Ring Transformation of 3-Hydroxy-1,2,5- and -1,2,4-thiadiazoles and -isothiazoles into Isothiazole, Thiazole and Thiophene Derivatives

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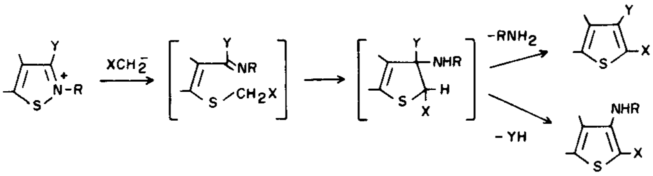
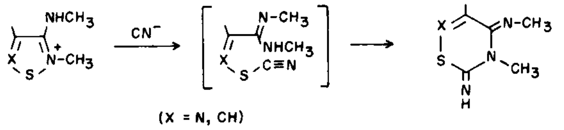
Received March 1, 1985

Ring transformation of 3-hydroxy-1,2,5-thiadiazole (**1**), 3-hydroxy-1,2,4-thiadiazole (**14**), and 3-hydroxyisothiazole (**18**) by the reaction with acetic anhydride in the presence of DBU afforded isothiazoles **2-5** and **13**, thiazoles **15** and **16** and thiophenes **21-25**, respectively. The reaction of **1** with propionic anhydride gave isothiazole **13**. The formation pathway of the products is mentioned.

J. Heterocyclic Chem., **22**, 1497 (1985).

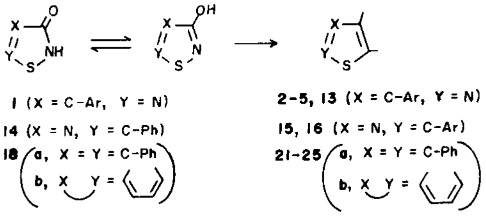
Recently, ring transformations of isothiazolium and 1,2,5-thiadiazolium salts were reported [1-3]. In both cases, a nucleophilic attack of an anion on the sulfur atom of the ring caused ring opening which was followed by ring closure into a new heterocyclic system.





(X = N, CH)

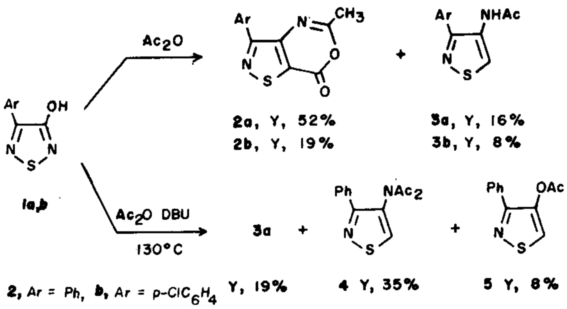
We now report the conversion of five-membered heterocycles having a 3-hydroxyisothiazole skeleton into five-membered heterocycles bearing one less nitrogen atom in a newly constructed ring. Namely, the transformation of 1,2,5-thiadiazole **1** into isothiazoles **2-5** and **13**, 1,2,4-thiadiazole **14** into thiazoles **15** and **16** and isothiazole **18** into thiophenes **21-25**, respectively, is described below.



Results and Discussion.

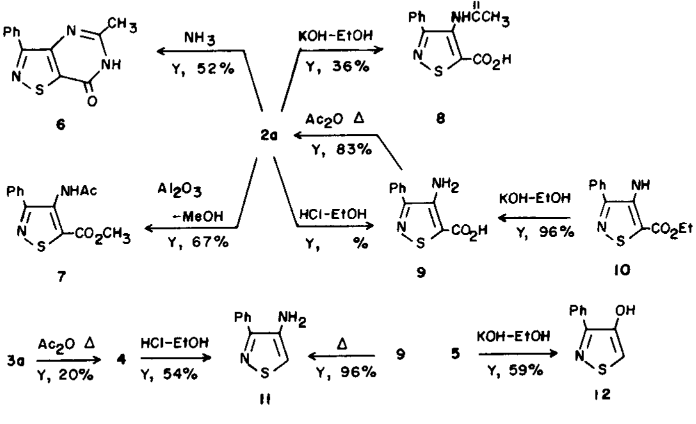
Though **1** is inert toward acetic anhydride at 100°, a slightly exothermic reaction occured when a mixture of **1** and acetic anhydride was treated with DBU at room temperature. The initially colorless reaction mixture became dark green, and in a few minutes, colorless needles of **2** precipitated. Column chromatography of the filtrate afforded **3**. When the reaction of **1a** was carried out at 130° for one hour, **3a**, **4** and **5** were obtained. Their yields are shown in Scheme 1.

