Reactions of 3-Methylamino-5-phenylthiophene with α,β-Unsaturated Esters and α,β-Unsaturated Nitriles

Jong Seok Lee and Kyongtae Kim*

Department of Chemistry, Seoul National University, Seoul 151-742, Korea
Received July 7, 1999

Treatment of 3-methylamino-5-phenylthiophene with α,β-unsaturated esters, *i.e.*, methyl acrylate, (*E*)-methyl crotonate, diethyl fumarate, diethyl maleate and ethyl propiolate, in tetrahydrofuran for several days at reflux gave 1-methyl-3,4-dihydrothieno[2,3-*e*]pyridin-2-ones **4** and/or 1-methylthieno[2,3-*e*]pyridin-2-ones **5**, depending on the structure of the esters. On the other hand, the same reactions with α,β-unsaturated nitriles such as acrylonitrile and tetracyanoethene, gave the corresponding thiophenes **7** and **10** bearing 2-cyanoethyl and 1,2,2–tricyanoethenyl groups at C-2, respectively. The reaction with (*Z*)-1,2-dicyanoethene under the same conditions produced the corresponding thiophene **9** bearing the 1,2-dicyanoethenyl group and 1,2-dicyano-5-methylaminobiphenyl.

J. Heterocyclic Chem., **37**, 363 (2000).

Inter- and intra-molecular cyclizations of thiophenes bearing appropriate substituents have attracted considerable attention owing to their potential for the synthesis of a variety of cycloadducts [1]. However, there has been little investigation of such cyclization reactions involving 3-aminothiophene derivatives. A survey of the literature shows that there are two types of reactions, namely thermal [2 + 2] reactions and simple substitution reactions involving 3-(1-pyrrolidinyl)thiophenes. For example, 3-(1-pyrrolidinyl)thiophenes reacted with dimethyl acetylenedicarboxylate (DMAD) in an apolar solvent at -30° C gave a 1:1 reaction product of 2-thiabicyclo[3.2.0]hepta-3,6-dienes, which were ultimately converted to phthalic esters *via* thiepins, whereas in a polar solvent 6,7,7a,8-tetrahydro-5*H*-thieno[2,3-*b*]pyrrolizines were formed in 60 to 63% yields [2]. The reactions of 5-methyl- and 5-phenyl-3-(1-pyrrolidinyl)thiophene derivatives with diphenylketene in chloroform at room temperature gave 1:1 addition products, 2-diphenylacetyl-3-(1-pyrrolidinyl)thiophene derivatives in 17 and 16% yields [3]. Similarly, the reactions of 5-phenyl-3-(1-pyrrolidinyl)thiophene with β-nitrostyrene in chloroform at room temperature gave a 1:1 reaction product, 2-(2-nitro-1-phenyl)ethyl-3-(1-pyrrolidinyl)thiophene derivative in 53% yield [3]. Interestingly, treatment of 3-pyrrolidinothiophene with mesitonitrile oxide gave 3-(1-pyrrolidinyl)thienyl mesityl ketoxime [4]. No isoxazoline was detected. The results indicate that the activated 3-aminothiophenes react with either electron deficient dienophiles or dipolarophiles to give either cycloadducts or substitution products, which appear to be controlled by solvents, the electronic properties of the dienophiles and dipolarophiles, and other reaction conditions.

In order to obtain further insight into the intermolecular cycloaddition of 3-aminothiophenes, the reactions of a variety of α,β-unsaturated esters and α,β-unsaturated nitriles with 3-alkylamino-5-arylthiophenes **3**, prepared by methanolysis of 2-acetyl-3-alkylamino-5-arylthiophenes **2** in absolute methanol saturated with hydrogen chloride gas [5] have been studied (Scheme 1). The results are described in this report.

Results and Discussion.

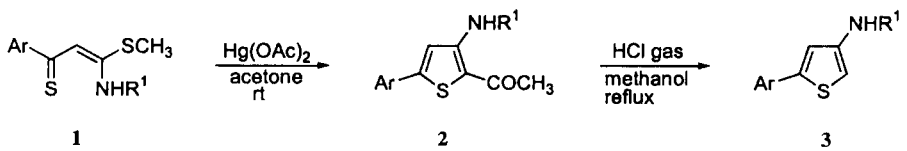
Synthesis of Compounds **3**.

Compounds **2** were dissolved in absolute methanol (5 ml) which was saturated with dried hydrogen chloride gas. Heating the solution at reflux, followed by a workup which gave **3**. Quantities of reactants, yields and melting points of **3** are summarized in Table 1, and the spectroscopic (^{1}H nmr, ir, ms) and analytical data are summarized in Table 2.

The Reactions of **3** with α,β-Unsaturated Esters.

α,β-Unsaturated esters (1.2 equivalents) were added to the solution of **3** in tetrahydrofuran. The progress of the reaction was monitored by thin layer chromatography (silica gel, ethyl acetate/*n*-hexane = 1:2), which indicated that the reactions proceeded very slowly at room temperature. It took several days for completion of the reactions even

Scheme 1



1 **2** **3**

Table 1

Quantities of Compounds **2** and Physical Data of Compounds **3**

Compound	Ar	R^1	mmole	Compound	Yield [a] %	Mp [b] (°C)
2a	Ph	CH_3	0.19	**3a**	98	40-43
2b	Ph	CH_2CH_3	0.16	**3b**	86	42
2c	4-$CH_3OC_6H_4$	CH_3	0.26	**3c**	79	122-124
2d	4-$CH_3OC_6H_4$	CH_2CH_3	0.33	**3d**	67	72-74
2e	3-ClC_6H_4	CH_3	0.19	**3e**	99	68-69
2f	3-ClC_6H_4	CH_2CH_3	0.16	**3f**	98	58-59
2g	3-$CH_3OC_6H_4$	CH_3	0.20	**3g**	67	oil
2h	3-$CH_3OC_6H_4$	CH_2CH_3	0.19	**3h**	93	oil

[a] Isolated yields; [b] From a mixture of dichloromethane and *n*-hexane.

at reflux temperature. Chromatography of the reaction mixture invariably showed a considerable number of unknown mixtures, which could not be separated by usual methods, and thieno compounds **4** and/or **5**, depending on the structure of the esters. Quantities of the reactants, reaction times, yields, melting points, and colors of the products **4** and **5** are summarized in Table 3 and their spectroscopic (ir, ^1H nmr, ms) and analytical data are summarized in Table 4.

