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SYNTHESIS OF 1,3-THIAZOLIDINES FROM AROMATIC THIOKETONES AND *N*-BENZYLIDENE α-AMINO ACID ESTERS *VIA* 1,3-DIPOLAR CYCLOADDITION OF AZOMETHINE YLIDES

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(Dedicated to Professor Sho Ito on the occasion of his 77th birthday)

Abstract – The reaction of *N*-benzylidenephenylglycine methyl ester (**2a**) and *N*-benzylidenalanine methyl ester (**2b**) with thiobenzophenone (**5a**) and fluorene-9-thione (**5b**) in acetonitrile in the presence of lithium bromide and DBU gave a mixture of two corresponding diastereoisomeric [2+3] cycloadducts of types (**6**) and (**7**). The products were formed regioselectively and in good yields from the *in situ* generated metallo-azomethine ylides (**8**). The relative configurations of the two products (**6c**) and (**7c**) formed from fluorene-9-thione (**5b**) and **2a** were established by X-Ray crystallography.

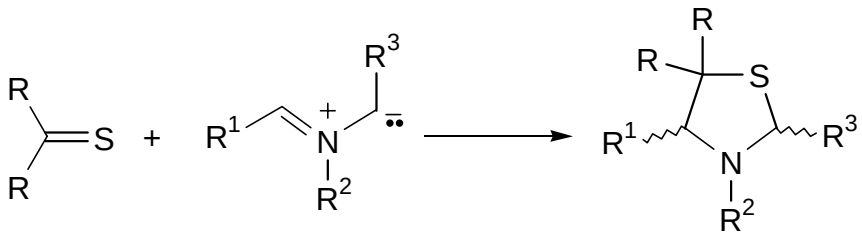
INTRODUCTION

Azomethine ylides are well-known nitrogen-centered 1,3-dipoles which have found many applications in the synthesis of five-membered nitrogen heterocycles.[2-5] *Huisgen* and coworkers were the first who described the classical experiments with thermal and photochemical ring opening of aziridines to give non-stabilized azomethine ylides as reactive intermediates.[6-8] The stereoselectivity of both the aziridine ring opening and the 1,3-dipolar cycloaddition was recognized as an attractive feature of azomethine ylide chemistry.[9-14]

Other methods for the generation of azomethine ylides are for example the desilylation of α-silylonium salts[15-17] and α-cyanosilylamino ethers,[18] the dehydratisation of tertiary amine oxides,[19] the addition of carbenes or carbenoids onto imines,[20-22] the 1,2-prototropic rearrangement of α-amino acid imines,[23] the condensation of secondary amines with

aldehydes,[24,25] the decarboxylation of amino acid immonium salts,[26-28] and *Lewis* acid catalyzed reactions *via* metallo-azomethine ylides.[29] The 1,3-dipolar cycloaddition of azomethine ylides with olefins or acetylenes yielding pyrrolidines or pyrrols with a wide range of substitution is well-known.[3,6,30-33] In contrast, the analogous reaction with thiocarbonyl compounds as dipolarophiles is rarely described. Only a few examples have been published in the last few years.[18,19,34-36] Recently, *Gallagher* and coworkers reported a synthesis of carbapenams and carbapenemes *via* cycloaddition of an azomethine ylide with thiocarbonyl compounds.[37] In their experiments, the intermediate 1,3-dipole was generated by decarboxylation of a 1,3-oxazolidinone derivative. Recently, we reported on the 1,3-dipolar cycloaddition of azomethine ylides, generated from aziridines, with 1,3-thiazole-5(4*H*)-thiones.[38] Therefore, it appears that the cycloaddition of azomethine ylides with C=S double bonds offers an attractive access to highly functionalized 1,3-thiazolidines (**1**) (*Scheme 1*).

Scheme 1



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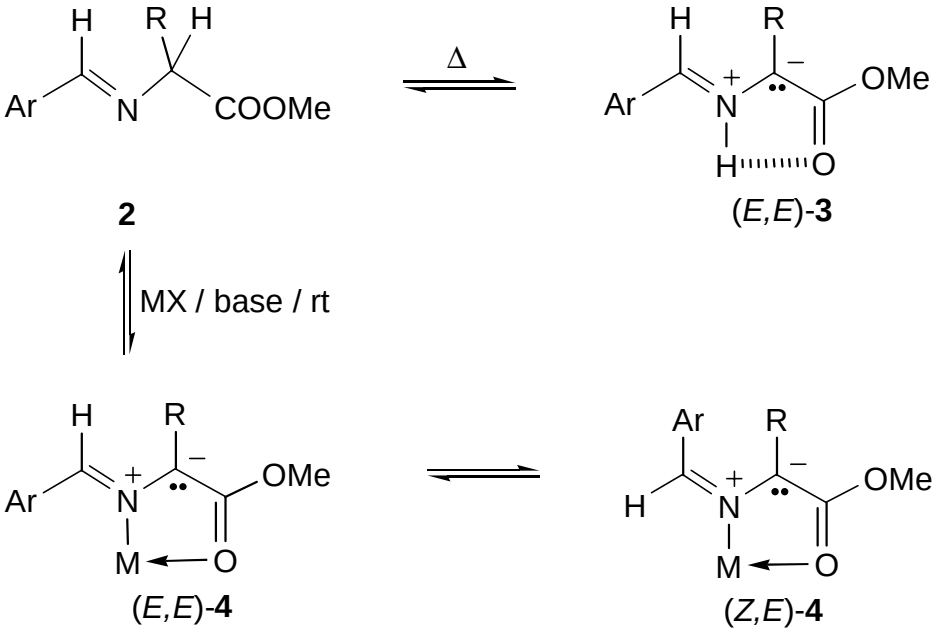
A few years ago, *Grigg et al.* developed the azomethine ylide generation *via* 1,2-prototropic rearrangement of α-amino acid imines (**2**), which offers a synthetic access to pyrrolidines that are not substituted at the *N*-atom (R^2 = H).[23] A large number of ylide precursors are readily available from condensations of α-amino acid esters with aldehydes.[23,39] Heating of these α-amino acid ester imines of type (**2**) generates azomethine ylides of type (**3**) (*Scheme 2*). The configuration of the dipoles (**3**) depends on the nature of the substituent R, as well as on the solvent and temperature effects. However, in many cases the corresponding (*E,E*)- or *syn*-azomethine ylides are formed stereospecifically.[23]

