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PREPARATION OF NEW NITROGEN-BRIDGED HETEROCYCLES. 68. ONE-POT SYNTHSIS OF 4-SUBSTITUTED 5-ACYLTHIENO[3,2-*d*]-THIAZOLE DERIVATIVES[1]

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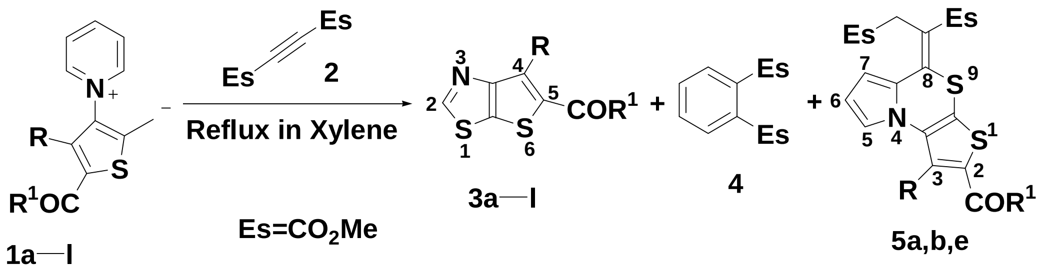
Abstract – The reactions of 5-acyl-3-(1-pyridinio)thiophene-2-thiolates with dimethyl acetylenedicarboxylate in xylene at the reflux temperature afforded the corresponding 2-unsubstituted 5-acylthieno[3,2-*d*]thiazoles in 25—69% yields together with dimethyl phthalate as another fragmentation product. In a few reactions, the unexpected products, dimethyl 2-[2-acylthieno[2',3':2,3]-1,4-thiazino[4,5-*a*]pyrrol-8-ylidene]succinate derivatives, were also isolated, though their yields were very low.

Thieno[3,2-*d*]thiazole derivatives have been prepared by the cyclizations of suitably substituted thiophenes[2,3] and thiazoles[4,5] or the thermolyses of thieno[3,2-*e*][1,2,4]triazines.[6] However, these methods are less useful from the preparative point of view, because the access to the substrates was not easy in the former methods and the yields of the products were low in the latter. In the continuation of our work in heterocyclic syntheses, we are interested in the development of a new construction method for this thieno[3,2-*d*]thiazole skeleton, since we previously observed a smooth thermolysis of dimethyl 3-alkylthio-4-thia-1-azatetracyclo[5.4.0.0^{5,11}.0^{6,8}]undeca-2,9-diene-5,6-dicarboxylates to the corresponding 5-(alkylthio)thiazoles and dimethyl phthalate,[7] and we thought that an extension of this type of reaction to the thiophene-fused substrates may lead to the corresponding thieno[3,2-*d*]thiazoles. Furthermore, the ready availabilities of the substrates and the reagent (dimethyl acetylenedicarboxylate, DMAD) and the simplicity of the operation also may be the main advantages of this reaction. Here we report a one-pot synthesis of the title compounds, 2-unsubstituted 5-acylthieno[3,2-*d*]thiazole derivatives, from the reactions of 5-acyl-3-(1-pyridinio)thiophene-2-thiolates with DMAD in xylene under the reflux temperature.

RESULTS AND DISCUSSION

When the reactions of 5-acyl-3-(1-pyridinio)thiophene-2-thiolates (**1a—l**), which were prepared from the alkaline treatment of 1-(acylmethyl)pyridinium chloride, carbon disulfide, and some acylmethyl halides such as chloroacetone, phenacyl bromide, *p*-chlorophenacyl bromide, and *p*-bromophenacyl bromide according to the procedure reported by us,[8,9] with DMAD (**2**) were carried out in xylene at the reflux temperature for 36 h and, by the column chromatographic separation of the resulting mixtures, the expected 5-acylthieno[3,2-*d*]thiazole (**3a—l**) were obtained as colorless crystals in 25—69% yields, together with dimethyl phthalate (**4**). In addition, the unexpected products, dimethyl 2-[2-acylthieno[2’,3’:2,3]-1,4-thiazino[4,5-*a*]pyrrol-8-ylidene]succinates **5a**,**b**,**e**, were also obtained as pale yellow products in the reactions of 3-(1-pyridinio)thiophene-2-thiolate (**1a,b,e**) with **2**, but their yields were in trace or very low.



Entry	R	R^1	Yield (%) 3	5
a	Me	Me	51	Trace
b	Me	Ph	53	Trace
c	Me	C_6H_4Cl-*p*	65	0
d	Me	C_6H_4Br-*p*	63	0
e	Ph	Me	25	9
f	Ph	Ph	29	0
g	Ph	C_6H_4Cl-*p*	33	0
h	Ph	C_6H_4Br-*p*	41	0
i	CH_2CO_2Et	Me	43	0
j	CH_2CO_2Et	Ph	62	0
k	CH_2CO_2Et	C_6H_4Cl-*p*	69	0
l	CH_2CO_2Et	C_6H_4Br-*p*	66	0

