Studies on Heteropentalenes. V.[1] Cycloadditions of 5-Aryl-3-methylimidazo-[5,1-*b*]thiazoles with Acetylenic Esters Leading to 5-Aryl-3-methyl-thiazolo[2,3-*c*]benzimidazoles and Related Heterocycles

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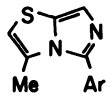
(Received December 10, 1981)

Cycloaddition of 5-aryl-3-methylimidazo[5,1-*b*]thiazoles with dialkyl acetylenedicarboxylate in an aprotic nonpolar solvent gives a number of products including epimeric thiazolo[2,3-*c*]benzimidazoles (**3** and **4**) [1:2-cycloadducts], epimeric 5,10b-ethenothiazolo[3′,2′:3,4]imidazo[1,5-*a*]pyridines (**5** and **6**) [1:3-cycloadducts], and thiazolo[3′,2′:3,4]imidazo[1,2-*a*]pyridines [1:3-adducts]. At higher temperature, formation of the 1:2-cycloadducts is favored over the 1:3-adducts, whereas the latter predominates at room temperature. In an aprotic polar medium, the 1:3-cycloadducts (**5** and **6**) and tetraalkyl 6-arylpyridine-2,3,4,5-tetracarboxylates are substantially produced. Epimerization of **3** and **4** has been found to compete well with fragmentation to 4*H*-1,4-benzothiazine.

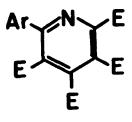
Although the chemistry of aromatic azapentalenes has been dealt with from various angles,[2] studies on cycloadditions to them had been undeservedly neglected before we first reported the 1,4-cycloadditions[3] of imidazo-[2,1-*b*]thiazoles and of imidazo[2,1-*b*]benzothiazoles with acetylenic esters (*e.g.*, dimethyl acetylenedicarboxylate (DMAD)[4] and methyl propiolate[5]). The present paper is concerned with the 1,4-cycloadditions[3] of imidazo[5,1-*b*]thiazoles (**1**). The result will prove of some interest for the synthesis of thiazolo[2,3-*c*]benzimidazoles (**3** and **4**) and 4*H*-1,4-benzothiazine rings (**10**).

The reactions of imidazo[5,1-*b*]thiazoles with acetylenic esters are highly solvent dependent, like those of imidazo[2,1-*b*]thiazoles[4] and of imidazo[2,1-*b*]benzothiazoles.[4] With DMAD in acetonitrile, 3-methyl-5-phenylimidazo[5,1-*b*]thiazole (**1a**) produced tetramethyl 6-phenylpyridine-2,3,4,5-tetracarboxylate (**2**),[6] two diastereoisomers **3a** and **4a** of tetramethyl 3-methyl-5-phenylthiazolo[2,3-*c*]benzimidazole-7,8,9,10-tetracarboxylate [1:2-cycloadducts], and two diastereoisomers **5a** and **6a** of hexamethyl 3-methyl-5-phenyl-5,10b-ethenothiazolo[3′,2′:3,4]imidazo[1,5-*a*]pyridine-7,8,9,10,11,12-hexacarboxylate [1:3-cycloadducts]. However, use of benzene, xylene, or tetrahydrofuran (THF) as a solvent resulted in the formation of a new 1:3-adduct [dimethyl 2-(5,6,7,8-tetramethoxycarbonyl-3-methyl-4a-phenylthiazolo[3′,2′:3,4]imidazo]1,2-*a*]pyridin-10-yl)fumarate (**8a**)] in addition to **3a**, **4a**, **5a**, and **6a**, but did not yield the pyridine (**2**).

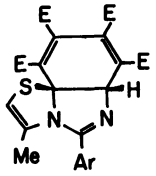
a series: E = CO_2Me, Ar = Ph
b series: E = CO_2Me, Ar = C_6H_4Me-p
c series: E = CO_2Et, Ar = Ph



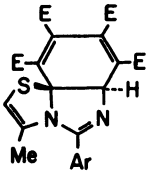
1a - b



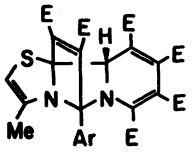
2a - b



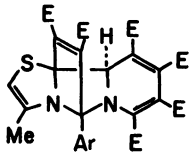
3a - c



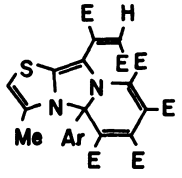
4a - c



5a - b



6a - b



8a - b

Likewise, the reaction of **1b** with DMAD afforded a series of the compounds **2b**, **3b**, **4b**, **5b**, and **6b** in

