# Reactions of Pyridinium or Isoquinolinium Ketene Dithioacetals with Aromatic *N*-Imines and *S*-Imines

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Reactions of ketene dithioacetals, 1-[1-substituted 2,2-bis(methylthio)ethenyl]pyridinium **1a-i** or -isoquinolinium **2a,b** iodides with aromatic *N*-imines, 1-aminopyridinium **3a-l**,1-aminoquinolinium (**4**), and 2-aminoisoquinolinium (**5**) mesitylene sulfonates gave the corresponding 2-methylthioimidazo[1,2-*a*]pyridines **9a-k**, 2-methylthiopyrazolo[1,5-*a*]pyridines **11a-q**, 2-methylthioimidazo[2,1-*a*]isoquinoline derivatives **10a,b** and 2-methylthiopyrazolo[1,5-*a*]quinoline (**12**). The benzoyl compounds, 1-[1-benzoyl-2,2-bis(methylthio)ethenyl]-pyridinium iodides **1g,h,i** reacted with *N*-imine **3a** to give the 3-benzoyl-2-methylthioimidazo[1,2-*a*]pyridines **9h-k**. The reaction of pyridinium ketene dithioacetals **1a,f,g** ($R^1$ = COOEt, COPh, and CN) with substituted pyridinium *N*-imines having an electron-withdrawing group on the pyridine ring afforded only the corresponding pyrazolo[1,5-*a*]pyridine derivatives **11j-r** in good yields. Reactions of ketene dithioacetals with various *S*-imines are also described. Possible mechanisms for the formation of **9** and **11** are described.

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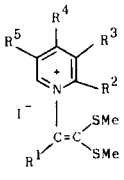
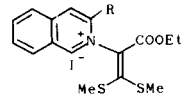
Pyridinium ketene dithioacetals are versatile precursors for the synthesis of various types of heterocyclic compounds [1,2]. We have recently reported a convenient method for the preparation of pyridinium ketene dithioacetals which display high reactivity towards nucleophiles such as active methylene compounds. These reactions give the corresponding stable pyridinium *N*-allylides and various functionalized indolizine derivatives. In an extension of our studies on ketene dithioacetals, we now wish to report the reaction of the ketene dithioacetals with aromatic *N*-imines or *S*-imines. The pyridinium and isoquinolinium ketene dithioacetals **1** and aromatic *N*-imines and *S*-imines as well as the products derived from them are shown in Charts 1 and 2.



**1a-i**

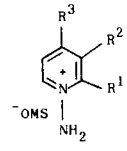
| No. | $R^1$ | $R^2$ | $R^3$ | $R^4$ | $R^5$ |
|---|---|---|---|---|---|
| 1a | COOEt | H | H | H | H |
| b | COOEt | Me | H | H | H |
| c | COOEt | H | Me | H | H |
| d | COOEt | H | H | Me | H |
| e | COOEt | H | Me | H | Me |
| f | CN | H | H | H | H |
| g | COPh | H | H | H | H |
| h | COPh | H | Me | H | H |
| i | COPh | H | Me | H | Me |



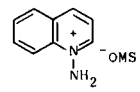
**2a, b**

a: R=H
b: R=Me

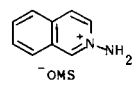
| No. | $R^1$ | $R^2$ | $R^3$ |
|---|---|---|---|
| 3a | H | H | H |
| b | Me | H | H |
| c | H | Me | H |
| d | H | H | Me |
| e | H | $NH_2$ | H |
| f | H | OH | H |
| g | H | $CONH_2$ | H |
| h | H | $CONEt_2$ | H |
| i | H | COOMe | H |
| j | H | H | $CONH_2$ |
| k | H | H | CN |
| l | H | H | COOEt |



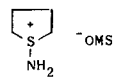
**3a-l**



**4**



**5**



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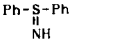

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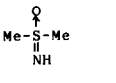
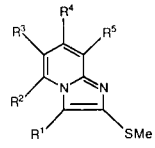


