Preparation of New Nitrogen-Bridged Heterocycles. 60.[1] Syntheses and Conformational Analyses of Bis(indolizin-1-yl) Disulfides

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Received April 29, 2007; accepted July 18, 2007; published online July 25, 2007

Some bis(indolizin-1-yl) disulfides, readily obtainable from the treatment of 1-(benzoylthio)indolizines with piperidine, were prepared and their conformations were investigated. In comparison with those of 1-(benzoylthio)indolizines, the ^{1}H-NMR spectra of these disulfides showed considerable high field shifts (δ 0.13—0.82 ppm) on each pyridine ring proton and the UV spectra exhibited significant bathochromic and hyperchromic shifts. These results supported strongly the participation of an intramolecular π–π interaction between the two indolizine rings in these molecules and, hence, of a particular *gauche* (*cis*) conformation. However, the conformational considerations and molecular calculations (Mopac PM3) for some bis(indolizin-1-yl) disulfides showed the presence of four more stable *gauche* forms in which two are enantiomeric, resulting in three types of *gauche* structures. These three types of *gauche* structures were confirmed by X-ray analyses.

Key words bis(indolizin-1-yl) disulfide; conformational stability; π–π interaction; *gauche* form; X-ray analysis

In our preceding papers we described that the conformational stability of a sulfide linkage is inherently in the following order: *gauche* form>*anti* form>*eclipse* form, irrespective of the presence of some attractive interaction between the substituents on the terminal atoms, but the difference in the formation energies of the optimized *gauche* and *anti* conformation is not large.[1,2] This order was also consistent with our experimental results observed for various 3-(*R*-thio)-thieno[3,4-*b*]indolizine derivatives,[1—5] and the extra presence of the intramolecular π–π interaction made one of the gauche conformations more predominant than the other *gauche* and *anti* ones in the solution state. These molecules can be novel candidates for investigating face selectivity or conformational control through a single bond. As an extension of this work, we are interested in the conformation about the disulfide linkage, since we previously found a similar phenomenon in the X-ray analysis of bis[thieno[3,4-*b*]indolizin-3-yl] disulfide.[6] According to the literature there are several MO calculations in which a preference of the *gauche* (*cis*) form over the *anti* (*trans*) form in relation to the disulfide linkage and an energy minimum in the dihedral angle near 90° have been shown.[7,8] Furthermore, some structural data for comparatively simple disulfides such as dimethyl disulfide,[9,10] dibenzyl disulfide,[11] and diphenyl disulfide[12,13] by other investigators were in agreement with this prediction. However, there have not been many studies on the conformations of disulfide compounds and a more detailed investigation of their conformations is still valuable. We selected bis(indolizin-1-yl) disulfide derivatives as the model compound for the following reasons: 1) an effective method for the preparation of these compounds has been already developed by us[14]; 2) their Mopac PM3 calculations[15] supported the appearance of exclusive or nearly exclusive *gauche* forms; and 3) the participation of the intramolecular π–π interaction between the two indolizin-1-yl groups can be expected. In this paper we report the facile syntheses and the conformations of some bis(indolizin-1-yl) disulfide derivatives.

Results and Discussion

Conformational Analyses of Some Bis(indolizin-1-yl) Disulfides by Molecular Calculations Considering the molecular structures of bis[2-(*R*-thio)indolizin-1-yl] disulfides (**5**) (see Chart 2), the 6 most probable conformations were selected for calculation (Fig. 1): two *anti* forms **A1** and **A2**, and 4 *gauche* forms **G1** with an intramolecular π–π interaction, **G2**, **G3**, and **G4**. Since the *gauche* forms **G3** and **G4** are enantiomeric, however, the Mopac PM3 calculations[15] were performed for the **A1**, **A2**, **G1**, **G2**, and **G3** of Compounds **5a**—**e**, **i**. The relative formation energy and one torsion angle (C–S–S–C) in the respective optimized conformations using the **G3** form as a standard are listed in Table 1. As expected, all or the majority of the **A1** or **A2** forms were changed to the **G1** and **G2** or **G3** and **G4** forms respectively during the optimized calculations. Though some of them converged in the anti forms, their formation energies were considerably high. These data suggest clearly that the *gauche* forms (**G1**, **G2**, **G3**, **G4**) are fairly more stable than the *anti* forms (**A1**, **A2**) and, though the energy differences between **G1**, **G2**, **G3**, and **G4** are small (below 0.6 kcal/mol), the **G3**

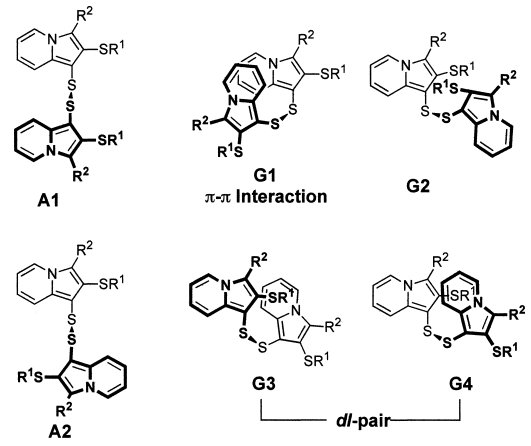

Fig. 1. Main Conformations of Bis(indolizin-1-yl) Disulfides for Molecular Calculations

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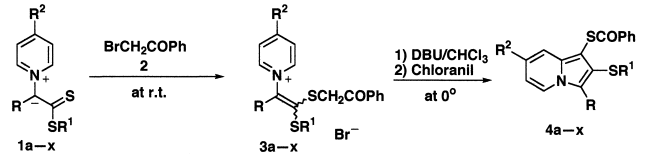
Table 1. Relative Energy Differences and the Dihedral Angles of the Disulfide Linkages for Some Bis(indolizin-1-yl) Disulfides by MOPAC (PM3) Calculations

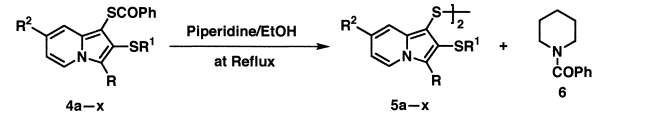
No.	A1	A2	G1	G2	G3 (G4)[a]
5a	5.3883 119.8[b]	to G3 or G4	0.5392 76.8[b]	0.0322 82.5[b]	0 (188.4218) 85.3[b]
5b	to G1 or G2	to G3 or G4	0.5668 76.9[b]	0.2520 78.5[b]	0 (180.1620) 85.3[b]
5c	2.9647 130.0[b]	to G3 or G4	0.5287 77.2[b]	0.1744 79.0[b]	0 (246.7626) 85.3[b]
5d	to G1 or G2	6.5588 148.3[b]	0.1227 76.2[b]	0.5588 85.3[b]	0 (282.3521) 88.3[b]
5e	to G1 or G2	to G3 or G4	0.1043 75.1[b]	0.5375 79.7[b]	0 (−54.0164) 85.2[b]
5i	to G1 or G2	to G3 or G4	0.1492 70.3[b]	0.1864 78.8[b]	0 (104.9178) 85.8[b]

a) The values (kcal/mol) in the parentheses are those obtained actually from the MOPAC calculations. *b*) The dihedral angle (°) about the disulfide linkage.



1,3,4	R	R¹	R²	Yield (%) 4 from 1	1,3,4	R	R¹	R²	Yield (%) 4 from 1
a	CN	Me	H	57	m	CN	Me	Me	44
b	CN	Et	H	50	n	CN	Et	Me	60
c	CN	CH_2Ph	H	37	o	CN	CH_2Ph	Me	45
d	CN	$CH_2$1-Naphthyl	H	32	p	CN	$CH_2$1-Naphthyl	Me	55
e	CO_2Et	Me	H	53	q	CO_2Et	Me	Me	51
f	CO_2Et	Et	H	63	r	CO_2Et	Et	Me	75
g	CO_2Et	CH_2Ph	H	70	s	CO_2Et	CH_2Ph	Me	82
h	CO_2Et	$CH_2$1-Naphthyl	H	70	t	CO_2Et	$CH_2$1-Naphthyl	Me	70
i	COPh	Me	H	38	u	COPh	Me	Me	65
j	COPh	Et	H	40	v	COPh	Et	Me	65
k	COPh	CH_2Ph	H	60	w	COPh	CH_2Ph	Me	60
l	COPh	$CH_2$1-Naphthyl	H	55	x	COPh	$CH_2$1-Naphthyl	Me	60

Chart 1



5	R	R¹	R²	Yield (%)
a	CN	Me	H	90
b	CN	Et	H	40
c	CN	CH_2Ph	H	96
d	CN	$CH_2$1-Naphthyl	H	92
e	CO_2Et	Me	H	73
f	CO_2Et	Et	H	64
g	CO_2Et	CH_2Ph	H	86
h	CO_2Et	$CH_2$1-Naphthyl	H	55
i	COPh	Me	H	88
j	COPh	Et	H	84
k	COPh	CH_2Ph	H	30
l	COPh	$CH_2$1-Naphthyl	H	60

5	R	R¹	R²	Yield (%)
m	CN	Me	Me	90
n	CN	Et	Me	50
o	CN	CH_2Ph	Me	94
p	CN	$CH_2$1-Naphthyl	Me	68
q	CO_2Et	Me	Me	96
r	CO_2Et	Et	Me	52
s	CO_2Et	CH_2Ph	Me	75
t	CO_2Et	$CH_2$1-Naphthyl	Me	48
u	COPh	Me	Me	80
v	COPh	Et	Me	82
w	COPh	CH_2Ph	Me	56
x	COPh	$CH_2$1-Naphthyl	Me	76

Chart 2

or **G4** form is the most stable conformation. On the other hand, the calculated torsion angles for the disulfide moiety in the **G1**, **G2**, and **G3** forms are in the range of 70.3—85.8° and these values are slightly lower than those (83.9—96.6°) in the MO calculations and structural data described above.[7—13)]

Syntheses of 1-(Benzoylthio)indolizine Derivatives According to the procedure described earlier by us[14)] these 1-benzoylthio-2-(*R*-thio)indolizine derivatives **4a**—**x** were synthesized from the *S*-alkylation of pyridinium 1-[2-(*R*-thio)-2-thioxo]ethanides (**1a**—**x**) with phenacyl bromide (**2**), followed by the treatment of the resulting pyridinium salts (**3a**—**x**) with 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) and chloranil in chloroform at 0 °C. These results are summarized in Chart 1.