Table 1. Conditions and yields for the reactions of **1** with acetylenic esters

Substrate	Reagent	Ratio	Solvent	Temp	Time/h	Products (%)						
1a	DMAD	1 : 1	MeCN	Reflux	1	**1a**(49)	**2a**(2)	**3a**(10)	**4a**(7)	**5a**(3)	**6a**(3)	
1a	DMAD	1 : 5	MeCN	Reflux	1		**2a**(10)	**3a**(21)	**4a**(5)	**5a**(22)	**6a**(34)	
1a	DMAD	1 : 5	MeCN	R.T.	20		**2a**(18)	**3a**(8)	**4a**(2)	**5a**(8)	**6a**(43)	
1a	DMAD	1 : 1	Benzene	Reflux	1	**1a**(47)		**3a**(10)	**4a**(9)	**5a**(4)	**6a**(4)	**8a**(6)
1a	DMAD	1 : 5	Benzene	Reflux	1			**3a**(27)	**4a**(26)	**5a**(14)	**6a**(20)	**8a**(7)
1a	DMAD	1 : 5	Benzene	R.T.	20			**3a**(4)	**4a**(4)	**5a**(10)	**6a**(34)	**8a**(3)
1a	DMAD	1 : 5	THF	Reflux	1			**3a**(21)	**4a**(7)	**5a**(10)	**6a**(18)	**8a**(9)
1a	DMAD	1 : 5	Xylene	Reflux	1			**3a**(22)	**4a**(20)	**5a**(5)	**6a**(7)	**8a**(5)
1b	DMAD	1 : 5	MeCN	Reflux	1		**2b**(11)	**3b**(7)	**4b**(16)	**5b**(19)	**6b**(37)	
1b	DMAD	1 : 5	Benzene	Reflux	1			**3b**(13)	**4b**(41)	**5b**(13)	**6b**(21)	**8b**(8)
1b	DMAD	1 : 5	Xylene	Reflux	1			**3b**(12)	**4b**(41)	**5b**(10)	**6b**(14)	**8b**(9)
1a	DEAD	1 : 5	MeCN	Reflux	1			**3c**(22)	**4c**(6)			
1a	DEAD	1 : 5	Benzene	Reflux	1			**3c**(51)	**4c**(5)			

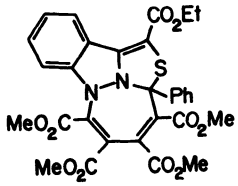
acetonitrile, and a series of the products **3b**, **4b**, **5b**, **6b**, and **8b** in benzene or xylene. With diethyl acetylenedicarboxylate (DEAD), **1a** yielded the diastereoisomers **3c** and **4c** alone in either of acetonitrile or benzene, however. Irrespective of the polarity of the solvent, formation of the 1:2-cycloadducts seems to become favorable at higher temperature than that of the 1:3-adducts. These results are provided in Table 1.

Structures of these new compounds were deduced from their elemental analyses and spectroscopic behaviors. Elemental analyses of **3a** and **4a** gave the same elemental composition of $C_{24}H_{22}N_2O_8S$. The compound **3a** exhibits three ν(C=O) absorptions at 1705, 1725, and 1750 cm^{-1} in the IR spectrum, and the ^{13}C NMR signals for two sp^3-carbons of the ring at δ 47.1 (d) (C-6a) and 118.9 (s) (C-10a) and one easily identified sp^2-carbon flanked by two nitrogens at δ 166.6 (s). Specific ^1H NMR resonances observed for **3a** include four ester Me singlets at δ 3.47, 3.51, 3.77, and 3.79, and two 1H-singlets at δ 7.12 (H-2) and 6.68 (H-6a).

The ^{13}C NMR signals of the compound **4a** are very similar to those of the compound **3a**, and the ^1H NMR spectra of **3a** and **4a** resemble each other except for the resonance of one ester Me and H-6a protons. As to the differences, **3a** has an ester Me signal at δ 3.51 and a methine singlet at δ 6.68 (H-6a), whereas **4a** at δ 3.73 and 6.27 respectively. These significant changes strongly suggest that stereochemical disposition of the hydrogen at C-6a of differs from that of **4a**. As the hydrogen disposed *syn* must be susceptible to anisotropic deshielding effect of the ring sulfur atom, the compound whose H-6a proton is seen at lower field should be *syn*-isomer **3a** and the one displaying its H-6a proton at higher field *anti*-isomer **4a**.

Interconversion of **3a** and **4a**, though not attained thermally (*e.g.*, heating in xylene), takes place readily in the presence of base. Heating of either **3a** or **4a** with sodium methoxide in methanol or 1,8-diazabicyclo-[5.4.0]undec-7-ene (DBU) in benzene produced a mixture of **3a**, **4a**, and tetramethyl 3-methyl-4*H*-1,4-benzothiazine-5,6,7,8-tetracarboxylate (**10a**)[7] whose structure is delineated later. These observations firmly show the compounds **3a** and **4a** to be epimers. Similarly, the epimerization of **3c** to **4c** was found to compete significantly with the fragmentation to **10c**.

