Annulated 1,2,4-Triazoles. A Convenient Synthesis of Thieno[2,3-*f*][1,2,4]triazolo[1,5-*a*]azepines: ANovel Triheterocyclic Ring System

Quanrui Wang,* Zheng Li, Haiyan Yang, Feng Li, Zongbiao Ding, Fenggang Tao

Department of Chemistry, Fudan University, 200433 Shanghai, P. R. China
Fax +86(21)65641740; E-mail: qrwangb@online.sh.cn

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Abstract: A synthetic approach to the previously unknown thieno[2,3-*f*][1,2,4]triazolo[1,5-*a*]azepine derivatives was efficiently accomplished by cycloaddition of the bicyclic 1-aza-2-azoniaallene salts **6**, derived from 6,7-dihydrobenzo[*b*]thiophen-4(5*H*)-one hydrazones **4**, to the triple bond of nitriles, followed by ring enlargement. The X-ray crystal diffraction analysis of the picrate **10a** provided affirmative proof for the structural assignment made.

Key words: 1-aza-2-azoniaallene cations, cycloaddition, nitriles, ring enlargement, thieno[2,3-*f*][1,2,4]triazolo[1,5-*a*]azepines

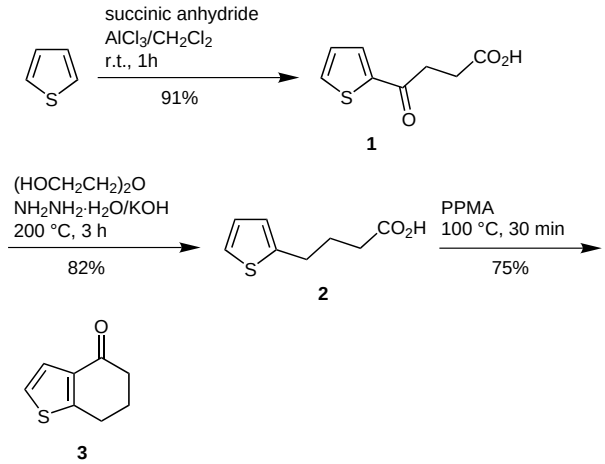
Many benzoazepine and benzoheteroazepine compounds with an additional triazolo ring fused on the seven-membered ring have been extensively investigated due to their wide spectrum of in vivo activities.[1–7] Nowadays, efforts are still being devoted to the structural modification of these pharmaceutically important molecules, for enhancing the activity or modifying the activity profile. By far the greatest attempts have been concentrated on thienotriazoloazepines, which differ from the benzo-fused analogues by replacing the benzene ring with a thiophene nucleus.[3–5] These novel tricyclic compounds have been described as having selective and potent blocking effects on D_4 receptor, antagonists for platelet activating factor, as having antiallergic properties, and also act as antipsychotic agents. However, to the best of our knowledge, only a very few fusion patterns of thieno[1,2,4]triazoloazepines have been reported as compared to the multitude of their benzo annulated counterparts. Included among these are derivates of the parent heterocycles 1*H*-thieno[3,4-*c*][1,2,4]triazolo[4,3-*a*]azepine,[3] 1*H*-thieno-[3,2-*c*][1,2,4]triazolo[4,3-*a*]azepine,[3] and 1*H*-thieno[3,2-*d*][1,2,4]triazolo[1,5-*a*]azepine.[4]

We have previously described the synthesis of various 1,2,4-triazolo[3,2-*d*][1,5]benzoxazepine[8,9] as well as 1,2,4-triazolo[3,2-*d*][1,5]benzothiazepine[9,10] compounds via reaction of the allenium ions derived from chroman-4-ones and respectively thiochroman-4-ones, with nitriles. Mechanistically, the reaction involves an initial cycloaddition followed by a ring enlargement. The present work is aimed at broadening the range of thieno[1,2,4]triazoloazepine heterocycles.

