Preparation of New Nitrogen-bridged Heterocycles. 7.[1] Reactions of 3-[Bis(methylthio)methylene]-2(3*H*)-indolizinones with Some Pyridinium *N*-Aminides

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Synopsis. The reactions of 3-[bis(methylthio)methylene]-2(3*H*)-indolizinones with pyridinium, quinolinium, and isoquinolinium *N*-aminides gave unstable 1,3-dipolar spiro-adducts with the elimination of a methanethiol, and some of these adducts isomerized thermally to afford the corresponding *N*-ylide derivatives.

Ketene dithioacetals are now widely recoginized as versatile intermediates in the syntheses of a variety of organic compounds. In particular, the members conjugated with a vinyl or a keto group serve as carbonyl umpolung reagents,[2] Diels-Alder dienes,[3] and reagents for the preparation of various heterocycles.[4] Recently, we reported the preparation of dihydroaromatic ketene dithioacetals, 3-[bis(methylthio)methylene]-2(3*H*)-indolizinone derivatives, and their transformation into 2*H*-pyrano[2,3-*b*]indolizinones by the reactions with various activated acetates in the presence of alkali.[5] The reaction with actates is the first case in which the high electrophilicity of these α-oxo ketene dithioacetals serves for the syntheses of fused heterocycles. In this note, we wish to report the reactivity of 3-[bis(methylthio)methylene]-2(3*H*)-indolizinones as a dipolarophile and thermal behavior of the resulting 1,3-dipolar spiro-adducts.

When an equimolar mixture of 3-[bis(methylthio)methylene]-1-methyl-2(3*H*)-indolizinone **1** and 1-aminopyridinium iodide **3** was treated with potassium carbonate in THF at room temperature and then separated carefully by column chromatography, red spiroadduct **4** was obtained in a quantitative yield. A similar treatment of 1-phenyl derivative **2** and *N*-aminide **3** gave the corresponding compound **5** in a 66% yield. In these reactions, methanethiol was detected by its unpleasant odor. These compounds **4** and **5**, however, were extremely unstable and converted rapidly to intractable tarry materials even at room temperature. So, we next examined the reactions of the stabilized bicyclic *N*-aminides instead of monocyclic one. As might be expected, the reactions of **1** and **2** with 1-aminoquinolinium iodide **6** and 2-aminoisoquinolinium iodide **9** in the presence of alkali afforded relatively stable crystalline spiro-adducts **7**, **8**, **10**, and **11** in 69—100% yields.

Interestingly, compounds **7**, **10**, and **11** isomerized smoothly into the corresponding quinolinium *N*-ylide **12**, and isoquinolinium *N*-ylides **14** and **15** on standing at room temperature or on heating in boiling xylene, while no *N*-ylide **13** could be obtained from the thermolysis of **8** under the same conditions. On the other hand, the reactions of acyclic ketene dithioacetals **16** and **17** with **3** in the presence of alkali afford-

