-methyl glycine and L-proline (Aldrich) were used as purchased, without further purification.

6.2. General procedure for cycloaddition of azomethine ylide 3 to methylene lactones 5–9

A 100 ml round bottom flask, equipped with a condenser and an air moisture-impermeable seal, was charged with lactone (2 mmol), sarcosine (0.35 g, 4 mmol) and paraformaldehyde (0.24 g, 8 mmol). The reaction mixture was refluxed in dry toluene (60 ml) until the starting lactone was consumed. Toluene was removed in vacuo. Residue was redissolved in chloroform, the solution filtered to remove a precipitate and dried over $MgSO_4$. After filtration and solvent removal at reduced pressure, the crude product was separated by column chromatography on alumina usually in diethyl ether (other eluents are noted below).

6.2.1. (5*R,9*S**)-7-Methyl-1-oxo-2-oxa-7-azaspiro[4.4]non-9-yl tosylate (10a).** Yield 0.41 g (63%) of a white solid, mp 91–92°C; [Found: C, 55.05; H, 6.12; N, 4.42. $C_{15}H_{19}NO_5S$ requires C, 55.37; H, 5.89; N, 4.30%]; LC in dichloromethane; ν_{max}(KBr) 2959, 2792, 1766, 1595, 1454, 1363, 1236, 1181, 1019, 819, 664, 554 cm^{-1}; δ_H 7.79 (2H, d, *J*=7.8 Hz, *o-H*-Ts), 7.36 (2H, d, *J*=7.8 Hz, *m-H*-Ts), 5.02 (1H, dd, *J*=6.3, 3.5 Hz, C*H*), 4.34 (1H, m, CH_2O), 4.23 (1H, m, CH_2O), 2.89 (2H, m, CHCH_2N), 2.86 (1H, m, $OCH_2CH_aH_b$), 2.81 (2H, m, CCH_2N), 2.70 (3H, s, N-*Me*), 2.46 (3H, s, *Me*), 2.22 (1H, m, $OCH_2CH_aH_b$); δ_C(75.47 MHz) 178.4, 145.5, 132.8, 130.1, 128.0, 81.9, 66.5, 64.2, 61.0, 52.6, 41.5, 30.5, 21.7; λ_{max} 273, 263, 226 nm.

6.2.2. (5*R,9*R**)-7-Methyl-1-oxo-2-oxa-7-azaspiro[4.4]non-9-yl tosylate (10b).** Yield 0.42 g (65%) of white solid, mp 88–89°C (petroleum ether); [Found: C, 55.28; H, 5.83; N, 4.16. $C_{15}H_{19}NO_5S$ requires C, 55.37; H, 5.89; N, 4.30%]; LC in dichloromethane; ν_{max}(KBr) 2972, 2801, 1775, 1596, 1453, 1362, 1186, 1017, 888, 662, 558 cm^{-1}; δ_H 7.78 (2H, d, *J*=7.8 Hz, *o-H*-Ts), 7.35 (2H, d, *J*=7.8 Hz, *m-H*-Ts), 4.91 (1H, t, *J*=6.6 Hz, C*H*), 4.26 (2H, m, CH_2O), 3.04 (1H, dd, *J*=9.9, 6.6 Hz, CHCH_aH_bN), 3.02 (1H, d, *J*=9.6 Hz, CCH_aH_bN), 2.72 (1H, d, *J*=9.5 Hz, CCH_aH_bN), 2.63 (1H, dd, *J*=9.9, 6.6 Hz, CHCH_aH_bN), 2.44 (3H, s, Me), 2.41 (1H, m, $OCH_2CH_aH_b$), 2.34 (1H, m, $OCH_2CH_aH_b$), 2.33 (3H, s, N*Me*); δ_C(75.47 MHz) 175.1, 145.5, 132.9, 130.0, 128.0, 82.9, 65.1, 63.2, 60.2, 52.2, 41.7, 35.8, 21.7; λ_{max} 274.0, 263.4, 224.6 nm.

6.2.3. (5*R,9′*S**)-7-Methyl-9-(2-thienyl)-2-oxa-7-azaspiro[4.4]nonan-1-one (10c).** Yield 0.36 g (75%), colorless oil; [Found: C, 60.63; H, 6.28; N, 6.12. $C_{12}H_{15}NO_2S$ requires C, 60.73, H, 6.37, N, 5.90%]; ν_{max}(liquid film) 2937, 2784, 1766, 1449, 1371, 1169, 1024, 700 cm^{-1}; δ_H 7.20 (1H, d, *J*=4.9 Hz, H5-thienyl), 6.95 (1H, m, H4-thienyl), 6.89 (1H, d, *J*=3.3 Hz, H3-thienyl), 4.08 (2H, m, CH_2O), 3.88 (1H, m, CH), 3.13 (1H, m, CHCH_aH_bN), 3.03 (1H, m, CHCH_aH_bN), 2.99 (1H, d, *J*=9.4 Hz, CCH_aH_bN), 2.82 (1H, d, *J*=9.4 Hz, CCH_aH_bN), 2.45 (3H, s, Me), 2.02 (2H, m, OCH_2CH_2); δ_C(75.47 MHz) 179.4, 141.2, 125.5, 125.1, 123.8, 65.4, 65.0, 61.3, 52.6, 45.6, 40.8, 32.2; λ_{max} 309.4, 250.6 nm.

