  Bull. Chem. Soc. Jpn., 64, 3289—3295 (1991)

Preparation of New Nitrogen-Bridged Heterocycles. 27.[1] First Syntheses of 1,3-Thiazino[6,5-*b*]indolizine Derivatives

Akikazu KAKEHI,* Suketaka ITO, Tosio SAKURAI,† Kunio URUSHIDO,†
Hidetoshi ISAWA, and Manabu ENOMOTO
Department of Chemistry and Material Engineering, Faculty of Engineering,
Shinshu University, Wakasato, Nagano 380
† Department of Chemistry, Faculty of Education, Shinshu University, Nishinagano, Nagano 380
(Received April 24, 1991)

Potassium 2-indolizinethiolates, generated in situ from the treatment of dialkyl 2-[(2-ethoxycarbonylethyl)thio]indolizine-1,3-dicarboxylates with potassium *t*-butoxide in *N*,*N*-dimethylformamide, reacted smoothly with various isothiocyanates and isocyanates with the elimination of alkoxide ions to give new heterocyclic compounds, alkyl 4(3*H*)-oxo-2-thioxo- and 2,4(3*H*)-dioxo-2*H*-1,3-thiazino[6,5-*b*]indolizine-10-carboxylates, in moderate to good yields. The structures of these 1,3-thiazino[6,5-*b*]indolizine derivatives were determined mainly by elemental analyses and spectral inspections, and the structural assignment was finally confirmed by the single crystal X-ray analyses of two compounds.

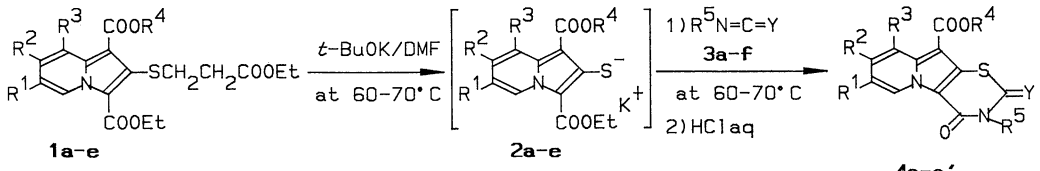
Recently, we reported the simple and convenient syntheses of various indolizine derivatives possessing an active methylene group at the 2-position and electron-withdrawing groups at the 1- and 3-positions and their smooth intramolecular cyclizations to the corresponding thieno[3,2-*a*]- and thieno[2,3-*b*]indolizine derivatives in the presence of a base.[2] In particular, potassium 2-indolizinethiolate derivatives[2c] generated in situ by the treatment of the corresponding 2-[(2-ethoxycarbonylethyl)thio]- or 2-[(2-cyanoethyl)thio]indolizines with potassium *t*-butoxide were key intermediates for the syntheses of these polyfunctionalized indolizines and thiophene-fused indolizines, and their very high reactivities toward various alkylating agents were shown.[2d] The ready availability, high nucleophilicity, and wide structural versatility of these potassium 2-indolizinethiolate derivatives promped us to investigate further their reactivity toward some heterocumulenes which are well known as reactive electrophilic species.[3] In this paper, we wish to report the reactions of 2-indolizinethiolate derivatives with some isothiocyanates and isocyanates, affording new heterocycles, 2-thioxo-2*H*-1,3-thiazino[6,5-*b*]indolizin-4(3*H*)-one and 2*H*-1,3-thiazino[6,5-*b*]indolizine-2,4(3*H*)-dione derivatives.

Results and Discussion

Reactions of Potassium 2-Indolizinethiolates with Isothiocyanates and Isocyanates. The treatment of dialkyl 2-[(2-ethoxycarbonylethyl)thio]indolizine-1,3-dicarboxylates (**1a**—**e**)[2c] with potassium *t*-butoxide in *N*,*N*-dimethylformamide (DMF) at 60—70 °C, the removal of the ethyl acrylate generated, and the addition of methyl isothiocyanate (**3a**) to the resulting potassium 2-indolizinethiolate derivatives (**2a**—**e**) afforded ethyl or *t*-butyl 3-methyl-4(3*H*)-oxo-2-thioxo-2*H*-1,3-thiazino-[6,5-*b*]indolizine-10-carboxylates (**4a**—**e**) in 41—97% yields. Similar reactions of indolizine derivatives **1a**—**d** with ethyl isothiocyanate (**3b**), phenyl isothiocyanate (**3c**), and allyl isothiocyanate (**3d**) gave the corresponding 4(3*H*)-oxo-2-thioxo-2*H*-1,3-thiazino[6,5-*b*]indolizine derivatives **4f**—**q** in moderate to good yields. The reactions of **2a**—**e** with ethyl isocyanate (**3e**), and propyl isocyanate (**3f**) also provided the expected products, alkyl 3-ethyl- or 3-propyl-2,4(3*H*)-dioxo-2*H*-1,3-thiazino[6,5-*b*]indolizine-10-carboxylates **4r**—**v**, **x**—**a′**, except compound **4w**. Interestingly, no product such as 4(3*H*)-oxo-2-thioxo- or 2,4(3*H*)-dioxo-2*H*-1,3-thiazino[5,6-*a*]indolizine **5** was formed even in the reactions of heterocumulenes **3a**—**f** with dialkyl 6,8-dimethylindolizine-1,3-dicarboxylates (**1d**, **e**), in which the reactivity of the 1-alkoxycarbonyl group is fairly enhanced owing to the steric hindrance of the 8-methyl group at the peri-position (Scheme 1).[2b,d] On the other hand, the reactions of indolizines **1f**, **g** having a cyano or an acetyl group at the 1- or 3-position with reagents **3a**—**f** did not afford any products such as **7** and **8** under the reaction conditions employed here, and only the deprotected 2-indolizinethiols **6a**, **b** were obtained in 64 and 71% yields, respectively. The reactions of 2-indolizinethiols **6a**, **b**, obtained in this reaction, with **3a**—**f** were also unsuccessful. (Scheme 2)