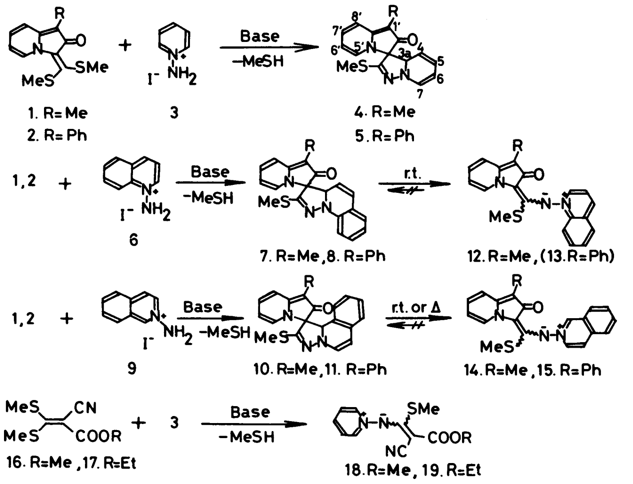

Table 1. NMR data of 1,3-dipolar spiro-adducts in $CDCl_3$

Compd	R	SMe	C-3a	C-4	C-5	C-6	C-6′	C-7, 5′,7′, and 8′
4	1.80	2.48	5.61	4.70	6.08	4.87	6.23	6.70—7.50
	s	s	br s	br d	m	br t	dt	m
	$J_{4,5}=9.0$, $J_{5,6}=J_{6,7}=J_{5',6'}=J_{6',7'}=7.0$, $J_{6',8'}=1.5$ Hz							
5	a)	2.48	5.70	4.77	6.09	4.87	6.30	6.60—7.80
		s	br s	br d	m	br t	m	m
	$J_{4,5}=9.0$, $J_{5,6}=J_{6,7}=7.0$ Hz							
7	1.84	2.57	5.70	5.27	6.60	b)	6.21	6.70—7.70
	s	s	t	dd	dd		dt	m
	$J_{4,5}=10.0$, $J_{4,3a}=J_{5,3a}=2.5$, $J_{5',6'}=J_{6',7'}=7.0$, $J_{6',8'}=1.5$ Hz							
8	c)	2.56	5.73	5.30	6.58	c)	6.23	6.70—7.90
		s	t	dd	dd		m	m
	$J_{4,5}=10.0$, $J_{4,3a}=J_{5,3a}=2.5$ Hz							
10	1.90	2.49	6.11	d)	d)	5.47	6.02	6.80—7.40
	s	s	s			d	dt	m
	$J_{6,7}=8.0$, $J_{5',6'}=J_{6',7'}=7.0$, $J_{6',8'}=1.5$ Hz							
11	e)	2.50	6.17	e)	e)	5.42	6.03	6.80—7.80
		s	s			d)	m	m
	$J_{6,7}=8.0$ Hz							

a) Overlapped with each others at δ 6.60—7.80. b) Overlapped with each others at δ 6.70—7.70. c) Overlapped with each others at δ 6.70—7.90. d) Overlapped with each others at δ 6.80—7.40. e) Overlapped with each others at δ 6.80—7.80.

Table 2. Preparations and some properties of spiro-adducts and ylidic compounds

Compd[a)] No.	Yield %	Mp θ_m/°C	$\nu_{C=O}^{KBr}$/cm^{-1}	Formula	Calcd(%)			Found(%)		
					C	H	N	C	H	N
4	100	decomp	1602	b)						
5	66	decomp	1610	b)						
7	69	76—79(decomp)	1600	$C_{20}H_{17}N_3OS$	69.14	4.93	12.10	69.11	5.09	11.97
8	100	199—200(decomp)	1600	$C_{25}H_{19}N_3OS$	73.32	4.68	10.26	73.41	4.70	10.16
10	83	106—109	1594	$C_{20}H_{17}N_3OS$	69.14	4.93	12.10	69.00	5.09	12.23
11	100	100(decomp)	1592	$C_{25}H_{19}N_3OS$	73.32	4.68	10.26	73.41	4.73	10.11
12	53	139—140	1600	$C_{20}H_{17}N_3OS$	69.14	4.93	12.10	69.21	4.87	11.96
14	80	156—158	1587	$C_{20}H_{17}N_3OS$	69.14	4.93	12.10	69.12	5.07	11.98
15	80	249—250	1591	$C_{25}H_{19}N_3OS$	73.32	4.68	10.26	73.25	4.73	10.28
18	87	125—127	1662[c)]	$C_{11}H_{11}N_3O_2S$	53.00	4.45	16.86	52.98	4.40	16.92
19	97	128—130	1662[d)]	$C_{12}H_{13}N_3O_2S$	54.76	4.98	15.96	54.47	4.92	16.02