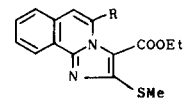
**8**

Chart 1



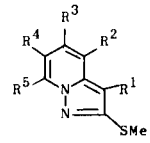
**9a-k**

| No. | $R^1$ | $R^2$ | $R^3$ | $R^4$ | $R^5$ |
|---|---|---|---|---|---|
| 9a | COOEt | H | H | H | H |
| b | COOEt | Me | H | H | H |
| c | COOEt | H | Me | H | H |
| d | COOEt | H | H | Me | H |
| e | COOEt | H | H | H | Me |
| f | COOEt | H | Me | H | Me |
| g | CN | H | H | H | H |
| h | COPh | H | H | H | H |
| i | COPh | H | Me | H | H |
| j | COPh | H | H | H | Me |
| k | COPh | H | Me | H | Me |



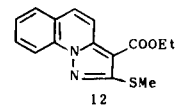
**10a, b**

a: R=H
b: R=Me

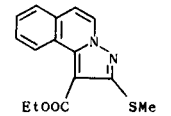


**11a-q**

| No. | $R^1$ | $R^2$ | $R^3$ | $R^4$ | $R^5$ |
|---|---|---|---|---|---|
| 11a | COOEt | H | H | H | H |
| b | COOEt | Me | H | H | H |
| c | COOEt | H | Me | H | H |
| d | COOEt | H | H | Me | H |
| e | COOEt | H | H | H | Me |
| f | CN | H | H | H | H |
| g | CN | H | Me | H | H |
| h | COOEt | $NH_2$ | H | H | H |
| i | COOEt | OH | H | H | H |
| j | COOEt | H | $CONH_2$ | H | H |
| k | COOEt | H | CN | H | H |
| l | COPh | H | COOEt | H | H |
| m | COOEt | H | H | $CONEt_2$ | H |
| n | COOEt | H | H | $CONH_2$ | H |
| o | CN | H | H | $CONH_2$ | H |
| p | COPh | H | H | $CONH_2$ | H |
| q | H | H | H | COOMe | H |



**12**



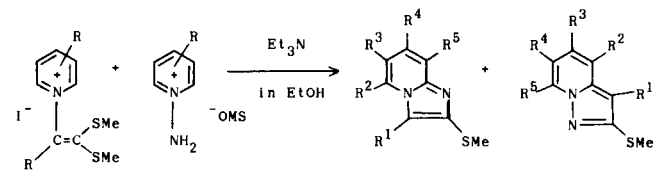
**13**

Chart 2

Pyridinium ketene dithioacetals **1a-i** are easily prepared by the condensation of the corresponding pyridinium salts with carbon disulfide followed by methylation with dimethyl sulfate and sodium hydroxide in ethanol [3].

The reaction of **1a-i** with 1-aminopyridinium mesitylenesulfonates **3a-l** in the presence of triethylamine in ethanol gave the corresponding 2-methylthioimidazo[1,2-*a*]pyridines **9a-k** and 2-methylthiopyrazolo[1,5-*a*]pyridines **11a-r** in ratios as shown in Chart 3. A possible reaction mechanism for the formation of **9** and **11** is shown in Chart 8. The pyridyl group acts effectively as a leaving group for the 1,5-dipolar cycloaddition in this reaction. The reaction of ketene dithioacetal **1a** with the *N*-imine **3a** gave a mixture of ethyl 2-methylthiopyrazolo[1,5-*a*]pyridine-3-carboxylate derivative (**11a**) and ethyl 2-methylthioimidazo[1,2-*a*]pyridine-3-carboxylate (**9a**) in a ratio of 81:19. When **3c** and **3d** bearing a methyl group on the pyridine ring of the pyridinium *N*-imines were used, the formation of **9a** increased in comparison with the previous case of the reaction of **1a** with **3a** as shown in Chart 3. The reaction of **1a** with **3d** gave a mixture of **9a** and **11c** in a ratio of 43:57. The reaction of **1a** with **3c** also gave a mixture of **9a, 11b,** and **11d** in a ratio of 37:8:55. However, the reaction of **1a** with 2-methylpyridinium salt (**3b**) produced the corresponding pyrazolo[1,5-*a*]pyridine **11e** in low yield, because of steric hindrance of the methyl group at the 2-position in **3b**. The 3-aminopyridinium *N*-imine (**3e**) was also reacted with **1a** to yield **9a** as a major product along with ethyl 4-amino-2-methylthiopyrazolo[1,5-*a*]pyridine-3-carboxylate (**11h**). The ratio of **9a** to **11h** was 55:45. Similarly, the reaction of **1a** with 3-hydroxypyridinium *N*-imine (**3f**) gave a mixture of **9a** and **11i** (58:42). The presence of the methyl group in the pyridinium ketene dithioacetal unilaterally leads to the formation of pyrazolo[1,5-*a*]pyridine as shown in Chart 3. Significantly, the reaction of the dimethyl compound, **1e**, with **3a** gave a mixture of pyrazolo[1,5-*a*]pyridine **11a** and a trace of 6,8-dimethylimidazo[1,2-*a*]pyridine **9f**. This impurity was readily removed from the reaction mixture by recrystallization from ethanol. Thus this method is convenient for the preparation of pyrazolo[1,5-*a*]pyridine derivatives exclusively.