Scheme 1

The structures of these thieno[3,2-*d*]thiazoles **3a—l** were assigned by their spectral inspection and elemental analyses. The IR spectra of **3a—l** showed a largely shifted absorption band (1611—1649 cm^{-1}) characteristics of carbonyl group at the 2-position of five-membered heteroaromatics such as furan and thiophene. The ^{1}H-NMR spectra exhibited the 2-proton on the thieno[3,2-*d*]thiazole ring as a sharp singlet at low magnetic fields (δ 8.89—8.98). The chemical shifts for the 2-proton in thieno[3,2-*d*]thiazole derivatives **3a**—**l** are almost parallel to those (δ 8.63—8.81) for the 2-proton in 5-(alkylthio)thiazole derivatives reported earlier by us.[7] The elementary analyses for these products **3a**—**l** were in good accord with our proposed compositions and the X-ray analysis for one compound, 5-(*p*-bromobenzoyl)-4-(ethoxycarbonylmethyl)thieno[3,2-*d*]-thiazole (**3l**), confirmed its structure. The ORTEP drawing[10] of **3l** is shown in Figure 1. On the other hand, the structures of by-products **5a**,**b**,**e** were presumed from the ^{1}H-NMR spectral inspection and finally determined by the X-ray analysis of one compound **5a** because of their low yields. In particular, the numbers of the hydrogen atoms in **5a**,**b**,**e** were indicated to be 17, 19, and 19 respectively and their numbers coincided with those in the molecular formulas ($C_{18}H_{17}NO_5S_2$, $C_{23}H_{19}NO_5S_2$, and $C_{23}H_{19}NO_5S_2$) expected for the 1:1 adducts between **1a**,**b**,**e** and reagent **2**. For example, the ^{1}H-NMR spectrum showed four methyl proton singlet signals (δ 2.51, 2.79, 3.78, and 3.85) due to a methyl and an acetyl group on the thiophene ring and to two methoxycarbonyl groups, a methylene singlet (δ 3.88), and three vicinal unsaturated protons (δ 6.50 (1H, dd, *J*=3.9 and 2.9 Hz), 6.53 (1H, dd, *J*=2.9 and 1.4 Hz), and 7.44 (1H, dd, *J*=3.9 and 1.4 Hz)). The disappearance of the vicinal five-proton configuration on the pyridine ring in starting materials **1a**,**b**,**e** and the new appearance of a vicinal three-proton one which has small vicinal couplings (*J*=3.9 and 2.9 Hz) in comparison with those in 6-menbered aza-heterocycles made us suspect the presence of an aromatic pyrrole ring in the structures of products **5a**,**b**,**e**. Since we had previously observed the formation of dimethyl 4-aryl-5-thia-2,3-diazatricyclo[4.3.2.$0^{2,7}$]undeca-3,8,10-triene-6,11-dicarboxylates (2,5-dihydropyrrole ring is involved) via the intervention of intermediates dimethyl 5a*H*-2-arylpyrido[1,2-*d*][1,3,4]-thiadiazepine-4,5-dicarboxylates (1,2-dihydropyridine ring is involved) in the reactions of pyridinium 1-(arylthiocarbonyl)-aminides with **2**,[11,12] it is not unimaginable such successive ring changes are possible: 1,2-dihydropyridine → 2,5-dihydropyrrole → aromatic pyrrole. However, we could not determine their structures with certainty only by these data. Fortunately, one (**5a**) of these products was obtained as single crystals, so X-ray analysis was performed and the structure was finally confirmed to be dimethyl 2-[2-acetyl-3-methylthieno[2',3':2,3]-1,4-thiazino[4,5-*a*]pyrrol-8-