Two principle protocols are available in the literature for the synthesis of 6,7-dihydrobenzo[*b*]thiophen-4(5*H*)-one **3**, which serves as the key starting material in our program. One involves the ring construction of 4-(2-thienyl)butyric acid with either CH_3SO_3H/P_2O_5 (PPMA) or CF_3SO_3H/P_2O_5 (PPTMA),[11] via acid chloride formation by Lewis acid catalysis.[12] The other protocol calls for the reaction of 3-mercaptocyclohexanone with aqueous glyoxal. The method we chose was based on the reagents available. Thus, according to the literature procedure,[11] thiophene was allowed to react with succinic anhydride under $AlCl_3$ catalysis, giving 4-oxo-4-(2-thienyl)butanoic acid (**1**). The Wolff–Kishner–Minlong reduction converted the γ-oxo acid **1** to 4-(2-thienyl)butyric acid **2**, from which 6,7-dihydrobenzo[*b*]thiophen-4(5*H*)-one **3** was prepared via intramolecular Friedel–Crafts acylation in the presence of PPMA in overall yield of 56% (Scheme 1).

Synthesis of the target heterocycles was started with the hydrazones **4**, which were prepared by condensation of cyclic ketone **3** with the corresponding hydrazine in ethanolic solution in the presence of a catalytic amount of glacial acetic acid. The hydrazones **4** were subjected to chlorination by addition of a stoichiometric amount of *tert*-butyl hypochlorite at low temperatures (–30 °C → –10 °C). Work-up afforded the α-chloroazo compounds **5** as red oils in essentially quantitative yields.

More recently it came to our attention that $BTMA^+ICl_4^-$ (benzyltrimethylammonium tetrachloroiodate) has been



Scheme 1

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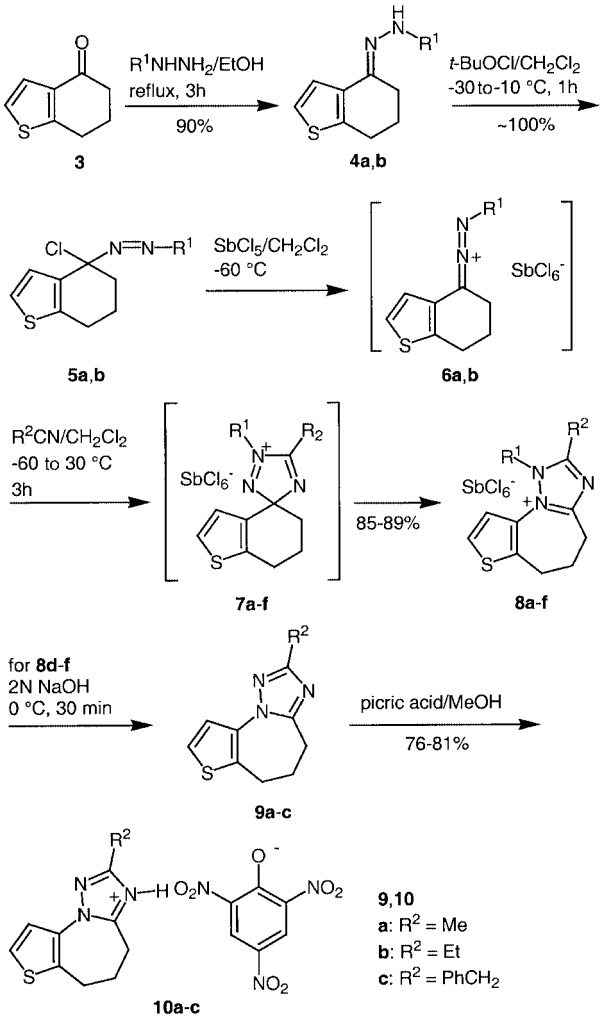
frequently used as an easy-to-prepare chlorination agent.[14] However, *tert*-butyl hypochlorite gave superior results. This reagent is readily availabile, offers mild reaction conditions, and is also convenient to use. Compounds **5a**,**b**, which are susceptible to thermal or photodecomposition, were employed for further transformation as described below.

The synthesis of the title compounds is outlined in Scheme 2. Thus, for example, a solution of the α-chloroazo compound **5a** in anhydrous dichloromethane was allowed to react with antimony pentachloride at low temperature (–60 °C), generating the allene-like cation **6a** upon departure of the chloride ion. In general, the salts **6** are highly reactive intermediates, thus precluding their isolation.