Furthermore, any condensation products were not given in the reactions of **1a**, **b** with phenylketene and dichloroketene generated in situ by the addition of phenylacetyl chloride or dichloroacetyl chloride to the reaction mixtures.

The structural assignments for the products **4a**—**v**,**x**—**a′** were accomplised mainly by their elemental and spectral analyses and mechanistic considerations. For example, their elemental analyses coincided well with the compositions for our proposed structures and their IR spectra (see Table 5) distinctly showed the carbonyl absorption bands due to an aromatic ester and an amide group in the ranges of 1659—1721 and 1637—1664 cm^{-1}, respectively. The ^1H NMR spectra (Table 1) of **4a**—**v**, **x**—**a′** showed the presence of an alkyl, allyl, or phenyl group derived from isothiocyanates **3a**—**d** or isocyanates **3e**, **f** employed here, and the absence of an ethoxyl group of two ester alkoxyl groups which were present at the 1-



1	R^1	R^2	R^3	R^4
a	H	H	H	Et
b	H	Me	H	Et
c	H	Et	H	Et
d	Me	H	Me	Et
e	Me	H	Me	*t*-Bu

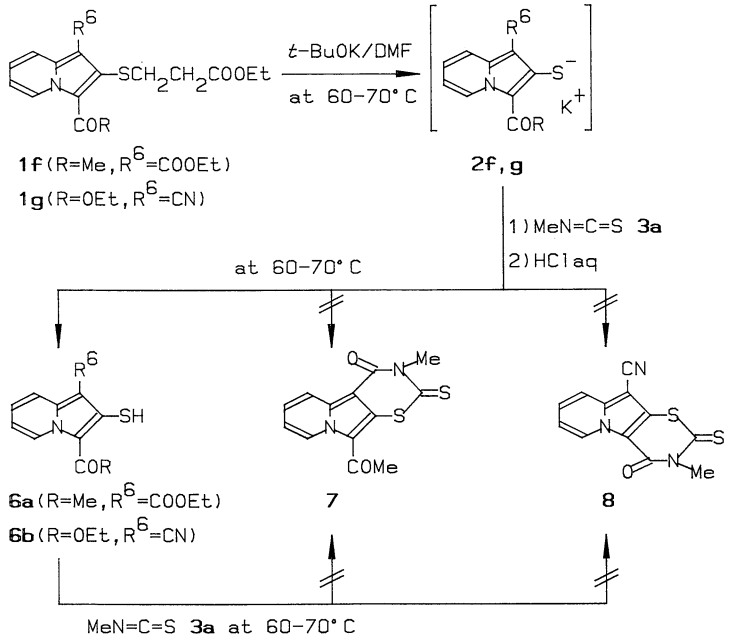
3	R^5	Y
a	Me	S
b	Et	S
c	Ph	S
d	Allyl	S
e	Et	O
f	Pr	O

4	R^1	R^2	R^3	R^4	R^5	Y
a	H	H	H	Et	Me	S
b	H	Me	H	Et	Me	S
c	H	Et	H	Et	Me	S
d	Me	H	Me	Et	Me	S
e	Me	H	Me	*t*-Bu	Me	S
f	H	H	H	Et	Et	S
g	H	Me	H	Et	Et	S
h	H	Et	H	Et	Et	S
i	Me	H	Me	Et	Et	S

4	R^1	R^2	R^3	R^4	R^5	Y
j	H	H	H	Et	Ph	S
k	H	Me	H	Et	Ph	S
l	H	Et	H	Et	Ph	S
m	Me	H	Me	Et	Ph	S
n	H	H	H	Et	Allyl	S
o	H	Me	H	Et	Allyl	S
p	H	Et	H	Et	Allyl	S
q	Me	H	Me	Et	Allyl	S
r	H	H	H	Et	Et	O

