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Paper

Diastereoselective Synthesis of Spiro[pyrazolone-4,3'-tetrahydrothiophenes] via a Sulfa-Michael/Aldol Domino Reaction

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42–98% 3:2:1 to 20:1 d.r. 17 examples

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Abstract A new approach for the diastereoselective synthesis of spiro[pyrazolone-4,3'-tetrahydrothiophenes] was developed. The *N*,*N*-diisopropylethylamine-catalyzed reaction of arylidenepyrazolones with *in situ* generated 2-sulfanylacetaldehyde provides the corresponding spiro-heterocycles via a domino sulfa-Michael/aldol reaction in 42–98% yield and 3:2:1 to 20:1 d.r. under mild reaction conditions.

Key words spiro compounds, domino reaction, tetrahydrothiophene, pyrazolone, sulfa-Michael addition

The development of new and efficient synthetic routes to access bioactive heterocyclic compounds is fundamental for the synthesis of valuable natural products, pharmaceuticals and agrochemicals. Tetrahydrothiophenes are present in many natural products and pharmaceuticals,¹ such as the essential coenzyme biotin² or analogues of penicillin.³ In addition, bioactive compounds bearing a pyrazolone moiety display a wide range of biological and pharmaceutical properties, and especially spiro-pyrazolones,⁴ such as the spiro compounds **A**,⁵ with antimicrobial activity, **B**, a phosphodiesterase inhibitor,⁶ **C**, with antitumor activity,⁷ and **D**, with antibacterial activity,⁸ have attracted much interest in medicinal chemistry (Figure 1).

Recently, arylidenepyrazolones have been recognized as very good substrates to provide new pyrazole and pyrazolone derivatives.⁹ 1,4-Dithiane-2,5-diol, the dimer of 2sulfanylacetaldehyde, emerged as an excellent precursor for the development of domino sulfa-Michael/aldol reactions to provide tetrahydrothiophene rings (Scheme 1).¹⁰ Similar domino transformations of 1,4-dithiane-2,5-diol resulted in the construction of spiro-tetrahydrothiophenes containing



Figure 1 Typical examples of bioactive spiro-pyrazolone compounds

oxindole,^{11a,c} 1,3-indanedione,^{11e} and chromanone cores.^{11b,d} However, to the best of our knowledge, there is no report in the literature on the formation of spiro-tetrahydrothiophenes bearing a pyrazolone moiety.

Herein we report a diastereoselective sulfa-Michael/ aldol domino reaction of arylidenepyrazolones **1** and 1,4dithiane-2,5-diol (**2**) to provide spiro[pyrazolone-4,3'-tetrahydrothiophenes] **3** (Scheme 1). In our initial investigations, different organic and inorganic bases were tested (Table 1). The first attempt using DMAP (10 mol%) in CH₂Cl₂ at room temperature afforded the spirocyclic product **3a** in 83% yield and 12:2:1 d.r (entry 1). The product was acetylated *in situ* to ease the analysis of the NMR spectra. The screening of other organic bases such as Et₃N, DABCO, or DBU provided **3a** in moderate to very good yields and good diastereomeric ratios, but the reaction time extended to 19 hours when the base DABCO was used (entries 2–4). The sulfa-



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Scheme 1 Synthetic catalytic approaches to spirocyclic tetrahydrothiophenes

Michael/aldol domino reaction proceeded well when the inorganic base K_2CO_3 was used, to afford **3a** in 97% yield and 9:2:1 d.r., but in a longer reaction time (entry 5).

After further screening of organic bases, DIPEA was found to be the best catalyst, providing the spirocyclic product **3a** in 98% yield and 12:2:1 d.r. within 15 minutes (Table 1, entry 9). The reaction was further optimized by conducting the reaction in different solvents and varying the catalyst loading to determine the optimal reaction conditions. We found that DIPEA (5 mol%) in CH_2Cl_2 at room temperature provided **3a** in the best yield of 98% and a d.r. of 15:2:1 within 15 minutes (entry 16).

The optimized reaction conditions were then used to probe the general applicability of the domino sequence (Scheme 2). The sulfa-Michael/aldol reaction of arylidenepyrazolones bearing electron-donating (**1a**–**f**) and electronwithdrawing groups (**1g**–**j**) provided the spirocyclic compounds **3a**–**j** in good to excellent yields and moderate to excellent diastereomeric ratios. Good results in terms of yield and d.r. were also obtained by using a thionyl substituent at the arylidenepyrazolone, showing the presence of heterocyclic substituents in this reaction. The substrate scope was extended by varying the substituents at the N-1 and C-3 positions of the alkylidenepyrazolone. The reaction with different aryl substituents at the N-1 position provided good yields and moderate to very good diastereomeric ratios (**3l**–**n**). Moderate to good yields and moderate to excel-

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Table 1 Catalyst and Solvent Screening^a

	,,		5		
Ph	Ph +		1) cat. (10 mol% solvent, r.t. 2) Ac ₂ O (1.2 equ DMAP (20 m Py (1.2 equiv)	s) 	OAc CH ₃
	iu -	2			rac- 3a
Entry	Catalyst	Solvent	Reaction time	Yield (%) ^b	d.r. ^c
1	DMAP	CH ₂ Cl ₂	55 min	83	12:2:1
2	Et_3N	CH_2CI_2	50 min	73	7:2:1
3	DABCO	CH_2CI_2	19 h	93	10:2:1
4	DBU	CH_2CI_2	90 min	81	12:2:1
5	K ₂ CO ₃	CH_2CI_2	48 h	97	9:2:1
6	DBN	CH_2CI_2	3.5 h	83	11:2:1
7	HMTA ^d	CH_2CI_2	4 h	77	13:2:1
8	TMEDA	CH_2CI_2	30 min	98	12:2:1
9	DIPEA	CH_2CI_2	15 min	98	12:2:1
10	DIPEA	DCE	30 min	79	15:2:1
11	DIPEA	toluene	5 h	96	15:2:1
12	DIPEA	THF	20 min	74	6:1:1

14^f DIPEA CH₂Cl₂ 20 min 37 17:2:1 15^g DIPEA CH₂Cl₂ 55 16:2:1 25 min 16^h DIPEA CH_2CI_2 15 min 98 15:2:1 ^a Reaction conditions: 1a (0.25 mmol), 2 (0.15 mmol), cat. (10 mol%), sol-

7 d

n.d.

n.d.

vent (2.5 mL, 0.1 M).

CH₂Cl₂

^b Yield of **3a** after flash chromatography.

^c The diastereomeric ratio was determined by ¹H NMR.

^d HMTA = hexamethylenetetramine.

DIPFA

13e

• The reaction was carried out at 0 °C.

^f The reaction was carried out with DIPEA (30 mol%) at 0 °C.