In the presence of a slight excess amount of acetonitrile, cycloaddition of **6a** to the triple bond of acetonitrile occurred smoothly leading to the formation of the 3-spiro substituted 3*H*-1,2,4-triazolium salt **7a**. On elevation of the temperature to about 35 °C, **7a** underwent spontaneous rearrangement with insertion of the nitrogen atom into the carbon skeleton providing the tricyclic product **8a** as white crystals in 87% yield. The other two thieno[2,3-*f*][1,2,4]triazolo[1,5-*a*]azepinium salts **8b** and **8c** were synthesized in high yields under comparable conditions.

With the aim of conducting physiological evaluations, we next considered expanding this reaction to the synthesis of the N(3) unsubstituted neutral free bases. To this end, the *N*-ester group substituted chloroazo compound **5b** was prepared and employed as the reactant. In a similar way as described for **8a**–**c**, the N(3)-carbethoxy substituted **8d**–**f** were produced. Since salts **8d**–**f** are extremely moisture-sensitive, they were treated directly in the same reaction vessel with a cold solution of aqueous sodium hydroxide. The neutral products **9a**–**c** were obtained after usual work-up as brown oils, which were transformed to the picrates **10a**–**c** for characterization (Scheme 2).

Mechanistically, the reaction begins with the cycloaddition of the allene-like ions **6** to the triple bond. The five-membered heterocyclic ring of the initial spiro adducts **7** contains, as a characteristic feature, a diazenium function, in which the nitrogen atom in the β-position to the aryl or ester substituent exhibits a latent nitrenium character. Subsequent migration of a substituent adjacent to the nitrogen atom mentioned above takes place with simultaneous ring enlarging annulation. We have previously shown that the 1,2-rearrangement of carbon to electron-deficient nitrogen in 3*H*-1,2,4-triazolium ions occurs with exclusive selectivity. Although the precise factors that govern migratory aptitude are not completely understood, given two different substituents, the migratory aptitude seems to parallel their ability to accommodate the respective carbocation. Studies of other substituents have shown that the migratory aptituide of groups is H > phenyl (aryl) > 3° alkyl > 2° alkyl > 1° alkyl > methyl approx. = cyclopropyl.[15,16] This behavior is just what we would expect in the present circumstances. We found that the ring enlargement proceeded smoothly under mild conditions with migration of the thiophene side of the spiro compounds **7**, leading to the formation of the tricyclic compounds **8** as the sole isolated products. Otherwise isomer **8′** would have formed through migration of the aliphatic side of the ring (Figure 1).



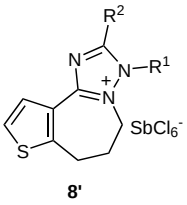
3 4a,b 5a,b 6a,b 7a-f 8a-f 9a-c 10a-c

4-6a: R^1 = 2,4,6-$Cl_3C_6H_2$; **b**: R^1 = CO_2Et

7, 8	a	b	c	d	e	f
R^1	a	a	a	b	b	b
R^2	Me	Et	n-Pr	Me	Et	$PhCH_2$

[a] 2,4,6-$Cl_3C_6H_2$; [b] CO_2Et

Scheme 2



8'

Figure 1

On the other hand, it has been revealed that an electron-withdrawing group at N(1) in the 3*H*-triazolium rings accelerates the rearrangement dramatically.[15,16] In the present examination, we chose **4a** and **4b** bearing a trichlorophenyl group as the starting material in order to facilitate the final rearrangement **7**→**8**. However, the employment of the substrate **5c** derived from pentafluorophenyl hydrazone **4c** ($R^1 = C_6F_5$) failed to furnish the expected tricyclic compounds **8** in practically useful yields, even if other Lewis acids such as $AlCl_3$, $TiCl_4$, CF_3CO_2Ag, etc. were used instead of $SbCl_5$.

The structures of compounds **8** and **10** were principally assigned by ^1H NMR and ^{13}C NMR spectroscopy along with microanalyses (see experimental). For each compound, the chemical shifts around 2.50–3.10 ppm arise from the $CH_2CH_2CH_2$ group and at 8.30 ppm is due to the aryl group (R^1). In the ^{13}C NMR spectra of compounds **8** and **10** the two C=N signals are found between 155 and 164 ppm. The IR absorption at about 1560 cm^{-1} can be accounted for by the triazole ring.