6.2.4. (5*R,9′*R**)-7-Methyl-9-(2-thienyl)-2-oxa-7-azaspiro[4.4]nonan-1-one (10d).** Yield 0.30 g (65%), colorless oil; [Found: C, 60.53; H, 6.62; N, 5.68. $C_{12}H_{15}NO_2S$ requires C, 60.73; H, 6.37; N, 5.90%.]; ν_{max}(liquid film) 2938, 2785, 1766, 1474, 1372, 1246, 1177, 1025, 701 cm^{-1}; δ_H(500 MHz) 7.17 (1H, dd, *J*=4.9, 1.3 Hz, H5-thienyl), 6.97 (1H, br d, *J*=3.6 Hz, H3-thienyl), 6.93 (1H, dd, *J*=4.9, 3.6 Hz, H4-thienyl), 4.17–4.07 (1H, m, OCH_aH_b), 4.03–3.93 (1H, m, OCH_aH_b), 3.71 (1H, dd, *J*=10.9, 6.6 Hz, CH), 3.22 (1H, dd, *J*=9.2, 6.6 Hz, CHCH_aH_bN), 3.06 (1H, d, *J*=10.2 Hz, CCH_aH_bN), 3.03 (1H, d, *J*=10.2 Hz, CCH_aH_bN), 2.95 (1H, dd, *J*=10.9, 9.2 Hz, CH_2), 2.48 (2H, m, OCH_2CH_2), 2.45 (3H, s, Me); δ_C(75.47 MHz) 178.8, 139.2, 127.4, 126.0, 124.7, 65.4, 65.2, 62.8, 54.3, 51.2, 42.1, 37.2; λ_{max} 309.4, 250.6 nm.

6.2.5. (5*R,9*S**)-7-Methyl-9-(2-phenylethynyl)-2-oxa-7-azaspiro[4.4]nonan-1-one (10e).** Yield 0.34 g (66%), colorless oil; [Found: C, 75.06; H, 6.82; N, 5.91. $C_{16}H_{17}NO_2$ requires C, 75.26; H, 6.71; N, 5.49%]; ν_{max}(liquid film) 2941, 2785, 2227, 1770, 1489, 1444, 1373, 1166, 1025, 758, 691 cm^{-1}; δ_H(500 MHz) 7.40–7.37 (2H, m, *o*-H-Ph), 7.28–7.32 (3H, m, *p*,*m*-H-Ph), 4.46–4.40 (1H, m, OCH_aH_b), 4.22–4.25 (1H, m, OCH_aH_b), 3.65 (1H, t, *J*=7.7 Hz, CH), 3.11 (1H, pt, *J*=8.8 Hz, CHCH_aH_bN), 3.01 (2H, d, *J*=9.5 Hz, CCH_aH_bN), 2.95–2.88 (1H, m, $OCH_2CH_aH_b$), 2.88 (1H, dd, *J*=8.9, 7.7 Hz, CHCH_aH_bN), 2.65 (2H, d, *J*=9.5 Hz, CCH_aH_bN), 2.40 (3H, s, Me), 2.25 (1H, m, $OCH_2CH_aH_b$); δ_C(75.47 MHz) 180.2, 131.6, 128.4, 128.3, 122.9, 86.7, 85.4, 66.4, 65.5, 62.2, 51.5, 41.8, 38.6, 33.2; λ_{max} 251.3, 245.1 nm.

6.2.6. (5*R,9*R**)-7-Methyl-9-(2-phenylethynyl)-2-oxa-7-azaspiro[4.4]nonan-1-one (10f).** Yield 0.33 g (64%), colorless oil; [Found: C, 74.99; H, 6.66; N, 5.28. $C_{16}H_{17}NO_2$ requires C, 75.26; H, 6.71; N, 5.49%]; ν_{max} (liquid film) 2940, 2911, 2789, 2227, 1768, 1487, 1448, 1372, 1175, 1024, 758, 693, 534 cm^{-1}; δ_H(500 MHz) 7.43–7.36 (2H, m, *o*-H-Ph), 7.30–7.24 (3H, m, *p*,*m*-H-Ph), 4.45–4.26 (2H, m, CH_2O), 3.25 (1H, d, *J*=11.6 Hz, CHCH_aH_bN), 3.23 (1H, d, *J*=12 Hz, CHCH_aH_bN), 3.01 (1H, d, *J*=9.9 Hz, CCH_aH_bN), 2.97 (1H, d, *J*=9.9 Hz, CCH_aH_bN), 2.68 (1H, dd, *J*=11.5, 12.6 Hz, CH) 2.49–2.42 (2H, m, OCH_2CH_2), 2.42 (3H, s, Me); δ_C(75.47 MHz) 178.5, 131.9, 128.43, 128.39 122.9, 85.5, 85.3, 65.6, 64.3, 61.8, 53.9, 41.8, 41.7, 37.9; λ_{max} 255.1, 272.7, 279.3 nm.

6.2.7. (5*R,9*S**)-7-Methyl-9-(2-trimethylsilylethynyl)-2-oxa-7-azaspiro[4.4]nonan-1-one (10g).** Yield 0.34 g (68%), colorless oil; [Found: C, 62.08; H, 8.82; N, 5.71. $C_{13}H_{21}NO_2Si$ requires C, 62.11; H, 8.42; N, 5.57%]; ν_{max} (liquid film) 2981, 2856, 2773, 2222.6, 1776, 1577, 1436, 1389, 1253, 1175, 1126, 856, 769, 691 cm^{-1}; δ_H(300 MHz) 4.38–4.26 (2H, m, CH_2O), 3.15 (1H, dd, *J*=8.7, 6.7 Hz, CHCH_aH_bN), 3.10 (1H, dd, *J*=9.9, 6.0 Hz, CHCH_aH_bN), 3.05 (1H, d, *J*=9.3 Hz, CCH_aH_bN), 2.93 (1H, d, *J*=9.3 Hz, CCH_aH_bN), 2.59 (1H dd, *J*=10.1, 8.8 Hz, CH), 2.43–2.39 (m, 2H, OCH_2CH_2), 2.39 (3H, s, NMe), 0.15 (s, 9H, TMS); δ_C(75.47 MHz) 179.5, 105.5, 93.9, 66.4, 63.7, 62.9, 56.1, 43.1, 42.1, 33.8, 0.08; λ_{max} 272.1, 252.0, 244.1 nm.

6.2.8. (5*R,9*R**)-7-Methyl-9-(2-trimethylsilylethynyl)-2-oxa-7-azaspiro[4.4]nonan-1-one (10h).** Yield 0.33 g (67%) colorless oil; [Found: C, 62.31; H, 8.28; N, 5.53.