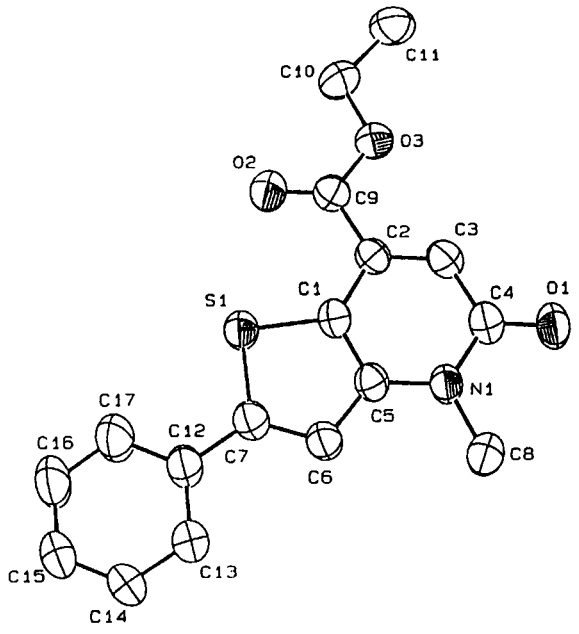


Figure 1. Molecular structure of compound **5b** with the atomic numbering scheme.

The derived structures of compounds **4** and **5** were based on the spectroscopic and analytical data. The X–Ray crystal structure of **5b** clearly shows the formation of thieno[2,3-*e*]pyridinone derivative rather than [2 + 2] cycloadducts shown in the foregoing examples [2]. Figure 1 shows the molecular structure of **5b** and the crystal and refinement parameters for compound **5b**; atomic coordinates and equivalent isotropic thermal parameters of non-hydrogen atoms of **5b** are listed in Tables 5 and 6, respectively. The selected bond distances and angles of **5b** are summarized in Tables 7 and 8, respectively.

In addition, Table 3 shows that the reactions of **3** with α,β-unsaturated esters produced two types of products, *i.e.*, 3,4-dihydrothieno[2,3-*e*]pyridin-2-ones **4** and thieno[2,3-*e*]pyridin-2-ones **5**. When compounds **4** had a substituent at C-4 such as **4c** (entry 3) and **4d** (entries 4 and 5), dehydrogenation occurred readily to give thieno-[2,3-*e*]pyridin-2-ones **5a** and **5b**, respectively. Dehydrogenation also occurred during the recrystallization process. Consequently, yields of **5** increased somewhat after recrystallization of **4**. However, it is uncertain what the oxidizing agent may be. It is envisaged that the gain in stabilization energy produced by forming a conjugate enone in the dihydropyridinone ring may be responsible for the ready formation of **5a** and **5b**.

The reactions of **3a** with diethyl fumarate (entry 4) and diethyl maleate (entry 5) gave the same products, *i.e.*, **4d** and **5b** with a different ratio. It is interesting to note that the reaction with ethyl propiolate (entry 6) yielding (*E*)-ethyl 3-(3-methylamino-5-phenyl-2-thienyl)propenoate (**6**) (8%) in addition to **5c** (11%) took sixteen days, whereas the same reaction with dimethyl acetylenedicarboxylate yielding **5d** (entry 7) took only three days for completion. Nonetheless, the yield of **5d** was more than 3-fold higher than that of **5c**. Compound **5d** was also obtained by the reaction with dimethyl 1,4-dimethyl-7-oxabicyclo[2.2.1]-

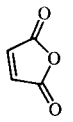
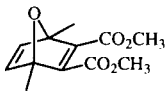
Table 2