In the case of metallo-azomethine ylides (**4**), generated from **2** in the presence of a metal salt and a base, the azomethine ylides ((*E,E*)-**4**) are formed stereospecifically due to the complexation of the metal ion to the imine *N*-atom and the ester carbonyl group.[29] Depending on the reaction conditions, stereomutation at C(2) forming the (*Z,E*)-ylides can occur (*Scheme 2*). In the present paper, we report on the reaction of *N*-benzylidenephenylglycine methyl ester (**2a**) (Ar = Ph, R = Ph) and *N*-benzylidenalanine methyl ester (**2b**) (Ar = Ph,

R = Me) with thiobenzophenone (**5a**) and fluorene-9-thione (**5b**) in acetonitrile in the presence of LiBr and DBU as the base. In all reactions, two diastereoisomeric 1,3-thiazolidine derivatives (**6a-d**) (main isomer) and (**7a-d**) (minor isomer), derived from the ylide ((*E*,*E*)-**8**) and ((*Z*,*E*)-**8**), respectively, were isolated (*Scheme 3*).

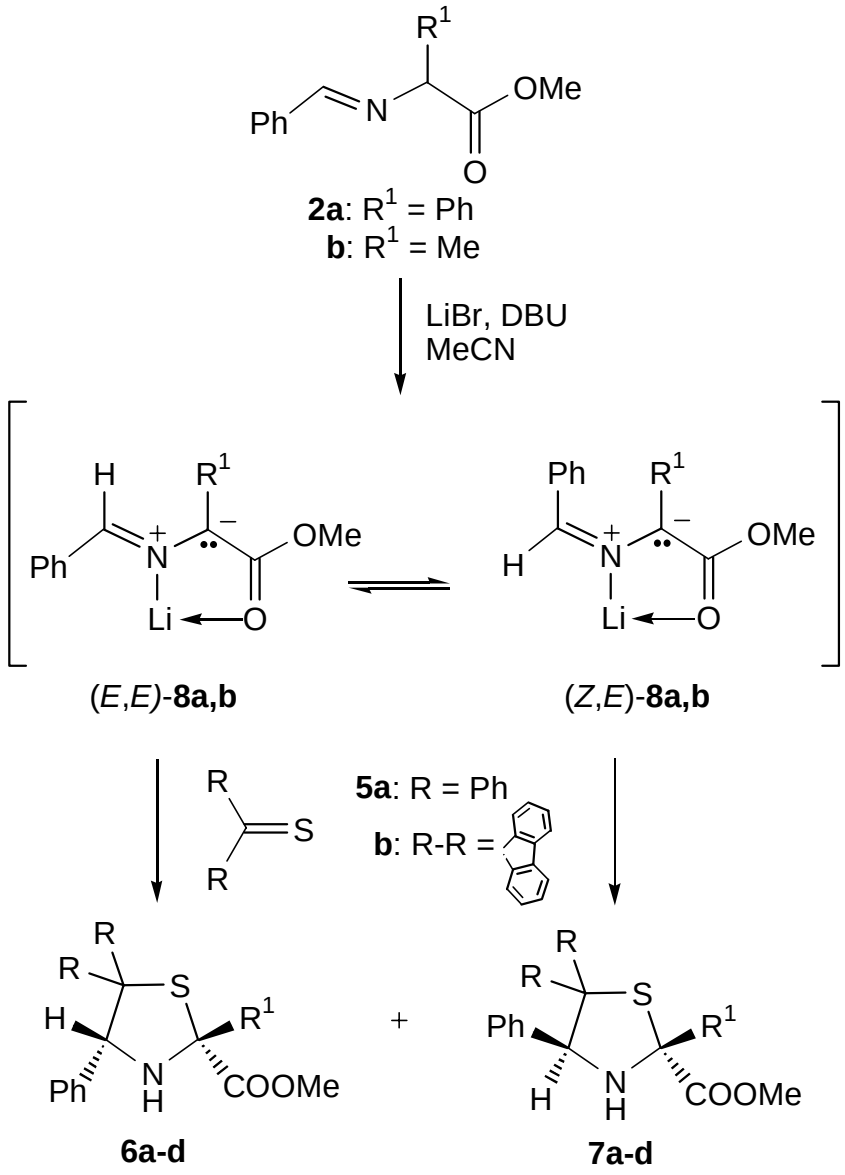
Scheme 2



RESULTS AND DISCUSSION

The reactions of **2a,b** with **5a** were carried out in acetonitrile as solvent, whereas in the case of **5b** a mixture of acetonitrile and toluene (5:1) was used to increase the solubility of **5b**. Compared with toluene, acetonitrile is the better solvent for the reaction because of the higher solubility of lithium bromide. All reactions were carried out with an excess (2 eq.) of thiocarbonyl compound (**5**), because the *in situ* generated azomethine ylides (**8**) can also be trapped by its precursor, the imine (**2**), yielding a side product of type (**9**). To avoid this reaction it is necessary to keep an excess of the thiocarbonyl compound in the solution. The used thioketones (**5a,b**) are highly reactive dipolarophiles.[40] In particular, **5b** undergoes cycloadditions very quickly. Furthermore, these compounds are sensitive to air and to moisture. Therefore, the reaction mixture was kept under an argon atmosphere. The reactions were performed at room temperature and the mixtures were stirred for the time shown in *Table 1*. When the imine (**2**) was completely consumed, the reaction was quenched by addition of a saturated aqueous