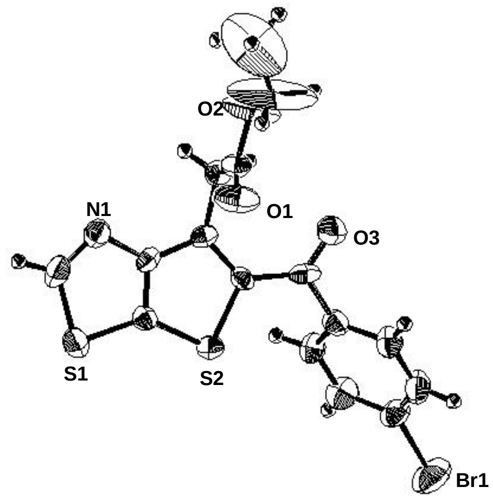


Figure 1. ORTEP drawing of **3l**

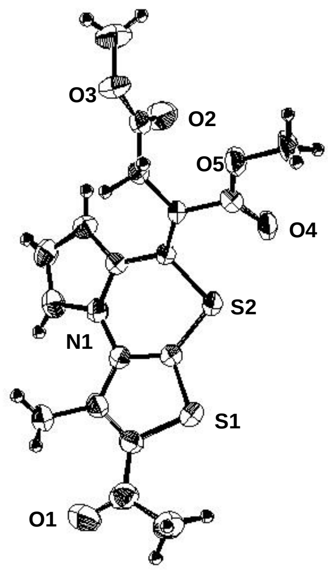
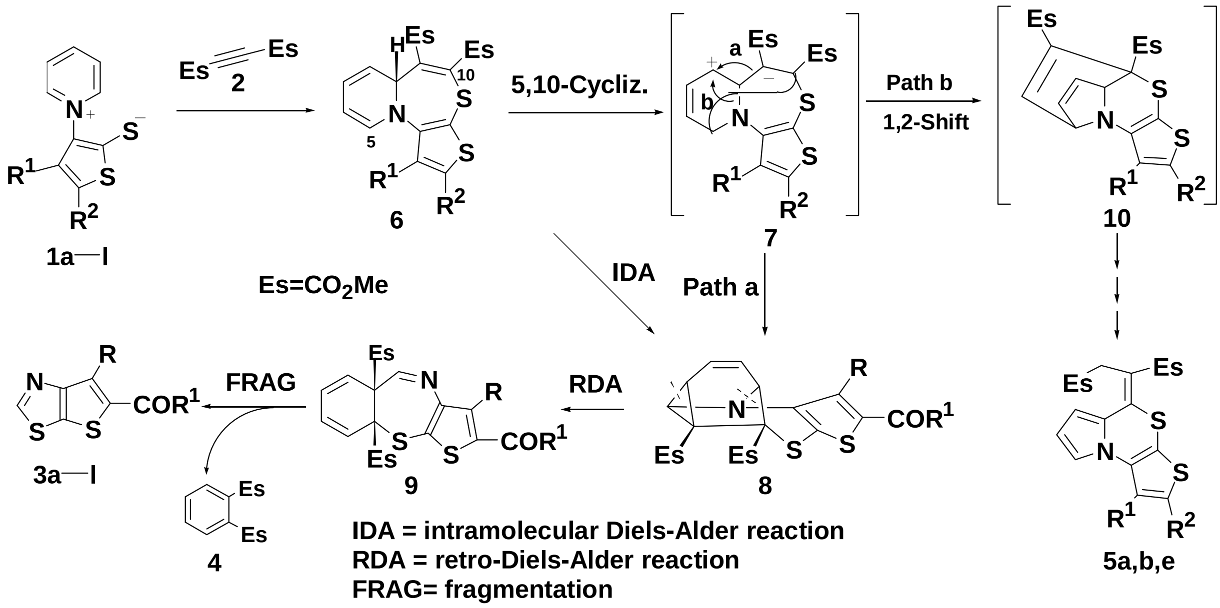


Figure 2. ORTEP drawing of **5a**

ylidene]succinate (see Figure 2).

The possible reaction mechanisms (Scheme 2) for the formation of products **3a—l** and **5a**,**b**,**e** are shown in Scheme 2. The formation mechanism of thieno[3,2-*d*]thiazoles **3a—l** is fundamentally the same as that proposed earlier by us for the formation of 5-(alkylthio)thiazoles.[7] On the other hand, that for by-products **5a**,**b**,**e** was unclear, but it must involve a key intermediate such as **10**.



Scheme 2

EXPERIMENTAL

Melting points were measured with a Yanagimoto micromelting point apparatus and were not corrected. Microanalyses were carried out on a Perkin-Elmer 2400 elemental analyzer. ^{1}H-NMR and ^{13}C-NMR spectra were determined with a JEOL JNM-LA400 (^{1}H: 400 MHz and ^{13}C: 100.4 MHz) spectrometer in deuteriochloroform with tetramethylsilane used as the internal standard; the chemical shifts were expressed in δ values. The IR spectra were taken with a JASCO FT/IR-5300 IR spectrophotometer.

Preparations of 3-(1-pyridinio)thiophene-2-thiolates (1a—l). Of these compounds 4-ethoxycarbonylmethyl-3-(1-pyridinio)thiophene-2-thiolates (**1i—l**) were prepared according to our previous paper,[8,9] and other 4-methyl- and 4-phenyl derivatives **1a—h** according to the following general procedure. An ethanolic solution (50 mL) of 1-acetonyl- or 1-phenacylpyridinium chloride (10 mmol) and carbon disulfide (1.140 g, 15 mmol) was treated with an aqueous solution (10 mL) of sodium hydroxide (1.000 g, 25 mmol) under stirring at room temperature for 0.5 h, and then an alkylating agent (10 mmol) such as chloroacetone, phenacyl chloride, *p*-chlorophenacyl bromide, and *p*-bromophenacyl bromide was added to the reaction mixture and the resulting solution was allowed to react at that temperature for another 12 h. The solution was poured into ice-water (300 mL) and the precipitates which separated were collected by suction. Recrystallization of the crude products from acetone afforded the corresponding 3-(1-pyridinio)thiophene-2-thiolates.

Some data for the new products **1a—i** are as follows:

5-Acetyl-4-methyl-3-(1-pyridinio)thiophene-2-thiolate (1a): From 1-acetonylpyridinium chloride, carbon disulfide, and chloroacetone, 69%, brown needles (from $CHCl_3$), mp 269—272 °C. IR (KBr): 1628 cm^{-1}. ^{1}H-NMR: 2.33 (3H, s, COMe), 2.39 (3H, s, 4-Me), 8.06 (2H, br dd, *J*=7.8, 5.6 Hz, Py-H), 8.45 (1H, br t, *J*=7.8 Hz, Py-H), 8.74 (2H, br d, *J*=5.6 Hz, Py-H). *Anal.* Calcd for $C_{12}H_{11}NOS_2$: C, 57.80; H, 4.45; N, 5.62. Found: C, 57.96; H, 4.32; N, 5.59.