IR, ^{1}H NMR and MS Spectroscopic and Analytical Data of Compounds **3**

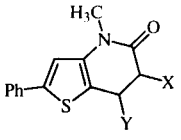
Compound	IR (cm^{-1})	^{1}H NMR (deuteriochloroform) δ (ppm)	MS m/z	Molecular Formula	Analysis % Calcd./Found C	H	N	S
3a	3392, 2912, 1562, 1491, 1082	2.84 (s, 3H, CH_3N), 5.92 (d, 1H, J = 1.5 Hz, HC=), 6.85 (d, 1H, J = 1.5 Hz, HC=), 7.24-7.40 (m, 3H, ArH), 7.54-7.60 (m, 2H, ArH)	189 (M^+, 100%)	$C_{11}H_{11}NS$	69.80 69.75	5.86 5.79	7.40 7.28	16.94 16.88
3b	3376, 2960, 1558, 1494, 1187	1.24 (t, 3H, J = 6.8 Hz, CH_3CH_2N), 3.13 (q, 2H, J = 7.2 Hz, CH_3CH_2N), 5.91 (s, 1H, HC=), 6.81 (s, 1H, HC=), 7.13-7.73 (m, 5H, ArH)	203 (M^+, 78%), 188 (100)	$C_{12}H_{13}NS$	70.89 70.91	6.45 6.52	6.89 6.82	15.77 15.69
3c	3392, 1597, 1562, 1504, 1280	2.86 (s, 3H, CH_3N), 3.65 (s, br, 1H, NH), 3.85 (s, 3H, CH_3O), 5.89 (d, 1H, J = 1.5 Hz, HC=), 6.76 (d, 1H, J = 1.5 Hz, HC=), 6.90-6.93 (m, 2H, ArH), 7.49-7.52 (m, 2H, ArH)	219 (M^+, 100%), 204 (47)	$C_{12}H_{13}NOS$	65.72 65.67	5.97 5.91	6.39 6.29	14.62 14.58
3d	3376, 1558, 1507, 1277, 1245	1.19 (t, 3H, J = 7.0 Hz, CH_3CH_2N), 3.06 (q, 2H, J = 7.1 Hz, CH_3CH_2N), 3.75 (s, 3H, CH_3O), 5.79 (s, 1H, HC=), 6.66 (s, 1H, HC=), 6.80 (d, 2H, J = 8.4 Hz, ArH), 7.39 (d, 2H, J = 8.5 Hz, ArH)	233 (M^+, 100%), 218 (94), 205 (20)	$C_{13}H_{15}NOS$	66.92 66.88	6.48 6.46	6.00 6.06	13.74 13.67
3e	3280, 1584, 1552, 1507, 1475	2.73 (s, 3H, CH_3N), 3.38 (s, br, 1H, NH), 5.84 (d, 1H, J = 1.6 Hz, HC=), 6.73 (d, 1H, J = 1.6 Hz, HC=), 7.13-7.19 (m, 2H, ArH), 7.30-7.33 (m, 1H, ArH), 7.43-7.44 (m, 1H, ArH)	223 (M^+, 100%), 207 (6)	$C_{11}H_{10}ClNS$	59.05 59.11	4.51 4.47	6.26 6.14	14.33 14.15
3f	3264, 2960, 1584, 1552, 1472	1.17 (t, 3H, J = 7.1 Hz, CH_3CH_2N), 3.03 (q, 2H, J = 7.1 Hz, CH_3CH_2N), 3.26 (s, br, 1H, NH), 5.85 (d, 1H, J = 1.5 Hz, HC=), 6.74 (d, 1H, J = 1.5 Hz, HC=), 7.11-7.20 (m, 2H, ArH), 7.31-7.34 (m, 1H, ArH), 7.43 (d, 1H, J = 1.6 Hz, ArH)	237 (M^+, 62%), 222 (100)	$C_{12}H_{12}ClNS$	60.62 60.73	5.09 5.18	5.89 5.75	13.49 13.32
3g	3392, 2928, 1594, 1565, 1491	2.86 (s, 3H, CH_3N), 3.65 (s, br, 1H, NH), 3.86 (s, 3H, CH_3O), 5.95 (d, 1H, J = 1.5 Hz, HC=), 6.87 (d, 1H, J = 1.5 Hz, HC=), 7.12-7.32 (m, 4H, ArH)	219 (M^+, 100%), 176 (16)	$C_{12}H_{13}NOS$	65.72 65.57	5.92 5.76	6.39 6.23	14.62 14.45
3h	3376, 2944, 1594, 1562, 1485	1.32 (t, 3H, J = 7.2 Hz, CH_3CH_2N), 3.21 (q, 2H, J = 7.1 Hz, CH_3CH_2N), 3.85 (s, 3H, CH_3O), 5.35 (s, 1H, HC=), 6.99 (s, 1H, HC=), 7.09-7.31 (m, 4H, ArH)	233 (M^+, 76%), 218 (100)	$C_{13}H_{15}NOS$	66.92 66.81	6.48 6.34	6.00 6.08	13.74 13.63

Table 3

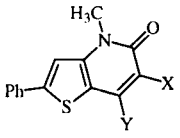
Quantities of Reactants and Reaction Times, Yields, Melting Points and Color of Products **4** and **5**

Entry	Compound mmole	α,β-Unsaturated Ester mmole	Reaction Time Day	Product	Yield [a] %	Mp (°C)	Color
1	**3a** 0.27	CH_2=$CHCO_2CH_3$ 0.33	10	**4a**	44	130-131 [c]	pale yellow
2	**3a** 0.27	CH_2=$C(CH_3)CO_2CH_3$ 1.35	16	**4b**	26	134-135 [c]	brown
3	**3a** 0.27	(*E*)-CH_3CH=$CHCO_2CH_3$ 0.54	10	**4c**	10	oil	yellow
				5a	9 (15) [b]	162-163 [d]	pale green
4	**3a** 0.27	(*E*)-$CH_3CH_2O_2CCH$=$CHCO_2CH_2CH_3$ 0.32	5	**4d**	8	129-130 [c]	pale yellow
				5b	37	152-153 [c]	yellow
5	**3a** 0.27	(*Z*)-$CH_3CH_2O_2CCH$=$CHCO_2CH_2CH_3$ 0.32	5	**4d**	39		
				5b	22 (51) [b]		
6	**3a** 0.27	HC ≡ $CCO_2CH_2CH_3$ 1.35	16	**5c**	11	167-168 [c]	white
7	**3a** 0.27	CH_3O_2CC ≡ CCO_2CH_3	3	**5d**	37	180-181 [c]	yellow
8	**3a** 0.26	 0.32	12	**5d**	11		
9	**3a** 0.27	 0.82	2.2	**5d**	39		
10	**3c** 0.23	CH_3O_2CC ≡ CCO_2CH_3 0.34	3	**5e**	79	204-205 [c]	yellow

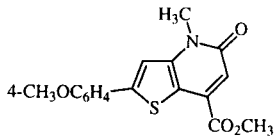
[a] Isolated yields; [b] A portion of compounds **4c** and **4d** were converted to **5a** and **5b**, respectively during recrystallization; [c] From a mixture of ethyl acetate and *n*-hexane; [d] From dichloromethane.