Crystal Structure of Compound 10a

To finally distinguish compounds **8** and the plausible isomers **8′,** a crystal of **10a** was developed and submitted for X-ray diffraction analysis. The results provided clear proof of the structural assignment. The X-ray structure for **10a** is shown in Figure 2 and some significant metric parameters are listed in Table 1.

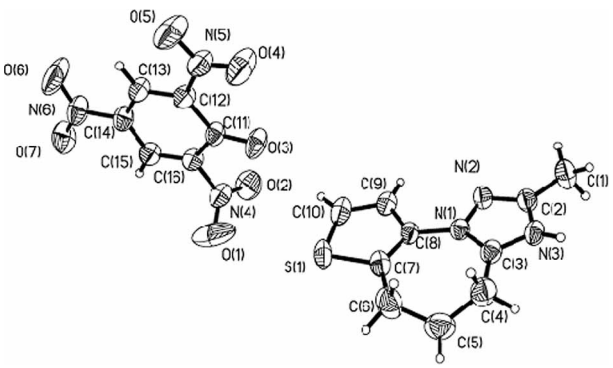


Figure 2 Molecular structure of compound **10a**.

The molecular skeleton is a [5-7-5] tricyclic system with a thiophene ring, an azepine ring, which adopts a twist-boat configuration, and an essentially planar triazole ring. The triazolo ring contains an apparently long N(1)–N(2) distance of 1.379 (3) Å, which is typical for a single N–N bond; however, it is slightly shorter than a N–N single bond with a value of 1.401 Å as given by Allen.[17] On the other hand, the bonds N(3)–C(2), N(3)–C(3) and N(1)–C(3) in the triazole ring are nearly equally long with values ranging from 1.323(4) to 1.353(4) Å which refer to a partial double bond length and are in accordance with those of delocalized systems such as 1.338 Å in pyridine,[18] whereas the bond length of N(2)–C(2) is significantly shorter in comparison to that found in structurally closely related systems.[16,19] From these bond lengths it can be surmised that there is a delocalization of electron density in the 5-membered ring. Finally, all the bond lengths and bond angles in the two aryl rings are normal.

Table 1 Selected Bond Lengths (Å) and Bond Angles (deg) for **10a**

Bond	Bond Length (Deg)	Bond	Bond Length (Deg)
S1–C10	1.705(4)	S1–C7	1.727(3)
N1–C3	1.332(4)	N1–N2	1.379(3)
N1–C8	1.423(4)	N2–C2	1.300(4)
N3–C3	1.323(4)	N3–C2	1.353(4)
C1–C2	1.485(5)	C3–C4	1.480(5)
C4–C5	1.516(6)	C6–C7	1.495(6)
C6–C5	1.499(6)	C7–C8	1.359(4)
C8–C9	1.426(4)	C9–C10	1.346(5)
C10–S1–C7	92.81(16)	C3–N1–N2	110.5(2)
C3–N1–C8	130.8(3)	N2–N1–C8	118.6(2)
C2–N2–N1	104.5(2))	C3–N3–C2	108.4(3)
N2–C2–N3	110.6(3)	N2–C2–C1	125.6(3)
N3–C2–C1	123.9(3)	N3–C3–N1	106.1(3)
N3–C3–C4	124.2(3)	N1–C3–C4	129.7(3)
C3–C4–C5	115.5(3)	C7–C6–C5	114.9(3)
C6–C5–C4	115.1(4)	C8–C7–C6	132.0(3)
C8–C7–S1	109.2(2)	C6–C7–S1	118.8(3)
C7–C8–N1	126.0(3)	C7–C8–C9	114.3(3)
N1–C8–C9	119.7(3)	C10–C9–C8	111.9(3)

In summary, we report in this paper a practical methodology for the synthesis of novel thieno[1,2,4]triazoloazepine derivatives. Full characterization data, along with an X-ray crystallographic analysis for **10a** have established the structure. The obvious advantages of this method include (i) the annulation mode of the products is unprecedented in the literature and this would offer us the opportunity to enhance the activity or modify the profile; (ii) the reagents employed are readily accessible; (iii) the route is short and the work-up procedure is simple; and (iv) the overall yields are from good to excellent. To provide additional synthetic scope, we are currently testing the possibility of incorporating a diverse range of substituents on the thiophene ring. We are also exploring the extension of the strategy to other interesting analogues with different fusion pattern of the thiophene ring, e.g., thieno[3,4-*f*]- as well as thieno[3,2-*f*]triazoloazepines by employing 2,3,6,7-tetrahydro-2-thiainden-4-ones and respectively 4,5-dihydrobenzo[*b*]thiophen-7(6*H*)-ones.