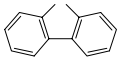
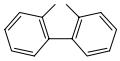
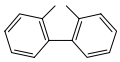
Scheme 3



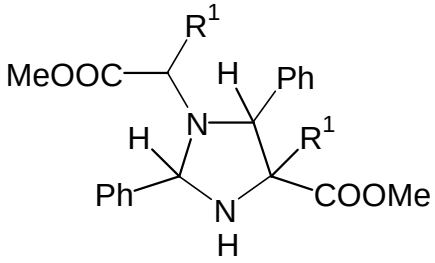
solution of ammonium chloride, the mixture was extracted with ether, and the products were isolated by column chromatography. When **5a** was reacted with **2a** according to the method described above (*cf. Scheme 3*), the imine (**2a**) was consumed after 6 h. After chromatographic workup, a mixture of the two diastereoisomers (**6a**) and (**7a**) was obtained in 75% yield. The separation of this mixture by preparative TLC (SiO_2) yielded the two isomers in a ratio of 2:1 (*Table 1*). The reaction of **5a** with **2b** gave, after 8 h, the two diastereoisomeric products (**6b**) and (**7b**) in 81% yield with a ratio of 3.9:1. In analogous reactions of **5b** with **2a** and **2b**, respectively, the color of the reaction mixture changed immediately from olive-green to orange-yellow. The monitoring by TLC showed that after two min the starting material was consumed, indicating once more that fluorene-9- thione (**5b**) is one of the most reactive dipolarophiles. After

column chromatography, a 2.4:1 mixture of the two diastereoisomers (**6c**) and (**7c**) was isolated from the reaction involving **2a**. Furthermore, only traces of the starting thione (**5b**) and

Table 1. *Reaction of **2a,b** with thioketones (**5a,b**)*

Imine (**2**)	Thioketone (**5**)	Reaction time	1,3-Thiazolidine (**6,7**)	Yield (%)	Ratio **6**:**7**
a R^1 = Ph	**a** R = Ph	6 h	**a** R^1 = R = Ph	75	2:1
b R^1 = Me		8 h	**b** R^1 = Me; R = Ph	81	3.9:1
a R^1 = Ph	**b** R-R = 	2 min	**c** R^1 = Ph; R-R = 	82	2.4:1
b R^1 = Me		2 min	**d** R^1 = Me; R-R = 	69	3.2:1

bisfluorenylidene (**10**)[41] could be isolated. The latter is a well-known side product in many reactions of **5b**. Under the same conditions, the reaction of **5b** with imine (**2b**) gave similar results; the diastereoisomers (**6d**) and (**7d**) were isolated in a ratio of 3.2:1 (*cf. Table 1*).



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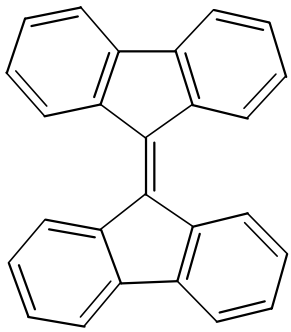