^g The reaction was carried out with DIPEA (1 mol%).

^h The reaction was carried out with DIPEA (5 mol%).

lent diastereomeric ratios were achieved by varying the alkyl substituent at C-3 (**30–q**). It was observed that an increase in the steric hindrance at C-3 resulted in a lower yield (**3n–p**).

Furthermore, an enantioselective sulfa-Michael/aldol domino sequence was investigated, catalyzed by different chiral bifunctional organocatalysts such as squaramides¹² and thioureas.¹³ Initially different squaramide and thiourea catalysts (Table 2, **I–IV**) were tested to provide the product **3a**. In all approaches good to excellent yields could be achieved with good diastereomeric ratios, but the best enantioselectivity of only 19% *ee* was obtained with catalyst **I**. The reaction was then conducted in different solvents and at low temperature employing catalyst **I**, but so far the *ee* value could not be increased beyond 23% (entry 6).





tal structure analysis of compound **3i** (Figure 2).¹⁴ In conclusion, we have developed a diastereoselective sulfa-Michael/aldol domino reaction of arylidenepyrazolones with 1,4-dithiane-2,5-diol to afford spiro[pyrazolone-4,3'-tetrahydrothiophenes] in moderate to excellent yields and diastereomeric ratios. An attempt to develop an enantioselective variant of this protocol has also been carried out, but so far only 23% ee could be reached.

 Table 2
 Test of an Enantioselective Sulfa-Michael/Aldol Domino Reac tion^a

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Entry	Catalyst	Solvent	Reaction time	Yield (%) [⊾]	ее (%) ^с	d.r. ^d
1	I	CH_2CI_2	1 h	98	19	10:2:1
2	П	CH_2CI_2	2.5 h	88	4	12:2:1
3	ш	CH_2CI_2	5.5 h	98	18	8:2:1
4	IV	CH_2CI_2	5.5 h	98	14	10:2:1
5	I.	toluene	3 d	97	17	6:1:1
6	I.	THF	24 h	66	23	12:3:1
7 ^e	I	THF	2 d	45	21	13:3:1



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Figure 2 X-ray crystal structure of spiro[pyrazolone-4,3'-tetrahydrothiophene] **3i**. Interestingly, one enantiomer of **3i** was obtained after crystallization from *n*-hexane–ethyl acetate (1:1).

Unless otherwise noted, all commercially available chemicals were used without purification. All solvents were distilled and purified according to standard procedures. Analytical TLC was performed using SIL G-25 UV₂₅₄ from Macherey & Nagel (particle size 0.040–0.063 nm; 230-240 mesh flash) and visualized with UV radiation at 254 nm. ¹H, ¹³C, and ¹⁹F NMR spectra were recorded at ambient temperature on a Varian Innova 400 or Innova 600 instrument. Chemical shifts of the major diastereomer for the ¹H NMR and ¹³C NMR spectra are reported in ppm with coupling constants given in Hz. Melting points were measured on a LLG MPM-H2 melting point instrument. Mass spectra were acquired on a Finnigan SSQ7000 (EI, 70 eV) spectrometer and on a ThermoFinnigan LCO Deca XP plus (ESI) spectrometer, and high resolution ESI spectra were obtained on a ThermoFisher Scientific LTQ Orbitrap XL. Analytical HPLC was performed on a Agilent 1260 instrument by using chiral stationary phases (Daicel Chiralpak IA column). The alkylidenepyrazolones 1 were prepared according to known procedures.15

Compounds rac-3a-q; General Procedure

1,4-Dithiane-2,5-diol (**2**; 0.15 mmol) and DIPEA (5 mol%) were added to a solution of **1** (0.25 mmol) in CH₂Cl₂ (2.5 mL). The reaction mixture was stirred at r.t. until **1** was completely consumed as indicated by TLC. The solution of the crude product was cooled to 0 °C and treated with Ac₂O (0.30 mmol), DMAP (0.05 mmol), and pyridine (0.30 mmol). The crude product was then subjected to flash chromatography (silica gel, *n*-pentane–Et₂O, 20:1 to 6:1); this afforded the spiro product **3**.

1-Methyl-4-oxo-3,6-diphenyl-7-thia-2,3-diazaspiro[4.4]non-1-en-9-yl Acetate (3a)

Yield: 93 mg (98%); colorless solid; mp 78–80 °C; $R_f = 0.60$ (*n*-pentane–Et₂O, 1:1).

IR (ATR): 1750, 1709, 1595, 1495, 1452, 1401, 1364, 1323, 1292, 1216, 1148, 1053, 918, 839, 798, 758, 696 cm⁻¹.

¹H NMR (600 MHz, $CDCI_3$): δ = 7.70 (m, 2 H, Ar-H), 7.39–7.33 (m, 4 H, Ar-H), 7.25–7.15 (m, 4 H, Ar-H), 5.75 (t, *J* = 8.5 Hz, 1 H, CHOAc), 5.14 (s, 1 H, CHAr), 3.81 (dd, *J* = 11.1, 8.3 Hz, 1 H, SCHH), 3.19 (dd, *J* = 11.1, 8.8 Hz, 1 H, SCHH), 2.38 (s, 3 H, CH₃), 1.98 (s, 3 H, CH₃).

 ^{13}C NMR (151 MHz, CDCl₃): δ = 170.9 (C=O), 169.3 (C=O), 157.5 (Cq), 137.4 (Cq), 133.1 (Cq), 128.9 (2 C, Ar-C), 128.8 (Ar-C), 128.6 (2 C, Ar-C), 127.2 (2 C, Ar-C), 125.5 (Ar-C), 119.2 (2 C, Ar-C), 79.3 (CHOAc), 69.2 (Cq), 54.3 (CHAr), 33.0 (SCH_2), 20.6 (CH_3), 17.8 (CH_3).



$$\begin{split} \mathsf{MS}\,(\mathsf{EI}, \mathsf{70~eV});\, m/z\,(\%) &= 381.3\,(\mathsf{7})\,[\mathsf{M}+\mathsf{H}]^+, 380.1\,(33)\,[\mathsf{M}]^+, 320.1\,(55)\\ [\mathsf{M}-\mathsf{OAc}]^+, 263.1\,(100)\,[\mathsf{M}-\mathsf{C}_4\mathsf{H}_5\mathsf{O}_2\mathsf{S}]^+. \end{split}$$

HRMS (ESI): m/z [M + H]⁺ calcd for C₂₁H₂₁N₂O₃S: 381.1267; found: 381.1268.

6-(4-Methoxyphenyl)-1-methyl-4-oxo-3-phenyl-7-thia-2,3-diazaspiro[4.4]non-1-en-9-yl Acetate (3b)

Yield: 83 mg (81%); yellow solid; mp 38–40 °C; $R_f = 0.47$ (*n*-pentane–Et₂O, 1:1).