The structures of products **4a**—**x** were determined by their elemental analyses, IR, UV, and ^{1}H-NMR spectral analyses and by comparison with those of known compounds (**4a**, **e**, **i**, **m**, **q**, **u**). In particular, the IR spectra of **4a**—**x** showed an unsaturated carbonyl absorption band at 1663—1686 cm^{-1}, together with an unsaturated cyano band (2199—2213 cm^{-1}) in **4a**—**d**, **m**—**p** and a largely shifted carbonyl band (1591—1609 cm^{-1}) due to the 3-benzoyl group in **4i**—**l**, **u**—**x**. Compounds **4a**—**h**, **m**—**t** having a cyano or ethoxycarbonyl group at the 3-position showed a absorption maximum at 330—351 nm in the UV spectra and were colorless crystals. On the other hand, products **4i**—**l**, **u**—**x** bearing a 3-benzoyl group exhibited a maximum at a higher region (384—389 nm) and were yellow crystals.

Syntheses and Their Structures of Bis(indolizin-1-yl) Disulfide Derivatives The treatment of 1-(benzoylthio)indolizines (**4a**—**x**) with piperidine in ethanol at the reflux temperature afforded the corresponding bis[2-(*R*-thio)indolizin-1-yl] disulfides (**5a**—**x**) in moderate to good yields (Chart 2).

The elemental analyses for new products (**5a**—**d**, **f**—**l**, **n**—**p**, **r**—**x**) were in good accord with our proposed structures. Their IR spectra showed an cyano band near 2200 cm^{-1} (**5a**—**d**, **m**—**p**), an ester carbonyl band at 1674—1688 cm^{-1} (**5e**—**h**, **q**—**t**), and a benzoyl carbonyl band at 1596—1620 cm^{-1} (**5i**—**l**, **u**—**x**). The UV spectra of **5a**—**h**, **m**—**t** exhibited an absorption band at 334—349 nm and those of **5i**—**l**, **u**—**x** showed an absorption band at 393—400 nm. The bathochromic shifts of each absorption maximum in comparison with those of **4a**—**x** were not large (5 nm maximum) but the end absorption bands were spread largely to a higher region and, hence, even compounds (**5a**—**h**, **m**—**t**) having the 3-cyano or 3-ethoxycarbonyl group were pale yellow in color. In the ^{1}H-NMR spectra of disulfides **5a**—**x** the 2 sets of pyridine ring protons in the molecule completely overlapped each other suggesting the presence of a symmetric factor. In addition, all the pyridine ring protons of **5a**—**x** were shifted considerably at higher magnetic regions com-

pared to those of 1-benzoylthio-2-(*R*-thio)indolizines (**4a**, **e**, **i**, **m**, **q**, **u**) (see Table 2). These results indicated that the predominant conformation of **5a**—**x** in the solution state must be the **G1** form with a C_2 symmetry in which the intramolecular π–π interaction is possible. Unexpectedly, the X-ray analyses of bis(indolizin-1-yl) disulfides **5a**, **k**, **n**, **q** showed the **G2**, **G4**, **G1**, and **G1** forms respectively. Furthermore, the crystal of the 2-benzylthio derivative (**5k**) had a *gauche* and an *anti* sulfide linkage and did not have any symmetric structure. The dihedral angles for the disulfide moiety in **5a**, **k**, **n**, **q** are 68.4(2)°, 69.6(3)°, 96.4(2)°, and 68.4(5)° respectively, and the values for **5a**, **k**, **q** are significantly smaller than those (78.5—85.3, 85.2—85.8, and 70.3—77.2°) calculated for **G2**, **G4**, and **G1** respectively (see Table 1). The larger angle (96.4(2)°) for **5n** (**G1** form) must be attributable to the steric interaction between the two ethylthio moieties facing inward. The ORTEP drawings[16] of compounds (**5a**, **k**, **n**, **q**) are shown in Figs. 2—5. From these results we could deduce the predominance of the *gauche* forms over the *anti* forms in our model compounds and a particular *gauche* form (**G1**) having an intramolecular π–π interaction between the two indolizine rings is the most stable conformation in the solution state. However, the difference in the conformational stability between the *gauche* forms is not so large and even though such attractive interaction worked only on the **G1** form, the other *gauche* forms (**G2**, and **G3** or **G4**) also appeared in the crystalline state.

In conclusion, we synthesized some bis[2-(*R*-thio)indolizin-1-yl] disulfides and could confirm that the *gauche* conformations predominate over the *anti* ones and also that the π–π interaction is the main factor for the **G1** conformation in the solution state.

Table 2. ^{1}H-NMR Spectral Data for the Pyridine Ring Protons of Bis(indolizin-1-yl) Disulfides (**5a**—**x**)

No.	C-5	C-6	C-7	C-8	δC-5	δC-6	δC-7	δC-8
4a	8.29	6.94	7.17	7.47	0.00	0.00	0.00	0.00
5a	8.11	6.80	6.94	7.01	0.18	0.14	0.23	0.46
5b	8.13	6.81	6.94	7.02	0.16	0.13	0.23	0.45
5c	8.03	6.73	6.80	6.80	0.26	0.21	0.37	0.67
5d	8.02	6.74	6.87	6.95	0.27	0.20	0.30	0.52
4e	9.55	6.90	7.15	7.51	0.00	0.00	0.00	0.00
5e	9.29	6.65	6.73	6.90	0.26	0.25	0.42	0.61
5f	9.30	6.66	6.71	6.91	0.25	0.24	0.44	0.60
6g	9.29	6.66	6.72	6.89	0.26	0.24	0.43	0.62
5h	9.28	6.66	6.74	6.93	0.27	0.24	0.41	0.58
4i	9.47	6.93	7.22	7.52	0.00	0.00	0.00	0.00
5i	9.28	6.79	6.97	7.18	0.19	0.14	0.25	0.34
5j	9.29	6.79	6.98	7.21	0.18	0.14	0.24	0.31
5k	9.25	6.78	6.98	7.23	0.22	0.15	0.24	0.29
5l	9.24	6.80	7.01	7.15	0.23	0.13	0.21	0.37
4m	8.15	6.76	2.37	7.22	0.00	0.00	0.00	0.00
5m	7.96	6.61	2.22	6.63	0.19	0.15	0.15	0.59
5n	7.98	6.62	2.21	6.64	0.17	0.14	0.16	0.58
5o	7.88	6.52	2.07	6.40	0.27	0.24	0.30	0.82
5p	7.90	6.56	2.16	6.62	0.25	0.20	0.21	0.60
4q	9.43	6.73	2.36	7.26	0.00	0.00	0.00	0.00
5q	9.14	6.44	2.03	6.50	0.29	0.29	0.33	0.76
5r	9.15	6.44	2.02	6.49	0.28	0.29	0.34	0.77
5s	9.14	6.44	1.99	6.45	0.29	0.29	0.37	0.81
5t	9.15	6.46	2.03	6.55	0.28	0.27	0.33	0.71
4u	9.42	6.78	2.39	7.28	0.00	0.00	0.00	0.00
5u	9.24	6.59	2.16	6.78	0.18	0.19	0.23	0.50
5v	9.26	6.60	2.16	6.80	0.16	0.18	0.23	0.48
5w	9.19	6.57	2.11	6.76	0.23	0.21	0.28	0.52
5x	9.20	6.62	2.18	6.91	0.22	0.16	0.21	0.37

The coupling constants are as follows: $J_{5,6}$=6.8—7.2 Hz, $J_{6,7}$=6.8—7.2 Hz, $J_{7,8}$=8.8—9.0 Hz, $J_{6,8}$=1.5—2.0 Hz.

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. The ^{1}H-NMR spectra were determined with a Hitachi R-600 spectrometer (60 MHz) or a JEOL JNM-LA400 (^{1}H: 400 MHz) spectrometer in deuteriochloroform with tetramethylsilane used as the internal standard; the chemical shifts are expressed in δ values. The IR and UV spectra were taken with JASCO FT/IR-5300 IR and SHIMADZU UV-2450 spectrophotometers, respectively.

Preparation of Pyridinium 1-[2-(*R*-thio)-2-thioxo]ethanides These pyridinium methylides were prepared according to the procedure described by Tominaga *et al.*[17] The results and some properties of new pyridinium methylides (**1b**—**d**, **f**—**h**, **j**—**l**, **n**—**p**, **r**—**t**, **v**—**x**) are as follows:

Pyridinium 1-(1-Cyano-2-ethylthio-2-thioxo)ethanides (**1b**): 64% (from 1-(cyanomethyl)pyridinium chloride, carbon disulfide, and diethyl sulfate), pale yellow needles (from $CHCl_3$–ether), mp 120—122 °C. IR (KBr) cm^{-1}: 2170. ^{1}H-NMR (60 MHz) δ: 1.36 (3H, t, J=7.0 Hz), 3.38 (2H, q, J=7.0 Hz), 7.88 (2H, br t, J=7.0 Hz, 3-, 5-H), 8.26 (1H, br t, J=7.0 Hz, 4-H), 9.07 (2H, br d, J=7.0 Hz, 2-, 6-H). *Anal.* Calcd for $C_{10}H_{10}N_2S_2$: C, 54.02; H, 4.53; N, 12.60. Found: C, 54.06; H, 4.52; N, 12.58.