5-Benzoyl-4-methyl-3-(1-pyridinio)thiophene-2-thiolate (1b): From 1-acetonylpyridinium chloride, carbon disulfide, and phenacyl chloride, 95%, brown needles (from $CHCl_3$), mp 279—281 °C. IR (KBr): 1615 cm^{-1}. ^{1}H-NMR: 2.39 (3H, s, 4-Me), 7.43 (2H, br dd, *J*=7.6, 7.1 Hz, Ph-H), 7.51 (1H, br t, *J*=7.6 Hz, Ph-H), 7.80 (2H, br d, *J*=7.1 Hz, Ph-H), 8.08 (2H, br dd, *J*=7.8, 5.6 Hz, Py-H), 8.47 (1H, br t, *J*=7.8 Hz, Py-H), 8.76 (2H, br d, *J*=5.6 Hz, Py-H). *Anal.* Calcd for $C_{17}H_{13}NOS_2$: C, 65.57; H, 4.21; N, 4.50. Found: C, 65.79; H, 4.09; N, 4.39.

5-(*p*-Chlorobenzoyl)-4-methyl-3-(1-pyridinio)thiophene-2-thiolate (1c): From 1-acetonylpyridinium chloride, carbon disulfide, and *p*-chlorophenacyl bromide, 94%, brown needles (from $CHCl_3$), mp 260—263 °C. IR (KBr): 1620 cm^{-1}. ^{1}H-NMR: 2.38 (3H, s, 4-Me), 7.41 (2H, br d, *J*=8.3 Hz, Ph-H), 7.76 (2H, br d, *J*=8.3 Hz, Ph-H), 8.09 (2H, br dd, *J*=7.8, 5.6 Hz, Py-H), 8.47 (1H, br t, *J*=7.8 Hz, Py-H), 8.76 (2H, br d, *J*=5.6 Hz, Py-H). *Anal.* Calcd for $C_{17}H_{12}ClNOS_2$: C, 59.04; H, 3.50; N, 4.05. Found: C, 58.99; H, 3.56; N, 4.03.

4-(*p*-Bromobenzoyl)-4-methyl-3-(1-pyridinio)thiophene-2-thiolate (1d): From 1-acetonylpyridinium chloride, carbon disulfide, and *p*-bromophenacyl chloride, 89%, brown needles (from $CHCl_3$), mp 243—245 °C. IR (KBr): 1618 cm^{-1}. ^{1}H-NMR: 2.37 (3H, s, 4-Me), 7.57 (2H, br d, *J*=8.3 Hz, Ph-H), 7.68 (2H, br d, *J*=8.3 Hz, Ph-H), 8.09 (2H, br dd, *J*=7.8, 5.6 Hz, Py-H), 8.48 (1H, br t, *J*=7.8 Hz, Py-H), 8.76 (2H, br d, *J*=5.6 Hz, Py-H). *Anal.* Calcd for $C_{17}H_{12}BrNOS_2$: C, 52.31; H, 3.10; N, 3.59. Found: C, 52.55; H, 3.09; N, 3.36.

5-Acetyl-4-phenyl-3-(1-pyridinio)thiophene-2-thiolate (1e): From 1-phenacylpyridinium chloride, carbon disulfide, and chloroacetone, 71%, brown needles (from $CHCl_3$), mp 279—281 °C. IR (KBr): 1603 cm^{-1}. ^{1}H-NMR: 1.96 (3H, s, COMe), 7.15—7.21 (2H, m, Ph-H), 7.29—7.35 (3H, m, Ph-H), 7.77 (2H, br dd, *J*=7.8, 5.6 Hz, Py-H), 8.20 (1H, br t, *J*=7.8 Hz, Py-H), 8.60 (2H, br d, *J*=5.6 Hz, Py-H). *Anal.* Calcd for $C_{17}H_{13}NOS_2$: C, 65.57; H, 4.21; N, 4.50. Found: C, 65.61; H, 4.19; N, 4.47.

5-Benzoyl-4-phenyl-3-(1-pyridinio)thiophene-2-thiolate (1f): From 1-phenacylpyridinium chloride, carbon disulfide, and phenacyl chloride, 84%, orange needles (from $CHCl_3$), mp 272—274 °C. IR

(KBr): 1620 cm^{-1}. ^{1}H-NMR: 6.93 (2H, br d, *J*=6.8 Hz, Ph-H), 7.04—7.14 (3H, m, Ph-H), 7.17 (2H, br dd, *J*=7.8, 7.3 Hz, Ph-H), 7.30 (1H, br t, *J*=7.3 Hz, Ph-H), 7.58 (2H, br d, *J*=7.8 Hz, Ph-H), 7.78 (2H, br dd, *J*=7.8, 5.6 Hz, Py-H), 8.22 (1H, br t, *J*=7.8 Hz, Py-H), 8.61 (2H, br d, *J*=5.6 Hz, Py-H). *Anal.* Calcd for $C_{22}H_{15}NOS_2$: C, 70.75; H, 4.05; N, 3.75. Found: C, 70.70; H, 3.86; N, 3.98.

