Intramolecular dipolar cycloaddition reaction of 5*H*,7*H*-thiazolo[3,4-*c*]oxazol-4-ium-1-olates: synthesis of chiral 1*H*-pyrrolo[1,2-*c*]thiazole derivatives

Teresa M. V. D. Pinho e Melo,*[a] Dália M. Barbosa,[a] Paulo J. R. S. Ramos,[a] António M. d'A. Rocha Gonsalves,[a] Thomas L. Gilchrist,[b] Ana M. Beja,[c] José A. Paixão,[c] Manuela R. Silva[c] and Luiz Alte da Veiga[c]

[a] *Departamento de Química, Universidade de Coimbra, 3000 Coimbra, Portugal*
[b] *Chemistry Department, University of Liverpool, Liverpool, UK L69 7ZD*
[c] *Departamento de Fìsica, Universidade de Coimbra, 3000 Coimbra, Portugal*

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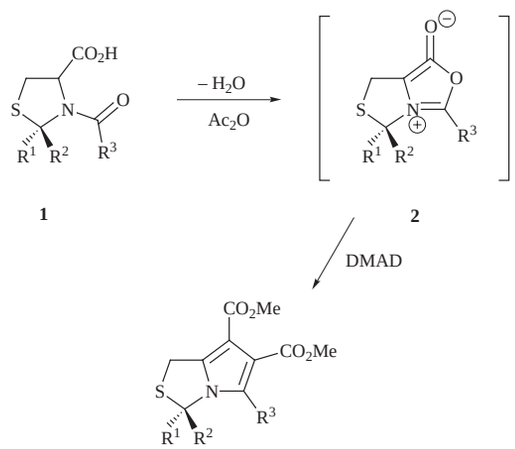
(2*R*,4*R*)-*N*-Acyl-2-phenylthiazolidine-4-carboxylic acids were used to generate 5*H*,7*H*-thiazolo[3,4-*c*]oxazol-4-ium-1-olates with internal dipolarophiles. The intramolecular 1,3-dipolar cycloaddition of these mesoionic species led to the synthesis of new 1*H*-pyrrolo[1,2-*c*]thiazole derivatives (**8a**, **8b** and **12**) as single enantiomers. The structure of **8a** was determined by X-ray crystallography.

Introduction

1,3-Dipolar cycloaddition reactions of oxazolium-5-olates (münchnones) have proved to be a useful method of synthesis of pyrroles.[1] The method can also be used as a route to heterocycles in which another ring system is annulated to pyrrole. Thus, 2-substituted-*N*-acylthiazolidine-4-carboxylic acids **1** have been used to generate 5*H*,7*H*-thiazolo[3,4-*c*]oxazol-4-ium-1-olates **2** which give some examples of 1,3-dipolar addition, namely the addition to dimethyl acetylenedicarboxylate (Scheme 1),[2] to α-chloroacrylonitrile[3] and to imines.[4] The



Scheme 1

products from dimethyl acetylenedicarboxylate are 1*H*-pyrrolo[1,2-*c*]thiazole derivatives.

Györgydeák *et al.*[2b] have shown that chiral 3-substituted pyrrolo[1,2-*c*]thiazole-6,7-dicarboxylic acid esters can be obtained from 2-substituted-*N*-acyl-1,3-thiazolidine-4-carboxylic acids with high enantiomeric excess. The chirality at C-4 of the thiazolidine is lost and the chirality at C-2 (C-3 in the product) is retained.

Previous examples of intramolecular 1,3-dipolar addition reactions of münchnones have been described.[5,6] These have shown that müchnone derivatives containing an internal unactivated olefinic π-bond undergo intramolecular 1,3-dipolar cycloaddition giving the corresponding cycloadducts with retention of the elements of carbon dioxide.[5] On the other hand, Nayyar *et al.*[6] have shown that to promote the intramolecular 1,3-dipolar cycloaddition of münchnones with tethered alkynes, the internal dipolarophile needs to be electron deficient or at least polarized. In particular, attempts to promote the cycloaddition of an *N*-acylproline derivative with a terminal alkylacetylene were not successful.[6]

This paper describes an extension to the use of 5*H*,7*H*-thiazolo[3,4-*c*]oxazol-4-ium-1-olate **2** in intramolecular 1,3-dipolar cycloadditions. An important feature of this intramolecular cycloaddition is that it can be carried out with dipolarophiles lacking any activating substituents.