The reaction of benzoyl compounds, 1-[1-benzoyl-2,2-bis(methylthio)ethenyl]pyridinium iodides **1g-i**, with the *N*-imine **3a** under the same conditions gave only the 3-benzoyl-2-methylthioimidazo[1,2-*a*]pyridines **9h-k**. The formation of **9h-k** may be explained by a stronger interaction of the benzoyl carbonyl oxygen with the sulfur atom of the methylthio group than the corresponding ester carbonyl oxygen the sulfur atom [6] and/or by the steric hindrance due to a phenyl group as shown in Route B of Chart 8. The reaction of the cyanopyridinium ketene dithioacetal **1f** with the *N*-imine **3a** gave a mixture of **9g** and **11f** in equal amounts and also in a good yield. Compound **1f** was allowed to react with 4-methyl *N*-imine **3d** to give **9g** as the major product along with a minor amount of 3-cyano-7-methyl-2-methylthiopyrazolo[1,5-*a*]pyridine (**11g**), because of the inductive effect of methyl group at

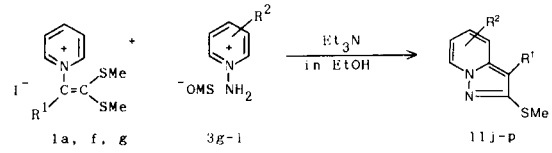



1a-i 3a-f 9a-k 11a-i

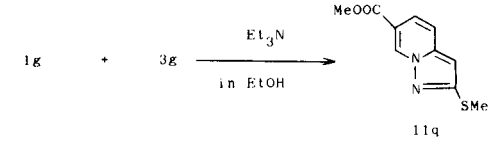
| entry | Starting Materiales KDA | N-imines | Products IP( ) | PP( ) | Total Yield(%) |
|---|---|---|---|---|---|
| 1 | 1a | 3a | 9a(19) | 11a(81) | 83 |
| 2 | 1a | 3b | 9a(2) | 11e(98)(7) | 11 |
| 3 | 1a | 3c | 9a(37) | 11b(8), 11d(55) | 89 |
| 4 | 1a | 3d | 9a(43) | 11c(57) | 88 |
| 5 | 1f | 3a | 9g(50) | 11f(50) | 93 |
| 6 | 1f | 3d | 9g(85) | 11g(15) | 85 |
| 7 | 1a | 3e | 9a(55) | 11h(45) | 56 |
| 8 | 1a | 3f | 9a(58) | 11i(42) | 94 |
| 9 | 1b | 3a | 9b(2) | 11a(98) | 21 |
| 10 | 1c | 3a | 9c(1),9e(1) | 11a(98)(76) | 89 |
| 11 | 1d | 3a | 9d(2) | 11a(98) | 78 |
| 12 | 1e | 3a | 9f(1) | 11a(99)(81) | 93 |
| 13 | 1e | 3d | 9f(10) | 11c(90)(77) | 95 |
| 14 | 1e | 3e | 9f(32) | 11h(68)(42) | 75 |
| 15 | 1e | 3f | 9f(32) | 11i(68)(37) | 78 |
| 16 | 1g | 3a | 9h(100) | | 54 |
| 17 | 1h | 3a | 9i(39),9j(61) | | 26 |
| 18 | 1i | 3a | 9k(100) | | 17 |