IR (ATR): 2944, 1719, 1596, 1493, 1363, 1216, 1044, 918, 829, 753, 692 $\rm cm^{-1}.$

¹H NMR (600 MHz, $CDCl_3$): δ = 7.72 (d, *J* = 8.6 Hz, 2 H, Ar-H), 7.36 (m, 2 H, Ar-H), 7.29–7.23 (m, 2 H, Ar-H), 7.17 (m, 1 H, Ar-H), 6.74 (t, *J* = 7.7 Hz, 2 H, Ar-H), 5.72 (t, *J* = 8.5 Hz, 1 H, CHOAc), 5.09 (s, 1 H, CHAr), 3.80 (dd, *J* = 11.0, 8.5 Hz, 1 H, SCHH), 3.72 (s, 3 H, OCH₃), 3.17 (m, 1 H, SCHH), 2.40 (s, 3 H, CH₃), 1.97 (s, 3 H, CH₃).

¹³C NMR (151 MHz, CDCl₃): δ = 171.0 (C=O), 169.3 (C=O), 159.7 (C_q), 157.6 (C_q), 137.4 (C_q), 129.6 (C_q), 128.8 (2 C, Ar-C), 128.4 (2 C, Ar-C), 125.4 (Ar-C), 119.1 (2 C, Ar-C), 113.9 (2 C, Ar-C), 79.2 (CHOAc), 69.2 (C_q), 55.2 (OCH₃), 53.9 (CHAr), 33.0 (SCH₂), 20.6 (CH₃), 17.8 (CH₃).

 $\begin{array}{l} MS \; (EI, \, 70 \; eV): \; m/z \; (\%) = 411.1 \; (16) \; [M + H]^{+}, \, 410.1 \; (62) \; [M]^{+}, \, 350.1 \\ (50) \; [M - HOAc]^{+}, \, 293.1 \; (100) \; [M - C_4H_5O_2S]^{+}. \end{array}$

HRMS (ESI): $m/z \,[M + Na]^+$ calcd for $C_{22}H_{22}N_2O_4SNa:$ 433.1193; found: 433.1192.

1-Methyl-4-oxo-3-phenyl-6-*p*-tolyl-7-thia-2,3-diazaspiro[4.4]non-1-en-9-yl Acetate (3c)

Yield: 91 mg (92%); colorless solid; mp 35–37 °C; $R_f = 0.68$ (*n*-pen-tane–Et₂O, 1:1).

 $IR (ATR): 2951, 1750, 1709, 1596, 1497, 1434, 1402, 1364, 1291, 1216, 1146, 1052, 920, 821, 798, 757, 727, 689 \ cm^{-1}.$

¹H NMR (600 MHz, CDCl₃): δ = 7.72 (m, 2 H, Ar-H), 7.36 (m, 2 H, Ar-H), 7.22 (d, *J* = 8.1 Hz, 2 H, Ar-H), 7.18 (m, 1 H, Ar-H), 7.01 (d, *J* = 7.9 Hz, 2 H, Ar-H), 5.73 (t, *J* = 8.5 Hz, 1 H, CHOAc), 5.11 (s, 1 H, CHAr), 3.80 (dd, *J* = 11.1, 8.3 Hz, 1 H, SCHH), 3.17 (dd, *J* = 11.1, 8.8 Hz, 1 H, SCHH), 2.39 (s, 3 H, CH₃), 2.25 (s, 3 H, CH₃), 1.98 (s, 3 H, CH₃).

¹³C NMR (151 MHz, CDCl₃): δ = 171.0 (C=O), 169.3 (C=O), 157.6 (C_q), 138.6 (C_q), 137.5 (C_q), 129.9 (C_q), 129.3 (2 C, Ar-C), 128.8 (2 C, Ar-C), 127.0 (2 C, Ar-C), 125.4 (Ar-C), 119.1 (2 C, Ar-C), 79.4 (CHOAc), 69.2 (C_q), 54.1 (CHAr), 33.0 (SCH₂), 21.1 (CH₃), 20.6 (CH₃), 17.8 (CH₃).

 $\begin{array}{l} MS \; (EI, \, 70 \; eV): \; m/z \; (\%) = 395.2 \; (11) \; [M + H]^{+}, \, 394.2 \; (31) \; [M]^{+}, \, 334.1 \\ (64) \; [M - HOAc]^{+}, \, 277.1 \; (100) \; [M - C_4H_5O_2S]^{+}. \end{array}$

HRMS (ESI): $m/z~[{\rm M} + Na]^{*}$ calcd for $C_{22}H_{22}N_{2}O_{3}SNa:$ 417.1243; found: 417.1240.

6-(3-Methoxyphenyl)-1-methyl-4-oxo-3-phenyl-7-thia-2,3-diazaspiro[4.4]non-1-en-9-yl Acetate (3d)

Yield: 92 mg (90%); brown oil; $R_f = 0.55$ (*n*-pentane-Et₂O, 1:1).

IR (ATR): 2951, 1751, 1709, 1595, 1493, 1458, 1433, 1402, 1366, 1270, 1216, 1153, 1045, 923, 872, 756, 713, 692 $\rm cm^{-1}.$

¹H NMR (400 MHz, CDCl₃): δ = 7.72 (d, *J* = 7.8 Hz, 2 H, Ar-H), 7.34 (t, *J* = 7.9 Hz, 2 H, Ar-H), 7.19–7.08 (m, 2 H, Ar-H), 6.93 (d, *J* = 7.5 Hz, 1 H, Ar-H), 6.84 (s, 1 H, Ar-H), 6.75 (d, *J* = 8.4 Hz, 1 H, Ar-H), 5.72 (t, *J* = 8.6 Hz, 1 H, CHOAc), 5.09 (s, 1 H, CHAr), 3.78 (dd, *J* = 11.0, 8.3 Hz, 1 H, SCHH), 3.56 (s, 3 H, OCH₃), 3.16 (dd, *J* = 10.9, 9.0 Hz, 1 H, SCHH), 2.36 (s, 3 H, CH₃), 1.96 (s, 3 H, CH₃).

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¹³C NMR (101 MHz, CDCl₃): δ = 171.0 (C=O), 169.2 (C=O), 159.6 (C_q), 157.5 (C_q), 137.4 (C_q), 134.6 (C_q), 129.6 (Ar-C), 128.8 (2 C, Ar-C), 125.4 (Ar-C), 119.3 (Ar-C), 119.0 (2 C, Ar-C), 114.8 (Ar-C), 112.2 (Ar-C), 79.3 (CHOAc), 69.1 (C_q), 55.0 (OCH₃), 54.1 (CHAr), 33.0 (SCH₂), 20.6 (CH₃), 17.8 (CH₃).