$C_{13}H_{21}NO_2Si$ requires C, 62.11; H, 8.42; N, 5.57%]; ν_{max} (liquid film) 2959, 2742, 2787, 2181, 1772, 1476, 1451, 1372, 1175, 1120, 843, 651 cm^{-1}; δ_H(300 MHz) 4.29–4.17 (2H, m, CH_2O), 3.05 (1H, dd, J=8.7, 6.7 Hz, CHCH_aH_bN), 2.95 (1H, dd, J=10.7, 6.6 Hz, CHCH_aH_bN), 2.87 (1H, d, J=9.9 Hz, CCH_aH_bN), 2.82 (1H, d, J=9.9 Hz, CCH_aH_bN), 2.48 (1H, dd, J=10.7, 8.8 Hz, CH), 2.40–2.31 (2H, m, OCH_2CH_2), 2.30 (3H, s, NMe), 0.05 (9H, s, TMS); δ_C(75.47 MHz) 178.3, 102.5, 89.9, 65.4, 62.5, 61.7, 54.0, 42.1, 41.8, 37.8, 0.02; λ_{max} 276.2, 251.0, 245.2 nm.

6.2.9. 7-Methyl-2-oxa-7-azaspiro[4.4]nonan-1-one (10i). Yield 0.19 g (62%), colorless oil; [Found: C, 61.71; H, 8.62; N, 8.87. $C_8H_{13}NO_2$ requires C, 61.91; H, 8.44; N, 9.03%]; ν_{max}(liquid film) 2945, 2789, 1769, 1451, 1373, 1249, 1175, 1152, 1021, 683 cm^{-1}; δ_H(300 MHz) 4.16–4.01 (2H, m, CH_2O), 2.70 (1H, dt, J=8.3, 4.4 Hz, CHCH_aH_bN), 2.58 (1H, d, J=9.4 Hz, CCH_aH_bN), 2.49 (1H, d, J=9.4 Hz, CCH_aH_bN), 2.35 (1H, pq, J=8.2 Hz, CHCH_aH_bN), 2.25–2.04 (3H, m, OCH_2CH_2, CC$H_aH_bCH_2$N), 2.21 (3H, t, NMe) 1.70 (1H, dt, J=12.6, 7.6 Hz, CC$H_aH_bCH_2$N); δ_C(75.47 MHz) 181.4, 65.8, 65.2, 56.1, 48.5, 41.9, 37.9, 36.6; λ_{max} 314.4, 244.4 nm.

6.3. Reactions of azomethine ylide 4 with lactones 5–9

The general procedure for the reactions of **3** was followed using L-proline instead. Four spiropyrrolizidine isomers **11**–**14** were detected in each reaction mixture. The major isomers **11** and **13** were isolated by column chromatography on alumina using diethyl ether as an eluent if not stated otherwise. Reaction times and isomer ratios in the crude reaction mixtures are given in Table 2.

6.3.1. (1′*R,2′*S**,7a′*S**)-2-Oxohexahydrospiro[furan-3(3*H*),1′-pyrrolizine]-2′-yl tosylate (11a).** Yield 0.21 g (30%), white solid, mp 102–103°C (petroleum ether); [Found: C, 58.23; H, 6.25; N, 3.83. $C_{17}H_{21}NO_5S$ requires C, 58.10; H, 6.02; N, 3.99%]; ν_{max}(KBr) 2965, 2943, 2868, 2809, 1762, 1598, 1369, 1188, 1019, 899, 666, 560 cm^{-1}; δ_H(500 MHz) 7.71 (2H, d, J=7.8 Hz, *o*-H-Ts), 7.29 (2H, d, J=7.8 Hz, *m*-H-Ts), 5.03 (1H, dd, J=4.6, 2.9 Hz, H-10), 4.28 (1H, dt, J=6.4, 2.6 Hz, OCH_aH_b), 4.08 (1H, m, OCH_aH_b), 3.62 (1H, t, J=7.3 Hz, H-5), 3.11 (1H, dd, J=12.1, 4.8 Hz, H-9a), 2.97 (1H, dd, J=12.1, 2.8, H-9b), 2.94 (1H, m, H-8a), 2.64 (1H, m, H-3a), 2.49 (1H, m, H-8b), 2.38 (3H, s, Me), 2.11 (1H, m, H-3b), 1.99 (3H, m, H-6a,7ab), 1.86 (1H, m, H-6b); δ_C(75.47 MHz) 176.5, 145.3, 133.3, 130.0, 127.9, 85.9, 71.9, 65.8, 58.4, 55.8, 54.8, 30.9, 27.9, 27.8, 21.6; λ_{max} 274.0, 263.0, 243.0 nm.

6.3.2. (1′*R,2′*S**,7a′*S**)-2-Oxohexahydrospiro[furan-3(3*H*),2′-pyrrolizine]-1′-yl tosylate (13a).** Yield 0.08 g (11%), white solid. mp 77–78°C (petroleum ether); [Found: C, 57.98; H, 6.19; N, 3.92. $C_{17}H_{21}NO_5S$ requires C, 58.10; H, 6.02; N, 3.99%]; ν_{max}(KBr) 2969, 2876, 2822, 1767, 1599, 1362, 1183, 1030, 1005, 853, 670, 557 cm^{-1}; δ_H(300 MHz) 7.71 (2H, d, J=7.8 Hz, *o*-H-Ts), 7.30 (2H, d, J=7.8 Hz, *m*-H-Ts), 4.57 (1H, d, J=7.6 Hz, H-10), 4.34–4.29 (1H, m, OCH_aH_b), 4.29–4.23 (1H, m, OCH_aH_b), 3.49 (1H, dd, J=12.2, 7.0 Hz, H-5), 3.25 (1H, d, J=10.6 Hz, H-9a), 3.00 (1H, d, J=10.6 Hz, H-9b), 3.00–2.93 (1H, m, H-8a), 2.90–2.84 (1H, m, H-8b), 2.73–2.67 (1H, m, H-3a), 2.55 (3H, s, Me), 2.40–2.34 (1H, m, H-3b), 1.91–1.89 (3H, m, H-6a,b, H-7a), 1.67–1.61 (1H, m, H-7b); δ_C(75.47 MHz) 176.8, 145.8, 132.2, 130.1, 128.2, 85.5, 68.2, 66.4, 61.2, 54.7, 53.8, 29.3, 28.5, 25.3, 21.7; λ_{max} 274.0, 263.4, 243.5 nm.