Melting points are uncorrected. Commercially available solvents were dried by standard methods prior to use. IR spectra were recorded using a Mattson Alpha-centauri FT-IR spectrometer, for solids in KBr discs and for liquids by placing a thin layer of the CCl_4 soln between two KBr discs, and absorptions are given in wavenumbers (cm^{-1}). ^1H and ^{13}C NMR spectra were measured in DMSO-d_6, or $CDCl_3$ solns on a Bruker 500 or Varian 400 spectrometer with TMS as internal reference. Coupling constant (*J*) values are given in Hz. The elemental analyses for C, H, N were obtained on a Carlo Erba 1106 elemental analyzer. Satisfactory microanalysis (C ± 0.20, H ± 0.20, N ± 0.30) was obtained for all new compounds. X-ray diffraction analysis of **7a** was measured with a Rigaku AFC7R diffractometer.

6,7-dihydrobenzo[*b*]thiophen-4(5*H*)-one,[11–13] *tert*-butyl hypochlorite[20] were prepared according to literature procedures. All non-aq reactions were performed with exclusion of moisture.

Hydrazones (4); General Procedure

A mixture of 6,7-dihydrobenzo[*b*]thiophen-4(5*H*)-one (3.05 g, 20 mmol) and the appropriate hydrazine (20 mmol) in EtOH (30 mL) containing a catalytic amount of HOAc (ca. 1 mL) was refluxed for 3 h. After removal of solvent in vacuo, the residual solids were recrystallized from a suitable solvent to afford pure hydrazone **4**.

6,7-Dihydrobenzo[*b*]thiophen-4(5*H*)-one (2,4,6-Trichlorophenyl)hydrazone (4a)

From 6,7-dihydrobenzo[*b*]thiophen-4(5*H*)-one and (2,4,6-trichlorophenyl)hydrazine. Crystallization from EtOH (95%) afforded **4a** as white-needles.

Yield: 90%; mp 127–129 °C.

IR (KBr): 1122, 1470, 1556, 3298 cm^{-1}.

^1H NMR ($CDCl_3$): δ = 2.10–2.81 (m, 6 H, 3 × CH_2), 6.77 (d, *J* = 5.5 Hz, 1 H), 7.00 (d, *J* = 5.5 Hz, 1 H, SC_4H_2), 7.10 (2 H, s, ArH), 7.20 (1 H, s, NH).

Anal. Calcd for $C_{14}H_{11}Cl_3N_2S$: C, 48.64; H, 3.21; N, 8.10. Found: C, 48.68; H, 3.20; N, 8.16.

6,7-Dihydrobenzo[*b*]thiophen-4(5*H*)-one Ethoxy Carbonylhydrazone (4b)

From 6,7-dihydrobenzo[*b*]thiophen-4(5*H*)-one and ethyl carbazate. Crystallization from petroleum ether (bp 60–90 °C) afforded **4b** as a white solid.

Yield: 90%; mp 112–114 °C.

IR (KBr): 1328, 1540, 1692, 3249 cm^{-1}.

^1H NMR ($CDCl_3$): δ = 1.26 (t, *J* = 6.0 Hz, 3 H, CH_3), 2.03–2.77 (m, *J* = 6.0 Hz, 6 H, 3 × CH_2), 4.10 (q, *J* = 6.0 Hz, 2 H, OCH_2), 6.76 (d, *J* = 5.5 Hz, 1 H), 7.28 (d, *J* = 5.5 Hz, 1 H, SC_4H_2), 8.33 (s, 1 H, NH).