a) NMR data of ylidic compounds in $CDCl_3$ as follows: **12**, δ 1.89 (3H, s, 1′-Me), 2.68 (3H, s, SMe), and 7.00—8.80 (11H, m, other protons). **14**, δ 1.93 (3H, s, 1′-Me), 2.70 (3H, s, SMe), and 7.00—8.80 (11H, m, other protons). **15**, δ 2.55 (3H, s, SMe) and 6.80—8.70 (16H, m, other protons). **18**, δ 2.47 (3H, s, SMe), 3.51 (3H, s, OMe), and 7.70—8.80 (5H, m, pyridine protons). **19**, δ 1.12 (3H, t, *J*=7.0 Hz, $CH_2\underline{CH_3}$), 2.47 (3H, s, SMe), 3.98 (2H, q, *J*=7.0 Hz, $O\underline{CH_2}CH_3$), and 7.70—8.80 (5H, m, pyridine protons). b) The analysis could not be performed because of its thermal instability. c) The cyano absorption band appeared at 2162 cm^{-1}. d) The cyano absorption band appeared at 2178 cm^{-1}.

ed only stable pyridinium *N*-ylides **18** and **19** in good yields, respectively, but did not cycloadducts at all.

Structural elucidation of these spiro-adducts **4**, **5**, **7**, **8**, **10**, and **11** was mainly accomplished by their NMR and IR spectral inspection and partly by their elemental analyses. In particular, their NMR spectra (See Table 1) supported clearly the presences of 2(3*H*)-indolizinone[5)] and 3,3a-dihydropyrazolo[1,5-*a*]pyridine moieties.[6)] The IR spectra exhibited also the presence of a carbonyl band (near 1600 cm^{-1}) characteristic of 2(3*H*)-indolizinone derivative.[5)] Similarly, the structures of *N*-ylides **12**, **14**, **15**, **18**, and **19** were determined by their elemental analyses and by comparison of their spectral data with those of known pyridinium *N*-ylides.[6,7)]

The formation of the spiro-adducts **4**, **5**, **7**, **8**, **10**, and **11** may be considered by 1,3-dipolar cycloaddition between ketene dithioacetals **1** and **2** and *N*-amimides **3**, **6**, and **9** followed by the elimination of one molecule of methanethiol from the resulting primary spiro-adducts. Since facile transformations from these spiro-adducts **7**, **10**, and **11** to the corresponding *N*-ylides **12**, **14**, and **15** were observed but the reverse reaction was not, an alternative path *via* 1,5-dipolar cyclization of the *N*-ylides such as **12**—**15** which were formed initially by the nucleophilic substitutions of *N*-aminides onto dithioacetals may be discarded.

Experimental

Melting points were measured with a Yanagimoto micro melting point apparatus and are uncorrected. Microanalyses were carried out on a Perkin-Elmer 240 Elemental Analyzer. The NMR spectra were determined with a Varian EM360A Spectrometer in deuteriochloroform with tetramethylsilane as an internal standard. The chemical shifts are expressed in δ values. The IR spectra were taken with a Hitachi 260-10 Infrared Spectrophotometer.

Reactions of Ketene Dithioacetals with N*-Aminides. General Procedure*: A solution of acetal (*1* or *2*, 1 mmol) and pyridinium salt (1 mmol) in THF (30 mol) was treated with anhydrous potassium carbonate (5 g) under stirring at room temperature for 30 min. Insoluble inorganic substances were filtered and the filtrate was immediately concentrated *in vacuo* at below 10 °C. The residue was separated by column chromatography (alumina) using ether and then chloroform as eluents and the chloroform layer was concentrated carefully by centrifugal freezing dryer (Yamato, RC-11). Recrystallizations from chloroform–hexane at below 5 °C gave pure adducts **7**, **8**, **10**, and **11**, but those of **4** and **5** were unsuccessful because of their thermal instability. On the other hand, only pyridinium *N*-ylides **18** and **19** were formed from the reactions of acyclic acetals **16** and **17** with **3**. The results and data are shown in Tables 1 and 2.

Isomerization of Spiro-adducts to N*-Ylides*. Spiro-adducts **7** and **10** smoothly isomerized to the corresponding *N*-ylides **12** and **14** on standing at room temperature for 3—4 d, but the conversion of **11** to **15** was accomplished by heating for 30 min in boiling xylene. On the other hand, adduct **8** decomposed under above conditions and no ylide could be obtained. The results and data are summarized in Table 2.

References

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