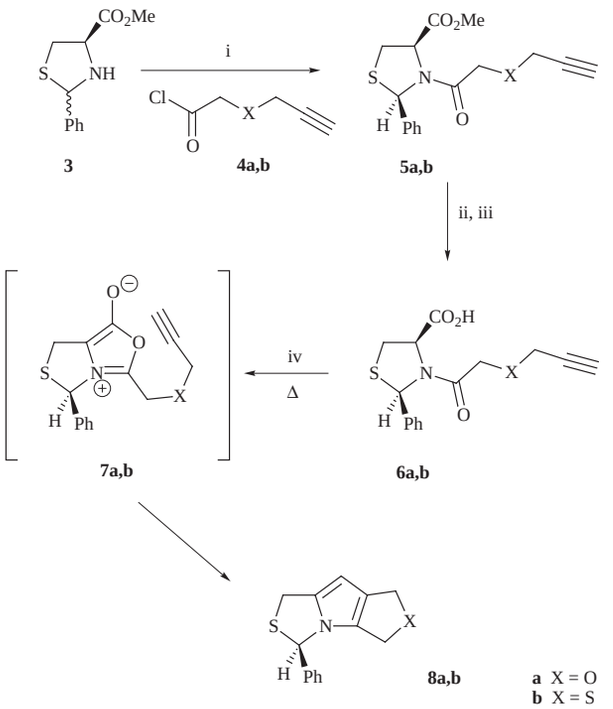
Results and discussion

Our objective was to obtain 5*H*,7*H*-thiazolo[3,4-*c*]oxazol-4-ium-1-olates **2** containing an internal dipolarophile in order to promote intramolecular cycloaddition reactions. Scheme 2 illustrates the synthetic approach used. Prop-2-ynyloxyacetic acid was prepared from the reaction of propargyl alcohol (prop-2-ynol) and chloroacetic acid by a known method.[7] The reaction of this acetylenic acid with thionyl chloride gave the acid chloride **4a** which was used to acylate a mixture of the (2*R*,4*R*) and (2*S*,4*R*) diastereoisomers of methyl 2-phenylthiazolidine-4-carboxylate[8] **3** in the presence of potassium carbonate.

As previous studies have shown,[9] the NMR spectra of *N*-acylthiazolidines at ambient temperature are complicated by the existence of separate rotamers but the spectrum is simplified at higher temperature. In agreement with this we found that the NMR spectra of **5a**, when recorded in DMSO-d_6 at 100 °C, showed signals for a single diasteriomer. By comparision with literature analogies the spectrum was consistent with an assignment of (2*R*,4*R*) stereochemistry. This was also suggested by the positive value of the optical rotation.[9a]

Hydrolysis of the ester group of compound **5a** with KOH in EtOH–H_2O or with LiOH did not give a clean result. However the reaction of compound **5a** with lithium iodide in ethyl acetate followed by treatement with aqueous HCl led to the formation of thiazolidine **6a** in 67% yield.

Attempts were made to prepare compound **6a** directly from the reaction of 2-phenylthiazolidine-4-carboxylic acid with the acid chloride **4a**. However the acylation reaction led to a complex mixture of products.



Scheme 2 *Reagents:* i, K_2CO_3, CH_2Cl_2; ii, LiI; iii, HCl aq.; iv, Ac_2O.

N-Acylthiazolidine **6a** was heated in a solution of acetic anhydride to generate the mesoionic species **7a**. At 95–100 °C there was no reaction but at a higher temperature (135 °C) the 3,7-dihydro-1*H*-furo[3′,4′ : 4,5]pyrrolo[1,2-*c*]thiazole **8a** was obtained in 44% yield.

The reaction of *N*-acetyl-2-phenylthiazolidine-4-carboxylic acid in a diastereoisomerically pure form with dimethyl acetylenedicarboxylate in Ac_2O gives chiral 1*H*-pyrrolo[1,2-*c*]thiazole derivatives.[2b] The chirality at C-4 of the starting carboxylic acid is eliminated in the product and the chirality at C-2 (C-3 in the product) is maintained. By analogy, we obtained compound **8a** as a single enantiomer (Scheme 2) and having $[\alpha]_D^{25} = +210$.