Pyridinium 1-(2-Benzylthio-1-cyano-2-thioxo)ethanides (**1c**): 70% (from 1-(cyanomethyl)pyridinium chloride, carbon disulfide, and benzyl bromide), pale yellow needles (from $CHCl_3$–ether), mp 151—156 °C. IR (KBr) cm^{-1}:

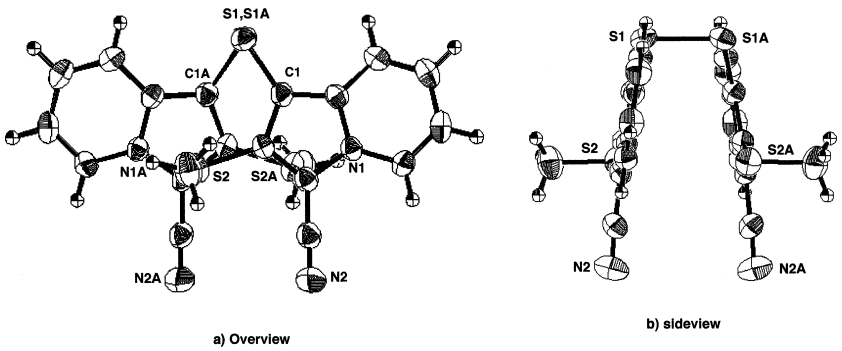


Fig. 2. ORTEP Drawings of Bis[3-cyano-2-(methylthio)indolizin-1-yl] Disulfide (**5a**)

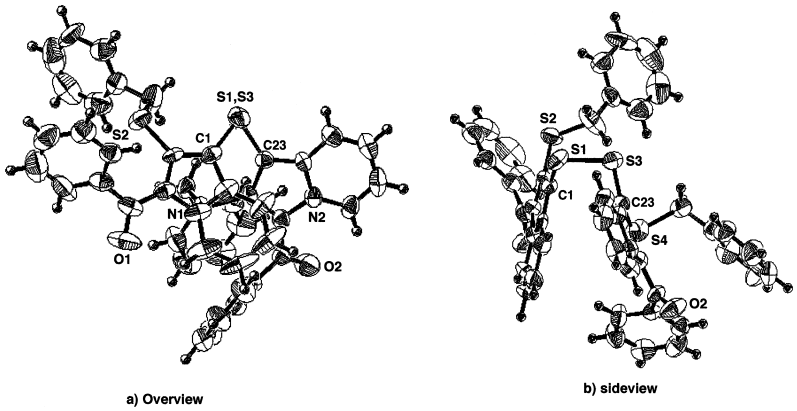


Fig. 3. ORTEP Drawings of Bis[3-benzoyl-2-(benzylthio)indolizin-1-yl] Disulfides (**5k**)

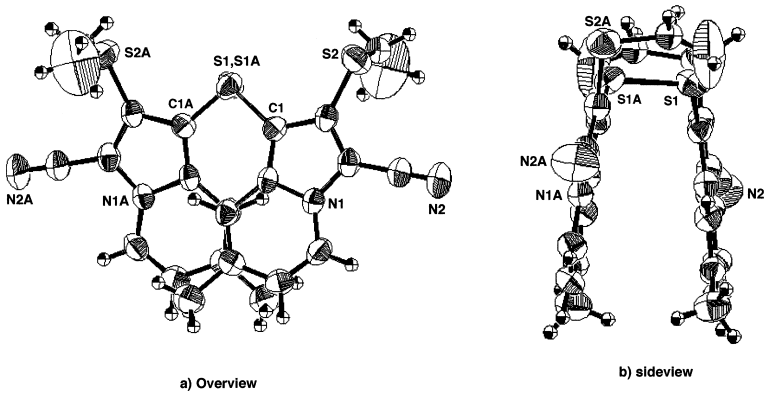


Fig. 4. ORTEP Drawings of Bis[3-cyano-2-(ethylthio)indolizin-1-yl] Disulfides (**5n**)

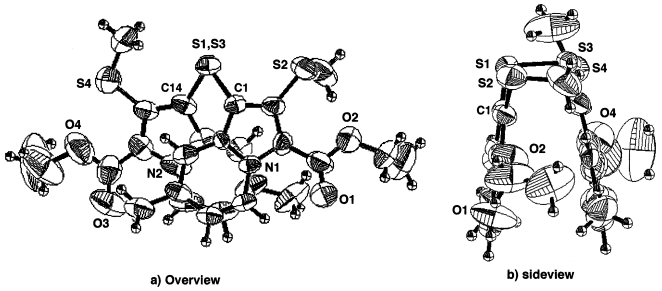


Fig. 5. ORTEP Drawings of Bis[3-ethoxycarbonyl-2-(methylthio)indolizin-1-yl] Disulfides (**5q**)

2179. ^{1}H-NMR (60 MHz) δ: 4.65 (2H, s, SC$\underline{H}_2$), 7.0—7.5 (5H, m), 7.82 (2H, br t, J=7.0 Hz), 8.21 (1H, br t, J=7.0 Hz), 9.03 (2H, br d, J=7.0 Hz). *Anal.* Calcd for $C_{15}H_{12}N_2S_2$: C, 63.35; H, 4.25; N, 9.85. Found: C, 63.49; H, 4.25; N, 9.68.

Pyridinium 1-[1-Cyano-2-(1-naphthylmethylthio)-2-thioxo]ethanides (**1d**): 77% (from 1-(cyanomethyl)pyridinium chloride, carbon disulfide, and 1-(chloromethyl)naphthalene), pale yellow needles (from $CHCl_3$), mp 132—136 °C. IR (KBr) cm^{-1}: 2172. ^{1}H-NMR (60 MHz) δ: 5.10 (2H, s, SC$\underline{H}_2$), 7.1—8.4 (10H, m), 8.89 (2H, br d, J=7.0 Hz). *Anal.* Calcd for $C_{19}H_{14}N_2S_2$: C, 68.23; H, 4.22; N, 8.58. Found: C, 68.44; H, 4.24; N, 8.35.

Pyridinium 1-(1-Ethoxycarbonyl-2-ethylthio-2-thioxo)ethanides (**1f**): 50% (from 1-(ethoxycarbonylmethyl)pyridinium chloride, carbon disulfide, and diethyl sulfate), pale yellow needles (from $CHCl_3$–ether), mp 180—181 °C. IR (KBr) cm^{-1}: 1655. ^{1}H-NMR (60 MHz) δ: 1.17 (3H, t, J=7.0 Hz), 1.34 (3H, t, J=7.0 Hz), 3.31 (2H, q, J=7.0 Hz), 4.16 (2H, q, J=7.0 Hz), 7.87 (2H, br t, J=7.0 Hz), 8.23 (1H, br t, J=7.0 Hz), 8.51 (2H, br d, J=7.0 Hz). *Anal.* Calcd for $C_{12}H_{15}NO_2S_2$: C, 53.51; H, 5.61; N, 5.20. Found: C, 53.77; H, 5.69; N, 4.92.

Pyridinium 1-(2-Benzylthio-1-ethoxycarbonyl-2-thioxo)ethanides (**1g**): 52% (from 1-(ethoxycarbonylmethyl)pyridinium chloride, carbon disulfide, and benzyl bromide), pale yellow needles (from $CHCl_3$–ether), mp 171—173 °C. IR (KBr) cm^{-1}: 1658. ^{1}H-NMR (60 MHz) δ: 1.12 (3H, t, J=7.0 Hz), 4.11 (2H, q, J=7.0 Hz), 4.59 (2H, s), 6.9—7.5 (5H, m), 7.79 (2H, br t, J=7.0 Hz), 8.27 (1H, br t, J=7.0 Hz), 8.48 (2H, br d, J=7.0 Hz). *Anal.* Calcd for $C_{17}H_{17}NO_2S_2$: C, 61.60; H, 5.17; N, 4.23. Found: C, 61.80; H, 5.15; N, 4.05.

Pyridinium 1-[1-Ethoxycarbonyl-2-(1-naphthylmethylthio)-2-thioxo]-ethanides (**1h**): 54% (from 1-(ethoxycarbonylmethyl)pyridinium chloride, carbon disulfide, and 1-(chloromethyl)naphthalene), pale yellow needles (from $CHCl_3$), mp 203—205 °C. IR (KBr) cm^{-1}: 1657. ^{1}H-NMR (60 MHz) δ: 1.07 (3H, t, J=7.0 Hz), 4.09 (2H, q, J=7.0 Hz), 4.84 (2H, s), 7.0—8.4 (10H, m), 8.53 (2H, br d, J=7.0 Hz). *Anal.* Calcd for $C_{21}H_{19}NO_2S_2$: C, 66.11; H, 5.02; N, 3.67. Found: C, 66.28; H, 5.03; N, 3.47.

Pyridinium 1-(1-Benzoyl-2-ethylthio-2-thioxo)ethanides (**1j**): 60% (from 1-phenacylpyridinium chloride, carbon disulfide, and diethyl sulfate), pale yellow needles (from $CHCl_3$–ether), mp 205—208 °C. IR (KBr) cm^{-1}: 1622. ^{1}H-NMR (60 MHz) δ: 1.31 (3H, t, J=7.0 Hz), 3.26 (2H, q, J=7.0 Hz), 7.27 (5H, s, COPh), 7.73 (2H, br t, J=7.0 Hz), 8.23 (1H, br t, J=7.0 Hz), 8.53 (2H, br d, J=7.0 Hz). *Anal.* Calcd for $C_{16}H_{15}NOS_2$: C, 63.76; H, 5.02; N, 4.65. Found: C, 64.06; H, 5.02; N, 4.36.

Pyridinium 1-(1-Benzoyl-2-benzylthio-2-thioxo)ethanides (**1k**): 56% (from 1-phenacylpyridinium chloride, carbon disulfide, and benzyl bromide), pale yellow needles (from $CHCl_3$–ether), mp 198—200 °C. IR (KBr) cm^{-1}: 1622. ^{1}H-NMR (60 MHz) δ: 4.53 (2H, s, SC$\underline{H}_2$), 7.26 (10H, s), 7.73 (2H, br t, J=7.0 Hz), 8.22 (1H, br t, J=7.0 Hz), 8.56 (2H, br d, J=7.0 Hz). *Anal.* Calcd for $C_{21}H_{17}NOS_2$: C, 69.39; H, 4.71; N, 3.85. Found: C, 69.60; H, 4.81; N, 3.54.