5-(*p*-Chlorobenzoyl)-4-phenyl-3-(1-pyridinio)thiophene-2-thiolate (1g): From 1-phenacylpyridinium chloride, carbon disulfide, and *p*-chlorophenacyl bromide, 83%, brown needles (from $CHCl_3$), mp 262—264 °C. IR (KBr): 1620 cm^{-1}. ^{1}H-NMR: 6.91 (2H, br d, *J*=7.3 Hz, Ph-H), 7.04—7.20 (5H, m, Ph-H), 7.48 (2H, br d, *J*=8.3 Hz, Ph-H), 7.79 (2H, br dd, *J*=7.8, 5.6 Hz, Py-H), 8.24 (1H, br t, *J*=7.8 Hz, Py-H), 8.60 (2H, br d, *J*=5.6 Hz, Py-H). *Anal.* Calcd for $C_{22}H_{14}ClNOS_2$: C, 64.78; H, 3.46; N, 3.43. Found: C, 64.98; H, 3.48; N, 3.21.

5-(*p*-Bromobenzoyl)-4-phenyl-3-(1-pyridinio)thiophene-2-thiolate (1h): From 1-phenacylpyridinium chloride, carbon disulfide, and *p*-bromophenacyl bromide, 85%, orange needles (from $CHCl_3$), mp 247—250 °C. IR (KBr): 1620 cm^{-1}. ^{1}H-NMR: 6.90 (2H, br d, *J*=7.1 Hz, Ph-H), 7.08 (2H, br dd, *J*=7.2, 7.1 Hz, Ph-H), 7.16 (1H, br t, *J*=7.2 Hz, Ph-H), 7.28 (2H, br d, *J*=8.3 Hz, Ph-H), 7.41 (2H, br d, *J*=8.3 Hz, Ph-H), 7.78 (2H, br dd, *J*=7.8, 5.6 Hz, Py-H), 8.23 (1H, br t, *J*=7.8 Hz, Py-H), 8.60 (2H, br d, *J*=5.6 Hz, Py-H). *Anal.* Calcd for $C_{22}H_{14}BrNOS_2$: C, 58.41; H, 3.12; N, 3.10. Found: C, 58.30; H, 3.19; N, 3.14.

5-Acetyl-4-ethoxycarbonylmethyl-3-(1-pyridinio)thiophene-2-thiolate (1i): From 1-(3-ethoxycarbonylacetonyl)pyridinium chloride, carbon disulfide, and chloroacetone, 54%, brown needles (from $CHCl_3$), mp 205—210 °C. IR (KBr): 1618, 1711 cm^{-1}. ^{1}H-NMR: 1.25 (3H, t, *J*=7.1 Hz, OCH_2CH_3), 2.38 (3H, s, COMe), 3.73 (2H, s, CH_2CO), 4.13 (2H, q, *J*=7.1 Hz, OCH_2CH_3), 8.04 (2H, br dd, *J*=7.8, 5.6 Hz, Py-H), 8.44 (1H, br t, *J*=7.8 Hz, Py-H), 8.88 (2H, br d, *J*=5.6 Hz, Py-H). *Anal.* Calcd for $C_{15}H_{15}NO_3S_2$: C, 56.05; H, 4.70; N, 4.36. Found: C, 56.04; H, 4.78; N, 4.30.

Reactions of 3-(1-pyridinio)thiophene-2-thiolates (1) with dimethyl acetylenedicarboxylate (2) at the xylene reflux temperature. General Method. A xylene solution (30 mL) of 3-(1-pyridinio)thiophene-2-thiolate (**1**, 1 mmol) and dimethyl acetylenedicarboxylate (**2**, 0.156g, 1.1 mmol) was heated at the reflux temperature for 36 h. The resulting solution was concentrated under reduced pressure to remove the solvent. The residue was separated by column chromatography on alumina using hexane and then ether as an eluent. The combined ether fraction was concentrated under reduced pressure, and recrystallization of the residue from chloroform-hexane afforded the corresponding thieno[3,2-*d*]thiazole derivative (**3**).

In these reactions the formation of dimethyl phthalate (4) was always confirmed by ^{1}H-NMR spectra of the crude products. Some data for these products **3a—i** are as follows:

5-Acetyl-4-methylthieno[3,2-*c*]thiazole (3a): From **1a** and **2**, 51%, colorless needles, mp 68—71 °C (from $CHCl_3$-hexane). IR (KBr): 1634 cm^{-1}. ^{1}H-NMR: 2.62 (3H, s, 4-Me), 2.87 (3H, s, COMe), 8.92 (1H, s, 2-H). ^{13}C-NMR: 15.00, 29.34, 134.48, 135.08, 141.48, 155.82 (2-C), 162.61, 191.26. *Anal.* Calcd for $C_8H_7NOS_2$: C, 48.71; H, 3.58; N, 7.10. Found: C, 48.64; H, 3.61; N, 7.14.