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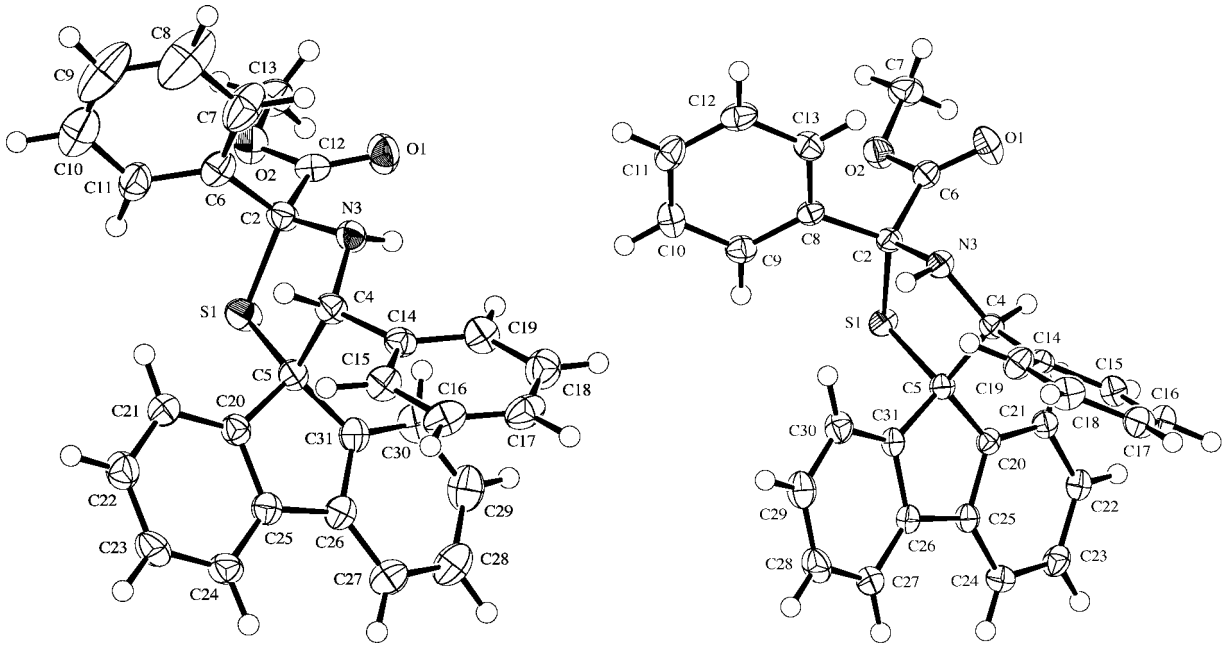
In the case of the pair of cycloadducts (**6c**) and (**7c**), the structures have been established by X-Ray crystal structure analyses (*Figure 1*). It was shown that the two adducts are diastereoisomeric methyl 1,3-thiazolidine-2-carboxylates. Whereas the two phenyl groups at C(2) and C(4) of the main product (**6c**) are *trans* oriented, they are in the *cis* position in the minor product (**7c**).

On the basis of the spectral data, especially ^{1}H- and ^{13}C-NMR data, and comparison with those of **6c** and **7c**, the structures of the other diastereoisomeric pairs were assigned. In all cases, the

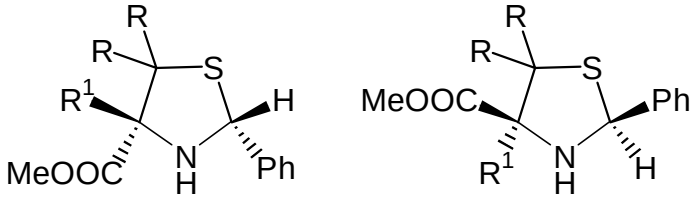
main product of type (**6**), with R^1 at C(2) and Ph at C(4) in a *trans* relationship, is the expected one. It results from the cycloaddition of the azomethine ylides ((*E*,*E*)-**8**) onto the C=S group



6c **7c**

Figure 1. ORTEP plots[42] of the molecular structures of **6c** and **7c**

(*cf. Scheme 4*). The (*E*,*E*)-configuration of the complexed azomethine ylide should be preferred because of the steric repulsion between Ph and R^1 in the (*Z*,*E*)-configured ylide (*cf. Scheme 3*). For this reason, we expected **11** to be the minor adduct, which would result from a transition state that is regioisomeric compared with that leading to **6**. However, neither **11** nor **12** could be detected in the reaction mixture. Therefore, the cycloaddition of the complexed azomethine ylides (**8**) with the thioketones (**5a,b**) occurred regioselectively leading exclusively to 1,3-thiazolidine-2-carboxylates.

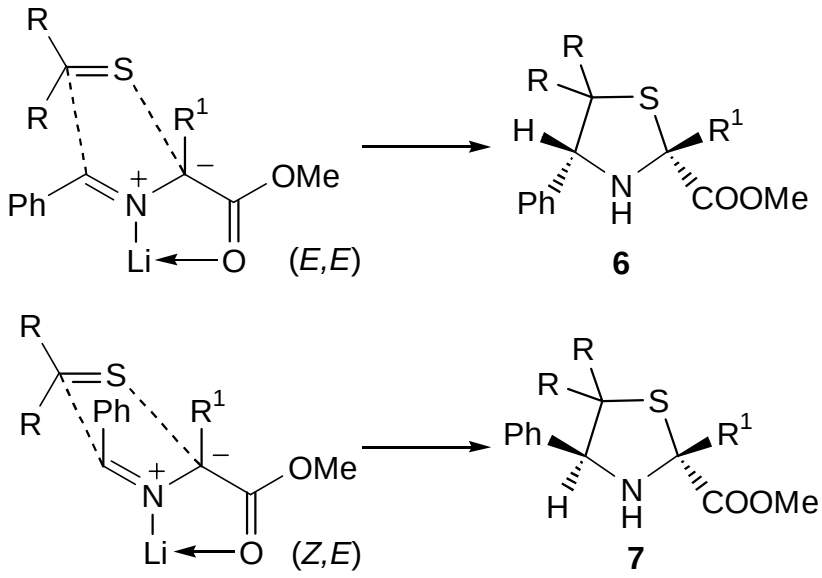


11 **12**

R^1 = Ph, Me

The minor isomer (**7**) isolated from the mixture was in all cases the diastereoisomer of **6**, resulting from the cycloaddition of the azomethine ylide ((*Z,E*)-**8**).