Scheme 1



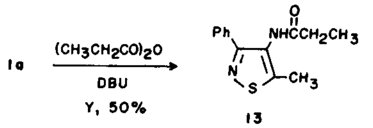
The structures of **2**, **3**, **4** and **5** were determined on the basis of chemical conversions which are summarized in Scheme 2. Treatment of **2a** with ammonia gave **6** in 52% yield and with alumina in methanol gave **7** in 67% yield. Hydrolysis of **2a** in ethanolic potassium hydroxide afforded **8**, while **9** was obtained in the hydrolysis in ethanolic hydrochloric acid. An authentic specimen of **9** was prepared by the hydrolysis of the already known ester **10** [4] in refluxing ethanoic potassium hydroxide in quantitative

Scheme 2

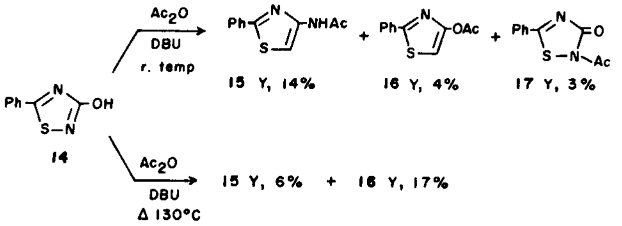


yield. Cyclization of **9** with acetic anhydride at 70° afforded **2a** in 83% yield. Thus, the structure of **2a** was established as 3-phenyl-4-methyl-6*H*-isothiazolo[4,5-*d*]-1,3-oxazin-6-one. Acetylation of **3a** gave **4a** in 20% yield and the hydrolysis of **4a** in etanolic hydrochloric acid afforded 3-phenyl-4-aminoisothiazole (**11**) which is identical with the pyrolytic decarboxylation product of **9**. Hydrolysis of **5** in alkaline media gave 3-phenyl-4-hydroxyisothiazole (**12**) [5].

The reaction of **1a** with propionic anhydride at room temperature gave the expected **13** in 50% yield. The reaction with succinic anhydride did not proceed at room temperature. When the mixture was heated at 70-80°, an explosive reaction occured, giving only tars.



The reaction of 3-hydroxy-5-phenyl-1,2,4-thiadiazole (**14**) with acetic anhydride also afforded the expected thiazoles **15** and **16** [6], along with 2-acetyl-1,2,4-thiadiazolin-3-one (**17**). Although the yields are poor, it is noted



that 4-acetoaminothiazole **15** was the main product in the reaction at room temperature, while **16** was obtained as a major product in the reaction at 130°.

Next, the reaction of 3-hydroxyisothiazoles **18a** and **b** with acetic anhydride was investigated and the results are shown in Scheme 3.

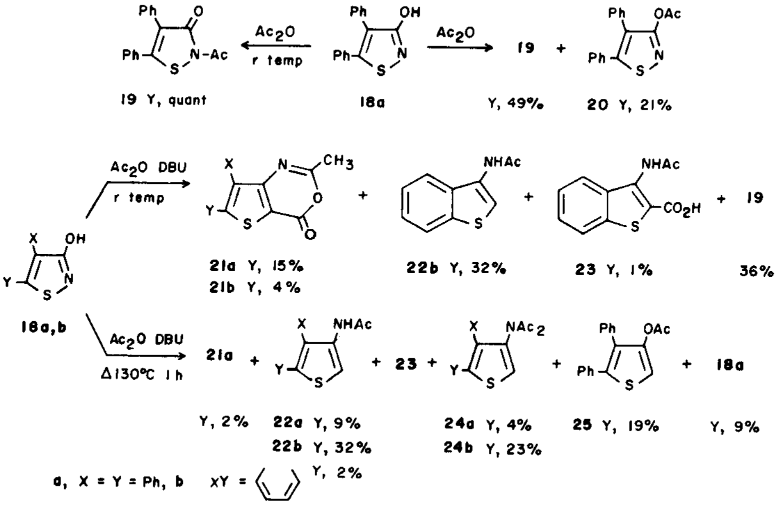
Compound **18a** reacted with acetic anhydride in the absence of DBU at room temperature, giving **19** in a quantitative yield, and at 130°, giving a mixture of **19** and **20**.

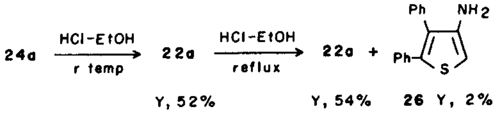
When acetic anhydride was added to a mixture of **18a** and DBU, the color of the reaction mixture changed from colorless to dark green and the expected **21a** was obtained in 15% yield, accompanied by **19** in 36% yield. When the reaction was carried out at 130°, **21a** was formed in only 2% yield and another thiophene derivatives **22a**, **25a**, and **26** were obtained in 9, 4, and 19% yields, respectively, along with **23** and **18a**, but **19** was not obtained. Compound **18a** may be formed by the hydrolysis of **20** during work-up.

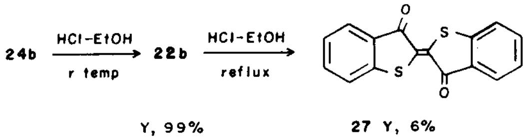
The reaction of **18b** with acetic anhydride at room temperature afforded the corresponding **21b**, **22b**, and **23** in 4, 32, and 1% yields, respectively. At 130°, diacetylaminothiophene (**24b**) was obtained in 23% yield, together with **22b** in 32% yield. Compound **21b** and 3-acetoxybenzo[*b*]thiophene were formed.