Pyridinium 1-[1-Benzoyl-2-(1-naphthylmethylthio)-2-thioxo]ethanides (**1l**): 68% (from 1-phenacylpyridinium chloride, carbon disulfide, and 1-(chloromethyl)naphthalene), pale yellow needles (from $CHCl_3$), mp 222—225 °C. IR (KBr) cm^{-1}: 1620. ^{1}H-NMR (60 MHz) δ: 4.84 (2H, s, SC$\underline{H}_2$), 7.0—8.5 (15H, m), 8.59 (2H, br d, J=7.0 Hz). *Anal.* Calcd for $C_{25}H_{19}NOS_2$: C, 72.61; H, 4.63; N, 3.39. Found: C, 72.79; H, 4.64; N, 3.19.

4-Methylpyridinium 1-(1-Cyano-2-ethylthio-2-thioxo)ethanides (**1n**): 71%

(from 1-cyanomethyl-4-methylpyridinium chloride, carbon disulfide, and diethyl sulfate), pale yellow needles (from $CHCl_3$–ether), mp 129—130 °C. IR (KBr) cm^{-1}: 2164. ^{1}H-NMR (60 MHz) δ: 1.36 (3H, t, J=7.0 Hz), 2.67 (3H, s, 4-Me), 3.36 (2H, q, J=7.0 Hz), 7.66 (2H, br d, J=7.0 Hz), 8.79 (2H, br d, J=7.0 Hz). *Anal.* Calcd for $C_{11}H_{12}N_2S_2$: C, 55.90; H, 5.12; N, 11.85. Found: C, 55.95; H, 5.12; N, 11.80.

4-Methylpyridinium 1-(2-Benzylthio-1-cyano-2-thioxo)ethanides (**1o**): 71% (from 1-cyanomethyl-4-methylpyridinium chloride, carbon disulfide, and benzyl bromide), pale yellow needles (from $CHCl_3$–ether), mp 160—166 °C. IR (KBr) cm^{-1}: 2173. ^{1}H-NMR (60 MHz) δ: 2.59 (3H, s), 4.64 (2H, s), 7.0—7.6 (5H, m), 7.60 (2H, br d, J=7.0 Hz), 8.72 (2H, br d, J=7.0 Hz). *Anal.* Calcd for $C_{16}H_{14}N_2S_2$: C, 64.40; H, 4.73; N, 9.39. Found: C, 64.44; H, 4.72; N, 9.37.

4-Methylpyridinium 1-[1-Cyano-2-(1-naphthylmethylthio)-2-thioxo)-ethanides (**1p**): 63% (from 1-cyanomethyl-4-methylpyridinium chloride, carbon disulfide, and 1-(chloromethyl)naphthalene), pale yellow needles (from $CHCl_3$), mp 185—187 °C. IR (KBr) cm^{-1}: 2166. ^{1}H-NMR (60 MHz) δ: 2.57 (3H, s), 5.09 (2H, s), 7.0—8.0 (9H, m), 8.75 (2H, br d, J=7.0 Hz). *Anal.* Calcd for $C_{20}H_{16}N_2S_2$: C, 68.93; H, 4.63; N, 8.04. Found: C, 68.76; H, 4.85; N, 8.00.

4-Methylpyridinium 1-(1-Ethoxycarbonyl-2-ethylthio-2-thioxo)ethanides (**1r**): 50% (from 1-ethoxycarbonylmethyl-4-methylpyridinium chloride, carbon disulfide, and diethyl sulfate), pale yellow needles (from $CHCl_3$–ether), mp 185—188 °C. IR (KBr) cm^{-1}: 1615. ^{1}H-NMR (60 MHz) δ: 1.16 (3H, t, J=7.0 Hz), 1.35 (3H, t, J=7.0 Hz), 2.67 (3H, s), 3.30 (2H, q, J=7.0 Hz), 4.15 (2H, q, J=7.0 Hz), 7.63 (2H, br d, J=7.0 Hz), 8.32 (2H, br d, J=7.0 Hz). *Anal.* Calcd for $C_{13}H_{17}NO_2S_2$: C, 55.10; H, 6.05; N, 4.94. Found: C, 55.33; H, 6.16; N, 4.65.

4-Methylpyridinium 1-(2-Benzylthio-1-ethoxycarbonyl-2-thioxo)-ethanides (**1s**): 45% (from 1-ethoxycarbonylmethyl-4-methylpyridinium chloride, carbon disulfide, and benzyl bromide), pale yellow needles (from $CHCl_3$–ether), mp 182—183 °C. IR (KBr) cm^{-1}: 1661. ^{1}H-NMR (60 MHz) δ: 1.14 (3H, t, J=7.0 Hz), 2.66 (3H, s), 4.12 (2H, q, J=7.0 Hz), 4.57 (2H, s), 7.0—7.5 (5H, m), 7.60 (2H, br d, J=7.0 Hz), 8.33 (1H, br d, J=7.0 Hz). *Anal.* Calcd for $C_{18}H_{19}NO_2S_2$: C, 62.58; H, 5.54; N, 4.05. Found: C, 62.39; H, 5.55; N, 3.78.

4-Methylpyridinium 1-(1-Ethoxycarbonyl-2-(1-naphthylmethylthio)-2-thioxo)ethanides (**1t**): 40% (from 1-ethoxycarbonylmethyl-4-methylpyridinium chloride, carbon disulfide, and 1-(chloromethyl)naphthalene), pale yellow needles (from $CHCl_3$), mp 188—191 °C. IR (KBr) cm^{-1}: 1658. ^{1}H-NMR (60 MHz) δ: 1.14 (3H, t, J=7.0 Hz), 2.64 (3H, s), 4.11 (2H, q, J=7.0 Hz), 4.55 (2H, s), 7.0—7.6 (7H, m), 7.58 (2H, br d, J=7.0 Hz). 8.32 (2H, br d, J=7.0 Hz). *Anal.* Calcd for $C_{22}H_{21}NO_2S_2$: C, 66.80; H, 5.35; N, 3.54. Found: C, 66.77; H, 5.53; N, 3.40.

4-Methylpyridinium 1-(1-Benzoyl-2-ethylthio-2-thioxo)ethanides (**1v**): 59% (from 4-methyl-1-phenacylpyridinium chloride, carbon disulfide, and diethyl sulfate), pale yellow needles (from $CHCl_3$–ether), mp 190—194 °C. IR (KBr) cm^{-1}: 1633. ^{1}H-NMR (60 MHz) δ: 1.31 (3H, t, J=7.0 Hz), 2.56 (3H, s), 3.26 (2H, q, J=7.0 Hz), 7.1—7.4 (5H, m), 7.49 (2H, br d, J=7.0 Hz), 8.32 (1H, br d, J=7.0 Hz). *Anal.* Calcd for $C_{17}H_{17}NOS_2$: C, 64.73; H, 5.43; N, 4.44. Found: C, 64.87; H, 5.45; N, 4.27.

4-Methylpyridinium 1-(1-Benzoyl-2-benzylthio-2-thioxo)ethanides (**1w**): 70% (from 4-methyl-1-phenacylpyridinium chloride, carbon disulfide, and benzyl bromide), pale yellow needles (from $CHCl_3$–ether), mp 176—177 °C. IR (KBr) cm^{-1}: 1630. ^{1}H-NMR (60 MHz) δ: 2.55 (3H, s), 4.59 (2H, s), 7.0—7.5 (10H, m), 7.49 (2H, br d, J=7.0 Hz), 8.37 (1H, br d, J=7.0 Hz). *Anal.* Calcd for $C_{22}H_{19}NOS_2$: C, 69.99; H, 5.07; N, 3.71. Found: C, 70.27; H, 5.19; N, 3.39.

4-Methylpyridinium 1-[1-Benzoyl-2-(1-naphthylmethylthio)-2-thioxo)-ethanides (**1x**): 88% (from 4-methyl-1-phenacylpyridinium chloride, carbon disulfide, and 1-(chloromethyl)naphthalene), pale yellow needles (from $CHCl_3$), mp 208—211 °C. IR (KBr) cm^{-1}: 1633. ^{1}H-NMR (60 MHz) δ: 2.62 (3H, s), 5.00 (2H, s), 7.0—8.2 (14H, m), 8.38 (2H, br d, J=7.0 Hz). *Anal.* Calcd for $C_{26}H_{21}NOS_2$: C, 73.04; H, 4.95; N, 3.28. Found: C, 73.36; H, 4.88; N, 3.03.

Preparation of 1-(Benzoylthio)indolizine Derivatives. General Method A mixture of pyridinium 1-[*R*-thio(thiocarbonyl)]methylide (**1**, 2 mmol) and phenacyl bromide (**2**, 0.420 g, 2.1 mmol) was dissolved in chloroform (15 ml) and the resulting solution was kept at room temperature for 2 h. The solution was concentrated at reduced pressure and the residue was washed 3 times with ether to remove unaltered phenacyl bromide. Pyridinium salt was then dissolved in chloroform (30 ml) and allowed to react with DBU (0.302 g, 2 mmol) under stirring in an ice bath for 5 min. Chloranil (0.500 g, 2 mmol) was then added to the resulting reaction mixture at that temperature and stirred for a further 4 h. The solution was concentrated at reduced pressure and the residual oil was separated by column chromatography on alumina using chloroform as an eluent. The collected fraction of 1-(benzoylthio)indolizine was concentrated at reduced pressure, and recrystallization from ethanol gave the pure products (**4a**—**x**). Some data for the new compounds (**4b**—**d**, **f**—**l**, **n**—**p**, **r**—**x**) are as follows:

1-Benzoylthio-2-(ethylthio)indolizine-3-carbonitrile (**4b**): From **1b** and phenacyl bromide (**2**), colorless needles (from ethanol), mp 128—129 °C. IR (KBr) cm^{-1}: 1676, 2209. ^{1}H-NMR (60 MHz) δ: 1.29 (3H, t, J=7.0 Hz), 3.07 (2H, q, J=7.0 Hz), 7.0—8.3 (6H, m, 8-H, COPh), 6.93 (1H, dt, J=7.0, 7.0, 1.0 Hz, 6-H), 7.18 (1H, q, J=9.0, 7.0 Hz, 7-H), 8.29 (1H, d, J=7.0 Hz, 5-H). UV λ_{max} ($CHCl_3$) nm (log ε): 259 (4.51), 330 (3.95). *Anal.* Calcd for $C_{18}H_{14}N_2OS_2$: C, 63.88; H, 4.17; N, 8.28. Found: C, 63.90; H, 4.05; N, 8.38.