Scheme 4



In conclusion, the experiments discussed above show that the *in situ* generated azomethine ylides ((*E,E*)-**8**) and ((*Z,E*)-**8**) can be trapped with highly reactive thioketones like thiobenzophenone (**5a**) and fluorene-*9*-thione (**5b**). The regioselective cycloaddition reaction afforded the corresponding cycloadducts in good yield as a pair of two diastereoisomers (**6**) and (**7**) in a ratio of 2:1 to 4:1. The main diastereoisomer (**6**) is the result of the cycloaddition with the (*E,E*)-configurated ylide of type (**8**).

EXPERIMENTAL

General remarks. If not otherwise stated, IR spectra were recorded on a *Perkin-Elmer-781* instrument (KBr, cm^{-1}), ^{1}H-NMR and ^{13}C-NMR spectra on a *Bruker-AC-300* or *ARX-300* instrument ($CDCl_3$, 300 and 75.5 MHz, respectively, δ in ppm, *J* in Hz), and MS spectra on a *Finnigan-MAT-90* (70 eV, CI with NH_3) or *Finnigan-SSQ-700* spectrometer (ESI). Column chromatography (CC) and prep. TLC on silica gel (SiO_2).

Synthesis of the starting materials. *N*-Benzylidenephenylglycine methyl ester (**2a**) and *N*-benzylidenalanine methyl ester (**2b**) were prepared according to ref.[39] from methyl phenylglycinate hydrochloride and methyl alaninate hydrochloride, respectively, with

benzaldehyde. The crude imine (**2a**) was recrystallized from petroleum ether (mp 62-63°C), **2b** was obtained as pale yellow liquid. Thiobenzophenone (**5a**) was prepared from benzophenone using *Lawesson*-reagent.[43] Purification by column chromatography using first pentane/Et_2O (4:2) and then pentane yielded the pure thioketone. Fluorene-9-thione (**5b**) was obtained from fluoren-9-one using the method of *Mloston et al.*[44] The crude **5b** was purified by column chromatography using pentane/CH_2Cl_2 as solvent. Acetonitrile (MeCN) was dried over molecular sieves (4Å), toluene over sodium, LiBr was dried in a desiccator over $CaCl_2$ and DBU was freshly distilled before using.

General procedure for the cycloaddition reactions. A mixture of imine (**2**) (1 mmol), thiocarbonyl compound (**5**) (2 mmol), and LiBr (130 mg, 1.5 mmol) was dissolved in dry MeCN (5 mL), and then the base (DBU) was added dropwise to the reaction mixture. The mixture was stirred at rt for the time shown in *Table 1*. The reaction was quenched by addition of a saturated aqueous solution of NH_4Cl and extracted (2x) with Et_2O. The combined organic layers were washed with brine, dried over $MgSO_4$, and the solvent was evaporated. The crude products were purified by CC using hexane/AcOEt followed by preparative TLC.

*Methyl (2*RS*),(4*RS*)-2,4,5,5-tetraphenyl-1,3-thiazolidine-2-carboxylate* (**6a**). Prep. TLC with hexane/AcOEt 20:1, less polar fraction. Yield: 50% (225 mg). Colorless foam. ^{1}H-NMR: 4.05 (*s*, 3H, MeO), 4.61 (br *d*, *J* = 14.4, NH), 5.44 (br *d*, *J* = 14.4, H-C(4)), 6.96 (*d*, *J* = 7.3, 2 arom. H), 7.25-8.09 (4*m*, 16 arom. H), 8.10-8.12 (*dd*, ^2J = 4.0, ^3J = 2.1, 2 arom. H). ^{13}C-NMR: 53.5 (*t*, MeO), 71.7 (*d*, C(4)), 78.2, 78.7 (2*s*, C(2), C(5)), 126.8, 126.9, 127.1, 127.6, 127.7, 127.9, 128.1, 128.2, 128.4, 128.8, 131.3 (11*d*, 20 arom. CH), 136.3, 139.5, 141.4, 142.7 (4*s*, 4 arom. C), 171.4 (*s*, C=O). IR: 3310*w*, 3056*m*, 3030*m*, 2950*m*, 1954*w*, 1731*s*, 1659*m*, 1596*m*, 1491*m*, 1445*s*, 1312*m*, 1258*s*, 1204*s*, 1128*m*, 1079*m*, 1033*m*, 1015*m*, 941*m*, 898*m*, 826*m*, 769*s*, 739*s*, 696*s*, 638*m*, 622*m*. ESI-MS: 452 (100, $[M+1]^+$).

*Methyl (2*RS*),(4*SR*)-2,4,5,5-tetraphenyl-1,3-thiazolidine-2-carboxylate* (**7a**). Prep. TLC with hexane/AcOEt 20:1, more polar fraction. Yield: 24.6% (111 mg). Colorless foam. ^{1}H-NMR: 3.22 (br *s*, NH), 3.59 (*s*, 3H, MeO), 5.74 (br *s*, H-C(4)), 6.65 (*d*, *J* = 7.2, 2 arom. H), 6.76-7.76 (4*m*, 16 arom. H), 7.77 (*dd*, ^2J = 6.4, ^3J = 1.8, 2 arom. H). ^{13}C-NMR: 53.1 (*t*, MeO), 72.5 (*d*, C(4)), 74.9, 78.5 (2*s*, C(2), C(5)), 126.6, 126.9, 127.0, 127.6, 127.7, 128.2, 128.4, 128.5, 128.55, 128.6, 131.2 (11*d*, 20 arom. CH), 136.5, 139.7, 140.5, 142.7 (4*s*, 4 arom. C), 172.6 (*s*, C=O). IR: 3309*m*, 3083*m*, 3057*m*, 3029*m*, 2950*m*, 1731*s*, 1701*m*, 1658*s*, 1597*s*, 1537*w*, 1492*s*, 1445*s*, 1348*w*, 1317*m*, 1276*s*, 1256*s*, 1204*s*, 1176*s*, 1157*m*, 1131*s*, 1075*s*, 1032*s*, 1000*m*, 941*m*, 919*m*, 899*m*, 886*w*, 824*w*, 768*s*, 738*s*, 696*s*, 638m, 623*m*. ESI-MS: 542 (100, $[M+1]^+$).