 $\begin{array}{l} \mathsf{MS}\,(\mathsf{EI}, \mathsf{70\ eV});\, m/z\,(\%) = 411.0\,(9)\,[\mathsf{M}+\mathsf{H}]^+, 410.0\,(21)\,[\mathsf{M}]^+, 350.0\,(38) \\ [\mathsf{M}-\mathsf{HOAc}]^+, 292.9\,(100)\,[\mathsf{M}-\mathsf{C_4H_5O_2S}]^+. \end{array}$

HRMS (ESI): $m/z [M + Na]^+$ calcd for $C_{22}H_{22}N_2O_4SNa$: 433.1193; found: 433.1193.

1-Methyl-4-oxo-3-phenyl-6-o-tolyl-7-thia-2,3-diazaspiro[4.4]non-1-en-9-yl Acetate (3e)

Yield: 69 mg (70%); colorless solid; mp 127–129 °C; $R_f = 0.59$ (*n*-pentane–Et₂O, 1:1).

IR (ATR): 2958, 2312, 2093, 1724, 1476, 1361, 1212, 1025, 737 cm⁻¹.

¹H NMR (400 MHz, CDCl₃): δ = 7.75–7.65 (m, 3 H, Ar-H), 7.35–7.28 (m, 2 H, Ar-H), 7.17–7.09 (m, 3 H, Ar-H), 7.02 (m, 1 H, Ar-H), 5.73 (t, J = 8.3 Hz, 1 H, CHOAc), 5.41 (s, 1 H, CHAr), 3.82 (dd, J = 11.2, 8.1 Hz, 1 H, SCHH), 3.21 (dd, J = 11.2, 8.5 Hz, 1 H, SCHH), 2.53 (s, 3 H, CH₃), 2.26 (s, 3 H, CH₃), 1.98 (s, 3 H, CH₃).

 ^{13}C NMR (101 MHz, CDCl₃): δ = 170.9 (C=O), 169.2 (C=O), 157.8 (C_q), 137.5 (C_q), 137.3 (C_q), 131.6 (C_q), 131.0 (Ar-C), 128.8 (2 C, Ar-C), 128.5 (Ar-C), 128.1 (Ar-C), 125.9 (Ar-C), 125.3 (Ar-C), 118.8 (2 C, Ar-C), 79.6 (CHOAc), 68.2 (C_q), 50.3 (CHAr), 33.4 (SCH₂), 20.7 (CH₃), 19.6 (CH₃), 18.6 (CH₃).

MS (EI, 70 eV): m/z (%) = 395.2 (1) [M + H]⁺, 335.0 (1) [M - OAc]⁺.

HRMS (ESI): $m/z \,[M + Na]^+$ calcd for $C_{22}H_{22}N_2O_3SNa$: 417.1243; found: 417.1226.

6-(Benzo[d][1,3]dioxol-5-yl)-1-methyl-4-oxo-3-phenyl-7-thia-2,3diazaspiro[4.4]non-1-en-9-yl Acetate (3f)

Yield: 69 mg (65%); orange solid; mp 42–44 °C; $R_f = 0.63$ (*n*-pentane–Et₂O, 1:1).

IR (ATR): 2902, 1717, 1598, 1488, 1362, 1221, 1037, 922, 758 cm⁻¹.

¹H NMR (600 MHz, $CDCl_3$): δ = 7.73 (m, 2 H, Ar-H), 7.40–7.34 (m, 2 H, Ar-H), 7.18 (m, 1 H, Ar-H), 6.91 (d, *J* = 1.8 Hz, 1 H, Ar-C), 6.80 (dd, *J* = 8.2, 1.9 Hz, 1 H, Ar-H), 6.62 (d, *J* = 8.1 Hz, 1 H, Ar-H), 5.90 (dd, *J* = 12.0, 1.5 Hz, 2 H, -OCH₂O-), 5.70 (t, *J* = 8.6 Hz, 1 H, CHOAc), 5.05 (s, 1 H, CHAr), 3.79 (dd, *J* = 11.1, 8.3 Hz, 1 H, SCHH), 3.17 (dd, *J* = 11.1, 8.9 Hz, 1 H, SCHH), 2.42 (s, 3 H, CH₃), 1.98 (s, 3 H, CH₃).

 ^{13}C NMR (151 MHz, CDCl₃): δ = 170.8 (C=O), 169.2 (C=O), 157.5 (C_q), 147.9 (C_q), 147.8 (C_q), 137.4 (C_q), 128.9 (2 C, Ar-C), 126.6 (C_q), 125.5 (Ar-C), 121.0 (Ar-C), 119.2 (2 C, Ar-C), 108.2 (Ar-C), 107.5 (Ar-C), 101.3 (-OCH_2O-), 79.1 (CHOAc), 69.2 (C_q), 54.2 (CHAr), 33.0 (SCH₂), 20.6 (CH₃), 17.9 (CH₃).

MS (EI, 70 eV): m/z (%) = 425.3 (2) [M + H]⁺, 424.2 (7) [M]⁺, 364.2 (16) [M - HOAc]⁺, 307.1 (100) [M - C₄H₅O₂S]⁺.

HRMS (ESI): $m/z [M + Na]^+$ calcd for $C_{22}H_{20}N_2O_5SNa$: 447.0985; found: 447.0984.

6-(4-Chlorophenyl)-1-methyl-4-oxo-3-phenyl-7-thia-2,3-diazaspiro[4.4]non-1-en-9-yl Acetate (3g)

Yield: 81 mg (78%); colorless solid; mp 37–39 °C; R_f = 0.50 (n-pentane–Et_2O, 1:1).

IR (ATR): 2939, 2291, 2083, 1715, 1596, 1491, 1361, 1213, 1043, 917, 828, 751, 691 $\rm cm^{-1}.$

¹H NMR (600 MHz, CDCl₃): δ = 7.74–7.70 (m, 2 H, Ar-H), 7.37 (m, 2 H, Ar-H), 7.31–7.27 (m, 2 H, Ar-H), 7.22–7.18 (m, 3 H, Ar-H), 5.73 (t, *J* = 8.6 Hz, 1 H, CHOAc), 5.09 (s, 1 H, CHAr), 3.81 (dd, *J* = 11.1, 8.3 Hz, 1 H, SCHH), 3.19 (dd, *J* = 11.1, 8.9 Hz, 1 H, SCHH), 2.37 (s, 3 H, CH₃), 1.98 (s, 3 H, CH₃).