KDA: ketene dithioacetal; IP: imidazo[1,2-a]pyridine; PP: pyrazolo[1,5-a]pyridine; ( ): product ratio determined by GC; ( ): isolated yields (%)

Chart 3




1a, f, g 3g-i 11j-p




1g + 3g 11q

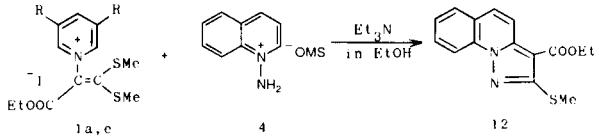
| | $R^1$ | $R^2$ | Yield(%) |
|---|---|---|---|
| 11j: | COOEt | 5-$CONH_2$ | 52 |
| k: | COOEt | 5-CN | 40 |
| l: | COOEt | 6-$CONH_2$ | 86 |
| m: | COOEt | 6-$CONEt_2$ | 64 |
| n: | CN | 6-$CONH_2$ | 61 |
| o: | COPh | 5-COOEt | 44 |
| p: | COPh | 6-$CONH_2$ | 29 |
| q: | H | 6-COOMe | 31 |

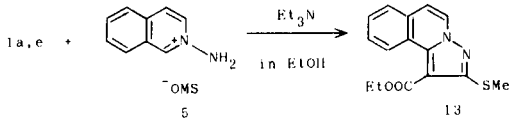
Chart 4

4-position of pyridinium *N*-imine. The separation of a mixture of these products (**9g** and **11f**, **9g** and **11g**) by column chromatography on alumina was unsuccessful. This result suggests the absence of an interaction between the methylthio and the cyano groups. The reaction of ketene dithio-

acetals **1a** ($R^1$ = COOEt), **1f** ($R^1$ = CN), and **1g** ($R^1$ = COPh) with substituted pyridinium *N*-imines **3g-l** having an electron-withdrawing group (CN, $CONH_2$, $CONEt_2$, COOMe) on the pyridine ring gave only pyrazolo[1,5-*a*]-pyridine derivatives **11j-q** in good yields, because of more electron deficient carbon at the 2- or 6-position on pyridine ring.

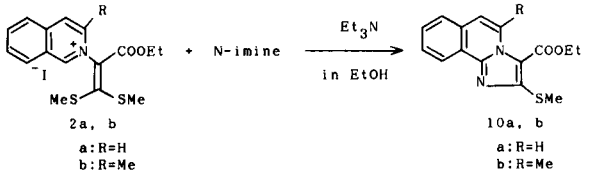
The reaction of **1a** with 1-aminoquinolinium methylenesulfonate (**4**) gave only pyrazolo[1,5-*a*]quinoline derivatives **12** in 81% yield. Under similar conditions the reaction of **1a** with 2-aminoisoquinolinium mesitylenesulfonate (**5**) also afforded pyrazolo[5,1-*a*]isoquinoline **13** in 78% yield. When **4** or **5** was allowed to react with **1e**, **12** and **13** were obtained in 87 and 94% yields, respectively.




| entry | KDA | N-imine | Product | Yield(%) |
|---|---|---|---|---|
| 1 | 1a | 4 | 12 | 81 |
| 2 | 1e | 4 | 12 | 87 |
| 3 | 1a | 5 | 13 | 78 |
| 4 | 1e | 5 | 13 | 94 |