4	R^1	R^2	R^3	R^4	R^5	Y
s	H	Me	H	Et	Et	O
t	H	Et	H	Et	Et	O
u	Me	H	Me	Et	Et	O
v	Me	H	Me	*t*-Bu	Et	O
(w)	H	H	H	Et	Pr	O
x	H	Me	H	Et	Pr	O
y	H	Et	H	Et	Pr	O
z	Me	H	Me	Et	Pr	O
a'	Me	H	Me	*t*-Bu	Pr	O

Scheme 1.



Scheme 2.

Table 1. ^{1}H NMR Spectral Data of 1,3-Thiazino[6,5-*b*]indolizines

No[a)]	C-6	C-7	C-8	C-9	R^6	R^5
4a	9.70	7.06	7.49	8.31	1.43 4.38	3.88
	br d	dt	br t	br d	t q	s
4b	9.48	6.87	2.47	8.00	1.42 4.36	3.83
	d	dd	s	br s	t q	s
4c	9.57	6.92	1.30 2.78	8.08	1.43 4.37	3.86
	d	dd	t q	br s	t q	s
4d	9.53	2.37	7.09	2.74	1.46 4.37	3.88
	br s	s	br s	s	t q	s
4e	9.59	2.38	7.11	2.74	1.66	3.91
	br s	s	br s	s	s	s
4f	9.74	7.11	7.53	8.35	1.47 4.43	1.37 4.73
	br d	dt	br t	br d	t q	t q
4g	9.52	6.92	2.49	8.08	1.43 4.38	1.33 4.72
	d	dd	s	br s	t q	t q
4h	9.56	6.94	1.31 2.80	8.08	1.43 4.36	1.31 4.68
	d	dd	t q	br s	t q	t q
4i	9.59	2.36	7.09	2.73	1.44 4.36	1.33 4.72
	br s	s	br s	s	t q	t q
4j	9.66	7.08	b)	8.40	1.48 4.45	7.1—7.7
	br d	dt		br d	t q	m
4k	9.51	6.91	2.49	8.17	1.44 4.42	7.1—7.7
	d	dd	s	br s	t q	m
4l	9.53	6.95	1.32 2.79	8.18	1.48 4.44	7.1—7.7
	d	dd	t q	br s	t q	m
4m	9.58	2.32	b)	2.80	1.47 4.42	7.0—7.7
	br s	s		s	t q	m
4n	9.66	7.05	7.48	8.27	1.43 4.38	5.0—5.5 5.6—6.4
	br d	dt	br t	br d	t q	m m
4o	9.48	6.87	2.47	8.01	1.42 4.38	5.0—5.5 5.6—6.4
	d	dd	s	br s	t q	m m
4p	9.53	6.92	1.32 2.80	8.07	1.44 4.38	5.0—5.5 5.6—6.4
	d	dd	t q	br s	t q	m m
4q	9.59	2.36	7.13	2.74	1.44 4.37	5.0—5.5 5.6—6.4
	br s	s	br s	s	t q	m m
4r	9.76	7.06	7.48	8.32	1.43 4.41	1.28 4.23
	br d	dt	br t	br d	t q	t q
4s	9.59	6.87	2.48	8.05	1.43 4.43	1.28 4.18
	d	dd	s	br s	t q	t q
4t	9.63	6.93	1.29 2.80	8.10	1.45 4.41	1.33 4.18
	d	dd	t q	br s	t q	t q
4u	9.57	2.31	7.00	2.68	1.41 4.32	1.26 4.14
	br s	s	br s	s	t q	t q
4v	9.59	2.34	7.02	2.71	1.65	1.27 4.17
	br s	s	br s	s	s	t q
4x	9.56	6.84	2.47	8.03	1.43 4.37	0.96 1.3—2.1 4.03
	d	dd	s	br s	t q	t m q
4y	9.61	6.88	1.31 2.79	8.08	1.44 4.36	0.96 1.3—2.1 4.06
	d	dd	t q	br s	t q	t m q
4z	9.59	2.34	7.06	2.72	1.44 4.37	0.97 1.3—2.1 4.06
	br s	s	br s	s	t q	t m q
4a′	9.59	2.32	7.01	2.69	1.67	0.98 1.3—2.1 4.04
	br s	s	br s	s	s	t m q

a) The coupling constants were as follows: $J_{6,7}=J_{7,8}=7.0$, $J_{8,9}=9.0$, $J_{6,8}=2.0$, and $J_{Et}=7.0$ Hz. b) Overlapped with the phenyl proton signals.

and 3-positions in starting indolizines **1a**—**e**. However, these considerations for products **4a**—**d**, **f**—**u**,**x**—**z**, except **4e**, **v**, **a′** which bear a *t*-butoxycarbonyl group, were not only true for the structures of the 1,3-thiazino[6,5-*b*]indolizines but also for an alternative structure, 1,3-thiazino[5,6-*a*]indolizine **5**. Finally, the structures of compounds **4a**—**d**, **f**—**u**, **x**—**z** were determined by analogy with the high reactivity of the 3-alkoxycarbonyl group superior to the 1-alkoxycarbonyl group[2d)] and confirmed by the X-ray analyses of compounds **4i**, **u** (see below).