The structures **5a** and **6a**, both being analyzed as $C_{30}H_{28}N_2O_{12}S$, were assigned as follows. Their UV spectra resemble each other, possessing a maximum absorption even at the wavelength greater than 400 nm. As the ^{13}C NMR spectra of **5a** and **6a** also resemble each other, they must be stereoisomers. Besides signals for carbons associated with Me, Ph, and CO_2Me groups, eleven carbons are seen, among which six singlets at δ 120—150 are assigned to =C–CO_2Me groups by reference to the spectra of **3a** and **4a**. Signals at δ 117—118 and at δ 153—154 are assigned to a CH=CH–Me group. Two sp^3-carbons which appear at δ 56—58 and δ 71—72 are assigned to >CH and >C–Ph groups with the aid of proton-decoupled off resonance spectra. The remaining singlet observed at lower field (δ 113—114) must be due to a quarternary carbon flanked by sulfur and nitrogen atoms. This is supported by the ^{13}C NMR spectrum of **7** whose C-4a has been reported to resonate at δ 114.[8]



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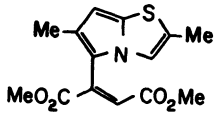
It is therefore deduced that a new six membered ring incorporating 2 mol of DMAD is annelated to **1** at the N(6)–C(7) bond and the remaining DMAD forms an etheno bridge whose termini are at C-5 and C-8 of **1**. The isomers **5a** and **6a** reveal their H-10a proton at δ 5.12 and 5.15 respectively. With the same reasonings for the stereochemical assignments of **3a** and **4a**, the *syn*-hydrogen at C-10a of a 5,10b-ethenothiazolo-[3′,2′:3,4]imidazo[1,5-*a*]pyridine ring must resonate at lower field than its counterpart, and hence the compound whose methine hydrogen is seen at δ 5.12 is assigned the *anti*-structure (**5a**) and the one displaying the methine hydrogen at δ 5.15 the *syn*-structure (**6a**).



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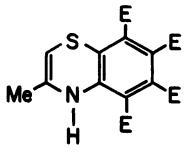
The ^1H NMR spectrum of **8a**, $C_{30}H_{28}N_2O_{12}S$, confirmed the presence of six ester Me groups and two olefinic protons, one Me group and a phenyl group. Of the two olefinic protons, the one has its chemical shift (δ 6.72) close to the olefinic proton of dimethyl fumarate (δ 6.83) and of the compound **9** (δ 6.79).[9] As both of the other olefinic singlet (δ 6.96) and a Me singlet at δ 2.38 broaden, as seen for the ^1H NMR spectra of **1a**, **3a**, **4a**, **5a**, and **6a**, the thiazole ring of **1a** would have remained intact. These observations, together with the disappearance of the H-7 proton of **1a** and complete difference of the UV spectrum of **8a** from those of the other 1 : 3-adducts **5a** and **6a**, allowed the structure to be proposed.

UV, IR, and ^1H NMR spectroscopic properties of the compounds **2a**—**2b**, **3a**—**3c**, **4a**—**4c**, **5a**—**5b**, **6a**—**6b**, and **8a**—**8b** are collected in Table 2 and full ^{13}C NMR spectral assignments of **3a**, **4a**, **4b**, **5a**, and **6a** in Table 3.

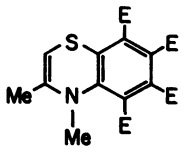
The structure **10a**, $C_{17}H_{17}NO_8S$, was determined as follows. The ^1H NMR spectrum shows a Me doublet at δ 2.41 which couples (J=0.5 Hz) with an olefinic proton at δ 6.74. Of the two singlets at δ 3.83 and 3.90 associated with four ester Me groups, the latter was found to be overlapped with an additional proton, which could be exchangeable. Furthermore, the spectrum indicated the absence of a benzene ring. The IR spectrum had ν(C=O) bands at 1695, 1715, and 1730 cm^{-1} and a broad ν(NH) band at 2300—2850 cm^{-1}