*Methyl (2*RS*),(4*RS*)-2-methyl-4,5,5-triphenyl-1,3-thiazolidine-2-carboxylate* (**6b**). Prep. TLC with hexane/AcOEt 20:1, less polar fraction. Yield: 64.5% (251 mg). Pale yellow foam. ^{1}H-NMR: 1.98 (*s*, 3H, Me), 3.86 (*s*, 3H, MeO), 4.08 (br *d*, *J* = 12.7, NH), 5.53 (br *d*, *J* = 12.1, H-C(4)), 6.75 (*d*, *J* = 7.2, 2 arom. H), 6.93-7.27 (2*m*, 11 arom. H), 7.46 (*d*, *J* = 7.2, 2 arom. H). ^{13}C-NMR: 28.7 (*t*, Me), 53.3 (*t*, MeO), 71.8, 77.9 (2*s*, C(2), C(5)), 71.9 (*d*, C(4)), 126.8, 127.0, 127.1, 127.7, 127.8, 127.9, 128.2, 128.7, 131.4 (9*d*, 15 arom. CH), 136.2, 139.4, 142.9 (3*s*, 3 arom. C), 172.8 (*s*, C=O). IR: 3308*w*, 3057*m*, 3031*m*, 2975*m*, 2951*m*, 2924*m*, 1952*w*, 1733*s*, 1597*w*, 1493*m*, 1439*s*, 1378*m*, 1264*s*, 1198*s*, 1141*s*, 1066*m*, 1034*m*, 982*m*, 931*w*, 896*m*, 859*m*, 824*m*, 770*s*, 738*s*, 697*s*, 650*w*, 616*w*. ESI-MS: 390 (100, $[M+1]^+$). Anal. Calcd for $C_{24}H_{23}NO_2S$: C, 74.01; H, 5.95; N 3.60; S 8.23. Found: C, 73.69; H, 5.79; N, 3.52; S, 8.15.

*Methyl (2*RS*),(4*SR*)-2-methyl-4,5,5-triphenyl-1,3-thiazolidine-2-carboxylate* (**7b**). Prep. TLC with hexane/AcOEt 20:1, more polar fraction. Yield: 16.7% (65 mg). Yellow foam. ^{1}H-NMR: 2.03 (*s*, 3H, Me), 2.86 (br *s*, NH), 3.78 (*s*, 3H, MeO), 5.83 (*s*, H-C(4)), 6.72 (*d*, *J* = 7.2, 2 arom. H), 7.00-7.29 (*m*, 11 arom. H), 7.43 (*d*, *J* = 7.2, 2 arom. H). ^{13}C-NMR: 25.9 (*t*, Me), 52.7 (*t*, MeO), 72.1, 75.6 (2*s*, C(2), C(5)), 73.0 (*d*, C(4)), 126.6, 126.8, 126.9, 127.0, 127.6, 128.0, 128.1, 128.5, 131.3 (9*d*, 15 arom. CH), 136.5, 140.2, 143.2 (3*s*, 3 arom. C), 173.5 (*s*, C=O). IR: 3312*m*, 3084*m*, 3057*m*, 3030*m*, 2949*m*, 2924*s*, 2852*m*, 2318*w*, 1732*s*, 1658*m*, 1597*m*, 1492*s*, 1467*s*, 1441*s*, 1404*m*, 1375*m*, 1344*m*, 1310*m*, 1252*s*, 1195*s*, 1141*s*, 1091*s*, 1032*m*, 1001*m*, 980*m*, 926*w*, 897*m*, 843*w*, 823w, 813*m*, 738*s*, 697*s*, 668*m*, 639*m*, 627*m*, 617*m*. ESI-MS: 390 (100, $[M+1]^+$).