Crystallography of 1,3-Thiazino[6,5-*b*]indolizines (4i,u).

Single crystals of ethyl 3-ethyl-7,9-dimethyl-4(3*H*)-

Table 2. Crystal and Structure Analysis Data of Compounds **4i**, **u**

	4i	**4u**
Formula	$C_{17}H_{18}N_2O_3S_2$	$C_{17}H_{18}N_2O_4S$
Formula weight	362.46	346.40
Crystal system	Monoclinic	Triclinic
Space group	$P2_1/a$; Z=4	$P\bar{1}$; Z=2
Lattice parameters		
a/Å	7.514 (3)	9.788 (6)
b/Å	19.469 (4)	10.571 (10)
c/Å	11.666 (4)	8.324 (10)
α/°	90	103.63 (11)
β/°	97.1 6 (3)	101.27 (8)
γ/°	90	87.74 (6)
V/Å^3	1693.4 (9)	820.9 (14)
D_{calcd}/g cm^{-3}	1.422	1.401
Crystal size/mm^3	0.12×0.08×0.80	0.10×0.10×0.60
Diffractometer	Rigaku AFC5S	Rigaku AFC5S
Radiation	Mo$K\alpha$ (λ=0.71069 Å)	Mo$K\alpha$ (λ=0.71069 Å)
Monochrometer	Graphite	Graphite
Scan type	ω–2θ	ω–2θ
2θ Max	55.0°	55.1°
Computer program	TEXSAN System[a)]	TEXSAN System[a)]
Structure solution	Direct method; SIR[b)]	Direct method; SIR[b)]
Hydrogen atom treatment	Calculated, not refined	Calculated, not refined
Refinement	Full-matrix, anisotropic	Full-matrix, anisotropic
Least-squares weight	$4F_o^2/\sigma^2$ (F_o^2)	$4F_o^2/\sigma^2$ (F_o^2)
No. of measurement ref.	Total: 4311, Unique: 4017	Total: 3981, Unique: 3750
No. of observations[c)]	1152	1932
No. of variables	217	217
Residuals R; R_w	0.062; 0.067	0.066; 0.079
Max Shift/Error	0.15	0.17
$\Delta\rho_{max}$/e$^-$ Å^{-3}	0.31	0.45

a) See Ref. 6. b) See Ref. 7. c) $I<3.00\sigma(I)$.

Table 3. Atomic Coordinates (×10^3) and Equivalent Temperature Factors for Non-Hydrogen Atoms in Compound **4i** (esd's, where given, are in parentheses)

Atom	x	y	z	B_{eq}[a)]/Å^2
S1	−66.1 (3)	190.7 (1)	−119.6 (2)	4.0 (1)
S2	−121.6 (3)	244.4 (2)	97.8 (2)	5.8 (1)
O1	−35.3 (9)	410.1 (3)	−211.4 (5)	5.4 (3)
O2	104 (1)	83.6 (4)	−428.9 (7)	8.3 (5)
O3	−38.8 (9)	85.9 (3)	−274.5 (6)	5.8 (4)
N1	31.7 (8)	305.0 (4)	−378.1 (6)	3.6 (4)
N2	−83 (1)	328.5 (4)	−77.6 (7)	4.2 (4)
C1	−87 (1)	264.1 (5)	−35.0 (7)	3.6 (4)
C2	−41 (1)	348.8 (5)	−189.7 (8)	4.0 (5)
C3	−12 (1)	294.2 (4)	−266.4 (7)	3.1 (4)
C4	54 (1)	366.3 (5)	−431.9 (9)	4.5 (5)
C5	98 (1)	367.1 (5)	−542.2 (8)	4.4 (5)
C6	116 (1)	303.8 (6)	−595.9 (7)	4.3 (5)
C7	94 (1)	242.4 (5)	−548.2 (7)	3.6 (5)
C8	53 (1)	240.5 (5)	−431.8 (8)	3.6 (4)
C9	21 (1)	190.7 (5)	−349.1 (7)	3.5 (4)
C10	−21 (1)	225.2 (4)	−250.1 (7)	3.1 (4)
C11	128 (2)	435.2 (6)	−598.8 (9)	7.1 (6)
C12	109 (1)	178.3 (5)	−615.6 (8)	5.2 (5)
C13	35 (1)	115.8 (5)	−359 (1)	5.0 (6)
C14	−28 (2)	10.9 (6)	−270 (1)	9.0 (8)
C15	−91 (2)	−13.8 (7)	−179 (1)	12 (1)
C16	−113 (1)	386.2 (5)	0.6 (8)	5.4 (5)
C17	57 (2)	414.5 (5)	59.3 (9)	6.9 (6)

a) $B_{eq}=\frac{8\pi^2}{3}\sum_{i=1}^{3}\sum_{j=1}^{3}U_{ij}a_i^*a_j^*\boldsymbol{a}_i\cdot\boldsymbol{a}_j$.