5-Benzoyl-4-methylthieno[3,2-*c*]thiazole (3b): From **1b** and **2**, 53%, colorless needles, mp 69—70 °C (from $CHCl_3$-hexane). IR (KBr): 1616 cm^{-1}. ^{1}H-NMR: 2.65 (3H, s, 4-Me), 7.50 (2H, br dd, *J*=8.0, 7.4 Hz, Ph-H), 7.60 (1H, br t, *J*=7.4 Hz, Ph-H), 7.82 (2H, br d, *J*=8.0 Hz, Ph-H), 8.93 (1H, s, 2-H). *Anal.* Calcd for $C_{13}H_9NOS_2$: C, 60.21; H, 3.50; N, 5.40. Found: C, 60.08; H, 3.52; N, 5.28.

5-(*p*-Chlorobenzoyl)-4-methylthieno[3,2-*c*]thiazole (3c): From **1c** and **2**, 65%, colorless needles, mp 140—143 °C (from $CHCl_3$-hexane). IR (KBr): 1640 cm^{-1}. ^{1}H-NMR: 2.66 (3H, s, 4-Me), 7.48 (2H, br d, *J*=8.4 Hz, Ph-H), 7.78 (2H, br d, *J*=8.4 Hz, Ph-H), 8.94 (1H, s, 2-H). ^{13}C-NMR: 15.23, 128.64, 130.35, 135.13, 136.12, 137.16, 138.75, 138.95, 155.97 (2-C), 162.14, 188.34. *Anal.* Calcd for $C_{13}H_8ClNOS_2$: C, 53.15; H, 2.74; N, 4.77. Found: C, 53.11; H, 2.75; N, 4.80.

5-(p-Bromobenzoyl)-4-methylthieno[3,2-*c*]thiazole (3d): From **1d** and **2**, 63%, colorless needles, mp 152—153 °C (from $CHCl_3$-hexane). IR (KBr): 1640 cm^{-1}. ^{1}H-NMR: 2.66 (3H, s, 4-Me), 7.64 (2H, br d, *J*=8.5 Hz, Ph-H), 7.70 (2H, br d, *J*=8.5 Hz, Ph-H), 8.94 (1H, s, 2-H). ^{13}C-NMR: 15.25, 127.35, 130.45, 131.64, 135.19, 136.22, 137.63, 138.94, 155.96 (2-C), 162.19, 188.48. *Anal.* Calcd for $C_{13}H_8BrNOS_2$: C, 46.16; H, 2.38; N, 4.14. Found: C, 46.39; H, 2.25; N, 4.05.

5-Acetyl-4-phenylthieno[3,2-*c*]thiazole (3e): From **1e** and **2**, 25%, colorless needles, mp 137—139 °C (from $CHCl_3$-hexane). IR (KBr): 1636 cm^{-1}. ^{1}H-NMR: 2.15 (3H, s, COMe), 7.48—7.57 (5H, m, Ph-H), 8.89 (1H, s, 2-H). *Anal.* Calcd for $C_{13}H_9NOS_2$: C, 60.21; H, 3.50; N, 5.40. Found: C, 60.20; H, 3.53; N, 5.39.

5-Benzoyl-4-phenylthieno[3,2-*c*]thiazole (3f): From **1f** and **2**, 29%, colorless needles, mp 151—153 °C (from $CHCl_3$-hexane). IR (KBr): 1611 cm^{-1}. ^{1}H-NMR: 7.13 (2H, br dd, *J*=8.1, 7.5 Hz, Ph-H), 7.13—7.19 (3H, m, Ph-H), 7.30 (1H, br t, *J*=7.5 Hz, Ph-H), 7.38—7.44 (2H, m, Ph-H), 7.59 (2H, br d, *J*=8.1 Hz, Ph-H), 8.97 (1H, s, 2-H). ^{13}C-NMR: 127.66, 127.92, 128.20, 129.52, 130.14, 132.16, 133.11, 134.90, 136.79, 137.30, 141.61, 156.26 (2-C), 160.28, 190.09. *Anal.* Calcd for $C_{18}H_{11}NOS_2$: C, 67.27; H, 3.45; N, 4.36. Found: C, 67.40; H, 3.36; N, 4.32.

5-(*p*-Chlorobenzoyl)-4-phenylthieno[3,2-*c*]thiazole (3g): From **1g** and **2**, 33%, colorless needles, mp 162—164 °C (from $CHCl_3$-hexane). IR (KBr): 1622 cm^{-1}. ^{1}H-NMR: 7.09 (2H, br d, *J*=8.4 Hz, Ph-H), 7.17—7.25 (3H, m, Ph-H), 7.37—7.43 (2H, m, Ph-H), 7.51 (2H, br d, *J*=8.4 Hz, Ph-H), 8.98 (1H, s, 2-H). ^{13}C-NMR: *Anal.* Calcd for $C_{18}H_{10}ClNOS_2$: C, 60.75; H, 2.83; N, 3.94. Found: C, 60.92; H, 2.71; N, 3.88.