TABLE 2. SPECTROSCOPIC PROPERTIES OF **2**, **3**, **4**, **5**, **6**, AND **8**

Compound	λ_{max}/nm (log ε)	ν(C=O)/cm^{-1}	^{1}H MNR δ
2a	269 (4.22)	1740, 1730, 1715	3.68(3H, s), 3.93(3H, s), 3.95(3H, s), 3.98(3H, s), 7.25—7.75(5H, m)
2b	282 (4.06)	1740, 1725	2.38(3H, s), 3.70(3H, s), 3.89(3H, s), 3.92(3H, s), 3.96(3H, s), 7.21(2H, d, J=8 Hz), 7.48(2H, d, J=8 Hz),
3a	250^{sh} (4.21), 317 (4.32), 350^{sh} (4.16)	1750, 1725, 1705	2.45(3H, bs), 3.47(3H, s), 3.51(3H, s), 3.77(3H, s), 3.79(3H, s), 6.68(1H, s), 7.12(1H, bs), 7.2—7.6(5H, m)
3b	250 (4.08), 327 (4.31), 355^{sh} (4.17)	1750, 1725, 1710	2.38(3H, s), 2.47(3H, bs), 3.53(6H, s), 3.80(6H, s), 6.75(1H, s), 7.18(1H, bs), 7.25(2H, d, J=8 Hz), 7.44(2H, d, J=8 Hz)
3c	242(4.33), 313 (4.40), 345^{sh} (4.25)	1745, 1720, 1695	0.86(3H, t, J=7 Hz), 1.08(3H, t, J=7 Hz), 1.28(6H, t, J=7 Hz), 2.47(3H, bs), 3.90(2H, q, J=7 Hz), 3.96(2H, q, J=7 Hz), 4.24(2H, q, J=7 Hz), 4.25(2H, q, J=7 Hz), 6.70(1H, s), 7.13 (1H,bs), 7.25—7.6(5H, m)
4a	255 (4.28), 320 (4.13), 360 (4.16)	1740, 1725, 1695	2.42(3H, bs), 3.46(3H, s), 3.73(3H, s), 3.76(3H, s), 3.79(3H, s), 6.27(1H, s), 7.00(1H, bs), 7.3—7.6(3H, m), 7.9—8.2(2H, m)
4b	255 (4.31), 325 (4.26), 361 (4.26)	1750, 1740, 1720	2.42(6H, s), 3.47(3H, s), 3.75(3H, s), 3.78(3H, s), 3.82(3H, s), 6.27(1H, s), 7.03(1H, bs), 7.30(2H, d, J=8 Hz), 8.03(2H, d, J=8 Hz)
4c	253 (4.25), 320 (4.18), 360 (4.20)	1750, 1725, 1690	1.01(3H, t, J=7 Hz), 1.22(3H, t, J=7 Hz), 1.25(3H, t, J=7 Hz), 1.32(3H, t, J=7 Hz), 2.42(3H, bs), 3.97(2H, q, J=7 Hz), 4.26(2H, q, J=7 Hz), 4.27(2H, q, J=7 Hz), 4.30(2H, q, J=7 Hz), 6.12(1H, s), 7.03(1H, bs), 7.35—7.65(3H, m), 8.05—8.3(2H, m)
5a	260 (4.44), 405 (4.07)	1735, 1720	2.45(3H, bs), 3.10(3H, s), 3.38(3H, s), 3.48(3H, s), 3.57(3H, s), 3.84(3H, s), 3.94(3H, s), 5.12(1H, s), 7.15(1H, bs), 7.15—7.35(3H, m), 7.45—7.7(2H, m)
5b	261 (4.21), 406 (3.87)	1735, 1720	2.25(3H, s), 2.45(3H, bs), 3.12(3H, s), 3.36(3H, s), 3.48(3H, s), 3.55(3H, s), 3.81(3H, s), 3.91(3H, s), 5.10(1H, s), 6.98(2H, d, J=8 Hz), 7.13(1H, bs), 7.40(2H, d, J=8 Hz)
6a	262 (4.32), 290 (4.28), 408 (3.97), 430^{sh} (3.85)	1750, 1740, 1720, 1710	2.17(3H, bs), 3.20(3H, s), 3.48(3H, s), 3.77(3H, s), 3.80(3H, s), 3.87(6H, s), 5.15(1H, s), 6.61(1H, bs), 7.0—7.4(5H, m)
6b	263 (4.26), 300 (4.21), 410 (3.94), 430^{sh} (3.82)	1755, 1735, 1715	2.20(3H, bs), 2.26(3H, s), 3.26(3H, s), 3.50(3H, s), 3.79(3H, s), 3.82(3H, s), 3.88(6H, s), 5.16(1H, bs), 6.69(1H, bs), 6.90(2H, d, J=8 Hz), 7.23(2H, d, J=8 Hz)
8a	368 (3.56)	1755, 1730, 1720, 1700	2.38(3H, bs), 3.48(3H, s), 3.54(3H, s), 3.68(3H, s), 3.73(3H, s), 3.76(3H, s), 3.87(3H, s), 6.72(1H, s), 6.96(1H, bs),7.15—7.6(5H, m)
8b	362 (3.66)	1740, 1730, 1710	2.27(3H, s), 2.38(3H, bs), 3.47(3H, s), 3.54(3H, s), 3.63(3H, s), 3.70(3H, s), 3.74(3H, s), 3.82(3H, s), 6.65(1H, s), 6.92(1H, bs), 7.07(2H, d, J=8 Hz), 7.28(2H, d, J=8 Hz)