Table 4. Atomic Coordinates (×10^3) and Equivalent Temperature Factors for Non-Hydrogen Atoms in Compound **4u** (esd's, where given, are in parentheses)

Atom	x	y	z	B_{eq}[a)]/Å^2
S1	712.1 (1)	83.6 (1)	497.5 (2)	3.31 (5)
O1	909.4 (4)	−42.9 (4)	632.6 (5)	4.7 (2)
O2	625.9 (4)	−327.4 (3)	220.4 (5)	4.1 (2)
O3	552.9 (5)	289.9 (3)	439.6 (5)	5.1 (2)
O4	376.7 (4)	297.2 (3)	228.3 (5)	4.5 (2)
N1	437.8 (4)	−120.1 (4)	134.4 (5)	2.6 (1)
N2	760.4 (4)	−181.6 (4)	428.9 (5)	3.3 (2)
C1	804.7 (5)	−58.5 (5)	524.4 (7)	3.3 (2)
C2	644.2 (5)	−213.5 (5)	296.5 (6)	2.9 (2)
C3	558.3 (5)	−108.2 (4)	259.5 (6)	2.5 (2)
C4	381.5 (5)	−234.6 (5)	27.3 (6)	3.0 (2)
C5	263.7 (6)	−230.7 (5)	−87.2 (7)	3.6 (2)
C6	201.0 (5)	−111.3 (5)	−91.1 (6)	3.3 (2)
C7	252.7 (5)	4.5 (5)	15.6 (6)	2.9 (2)
C8	378.5 (5)	1.2 (4)	133.1 (6)	2.5 (2)
C9	467.3 (5)	93.0 (5)	261.4 (6)	2.7 (2)
C10	574.0 (5)	23.0 (5)	335.3 (6)	2.6 (2)
C11	201.4 (7)	−353.2 (6)	−206.9 (8)	5.1 (3)
C12	171.4 (6)	126.7 (5)	3.5 (7)	3.8 (2)
C13	469.2 (6)	235.0 (5)	317.8 (7)	3.4 (2)
C14	380.9 (7)	438.3 (6)	281 (1)	6.0 (3)
C15	260.6 (8)	488.9 (6)	184 (1)	6.6 (3)
C16	849.3 (6)	−290.2 (6)	464.9 (7)	4.1 (2)
C17	961.9 (6)	−317.9 (6)	360.8 (9)	5.7 (3)

a) $B_{eq}=\frac{8\pi^2}{3}\sum_{i=1}^{3}\sum_{j=1}^{3}U_{ij}a_i^*a_j^*\boldsymbol{a}_i\cdot\boldsymbol{a}_j$.

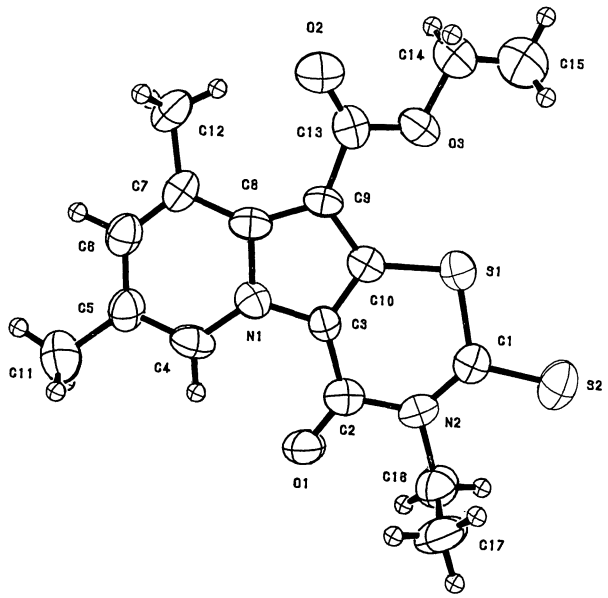


Fig. 1. ORTEP drawing of 4(3*H*)-oxo-2-thioxo-2*H*-1,3-thiazino[6,5-*b*]indolizine derivative **4i** showing the atom labeling scheme and 50% probability thermal ellipsoids.