Structural assignment of **22**, **24** and **25** was done on the basis of hydrolyses. Compounds **24a** and **b** were easily hydrolyzed to give **22a** and **b** in 52 and 99% yields, respectively. In ethanolic hydrochloric acid at reflux, **22a** afforded 4-aminothiophene **26** in 2% yield, together with unchanged **22a** in 54% yield, while **22b** did not give the corresponding thiophene but thio indigo **27** [7] as deep red needles. It is known that 3-aminobenzo[*b*]thiophene yields **27** *via* 3-hydroxybenzo[*b*]thiophene [7,8]. Compound **25** was hydrolyzed in ethanolic hydrochloric acid, giving

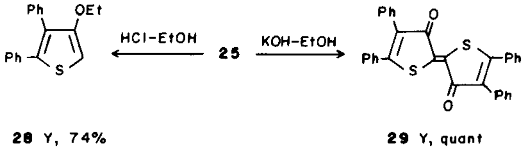
Scheme 3







ethoxythiophene **28** as colorless needles. Compound **28** is labile and gradually colored red in air. Under alkaline conditions, **25** gave red-colored **29** quantitatively.



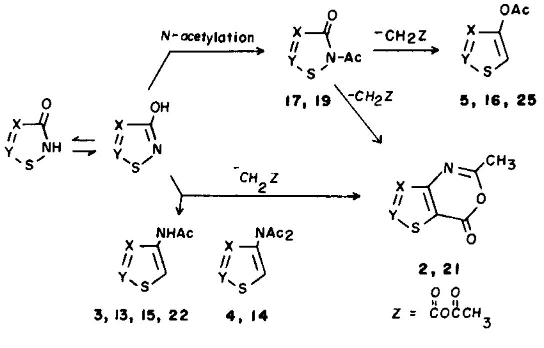
The reaction of **18a** and propionic anhydride in the presence of DBU was conducted at 80° for one hour and **18a** was recovered in 88% yield with a large amount of resinous materials.

Finally, it is briefly mentioned on the formation pathway of the products. Although the products are reasonably explained *via* a similar mechanism with that suggested by Mckinnon *et al* [1,2] for the reaction of isothiazolium salt with nucleophiles, it seems appropriate to check the possibility of *N*-acetylation prior to the ring opening of **1**, **14**, and **18**. Thus, **19** was treated with acetic anhydride in the presence of DBU. Though innert at room temperature, **19** afforded **21a** and **25** in 10 and 11% yields, respectively, in the reaction at 130° for one hour, but not **22a**, **23** and **24a**.

$$19 \xrightarrow[130°C\ 1\ h]{Ac_2O\ \ DBU} \underset{Y,\ 10\%}{21a} + \underset{Y,\ 11\%}{25}$$

This result suggests that acetoamido derivatives **3**, **4**, **13**, **15**, **22** and **24** may be formed directly from **1**, **14** and **18**, while acetoxy derivatives **5** **16** and **25** may be formed *via* *N*-acetylated **1**, **14** and **18b**, respectively. Compound **2** and **21** may be formed *via* the both pathways (Scheme 4).

Scheme 4



EXPERIMENTAL

All melting points were determined on a Yanagimoto micro melting point apparatus or a Mitamura-Riken MRK melt-thermo and are not corrected. The ir spectra were measured on a Nippon Bunko A-102 spectrophotometer as potassium bromide pellets or as liquid films on sodium chloride discs. The ^{1}H- and ^{13}C-nmr spectra were recorded on a Nippon Denshi JEOL FT-100 using TMS as an internal standard in deuteriochloroform unless otherwise stated. Mass spectra were obtained on a Nippon Denshi JMS-01SG-2 mass spectrometer at 75 eV using a direct inlet system. Column chromatography was carried out on silica gel (Wako C-300) unless otherwise stated.

Reaction of 1 with Acetic Anhydride.

To a mixture of **1a** (500 mg) and acetic anhydride (5 ml), DBU (2 ml) was added at room temperature. Precipitated **2a** (358 mg, 52%) was filtered and the filtrate was chromatographed on alumina using benzene as an eluent, giving **3a** (97 mg, 16%).

Compounds **2b** (75 mg, 19%) and **3b** (30 mg, 8%) were similarly obtained by the reaction of **1b** (300 mg), acetic anhydride (3 ml) and DBU (1 ml).

3-Phenyl-5-methyl-6*H*-isothiazolo[4,5-*d*]-1,3-oxazin-6-one (**2a**).

This compound was obtained as colorless needles (hexane), mp 300°; ir: ν CO 1760 cm^{-1}; ^{1}H-nmr: δ 2.57 (s, 3H), 7.42-7.56 (m, 3H), 8.28-8.39 (m, 2H); ^{13}C-nmr: δ 21.3, 128.4, 128.9, 130.5, 133.1, 137.0, 148.7, 153.9, 162.4, 163.9; ms: m/e 244.

Anal. Calcd. for $C_{12}H_8N_2O_2S$: C, 59.01; H, 3.30; N, 11.47. Found: C, 59.13; H, 3.35; N, 11.17.

3-Phenyl-4-acetoamidoisothiazole (**3a**).

This compound was obtained as colorless needles (a 5:1-mixture of hexane and benzene), mp 99-100.5°; ir: ν NH 3255, ν CO 1660 cm^{-1}; ^{1}H-nmr: δ 2.09 (s, 3H), 7.21-7.67 (m, 5H), 7.92 (br s, 1H), 9.13 (s, 1H); ^{13}C-nmr: δ 23.6, 127.9, 129.1, 129.3, 130.6, 133.8, 135.6, 159.3, 167.8; ms: m/e (relative intensity) 218 (59), 176 (100).

Anal. Calcd. for $C_{11}H_{10}N_2OS$: C, 60.53; H, 4.62; N, 12.83. Found: C, 60.26; H, 4.72; N, 12.44.