10a,c



11a

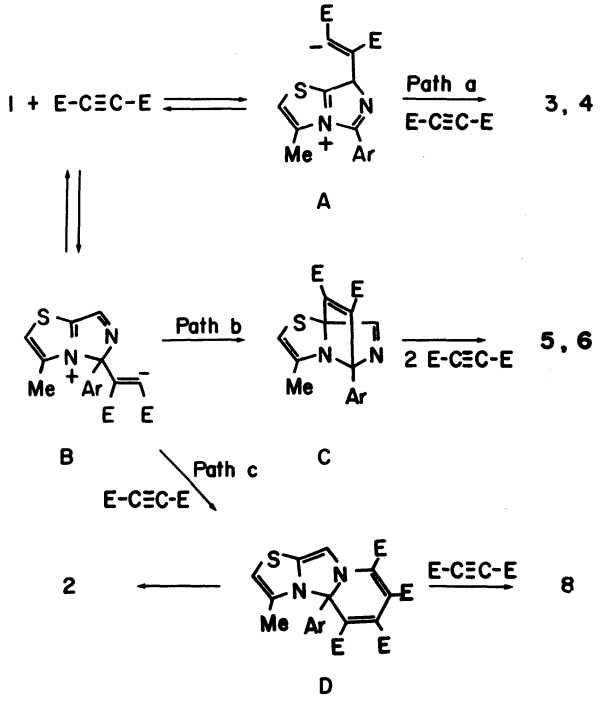
indicative of hydrogen-bonding with the CO_2Me absorbing at 1695 cm^{-1}. This compound, though resistant toward acetylation, was found to react with methyl fluorosulfate giving the corresponding *N*-methyl derivative (**11a**). These data are accounted for in terms of the structure **10a**.

Plausible mechanisms for the reactions of imidazo-[5,1-*b*]thiazoles (**1**) with acetylenic esters are given in Scheme 1. Electrophilic attack of the acetylenic ester would occur at either C-5 or C-7 of **1**. The attack at C-7 gives an intermediate **A**, from which the 1:2-cycloadducts **3** and **4** are formed (Path a). When the attack takes place at C-5, the position presumed to be more electron-rich than C-7 due to electron release from the sulfur and the nitrogen at the 4-position, an intermediate **B** is generated. Cyclization of **B** to **C**

Table 3. ^{13}C NMR spectra of **3a**, **4a**, **4b**, **5a**, and **6a**

Carbon	3a	4a	4b	5a	6a
2	121.2d	117.5d	117.4d	118.5d	117.4d
3	152.8s	154.9s	154.8s	153.6s	152.9s
5	166.6s	166.8s	166.9s	71.2s	72.4s
6a	47.1d	52.6d	47.4d	—	—
7	141.3s	146.7s	147.0s	152.9s	148.8s
8	137.8s	134.5s	131.8s	137.4s	133.3s
9	138.8s	139.6s	139.4s	137.8s	138.3s
10	154.8s	150.5s	150.2s	144.8s	146.5s
10a	118.9s	116.4s	116.1s	57.9d	56.0d
10b	—	—	—	113.1s	114.2s
11	—	—	—	124.9s	126.6s
12	—	—	—	127.4s	126.8s
Me	17.1q	17.4q	17.3q	16.7q	16.6q
			21.5q		
OMe	52.3q	52.9q	52.6q	51.7q	51.5q
	52.9q[a]	53.0q[b]	52.9q[b]	51.8q	51.6q
		53.2q	53.2q	52.2q	52.3q
				52.7q[b]	52.6q
				52.8q	52.8q
					53.6q
C=O	163.7s	164.1s	163.8s	161.7s	162.8s
	164.6s	164.3s	164.3s	163.3s	163.5s
	167.0s	166.6s	166.7s	163.8s	165.4s
	167.8s	166.9s	167.2s	164.6s	166.8s
				166.1s	168.8s
				168.6s	170.2s
Ph	128.1d[b]	128.8d	129.7d[b]	127.0s	126.9s
	128.3d[b]	129.0d[b]	129.8d[b]	127.1d[b]	127.3d[b]
	129.0s	129.0d[b]	131.6s	127.6d[b]	129.6d
	129.7d	132.3d	139.4s	128.7d	130.4d[b]

a) Three peaks degenerate. b) Two peaks degenerate.