1-Benzoylthio-2-(benzylthio)indolizine-3-carbonitrile (**4c**): From **1c** and **2**, colorless needles (from ethanol), mp 142—145 °C. IR (KBr) cm^{-1}: 1676, 2199. ^{1}H-NMR (60 MHz) δ: 4.16 (2H, s, SC$\underline{H}_2$), 6.89 (1H, dt, J=7.0, 7.0, 1.0 Hz), 7.0—8.2 (6H, m), 7.23 (5H, s), 7.45 (1H, d, J=9.0 Hz), 8.23 (1H, d, J=7.0 Hz). UV λ_{max} ($CHCl_3$) nm (log ε): 261 (shoulder), 330 (3.88). *Anal.* Calcd for $C_{23}H_{16}N_2OS_2$: C, 68.97; H, 4.03; N, 6.99. Found: C, 68.84; H, 3.90; N, 7.26.

1-Benzoylthio-2-(1-naphthylmethylthio)indolizine-3-carbonitrile (**4d**): From **1d** and **2**, colorless needles (from ethanol), mp 166—167 °C. IR (KBr) cm^{-1}: 1672, 2207. ^{1}H-NMR (60 MHz) δ: 4.62 (2H, s), 6.90 (1H, dt, J=7.0, 7.0, 1.0 Hz), 7.0—8.2 (12H, m), 7.14 (1H, br q, J=9.0, 7.0 Hz), 8.22 (1H, d, J=7.0 Hz). UV λ_{max} ($CHCl_3$) nm (log ε): 258 (4.50), 333 (shoulder). *Anal.* Calcd for $C_{27}H_{18}N_2OS_2$: C, 71.97; H, 4.03; N, 6.22. Found: C, 71.89; H, 4.04; N, 6.01.

Ethyl 1-Benzoylthio-2-(ethylthio)indolizine-3-carboxylate (**4f**): From **1f** and **2**, colorless needles (from ethanol), mp 100—102 °C. IR (KBr) cm^{-1}: 1682. ^{1}H-NMR (60 MHz) δ: 1.18 (3H, t, J=7.0 Hz), 1.47 (3H, t, J=7.0 Hz), 2.96 (2H, q, J=7.0 Hz), 4.48 (2H, q, J=7.0 Hz), 6.90 (1H, dt, J=7.0, 7.0, 1.0 Hz), 7.0—8.3 (6H, m), 7.14 (1H, br q, J=9.0, 7.0 Hz), 9.55 (1H, d, J=7.0 Hz). UV λ_{max} ($CHCl_3$) nm (log ε): 263 (4.45), 339 (4.04), 350 (4.03). *Anal.* Calcd for $C_{20}H_{19}NO_3S_2$: C, 62.31; H, 4.97; N, 3.63. Found: C, 62.11; H, 5.06; N, 3.75.

Ethyl 1-Benzoylthio-2-(benzylthio)indolizine-3-carboxylate (**4g**): From **1g** and **2**, colorless needles (from ethanol), mp 96—97 °C. IR (KBr) cm^{-1}: 1671. ^{1}H-NMR (60 MHz) δ: 1.46 (3H, t, J=7.0 Hz), 4.43 (2H, q, J=7.0 Hz), 4.12 (2H, s), 6.88 (1H, dt, J=7.0, 7.0, 1.0 Hz), 7.0—8.3 (12H, m), 9.54 (1H, d, J=7.0 Hz). UV λ_{max} ($CHCl_3$) nm (log ε): 262 (shoulder), 340 (4.06). *Anal.* Calcd for $C_{25}H_{21}NO_3S_2$: C, 67.09; H, 4.73; N, 3.13. Found: C, 67.09; H, 4.80; N, 3.11.

Ethyl 1-Benzoylthio-2-(1-naphthylmethylthio)indolizine-3-carboxylate (**4h**): From **1h** and **2**, colorless needles (from ethanol), mp 174—177 °C. IR (KBr) cm^{-1}: 1678. ^{1}H-NMR (60 MHz) δ: 1.34 (3H, t, J=7.0 Hz), 4.28 (2H, q, J=7.0 Hz), 4.55 (2H, s), 6.89 (1H, dt, J=7.0, 7.0, 1.0 Hz), 7.0—8.4 (14H, m), 9.54 (1H, d, J=7.0 Hz). UV λ_{max} ($CHCl_3$) nm (log ε): 261 (shoulder), 340 (4.02). *Anal.* Calcd for $C_{29}H_{23}NO_3S_2$: C, 72.32; H, 4.81; N, 2.91. Found: C, 72.41; H, 4.74; N, 2.89.

3-Benzoyl-1-benzoylthio-2-(methylthio)indolizine (**4i**): From **1i** and **2**, yellow needles (from ethanol), mp 113—116 °C. IR (KBr) cm^{-1}: 1622, 1678. ^{1}H-NMR (60 MHz) δ: 2.12 (3H, s), 6.93 (1H, dt, J=7.0, 7.0, 1.0 Hz), 7.0—8.2 (10H, m), 7.22 (1H, br q, J=9.0, 7.0 Hz), 7.52 (1H, d, J=9.0 Hz), 9.47 (1H, d, J=7.0 Hz). UV λ_{max} ($CHCl_3$) nm (log ε): 320 (3.89), 384 (4.08). *Anal.* Calcd for $C_{23}H_{17}NO_2S_2$: C, 68.46; H, 4.25; N, 3.47. Found: C, 68.48; H, 4.17; N, 3.53.

3-Benzoyl-1-benzoylthio-2-(ethylthio)indolizine (**4j**): From **1j** and **2**, yellow needles (from ethanol), mp 113—116 °C. IR (KBr) cm^{-1}: 1609, 1663. ^{1}H-NMR (60 MHz) δ: 0.90 (3H, t, J=7.0 Hz), 2.55 (2H, q, J=7.0 Hz), 6.90 (1H, dt, J=7.0, 7.0, 1.0 Hz), 7.0—8.3 (12H, m), 9.47 (1H, d, J=7.0 Hz). UV λ_{max} ($CHCl_3$) nm (log ε): 262 (shoulder), 284 (shoulder), 323 (3.86), 384 (4.08). *Anal.* Calcd for $C_{24}H_{19}NO_2S_2$: C, 69.04; H, 4.59; N, 3.35. Found: C, 69.29; H, 4.42; N, 3.27.

3-Benzoyl-1-benzoylthio-2-(benzylthio)indolizine (**4k**): From **1k** and **2**, yellow needles (from ethanol), mp 117—118 °C. IR (KBr) cm^{-1}: 1591, 1686. ^{1}H-NMR (60 MHz) δ: 3.69 (2H, s), 6.6—8.3 (16H, m), 6.93 (1H, dt, J=7.0, 7.0, 1.0 Hz), 7.22 (1H, br q, J=9.0, 7.0 Hz), 9.41 (1H, d, J=7.0 Hz). UV λ_{max} ($CHCl_3$) nm (log ε): 286 (shoulder), 385 (4.09). *Anal.* Calcd for $C_{29}H_{21}NO_2S_2$: C, 72.63; H, 4.41; N, 2.92. Found: C, 72.58; H, 4.66; N, 2.72.

3-Benzoyl-1-benzoylthio-2-(1-naphthylmethylthio)indolizine (**4l**): From **1l** and **2**, yellow needles (from ethanol), mp 163—165 °C. IR (KBr) cm^{-1}: 1607, 1669. ^{1}H-NMR (60 MHz) δ: 4.10 (2H, s, SC$\underline{H}_2$), 6.7—8.3 (19H, m), 7.23 (5H, s), 6.93 (1H, dt, J=7.0, 7.0, 1.0 Hz), 9.40 (1H, d, J=7.0 Hz). UV λ_{max} ($CHCl_3$) nm (log ε): 288 (shoulder), 385 (4.05). *Anal.* Calcd for

$C_{33}H_{23}NO_2S_2$: C, 74.83; H, 4.38; N, 2.64. Found: C, 74.89; H, 4.45; N, 2.52.

1-Benzoylthio-2-ethylthio-7-methylindolizine-3-carbonitrile (**4n**): From **1n** and **2**, colorless needles (from ethanol), mp 152—154 °C. IR (KBr) cm^{-1}: 1674, 2205. ^{1}H-NMR (60 MHz) δ: 1.28 (3H, t, J=7.0 Hz), 2.37 (3H, s, 7-Me), 3.05 (2H, q, J=7.0 Hz), 6.76 (1H, dd, J=7.0, 1.0 Hz), 7.0—8.2 (5H, m), 7.23 (1H, br s), 8.14 (1H, d, J=7.0 Hz). UV λ_{max} ($CHCl_3$) nm (log ε): 259 (4.52), 330 (4.01). *Anal.* Calcd for $C_{19}H_{16}N_2OS_2$: C, 64.75; H, 4.58; N, 7.95. Found: C, 64.48; H, 4.73; N, 7.87.