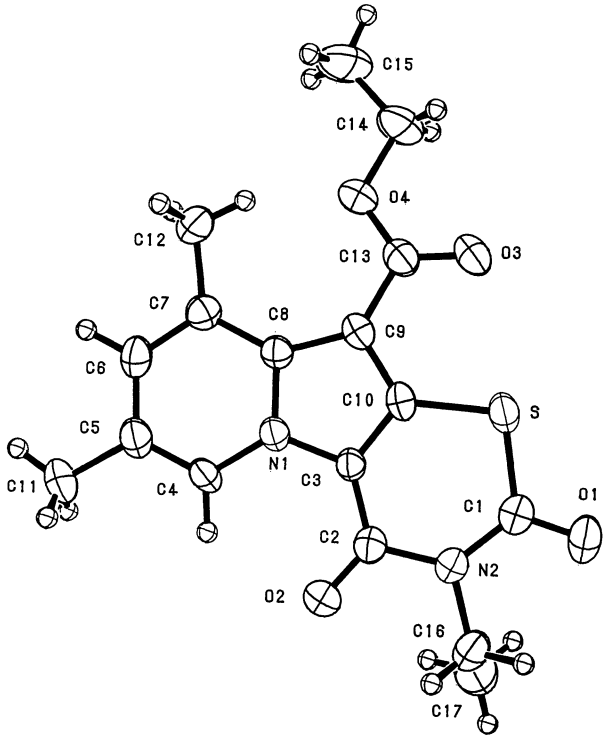


Fig. 2. ORTEP drawing of 2,4(3*H*)-dioxo-2*H*-1,3-thiazino[6,5-*b*]indolizine derivative **4u** showing the atom labeling scheme and 50% probability thermal ellipsoids.

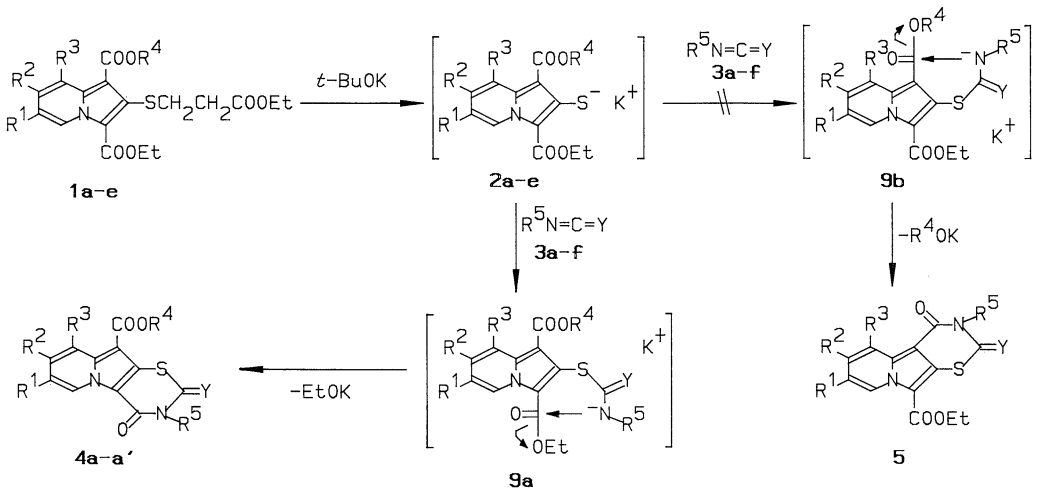
oxo-2-thioxo- (**4i**) and ethyl 3-ethyl-7,9-dimethyl-2,4-(3*H*)-dioxo-2*H*-1,3-thiazino[6,5-*b*]indolizine-10-carboxylate (**4u**) were grown from their ethanolic solutions, respectively. A yellow monoclinic crystal for **4i** and a white triclinic crystal for **4u** were used for structure determinations. Crystal data and details of structure analyses are shown in Tables 2—4.[4] The ORTEP drawings[5] of compounds **4i**, **u** are shown in Figs. 1 and 2, respectively. Interestingly, the only difference between the structures of **4i**, **u** was observed in the conformations of their 10-ethoxycarbonyl groups, but the reason for their different packings in the crystal lattices is still unclear.