 ^{13}C NMR (151 MHz, CDCl₃): δ = 170.7 (C=O), 169.2 (C=O), 157.2 (Cq), 137.3 (Cq), 134.6 (Cq), 131.8 (Cq), 128.9 (2 C, Ar-C), 128.8 (2 C, Ar-C), 128.6 (2 C, Ar-C), 125.6 (Ar-C), 119.1 (2 C, Ar-C), 79.2 (CHOAc), 69.1 (Cq), 53.5 (CHAr), 33.1 (SCH_2), 20.6 (CH_3), 17.8 (CH_3).

MS (EI, 70 eV): m/z (%) = 416.1 (16) [M, ³⁷Cl]⁺, 414.1 (39) [M, ³⁵Cl]⁺, 356.0 (17) [M – HOAc, ³⁷Cl]⁺, 354.0 (65) [M – HOAc, ³⁵Cl]⁺, 299.1 (31) [M – C₄H₅O₂S, ³⁷Cl]⁺, 297.0 (100) [M – C₄H₅O₂S, ³⁵Cl]⁺.

HRMS (ESI): $m/z [M + Na]^+$ calcd for $C_{21}H_{19}ClN_2O_3SNa$: 437.0697; found: 437.0698.

6-(4-Bromophenyl)-1-methyl-4-oxo-3-phenyl-7-thia-2,3-diazaspiro[4.4]non-1-en-9-yl Acetate (3h)

Yield: 90 mg (78%); colorless solid; mp 38–40 °C; R_f = 0.53 (*n*-pen-tane–Et₂O, 1:1).

 $IR (ATR): 1750, 1708, 1595, 1492, 1430, 1398, 1365, 1279, 1214, 1147, 1105, 1054, 1009, 955, 920, 881, 827, 793, 757, 725, 691 \ cm^{-1}.$

¹H NMR (600 MHz, CDCl₃): δ = 7.74–7.70 (m, 2 H, Ar-H), 7.40–7.33 (m, 4 H, Ar-H), 7.24–7.17 (m, 3 H, Ar-H), 5.73 (t, J = 8.6 Hz, 1 H, CHOAc), 5.07 (s, 1 H, CHAr), 3.80 (dd, J = 11.1, 8.3 Hz, 1 H, SCHH), 3.19 (dd, J = 11.1, 8.9 Hz, 1 H, SCHH), 2.37 (s, 3 H, CH₃), 1.98 (s, 3 H, CH₃).

 ^{13}C NMR (151 MHz, CDCl₃): δ = 170.7 (C=O), 169.2 (C=O), 157.1 (Cq), 137.3 (Cq), 132.3 (Cq), 131.8 (2 C, Ar-C), 128.9 (2 C, Ar-C), 128.9 (2 C, Ar-C), 125.6 (Ar-C), 122.8 (Cq), 119.1 (2 C, Ar-C), 79.2 (CHOAc), 68.98 (Cq), 53.5 (CHAr), 33.1 (SCH_2), 20.6 (CH_3), 17.8 (CH_3).

MS (EI, 70 eV): m/z (%) = 460.1 (34) [M, ⁸¹Br]⁺, 458.0 (33) [M, ⁷⁹Br]⁺, 400.0 (62) [M – OAc, ⁸¹Br]⁺, 398.0 (60) [M – OAc, ⁷⁹Br]⁺, 343.1 (94) [M – C₄H₆O₂S, ⁸¹Br]⁺, 341.0 (100) [M – C₄H₆O₂S, ⁷⁹Br]⁺.

HRMS (ESI): m/z [M + Na]⁺ calcd for $C_{21}H_{19}N_2O_3S^{79}BrNa$: 481.0192; found: 481.0193.

6-(3-Chlorophenyl)-1-methyl-4-oxo-3-phenyl-7-thia-2,3-diazaspiro[4.4]non-1-en-9-yl Acetate (3i)

Yield: 87 mg (84%); colorless solid; mp 119–121 °C; $R_f = 0.59$ (*n*-pentane–Et₂O, 1:1).

IR (ATR): 2950, 1728, 1589, 1489, 1361, 1219, 1041, 913, 768, 698 cm⁻¹.

¹H NMR (400 MHz, CDCl₃): δ = 7.72–7.66 (m, 2 H, Ar-H), 7.43 (m, 1 H, Ar-H), 7.39–7.32 (m, 2 H, Ar-H), 7.23–7.10 (m, 4 H, Ar-H), 5.71 (t, *J* = 8.6 Hz, 1 H, CHOAc), 5.07 (s, 1 H, CHAr), 3.79 (dd, *J* = 11.1, 8.3 Hz, 1 H, SCHH), 3.18 (dd, *J* = 11.1, 8.9 Hz, 1 H, SCHH), 2.36 (s, 3 H, CH₃), 1.97 (s, 3 H, CH₃).

 ^{13}C NMR (101 MHz, CDCl₃): δ = 170.7 (C=O), 169.2 (C=O), 157.1 (Cq), 137.2 (Cq), 135.4 (Cq), 134.6 (Cq), 129.9 (Ar-C), 129.0 (Ar-C), 128.9 (2 C, Ar-C), 127.3 (Ar-C), 125.7 (Ar-C), 125.5 (Ar-C), 119.3 (2 C, Ar-C), 79.1 (CHOAc), 69.0 (Cq), 53.5 (CHAr), 33.1 (SCH_2), 20.6 (CH_3), 17.7 (CH_3).

 $\begin{array}{l} MS \ (EI, \ 70 \ eV): \ m/z \ (\%) = 415.9 \ (14) \ [M, \ ^{37}Cl]^+, \ 414.0 \ (35) \ [M, \ ^{35}Cl]^+, \\ 356.0 \ (19) \ [M - HOAc, \ ^{37}Cl]^+, \ 354.0 \ (48) \ [M - HOAc, \ ^{35}Cl]^+, \ 298.9 \ (29) \\ [M - C_4H_5O_2S, \ ^{37}Cl]^+, \ 297.0 \ (100) \ [M - C_4H_5O_2S, \ ^{35}Cl]^+. \end{array}$

HRMS (ESI): m/z [M + Na]⁺ calcd for C₂₁H₁₉N₂O₃SClNa: 437.0697; found: 437.0696.



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1-Methyl-4-oxo-3-phenyl-6-[4-(trifluoromethyl)phenyl]-7-thia-2,3-diazaspiro[4.4]non-1-en-9-yl Acetate (3j)

Yield: 107 mg (95%); colorless solid; mp 40–42 °C; R_f = 0.53 (*n*-pentane–Et₂O, 1:1).

IR (ATR): 2101, 1712, 1600, 1497, 1322, 1219, 1119, 1053, 921, 846, 755, 688 cm⁻¹.