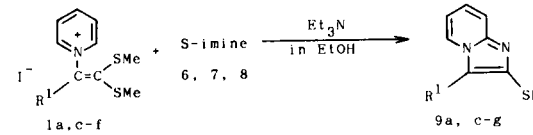
Chart 5




| entry | KDA | N-imine | Product | Yield(%) |
|---|---|---|---|---|
| 1 | 2a | 3a | 10a(100) | 66 |
| 2 | 2b | 3a | 10b(100) | 89 |
| 3 | 2a | 4 | 10(6),12(94) | 89 |
| 4 | 2a | 5 | 10(19),13(81) | 73 |

Chart 6

Reaction of 2-[1-ethoxycarbonyl-2,2-bis(methylthio)-ethenyl]isoquinolinium iodides **2a,b** with aromatic *N*-imines (**3a**) gave the corresponding imidazo[2,1-*a*]isoquinolines **10a,b** in 66 and 62% yields, respectively. The corresponding pyrazolo[1,5-*a*]pyridines were not obtained in this reaction. Therefore, it is suggested that the 1-position of isoquinolinium ring is more active than the




| entry | KDA | S-imine | Product | Yield(%) |
|---|---|---|---|---|
| 1 | 1a | 6 | 9a | 25 |
| 2 | 1c | 6 | 9c(74),9e(26) | 22 |
| 3 | 1d | 6 | 9d | 24 |
| 4 | 1e | 6 | 9f | 6 |
| 5 | 1a | 6 | 9g | 32 |
| 6 | 1a | 7 | 9a | 11 |
| 7 | 1f | 7 | 9g | 45 |
| 8 | 1a | 8 | 9a | 2 |

Chart 7

2-position of pyridinium ring. The reaction of compound **2a** with **4** gave the corresponding two products, **10a** and **12**, in a ratio of 6:94. When **2a** was reacted with the isoquinolinium *N*-imine **5**, a mixture of **10a** and **13** was obtained in a ratio of 19:81.

For the purpose of obtaining only the imidazo[1,2-*a*]-pyridines **9**, we tried to use the *S*-imine derivatives as the nitrogen atom source. Reaction of ketene dithioacetals **1a,c,d,e,f** with various *S*-imines **6,7,8** gave imidazo-[1,2-*a*]pyridines derivatives **9a,c,d,e,f,g**, but the yields were poor. Thus the 1,5-dipolar cyclization of pyridinium ketene dithioacetals with *S*-imines provides a direct and efficient synthesis of imidazo[1,2-*a*]pyridine derivatives and opens the way to the various annelated imidazoles.

An outline of the reaction mechanism is shown in Chart 8.

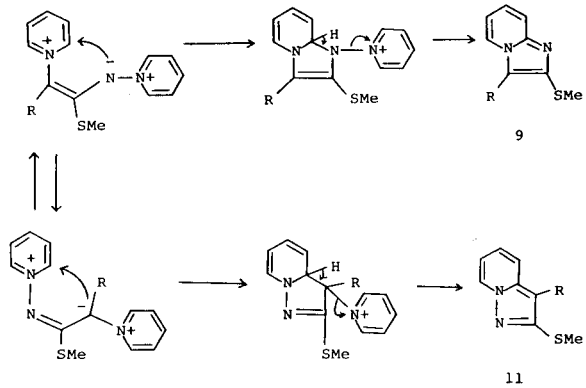



Chart 8

Pyridinium and isoquinolinium ketene dithioacetals are useful reagents for the synthesis of fused pyrazole and imidazole derivatives. The compounds prepared in this report are important precursors for the synthesis of biolog-

ically active heterocycles because of the possibility of introducing various functional groups which can then be further elaborated.

## EXPERIMENTAL

All melting points were determined on MEL-TEMP (Mitamura Riken Kogyo) capillary melting point apparatus and are uncorrected. Infrared (ir) spectra were recorded in potassium bromide pellets on a JASCO IRA-2 spectrometer, ultraviolet (uv) absorption spectra were determined on a Hitachi EP-S2 spectrometer in 95% ethanol, and nuclear magnetic resonance (nmr) spectra were obtained with a JNM-PS-100 (100 MHz) spectrometer with tetramethylsilane as an internal standard. Mass spectra were recorded on a JEOL JMS-01SG spectrometer.