3-(4'-Chlorophenyl)-5-methyl-6*H*-isothiazolo[4,5-*d*]-1,3-oxazin-6-one (**2b**).

This compound was obtained as colorless plates (chloroform), mp 174-175°; ir: ν CO 1765, 1750 cm^{-1}; ms: m/e (relative intensity) 280 (39), 278 (100).

Anal. Calcd. for $C_{12}H_7ClN_2O_2S$: C, 51.71; H, 2.53; N, 10.05. Found: C, 51.72; H, 2.67; N, 10.04.

3-(4'-Chlorophenyl)-4-acetoamidoisothiazole (**3b**).

This compound was obtained as colorless needles (chloroform), mp 155-156°; ir: ν NH 3250, ν CO 1650 cm^{-1}; ^{1}H-nmr (tetradeuteriomethanol): δ 2.06 (s, 3H), 7.38-7.64 (m, 4H), 8.95 (s, 1H); ^{13}C-nmr (tetradeuteriomethanol): δ 23.4, 130.4, 131.1, 132.9, 134.7, 136.8, 142.6, 162.4, 172.6; ms: m/e (relative intensity) 254 (26), 252 (70), 212 (40), 210 (100).

Anal. Calcd. for $C_{11}H_9ClN_2OS$: C, 52.28; H, 3.59; N, 11.08. Found: C, 52.39; H, 3.66; N, 11.11.

Reaction of 1a with Acetic Anhydride at 130°.

After a mixture of **1a** (1000 mg), acetic anhydride (10 ml), and DBU (5 ml) was heated in oil bath at 130° for one hour, it was poured into water (50 ml), extracted with benzene (30 ml × 2), dried over sodium sulfate and evaporated *in vacuo* to leave the residue which was chromatographed. Compound **5** (96 mg, 8%) was eluted with a 2:1-mixture of hexane and benzene, **4** (516 mg, 35%) with benzene and **3a** (236 mg 19%) with chloroform, respectively.

3-Phenyl-4-(diacetyl)aminoisothiazole (**4**).

This compound was obtained as colorless plates (hexane), mp 113-114°; ir: ν CO 1705 cm^{-1}; ^{1}H-nmr: δ 2.21 (s, 6H), 7.32-7.83 (m, 5H), 8.62 (s, 1H); ^{13}C-nmr; δ 26.5, 127.1, 128.8, 129.6, 132.1, 132.9, 147.9,

164.1, 172.3; ms: m/e (relative intensity) 260 (24), 218 (41), 176 (100).
Anal. Calcd. for $C_{13}H_{12}N_2O_2S$: C, 59.98; H, 4.65; N, 10.76. Found: C, 59.89; H, 4.60; N, 10.37.

3-Phenyl-4-acetoxyisothiazole (**5**).

This compound was obtained as pale yellow oil; ir: ν CO 1770 cm^{-1}; ^{1}H-nmr: δ 2.27 (s, 3H), 7.30-7.54 (m, 3H), 7.72-7.98 (m, 2H), 8.61 (s, 1H); ^{13}C-nmr: δ 21.1, 127.7, 128.5, 129.3, 133.4, 136.1, 142.1, 159.0, 167.6; ms: m/e (relative intensity) 219 (13), 177 (46), 104 (100).
Anal. Calcd. for $C_{11}H_9NO_2S$: C, 60.26; H, 4.14; N, 6.39. Found: C, 60.59; H, 4.23; N, 6.20.

Reaction of **2a** with Ammonia.

A mixture of **2a** (100 mg) and concentrated aqueous ammonia (5 ml) in ethanol (12 ml) was stirred at 50° for one hour and evaporated *in vacuo* to dryness, giving **6** (52 mg, 52%).

3-Phenyl-5-methylisothiazolo[5,4-*e*]-3,4-dihydropyrimidin-4-one (**6**).

This compound was obtained as colorless needles (ethanol), mp 318-319°; ir: ν NH 3200-2800, ν CO 1675 cm^{-1}; ^{1}H-nmr (hexadeuteriodimethyl sulfoxide): δ 2.47 (s, 3H), 7.44-7.61 (m, 3H), 8.23-8.48 (m, 2H); ^{13}C-nmr (hexadeuteriodimethyl sulfoxide): δ 21.3, 127.7, 128.4, 129.8, 133.2, 139.7, 150.7, 156.5, 157.3, 161.3; ms: m/e, 243.
Anal. Calcd. for $C_{12}H_9N_3OS$: C, 59.24; H, 3.73; N, 17.27. Found: C, 59.26; H, 3.82; N, 17.27.

Methanolysis of **2a**.

Compound **2a** (200 mg) was chromatographed on alumina using methanol as an eluent to give **7** (153 mg, 67%).

Methyl 3-Phenyl-4-acetoamidoisothiazole-5-carboxylate (**7**).