¹H NMR (600 MHz, CDCl₃): δ = 7.70 (m, 2 H, Ar-H), 7.48 (m, 4 H, Ar-H), 7.37 (m, 2 H, Ar-H), 7.20 (t, *J* = 7.4 Hz, 1 H, Ar-H), 5.75 (t, *J* = 8.6 Hz, 1 H, CHOAc), 5.16 (s, 1 H, CHAr), 3.83 (dd, *J* = 11.1, 8.3 Hz, 1 H, SCHH), 3.21 (dd, *J* = 11.1, 8.9 Hz, 1 H, SCHH), 2.37 (s, 3 H, CH₃), 1.99 (s, 3 H, CH₃).

¹³C NMR (151 MHz, CDCl₃): δ = 170.6 (C=O), 169.2 (C=O), 157.0 (C_q), 137.46 (C_q), 137.2 (C_q), 130.9 (q, *J* = 32.7 Hz, C_q), 128.9 (2 C, Ar-C), 127.7 (2 C, Ar-C), 125.7 (Ar-C), 125.6 (2 C, Ar-C), 123.7 (q, *J* = 272.3 Hz, CF₃), 119.1 (2 C, Ar-C), 79.3 (CHOAc), 69.0 (C_q), 53.5 (CHAr), 33.1 (SCH₂), 20.6 (CH₃), 17.7 (CH₃).

¹⁹F NMR (376 MHz, CDCl₃): δ = -62.78 (s).

 $\begin{array}{l} \mathsf{MS}\,(\mathsf{EI}, \mathsf{70~eV});\, m/z\,(\%) = 449.0\,(7)\,[\mathsf{M}+\mathsf{H}]^+, 447.9\,(31)\,[\mathsf{M}]^+, 387.9\,(33)\,[\mathsf{M}-\mathsf{HOAc}]^+, 330.6\,(100)\,[\mathsf{M}-\mathsf{C_4H_6O_2S}]^+. \end{array}$

HRMS (ESI): m/z [M + Na]⁺ calcd for C₂₂H₁₉N₂O₃S F₃Na: 471.0961; found: 471.0961.

1-Methyl-4-oxo-3-phenyl-6-(2-thienyl)-7-thia-2,3-diazaspiro[4.4]non-1-en-9-yl Acetate (3k)

Yield: 82 mg (85%); orange solid; mp 39–41 °C; $R_f = 0.46$ (*n*-pentane–Et₂O, 1:1).

IR (ATR): 3073, 2953, 1750, 1708, 1595, 1495, 1431, 1363, 1274, 1215, 1141, 1050, 919, 849, 800, 757, 697 $\rm cm^{-1}.$

¹H NMR (600 MHz, CDCl₃): δ = 7.81–7.77 (m, 2 H, Ar-H), 7.40–7.35 (m, 2 H, Ar-H), 7.19 (m, 1 H, Ar-H), 7.16 (m, 1 H, Ar-H_{2-Thienyl}), 6.97 (m, 1 H, Ar-H_{2-Thienyl}), 6.85 (m, 1 H, Ar-H_{2-Thienyl}), 5.69 (t, *J* = 8.6 Hz, 1 H, CHOAc), 5.32 (s, 1 H, CHAr), 3.80 (dd, *J* = 11.1, 8.3 Hz, 1 H, SCHH), 3.21 (dd, *J* = 11.0, 9.0 Hz, 1 H, SCHH), 2.47 (s, 3 H, CH₃), 1.98 (s, 3 H, CH₃).

 13 C NMR (151 MHz, CDCl₃): δ = 170.4 (C=O), 169.2 (C=O), 157.4 (Cq), 137.5 (Cq), 136.6 (Cq), 128.9 (2 C, Ar-C), 127.1 (Ar-C), 126.4 (Ar-C), 125.8 (Ar-C), 125.5 (Ar-C), 119.1 (2 C, Ar-C), 78.8 (CHOAc), 69.0 (Cq), 49.3 (CHAr), 33.3 (SCH_2), 20.6 (CH_3), 17.8 (CH_3).

MS (EI, 70 eV): m/z (%) = 387.0 (10) [M + H]⁺, 385.9 (36) [M]⁺, 325.8 (38) [M - HOAc]⁺, 268.7 (100) [M - C₄H₅O₂S]⁺.

HRMS (ESI): m/z [M + Na]⁺ calcd for C₁₉H₁₈N₂O₃S₂Na: 409.0651; found: 409.0651.

3-(2-Chlorophenyl)-1-methyl-4-oxo-6-phenyl-7-thia-2,3-diazaspiro[4.4]non-1-en-9-yl Acetate (31)

Yield: 78 mg (75%); colorless solid; mp 153–155 °C; $R_f = 0.50$ (*n*-pentane–Et₂O, 1:1).

IR (ATR): 3016, 2969, 2040, 1740, 1592, 1486, 1443, 1366, 1218, 1052, 919, 763, 701 $\rm cm^{-1}.$

¹H NMR (400 MHz, $CDCI_3$): δ = 7.43 (m, 3 H, Ar-H), 7.31–7.25 (m, 5 H, Ar-H), 7.08–7.04 (m, 1 H, Ar-H), 5.76 (t, *J* = 8.6 Hz, 1 H, CHOAc), 5.14 (s, 1 H, CHAr), 3.78 (dd, *J* = 11.0, 8.3 Hz, 1 H, SCHH), 3.20 (dd, *J* = 11.0, 8.9 Hz, 1 H, SCHH), 2.39 (s, 3 H, CH₃), 2.02 (s, 3 H, CH₃).

¹³C NMR (101 MHz, CDCl₃): δ = 169.7 (C=O), 168.9 (C=O), 156.5 (C_q), 133.9 (C_q), 133.8 (C_q), 131.9 (C_q), 130.3 (Ar-C), 129.8 (Ar-C), 128.7 (4 C, Ar-C), 128.5 (2 C, Ar-C), 127.3 (Ar-C), 75.8 (CHOAc), 66.5 (C_q), 49.6 (CHAr), 30.9 (SCH₂), 20.7 (CH₃), 13.7 (CH₃).

MS (EI, 70 eV): m/z (%) = 356.1 (11) [M – HOAc, ³⁷Cl]⁺, 354.1 (27) [M – HOAc, ³⁵Cl]⁺, 299.1 (35) [M – C₄H₅O₂S, ³⁷Cl]⁺, 297.1 (100) [M – C₄H₅O₂S, ³⁵Cl]⁺.

HRMS (ESI): m/z [M + Na]⁺ calcd for C₂₁H₁₉N₂O₃SCINa: 437.0697; found: 437.0685.

3-(4-Chlorophenyl)-1-methyl-4-oxo-6-phenyl-7-thia-2,3-diazaspiro[4.4]non-1-en-9-yl Acetate (3m)

Yield: 92 mg (89%); yellow oil; *R*_f = 0.61 (*n*-pentane–Et₂O, 1:1).