4a X = Y = H
4b X = CH_3, Y = H
4c X = H, Y = CH_3
4d X = H, Y = $CO_2CH_2CH_3$



5a X = H, Y = CH_3
5b X = H, Y = $CO_2CH_2CH_3$
5c X = Y = H
5d X = H, Y = CO_2CH_3



5e

Table 4

IR, ^{1}H NMR and MS Spectroscopic and Analytical Data of Compounds **4a-4d** and **5a-5e**

Compound	IR (cm^{-1})	^{1}H NMR (deuteriochloroform) δ (ppm)	Molecular Formula	Analysis % Calcd./Found C	H	N	S
4a	3072, 2912, 1658, 1638, 1414, 1350	2.79 (t, 2H, J = 7.6 Hz, CH_2CH_2), 2.97 (t, 2H, J = 7.5 Hz, CH_2CH_2), 3.35 (s, 3H, CH_3N), 6.99 (s, 1H, HC=), 7.27-7.41 (m, 3H, ArH), 7.54-7.57 (m, 2H, ArH)	$C_{14}H_{13}NOS$	69.10 68.95	5.39 5.27	5.76 5.67	13.18 13.22
4b	2912, 1658, 1568, 1456, 1414, 1347	1.34 (d, 3H, J = 6.7 Hz, CH_3CH), 2.65-2.84 (m, 2H, CH_2), 3.04 (m, 1H, CH_3CH), 3.36 (s, 3H, CH_3N), 6.99 (s, 1H, HC=), 7.26-7.41 (m, 3H, ArH) 7.54-7.57 (m, 2H, ArH)	$C_{15}H_{15}NOS$	70.01 70.17	5.87 5.76	5.44 5.29	12.46 12.51
4c	2961, 2926, 1673, 1564, 1421, 1345	1.37 (d, 3H, J = 6.8 Hz, CH_3CH), 2.41-2.55 (m, 2H, CH_2), 2.81-2.88 (m, 1H, CH_3CH), 3.36 (s, 3H, CH_3N), 7.01 (s, 1H, HC=), 7.40-7.47 (m, 3H, ArH), 7.53-7.68 (m, 2H, ArH)	$C_{15}H_{15}NOS$	70.01 69.89	5.87 6.03	5.44 5.26	12.46 12.38
4d	3088, 2976, 1715, 1661, 1459, 1414, 1347	1.24 (t, 3H, J = 7.1 Hz, $COCH_2CH_3$), 2.91 (dd, 1H, J = 7.1 Hz, J = 16.4 Hz, $CHCH_aH_b$), 2.99 (dd, 1H, J = 8.1 Hz, J = 16.4 Hz, $CHCH_aH_b$), 3.28 (s, 3H, CH_3N), 3.94 (m, 1H, $CHCO_2CH_2CH_3$), 4.17 (q, 2H, J = 7.2 Hz, $COCH_2CH_3$) 6.92 (s, 1H, HC=), 7.24-7.34 (m, 3H, ArH), 7.48-7.51 (m, 2H, ArH)	$C_{17}H_{17}NO_3S$	64.74 64.66	5.43 5.34	4.44 4.32	10.17 10.22
5a	3072, 2912, 1638, 1565, 1530, 1478	2.41 (s, 3H, CH_3), 3.75 (s, 3H, CH_3N), 6.43 (s, 1H, HC=), 7.40-7.50 (m, 4H, ArH, HC=), 7.68-7.71 (m, 2H, ArH)	$C_{15}H_{13}NOS$	70.56 70.42	5.13 5.19	5.49 5.43	12.56 12.48
5b	3088, 2928, 1712, 1632, 1526, 1478	1.37 (t, 3H, J = 7.1 Hz, $COCH_2CH_3$), 3.70 (s, 3H, CH_3N), 4.38 (q, 2H, J = 7.2 Hz, $COCH_2CH_3$), 7.15 (s, 1H, HC=), 7.18 (s, 1H, HC=), 7.32-7.41 (m, 3H, ArH), 7.62-7.65 (m, 2H, ArH)	$C_{17}H_{15}NO_3S$	65.16 65.33	4.82 5.53	4.47 4.29	10.23 10.26
5c	3072, 2912, 1635, 1526, 1469, 1392	3.69 (s, 3H, CH_3N), 6.52 (d, 1H, J = 9.4 Hz, HC=), 7.19 (s, 1H, HC=), 7.33-7.42 (m, 3H, ArH, HC=), 7.59-7.62 (m, 3H, ArH)	$C_{14}H_{11}NOS$	69.68 69.61	4.59 4.55	5.80 5.69	13.29 13.23
5d	3072, 2928, 1718, 1632, 1530, 1478	3.79 (s, 3H, CH_3N), 4.01 (s, 3H, CO_2CH_3), 7.22 (s, 1H, HC=), 7.27 (s, 1H, HC=), 7.41-7.49 (m, 3H, ArH), 7.70-7.74 (m, 2H, ArH)	$C_{16}H_{13}NO_3S$	64.20 64.24	4.38 4.54	4.68 4.57	10.71 10.64
5e	3088, 2928, 1718, 1638, 1530, 1482	3.73 (s, 3H, CH_3N), 3.84 (s, 3H, CH_3O), 3.97 (s, 3H, CO_2CH_3), 6.94 (d, 2H, J = 8.7 Hz, ArH), 7.11 (s, 1H, HC=), 7.14 (s, 1H, HC=), 7.61 (d, 2H, J = 8.7 Hz, ArH)	$C_{17}H_{15}NO_4S$	61.99 61.97	4.59 4.48	4.25 4.17	9.74 9.68