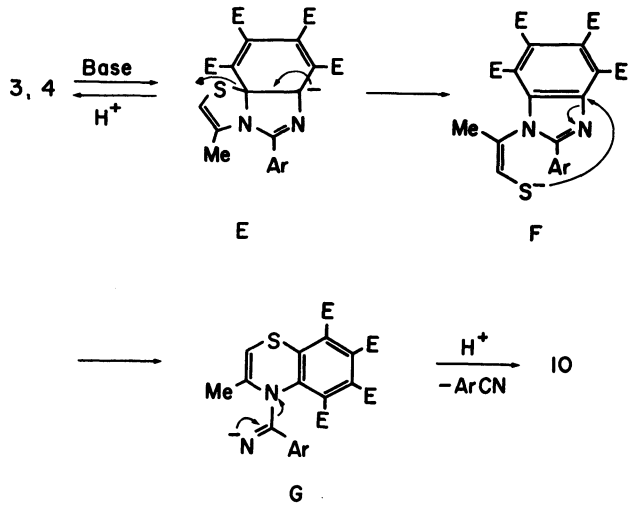


Scheme 1.

followed by a 1,4-dipolar cycloaddition[3] affords the 1:3-cycloadducts **5** and **6** (Path b). Alternatively, cycloaddition of **B** with an additional acetylenic ester would lead to an intermediate **D**, which undergoes either the Michael-type addition in a nonpolar solvent to produce **8** or fragmentation in polar medium to the pyridine **2** (Path c).

Conceivably, an equilibrium will be established between **1** and the dipolar species **A** and **B**. As cyclization of **A** leading to **3** or **4** (Path a) would be unfavorable because the acetylenic ester has to approach from a sterically crowded site, formation of **3** or **4** will require higher temperature. By comparison with the Path a, the pathways b and c would be easier to proceed because neither cyclizations of **B** to **C** nor **D** is sterically disturbed by the C-3-Me or C-5-Ar groups.

A likely mechanism for the base-promoted fragmentation of **3** or **4** to the benzothiazine (**10**) is depicted in Scheme 2. Abstraction of the hydrogen at C-6a by base gives rise to a carbanion **E** and a sulfide anion **F**, successively. Cyclization of the sulfide anion **F** leads to a new anion **G**, which subsequently undergoes loss of a nitrile followed by protonation to give **10**.



Scheme 2.

Experimental

Melting points were uncorrected. IR spectra were determined as Nujol mulls unless otherwise stated. ^1H NMR spectra were recorded in $CDCl_3$ with Me_4Si as internal standard with a Hitachi R-24B (60 MHz) or JEOL FX-100 (100 MHz) spectrometers, and ^{13}C NMR spectra with a Varian FT-80A instrument (20 MHz; solutions in $CDCl_3$ with Me_4Si as internal standard). Mass spectra were determined with a Hitachi M-80 spectrometer by means of either electron impact or field desorption ionization methods. Kieselgel 60 was used for chromatography.

3-Methyl-5-phenylimidazo[5,1-*b*]thiazole (**1a**) was prepared as reported.[10] **1a**: mp 105—106 °C (lit,[10] 106 °C), UV_{max} (chloroform) 303 nm (log ε 4.08), IR 775 and 700 cm^{-1} (phenyl), ^1H NMR δ=2.02 (3H, d, J=1 Hz), 6.27 (1H, q, J=1 Hz), 7.04 (1H, s), 7.15—7.6 (5H, m). Found: C, 67.20; H, 4.75; N, 13.12; S, 14.88%.

*3-Methyl-5-(*p*-tolyl)imidazo[5,1-*b*]thiazole (**1b**).* A mix-

Table 4. Analytical data of **2**, **3**, **4**, **5**, **6**, and **7**

Compound	Appearance	Mp θ_m/°C	Formula	Found (Calcd) (%) C	H	N	S	MS *m/e* (M^+)
2a	Colorless needles[a]	126—128[e]	$C_{19}H_{17}NO_8$	58.47 (58.91)	4.50 (4.42)	3.35 (3.62)		387
2b	Colorless needles[b]	85—87	$C_{20}H_{19}NO_8$	59.75 (59.85)	4.82 (4.77)	3.55 (3.49)		
3a	Yellow prisms[c]	191—193	$C_{24}H_{22}N_2O_8S$	57.90 (57.82)	4.42 (4.45)	5.61 (5.62)	6.46 (6.43)	498
3b	Yellow prisms[c]	176—178	$C_{25}H_{24}N_2O_8S$	58.82 (58.59)	4.79 (4.72)	5.52 (5.46)	6.12 (6.26)	
3c	Yellow needles[b]	140—142	$C_{28}H_{30}N_2O_8S$	60.82 (60.64)	5.53 (5.45)	5.16 (5.05)	5.66 (5.78)	554
4a	Yellow needles[c]	151—152	$C_{24}H_{22}N_2O_8S$	57.93 (57.82)	4.46 (4.45)	5.55 (5.62)	6.43 (6.43)	498
4b	Yellow needles[c]	196—198	$C_{25}H_{24}N_2O_8S$	58.77 (58.59)	4.63 (4.72)	5.44 (5.46)	6.21 (6.26)	
4c	Yellow needles[d]	57—61	$C_{28}H_{30}N_2O_8S$	60.78 (60.64)	5.62 (5.45)	5.28 (5.05)	5.48 (5.78)	554
5a	Yellow prisms[c]	180—181	$C_{30}H_{26}N_2O_{12}S$	56.48 (56.25)	4.46 (4.41)	4.33 (4.37)	5.30 (5.00)	640
5b	Yellow needles[d]	137—139	$C_{31}H_{30}N_2O_{12}S$	57.14 (56.88)	4.84 (4.62)	4.06 (4.28)	4.75 (4.90)	
6a	Yellow prisms[c]	180—181	$C_{30}H_{28}N_2O_{12}S$	56.12 (56.25)	4.54 (4.41)	4.09 (4.37)	4.81 (5.00)	
6b	Yellow prisms[d]	200—201	$C_{31}H_{30}N_2O_{12}S$	57.09 (56.88)	4.58 (4.62)	4.34 (4.28)	5.17 (4.90)	
8a	Yellow needles[c]	118—121	$C_{30}H_{28}N_2O_{12}S$	56.31 (56.25)	4.45 (4.41)	4.30 (4.37)	4.95 (5.00)	
8b	Yellow needles[c]	179—181	$C_{31}H_{30}N_2O_{12}S$	56.69 (56.88)	4.55 (4.62)	4.09 (4.28)	5.12 (4.90)	