5-(*p*-Bromobenzoyl)-4-phenylthieno[3,2-*c*]thiazole (3h): From **1h** and **2**, 41%, colorless needles, mp 174—176 °C (from $CHCl_3$-hexane). IR (KBr): 1622 cm^{-1}. ^{1}H-NMR: 7.16—7.25 (3H, m, Ph-H), 7.26

(2H, br d, *J*=8.5 Hz, Ph-H), 7.36—7.41 (2H, m, Ph-H), 7.43 (2H, br d, *J*=8.5 Hz, Ph-H), 8.98 (1H, s, 2-H). *Anal.* Calcd for $C_{18}H_{10}BrNOS_2$: C, 54.01; H, 2.52; N, 3.50. Found: C, 54.02; H, 2.45; N, 3.56.

5-Acetyl-4-(ethoxycarbonylmethyl)thieno[3,2-*c*]thiazole (3i): From **1i** and **2**, 43%, colorless needles, mp 126—129 °C (from $CHCl_3$-hexane). IR (KBr): 1649, 1732 cm^{-1}. ^{1}H-NMR: 1.28 (3H, t, *J*=7.2 Hz, OCH_2CH_3), 2.59 (3H, s, COMe), 4.20 (2H, q, *J*=7.2 Hz, OCH_2CH_3), 4.39 (2H, s, CH_2CO), 8.94 (1H, s, 2-H). ^{13}C-NMR: 14.15, 28.77, 34.02, 61.10, 131.08, 133.92, 141.10, 156.50 (2-C), 161.94, 169.61, 190.73. *Anal.* Calcd for $C_{11}H_{11}NO_3S_2$: C, 49.05; H, 4.12; N, 5.20. Found: C, 49.10; H, 4.08; N, 5.19.

5-Benzoyl-4-(ethocycarbonylmethyl)thieno[3,2-*c*]thiazole (3j): From **1j** and **2**, 62%, colorless needles, mp 130—131 °C (from $CHCl_3$-hexane). IR (KBr): 1632, 1730 cm^{-1}. ^{1}H-NMR: 1.25 (3H, t, *J*=7.2 Hz, OCH_2CH_3), 4.17 (2H, q, *J*=7.2 Hz, OCH_2CH_3), 4.27 (2H, s, CH_2CO), 7.49 (2H, br dd, *J*=7.7, 7.4 Hz, Ph-H), 7.60 (1H, br t, *J*=7.4 Hz, Ph-H), 7.86 (2H, br d, *J*=7.7 Hz, Ph-H), 8.94 (1H, s, 2-H). ^{13}C-NMR: 14.23, 34.12, 61.12, 128.37, 129.05, 131.86, 132.53, 135.09, 138.68, 140.48, 156.37 (2-C), 161.77, 169.67, 189.06. *Anal.* Calcd for $C_{16}H_{13}NO_3S_2$: C, 57.99; H, 3.95; N, 4.23. Found: C, 58.17; H, 4.07; N, 3.93.

5-(*p*-Chlorobenzoyl)-4-(ethoxycarbonylmethyl)thieno[3,2-*c*]thiazole (3k): From **1k** and **2**, 69%, colorless needles, mp 122—124 °C (from $CHCl_3$-hexane). IR (KBr): 1632, 1738 cm^{-1}. ^{1}H-NMR: 1.25 (3H, t, *J*=7.2 Hz, OCH_2CH_3), 4.17 (2H, q, *J*=7.2 Hz, OCH_2CH_3), 4.28 (2H, s, CH_2CO), 7.47 (2H, br d, *J*=8.5 Hz, Ph-H), 7.82 (2H, br d, *J*=8.5 Hz, Ph-H), 8.95 (1H, s, 2-H). *Anal.* Calcd for $C_{16}H_{12}ClNO_3S_2$: C, 52.53; H, 3.31; N, 3.83. Found: C, 52.64; H, 3.24; N, 3.78.

5-(*p*-Bromobenzoyl)-4-(ethoxycarbonylmethyl)thieno[3,2-*c*]thiazole (3l): From **1l** and **2**, 66%, colorless needles, mp 147—149 °C (from $CHCl_3$-hexane). IR (KBr): 1630, 1738 cm^{-1}. ^{1}H-NMR: 1.25 (3H, t, *J*=7.2 Hz, OCH_2CH_3), 4.17 (2H, q, *J*=7.2 Hz, OCH_2CH_3), 4.28 (2H, s, CH_2CO), 7.64 (2H, br d, *J*=8.5 Hz, Ph-H), 7.74 (2H, br d, *J*=8.5 Hz, Ph-H), 8.95 (1H, s, 2-H). *Anal.* Calcd for $C_{16}H_{12}BrNO_3S_2$: C, 46.84; H, 2.95; N, 3.41. Found: C, 46.86; H, 2.92; N, 3.42.