1-Benzoylthio-2-benzylthio-7-methylindolizine-3-carbonitrile (**4o**): From **1o** and **2**, colorless needles (from ethanol), mp 131—132 °C. IR (KBr) cm^{-1}: 1676, 2213. ^{1}H-NMR (60 MHz) δ: 2.37 (3H, s), 4.15 (2H, s), 6.75 (1H, dd, J=7.0, 1.0 Hz), 7.0—8.2 (6H, m), 7.15 (5H, s), 8.12 (1H, d, J=7.0 Hz). UV λ_{max} ($CHCl_3$) nm (log ε): 262 (shoulder), 330 (4.05). *Anal.* Calcd for $C_{24}H_{18}N_2OS_2$: C, 69.54; H, 4.38; N, 6.76. Found: C, 69.64; H, 4.43; N, 6.59.

1-Benzoylthio-7-methyl-2-(1-naphthylmethylthio)indolizine-3-carbonitrile (**4p**): From **1p** and **2**, colorless needles (from ethanol), mp 198—201 °C. IR (KBr) cm^{-1}: 1674, 2206. ^{1}H-NMR (60 MHz) δ: 2.37 (3H, s), 4.61 (2H, s), 6.76 (1H, dd, J=7.0, 1.0 Hz), 7.1—8.3 (13H, m), 8.14 (1H, d, J=7.0 Hz). UV λ_{max} ($CHCl_3$) nm (log ε): 260 (shoulder), 333 (3.98). *Anal.* Calcd for $C_{28}H_{20}N_2OS_2$: C, 72.39; H, 4.34; N, 6.03. Found: C, 72.65; H, 4.19; N, 5.91.

Ethyl 1-Benzoylthio-2-ethylthio-7-methylindolizine-3-carboxylate (**4r**): From **1r** and **2**, colorless needles (from ethanol), mp 115—116 °C. IR (KBr) cm^{-1}: 1672. ^{1}H-NMR (60 MHz) δ: 1.18 (3H, t, J=7.0 Hz), 1.46 (3H, t, J=7.0 Hz), 2.36 (3H, s), 2.97 (2H, q, J=7.0 Hz), 4.48 (2H, q, J=7.0 Hz), 6.74 (1H, dd, J=7.0, 1.0 Hz), 7.27 (1H, br s), 7.3—8.3 (5H, m), 9.45 (1H, d, J=7.0 Hz). UV λ_{max} ($CHCl_3$) nm (log ε): 264 (4.47), 342 (4.10). *Anal.* Calcd for $C_{21}H_{21}NO_3S_2$: C, 63.13; H, 5.30; N, 3.51. Found: C, 63.46; H, 5.15; N, 3.33.

Ethyl 1-Benzoylthio-2-benzylthio-7-methylindolizine-3-carboxylate (**4s**): From **1s** and **2**, colorless needles (from ethanol), mp 136—137 °C. IR (KBr) cm^{-1}: 1671. ^{1}H-NMR (60 MHz) δ: 1.41 (3H, t, J=7.0 Hz), 2.34 (3H, s), 4.37 (2H, s), 4.55 (2H, q, J=7.0 Hz), 6.74 (1H, dd, J=7.0, 1.0 Hz), 7.30 (5H, s), 7.0—8.3 (5H, m), 9.44 (1H, d, J=7.0 Hz). UV λ_{max} ($CHCl_3$) nm (log ε): 262 (shoulder), 344 (4.10). *Anal.* Calcd for $C_{26}H_{23}NO_3S_2$: C, 67.65; H, 5.02; N, 3.03. Found: C, 67.63; H, 5.14; N, 2.94.

Ethyl 1-Benzoylthio-2-(1-naphthylmethylthio)-7-methylindolizine-3-carboxylate (**4t**): From **1t** and **2**, colorless needles (from ethanol), mp 183—184 °C. IR (KBr) cm^{-1}: 1680. ^{1}H-NMR (60 MHz) δ: 1.35 (3H, t, J=7.0 Hz), 2.36 (3H, s), 4.30 (2H, q, J=7.0 Hz), 4.57 (2H, s), 6.74 (1H, dd, J=7.0, 1.0 Hz), 7.0—8.3 (13H, m), 9.46 (1H, d, J=7.0 Hz). UV λ_{max} ($CHCl_3$) nm (log ε): 264 (shoulder), 344 (4.11). *Anal.* Calcd for $C_{30}H_{25}NO_3S_2$: C, 70.42; H, 4.93; N, 2.74. Found: C, 70.71; H, 4.94; N, 2.66.

3-Benzoyl-1-benzoylthio-2-methylthio-7-methylindolizine (**4u**): From **1u** and **2**, yellow needles (from ethanol), mp 150—155 °C. IR (KBr) cm^{-1}: 1604, 1678. ^{1}H-NMR (400 MHz) δ: 2.11 (3H, s), 2.56 (3H, s), 2.39 (3H, s), 6.78 (1H, dd, J=7.0, 1.0 Hz), 7.4—8.2 (10H, m), 7.28 (1H, br s), 9.42 (1H, d, J=7.0 Hz). UV λ_{max} ($CHCl_3$) nm (log ε): 319 (3.86), 388 (4.13). *Anal.* Calcd for $C_{24}H_{19}NO_2S_2$: C, 69.04; H, 4.59; N, 3.35. Found: C, 69.26; H, 4.51; N, 3.20.

3-Benzoyl-1-benzoylthio-2-ethylthio-7-methylindolizine (**4v**): From **1v** and **2**, yellow needles (from ethanol), mp 154—156 °C. IR (KBr) cm^{-1}: 1599, 1667. ^{1}H-NMR (60 MHz) δ: 0.89 (3H, t, J=7.0 Hz), 2.38 (3H, s), 2.53 (2H, q, J=7.0 Hz), 6.78 (1H, dd, J=7.0, 1.0 Hz), 7.0—8.3 (11H, m), 9.42 (1H, d, J=7.0 Hz). UV λ_{max} ($CHCl_3$) nm (log ε): 262 (shoulder), 322 (3.87), 388 (4.17). *Anal.* Calcd for $C_{25}H_{21}NO_2S_2$: C, 69.58; H, 4.90; N, 3.25. Found: C, 69.63; H, 4.95; N, 3.15.

3-Benzoyl-1-benzoylthio-2-benzylthio-7-methylindolizine (**4w**): From **1w** and **2**, yellow needles (from ethanol), mp 137—138 °C. IR (KBr) cm^{-1}: 1604, 1678. ^{1}H-NMR (60 MHz) δ: 2.37 (3H, s), 3.67 (2H, s), 6.75 (1H, dd, J=7.0, 1.0 Hz), 6.7—8.3 (11H, m), 9.39 (1H, d, J=7.0 Hz). UV λ_{max} ($CHCl_3$) nm (log ε): 266 (shoulder), 388 (4.16). *Anal.* Calcd for $C_{30}H_{23}NO_2S_2$: C, 72.99; H, 4.70; N, 2.84. Found: C, 73.03; H, 4.82; N, 2.68.

3-Benzoyl-1-benzoylthio-2-(1-naphthylmethylthio)-7-methylindolizine (**4x**): From **1x** and **2**, yellow needles (from ethanol), mp 139—141 °C. IR (KBr) cm^{-1}: 1597, 1672. ^{1}H-NMR (60 MHz) δ: 2.39 (3H, s), 4.09 (2H, s), 6.78 (1H, dd, J=7.0, 1.0 Hz), 6.8—8.3 (18H, m), 9.35 (1H, d, J=7.0 Hz). UV λ_{max} ($CHCl_3$) nm (log ε): 284 (shoulder), 389 (4.16). *Anal.* Calcd for $C_{34}H_{25}NO_2S_2$: C, 75.11; H, 4.63; N, 2.58. Found: C, 75.27; H, 4.60; N, 2.46.

Preparation of Bis(indolizin-1-yl) Disulfide Derivatives. General Method An ethanolic solution (30 ml) of 1-(benzoylthio)indolizine (**4**, 0.5 mmol) and piperidine (0.200 g, 2.4 mmol) was heated under reflux conditions in a water bath for 12 h—1 d. The resulting reaction solution was then cooled in a refrigerator for 12 h and the precipitates which separated were collected by suction. Recrystallization from ethanol afforded the corresponding bis(indolizin-1-yl) disulfides as pale yellow needles or prisms. The chemical shifts for the protons and the methyl protons on the pyridine ring in the ^{1}H-NMR spectra were listed in the Table 1. The results and other data of **5a**—**x** are as follows:

Bis[3-cyano-2-(methylthio)indolizin-1-yl] Disulfide (**5a**)[9]: ^{1}H-NMR (400 MHz) δ: 2.63 (3H, s, SMe). UV λ_{max} ($CHCl_3$) nm (log ε): 276 (4.59), 334 (4.26), 374 (shoulder).

Bis[3-cyano-2-(ethylthio)indolizin-1-yl] Disulfide (**5b**): From **4b**, pale yellow needles (from ethanol), mp 118—120 °C. IR (KBr) cm^{-1}: 2201. ^{1}H-NMR (400 MHz) δ: 1.28 (3H, t, J=7.6 Hz), 3.10 (2H, q, J=7.6 Hz). UV λ_{max} ($CHCl_3$) nm (log ε): 279 (4.55), 335 (4.15), 374 (shoulder). *Anal.* Calcd for $C_{22}H_8N_4S_4$: C, 56.62; H, 3.89; N, 12.01. Found: C, 56.94; H, 3.84; N, 11.73.

Bis(2-benzylthio-3-cyanoindolizin-1-yl) Disulfide (**5c**): From **4c**, pale yellow needles (from ethanol), mp 176—177 °C. IR (KBr) cm^{-1}: 2199. ^{1}H-NMR (400 MHz) δ: 4.26 (2H, s), 7.17—7.32 (5H, m). UV λ_{max} ($CHCl_3$) nm (log ε): 280 (4.52), 335 (4.18). *Anal.* Calcd for $C_{32}H_{22}N_4S_4$: C, 65.75; H, 3.68; N, 9.29. Found: C, 65.72; H, 3.66; N, 9.34.