Scheme 2

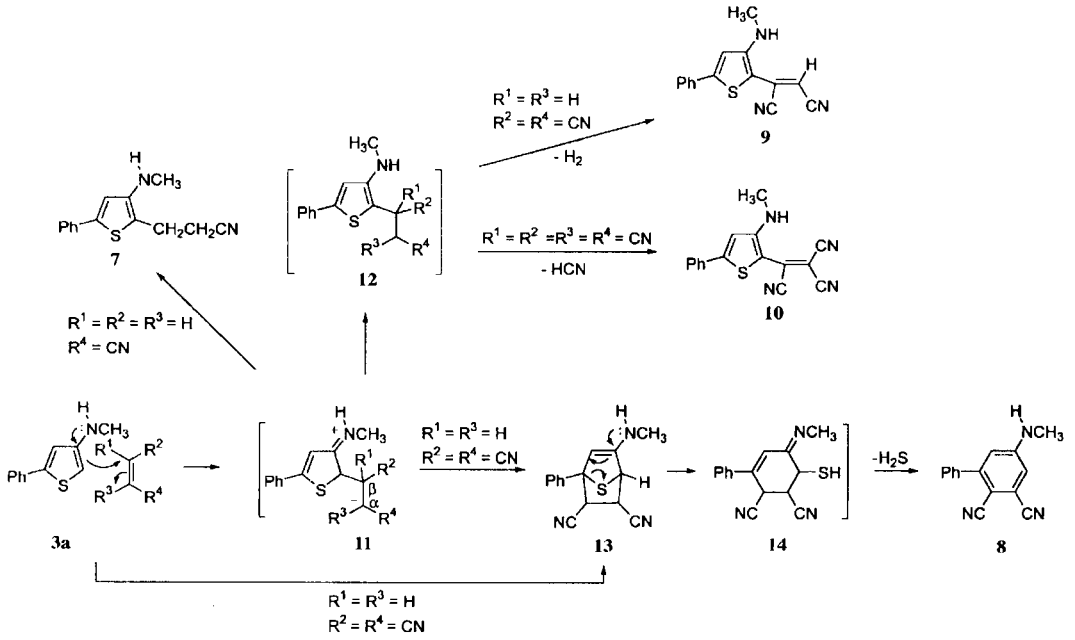


Table 5

Crystal and Refinement Parameters for Compound **5b**

Molecular Formula	$C_{17}H_{15}NO_3S$
Molecular weight	313.36
Color	Yellow
Crystal system	Triclinic
Space group	P1 bar (No. 2)
a, Å	10.618 (2)
b, Å	11.272 (2)
c, Å	20.056 (4)
α, deg	103.46 (2)
β, deg	92.44 (2)
γ, deg	100.19 (2)
V, Å^3	2288.9 (7)
Z	6
Density calculated, mg/mm^{-1}	1.364
Crystal size, mm	0.25 X 0.25 X 0.5
Absorption coefficient, mm^{-1}	0.224
F(000)	984
Index ranges	0<=h<=10, -13<=k<=13, -23<=l<=23
Reflection collected	6208
Independent reflections	5843 [R (int) = 0.0345]
Refinement method	Full-matrix least-squares on F^2
Data/restraints/parameters	5843/0/595
Goodness-of-fit on F^2	1.187
Final R indices [I>2σ (I)]	R_1 = 0.0489, wR_2 = 0.1366
R indices (all data)	R_1 = 0.0497, wR_2 = 0.1379
Largest diffraction peak and hole	0.330 and -0.340 e.A^{-3}

hepta-2,5-diene-2,3-dicarboxylate (entry 9). In view of the nearly identical yields of **5d** from both reactions (*cf.* entries 7 and 9), dimethyl acetylenedicarboxylate formed by retro-Diels-Alder reaction at high temperature is conceived to participate in the reaction with **3a** to give **5d**. The reaction of **3c** with dimethyl acetylenedicarboxylate gave **5e** in 79% yield (entry 10), which is a much higher yield than that of **5d** obtained from **3a** and dimethyl acetylenedicarboxylate for the same reaction time. Activation of position 2 of the thienyl moiety by the *para* methoxy group may be responsible for the increase in yield.

The Reaction of **3a** with α,β-Unsaturated Nitriles.

The reaction with acrylonitrile for five days under the same conditions as in the reactions with α,β-unsaturated esters gave 2-(2-cyanoethyl)thiophene derivative **7** in 61% yield (Scheme 2). However, treatment with (*Z*)-1,2-dicyanoethene under the same conditions gave 2,3-dicyano-5-methylaminobiphenyl **8** and 2-(1,2-dicyanoethenyl)-3-methylamino-5-phenylthiophene **9** in 6 and 14% yields, respectively. The reaction with tetracyanoethene (TCNE) was completed in 5 minutes yielding (3-methylamino-5-phenyl-2-thienyl)(cyano)methylidenemalononitrile **10** in 58% yield. The results clearly show the

Table 6

Positional and Equivalent Isotropic Thermal Parameters of Nonhydrogen Atoms for **5b**

Atom	X	Y	Z	U (eq)	Atom	X	Y	Z	U (eq)
S1	3404 (1)	4052 (1)	1514 (1)	51 (1)	C11	5483 (3)	6861 (3)	4839 (2)	74 (1)
C1	4037 (2)	5624 (2)	1790 (1)	47 (1)	C12	2698 (2)	3043 (2)	123 (1)	55 (1)
C2	4490 (2)	6334 (2)	2463 (1)	47 (1)	C13	2552 (3)	3112 (3)	-558 (2)	70 (1)
C3	4983 (2)	7556 (2)	2555 (1)	52 (1)	C14	2076 (4)	2058 (3)	-1067 (2)	51 (1)
C4	5033 (2)	8184 (2)	2005 (1)	53 (1)	C15	1731 (3)	929 (3)	-920 (2)	65 (1)
C5	4075 (2)	6191 (2)	1246 (1)	47 (1)	C16	1869 (4)	843 (3)	-260 (2)	74 (1)
C6	3612 (2)	5351 (2)	606 (1)	51 (1)	C17	2353 (4)	1887 (3)	258 (2)	55 (1)
C7	3222 (2)	4164 (2)	671 (1)	50 (1)	O1	5464 (2)	9301 (2)	2087 (1)	69 (1)
C8	4493 (3)	8057 (3)	788 (2)	70 (1)	O2	3930 (2)	4620 (2)	2966 (1)	69 (1)
C9	4387 (2)	5696 (2)	3043 (1)	51 (1)	O3	4853 (2)	6467 (2)	3646 (1)	59 (1)
C10	4761 (3)	5926 (3)	4239 (1)	65 (1)	N1	4542 (2)	7445 (2)	1359 (1)	50 (1)

enaminic activity of the 3-methylamino group of **3a**. In these reactions, no intermolecular cycloadducts analogous to **5** were isolated.