Reaction Mechanisms. These reactions were considered to proceed via the nucleophilic attack of 2-indolizinethiolate derivatives **2a**—**e** on the central carbon of heterocumulenes **3a**—**f** followed by the intramolecular nucleophilic reaction of the resulting intermediate, such as **9a**, with the elimination of an ethoxide ion. (See Scheme 3) As has been described in the transformations of 8-unsubstituted diethyl 2-(substituted methylthio)indolizine-1,3-dicarboxylates to 3-hydroxythieno[2,3-*b*]indolizines, the exclusive formation of 1,3-thiazino[6,5-*b*]indolizine derivatives **4a**—**c**, **f**—**h**, **j**—**l**,**n**—**p**, **r**—**t**, **x**, **y** from the reactions of 8-unsubstituted 2-indolizinethiolates **2a**—**c** with heterocumulenes **3a**—**f** was easily supported owing to the higher reactivity of the 3-alkoxycarbonyl group over the 1-alkoxycarbonyl group.[2b,d] However, the unavailability of 1,3-thiazino[5,6-*a*]indolizine derivatives, such as **5**, in the reactions of 6,8-dimethyl-2-indolizinethiolates **2d**, **e**, whose 1-alkoxycarbonyl group is activated by the steric hindrance of the 8-methyl group at the peri position, with **3a**—**f** was mysterious. The examination of the molecule of **5** using Dreiding models clearly showed the presence of severe repulsive interaction between the 4-oxo oxygen and the 8-methyl group. In order to avoid an unfavorable interaction like this, the exclusive intramolecular nucleophilic attack of the nitrogen anion to the carbonyl carbon of the 3-position could have occurred. On the other hand, the reason why some reactions of **2** with ketenes were unsuccessful is still unclear, but it may have been attributable in part to the bulkiness of these ketenes against the approach to the thiolate anion **2**.

In conclusion, the reactions of potassium 2-indolizinethiolate derivatives **2a**—**e** with some heterocumulenes **3a**—**f** was found to be a useful method for the preparation of new condensed indolizine derivatives.

Experimental

Melting points were measured with a Yanagimoto micromelting point apparatus and were not corrected. The microanalyses were carried out on a Perkin-Elmer 240 elemental analyzer. The ^{1}H NMR spectra were determined with a Varian EM360A spectrometer in deuteriochloroform with tetramethylsilane as an internal standard and the chemical



Scheme 3.

shifts are expressed in δ values. The IR spectra were taken with a Hitachi 260-10 infrared spectrophotometer.

Reaction of Indolizines with Isothiocyanates and Isocyanates in the Presence of Base. General Method. A solution of a dialkyl 2-[(2-ethoxycarbonylethyl)thio]indolizine-1,3-dicarboxylate (**1**, 1 mmol) in 2 ml of DMF was treated with potassium *t*-butoxide (0.168 g, 1.5 mmol) at 60—70 °C in a water bath for 1 h, and ethyl acrylate generated in this reaction was removed completely by a rotatory evaporator under reduced pressure. An isothiocyanate or isocyanate (**3**, 1.2 mmol) was added to the mixture and the resulting solution was allowed to react at 60—70 °C for an additional 2 h. The reaction mixture was acidified with diluted hydrochloric acid and water was then added to bring the total volume to 30 ml. The precipitates were colleted by filtration. The precipitates were then dissolved in 30 ml of chloroform and water was removed from the solution by filtration through phase-separating filter paper. The filtrate was concentrated under reduced pressure and the residue was separated by column chromatography on activated alumina using chloroform as an

Table 5. Some Data of the 1,3-Thiazino[6,5-*b*]indolizines

No[a]	React	Yield %	Mp °C	ν (KBr) cm^{-1}	Formula[b]
4a	**1a 3a**	80	234—237	1699 1657	$C_{14}H_{12}N_2O_3S_2$
4b	**1b 3a**	97	222—224	1692 1655	$C_{15}H_{14}N_2O_3S_2$
4c	**1c 3a**	41	199—201	1676 1657	$C_{16}H_{16}N_2O_3S_2$
4d	**1d 3a**	71	211—212	1718 1660	$C_{16}H_{16}N_2O_3S_2$
4e	**1e 3a**	55	232—235	1708 1661	$C_{18}H_{20}N_2O_3S_2$
4f	**1a 3b**	68	183—186	1700 1656	$C_{15}H_{14}N_2O_3S_2$
4g	**1b 3b**	82	232—235	1699 1650	$C_{16}H_{16}N_2O_3S_2$
4h	**1c 3b**	41	181—184	1694 1647	$C_{17}H_{18}N_2O_3S_2$
4i	**1d 3b**	48	210—213	1718 1659	$C_{17}H_{18}N_2O_3S_2$
4j	**1a 3c**	16	281—283	1696 1660	$C_{19}H_{14}N_2O_3S_2$
4k	**1b 3c**	19	280—283	1690 1657	$C_{20}H_{16}N_2O_3S_2$
4l	**1c 3c**	17	245—249	1693 1660	$C_{21}H_{18}N_2O_3S_2$
4m	**1d 3c**	22	283—285	1721 1661	$C_{21}H_{18}N_2O_3S_2$
4n	**1a 3d**	25	149—151	1690 1653	$C_{16}H_{14}N_2O_3S_2$
4o	**1b 3d**	61	152—155	1676 1653	$C_{17}H_{16}N_2O_3S_2$
4p	**1c 3d**	60	147—149	1691 1655	$C_{18}H_{18}N_2O_3S_2$
4q	**1d 3d**	55	172—174	1715 1663	$C_{18}H_{18}N_2O_3S_2$
4r	**1a 3e**	68	145—147	1696 1656	$C_{15}H_{14}N_2O_4S$
4s	**1b 3e**	86	188—190	1690 1661	$C_{16}H_{16}N_2O_4S$
4t	**1c 3e**	33	190—193	1691 1664	$C_{17}H_{18}N_2O_4S$
4u	**1d 3e**	42	178—181	1715 1662	$C_{17}H_{18}N_2O_4S$
4v	**1e 3e**	59	234—237	1720 1653	$C_{19}H_{22}N_2O_4S$
4x	**1b 3f**	67	159—161	1684 1660	$C_{17}H_{18}N_2O_4S$
4y	**1c 3f**	16	134—135	1698 1661	$C_{18}H_{20}N_2O_4S$
4z	**1d 3f**	34	187—188	1703 1655	$C_{18}H_{20}N_2O_4S$
4a′	**1e 3f**	34	190—191	1659 1637	$C_{20}H_{24}N_2O_4S$