α-Chloroazo Compounds (5); General Procedure

The reaction was carried out in the dark. To a soln of hydrazone **4** (10 mmol) in CH_2Cl_2 (10 mL) cooled between –30 °C and –10 °C in an ice-salt bath was added dropwise over 10 min a soln of *t*-BuOCl (1.25 g, 10 mmol) in CH_2Cl_2 (10 mL). After the mixture was stirred for about 1 h, the resulting soln was dried ($CaCl_2$). Thorough removal of volatiles by rotary evaporation left the α-chloroazo compound **5** as a red oil, which can be stored under air at low temperatures for prolonged times and was used without further purification.

4-Chloro-4-(2,4,6-trichlorophenylazo)-6,7-dihydrobenzo[*b*]-thiophene (5a)

Yield: 90%; deep-red oil.

IR (neat): 1141, 1551, 1571, 2968 cm^{-1}.

^1H NMR ($CDCl_3$): δ = 2.10–2.81 (m, 6 H, 3 × CH_2), 6.77 (d, *J* = 5.5 Hz, 1 H), 7.00 (d, *J* = 5.5 Hz, 1 H, SC_4H_2), 7.10 (s, 2 H, ArH).

4-Chloro-4-(ethoxycarbonylazo)-6,7-dihydrobenzo[*b*]-thiophene (5b)

Yield: 92%; orange oil.

IR (neat): 1236, 1576, 1764, 2935 cm^{-1}.

^1H NMR ($CDCl_3$): δ = 1.26 (t, *J* = 6.0 Hz, 3 H, CH_3), 2.03–2.77 (m, 6 H, 3 × CH_2), 4.10 (q, *J* = 6.0 Hz, 2 H, OCH_2), 6.76 (d, *J* = 5.5 Hz, 1 H), 7.28 (d, *J* = 5.5 Hz, 1 H, SC_4H_2).

1,2-Disubstituted-5,6-dihydro-4*H*-thieno[2,3-*f*][1,2,4]triazolo[1,5-*a*]azepinium Salts 8; General Procedure

The reaction was carried out in a nitrogen atmosphere. To a soln of **5** (2 mmol) and the appropriate nitrile (3 mmol) in anhyd CH_2Cl_2 (10 mL) was added dropwise a soln of $SbCl_5$ (0.73 g, 2.4 mmol) in CH_2Cl_2 (10 mL) at about –60 °C. The mixture was stirred at this temperature for 2 h, then allowed gradually to warm to 30 °C (bath temperature) and was stirred further for 1 h. The crude product was precipitated by slow addition of Et_2O. Recrystallization from MeOH–MeCN gave pure 1,2-disubstituted-5,6-dihydro-4*H*-thieno-[2,3-*f*][1,2,4]triazolo[1,5-*a*]azepinium hexachloroantimonate **8** as crystals.

5,6-Dihydro-2-methyl-1-(2,4,6-trichlorophenyl)-4*H*-thieno[2,3-*f*][1,2,4]triazolo[1,5-*a*]azepinium Hexachloroantimonate (8a)

Yield: 87%; white crystals (MeOH–MeCN, 1:1); mp 192–194 °C (decomp).

IR (KBr): 1455, 1564, 2931, 3084 cm^{-1}.

^1H NMR (DMSO-d_6): δ = 2.70 (s, 3 H, CH_3), 2.53–3.14 (m, 6 H, 3 × CH_2), 6.58 (d, 1 H, *J* = 5.6 Hz), 7.57 (d, 1 H, *J* = 5.6 Hz, SC_4H_2), 8.27 (s, 2 H, $Cl_3C_6H_2$).

^{13}C NMR (DMSO-d_6): δ = 164.1, 161.1 (C=N), 141.8, 141.0, 135.7, 131.0, 127.5, 124.4, 123.9, 120.8 (aryl), 31.9, 24.9, 23.9 (CH_2), 12.8 (CH_3).

Anal. Calcd for $C_{16}H_{13}Cl_9N_3SSb$: C, 26.68; H, 1.82; N, 5.84. Found: C, 26.56; H, 1.78; N, 5.85.

5,6-Dihydro-2-ethyl-1-(2,4,6-trichlorophenyl)-4*H*-thieno[2,3-*f*][1,2,4]triazolo[1,5-*a*]azepinium Hexachloroantimonate (8b)

Yield 89%; brown solid (MeOH–MeCN, 1:1); mp 180–183 °C (decomp).