6.3.3. (1′*R,2′*R**,7a′*S**)-2-Oxohexahydrospiro[furan-3(3*H*),1′-pyrrolizine]-2′-yl tosylate (11b).** Yield 0.25 g (35%), white solid, mp 114–116°C (petroleum ether); [Found: C, 58.31; H, 6.22; N, 4.36. $C_{17}H_{21}NO_5S$ requires C, 58.10; H, 6.02; N, 3.99%]; ν_{max}(KBr) 2953, 2864, 2811, 1756, 1339, 1190, 1019, 1173, 1113, 999, 863, 789, 566 cm^{-1}; δ_H(300 MHz) 7.76 (2H, d, J=7.8 Hz, *o*-H-Ts), 7.32 (2H, d, J=7.8 Hz, *m*-H-Ts), 5.13 (1H, dd, J=9.8, 6.9 Hz, H-10), 4.32–4.26 (1H, m, OCH_aH_b), 4.18–4.11 (1H, m, OCH_aH_b), 3.49 (1H, t, J=7.7 Hz, H-5), 3.07–2.99 (2H, m, H-9b,8b), 2.94–2.89 (1H, m, H-9a), 2.68–2.61 (1H, m, H-8a), 2.55–2.45 (1H, m, H-3b), 2.42 (3H, s, Me), 2.25–2.18 (1H, m, H-3a), 2.05–1.97 (1H, m, H-7a), 1.90–1.82 (1H, m, H-6b), 1.82–1.73 (1H, m, H-7b), 1.68–1.58 (1H, m, H-6a); δ_C(75.47 MHz) 174.2, 145.3, 133.0, 129.9, 127.8, 83.8, 69.2, 65.3, 54.7, 54.6, 54.0, 31.1, 27.6, 27.3, 21.6; λ_{max} 274.0, 263.4, 256.8 nm.

6.3.4. (1′*R,2′*R**,7a′*R**)-2-Oxohexahydrospiro[furan-3(3*H*),2′-pyrrolizine]-1′-yl tosylate (13b).** Yield 0.063 g (9%), white solid, mp 166–167°C (petroleum ether); [Found: C, 58.22; H, 5.86; N, 3.89. $C_{17}H_{21}NO_5S$ requires C, 58.10; H, 6.02; N, 3.99%]; ν_{max}(KBr) 2979, 2822, 1759, 1595, 1360, 1178, 1127, 1021, 901, 675, 555 cm^{-1}; δ_H(300 MHz) 7.83 (2H, d, J=7.8 Hz, *o*-H-Ts), 7.36 (2H, d, J=7.8 Hz, *m*-H-Ts), 4.80 (1H, d, J=4.7 Hz, H-10), 4.34–4.28 (1H, m, OCH_aH_b), 4.19 (1H, pseudo q, J=9.0 Hz, OCH_aH_b), 3.81–3.75 (1H, m, H-5), 3.23 (1H, d, J=10.2 Hz, H-9a), 3.12 (1H, d, J=10.2 Hz, H-9b), 2.94–2.88 (1H, m, H-8a), 2.64–2.58 (1H, m, H-8b), 2.38 (3H, s, Me), 2.32–2.28 (2H, m, H-3a,b), 1.95–1.62 (4H, H-6a,b, H-7a,b); δ_C(75.47 MHz) 176.5, 145.3, 133.3, 130.0, 127.9, 85.9, 71.9, 65.8, 58.4, 55.8, 54.8, 30.9, 27.9, 27.8, 21.6; λ_{max} 273.9, 263.6, 243.3 nm.

6.3.5. (1′*R,2′*R**,7a′*R**)-2′-(2-Thienyl)hexahydrospiro-[furan-3(3*H*),1′-pyrrolizine]-2-one (11c).** Yield 0.14 g (26%), colorless oil; [Found: C, 63.93; H, 6.13; N, 5.65. $C_{14}H_{17}NO_2S$ requires C, 63.85; H, 6.51; N, 5.32%]; ν_{max} (liquid film) 2958, 2868, 1761, 1450, 1371, 1169, 1024, 850, 701 cm^{-1}; δ_H(500 MHz) 7.20 (1H, d, J=4.9 Hz, H5-thienyl), 6.97–6.93 (1H, m, H4-thienyl), 6.89 (1H, d, J=3.3 Hz, H3-thienyl), 4.16–4.06 (2H, m, CH_2O), 4.00 (1H, t, J=8.2 Hz, H-10), 3.66 (1H, t, J=6.2 Hz, H-5), 3.35–3.27 (2H, m, H-9a,b), 3.23–3.17 (1H, m, H-8a), 2.71–2.63 (1H, m, H-8b), 2.21–2.09 (1H, m, H-3a), 2.04–1.92 (2H, m, H-3b,6a), 1.92–1.80 (3H, m, H-6b,7a,b); δ_C(75.47 MHz) 178.7, 140.5, 127.0, 125.7, 124.6, 72.9, 65.5, 59.2, 56.6, 56.0, 44.9, 31.9, 29.0, 26.9; λ_{max} 251.5, 308.0 nm.

6.3.6. (1′*R,2′*R**,7a′*S**)-1′-(2-Thienyl)hexahydrospiro-[furan-3(3*H*),2′-pyrrolizin]-2-one (13c).** Yield 0.12 g (22%), colorless oil; [Found: C, 63.69; H, 6.32; N, 5.60. $C_{14}H_{17}NO_2S$ requires C, 63.85; H, 6.51; N, 5.32%]; ν_{max} (liquid film) 2957, 2869, 1763, 1449, 1374, 1181, 1099, 1024, 799, 700, 649 cm^{-1}; δ_H(300 MHz) 7.22 (1H, d,

J=4.9 Hz, H5-thienyl), 6.97 (1H, m, H4-thienyl), 6.91 (1H, d, J=3.3 Hz, H3-thienyl), 4.16–4.04 (1H, m, OCH_aH_b), 3.90–3.80 (1H, m, H-10), 3.69–3.62 (1H, m, OCH_aH_b), 3.62 (1H, d, J=10.8 Hz, H-5), 3.27 (1H, d, J=9.7 Hz, H-9a), 3.04 (1H, d, J=9.7 Hz, H-9b), 3.05–2.96 (1H, m, H-8a), 2.81–2.72 (1H, m, H-8b), 2.40–2.30 (1H, m, H-3a), 2.26–2.17 (1H, m, H-3b), 2.05–1.82 (3H, m, H-6a,b, H-7a), 1.74–1.62 (1H, m, H-7b); δ_C(75.47 MHz) 179.1, 139.1, 127.4, 126.0, 124.7, 69.5, 66.0, 64.1, 56.8, 55.3, 52.7, 30.7, 29.9, 26.0; λ_{max} 251.0, 305.5 nm.