This compound was obtained as colorless plates (hexane), mp 178-179°; ir: ν NH 3270, ν CO 1730, 1670 cm^{-1}; ^{1}H-nmr (hexadeuteriodimethyl sulfoxide): δ 3.02 (s, 3H), 3.84 (s, 3H), 7.38-7.57 (m, 3H), 7.62-7.80 (m, 2H), 9.95 (br s, 1H); ^{13}C-nmr (hexadeuteriodimethyl sulfoxide): δ 22.7, 52.6, 127.3, 128.5, 129.3, 133.7, 133.8, 147.8, 159.1, 164.9, 169.1; ms: m/e (relative intensity) 276 (32), 234 (100).
Anal. Calcd. for $C_{13}H_{12}N_2O_3S$: C, 56.51; H, 4.38; N, 10.14. Found: C, 56.50; H, 4.51; N, 9.96.

Hydrolysis of **2a** in Ethanolic Potassium Hydroxide.

A mixture of **2a** (50 mg), potassium hydroxide (3 g), ethanol (20 ml), and water (10 ml) was stirred at room temperature for 2 hours. It was poured into 10% aqueous hydrochloric acid (100 ml) and continuously extracted with chloroform overnight. Evaporation of the extract afforded **8** (19 mg, 36%).

3-Phenyl-4-acetoamidoisothiazole-5-carboxylic Acid (**8**).

This compound was obtained as colorless prisms (chloroform), mp 178-179°; ir: ν NH 3200, ν COOH 3100-2500, ν CO 1710-1640 cm^{-1}; ms: m/e (relative intensity) 262 (27), 220 (100).
Anal. Calcd. for $C_{12}H_{10}N_2O_3S$: C, 54.95; H, 3.84; N, 10.68. Found: C, 55.00; H, 3.82; N, 10.56.

Hydrolysis of **2a** in Ethanolic Hydrochloric Acid.

Compound **2a** (45 mg) was stirred in a mixture of concentrated hydrochloric acid (10 ml) and ethanol (10 ml) at room temperature for one hour. It was continuously extracted with chloroform overnight and evaporation of the extract gave **9** (10 mg, 25%).

3-Phenyl-4-aminoisothiazole-5-carboxylic Acid (**9**).

This compound was obtained as colorless prisms (benzene), mp 247-248° dec; ir: ν NH 3580, 3355, ν COOH 3200-2400, ν CO 1665 cm^{-1}; ms: m/e 220.
Anal. Calcd. for $C_{10}H_8N_2O_2S$: C, 54.53; H, 3.66; N, 12.72. Found: C, 54.68; H, 3.68; N, 12.41.

Hydrolysis of **10**.

After **10** (400 mg) was refluxed in 20% ethanolic potassium hydroxide (20 ml) for 14 hours, it was poured into 10% hydrochloric acid (100 ml) to give **9** (341 mg, 96%).

Cyclization of **9** with Acetic Anhydride.

A mixture of **9** (50 mg) and acetic anhydride (5 ml) was heated at 70° for 30 minutes and cooled to room temperature, affording **2a** (46 mg, 83%).

Decarboxylation of **9**.

Compound **9** (30 mg) was heated at 480° for 2 minutes, giving **11** (22 mg, 96%).

3-Phenyl-4-aminoisothiazole (**11**).

This compound was obtained as pale yellow prisms (hexane), mp 79-80.5°; ir: ν NH 3450, 3350 cm^{-1}; ^{1}H-nmr: δ 3.72 (br s, 2H), 7.32-7.48 (m, 3H), 7.49 (s, 1H), 7.63-7.77 (m, 2H); ^{13}C-nmr: δ 124.4, 127.5, 128.7, 128.8, 134.6, 140.5, 158.6; ms: m/e (relative intensity) 176 (100), 104 (74).
Anal. Calcd. for $C_9H_8N_2S$: C, 61.34; H, 4.58; N, 15.89. Found: C, 61.10; H, 4.55; N, 15.56.

Acetylation of **3a**.

After a mixture of **3a** (200 mg) and acetic anhydride (1 ml) was heated at 130° for 30 minutes, it was poured into water (50 ml) and extracted with benzene (50 ml × 2). The extract was condensed *in vacuo* and chromatographed. Compound **4** (47 mg, 20%) and unreacted **3a** (69 mg) were eluted with benzene and chloroform, respectively.

Hydrolysis of **4**.

After a mixture of **4** (300 mg), concentrated hydrochloric acid (5 ml), and ethanol (5 ml) was refluxed for 30 minutes, it was poured into water (50 ml), extracted with benzene (30 ml × 3) and evaporated *in vacuo* to give **11** (110 mg, 54%).

Hydrolysis of **5**.

After a mixture of **5** (90 mg) in 20% ethanolic potassium hydroxide (5 ml) was refluxed for one hour, it was poured into 10% hydrochloric acid (50 ml), extracted with benzene (30 ml × 3) and evaporated *in vacuo* to afford **12** (43 mg, 59%).

3-Phenyl-4-hydroxyisothiazole (**12**).

This compound was obtained as colorless prisms, mp 168-169° or colorless needles, mp 161-162° (1:1-mixture of hexane and benzene) (lit [5] mp 156-158°); ^{1}H-nmr (hexadeuteriodimethyl sulfoxide): δ 7.34-7.58 (m, 3H), 7.95 (s, 1H), 8.06-8.19 (m, 2H); ^{13}C-nmr (hexadeuteriodimethyl sulfoxide): δ 124.5, 126.8, 128.2, 128.5, 134.0, 150.8, 155.9; ms: m/e (relative intensity) 177 (91), 104 (100).
Anal. Calcd. for C_9H_7NOS: C, 61.00; H, 3.98; N, 7.90. Found: C, 61.15; H, 4.03; N, 7.73.