a) Compounds **4a**—**q** were obtained as pale yellow needles and **4r**—**v**, **x**—**a′** as colorless needles.
b) Satisfactory analytical data (within 0.3% for C, H, and N) were obtained for all compounds.

eluent. Evaporation of the chloroform and recrystallization of the crude products from ethanol afforded the corresponding ethyl or *t*-butyl 4(3*H*)-oxo-2-thioxo- (**4a**—**q**) and 2,4(3*H*)-dioxo-2*H*-1,3-thiazino[6,5-*b*]indolizine-10-carboxylates (**4r**—**v**, **x**—**a'**). These results and some spectral data are summarized in Tables 1 and 5.

On the other hand, similar treatment of ethyl 3-acetyl-2-[(2-ethoxycarbonylethyl)thio]indolizine-1-carboxylate **1f** and ethyl 1-cyano-2-[(2-ethoxycarbonylethyl)thio]indolizine-3-carboxylate **1g** with methyl isothiocyanate **3a** gave only the corresponding 2-thiol derivatives, ethyl 3-acetyl-2-mercaptoindolizine-1-carboxylate (**6a**, mp 114—116 °C, 64% yield) and ethyl 1-cyano-2-mercaptoindolizine-3-carboxylate (**6b**, mp 130—131 °C, 71% yield), and did not afford any condensation products. Compounds **6a**, **b** were completely in accord with authentic samples in all respects.[2c] The 2-indolizinethiols **6a**, **b** did not react with reagents **3a**—**f** even under heating conditions.

The reactions of indolizines **1a**, **b** with ketene precursors such as phenylacetyl chloride and dichloroacetyl chloride under the alkaline conditions employed here were also unsuccessful.

References

1) For part 26 of this series, see A. Kakehi, S. Ito, T. Sakurai, and K. Urushido, *Chem. Pharm. Bull.*, **39**, 1949 (1991).

2) a) A. Kakehi, S. Ito, S. Matsumoto, and Y. Morimoto, *Chem. Lett.*, **1987**, 2043; b) A. Kakehi, S. Ito, T. Fujii, Y. Morimoto, S. Matsumoto, and M. Shiohara, *Bull. Chem. Soc. Jpn.*, **62**, 119 (1989); c) A. Kakehi, S. Ito, N. Yamada, and K. Yamaguchi, *Bull. Chem. Soc. Jpn.*, **63**, 829 (1990); d) *idem.*, *Chem. Pharm. Bull.*, **38**, 1527 (1990).

3) R. Richter and H. Ulrich, "The Chemistry of Functional Groups. The Chemistry of Cyanate and Their Thio Derivatives II," ed by S. Patai, John Wiley & Sons, New York (1977), Chap. 17, pp. 619—818; L. Drobnica, P. Kristian, and J. Augustin, *ibid.*, Chap. 22, pp. 1003—1221; S. Ozaki, *Chem. Rev.*, **72**, 457 (1972).

4) Bond lengths, bond and torsion angles, and F_o-F_c tables are deposited as Document No. 8965 at the Office of the Editor of Bull. Chem. Soc. Jpn.

5) C. K. Johnson, ORTEPII, Report ORNL-5138. Oak Ridge National Laboratory, Oak Ridge, Tennessee (1976).

6) TEXSAN TEXRAY, Structure Analysis Package, Molecular Structure Corporation (1985).

7) M. C. Burla, M. Camalli, G. Cascarano, C. Giacovazzo, G. Polidori, R. Spagna, and D. Viterbo, *J. Appl. Crystallogr.*, **22**, 389 (1989).