6.3.7. (1′*R,2′*S**,7a′*R**)-2′-(2-Thienyl)hexahydrospiro-[furan-3(3*H*),1′-pyrrolizine]-2-one (11d).** Yield 0.21 g (40%), colorless oil; [Found: C, 63.99; H, 6.68; N, 5.59. $C_{14}H_{17}NO_2S$ requires C, 63.85; H, 6.51; N, 5.32%]; ν_{max} (liquid film) 2937, 2869, 1758, 1451, 1374, 1291, 1214, 1171, 1027, 851, 702 cm^{-1}; δ_H(300 MHz) 7.16 (1H, dd, J=5.2, 1.1 Hz, H5-thienyl), 6.99 (1H, broad d, J=3.2 Hz, H3-thienyl), 6.93 (1H, dd, J=3.3, 5.2 Hz, H4-thienyl), 4.02 (1H, dt, J=6.4, 8.5 Hz, OCH_aH_b), 3.93 (1H, t, J=9.6 Hz, H-10), 3.88 (1H, t, J=7.6 Hz, H-5), 3.79 (1H, dt, J=6.4, 8.5 Hz, OCH_aH_b), 3.52 (2H, d, J=9.6 Hz, H-9a,b), 3.19–3.10 (1H, m, H-8a), 2.88 (1H, dt, J=5.8, 9.4 Hz, H-8b), 2.50–2.38 (1H, m, H-3a), 2.35–2.20 (1H, m, H-3b), 2.20–2.07 (1H, m, H-7a), 2.05–1.89 (2H, m, H-6a,7b), 1.76–1.61 (1H, m, H-6b); δ_C(75.47 MHz) 176.7, 137.2, 127.3, 126.4, 124.9, 73.3, 65.5, 58.4, 56.3, 54.4, 51.9, 31.8, 28.7, 27.2; λ_{max} 253.0, 306.5 nm.

6.3.8. (1′*R,2′*S**,7a′*R**)-1′-(2-Thienyl)hexahydrospiro-[furan-3(3*H*),2′-pyrrolizine]-2-one (13d).** Yield 0.041 g (8%), colorless oil; [Found: C, 64.16; H, 6.46; N, 5.19. $C_{14}H_{17}NO_2S$ requires C, 63.85; H, 6.51; N, 5.32%]; ν_{max} (liquid film) 2972, 2933, 1763, 1463, 1363, 1215, 1179, 911, 531 cm^{-1}; δ_H(300 MHz) 7.15 (1H, dd, J=1.2, 5.3 Hz, H5-thienyl), 6.90 (1H, br d, J=3.5 Hz, H3-thienyl), 6.87 (1H, dd, J=3.5, 5.3 Hz, H4-thienyl), 3.95–3.75 (2H, m, OCH_2), 3.91 (1H, buried d, J=7.6 Hz, H-10), 3.54 (1H, d, J=9.1 Hz, H-9a), 3.49 (1H, pseudo q, J=7.6 Hz, H-5), 3.47 (1H, d, J=9.1 Hz, H-9b), 3.06–2.95 (1H, m, H-8a), 2.83–2.75 (1H, m, H-8b), 2.50–2.39 (1H, m, H-3a), 2.30–2.21 (1H, m, H-3b), 2.20–2.10 (1H, m, H-7a), 1.91 (2H, m, H-6a, H-7b), 1.78–1.66 (1H, m, H-6b); δ_C(75.47 MHz) 176.8, 137.9, 127.2, 126.3, 124.7, 73.6, 65.3, 58.8, 56.6, 54.5, 52.1, 32.1, 28.7, 27.4; λ_{max} 251.5, 325.5 nm.

6.3.9. (1′*R,2′*R**,7a′*R**)-2′-(2-Phenylethynyl)hexahydrospiro[furan-3(3*H*),1′-pyrrolizine]-2-one (11e).** Yield 0.11 g (19%), colorless oil; [Found: C, 76.59; H, 6.65; N, 4.63. $C_{18}H_{19}NO_2$ requires C, 76.84; H, 6.81; N, 4.98%]; ν_{max}(liquid film) 2952, 2900, 2863, 2178, 1765, 1431, 1356, 1232, 1199, 1066, 1029, 736, 690 cm^{-1}; δ_H(500 MHz) 7.43–7.37 (2H, m, *o*-H-Ph), 7.33–7.26 (3H, m, *p*,*m*-H-Ph), 4.44 (1H, dt, J=9.1, 2.3 Hz, OCH_aH_b), 4.25 (1H, dt, J=6.4, 9.2 Hz, OCH_aH_b), 3.68 (1H, t, J=7.3 Hz, H-5), 3.60 (1H, dd, J=9.7, 7.0 Hz, H-10), 3.30 (1H, dd, J=7.0, 11.4 Hz, H-9a), 3.24–3.16 (1H, m, H-8a), 3.17 (1H, dd, J=7.0, 11.4 Hz, H-9b), 2.88 (1H, ddd, J=8.8, 10.2, 12.9 Hz, H-3a), 2.64 (1H, m, H-8b), 2.24 (1H, ddd, J=2.3, 6.4, 12.9 Hz, H-3b), 2.05–1.70 (4H, m, H-6a,b, H-7a,b); δ_C(75.47 MHz) 178.2, 131.9, 128.4 (*o*-C and *p*-C), 123.0, 85.7, 85.6 (2C≡), 73.1, 65.8, 59.4, 55.8, 37.6, 33.0, 28.8, 26.8; λ_{max} 269.2, 255.3, 242.4 nm.