The structure of **8a** was established by X-ray crystallography (Fig. 1) which confirms that compound **8a** has an *R* configuration at C-3. Selected bond angles and lengths obtained are given in Table 1.

(Prop-2-ynylthio)acetic acid was also prepared from the reaction of propargyl bromide and mercaptoacetic acid in the presence of aqueous ammonia. The reaction of this acetylenic acid with thionyl chloride gave the acid chloride **4b**. Thiazolidine **3** reacted with **4b** giving the acylated product **5b** (in 47% yield). The ^{1}H NMR spectrum of **5b** recorded in DMSO-d_6 at 100 °C showed a single diastereoisomer. The reaction conditions used in the acylation of **3** with **4a** and **4b** were the same giving only in both cases the (2*R*,4*R*) isomer. This was confirmed by comparison of the **5a** and **5b** ^{1}H NMR spectra. Compound **5b** was converted into the acid **6b** by reaction with lithium iodide in ethyl acetate followed by treatment with aqueous HCl. Heating compound **6b** in acetic anhydride allowed the synthesis of (5*R*)-5-phenyl-3,7-dihydro-1*H*-thieno[3′,4′ : 4,5]-pyrrolo[1,2-*c*][1,3]thiazole **8b** in 47% yield; $[\alpha]_D^{25} = +196.8$.

Another class of 5*H*,7*H*-thiazolo[3,4-*c*]oxazol-4-ium-1-olates containing an internal dipolarophile was investigated (Scheme 3). In the first step acid chloride **13** was prepared. The reaction of methyl salicylate with propargyl bromide in the presence of K_2CO_3 gave compound **14**. Hydrolysis with KOH–EtOH afforded the acid **15** which reacted with thionyl chloride to give the acid chloride **13**.

The reaction of compound **13** with the thiazolidine **3** in the presence of K_2CO_3 gave the corresponding *N*-acylated thiazolidine **9** (Scheme 3). The ^{1}H NMR spectra recorded in DMSO-d_6 at high temperature again showed that **9** is exclusively the (2*R*,4*R*) isomer. Reaction of **9** with lithium iodide in ethyl acetate gave the corresponding acid **10** in 85% yield.

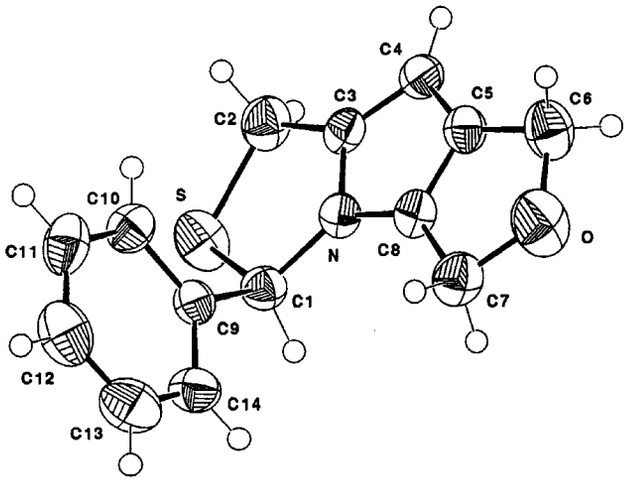
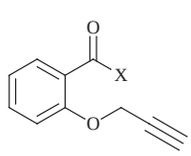


Fig. 1 X-Ray crystal structure of compound **8a**.

Table 1 Selected bond lengths and angles for **8a**

Bond lengths/Å			
S–C1	1.7812(17)	C7–C8	1.446(2)
S–C2	1.816(2)	O–C7	1.421(3)
C2–C3	1.455(2)	O–C6	1.433(3)
C3–C4	1.357(2)	N–C8	1.336(2)
C4–C5	1.385(2)	N–C3	1.353(2)
C5–C8	1.349(2)	N–C1	1.446(2)
C5–C6	1.459(2)		
Bond angles (°)			
C3–C2–S	105.68(13)	N–C8–C5	109.27(14)
N–C3–C2	112.87(15)	C8–N–C3	106.78(13)
C3–N–C1	121.66(13)	C5–C8–C7	113.11(15)
N–C1–S	102.59(11)	O–C7–C8	101.12(16)
N–C3–C4	110.67(14)	C7–O–C6	114.17(13)
C3–C4–C5	104.82(15)	O–C6–C5	102.42(15)
C8–C5–C4	108.46(14)	C8–C5–C6	109.17(15)
Torsion angles			
C3–N–C1–C9	−114.87(16)		
C8–N–C1–C9	66.0(2)		
C2–S–C1–C9	115.20(12)		