a) Recrystallized from petroleum ether. b) Recrystallized from ligroine. c) Recrystallized from ethanol. d) Recrystallized from ligroine–dichloromethane. e) Lit,[6] mp 128—129 °C.

tuer of 4-methyl-2-(*p*-toluoylaminomethyl)thiazole (7.4 g) and $POCl_3$ (25 ml) in dry benzene (50 ml) was heated under reflux for 6 h and evaporated under reduced pressure. Water was added to the residue and the solution was neutralized with NH_3 to deposit **1b** (4.0 g, 58%), which crystallized as colorless prisms from ligroine [mp 123—124 °C, UV_{max} (chloroform) 300 nm (log ε 4.14), IR 825 cm^{-1} (phenyl), ^1H NMR δ=2.07 (3H, d, J=1 Hz), 2.42 (3H, s), 6.36 (1H, q, J=1 Hz), 7.10 (1H, s), 7.20 (2H, d, J=8 Hz), 7.42 (2H, d, J=8 Hz). Found: C, 68.50; H, 5.14; N, 12.13; S, 14.14%. Calcd for $C_{13}H_{12}N_2S$: C, 68.39; H, 5.30; N, 12.27; S, 14.04%].

General Procedure for the Reactions of ***1*** *with DMAD.* A mixture of **1** (2.0 mmol), DMAD, and the solvent (30 ml) was allowed to react under the conditions specified in Table 1 and evaporated to dryness under reduced pressure. Chromatography of the residue with benzene, benzene–chloroform (1 : 1), and chloroform, successively, gave the compounds, **1**, **2**, **3**, **4**, **5**, and **6**, in the order. Analytical data are collected in Table 4 and spectroscopic data in Tables 2 and 3.

Reaction of ***1a*** *with DEAD.* A mixture of **1a** (2.0 mmol), DEAD, and the solvent (30 ml) was allowed to react under the conditions specified in Table 1 and evaporated to dryness under reduced pressure. Chromatography of the residue with benzene–chloroform (1 : 1) gave **3c** and **4c**, successively. Analytical data are given in Table 4 and spectroscopic data in Table 2.

Epimerization of ***3*** *and* ***4****.* *a)*: **3a** (0.150 g) was added to a sodium methoxide solution prepared from sodium (0.069 g) and abs methanol (30 ml). The mixture was heated under reflux, cooled, acidified with dil hydrochloric acid, and extracted with chloroform. The extracts were washed with water, dried (Na_2SO_4), and evaporated. Chromatography of the residue with benzene–chloroform (2:1) gave **3a** followed by **4a**. Elution with chloroform gave **10a**, which crystallized as yellow needles from benzene and had mp 223—225 °C, UV_{max} (ethanol) 238 nm (log ε 4.28), 275 (4.42), 394 (4.37), IR (chloroform) 2300—2850 (NH), 1730, 1715, and 1695 cm^{-1} (C=O), ^1H NMR δ=2.41 (3H, d, J=0.5 Hz), 3.83 (6H, s), 3.90 (7H, s) (one proton is exchangeable), 6.74 (1H, q, J=0.5 Hz), δ (CF_3CO_2H)=2.72 (3H, bs), 3.93 (6H, s), 4.18 (6H, s), 7.70 (1H, bs), 10.47 (1H, bs) (exchangeable). Found: C, 51.94; H, 4.23; N, 3.55; S, 8.16%. Calcd for $C_{17}H_{17}NO_8S$: C, 51.64; H, 4.33; N, 3.54; S, 8.11%. MS *m/e* (rel intensity) 395 (9%, M^+), 363 (61), 332 (100). Treatment of **8a** with methyl fluorosulfate in $CDCl_3$ in an NMR tube produced **11a**; ^1H NMR δ=2.50 (3H, bs), 3.87 (12H, s), 3.96 (3H, s), 6.87 (1H, bs). Yields of **3a**, **4a**, and **8a** are given in Table 5.