6.3.10. (1′*R,2′*R**,7a′*S**)-1′-(2-Phenylethynyl)hexahydrospiro[furan-3(3*H*),2′-pyrrolizine]-2-one (13e).** Yield 0.084 g (15%), colorless oil; [Found: C, 76.63; H, 6.79; N, 5.11. $C_{18}H_{19}NO_2$ requires C, 76.84; H, 6.81; N, 4.98%]; ν_{max}(liquid film) 2976, 2920, 2838, 2199, 1772, 1486, 1395, 1222, 1189, 1105, 1058, 769, 681 cm^{-1}; δ_H(300 MHz) 7.43 (2H, m, *o*-H-Ph), 7.31 (3H, m, *p*,*m*-H-Ph), 4.50 (1H, dt, J=6.1, 8.8 Hz, OCH_aH_b), 4.34 (1H, dt, J=6.1, 8.5 Hz, OCH_aH_b), 3.70–3.63 (1H, m, H-5), 3.26 (1H, d, J=9.9 Hz, H-9a), 3.13 (1H, d, J=9.9 Hz, H-9b), 3.08–2.99 (1H, buried m, H-8a) 3.06 (1H, d, J=10.2 Hz, H-10), 2.88 (1H, ddd, J=6.1, 8.2, 13.2 Hz, H-3a), 2.76 (1H, dt, J=10.5, 6.4 Hz, H-8b), 2.41–2.32 (1H, m, H-3b), 2.17–1.81 (4H, br m, H-6a,b, H-7a,b); δ_C(75.47 MHz) 179.0, 132.0, 128.6, 128.5, 122.9, 85.5, 85.3, 71.1, 66.6, 64.0, 55.1, 55.0, 45.4, 31.3, 30.3, 25.4; λ_{max} 283.1, 255.6, 240.4 nm.

6.3.11. (1′*R,2′*S**,7a′*R**)-2′-(2-Phenylethynyl)hexahydrospiro[furan-3(3*H*),1′-pyrrolizine]-2-one (11f).** LC in diethyl ether/acetone (6:1) yielded 0.15 g (26%) of white solid, mp 36–39 °C (petroleum ether); [Found: C, 77.12; H, 6.77; N, 4.89. $C_{18}H_{19}NO_2$ requires C, 76.84; H, 6.81; N, 4.98%]; ν_{max}(KBr) 2969, 2876, 2822, 1767, 1362, 1183, 1030, 1005, 853, 670, 557 cm^{-1}; δ_H(500 MHz) 7.40–7.35 (2H, m, *o*-H-Ph), 7.28–7.23 (3H, m, *p*,*m*-H-Ph), 4.39 (1H, dt, J=6.1, 8.4 Hz, OCH_aH_b), 4.22–4.12 (1H, m, OCH_aH_b), 3.67 (1H, t, J=7.6 Hz, H-5), 3.45 (1H, dd, J=10.8, 6,7 Hz, H-9a), 3.39 (1H, t, J=6.7 Hz, H-10), 3.29–3.15 (1H, m, H-9b), 3.02–2.92 (1H, m, H-8a), 2.75 (1H, dt, J=9.0, 5.6 Hz, H-8b), 2.54–2.42 (1H, m, H-3a), 2.29–2.18 (m, 1H, H-3b), 2.13–2.00(1H, m, H-7a), 1.95–1.78 (2H, m, H-7b,6a), 1.73–1.57 (1H, m, H-6b); δ_C(75.47 MHz) 176.2, 131.8, 128.29, 128.24, 122.8, 85.1, 83.7, 72.3, 65.4, 57.8, 55.9, 54.5, 42.9, 32.8, 28.6, 27.4; λ_{max} 274.0, 263.4, 243.5 nm.

6.3.12. (1′*R,2′*S**,7a′*R**)-1′-(2-Phenylethynyl)hexahydrospiro[furan-3(3*H*),2′-pyrrolizine]-2-one (13f).** Yield 0.10 g (18%), LC in diethyl ether/acetone (6:1), white solid, mp 56–57°C (petroleum ether); [Found: C, 77.09; H, 6.95; N, 5.13. $C_{18}H_{19}NO_2$ requires C, 76.84; H, 6.81; N, 4.98%]; ν_{max}(KBr) 2963, 2924, 2854, 2228, 1775, 1491, 1383, 1216, 1192, 1094, 1028, 758, 693 cm^{-1}; δ_H(500 MHz) 7.45–7.41 (2H, m, *o*-H-Ph), 7.31–7.28 (3H, m, *p*,*m*-H-Ph), 4.37 (2H, dd, J=8.6, 5.1 Hz, CH_2O), 3.90 (1H, pseudo q, J=7.2 Hz, H-5), 3.36 (1H, d, J=10.7 Hz, H-9a), 3.32 (1H, d, J=7.1 Hz, H-10), 3.12 (1H, d, J=10.7 Hz, H-9b), 3.13–3.09 (1H, buried m, H-8a), 3.00–2.95 (1H, m, H-8b), 2.47–2.38 (2H, m, H-3a,b), 2.34–2.26 (1H, m, H-6a), 2.17–2.10 (1H, m, H-7a), 1.95–1.83 (2H, m, H-6b, H-7b); δ_C(75.47 MHz) 176.9, 131.9, 128.4 (*o*,*m*-C-Ph), 123.1, 88.1, 85.1, 68.5, 65.3, 61.6, 56.5, 55.2, 43.2, 36.8, 28.2, 26.6; λ_{max} 279.2, 252.3, 245.4 nm.