13 X = Cl
14 X = OMe
15 X = OH

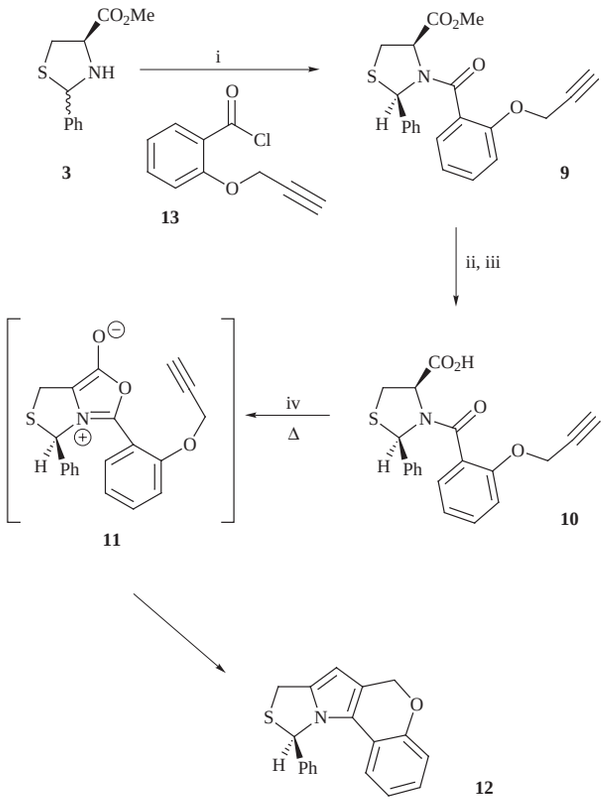
By heating thiazolidine **10** in acetic anhydride the mesoionic intermediate **11** was generated and this underwent an internal dipolar cycloaddition to give compound **12** in 38% yield. This showed $[\alpha]_D^{25} = +300$.

Conclusion

This study of intramolecular 1,3-dipolar cycloaddition reactions of 5*H*,7*H*-thiazolo[3,4-*c*]oxazol-4-ium-1-olate derivatives has shown that cycloaddition with non-activated internal dipolarophiles is a possible and useful reaction. New 1*H*-pyrrolo[1,2-*c*]thiazole derivatives (**8a**, **8b** and **12**) have been obtained as single enantiomers.

Experimental

^{1}H NMR spectra were recorded on a Bruker ACE200 spectrometer operating at 200 MHz (where indicated) or on a



Scheme 3 *Reagents:* i, K_2CO_3, CH_2Cl_2; ii, LiI; iii, HCl aq.; iv, Ac_2O.

Bruker AMX300 instrument operating at 300 MHz. ^{13}C spectra were recorded on a Bruker AMX300 instrument operating at 75.5 MHz. The solvent is deuteriochloroform except where indicated otherwise. IR spectra were recorded on a Perkin-Elmer 1720X FTIR spectrometer. Mass spectra were recorded under electron impact at 70 eV on a VG Micromass 7070E instrument. Optical rotations were measured on an Optical Activity AA-5 electrical polarimeter. Mps were recorded on a Reichert hot stage and are uncorrected. Flash column chromatography was performed with Merck 9385 silica as the stationary phase. Methyl 2-phenylthiazolidine-4-carboxylate **3** was prepared as described in the literature[8] and was isolated as a mixture of the (2*R*,4*R*) and (2*S*,4*R*) diastereoisomers.

Prop-2-ynyloxyacetic acid

This was prepared from propargyl (prop-2-ynyl) alcohol (9.51 g, 170 mmol) and chloroacetic acid (17.96 g, 190 mmol) by a procedure described in the literature[7] (Found: C, 52.3; H, 5.2. Calc. for $C_5H_6O_3$ C, 52.6; H, 5.3%); ν_{max}/cm^{-1} (film) 3480, 2053 and 1732; δ_H 2.53 (1 H, t, *J* 2.3) 4.27 (2 H, s) 4.33 (2 H, d, *J* 2.3) and 10.16 (1 H, br s, CO_2H); δ_C (75.5 MHz) 58.35, 65.63, 76.04, 78.10 and 175.33.