Reaction of **1a** with Propionic Anhydride.

After DBU (1 ml) was added to a mixture of **1a** (250 mg) and propionic anhydride (2 ml), it was stirred at room temperature for 15 minutes. It was poured into water (30 ml), extracted with benzene (30 ml × 2), concentrated to about 2 ml and chromatographed with chloroform as an eluent to give **13** (176 mg, 50%).

3-Phenyl-4-(1'-propionyl)amino-5-methylisothiazole (**13**).

This compound was obtained as colorless prisms (ethanol), mp 130-131°; ir: ν NH 3200, ν CO 1655 cm^{-1}; ^{1}H-nmr: δ 1.02 (t, 3H, J = 6 Hz), 2.15 (q, 2H, J = 6 Hz), 2.18 (s, 3H), 7.23-7.38 (m, 3H), 7.39-7.53 (m, 2H); ^{13}C-nmr: δ 9.8, 11.7, 29.3, 127.5, 128.4, 128.9, 134.5, 158.8, 164.0, 173.4; ms: m/e (relative intensity) 246 (34), 190 (100).
Anal. Calcd. for $C_{13}H_{14}N_2OS$: C, 63.39; H, 5.73; N, 11.37. Found: C, 63.27; H, 5.71; N, 11.12.

Reaction of **14** with Acetic Anhydride.

To a mixture of **14** (500 mg) and acetic anhydride (5 ml), DBU (2 ml) was added and treated as described above. Compound **16** (22 mg, 4%) was eluted with a 1:1-mixture of hexane and benzene, **15**, (88 mg, 14%) with benzene, and **17** (18 mg, 3%) with chloroform, respectively.

When the reaction was carried out at 130° for one hour, **15** (36 mg, 6%) and **16** (102 mg, 17%) were obtained.

2-Phenyl-4-acetoamidothiazole (**15**).

This compound was obtained as colorless plates (hexane), mp 175-176°; ir: ν NH 3300, 3200, ν CO 1645 cm^{-1}; ^{1}H-nmr: δ 2.10 (s, 3H), 7.23-7.47 (m, 3H), 7.54 (s, 1H), 7.69-7.92 (m, 2H), 8.60 (br s, 1H); ^{13}C-nmr: δ 23.6, 101.7, 126.1, 129.0, 130.3, 133.3, 147.8, 165.3, 167.8; ms: m/e (relative intensity) 218 (69), 176 (100), 104 (78).

Anal. Calcd. for $C_{11}H_{10}N_2OS$: C, 60.53; H, 4.62; N, 12.83. Found: C, 60.51; H, 4.64; N, 12.79.

2-Acetyl-5-phenyl-1,2,4-thiadiazolin-3-one (**17**).

This compound was obtained as colorless prisms (hexane), mp 147-149°; ir: ν CO 1725, 1695 cm^{-1}; ms: m/e (relative intensity) 200 (14), 178 (98), 104 (100).

Anal. Calcd. for $C_{10}H_8N_2O_2S$: C, 54.53; H, 3.66; N, 12.72. Found: C, 54.78; H, 3.73; N, 12.58.

Reaction of **18a** with Acetic Anhydride.

1) In the Absence of DBU.

Compound **18a** (200 mg) reacted with acetic anhydride)5 ml) at room temperature in a few minutes to give **19** (234 mg, 100%).

When the mixture of **18a** (200 mg) and acetic anhydride (10 ml) was heated at 130° for 40 minutes, poured into water (50 ml), extracted with benzene (30 ml × 2), condensed and chromatographed, **19** (115 mg, 49%) and **20** (49 mg, 21%) were obtained from the fractions eluted with a 1:1-mixture of benzene and hexane, and benzene, respectively.

2) In the Presence of DBU.

To a mixture of **18a** (1000 mg) and DBU (10 ml), was added acetic anhydride (30 ml) dropwisely and it was stirred at room temperature for 2 days. It was poured into water (150 ml), extracted with benzene (50 ml × 3), condensed and chromatographed. Pure **21a** (51 mg) was first eluted with a 4:1-mixture of hexane and benzene, then a mixture of **21a** and **19**. Their yields were determined by ^{1}H-nmr.

Next, a mixture of **18a** (1000 mg), DBU (8 ml) and acetic anhydride (20 ml) was heated at 130° for one hour and treated as described above. Compound **25** (219 mg, 19%) was eluted with a 1:1-mixture of hexane and benzene, **21a** (23 mg, 2%), **24a** (53 mg, 4%), and **18a** (90 mg, 9%) were eluted with benzene and **22a** (102 mg, 9%) with chloroform, respectively.

2-Acetyl-4,5-diphenylisothiazolin-3-one (**19**).

This compound was obtained as colorless needles (hexane), mp 152-154°; ir: ν CO 1690, 1680 cm^{-1}; ^{1}H-nmr: δ 2.73 (s, 3H), 7.20-7.43 (m, 10H); ms: m/e (relative intensity) 295 (22), 253 (100).

Anal. Calcd. for $C_{17}H_{13}NO_2S$: C, 69.13; H, 4.44; N, 4.74. Found: C, 69.43; H, 4.47; N, 4.52.

3-Acetoxy-4,5-diphenylisothiazole (**20**).