6.3.13. (1′*R,2′*R**,7a′*R**)-2′-(2-Trimethylsilylethynyl)-hexahydrospiro[furan-3(3*H*),1′-pyrrolizine]-2-one (11g).** Yield 0.11 g (20%), LC in dichloromethane, colorless oil; [Found: C, 64.88; H, 8.23; N, 4.89. $C_{15}H_{23}NO_2Si$ requires C, 64.94; H, 8.36; N, 5.05%]; ν_{max}(liquid film) 2960.7, 2903.3, 2876.5, 2169.9, 1767.5, 1376.0, 1249.9, 1026.1, 843.9, 761.0 cm^{-1}; δ_H(500 MHz) 4.45 (1H, dt, J=9.1, 2.6 Hz, OCH_aH_b), 4.27 (1H, dt, J=6.4, 9.6 Hz, OCH_aH_b), 3.94

Table 5. Crystallographic data and refinement parameters of **11a** and **11b**

Parameters	**11a**	**11b**
Empirical formula	$C_{12}H_{21}NO_5S$	$C_{12}H_{21}NO_5S$
Formula mass	351.41	351.41
Temperature (K)	150(2)	150(2)
Wavelength (Å)	0.71073	0.71073
Crystal system, space group	Monoclinic, *C*2/*c*	Triclinic, *P*-1
Crystal size (mm)	0.50×0.40×0.40	0.50×0.30×0.20
a (Å)	22,849(5)	6.521(1)
b (Å)	12.642(2)	11.093(2)
c (Å)	11.573(2)	11.761(2)
α (°)	90	108.82(3)
β (°)	97.05(2)	90.03(3)
γ (°)	90	95.10(3)
Volume (Å^3); *Z*	3317.7; 8	801.7
D (g cm^{-3})	1.407	1.236
Absorption coefficient (mm^{-1})	0.222	0.210
F_{000} (e)	1488	1488
Θ range for data collection (°)	2.48–25.07	2.48–25.07
Range of *hkl*	−27→26, −15→0, 0→13	0→7, −12→12, −13→13
Reflections collected/independent	3105/2943	3091/216
Completeness Θ=25.07 (%)	47.6	
Refinement method	Full-matrix least-squares on F^2	
Number of data/parameters	2943/302	1908/302
Goodness-of-fit on F^2	0.988	1.140
Final *R* indices [$I>2\sigma(I)$]	$R1$=0.0375, $_wR2$=0.0935	$R1$=0.0433
R indices (all data)	$R1$=0.0598, $_wR2$=0.1058	$R1$=7.05
Largest diff. peak and hole (e Å^3)	0.350 and −0.344	0.41 and −0.81

(1H, t, *J*=7.3 Hz, H-5), 3.58–3.46 (2H, m, H-10, H-8a), 3.40–3.23 (2H, m, H-9a,b), 2.88–2.68 (2H, m, H-3a,8b), 2.38 (1H, ddd, *J*=2.6, 6.4, 13.2 Hz, H-3b), 2.11–1.81 (4H, buried m, H-6a,b, H-7a,b), 0.15 (9H, s, TMS); δ_C(75.47 MHz) 176.6, 99.7, 92.3, 72.9, 66.0, 58.2, 56.1, 54.5, 37.9, 32.0, 28.2, 26.6, 0.06; λ_{max} 247.2, 292.3 nm.

6.3.14. (1′*R,2′*R**,7a′*S**)-1′-(2-Trimethylsilylethynyl)-hexahydrospiro[furan-3(3*H*),2′-pyrrolizine]-2-one (13g).** Yield 0.078 g (14%), LC in dichloromethane, colorless oil; [Found: C, 65.13; H, 8.62; N, 5.29. $C_{15}H_{23}NO_2Si$ requires C, 64.94; H, 8.36; N, 5.05%]; ν_{max}(liquid film) 2962, 2903, 2871, 2174, 1774, 1452, 1261, 1097, 1028, 801 cm^{-1}; δ_H(300 MHz) 4.42 (1H, dt, *J*=6.4, 8.5 Hz, OCH_aH$_b$), 4.29 (1H, dt, *J*=6.0, 8.5 Hz, OCH_aH$_b$), 3.60–3.51 (1H, m, H-5), 3.21 (1H, d, *J*=9.9 Hz, H-9a), 3.04–2.96(1H, buried m, H-8a), 3.00 (1H, d, *J*=9.9 Hz, H-9b), 2.89 (1H, d, *J*= 9.6 Hz, H-10), 2.83–2.67 (2H, m, H-3a, H-8b), 2.37–2.25 (1H, m, H-3b) 2.12–1.73 (4H, m, H-6a,b, H-7a,b) 0.15 (9H, s, TMS); δ_C(75.47 MHz) 179.0, 102.0, 90.4, 71.1, 66.6, 64.1, 55.1, 54.8, 45.6, 31.2, 30.1, 25.3, 0.2; λ_{max} 249.2, 260.6 nm.

6.3.15. (1′*R,2′*S**,7a′*R**)-2′-(2-Trimethylsilylethynyl)-hexahydrospiro[furan-3(3*H*),1′-pyrrolizine]-2-one (11h).** LC in dichloromethane yielded 0.12 g (21%) of white solid, mp 51–53°C (petroleum ether); [Found: C, 64.68; H, 8.22; N, 5.38. $C_{15}H_{23}NO_2Si$ requires C, 64.94; H, 8.36; N, 5.05%]; ν_{max}(KBr) 2959, 2913, 2870, 2172, 1767, 1450, 1249, 1173, 1106, 1035, 845, 760 cm^{-1}; δ_H(500 MHz) 4.38 (1H, dt, *J*=6.7, 8.5 Hz, OCH_aH$_b$), 4.17 (1H, dt, *J*=5.9, 8.5 Hz, OCH_aH$_b$), 3.64 (1H, t, *J*=7.6 Hz, H-5), 3.37–3.25 (2H, m, H-10, H-9a) 3.15 (1H, dd, *J*=10.5, 7.3 Hz, H-9b), 3.02–2.95 (1H, m, H-8a), 2.80–2.72 (1H, m, H-8b), 2.50–2.39 (1H, m, H-3a), 2.31–2.20 (1H, m, H-3b), 2.15–2.02 (1H, m, H-7a), 1.96–1.80 (2H, m, H-6b, H7a), 1.73–1.60 (1H, m, H-6b) 0.13 (9H, s, TMS); δ_C(75.47 MHz) 176.1, 102.0, 88.9, 72.3, 65.8, 57.8, 56.1, 54.6, 43.6, 32.9, 28.8, 27.3, 0.08; λ_{max} 247.4, 299.4 nm.