(Prop-2-ynylthio)acetic acid

A solution of propargyl bromide in toluene (7.33 g, 80% solution) was added to a solution of mercaptoacetic acid (3.00 g, 33 mmol) in aqueous ammonia (24%, 64 mL). The reaction mixture was stirred at 0 °C for 40 min. The solution was concentrated, filtered, a saturated aqueous solution of $NaHCO_3$ was added and the solution was washed with DCM. The aqueous solution was acidified with concentrated HCl and extracted with ethyl acetate. The organic phase was dried and the solvent was evaporated off giving (prop-2-ynylthio)acetic acid (83%), mp 55–60 °C; ν_{max}/cm^{-1} (KBr) 3168, 2109 and 1688; δ_H 2.32 (1 H, t, *J* 2.6) 3.44 (2 H, d, *J* 2.6) 3.47 (2 H, s) and 10.86 (1 H, br s, CO_2H); HRMS (EI+): found 130.0092. $C_5H_6SO_2$ requires 130.0088.

Methyl 2-prop-2-ynyloxybenzoate 14

Methyl salicylate (1.52 g, 10 mmol) was dissolved in acetone (25 mL). Potassium carbonate (1.38 g, 10 mmol) was added followed by a solution of propargyl bromide in toluene (2 mL, 80% solution). The reaction mixture was heated under reflux for 24 h. Cold water was added and the aqueous phase extracted with Et_2O. The organic phase was dried and the solvent evaporated off. The crude product was purified by flash chromatography [hexane–ethyl acetate (4:1)] giving compound **13** (1.4 g, 74%), mp 25.8–26 °C (Found: C, 69.4; H, 5.0. $C_{11}H_{10}O_3$ requires C, 69.5; H, 5.3%); ν_{max}/cm^{-1} (KBr) 3289, 2116 and 1726; δ_H 2.53 (1 H, t, *J* 2.4) 3.89 (3 H, s), 4.80 (2 H, d, *J* 2.4), 7.05 (1 H, dt, *J* 0.8 and 7.6, ArH), 7.14 (1 H, d, *J* 8.4, ArH), 7.48 (1 H, ddd, *J* 1.8, 8.5 and 9.2, ArH) and 7.82 (1 H, dd, *J* 1.8 and 7.6, ArH); *m/z* 190 (M^+, 11%), 189 (19), 175 (21), 159 (74), 131 (100) and 77 (88).

2-Prop-2-ynyloxybenzoic acid 15

To a solution of **14** (0.30 g, 1.57 mmol) in EtOH (12 mL) a saturated aqueous solution of KOH (10 drops) was added. The reaction mixture was stirred at room temperature for 25 h. Water (50 ml) was added and the resulting solution was acidified with HCl 1 M. The aqueous phase was extracted with AcOEt (4 × 20 mL). The organic phase was dried (Na_2SO_4) and the solvent evaporated off giving the acid **14** (0.20 g, 73%), mp 86–88 °C (from ether–hexane) (Found: C, 68.4; H, 4.6. $C_{10}H_8O_3$ requires C, 68.2; H, 4.6%); ν_{max}/cm^{-1} (KBr) 3281, 2096, 1705 and 1676; δ_H 2.66 (1 H, s), 4.94 (2 H, s), 7.15–7.20 (2 H, m, ArH), 7.58 (1 H, t, *J* 7.3, ArH) and 8.18 (1 H, d, *J* 7.3, ArH); δ_C (75.5 MHz) 45.08, 57.46, 77.81, 113.24, 122.82, 133.87, 134.82 and 156.22; *m/z* 176 (M^+, 7%), 147 (11), 134 (75) and 120 (100).

General procedure for the synthesis of methyl *N*-acylthiazolidine-4-carboxylate

(a) Acids chloride 4a, 4b and 13. Freshly distilled thionyl chloride (15 mL) was added to the acetylenic acid (28.5 mmol). After heating at reflux for 30 min the solvent was evaporated off. The residue was dissolved in toluene and the organic solvent evaporated off giving the corresponding acetylenic acid chloride which was used without further purification.