The formation of **9** and **10** can be explained by a Michael type of addition of **3a** to cyanoethene to give an intermediate **12** *via* the polar intermediate **11**. Dehydrogenation of **12** ($R^1 = R^3 = H$, $R^2 = R^4 = CN$) as in the formation of **5** yields **9**, whereas loss of hydrogen cyanide from **12** ($R^1 = R^2 = R^3 = R^4 = CN$) gives **10**. If the intermediate **11** undergoes an intramolecular cyclization to give a new intermediate **13** concomitant with cleavage of the C-S bond, an intermediate **14** would be produced. Aromatization by extrusion of hydrogen sulfide from **14** would give **8**.

Alternatively, cycloadduct **13** would be formed by a [4 + 2] cycloaddition of **3a**. Analogous types of reactions leading to benzene derivatives from reactive alkynes and thiophenes have been reported [7]. In cases where there is no cyano group at the β position to the cyano group such as in compound **7**, dehydrogenation does not take place. The spectroscopic (^1H nmr, ir, ms), analytical, and physical data for compounds **7**-**10** are summarized in Table 9.

In summary, the reactions of 3-methylamino-5-phenylthiophene **3a** with a variety of α,β-unsaturated esters in tetrahydrofuran at reflux gave 1-methyl-3,4-dihydrothieno[2,3-*e*]pyridin-2-ones **4**. However, when compounds **4** had a substituent at position **4**, dehydrogenation occurred readily to give 1-methylthieno[2,3-*e*]pyridin-2-ones **5**, presumably due to the gain in stabilization energy produced by forming a conjugate enone in the dihydropyridinone ring. It is envisaged that a Michael type of addition of **3a** to α,β-unsaturated esters, followed by intramolecular cyclization, yields **4**. However, the reactions with α,β-unsaturated nitriles generated products which are formed by a Michael type of addition reaction.

Table 7

Selected Bond Distances (Å) for **5b**

Atom 1	Atom 2	Distance	Atom 1	Atom 2	Distance
C1	S1	1.728 (2)	C5	N1	1.375 (3)
C1	C2	1.414 (3)	C6	C7	1.367 (3)
C1	C5	1.385 (3)	C7	C12	1.472 (3)
C2	C3	1.351 (3)	C8	N1	1.473 (3)
C2	C9	1.500 (3)	C9	O2	1.195 (3)
C3	C4	1.441 (4)	C9	O3	1.331 (3)
C4	O1	1.231 (3)	C10	O3	1.457 (3)
C5	C6	1.414 (3)	C10	C11	1.480 (4)

Table 8

Selected Bond Angles (degrees) for **5b**

Atom 1	Atom 2	Atom 3	Angle
C1	S1	C7	91.26(11)
C5	C1	C2	120.0(2)
C5	C1	S1	111.1(2)
C2	C1	S1	128.9(2)
C3	C2	C1	118.5(2)
C3	C2	C9	123.1(2)
C1	C2	C9	118.4(2)
C2	C3	C4	123.3(2)
O1	C4	N1	120.9(2)
O1	C4	C3	123.6(2)
N1	C4	C3	115.6(2)
N1	C5	C1	120.2(2)
N1	C5	C6	126.7(2)
C1	C5	C6	113.1(2)
C17	C12	C7	122.0(3)
O3	C10	C11	107.8(2)
O3	C9	C2	112.2(2)
O2	C9	C2	123.4(2)
O2	C9	O3	124.4(2)
C12	C7	S1	119.8(2)
C6	C7	S1	112.5(2)
C6	C7	C12	127.7(2)
C7	C6	C5	112.1(2)

Table 9

IR, ^{1}H NMR and MS Spectroscopic, Analytical, and Physical Data of Compounds **7-10**

Compound	Mp (°C)	IR [d] (cm^{-1})	^{1}H NMR (deuteriochloroform) δ (ppm)	MS m/z	Molecular Formula	Analysis Calcd./Found C	H	N	S
7	101-102 [a]	2240, 1622 1549, 1482, 1440	2.09-2.15 (m, 2H, CH_2), 2.25-2.50 (m, 3H, CH_2, CH), 3.40 (s, 3H, CH_3N), 6.77 (s, 1H, HC=), 7.43-7.53 (m, 3H, ArH), 7.63-7.67 (m, 2H, ArH) [e]	242 (M^+, 16%), 202 (100)	$C_{14}H_{14}N_2S$	69.39 69.36	5.82 5.78	11.56 11.49	13.23 13.12
8	181-182 [a]	2208, 1593, 1360	2.88 (d, 3H, J = 5.0 Hz, CH_3N), 4.58 (s, br, 1H, NH), 6.68 (d, 1H, J = 2.4 Hz, ArH), 6.80 (d, 1H, J = 2.3 Hz, ArH), 7.40-7.45 (m, 5H, ArH)	233 (M^+, 100%)	$C_{15}H_{11}N_3$	77.23 77.15	4.75 4.82	18.01 17.89	
9	155-156 [b]	2192, 1564, 1507, 1365	3.01 (d, 3H, J = 5.0 Hz, CH_3N), 5.40 (s, 1H, HC=), 5.52 (s, br, 1H, NH), 6.79 (s, 1H, CH=), 7.34-7.40 (m, 3H, ArH), 7.51-7.54 (m, 2H, ArH)	265 (M^+, 100%), 237 (36)	$C_{15}H_{11}N_3S$	67.90 67.79	4.18 4.32	15.84 15.73	12.09 11.97
10	240 [c]	2192, 1587, 1507, 1466, 1315	3.64 (s, 3H, CH_3N), 7.11 (s, 1H, HC=), 7.42-7.44 (m, 3H, ArH), 7.59-7.62 (m, 2H, ArH)	290 (M^+, 100%), 262 (16)	$C_{16}H_{10}N_4S$	66.19 65.23	3.47 3.35	19.30 19.45	11.04 10.87

[a] From ethyl acetate; [b] From dichloromethane; [c] Decomposed; [d] Recorded in potassium bromide; [e] Recorded in a mixture of deuteriodimethylsulfoxide and deuteriochloroform.