IR (ATR): 2951, 1723, 1595, 1490, 1357, 1215, 1143, 1044, 929, 825, 769, 697 cm⁻¹.

¹H NMR (400 MHz, CDCl₃): δ = 7.70–7.64 (m, 2 H, Ar-H), 7.29 (m, 4 H, Ar-H), 7.23–7.17 (m, 3 H, Ar-H), 5.72 (t, *J* = 8.5 Hz, 1 H, CHOAc), 5.10 (s, 1 H, CHAr), 3.79 (dd, *J* = 11.2, 8.3 Hz, 1 H, SCHH), 3.17 (dd, *J* = 11.2, 8.7 Hz, 1 H, SCHH), 2.36 (s, 3 H, CH₃), 1.96 (s, 3 H, CH₃).

 ^{13}C NMR (101 MHz, CDCl₃): δ = 170.9 (C=O), 169.2 (C=O), 157.8 (Cq), 135.9 (Cq), 132.9 (Cq), 130.5 (Cq), 128.8 (3 C, Ar-C), 128.6 (2 C, Ar-C), 127.1 (2 C, Ar-C), 120.1 (2 C, Ar-C), 79.3 (CHOAc), 69.3 (Cq), 54.5 (CHAr), 33.1 (SCH_2), 20.6 (CH_3), 17.8 (CH_3).

MS (EI, 70 eV): m/z (%) = 416.0 (14) [M, ³⁷Cl]⁺, 414.0 (36) [M, ³⁵Cl]⁺, 356.0 (18) [M – HOAc, ³⁷Cl]⁺, 354.0 (47) [M – HOAc, ³⁵Cl]⁺, 299.0 (31) [M – C₄H₅O₂S, ³⁷Cl]⁺, 297.0 (100) [M – C₄H₅O₂S, ³⁵Cl]⁺.

HRMS (ESI): m/z [M + Na]⁺ calcd for C₂₁H₁₉N₂O₃SCINa: 437.0697; found: 437.0697.

1-Methyl-4-oxo-6-phenyl-3-*p*-tolyl-7-thia-2,3-diazaspiro[4.4]non-1-en-9-yl Acetate (3n)

Yield: 85 mg (86%); brown solid; mp 37–39 °C; $R_f = 0.56$ (*n*-pentane–Et₂O, 1:1).

IR (ATR): 3479, 2940, 2655, 2333, 2099, 1719, 1613, 1510, 1362, 1215, 1044, 919, 814, 698 $\rm cm^{-1}$.

¹H NMR (600 MHz, CDCl₃): δ = 7.59–7.54 (m, 2 H, Ar-H), 7.36–7.33 (m, 2 H, Ar-H), 7.24–7.20 (m, 3 H, Ar-H), 7.17–7.14 (m, 2 H, Ar-H), 5.74 (t, *J* = 8.5 Hz, 1 H, CHOAc), 5.13 (s, 1 H, CHAr), 3.81 (dd, *J* = 11.1, 8.3 Hz, 1 H, SCHH), 3.18 (dd, *J* = 11.1, 8.8 Hz, 1 H, SCHH), 2.37 (s, 3 H, CH₃), 2.33 (s, 3 H, ArCH₃), 1.98 (s, 3 H, CH₃).

 13 C NMR (151 MHz, CDCl₃): δ = 170.7 (C=O), 169.3 (C=O), 157.3 (Cq), 135.3 (Cq), 135.0 (Cq), 133.1 (Cq), 129.3 (2 C, Ar-C), 128.7 (Ar-C), 128.6 (2 C, Ar-C), 127.2 (2 C, Ar-C), 119.2 (2 C, Ar-C), 79.3 (CHOAc), 69.1 (Cq), 54.2 (CHAr), 33.0 (SCH₂), 21.0 (CH₃), 20.6 (CH₃), 17.8 (CH₃).

MS (EI, 70 eV): m/z (%) = 395.2 (10) [M + H]⁺, 394.2 (26) [M]⁺, 334.1 (21) [M - HOAc]⁺, 277.1 (100) [M - C₄H₅O₂S]⁺.

HRMS (ESI): $m/z \; [M + Na]^+$ calcd for $C_{22}H_{22}N_2O_3SNa:$ 395.1424; found: 395.1423.

1-Isopropyl-4-oxo-3,6-diphenyl-7-thia-2,3-diazaspiro[4.4]non-1en-9-yl Acetate (30)

Yield: 55 mg (54%); yellow solid; mp 101–103 °C; $R_f = 0.63$ (*n*-pen-tane–Et₂O, 1:1).

IR (ATR): 2973, 1749, 1710, 1596, 1495, 1452, 1355, 1217, 1148, 1051, 979, 921, 883, 753, 693 $\rm cm^{-1}.$

¹H NMR (600 MHz, CDCl₃): δ = 7.79 (m, 2 H, Ar-H_{Diast}), 7.52 (m, 2 H, Ar-H), 7.47–7.43 (m, 2 H, Ar-H, Ar-H), 7.39 (m, 2 H, Ar-H_{Diast}), 7.33 (m, 2 H, Ar-H, Ar-H_{Diast}), 7.30–7.25 (m, 4 H, Ar-H, Ar-H_{Diast}), 7.24–7.19 (m, 4 H, Ar-H, Ar-H_{Diast}), 7.17 (m, 1 H, Ar-H_{Diast}), 7.11 (m, 1 H, Ar-H), 5.75 (dd, *J* = 10.1, 7.8 Hz, 1 H, CHOAc_{Diast}), 5.68 (dd, *J* = 9.9, 7.1 Hz, 1 H, CHO-Ac), 5.19 (s, 1 H, CHAr_{Diast}), 4.95 (s, 1 H, CHAr), 3.99 (t, *J* = 9.7 Hz, 1 H, SCHH), 3.75 (dd, *J* = 10.6, 7.8 Hz, 1 H, SCHH_{Diast}), 3.44 (dd, *J* = 9.5, 7.1

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Hz, 1 H, SCHH), 3.23 (t, J = 10.3 Hz, 1 H, SCH H_{Diast}), 3.12 (m, 1 H, C $H(CH_3)_{2\text{Diast}}$), 2.91 (m, 1 H, C $H(CH_3)_2$), 1.98 (s, 3 H, CH₃), 1.96 (s, 3 H, CH₃)_{2Diast}), 1.43 (d, J = 6.8 Hz, 3 H, CH₃ (ⁱPr)), 1.31 (d, J = 6.8 Hz, 3 H, CH₃ (ⁱPr))_{Diast}), 1.21 (d, J = 6.8 Hz, 3 H, CH₃ (ⁱPr)), 0.80 (d, J = 6.7 Hz, 3 H, CH₃ (ⁱPr)_{Diast}).