(b) Methyl *N*-acylthiazolidine-4-carboxylates. Methyl 2-phenylthiazolidine-4-carboxylate **3** (6.35 g, 28.5 mmol) was dissolved in dry dichloromethane (60 mL). Anhydrous potassium carbonate (6 g, 43.4 mmol) was added followed by a solution of the acid chloride in dichloromethane (20 mL). The reaction mixture was stirred under nitrogen at room temp. for 18 hours. The organic solution was washed with water and the solvent evaporated off. To the residue ethyl ether was added followed by filtration. The organic solvent was evaporated giving the methyl *N*-acylthiazolidine-4-carboxylate.

Methyl (2R,4R)-2-phenyl-3-(prop-2-ynyloxyacetyl)thiazolidine-4-carboxylate **5a.** Yield 43%, mp 110–112 °C (from DCM–hexane) (Found: C, 59.9; H, 5.6; N, 4.3. $C_{16}H_{17}NSO_4$ requires C, 60.2; H, 5.4; N, 4.4%); ν_{max}/cm^{-1} (KBr) 2954, 2925, 2854, 2125 and 1743; δ_H 2.35 (1 H, s), 3.21–3.32 (2 H, m), 3.84 (3 H, s), 4.08–4.21 (4 H, m), 5.03 (2 H, t, *J* 6.9), 6.14 (1 H, s), 7.29–7.45 (3 H, m, ArH) and 7.58–7.67 (2 H, m, ArH); *m/z* 319 (M^+, 2%), 318 (3), 260 (25), 233 (16), 222 (100) and 203 (96).

Methyl (2R,4R)-2-phenyl-3-(prop-2-ynylthioacetyl)thiazolidine-4-carboxylate **5b.** Yield 47%, mp 73–75 °C (from ether–hexane) (Found: C, 57.3; H, 5.1; N, 4.2; S, 19.1. $C_{16}H_{17}NS_2O_3$ requires C, 56.9; H, 5.1; N, 4.2; S, 19.6%); δ_H 2.17 (1 H, t, *J* 2.4), 3.17–3.42 (6 H, m), 3.84 (3 H, s), 4.99 (1 H, t, *J* 7.1), 6.27 (1 H, s), 7.29–7.42 (3 H, m, ArH) and 7.64–7.68 (2 H, m, ArH); *m/z* 335 (M^+, 5%), 264 (100), 222 (62) and 179 (25).

Methyl (2R,4R)-2-phenyl-3-[2-(prop-2-ynyloxybenzoyl]thiazolidine-4-carboxylate **9.** Yield 49%, mp 98–101 °C (from ether) (Found: C, 65.9; H, 5.2; N, 3.6. $C_{21}H_{19}NO_4S$ requires C, 66.1; H, 5.0; N, 3.7%); ν_{max}/cm^{-1} (KBr) 3246, 2115, 1755 and 1601; δ_H 2.55 (1 H, br s), 3.34–3.47 (2 H, m), 3.89 (3 H, s), 4.77 (2 H, br s), 5.31 (1 H, t, *J* 4.1), 5.94 (1 H, s), 7.12–7.40 (8 H, m, ArH) and 7.69 (1 H, d, *J* 7.5, ArH); *m*/*z* 381 (M^+, 12%), 222 (50), 192 (50) and 159 (100).

General procedure for the synthesis of thiazolidine-4-carboxylic acids

The methyl *N*-acyl-2-phenylthiazolidine-4-carboxylate (1 mmol) and LiI (4 mmol) were dissolved in ethyl acetate (1.3 mL). The reaction mixture was protected from light and heated at reflux for 6 h. Water was added (5 mL) and the solution was acidified with HCl 1 M and extracted with ethyl acetate. The organic phase was washed with water and with a saturated aqueous solution of NaCl. The organic solvent was evaporated off. To the residue a saturated aqueous solution of $NaHCO_3$ was added and the solution was washed with DCM. The aqueous solution was acidified with concentrated HCl and extracted with ethyl acetate. The organic phase was dried and the solvent was evaporated off giving the *N*-acyl-2-phenylthiazolidine-4-carboxylic acid. The following acids were isolated by this procedure:

(2*R*,4*R*)-2-Phenyl-*N*-(prop-2-ynyloxyacetyl)thiazolidine-4-carboxylic acid 6a. Yield 85%, mp 157–158 °C (from DCM–hexane) (Found: C, 58.9; H, 5.1; N, 4.3; S, 10.1. $C_{15}H_{15}NO_4S$ requires C, 59.0; H, 5.0; N, 4.6; S, 10.5%); ν_{max}/cm^{-1} (KBr) 2855, 2125 and 1747; δ_H 2.37 (1 H, br s), 3.35–3.37 (2 H, m), 4.09–4.14 (4 H, m), 5.09 (1 H, t, *J* 4.25), 6.16 (1 H, s), 7.26–7.38 (3 H, m, ArH), 7.58–7.61 (2 H, m, ArH) and 13.15 (1 H, br s); *m*/*z* 305 (M^+, 1%), 236 (8), 208 (45), 121 (90) and 104 (100).

(2*R*,4*R*)-2-Phenyl-*N*-(prop-2-ynylthioacetyl)thiazolidine-4-carboxylic acid 6b. Yield 61%, mp 190–192 °C (from ether); ν_{max}/cm^{-1} (KBr) 3061, 1743 and 1653; δ_H 2.08 (1 H, br s), 3.11–3.26 (2 H, m), 3.28–3.39 (4 H, m), 5.05 (1 H, t, *J* 6.9), 6.29 (1 H, s), 7.23–7.40 (3 H, m, ArH) and 7.55–7.65 (2 H, m, ArH); *m*/*z* 321 (M^+, 2%), 250 (100), 208 (78) and 162 (78).

(2*R*,4*R*)-2-Phenyl-3-[2-(prop-2-ynyloxybenzoyl)]thiazolidine-4-carboxylic acid 10. Yield 85%, mp 74–77 °C (from ether); δ_H 2.58 (1 H, br s), 3.38–3.61 (2 H, m), 4.76–4.87 (2 H, m), 5.32 (1 H, t, *J* 6.6), 5.96 (1 H, s) and 7.07–7.70 (9 H, m, ArH); *m*/*z* 367 (M^+, 8%), 311 (5), 208 (20), 192 (22) and 159 (100).

General procedure for the synthesis of adducts 8a, 8b and 12

The *N*-acyl-2-phenylthiazolidine-4-carboxylic acid **6a**, **6b** or **10** (5 mmol) was dissolved in Ac_2O (20 ml) and the solution was heated at reflux for 6 h. The reaction mixture was cooled to room temperature and was diluted with CH_2Cl_2 (50 ml). The organic phase was washed with a saturated aqueous solution of $NaHCO_3$ and with water, dried (Na_2SO_4) and evaporated off. The crude product was purified by flash chromatography [hexane–ethyl acetate (3 : 1)].

(5*R*)-5-Phenyl-3,7-dihydro-1*H*-furo[3′,4′ : 4,5]pyrrolo[1,2-*c*]-[1,3]thiazole 8a. Yield 44%, mp 123–124 °C (from ether–hexane) (Found: C, 69.5; H, 5.5; N, 5.6. $C_{14}H_{13}NSO$ requires C, 69.1; H, 5.4; N, 5.8%); ν_{max}/cm^{-1} (KBr) 3435, 2876, 2853 and 1473; δ_H 4.09–4.04 (1 H, m), 4.22 (2 H, s), 4.47–4.53 (1 H, m), 4.79–4.48 (2 H, m), 5.76 (1 H, s), 6.24 (1 H, s) 7.26–7.31 (2 H, m, ArH) and 7.34–7.37 (3 H, m, ArH); δ_C 29.43, 64.62, 65.88. 69.21, 94.17, 127.11, 128.50, 128.95, 129.29, 129.60, 138.48, 139.16; *m*/*z* 243 (M^+, 91%), 122 (100) and 77 (50); $[\alpha]_D^{25}$ = +210 (*c* = 0.1, $CHCl_3$).