Dimethyl 2-[2-acetyl-3-methylthieno[2',3':2,3]-1,4-thiazino[4,5-*a*]pyrrol-8-ylidene]succinate (5a): From **1a** and **2**, trace, pale yellow prisms. ^{1}H-NMR: 2.51 (3H, s, 3-Me), 2.79 (3H, s, COMe), 3.78 and 3.85 (each 3H, s, OMe), 3.88 (2H, s, CH_2CO), 6.50 (1H, dd, *J*=3.9, 2.9 Hz, 6-H), 6.53 (1H, dd, *J*=3.9, 1.4 Hz, 7-H), 7.44 (1H, dd, *J*=2.9, 1.4 Hz, 5-H).

Dimethyl 2-[2-benzoyl-3-methylthieno[2',3':2,3]-1,4-thiazino[4,5-*a*]pyrrol-8-ylidene]succinate (5b): From **1b** and **2**, trace, pale yellow powder. ^{1}H-NMR: 2.70 (3H, s, 3-Me), 3.78 and 3.85 (each 3H, s, OMe), 3.89 (2H, s, CH_2CO), 6.51 (1H, dd, *J*=3.9, 2.9 Hz, 6-H), 6.54 (1H, dd, *J*=3.9, 1.4 Hz, 7-H), 7.48 (2H, br dd, *J*=7.6, 7.5 Hz, Ph-H), 7.49 (1H, dd, *J*=1.9, 1.4 Hz, 5-H), 7.60 (1H, br t, *J*=7.5 Hz, Ph-H), 7.80(2H, br d, *J*=7.6 Hz, Ph-H).

Dimethyl 2-[2-acetyl-3-phenylthieno[2',3':2,3]-1,4-thiazino[4,5-*a*]pyrrol-8-ylidene]succinate (5e): From **1e** and **2**, 9%, pale yellow prisms (from $CHCl_3$-hexane), mp 189—191 °C (from $CHCl_3$-hexane). IR (KBr): 1642, 1672, 1738 cm^{-1}. ^{1}H-NMR: 1.92 (3H, s, COMe), 3.75 and 3.86 (each 3H, s, OMe), 3.87 (2H, s, CH_2CO), 6.11 (1H, dd, *J*=3.9, 2.9 Hz, 6-H), 6.23 (1H, dd, *J*=3.9, 1.4 Hz, 7-H), 6.43 (1H, dd, *J*=2.9, 1.4 Hz, 5-H), 7.37—7.42 (2H, m, Ph-H), 7.52—7.57 (3H, m, Ph-H). *Anal.* Calcd for $C_{23}H_{19}NO_5S_2$: C, 60.91; H, 4.22; N, 3.09. Found: C, 60.98; H, 4.18; N, 3.01.

Crystallography of 5-(*p*-bromobenzoyl)-4-ethoxycarbonylmethylthieno[3,2-*d*]thiazole (3l) A single crystal (0.68×0.54×0.22 mm) grown from $CHCl_3$–hexane was used for the unit-cell determinations and the data collection by a Rigaku AFC5S four-circle diffractometer with graphite-monochromated MoK_α radiation (λ=0.71069 Å). Crystal data of these compounds are as follows: **3a**: $C_{18}H_{17}NO_5S_2$; *M*=391.46; monoclinic, space group *P*-1 (#2), *Z*=4 with *a*=17.967 (18) Å, *b*=11.708 (10) Å, *c*=10.334 (11) Å, α=90.00(9)^o; β=102.33 (6)^o; γ=88.74(9)^o; *V*=1777.5 (29) Å^3, and $D_{calc.}$=1.463 g/cm^3. All calculations were performed using CrystalStructure.[13] The structure was solved by a direct method (SIR).[14] The non-hydrogen atoms were refined anisotropically, and the hydrogen atoms were attached at the idealized position and not refined. The final *R*- and R_w-factors after full-matrix least-squares refinements were 0.064 and 0.053 respectively for 5382 (I>2.00σ(I)) observed reflections.

Crystallography of dimethyl 2-[2-acetyl-3-methylthieno[2',3':2,3]-1,4-thiazino[4,5-a]pyrrol-8-ylidene]succinate (5a). A single crystal (0.68×0.54×0.22 mm) grown from $CHCl_3$–hexane was used for the unit-cell determinations and the data collection by a Rigaku AFC5S four-circle diffractometer with graphite-monochromated MoK_α radiation (λ=0.71069 Å). Crystal data of these compounds are as follows: **3a**: $C_{18}H_{17}NO_5S_2$; *M*=391.46; monoclinic, space group *P*-1 (#2), *Z*=4 with *a*=17.967 (18) Å, *b*=11.708 (10) Å, *c*=10.334 (11) Å, α=90.00(9)^o; β=102.33 (6)^o; γ=88.74(9)^o; *V*=1777.5 (29) Å^3, and $D_{calc.}$=1.463 g/cm^3. All calculations were performed using CrystalStructure.[13] The structure was solved by a direct method (SIR).[14] The non-hydrogen atoms were refined anisotropically, and the hydrogen atoms were attached at the idealized position and not refined. The final *R*- and R_w-factors after full-matrix least-squares refinements were 0.064 and 0.053 respectively for 5382 (I>2.00σ(I)) observed reflections.

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