Bis[3-cyano-2-(1-naphthylmethylthio)indolizin-1-yl] Disulfide (**5d**): From **4d**, pale yellow needles (from ethanol), mp 185—186 °C. IR (KBr) cm^{-1}: 2199. ^{1}H-NMR (400 MHz) δ: 4.64 (2H, s), 7.24—7.34 (2H, m), 7.46 (1H, ddd, J=7.0, 7.0, 1.0 Hz), 7.53 (1H, ddd, J=7.0, 7.0, 1.2 Hz), 7.73 (1H, d, J=7.8 Hz), 7.81 (1H, d, J=8.1 Hz), 8.14 (1H, d, J=8.3 Hz). UV λ_{max} ($CHCl_3$) nm (log ε): 284 (4.61), 338 (shoulder), 378 (shoulder). *Anal.* Calcd for $C_{40}H_{26}N_4S_4$: C, 69.54; H, 3.79; N, 8.11. Found: C, 69.48; H, 3.79; N, 8.17.

Bis[3-ethoxycarbonyl-2-(methylthio)indolizin-1-yl] Disulfide (**5e**)[9]: ^{1}H-NMR (400 MHz) δ: 1.47 (3H, t, J=7.2 Hz), 2.67 (3H, s), 4.45 (2H, q, J=7.1 Hz). UV λ_{max} ($CHCl_3$) nm (log ε): 284 (4.53), 354 (4.26).

Bis[3-ethoxycarbonyl-2-(ethylthio)indolizin-1-yl] Disulfide (**5f**): From **4f**, pale yellow needles (from ethanol), mp 118—120 °C. IR (KBr) cm^{-1}: 1687. ^{1}H-NMR (400 MHz) δ: 1.21 (3H, t, J=7.4 Hz), 1.47 (3H, t, J=7.0 Hz), 3.07 (2H, q, J=7.5 Hz), 4.46 (2H, q, J=7.1 Hz). UV λ_{max} ($CHCl_3$) nm (log ε): 284 (4.44), 353 (4.27). *Anal.* Calcd for $C_{26}H_{28}N_2O_4S_4$: C, 55.69; H, 5.03; N, 5.00. Found: C, 55.74; H, 4.76; N, 5.22.

Bis[2-benzylthio-3-(ethoxycarbonyl)indolizin-1-yl] Disulfide (**5g**) From **4g**, pale yellow needles (from ethanol), mp 126 °C. IR (KBr) cm^{-1}: 1686. ^{1}H-NMR (400 MHz) δ: 1.44 (3H, t, J=7.2 Hz), 4.23 (2H, s), 4.41 (2H, q, J=7.2 Hz), 7.13—7.26 (5H, m). UV λ_{max} ($CHCl_3$) nm (log ε): 284 (4.44), 351 (4.26). *Anal.* Calcd for $C_{36}H_{32}N_2O_4S_4$: C, 63.13; H, 4.71; N, 4.09. Found: C, 63.17; H, 4.74; N, 4.03.

Bis[3-ethoxycarbonyl-2-(1-naphthylmethylthio)indolizin-1-yl] Disulfide (**5h**): From **4h**, yellow needles (from ethanol), mp 111—114 °C. IR (KBr) cm^{-1}: 1691. ^{1}H-NMR (400 MHz) δ: 1.28 (3H, t, J=7.2 Hz), 4.24 (2H, q, J=7.2 Hz), 4.63 (2H, s), 7.18—7.26 (2H, m), 7.40—7.55 (2H, m), 7.68 (1H, d, J=7.6 Hz), 7.79 (1H, d, J=8.6 Hz), 8.21 (1H, d, J=8.3 Hz). UV λ_{max} ($CHCl_3$) nm (log ε): 290 (4.58), 349 (4.25). *Anal.* Calcd for $C_{40}H_{26}N_2O_4S_4$: C, 67.32; H, 4.62; N, 3.57. Found: C, 67.38; H, 4.65; N, 3.48.

Bis[3-benzoyl-2-(methylthio)indolizin-1-yl] Disulfide (**5i**): From **4i**, yellow needles (from ethanol), mp 73—75 °C. IR (KBr) cm^{-1}: 1608. ^{1}H-NMR (400 MHz) δ: 2.20 (3H, s), 7.43 (2H, t, J=7.5, 7.5 Hz), 7.56 (1H, br t, J=7.5, 7.5 Hz), 7.66 (2H, br d, J=7.5 Hz). UV λ_{max} ($CHCl_3$) nm (log ε): 293 (shoulder), 394 (4.35). *Anal.* Calcd for $C_{32}H_{24}N_2O_2S_4$: C, 64.40; H, 4.05; N, 4.69. Found: C, 64.58; H, 4.09; N, 4.45.

Bis[3-benzoyl-2-(ethylthio)indolizin-1-yl] Disulfide (**5j**): From **4j**, yellow needles (from ethanol), mp 118—120 °C. IR (KBr) cm^{-1}: 1616. ^{1}H-NMR (400 MHz) δ: 0.90 (3H, t, J=7.4 Hz), 2.66 (2H, q, J=7.3 Hz), 7.41 (2H, t, J=7.6, 7.6 Hz), 7.54 (1H, br t, J=7.4, 7.4 Hz), 7.62 (2H, br d, J=7.6 Hz). UV λ_{max} ($CHCl_3$) nm (log ε): 293 (shoulder), 394 (4.35). *Anal.* Calcd for $C_{34}H_{28}N_2O_2S_4$: C, 65.36; H, 4.52; N, 4.48. Found: C, 65.46; H, 4.56; N, 4.34.

Bis[3-benzoyl-2-(benzylthio)indolizin-1-yl] Disulfide (**5k**): From **4k**, yellow needles (from ethanol), mp 72—75 °C. IR (KBr) cm^{-1}: 1606. ^{1}H-NMR (400 MHz) δ: 3.82 (2H, s), 6.84 (2H, br d, J=7.6 Hz), 7.06—7.15 (3H, m), 7.34 (2H, t, J=7.6 Hz), 7.46—7.56 (3H, m). UV λ_{max} ($CHCl_3$) nm (log ε): 293 (shoulder), 394 (4.34). *Anal.* Calcd for $C_{44}H_{32}N_2O_2S_4$: C, 70.56; H, 4.31; N, 3.74. Found: C, 70.82; H, 4.27; N, 3.52.

Bis[3-benzoyl-2-(1-naphthylmethylthio)indolizin-1-yl] Disulfide (**5l**): From **4l**, yellow needles (from ethanol), mp 163—165 °C. IR (KBr) cm^{-1}: 1620. ^{1}H-NMR (400 MHz) δ: 4.21 (2H, s), 6.84 (1H, d, J=6.4 Hz), 7.07—7.17 (3H, m), 7.23—7.29 (3H, m), 7.35—7.44 (2H, m), 7.63 (1H, d, J=8.4 Hz), 7.74 (1H, d, J=8.4 Hz). UV λ_{max} ($CHCl_3$) nm (log ε): 291 (4.55),

393 (4.36). *Anal.* Calcd for $C_{52}H_{36}N_2O_2S_4$: C, 73.56; H, 4.27; N, 3.30. Found: C, 73.37; H, 4.11; N, 3.07.

Bis[3-cyano-7-methyl-2-(methylthio)indolizin-1-yl] Disulfide (**5m**)[9]: ^{1}H-NMR (400 MHz) δ: 2.65 (3H, s). UV λ_{max} ($CHCl_3$) nm (log ε): 279 (4.53), 332 (4.13), 376 (shoulder).

Bis[3-cyano-2-ethylthio-7-methylindolizin-1-yl] Disulfide (**5n**): From **4n**, pale yellow prisms (from ethanol), mp 234—246 °C. IR (KBr) cm^{-1}: 2207. ^{1}H-NMR (400 MHz) δ: 1.30 (3H, t, J=7.4 Hz), 3.11 (2H, q, J=7.3 Hz). UV λ_{max} ($CHCl_3$) nm (log ε): 276 (4.69), 333 (4.35), 376 (shoulder). *Anal.* Calcd for $C_{24}H_{22}N_4S_4$: C, 58.27; H, 4.48; N, 11.33. Found: C, 58.44; H, 4.46; N, 11.17.

Bis(2-benzylthio-3-cyano-7-methylindolizin-1-yl) Disulfide (**5o**): From **4o**, pale yellow needles (from ethanol), mp 172—173 °C. IR (KBr) cm^{-1}: 2201. ^{1}H-NMR (400 MHz) δ: 4.30 (2H, s), 7.17—7.30 (3H, m), 7.35 (2H, d, J=7.6 Hz). UV λ_{max} ($CHCl_3$) nm (log ε): 279 (4.51), 331 (4.27). *Anal.* Calcd for $C_{34}H_{26}N_4S_4$: C, 65.99; H, 4.23; N, 9.05. Found: C, 65.99; H, 4.15; N, 9.13.

Bis[3-cyano-7-methyl-2-(1-naphthylmethylthio)indolizin-1-yl] Disulfide (**5p**): From **4p**, pale yellow needles (from ethanol), mp 146—149 °C. IR (KBr) cm^{-1}: 2199. ^{1}H-NMR (400 MHz) δ: 4.67 (2H, s), 7.29 (1H, q, J=8.1, 6.8 Hz), 7.35 (1H, d, J=6.3 Hz), 7.46 (1H, br t, J=7.4 Hz), 7.53 (1H, br t, J=7.6 Hz), 7.73 (1H, d, J=8.0 Hz), 7.81 (1H, d, J=7.6 Hz), 8.18 (1H, d, J=8.3 Hz). UV λ_{max} ($CHCl_3$) nm (log ε): 283 (4.60), 338 (shoulder), 383 (shoulder). *Anal.* Calcd for $C_{42}H_{30}N_4S_4$: C, 70.16; H, 4.21; N, 7.79. Found: C, 70.15; H, 4.33; N, 7.68.

Bis[3-ethoxycarbonyl-7-methyl-2-(methylthio)indolizin-1-yl] Disulfide (**5q**)[9]: ^{1}H-NMR (400 MHz) δ: 1.47 (3H, t, J=7.2 Hz), 2.59 (3H, s), 4.46 (2H, q, J=7.1 Hz). UV λ_{max} ($CHCl_3$) nm (log ε): 283 (4.52), 344 (4.30).