*Methyl (2'*RS*),(4'*RS*)-diphenylspiro[fluorene-9,5'-(1',3'-thiazolidine)]-2'-carboxylate* (**6c**). Reaction in MeCN (5 mL)/toluene (1 mL). Prep. TLC with hexane/AcOEt 30:1 (2 x developed). Yield: 58.3% (262 mg). Colorless foam. ^{1}H-NMR: 3.80 (*s*, 3H, MeO), 4.63 (br *d*, *J* = 14.8, NH), 4.92 (br *d*, *J* = 14.8, H-C(4')), 6.44 (*d*, *J* = 7.5, 2 arom. H), 6.77-6.91 (*m*, 3 arom. H), 7.11-7.52 (2*m*, 10 arom. H), 7.70 (*d*, *J* = 7.5, 1 arom. H), 8.02 (*dd*, ^{2}J = 8.2, ^{3}J = 1.8, 2 arom. H). ^{13}C-NMR: 53.7 (*t*, MeO), 76.7 (*d*, C(4')), 74.2, 80.6 (2*s*, C(2'), C(5')), 119.5, 119.8, 124.1, 125.1, 125.9, 127.0, 127.2, 127.3, 127.6, 127.8, 128.0, 128.2, 128.3, 128.7 (14*d*, 18 arom. CH), 133.5, 138.9, 140.7, 141.1, 144.9, 147.4 (6*s*, 6 arom. C), 172.3 (*s*, C=O). IR: 3337*w*, 3060*m*, 2951*w*, 1733*s*, 1598*m*, 1474*m*, 1447*s*, 1430*s*, 1260*s*, 1206*s*, 1155*m*, 1138*m*, 1116*m*, 1037*m*, 1034*m*, 1016*m*, 1003*m*, 938*w*, 915*m*, 897*m*, 873*m*, 825*m*, 786*w*, 763*s*, 742*s*, 721*s*, 696*s*, 616*m*. CI-MS: 450 (5, $[M+1]^+$), 255 (16), 254 (100), 197 (18), 194 (5). Anal. Calcd for $C_{29}H_{23}NO_2S$: C, 77.48; H, 5.16; N 3.12; S 7.13. Found: C, 77.13; H, 5.09; N, 3.24; S, 7.34. Suitable crystals for an X-Ray crystal structure determination were grown from CH_2Cl_2/MeOH.

*Methyl (2'*RS*),(4'*SR*)-diphenylspiro[fluorene-9,5'-(1',3'-thiazolidine)]-2'-carboxylate* (**7c**). Prep. TLC with hexane/AcOEt 25:1 (2 x developed). Yield: 23.8% (107 mg). Pale yellow foam. ^{1}H-NMR: 3.67 (br *s*, NH), 3.77 (*s*, 3H, MeO), 5.36 (br *s*, H-C(4')), 6.59 (*d*, *J* = 7.2, 2 arom. H), 6.73-6.99 (*m*, 3 arom. H), 7.01-7.46 (2*m*, 10 arom. H), 7.81 (*d*, *J* = 7.5, 1 arom. H), 7.88 (*dd*, ^{2}J = 8.3, ^{3}J = 1.6, 2 arom. H). ^{13}C-NMR: 53.3 (*t*, MeO), 70.0, 79.2 (2*s*, C(2'), C(5')), 76.3 (*d*, C(4')), 119.5, 119.8, 124.6, 125.9, 126.6, 127.0, 127.1, 127.3, 127.5, 127.7, 127.9, 128.6, 128.7, 128.9 (14*d*, 18 arom. CH), 134.3, 139.2, 140.2, 140.9, 143.9, 147.5 (6*s*, 6 arom. C), 173.7 (*s*, C=O). IR: 3354*m*, 3058*m*, 2949*w*, 1742*s*, 1596*m*, 1491*m*, 1446*s*, 1343*m*, 1310*m*, 1259*m*, 1231*s*, 1201*s*, 1109*s*, 1031*m*, 1001*m*, 975*m*, 906*m*, 894*m*, 817*m*, 788*m*, 764*s*, 743*s*, 727*s*, 697*s*, 617*m*. ESI-MS: 472 (12, $[M+Na]^{+}$), 450 (100, $[M+1]^{+}$). Suitable crystals for an X-Ray crystal structure determination were grown from $CDCl_3$.

*Methyl (2'*RS*),(4'*RS*)-2'-methyl-5'-phenylspiro[fluorene-9,5'-(1',3'-thiazolidine)]-2'-carboxylate* (**6d**). Reaction in MeCN (5 mL)/toluene (1 mL). Prep. TLC with hexane/AcOEt 30:1 (2 x developed). Yield: 52.2% (202 mg). Pale yellow foam. ^{1}H-NMR: 2.13 (*s*, 3H, Me), 3.87 (*s*, 3H, MeO), 4.70 (br *d*, NH), 5.00 (*d*, *J* = 9.1, H-C(4')), 6.50 (*d*, *J* = 7.2, 2 arom. H), 6.75-6.89 (*m*, 3 arom. H), 7.06-7.41 (*m*, 6 arom. H), 7.69 (*d*, *J* = 7.5, 1 arom. H), 7.80 (*d*, *J* = 6.3, 1 arom. H). ^{13}C-NMR: 28.4 (*t*, Me), 53.5 (*t*, MeO), 73.4, 74.1 (2*s*, C(2'), C(5')), 77.2 (*d*, C(4')), 119.5, 119.9, 124.0, 125.1, 126.1, 127.1, 127.3, 127.4, 127.6, 127.8, 128.4 (11*d*, 13 arom. CH), 133.3, 138.9, 140.9, 144.3, 147.4 (5*s*, 5 arom. C), 173.9 (*s*, C=O). IR: 3320*m*, 3034*m*, 2952*m*, 1950*w*, 1729*s*, 1603*m*, 1584*w*, 1500*w*, 1448*s*, 1377*m*, 1268*s*, 1200*s*, 1145*s*, 1096*m*, 1063*m*, 1031*m*, 1004*w*, 979*m*, 944*w*, 913*w*, 897*m*, 874*w*, 859*m*, 825*s*, 766*s*, 743*s*, 714*s*, 694*s*, 660*m*, 618*m*. ESI-MS: 388 (100, $[M+1]^{+}$). Anal. Calcd for $C_{24}H_{21}NO_2S$: C, 74.39; H, 5.46; N 3.61; S 8.28. Found: C, 73.94; H, 5.46; N, 3.38; S, 8.34.