¹³C NMR (151 MHz, CDCl₃): δ = 171.0 (C=O_{Diast}), 169.9 (C=O), 169.1 (C=O), 168.7 (C=O_{Diast}), 165.4 (C_{q Diast}), 163.6 (C_q), 137.7 (C_{q Diast}), 137.3 (C_q), 134.0 (C_{q Diast}), 133.8 (C_q), 128.8 (2 C, Ar-C_{Diast}), 128.7 (2 C, Ar-C), 128.6 (2 C, Ar-C_{Diast}), 128.5 (2 C, Ar-C), 128.3 (2 C, Ar-C), 127.3 (2 C, Ar-C_{Diast}), 125.4 (2 C, Ar-C_{Diast}), 125.2 (2 C, Ar-C), 119.3 (2 C, Ar-C), 119.1 (2 C, Ar-C_{Diast}), 79.8 (CHOAc_{Diast}), 76.5 (CHOAc), 69.5 (C_{q Diast}), 67.7 (C_q), 53.0 (CHAr_{Diast}), 49.7 (CHAr), 32.3 (SCH_{2 Diast}), 30.7 (SCH₂), 29.7 (CH(CH₃)_{2 Diast}), 27.2 (CH(CH₃)₂), 22.8 (CH_{3 Diast}), 22.3 (CH₃), 20.8 (2 C, CH(CH₃)_{2 Diast}), 20.6 (2 C, CH(CH₃)₂).

MS (EI, 70 eV): m/z (%) = 408.1 (3) [M]⁺, 348.1 (13) [M – HOAc]⁺, 291.2 (67) [M – C₄H₅O₂S]⁺.

HRMS (ESI): m/z [M + Na]⁺ calcd for C₂₃H₂₄N₂O₃SNa: 409.1580; found: 409.1573.

1-*tert*-Butyl-4-oxo-3,6-diphenyl-7-thia-2,3-diazaspiro[4.4]non-1en-9-yl Acetate (3p)

Yield: 44 mg (42%); orange solid; mp 155–157 °C; $R_f = 0.70$ (*n*-pentane–Et₂O, 1:1).

IR (ATR): 2965, 1721, 1596, 1490, 1373, 1218, 1044, 967, 849, 748 cm⁻¹.

¹H NMR (600 MHz, CDCl₃): δ = 7.45 (m, 4 H, Ar-H), 7.28–7.24 (m, 2 H, Ar-H), 7.21 (m, 2 H, Ar-H), 7.17–7.12 (m, 1 H, Ar-H), 7.09 (m, 1 H, Ar-H), 5.91 (dd, J = 9.7, 7.2 Hz, 1 H, CHOAc), 5.32 (s, 1 H, CHAr), 4.01 (t, J = 9.6 Hz, 1 H, SCHH), 3.43 (dd, J = 9.5, 7.2 Hz, 1 H, SCHH), 1.98 (s, 3 H, CH₃), 1.47 (s, 9 H, 'Bu).

¹³C NMR (151 MHz, CDCl₃): δ = 170.0 (C=O), 168.9 (C=O), 163.6 (C_q), 137.1 (C_q), 134.3 (C_q), 128.5 (Ar-C), 128.5 (2 C, Ar-C), 128.4 (2 C, Ar-C), 128.1 (2 C, Ar-C), 125.2 (Ar-C), 119.2 (2 C, Ar-C), 77.0 (CHOAc), 68.4 (C_q), 48.5 (CHAr), 37.1 (C(CH₃)₃), 30.5 (SCH₂), 29.8 (3 C, ¹Bu), 20.7 (CH₃).

MS (EI, 70 eV): m/z (%) = 423.2 (36) [M + H]⁺, 422.2 (18) [M]⁺, 362.1 (89) [M - HOAc]⁺, 305.0 (100) [M - C₄H₅O₂S]⁺.

HRMS (ESI): m/z [M + H]⁺ calcd for C₂₄H₂₇N₂O₃S: 423.1737; found: 423.1736.

1-Ethyl-4-oxo-3,6-diphenyl-7-thia-2,3-diazaspiro[4.4]non-1-en-9-yl Acetate (3q)

Yield: 74 mg (76%); colorless oil; $R_f = 0.65$ (*n*-pentane-Et₂O, 1:1).

IR (ATR): 2978, 2940, 2106, 1751, 1708, 1596, 1495, 1453, 1353, 1218, 1142, 1049, 957, 913, 837, 800, 757, 728, 696 $\rm cm^{-1}.$

¹H NMR (600 MHz, CDCl₃): δ = 7.74 (m, 2 H, Ar-H), 7.39–7.31 (m, 5 H, Ar-H), 7.24–7.20 (m, 3 H, Ar-H), 5.73 (t, *J* = 8.6 Hz, 1 H, CHOAc), 5.13 (s, 1 H, CHAr), 3.79 (dd, *J* = 11.0, 8.2 Hz, 1 H, SCHH), 3.17 (dd, *J* = 10.9, 9.1 Hz, 1 H, SCHH), 2.68–2.58 (m, 2 H, CH₂CH3), 1.97 (s, 3 H, CH₃), 1.12 (t, *J* = 7.2 Hz, 3 H, CH₂CH₃).

 $^{13}C \ \text{NMR} \ (151 \ \text{MHz}, \ \text{CDCl}_3): \ \delta = 171.0 \ (\text{C=0}), \ 169.3 \ (\text{C=0}), \ 161.3 \ (\text{C}_q), \\ 137.6 \ (\text{C}_q), \ 133.3 \ (\text{C}_q), \ 128.8 \ (2 \ \text{C}, \ \text{Ar-C}), \ 128.7 \ (\text{Ar-C}), \ 128.5 \ (2 \ \text{C}, \ \text{Ar-C}), \\ 127.2 \ (\text{Ar-C}), \ 125.4 \ (2 \ \text{C}, \ \text{Ar-C}), \ 119.1 \ (2 \ \text{C}, \ \text{Ar-C}), \ 79.3 \ (\text{CHOAC}), \ 69.2 \ (\text{C}_q), \ 54.2 \ (\text{CHAr}), \ 33.1 \ (\text{SCH}_2), \ 24.5 \ (\text{CH}_2), \ 20.7 \ (\text{CH}_3), \ 9.0 \ (\text{CH}_2\text{CH}_3).$

MS (EI, 70 eV): m/z (%) = 394.0 (3) [M]⁺, 333.9 (12) [M – HOAc]⁺, 77.2 (100) [C₆H₅]⁺.

HRMS (ESI): m/z [M + Na]⁺ calcd for C₂₂H₂₂N₂O₃SNa: 417.1243; found: 417.1242.

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Paper

Supporting Information

Supporting information for this article is available online at http://dx.doi.org/10.1055/s-0035-1562473.

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