Bis[3-ethoxycarbonyl-2-ethylthio-7-methylindolizin-1-yl] Disulfide (**5r**): From **4r**, pale yellow needles (from ethanol), mp 257—259 °C. IR (KBr) cm^{-1}: 1674. ^{1}H-NMR (400 MHz) δ: 1.26 (3H, t, J=7.4 Hz), 1.47 (3H, t, J=7.2 Hz), 3.15 (2H, q, J=7.3 Hz), 4.44 (2H, q, J=7.2 Hz). UV λ_{max} ($CHCl_3$) nm (log ε): 282 (4.47), 347 (4.30). *Anal.* Calcd for $C_{28}H_{32}N_2O_4S_4$: C, 57.12; H, 5.48; N, 4.76. Found: C, 57.16; H, 5.58; N, 4.61.

Bis[2-benzylthio-3-ethoxycarbonyl-7-methylindolizin-1-yl] Disulfide (**5s**): From **4s**, pale yellow needles (from ethanol), mp 96—98 °C. IR (KBr) cm^{-1}: 1688. ^{1}H-NMR (400 MHz) δ: 1.41 (3H, t, J=7.1 Hz), 4.31 (2H, s), 4.40 (2H, q, J=7.1 Hz), 7.03—7.30 (5H, m). UV λ_{max} ($CHCl_3$) nm (log ε): 288 (shoulder), 345 (4.29). *Anal.* Calcd for $C_{38}H_{36}N_2O_4S_4$: C, 64.02; H, 5.09; N, 3.93. Found: C, 64.08; H, 5.09; N, 3.87.

Bis[3-ethoxycarbonyl-7-methyl-2-(1-naphthylmethylthio)indolizin-1-yl] Disulfide (**5t**): From **4t**, pale yellow needles (from ethanol), mp 139—140 °C. IR (KBr) cm^{-1}: 1674. ^{1}H-NMR (400 MHz) δ: 1.28 (3H, t, J=7.1 Hz), 4.22 (2H, q, J=7.2 Hz), 4.72 (2H, s), 7.22—7.28 (2H, m), 7.44 (1H, ddd, J=8.0, 7.1, 1.2 Hz), 7.50 (1H, ddd, J=8.3, 6.8, 1.5 Hz), 7.69 (1H, dd, J=6.6, 2.4 Hz), 7.80 (1H, d, J=7.8 Hz), 8.28 (1H, d, J=8.3 Hz). UV λ_{max} ($CHCl_3$) nm (log ε): 290 (4.59), 352 (shoulder). *Anal.* Calcd for $C_{46}H_{40}N_2O_4S_4$: C, 67.95; H, 4.96; N, 3.45. Found: C, 68.13; H, 4.93; N, 3.30.

Bis[3-benzoyl-7-methyl-2-(methylthio)indolizin-1-yl] Disulfide (**5u**): From **4u**, pale yellow needles (from ethanol), mp 158—160 °C. IR (KBr) cm^{-1}: 1602. ^{1}H-NMR (400 MHz) δ: 2.23 (3H, s), 7.43 (2H, t, J=7.7 Hz), 7.55 (1H, br t, J=7.4 Hz), 7.65 (2H, br d, J=7.7 Hz). UV λ_{max} ($CHCl_3$) nm (log ε): 264 (shoulder), 293 (shoulder), 400 (4.38). *Anal.* Calcd for $C_{34}H_{28}N_2O_2S_4$: C, 65.36; H, 4.52; N, 4.48. Found: C, 65.46; H, 5.56; N, 4.34.

Bis[3-benzoyl-2-ethylthio-7-methylindolizin-1-yl] Disulfide (**5v**): From **4v**, pale yellow needles (from ethanol), mp 148—150 °C. IR (KBr) cm^{-1}: 1596. ^{1}H-NMR (400 MHz) δ: 0.94 (3H, t, J=7.4 Hz), 2.71 (2H, q, J=7.3 Hz), 7.42 (2H, t, J=7.7 Hz), 7.54 (1H, br t, J=7.4 Hz), 7.62 (2H, br d, J=7.7 Hz). UV λ_{max} ($CHCl_3$) nm (log ε): 291 (shoulder), 400 (4.41). *Anal.* Calcd for $C_{36}H_{32}N_2O_2S_4$: C, 66.23; H, 4.94; N, 4.29. Found: C, 66.44; H, 5.00; N, 4.02.

Bis[3-benzoyl-2-benzylthio-7-methylindolizin-1-yl] Disulfide (**5w**): From **4w**, pale yellow needles (from ethanol), mp 73—75 °C. IR (KBr) cm^{-1}: 1602. ^{1}H-NMR (400 MHz) δ: 3.89 (2H, s), 6.91 (2H, m), 7.07—7.15 (3H, m), 7.37 (2H, t, J=7.7 Hz), 7.47—7.56 (3H, m). UV λ_{max} ($CHCl_3$) nm (log ε): 290 (shoulder), 399 (4.38). *Anal.* Calcd for $C_{46}H_{36}N_2O_2S_4$: C, 71.10; H, 4.67; N, 3.61. Found: C, 71.30; H, 4.62; N, 3.46.

Bis[3-benzoyl-7-methyl-2-(1-naphthylmethylthio)indolizin-1-yl] Disulfide (**5x**): From **4x**, pale yellow needles (from ethanol), mp 145—150 °C. IR (KBr) cm^{-1}: 1608. ^{1}H-NMR (400 MHz) δ: 4.28 (2H, s), 6.90 (1H, d, J=6.1 Hz), 7.10—7.20 (3H, m), 7.24—7.34 (3H, m), 7.36—7.45 (2H, m), 7.65 (1H, d, J=8.0 Hz), 7.69 (1H, d, J=8.6 Hz), 7.76 (1H, d, J=8.0 Hz). UV λ_{max} ($CHCl_3$) nm (log ε): 289 (4.54), 399 (4.38). *Anal.* Calcd for $C_{54}H_{40}N_2O_2S_4$+1/2H_2O: C, 73.19; H, 4.66; N, 3.16. Found: C, 73.37; H, 4.88; N, 2.87.

Crystallography of Bis[3-cyano-2-(methylthio)indolizin-1-yl] Disulfide (5a) A pale yellow prismatic single crystal (0.48×0.62×1.00 mm) grown from ethanol was used for the unit-cell determinations and data collection by a Rigaku AFC5S four-circle diffractometer with graphite-monochromated Mo$K\alpha$ radiation (λ=0.71069 Å). The crystal data of these compounds are as follows: **5a**: $C_{20}H_{14}N_4S_4$; M=438.60; monoclinic, space group $C2/c$ (#15), Z=4 with a=12.594(2) Å, b=12.889(2) Å, c=12.314(3) Å, β=100.00(2)°; V=1968.5(6) Å^3 and $D_{calc.}$=1.480 g/cm^3. All calculations were performed using the CrystalStructure crystallographic software package.[18] The structure was solved by a direct method (SIR92).[19] 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 0.048 and 0.045 respectively for 1643 (I>2.00σ(I)) observed reflections.

Crystallography of Bis[3-benzoyl-2-(benzylthio)indolizin-1-yl] Disulfide (5k) A yellow prismatic single crystal (0.28×0.28×0.72 mm) grown from ethanol was used for the unit-cell determinations and data collection by a Rigaku AFC5S four-circle diffractometer with graphite-monochromated Mo$K\alpha$ radiation (λ=0.71069 Å). Crystal data of these compounds are as follows: **5k**: $C_{44}H_{32}N_2O_2S_4$; M=788.99; monoclinic, space group $P2_1/n$ (#14), Z=4 with a=9.741(3) Å, b=18.209(3) Å, c=21.419(3) Å, β=99.51(2)°; V=3747(1) Å^3 and $D_{calc.}$=1.328 g/cm^3. All calculations were performed using the CrystalStructure crystallographic software package.[18] The structure was solved by a direct method (SIR92).[19] 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 0.063 and 0.047 respectively for 2695 (I>2.00σ(I)) observed reflections.

Crystallography of Bis[3-cyano-2-ethylthio-7-methylindolizin-1-yl] Disulfide (5n) A yellow prismatic single crystal (0.84×0.58×0.32 mm) grown from ethanol was used for the unit-cell determinations and data collection by a Rigaku AFC5S four-circle diffractometer with graphite-monochromated Mo$K\alpha$ radiation (λ=0.71069 Å). Crystal data of these compounds are as follows: **5n**: $C_{24}H_{22}N_4S_4$; M=494.70; monoclinic, space group $C2/c$ (#15), Z=4 with a=18.289(3) Å, b=9.359(3) Å, c=14.355(3) Å, β=97.42(2)°; V=2436.5(10) Å^3 and $D_{calc.}$=1.348 g/cm^3. All calculations were performed using the CrystalStructure crystallographic software package.[18] The structure was solved by a direct method (SIR).[19] 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 0.076 and 0.061 respectively for 1612 (I>2.00σ(I)) observed reflections.

Crystallography of Bis[3-ethoxycarbonyl-7-methyl-2-(methylthio)indolizin-1-yl] Disulfide (5q) A pale yellow prismatic single crystal (0.20×0.32×1.00 mm) grown from ethanol was used for the unit-cell determinations and data collection by a Rigaku AFC5S four-circle diffractometer with graphite-monochromated Mo$K\alpha$ radiation (λ=0.71069 Å). The crystal data of these compounds are as follows: **5q**: $C_{26}H_{28}N_2O_4S_4$; M=560.76; orthorhombic, space group $P2_1/a$ (#14), Z=4 with a=13.222(4) Å, b=8.895(5) Å, c=23.768(5) Å, β=95.91(2)°; V=2780(2) Å^3 and $D_{calc.}$=1.340 g/cm^3. All calculations were performed using the CrystalStructure crystallographic software package.[18] The structure was solved by a direct method (SIR).[19] 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 0.070 and 0.050 respectively for 1591 (I>2.00σ(I)) observed reflections.

References and Notes

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