EXPERIMENTAL

Proton nuclear magnetic resonance spectra were recorded at 300 MHz in deuteriochloroform solution containing tetramethylsilane as an internal standard. Infrared spectra were recorded in potassium bromide or in thin films on potassium bromide plates. Mass spectra were obtained by electron impact at 70 eV. Elemental analyses were determined by the Korea Basic Science Institute. Column chromatography was performed using silica gel (70-230 mesh, Merck). 2-Acetyl-3-alkylamino-5-arylthiophenes **2** were prepared by methods in the literature [5]. The spectroscopic (ir, ^{1}H nmr), physical, and analytical data for **2** are summarized in Table 10.

General Procedure for the Preparation of 3-Alkylamino-5-arylthiophenes **3a-3h**.

Dried hydrogen chloride gas was bubbled into a solution of **2** in absolute methanol (5 ml), which was heated for four hours at reflux. The color of the solution turned from yellow to dark blue. Water (30 ml) was added to the cooled reaction mixture, which was extracted with dichloromethane (3 x 30 ml). Drying the extracts over magnesium sulfate, followed by removal of the solvent, gave a residue which was chromatographed on a silica gel column (2 x 10 cm). Elution with a mixture of ethyl acetate and *n*-hexane (1:2) gave **3**. Consult Table 1 for quantities of reactants, yields, and melting points of compounds **3** and Table 2 for the spectroscopic (ir, ^{1}H nmr, ms) and analytical data for compounds **3**.

General Procedure for the Reactions of **3** with α,β-Unsaturated Esters.

To a solution in **3** in tetrahydrofuran (5 ml) was added α,β-unsaturated ester. The mixture was heated for an appropriate time at reflux. Removal of the solvent *in vacuo* gave a residue, which was chromatographed on a silica gel column (1 x 30 cm). Elution with a mixture of ethyl acetate and *n*-hexane (1:2) gave unknown mixtures. Subsequent elution with the same solvent mixture (9:1) gave 3,4-dihydrothieno[2,3-*e*]pyridin-2-ones **4** and thieno[2,3-*e*]pyridin-2-ones **5**. Consult Table 3 for quantities of reactants, reaction times, yields, melting points, and colors of the products **4a-4d** and **5a-5e** and Table 4 for the spectroscopic (ir, ^{1}H nmr, ms) and analytical data for compounds **4a-4d** and **5a-5e**.

General Procedure for the Reactions of **3a** with α,β-Unsaturated Nitriles.

The same procedure as for the reactions with α,β-unsaturated esters was followed. The reaction of **3a** (50 mg, 0.26 mmole) with acrylonitrile (28 mg, 0.52 mmole) in tetrahydrofuran for five days at reflux gave brown 2-(2-cyanoethyl)-3-methylimino-5-phenyl-2,3-dihydro-thiophene (**7**) (39 mg, 61%) and unknown mixtures (28 mg). The reaction of **3a** (52 mg, 0.27 mmole) with fumaronitrile (26 mg, 0.33 mmole) in tetrahydrofuran for five days at reflux gave both brown 2,3-dicyano-5-methylaminobiphenyl (**8**) (4 mg, 6%) and red 2-(1,2-dicyanoethenyl)-3-methylamino-5-phenylthiophene (**9**) (10 mg, 14%).

The reaction of **3a** (51 mg, 0.26 mmole) with tetracyanoethene (41 mg, 0.32 mmole) in tetrahydrofuran for five minutes at room temperature gave red (3-methylamino-5-phenyl-2-thienyl)(cyano)methylidenemalononitrile (**10**) (44 mg, 58%) and unknown mixtures (39 mg).

Consult Table 9 for spectroscopic (ir, ^{1}H nmr, ms), physical, and analytical data for compounds **7-10**.