IR (KBr): 1478, 1566, 2924, 3111 cm^{-1}.

^1H NMR (DMSO-d_6): δ = 1.35 (t, 3 H, *J* = 7.5 Hz, CH_3), 2.93 (q, 2 H, *J* = 7.5 Hz, CH_2), 2.54, 3.01, 3.16 (m, 6 H, 3 × CH_2), 6.58, 7.57 (d, 2 H, *J* = 5.6 Hz, SC_4H_2), 8.26 (2 H, s, $Cl_3C_6H_2$).

^{13}C NMR (DMSO-d_6): δ = 164.7, 164.3 (C=N), 141.9, 141.1, 135.8, 131.0, 127.5, 124.2, 123.9, 120.8 (aryl), 32.0, 24.9, 23.9 (3 × CH_2), 19.9 (CH_2), 10.8 (CH_3).

Anal. Calcd for $C_{17}H_{15}Cl_9N_3SSb$: C, 27.81; H, 2.06; N, 5.72. Found: C, 27.68; H, 2.07; N, 5.74.

5,6-Dihydro-2-propyl-1-(2,4,6-trichlorophenyl)-4*H*-thieno[2,3-*f*][1,2,4]triazolo[1,5-*a*] azepinium Hexachloroantimonate (8c)

Yield 85%; brown crystals (MeOH–MeCN, 1:1); mp 172–174 °C (decomp)

IR (KBr): 1480, 1566, 2959, 3072 cm^{-1}.

^1H NMR (DMSO-d_6): δ = 0.99 (t, 3 H, *J* = 7.3 Hz, CH_3), 1.83 (m, 2 H, CH_2), 2.89 (2 H, t, *J* = 7.3 Hz, CH_2), 2.55, 3.01, 3.16 (m, 6 H, 3 × CH_2), 6.58, 7.56 (d, 2 H, *J* = 5.6 Hz, SC_4H_2), 8.26 (s, 2 H, $Cl_3C_6H_2$).

^{13}C NMR (DMSO-d_6): δ = 164.2, 163.8 (C=N), 141.9, 141.0, 135.8, 131.0, 127.4, 124.2, 123.9, 120.8 (aryl), 32.0, 24.9, 23.9 (3 × CH_2), 27.5, 19.7 (CH_2), 13.7 (CH_3).

Anal. Calcd for $C_{18}H_{17}Cl_9N_3SSb$: C, 28.89; H, 2.29; N, 5.62. Found: C, 28.83; H, 2.29; N, 5.67.

Neutral 2-Substituted-5,6-dihydro-4*H*-thieno[2,3-*f*][1,2,4]triazolo[1,5-*a*]azepines 9 and their Picrates 10; Typical Procedure

The *N*-ethoxycarbonyl substituted α-chloroazo compound **5b** was employed as the substrate. Instead of precipitating the heterocycles **8d–f** by adding Et_2O upon completion of the reaction, the resulting mixture was chilled to 0 °C, and an aq soln of NaOH (2 N, 10 mL) was added dropwise with vigorous stirring. Stirring was continued for 20 min, and then the mixture was filtered. The filtrate was extracted with CH_2Cl_2 (3 × 20 mL), the combined extracts were washed with H_2O (2 × 20 mL) and dried over Na_2SO_4. Removal of the solvent under reduced pressure afforded the neutral tricyclic compounds **9a–c** as brownish oily residues, which were transformed to the picrates by addition of a sat. soln of picric acid in MeOH. The crystals formed were filtered and recrystallized from MeOH–$CHCl_3$ to furnish the analytically pure **10a–c** as yellow needles.

5,6-Dihydro-2-methyl-4*H*-thieno[2,3-*f*][1,2,4]triazolo[1,5-*a*]azepine Picrate (10a)

Yield 81%; yellow needles; mp 178–182 °C (decomp).

IR (KBr): 1313, 1530, 1608, 3057 cm^{-1}.