b): A mixture of **3a** (0.100 g) and DBU (1 drop) in dry benzene (5 ml) was heated under reflux for 1 h and evaporated under reduced pressure. The residue was chromatographed with benzene–chloroform (1 : 1) to give **3a**, **4a**, and **8a**, successively, whose yields are given in Table 5.

c): A mixture of **3c** (0.300 g) and a sodium ethoxide solution prepared from sodium (0.124 g) and abs ethanol (30 ml) was heated under reflux for 5 h and worked up as dercribed above. Elution with benzene–chloroform (2 : 1) gave **3c**

Table 5. Conditions and yields for the reactions of **3** and **4** with base

Substrate	Conditions	Time/h	(Yield/%)		
3a	NaOMe/MeOH	1	**3a**(68)	**4a**(24)	**10a**(7)
3a	NaOMe/MeOH	4	**3a**(26)	**4a**(4)	**10a**(62)
3a	DBU/Benzene	1	**3a**(70)	**4a**(14)	**10a**(13)
4a	NaOMe/MeOH	1	**3a**(65)	**4a**(25)	**10a**(5)
4b	NaOMe/MeOH	1	**3b**(17)	**4b**(54)	**10a**(17)
4b	NaOMe/MeOH	4	**3b**(5)	**4b**(18)	**10a**(45)

(0.050 g, 17%) followed by **4c** (0.055 g, 18%). Elution with chloroform gave **8c** (0.030 g, 12%), which crystallized as yellow needles from ligroine–dichloromethane and had mp 155—156 °C, UV_{max} (ethanol) 232 nm (log ε 4.50), 271 (4.55), 395 (4.48). IR 2850—2300 (NH), 1725, 1715, and 1695 cm^{-1} (C=O). ^1H NMR δ=1.32 (6H, t, J=7 Hz), 1.35 (6H, *t*, J=7 Hz), 2.45 (3H, d, J=0.5 Hz), 3.47 (1H, s) (exchangeable), 4.25 (4H, q, J=7 Hz), 4.32 (4H, q, J=7 Hz), 6.62 (1H, q, J=0.5 Hz). Found: C, 55.72; H, 5.45; N, 3.18; S, 7.15%, M^+ *m/e* 451. Calcd for $C_{21}H_{25}NO_8S$: C, 55.86; H, 5.58; N, 3.10; S, 7.10%, M 451.

We thank Dr. Masafumi Yasunami, Tohoku University, and Akira Mori, Kyushu University, for NMR spectral determinations.

References

1) Part IV, N. Abe, T. Nishiwaki, T. Omori, and E. Harada, *Bull. Chem. Soc. Jpn.*, **55**, 200 (1982).
2) J. Elguero, R. M. Claramunt, and A. J. Summers, *Adv. Heterocycl. Chem.*, **22**, 183 (1978); C. A. Ramsden, *Tetrahedron*, **33**, 3203 (1977); H. Volz and H. Kowarsch, *Heterocycles*, **7**, 1319 (1977); Th. Pyl and K.-H., Wunsch, *Z. Chem.*, **5**, 361 (1965).
3) R. Huisgen, "Topics in Heterocyclic Chemistry," ed by R. N. Castle, Wiley, New York (1969), p. 223.
4) N. Abe, T. Nishiwaki, and N. Komoto, *Bull. Chem. Soc. Jpn.*, **53**, 3308 (1980).
5) N. Abe and T. Nishiwaki, *Heterocycles*, **16**, 537 (1981).
6) R. Huisgen and K. Herbig, *Justus Liebigs Ann. Chem.*, **688**, 98 (1965).
7) Earlier we incorrectly proposed the 8a*H*-1,4-benzothiazine structure for this compound: N. Abe, T. Nishiwaki, and K. Ikeda, 14th Symposium on Nonbenzenoid Chemistry, Okayama, October 1981, Abstr. No. 1X05. The structure is now revised as shown.
8) K. T. Potts and J. L. Marshall, *J. Org. Chem.*, **41**, 129 (1976).
9) O. Ceder and B. Beijer, *Tetrahedron*, **28**, 4341 (1972).
10) Th. Pyl, O. Seitz, and K. Steage, *Justus Liebigs Ann. Chem.*, **679**, 144 (1964).