*Methyl (2'*RS*),(4'*SR*)-2'-methyl-5'-phenylspiro[fluorene-9,5'-(1',3'-thiazolidine)]-2'-carboxylate* (**7d**). Prep. TLC with hexane/AcOEt 30:1 (2 x developed). Yield: 16.5 % (64 mg). Pale yellow foam. ^{1}H-NMR: 2.13 (*s*, 3H, Me), 3.25 (br *s*, NH), 3.88 (*s*, 3H, MeO), 5.34 (*s*, 1H, H-C(4')), 6.57 (*d*, *J* = 7.1, 2 arom. H), 6.76-6.90 (*m*, 3 arom. H), 7.07-7.42 (*m*, 6 arom. H), 7.71 (*t*, *J* = 7.7, 2 arom. H). ^{13}C-NMR: 27.6 (*t*, Me), 52.9 (*t*, MeO), 70.4, 72.4 (2*s*, C(2'), C(5')), 76.3 (*d*, C(4')), 119.4, 119.7, 124.6, 125.7, 126.3, 126.9, 127.0, 127.3, 127.6, 127.8, 128.3 (11*d*, 13 arom. CH), 134.5, 139.2, 140.7, 144.7, 147.7 (5*s*, 5 arom. C), 174.6 (*s*, C=O). IR: 3304*m*, 3001*m*, 2949*m*, 1730*s*, 1603*w*, 1448*s*, 1372*m*, 1250*s*, 1184*s*, 1092*s*, 1030*m*, 1005w, 976*m*, 921*w*, 845*w*, 799*w*, 773*s*, 742*s*, 699*s*, 649*m*, 630*m*, 618*m*. ESI-MS: 388 (100, $[M+1]^{+}$).

Crystal Structure Determination of **6c** *and* **7c** (see *Table 2* and *Figure 1*).[45] The intensities were collected on a *Rigaku AFC5R* diffractometer in the $\omega/2\theta$-scan mode using graphite-monochromated MoK_α radiation (λ = 0.71069 Å) and a 12 kW rotating anode generator. The intensities were corrected for *Lorentz* and polarization effects, but not for absorption. Data collection and refinement parameters are listed in *Table 2*, views of the molecules are shown in *Figure 1*. The structures were solved by direct methods using SHELXS86,[46] which releaved the positions of all non-H atoms. The non-H atoms were refined anisotropically. All of the H-atoms of **6c** were located in a difference electron density map and their positions were allowed to refine together with individual isotropic displacement parameters. In the case of **7c**, the amine H-atom was placed in the position indicated by a difference electron density map and its position was allowed to refine together with an isotropic displacement parameter. All other H-atoms were fixed in geometrically calculated positions [*d*(C-H) = 0.95 Å] and were assigned fixed isotropic displacement parameters with values equal to $1.2U_{eq}$ of their parent C-atoms. The structures were refined on *F* using full-matrix least-squares procedures. For **7c**, a correction for secondary extinction was applied. Neutral atom scattering factors for non-H atoms were taken from ref.[47a], and the scattering factors for H-atoms were taken from ref.[48] Anomalous dispersion effects were included in F_{calc};[49] the values for *f'* and *f''* were those of ref.[47b] All calculations were performed using the TEXSAN crystallographic software package.[50]

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Table 2. Crystallographic Data for Compounds (**6c**) *and* (**7c**)

		6c	**7c**
Crystallised from		CH_2Cl_2/MeOH	$CDCl_3$
Empirical formula		$C_{29}H_{23}NO_2S$	$C_{29}H_{23}NO_2S$
Formula weight [g mol^{-1}]		449.57	449.57
Crystal color, habit		colorless, prism	colorless, prism
Crystal dimensions [mm]		0.20 x 0.32 x 0.44	0.40 x 0.50 x 0.60
Temperature [K]		173 (1)	173 (1)
Crystal system		monoclinic	orthorhombic
Space group		$P2_1/c$	$Pca2_1$
Z		4	4
Reflections for cell determination		20	25
2θ range for cell determination [°]		24-26	39-40
Unit cell parameters	a [Å]	8.681 (4)	19.662 (3)
	b [Å]	20.556 (3)	9.602 (1)
	c [Å]	13.298 (4)	11.787 (2)
	β [°]	104.53 (3)	90
	V [$Å^3$]	2297 (1)	2225.5 (4)
D_x [g cm^{-3}]		1.300	1.342
μ(MoK_α) [mm^{-1}]		0.168	0.173
$2\theta_{(max)}$ [°]		50	55
Total reflections measured		4464	3417
Symmetry independent reflect.		4045	2676
Reflections used [$I>2\sigma(I)$]		2880	2462
Parameters refined		390	302
Final R, wR		0.0463, 0.0438	0.0323, 0.0321
Weights: p in $w = [\sigma^2(F_o) + (pF_o)^2]^{-1}$		0.005	0.005
Goodness of fit		1.775	1.844
Secondary extinction coefficient		-	1.02(9) x 10^{-6}
Final Δ_{max}/σ		0.0002	0.0005
Δ (max; min) [e $Å^{-3}$]		0.23; -0.25	0.23; -0.19
$\sigma(d_{(C-C)})$ [Å]		0.004-0.006	0.003-0.004

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