^{1}H NMR (DMSO-d_6): δ = 2.31 (s, 3 H, CH_3), 2.06, 3.13, 3.17 (m, 6 H, 3 × CH_2), 4.46 (NH), 7.41, 7.47 (d, J = 5.5 Hz, 2 H, SC_4H_2), 8.59 [s, 2 H, $(NO_2)_3C_6H_2$].

^{13}C NMR (DMSO-d_6): δ = 160.6, 155.5 (C=N), 154.0, 141.8, 131.8, 128.8, 125.1, 124.2, 124.0, 122.3 (aryl), 27.9, 26.4, 20.8 (3 × CH_2), 12.2 (CH_3).

Anal. Calcd for $C_{16}H_{14}N_6O_7S$: C, 44.12; H, 3.22; N, 19.26. Found: C, 44.24; H, 3.25; N, 19.35.

5,6-Dihydro-2-ethyl-4*H*-thieno[2,3-*f*][1,2,4]triazolo[1,5-*a*]azepine Picrate (10b)

Yield 79%; yellow solid; mp 204–206 °C (decomp).

IR (KBr): 1318, 1547, 1634, 3081 cm^{-1}.

^{1}H NMR (DMSO-d_6): δ = 1.25 (t, J = 7.6 Hz, 3 H, CH_3), 2.70 (q, J = 7.6 Hz, 2 H, CH_2), 2.07, 3.14, 3.20 (m, 6 H, 3 × CH_2), 4.75 (NH), 7.43, 7.47 (d, J = 5.5 Hz, 2 H, SC_4H_2), 8.59 [s, 2 H, $(NO_2)_3C_6H_2$].

^{13}C NMR (DMSO-d_6): δ = 161.1, 159.8 (C=N), 154.4, 142.3, 132.2, 129.8, 125.6, 124.7, 124.6, 122.9 (aryl), 28.4, 26.8, 21.2 (3 × CH_2), 20.2 (CH_2), 12.1 (CH_3).

Anal. Calcd for $C_{17}H_{16}N_6O_7S$: C, 45.54; H, 3.60; N, 18.74. Found: C, 45.22; H, 3.54; N, 18.51.

2-Benzyl-5,6-dihydro-4*H*-thieno[2,3-*f*][1,2,4]triazolo[1,5-*a*]azepine Picrate (10c)

Yield 76%; yellow solid; mp 146–148 °C (decomp).

IR (KBr): 1320, 1536, 1619, 2998 cm^{-1}.

^{1}H NMR (DMSO-d_6): δ = 2.06, 3.13, 3.19 (m, 6 H, 3 × CH_2), 4.06 (s, 2 H, $ArCH_2$), 7.25–7.48 (m, 7 H, ArH), 8.00 (NH), 8.60 [s, 2 H, $(NO_2)_3C_6H_2$].

^{13}C NMR (DMSO-d_6): δ = 161.1, 158.7 (C=N), 155.1, 142.3, 137.3, 132.4, 129.4, 129.3, 128.9, 127.1, 125.6, 124.8, 124.5, 123.0 (aryl), 33.1 (CH_2), 28.5, 27.2, 21.4 (3 × CH_2).

Anal. Calcd for $C_{22}H_{18}N_6O_7S$: C, 51.76; H, 3.55; N, 16.46. Found: C, 51.14; H, 3.50; N, 16.11.

X-Ray Crystallographic Data for Compound 10a

Suitable crystals for an X-ray diffraction analysis were grown from $CHCl_3$–MeOH. [$C_{16}H_{14}N_6O_7S$], yellow prisms, FW = 434.39; triclinic, space group P–1, a = 8.136 (7), b = 8.692 (7), c = 14.158 (11) Å; α = 75.171(10), β = 84.314(9), γ = 72.098(11)°; V = 920.7(13) Å ^{3}; Z = 2; D_{calc} = 1.567 g cm^{-3}, F(000) = 448; μ (Mo–Kα) = 0.71073 Å; T = 193 (2) K. A total of 4556 reflections were measured on a Rigaku AFC7R diffractometer by employing graphite-monochromated Mo–Kα radiation and a 12 kW rotating anode generator; 3819 unique [R_{int} = 0.1033]. The structure was solved by direct methods and expanded using Fourier techniques. The refinement converged at $R1$ = 0.0884 and $wR2$ = 0.2086 for all data.

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