(5*R*)-5-Phenyl-3,7-dihydro-1*H*-thieno[3′,4′ : 4,5]pyrrolo[1,2-*c*]-[1,3]thiazole 8b. Yield 47%, mp 112–114 °C (from ether–hexane); ν_{max}/cm^{-1} (KBr) 3126, 3134, 1734 and 1695; δ_H 3.11 (1 H, m), 3.56 (1 H, m), 3.89 (2 H, t, *J* 3), 4.16 (1 H, d, *J* 12.9), 4.24 (1 H, d, *J* 12.9), 5.73 (1 H, s), 6.23 (1 H, s), 7.24–7.27 (2 H, m, ArH) and 7.34–7.37 (3 H, m, ArH); *m*/*z* 259 (M^+, 100%), 226 (28), 139 (47), and 122 (30); HRMS (EI+): found 259.0478. $C_{14}H_{13}NS_2$ requires 259.0489; $[\alpha]_D^{25}$ = +196.8 (*c* = 0.1, $CHCl_3$).

(10*R*)-10-Phenyl-6*H*,8*H*-chromeno[3′,4′ : 4,5]pyrrolo[1,2-*c*]-[1,3]thiazole 12. Yield 38%, mp 81–93 °C [with decomposition] (from ether–hexane); ν_{max}/cm^{-1} (KBr) 3131, 1638 and 1400; δ_H 4.01 (1 H, dd, *J* 13.5 and 0.6), 4.29 (1 H, dt, *J* 13.5 and 1.2), 5.23 (1 H, d, *J* 12.6), 5.27 (1 H, d, *J* 12.6), 5.85 (1 H, s), 6.61 (1H, s), 6.62–6.67 (1 H, m, Ar-H), 6.81–6.85 (2 H, m, Ar-H), 6.88–6.94 (1 H, m, Ar-H), 6.97–7.0 (2 H, m, Ar-H) and 7.22–7.34 (3H, m, Ar-H); *m*/*z* 305 (M^+, 83%), 182 (100) 154 (25) and 77 (9); $[\alpha]_D^{25}$ = +300 (*c* = 0.1, $CHCl_3$).

Crystal data for 8a †

$C_{14}H_{13}NOS$, M = 243.31, Monoclinic, a = 9.556(3) Å, b = 6.038(2) Å, c = 9.994(4) Å, α = 90°, β = 103.69(3)°, γ = 90°, V = 560(3) Å^3 (by least-squares refinement of diffractometer angles of 25 strong, well centered reflections with 10.5 ⩽ θ ⩽ 14.4°, λ = 0.71073 Å, T = 293(2) K), space group $P2_1$ (No 4), Z = 2, D_z = 1.442, prism 0.41 × 0.35 × 0.25 mm, μ(Mo-Kα) = 0.269 mm^{-1}.

Data collection and processing. CAD4 diffractometer, graphite monochromated Mo-Kα radiation, ω–2θ scans with ω scans width (0.85 + 0.35 tan θ)°, 4233 reflections measured (3.4 ⩽ θ ⩽ 25.9°, ±h, ±k, ±l), 2046 unique (merging, R_{int} > 0.0159, giving 1992 with $I > 2\sigma$, 2046 retained in all calculations). No absorption correction was required, an isotropic crystal decay (2%) was applied during data processing.

Structure solution and refinement. The structure was solved by direct methods[10] (all non-H atoms). Full matrix least-squares refinement[11] on F^2 with all non-H atoms anisotropic. H atoms were found on a ΔF synthesis. They were placed on idealized positions and refined as riding using $U_{iso}(H) = 1.2U_{iso}(C)$. The weighting scheme $\omega^{-1} = [\sigma^2(F_o^2) + (0.0377P)^2 + 0.0963P]$, $P = \frac{1}{3}[\max(F_o^2 + 2F_o^2)]$, gave a satisfactory flat variance. Final $R_1[F > 4\sigma F] = 0.0254$, ωR_2 all data = 0.0694, $S[F^2] = 1.063$ for 155 refined parameters (R indices defined as in ref. 11). An extinction correction[11] refined to 0.024(5) and the final ΔF synthesis showed no peaks outside the range −0.14→+0.14 e Å^{-3}. The absolute configuration was determined by Flack's method.[12] The refined η parameter was $\eta = -0.11(7)$ (η = 0,1 for the C(1) *R* and *S* configuration, respectively). Separated refinements for the two enantiomers gave $\omega R = 0.0694$ (*R*) and $\omega R = 0.0744$ (*S*). Hamilton's test[13] shows that the probability of error in rejecting the *S* configuration in face of the data was lower than 0.5%. Fig. 1 was produced with ORTEP II.[14]

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