This compound was obtained as colorless needles (hexane), mp 138-139°; ir: ν CO 1775 cm^{-1}; ^{1}H-nmr: δ 2.35 (s, 3H), 7.38-7.64 (m, 10H); ms: m/e (relative intensity) 295 (25), 253 (100), 178 (72).

Anal. Calcd. for $C_{17}H_{13}NO_2S$: C, 69.13; H, 4.44; N, 4.74. Found: C, 69.13; H, 4.47; N, 4.52.

2,3-Diphenyl-5-methyl-6*H*-thieno[3,2-*d*]-1,3-oxazin-6-one (**21a**).

This compound was obtained as colorless needles (hexane), mp 235-237°; ir: ν CO 1770 cm^{-1}; ^{1}H-nmr: δ 2.43 (s, 3H), 7.17-7.43 (m, 10H); ms: m/e (relative intensity) 319 (100), 318 (94).

Anal. Calcd. for $C_{19}H_{13}NO_2S$: C, 71.46; H, 4.10; N, 4.39. Found: C, 71.70; H, 4.19; N, 4.35.

2,3-Diphenyl-4-acetoamidothiophene (**22a**).

This compound was obtained as colorless plates (hexane), p 194-195°; ir: ν NH 3340, ν CO 1660 cm^{-1}; ^{1}H-nmr: δ 2.00 (s, 3H), 6.96-7.42 (m, 10H), 7.85 (s, 1H); ms: m/e (relative intensity) 293 (38), 251 (100), 217 (59), 178 (35).

Anal. Calcd. for $C_{18}H_{15}NOS$: C, 73.69; H, 5.15; N, 4.77. Found: C, 73.61; H, 5.14; N, 4.46.

2,3-Diphenyl-4-(diacetyl)aminothiophene (**24a**).

This compound was obtained as colorless prisms (pentane), mp 106.5-107.5°; ir: ν CO 1700 cm^{-1}; ^{1}H-nmr: δ 2.20 (s, 6H), 6.93-7.12 (m, 2H), 7.16-7.32 (m, 9H); ms: m/e (relative intensity) 335 (55), 293 (78), 251 (100).

Anal. Calcd. for $C_{20}H_{17}NO_2S$: C, 71.62; H, 5.11; N, 4.18. Found: C, 71.66; H, 5.09; N, 3.96.

2,3-Diphenyl-4-acetoxythiophene (**25**).

This compound was obtained as colorless needles (hexane), mp 107-108°; ir: ν CO 1755 cm^{-1}; ^{1}H-nmr: δ 2.08 (s, 3H), 7.09 (s, 1H), 7.16-7.34 (m, 10H); ms: m/e (relative intensity) 294 (26), 252 (100), 178 (29).

Anal. Calcd. for $C_{18}H_{14}O_2S$: C, 73.44; H, 4.79. Found: C, 73.42; H, 4.48.

Reaction of **18b** with Acetic Anhydride.

A mixture of **18b** (500 mg), acetic anhydride (5 ml) and DBU (2 ml) was treated in the same manner with the reaction of **14** with acetic anhydride. Compound **21b** (26 mg, 4%) and **23** (9 mg, 1%) were eluted with benzene and **22b** (225 mg, 32%) with chloroform, respectively.

Next, a mixture of **18b** (500 mg), acetic anhydride (5 ml) and DBU (2 ml) was treated in the same manner with the reaction of **1a** with acetic anhydride at 130°. Compound **23** (17 mg, 2%) was eluted with a 1:2-mixture of hexane and benzene, **24b** (200 mg, 23%) with benzene and **22b** (221 mg, 32%) with chloroform, respectively.

3-Methyl-6*H*-benzo[*b*]thieno[3,2-*d*]-1,3-oxazin-6-one (**21b**).

This compound was obtained as colorless needles (hexane), mp 183-185°; ir: ν CO 1760, 1740 cm^{-1}; ^{1}H-nmr: δ 2.56 (s, 3H), 7.38-7.68 (m, 2H), 7.82-7.96 (m, 1H), 8.14-8.26 (m, 1H); ms: m/e (relative intensity) 217 (100), 201 (45).

Anal. Calcd. for $C_{11}H_7NO_2S$: C, 60.82; H, 3.25; N, 6.25. Found: C, 60.74; H, 3.38; N, 6.28.

3-Acetoamidobenzo[*b*]thiophene (**22b**).

This compound was obtained as colorless plates (benzene), mp 175-177°; ir: ν NH 3295, ν CO 1645 cm^{-1}; ^{1}H-nmr: δ 2.23 (s, 3H), 7.28-7.43 (m, 2H), 7.53-7.67 (m, 1H), 7.76-7.91 (m, 1H), 7.93 (s, 1H); ^{13}C-nmr: δ 24.1, 112.8, 118.7, 123.2, 124.0, 124.9, 128.3, 132.8, 138.0, 168.0; ms: m/e (relative intensity) 191 (31), 149 (100).

Anal. Calcd. for $C_{10}H_9NOS$: C, 62.80; H, 4.74; N, 7.32. Found: C, 62.58; H, 4.88; N, 7.14.

3-Acetoamidobenzo[*b*]thiophene-2-carboxylic Acid (**23**).

This compound was obtained as colorless needles (chloroform), mp 239-241°; ir: ν COOH 3350-2500, ν NH 3300, ν CO 1670 cm^{-1}; ms: m/e (relative intensity) 235 (12), 175 (25), 121 (29), 43 (100).