6.3.16. (1′*R,2′*S**,7a′*R**)-1′-(2-Trimethylsilylethynyl)-hexahydrospiro[furan-3(3*H*),2′-pyrrolizine]-2-one (13h).** Yield 0.12 g (21%), LC in dichloromethane, white solid, mp 94–96°C (petroleum ether); [Found: C, 65.09; H, 8.61; N, 4.98. $C_{15}H_{23}NO_2Si$ requires C, 64.94; H, 8.36; N, 5.05%]; ν_{max}(KBr) 2959, 2922, 2868, 2175, 1775, 1482, 1251, 1029, 843, 716 cm^{-1}; δ_H(300 MHz) 4.31 (2H, dt, *J*=1.0, 6.4, Hz, OCH_2), 3.78 (1H, pseudo q, *J*=7.3 Hz, H-5), 3.27 (1H, d, *J*=11.0 Hz, H-9a), 3.11 (1H, d, *J*=7.3 Hz, H-10), 3.08–3.02 (1H, buried m, H-8a), 2.04 (1H, d, *J*=11.0 Hz, H-9b), 2.99–2.92 (1H, m, H-8b), 2.37–2.33 (2H, m, H-3a,b), 2.25–2.16 (1H, m, H-7a), 2.12–2.03 (1H, m, H-7b), 1.86–1.78 (2H, m, H-6a,b), 016 (9H, s, TMS); δ_C(75.47 MHz) 176.9, 101.9, 92.9, 68.4, 65.3, 61.6, 55.8, 55.2, 43.8, 36.9, 28.0, 22.3, −0.04; λ_{max} 292.0, 247.7 nm.

6.3.17. (1′*R,7a′*R**)-Hexahydrospiro[furan-3(3*H*),1′-pyrrolizine]-2-one (11i).** Yield 0.09 g (25%), LC in dichloromethane/diethyl ether (1:4), colorless oil; [Found: C, 66.19; H, 8.25; N, 7.46. $C_{10}H_{15}NO_2$ requires C, 66.27; H, 8.34; N, 7.73%]; ν_{max}(liquid film) 2955, 2780, 1772, 1431, 1352, 1249, 1195, 1149, 1028, 693 cm^{-1}; δ_H(300 MHz) 4.34–4.27 (1H, m, OCH_aH$_b$), 4.11 (1H, pseudo q, 8.8 Hz, OCH_aH$_b$), 3.45 (1H, t, *J*=7.3 Hz, H-5), 3.13 (1H, dt, *J*=10.8, 6.6 Hz, H-9a), 3.07–3.03 (1H, m, H-8a), 2.97 (1H, dt, *J*=10.8, 6.6 Hz, H-9b), 2.63 (1H, dt, *J*=6.1, 9.0 Hz, H-8b), 2.35 (1H, dt, *J*=12.7, 6.6 Hz, H-10a), 2.29 (2H, dd, *J*=8.1, 5.6 Hz, H-3a,b), 2.01–1.94 (1H, m, H-6a), 1.89 (1H, dt, *J*=12.7, 6.6 Hz,H-10b), 1.85–1.75 (2H, m, H-6b, H-7a), 1.70–1.62 (1H, m, H-7b); δ_C(75.47 MHz) 179.6, 73.2, 65.5, 55.0, 53.4, 51.6, 36.5, 36.3, 28.4, 27.3; λ_{max} 312.4, 251.4 nm.

6.3.18. (2′*R,7a′*S**)-Hexahydrospiro[furan-3(3*H*),2′-pyrrolizine]-2-one (13i).** Yield 0.025 g (7%), LC in dichloromethane/diethyl ether (1:4), colorless oil; [Found: C, 66.21; H, 8.35; N, 7.53. $C_{10}H_{15}NO_2$ requires C, 66.27; H, 8.34; N, 7.73%]; ν_{max}(liquid film) 2900, 2760, 1759, 1390, 1323, 1220, 1210, 1170, 1018, 685 cm^{-1}; δ_H(500 MHz) 4.39–4.30 (1H, m, OCH_aH_b), 4.22 (1H, pseudo q, J= 8.1 Hz, OCH_aH_b), 3.56–3.48 (1H, m, H-5), 3.17 (1H, d, J=9.1 Hz, H-9a), 3.11–3.03 (1H, m, H-8a), 2.91 (1H, d, J=9.1 Hz, H9b), 2.66–2.58 (1H, m, H-8b), 2.37–2.30 (1H, m, H-10a), 2.30–2.22 (2H, m, H-3a,b), 1.97–1.90 (1H, m, H-6a), 1.85–1.77 (1H, m, H-10b), 1.72–1.56 (3H, m, H-6b, H-7a,b); δ_C 178.2, 74.6, 64.8, 54.0, 52.8, 50.6, 36.4, 36.1, 28.0, 26.9; λ_{max} 320, 258 nm.

6.4. X-Ray crystallographic study

Crystals of **11a** and **11b** suitable for X-ray analysis were obtained by a careful recrystallization from diethyl ether. Experimental data were collected with a KUMA K4 kappa-axis four-circle diffractometer with graphite-monochromatized radiation. The data were corrected for Lp factor but no absorption correction was applied. The structures were solved by a direct method in a straightforward manner. The H atoms were placed in calculated positions with the temperature factors $1.2U_{eq}$ of the parent atoms and refined by using a 'ride-on' model. The structures were solved and refined using the SHELX97[29] program system and the drawings were prepared by ORTEP.[30] Crystal data and other details concerning the data collection are summarized in Table 5.

Crystallographic data (excluding structure factors) for the structures **11a** and **11b** in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication numbers CCDC 162247 and 162248, respectively. Copies of the data can be obtained, free of charge, on application to CCDC, 12 Union Road, Cambridge CB2 1 EZ, UK [fax: +44 (0) 1223-336033 or e-mail: deposit@ccdc.cam.ac.uk].

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