Table 10

IR and ^{1}H NMR Spectroscopic, Physical and Analytical Data for Compounds **2**

Compound	Mp [a] (°C)	Yield [b] %	IR [c] (cm^{-1})	^{1}H NMR (deuteriochloroform) δ (ppm)	Molecular Formula	Analysis % Calcd./Found C	H	N	S
2a	80-81	91	3315, 1620, 1575, 1421, 1377, 1217	2.28 (s, 3H, CH_3CO), 2.98 (d, 3H,J = 4.2 Hz, CH_3N), 6.78 (s, 1H, HC=), 7.28-7.35 (m, 3H, ArH), 7.55-7.58 (m, 2H, ArH), 8.15 (s, br, 1H, NH)	$C_{13}H_{13}NOS$	67.50 67.42	5.66 5.61	6.06 6.13	13.86 13.78
2b	77-78	86	3329, 1624, 1571, 1368, 1223	1.26 (t, 3H, J = 7.2 Hz, CH_3CH_2N), 2.32 (s, 3H, CH_3CO), 3.36 (quintet, 2H, J = 7.2 Hz, CH_3CH_2N), 6.82 (s, 1H, HC=), 7.35-7.40 (m, 3H, ArH), 7.63-7.68 (m, 2H, ArH), 8.16 (s, br, 1H, NH)	$C_{14}H_{15}NOS$	68.54 68.67	6.16 6.08	5.71 5.58	13.07 13.21
2c	67-68	50	3343, 1612, 1565, 1378, 1255, 1032	2.36 (s, 3H, CH_3CO), 3.04 (d, 3H, J = 5.2 Hz, CH_3N), 3.86 (s, 3H, CH_3O), 6.77 (s, 1H, HC=), 6.91-6.96 (m, 2H, ArH), 7.58-7.62 (m, 2H, ArH), 8.12 (s, br, 1H, NH)	$C_{14}H_{15}NO_2S$	64.34 64.28	5.79 5.63	5.36 5.27	12.27 12.30
2d	41-42	60	3302, 1612, 1576, 1261, 1185, 1032	1.26 (t, 3H, J = 8.6 Hz, CH_3CH_2N), 2.36 (s, 3H, CH_3CO), 3.37 (quintet, 2H, J = 8.6 Hz, CH_3CH_2N), 3.85 (s, 3H, CH_3O), 6.77 (s, 1H, HC=), 6.90-6.97 (m, 2H, ArH), 7.55-7.62 (m, 2H, ArH), 8.19 (s, br, 1H, NH)	$C_{15}H_{17}NO_2S$	65.43 65.35	6.22 6.25	5.09 4.98	11.64 11.55
2e	92-93	92	3313, 1600, 1555, 1367, 998, 774	2.35 (s, 3H, CH_3CO), 3.01 (d, 3H, J = 5.2 Hz, CH_3N), 6.82 (s, 1H, HC=), 7.30-7.34 (m, 2H, ArH), 7.47-7.50 (m, 1H, ArH), 7.60 (s, 1H, ArH), 8.07 (s, br, 1H, NH)	$C_{13}H_{12}ClNOS$	58.75 58.83	4.55 4.51	5.27 5.32	12.07 12.18
2f	58-59	84	3309, 1600, 1554, 1453 1382, 944 774	1.29 (t, 3H, J = 7.2 Hz, CH_3CH_2N), 2.35 (s, 3H, CH_3CO), 3.34 (quintet, 2H, J = 7.2 Hz, CH_3CH_2N), 6.83 (s, 1H, HC=), 7.30-7.34 (m, 2H, ArH), 7.47-7.50 (m, 1H, ArH), 7.59 (m, 1H, ArH), 8.12 (s, br, 1H, NH)	$C_{14}H_{14}ClNOS$	60.10 60.22	5.04 4.96	5.01 5.11	11.46 11.32
2g	50-51	90	3330, 1602, 1553, 1378, 1268, 1175, 780	2.36 (s, 3H, CH_3CO), 3.05 (d, 3H, J = 5.2 Hz, CH_3N), 3.86 (s, 3H, CH_3O), 6.86 (s, 1H, HC=), 6.88-6.97 (m, 1H, ArH), 7.11-7.34 (m, 3H, ArH), 8.06 (s, br, 1H, NH)	$C_{14}H_{15}NO_2S$	64.34 64.46	5.79 5.92	5.36 5.51	12.27 12.03
2h	liquid	81	3322, 1604, 1565, 1479, 1170, 1045, 775	1.31 (t, 3H, J = 7.2 Hz,, CH_3CH_2N), 2.37 (s, 3H, CH_3CO), 3.37 (quintet, 2H, J = 7.2 Hz, CH_3CH_2N), 3.87 (s, 3H, CH_3O), 6.86 (s, 1H, HC=), 6.87-6.99 (m, 1H, ArH), 7.17-7.40 (m, 3H, ArH), 8.15 (s, br, 1H, NH)	$C_{15}H_{17}NO_2S$	65.43 65.28	6.22 6.27	5.09 4.96	11.64 11.52

[a] From a mixture of dichloromethane and *n*-hexane; [b] Isolated yields; [c] Recorded in potassium bromide.

Crystallographic and refinement parameters for compound **5b** are summarized in Table 5. The data were collected by an Enraf-Nomius CAD4 diffractometer using graphite-monochromated M_o-K_α radiation. The structure was resolved by direct methods and subsequent Fourier maps. Refinements were carried out by full-matrix least-squares techniques. Non-hydrogen atoms were anisotropically refined. Atomic scattering factors were taken from International Tables for X-ray Crystallography, Vol **IV**, 1974. All calculations and drawings were performed using a Micro VAX II computer with the SDP system.

Acknowledgement.

The authors are grateful to KOSEF (project 981-0302-011-2) for financial support of this work.

REFERENCES AND NOTES

[1a] S. Rajappa, Comprehensive Heterocyclic Chemistry, A. R. Katritzky and C. W. Rees, eds, Pergamon Press, New York, 1984, Vol **4**, pp 741-861; [b] S. Rajappa and M. V. Natekar, Comprehensive Heterocyclic Chemistry II, A. R. Katritzky, C. W. Rees and E. F. V. Scriven, eds, Elsevier Science, New York, 1996, Vol **2**, pp 491-605.

[2a] H. Biere, C. Herrmann and G.-A. Hoyer, *Chem. Ber.*, **111**, 770 (1978); [b] D. N. Reinhoudt, G. Okay and W. P. Trompenaars, *Tetrahedron Letters*, 1529 (1979).

[3] H. C. Mutreja and D. N. Reinhoudt, *Recl. Trav. Chim. Pays-Bas.*, **99**, 241 (1980).

[4] D. N. Reinhoudt and C. G. Kouwenhoven, *Recl. Trav. Chim. Pays-Bas.*, **93**, 321 (1974).

[5] B. S. Kim, K. S. Choi and K. Kim, *J. Org. Chem.*, **63**, 6086 (1998).

[6] Reference [1a] p 788.

[7a] H. Wynberg and R. Helder, *Tetrahedron Letters*, 605 (1972); [b] H. J. Kuhn and K. Gollnick, *Tetrahedron Letters*, 1909 (1972); [c] H. J. Kuhn and K. Gollnick, *Chem. Ber.*, **106**, 674 (1973).