Anal. Calcd. for $C_{11}H_9NO_3S$: C, 56.15; H, 3.86; N, 5.95. Found: C, 55.96; H, 3.80; N, 5.85.

3-(Diacetylamino)benzo[*b*]thiophene (**24b**).

This compound was obtained as colorless prisms (benzene), mp 69-71°; ir: ν CO 1722, 1687 cm^{-1}; ^{1}H-nmr: δ 2.33 (s, 6H), 7.19-7.50 (m, 2H), 7.31 (s, 1H), 7.67-7.92 (m, 2H); ^{13}C-nmr: δ 26.2, 120.3, 123.3, 125.0, 125.2, 125.4, 131.7, 134.9, 138.6. 172.6; ms: m/e (relative intensity) 233 (7), 149 (35), 121 (49), 43 (100).

Anal. Calcd. for $C_{12}H_{11}NO_2S$: C, 61.78; H, 4.75; N, 6.00. Found: C, 61.99; H, 4.79; N, 6.13.

Hydrolysis of **24a**.

A mixture of **24a** (200 mg) in a mixture of concentrated acid (3 ml) and ethanol (7 ml) was refluxed for 30 minutes and poured into water (50 ml) to give **22a** (90 mg, 52%).

Hydrolysis of **22a**.

After a mixture of **22a** (200 mg), concentrated hydrochloric acid (7 ml) and ethanol (3 ml) was refluxed for one hour, it was poured into water (50 ml) giving unchanged **22a** (107 mg, 54%). The filtrate was extracted with benzene (30 ml × 2) and evaporated *in vacuo* to dryness to give **26** (3 mg, 2%).

2,3-Diphenyl-4-aminothiophene (**26**).

This compound was obtained as yellow prisms (ethanol) mp 71-72°; ir: ν NH 3455, 3430, 3350, 3210, 3200 cm^{-1}; ms: m/e 251.

Anal. Calcd. for $C_{16}H_{13}NS$: C, 76.46; H, 5.21; N, 5.57. Found: C, 76.56; H, 5.27; N, 5.52.

Hydrolysis of **24b**.

Compound **24b** (200 mg) was stirred in a mixture of ethanol (7 ml) and concentrated hydrochloric acid (3 ml) at room temperature for 30 minutes. It was poured into water (50 ml), giving **22b** (162 mg, 100%).

Hydrolysis of **22b**.

After a mixture of **22b** (300 mg), concentrated hydrochloric acid (10 ml) and ethanol (5 ml) was heated at reflux for 3 hours, then it was poured into water (75 ml), extracted with benzene (30 ml × 2), condensed and chromatographed using benzene as an eluent, affording **27** (15 mg, 6%).

Thioindigo (**27**).

This compound was obtained as red needles (ethanol), mp 295-305° (lit [7] mp >280°); ms: m/e 296.

Anal. Calcd. for $C_{16}H_{8}O_{2}S_{2}$: C, 64.84; H, 2.72. Found: C, 64.51; H, 3.09.

Hydrolysis of **25** in Ethanolic Hydrochloric Acid.

After a mixture of **25** (250 mg), concentrated hydrochloric acid (3 ml), and ethanol (7 ml) was heated at reflux for 30 minutes, it was poured into water (50 ml) to give **28** (176 mg, 74%).

2,3-Diphenyl-4-ethoxythiophene (**28**).

This compound was obtained as colorless needles (ethanol), mp 94-95°; ^{1}H-nmr: δ 1.33 (t, 3H, J = 6 Hz), 4.01 (q, 2H, J = 6 Hz), 6.21 (s, 1H), 7.12 (s, 5H), 7.17 (s, 5H); ms: m/e (relative intensity) 280 (69), 252 (69), 178 (100).

Anal. Calcd. for $C_{18}H_{16}OS$: C, 77.11; H, 5.75. Found: C, 76.83; H, 5.73.

Hydrolysis of **25** under Alkaline Conditions.

A mixture of **25** in 20% ethanolic potassium hydroxide (20 ml) was heated at reflux for one hour. It was poured into water (100 ml) and extracted with benzene (30 ml × 3). The color of the extract changed gradually from colorless to deep red with precipitation of **29** (200 mg, 94%).

2,2'-Bis(4,5-diphenyl-3*H*-thiophene-3-onylidene) (**29**).

This compound was obtained as deep red needles (benzene), mp 300°; ir: ν CO 1630 cm^{-1}; ^{1}H-nmr: δ 7.20-7.50 (m); ms: m/e 500.

Anal. Calcd. for $C_{32}H_{20}O_{2}S_{2}$: C, 76.77; H, 4.03. Found: C, 76.41; H, 4.06.

Reaction of **19** with Acetic Anhydride in the Presence of DBU.

A mixture of **19** (800 mg), acetic anhydride (6 ml) and DBU (3 ml) was stirred at 130° for one hour and treated in the same manner with the reaction of **18a**, affording **21a** (84 mg, 10%) and **25** (84 mg, 11%).

Acknowledgement.

The authors wish to express thanks to Professor S. Saeki of Kyushu University for a copy of the ir spectrum of **16** and Mr. T. Naito of Bristol-Myers Research Institute for the ir and ^{1}H-nmr spectral data of **12**.

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