(Ethoxycarbonyl)[(methylthio)thiocarbonyl][1-(3,5-dimethyl)pyridinio]-methylide (Intermediate of **1e**).

To a solution of 2.74 g (10 mmoles) of 1-ethoxycarbonylmethyl-3,5-dimethylpyridinium bromide and a solution of sodium hydroxide (sodium hydroxide 1.0 g + water 3 ml, 25 mmoles) in 100 ml of ethanol, was added 1.14 g (15 mmoles) of carbon disulfide below 5° over 20 minutes. After stirring at room temperature for 2 hours, dimethyl sulfate (1.8 g, 15 mmoles) was added dropwise to the reaction mixture with stirring for 1 hour at room temperature. The reaction mixture was diluted with water (200 ml) and the resulting precipitate was collected by filtration. After drying, the product was recrystallized from ethanol to give yellow needles, mp 237°, in 82% yield. This compound is a stable pyridinium dithiocarboxylate derivative; ir (potassium bromide): $\nu$ max $cm^{-1}$ 1640 (C=O); uv (ethanol): $\lambda$ max nm (log $\epsilon$) 286 (3.92), 327 (4.44); $^1H$ nmr (deuteriochloroform): $\delta$ 1.21 (3H, t, J = 7.0 Hz, O-$CH_2$-$CH_3$), 2.50 (3H, s, 3-Me), 2.51 (3H, s, 5-Me), 2.62 (3H, s, SMe), 4.17 (2H, q, J = 7.0 Hz, O-$CH_2$-), 7.91 (1H, s, 4-H), 8.13 (2H, s, 2, 6-H).

*Anal.* Calcd. for $C_{13}H_{17}O_2NS_2$: C, 55.09; H, 6.05; N, 4.94; S, 22.63. Found: C, 55.08; H, 6.01; N, 4.86; S, 22.75.

1-[1-Ethoxycarbonyl-2,2-bis(methylthio)ethenyl]-3,5-dimethylpyridinium Iodide (**1e**).

A solution of 2.83 g (10 mmoles) of the above methyl dithiocarboxylate and 2.83 g (20 mmoles) of methyl iodide in 100 ml of ethanol was refluxed for 30 minutes. After removal of the solvent and excess methyl iodide by rotary evaporation, the residue was recrystallized from ethanol to give pale yellow prisms, mp 112°, in 92% yield; ir (potassium bromide): $\nu$ max $cm^{-1}$ 1700 (C=O); uv (ethanol): $\lambda$ max nm (log $\epsilon$) 221 (4.33), 284 (3.92), 320 (3.95); $^1H$ nmr (deuteriochloroform): $\delta$ 1.25 (3H, q, J = 7.0 Hz, O-$CH_2$-$CH_3$), 2.66 (3H, s, SMe), 2.69 (3H, s, 3 or 5-Me), 2.70 (3H, s, 3 or 5-Me), 2.80 (3H, s, SMe), 8.30 (1H, bs, 4-H), 8.92 (1H, bs, 2, 6-H).

*Anal.* Calcd. for $C_{14}H_{20}IO_2NS_2$: C, 39.53; H, 4.74; N, 3.29; S, 15.08. Found: C, 39.38; H, 4.88; N, 3.09; S, 14.99.

(Ethoxycarbonyl)(1-isoquinolino)[(methylthio)thiocarbonyl]methylide (Intermediate of **2a**).

To a solution of 2.96 g (10 mmoles) of 2-ethoxycarbonylmethylisoquinolinium bromide, 1.14 g (15 mmoles) of carbon disulfide, and 1.89 g (15 mmoles) of dimethyl sulfate in 100 ml of ethanol, a solution of sodium hydroxide (sodium hydroxide: 0.8 g + water 3 ml, 15 mmoles) was added at below 5° over 20 minutes. After stirring at room temperature for 2 hours, the reaction mixture was diluted with water (200 ml) and the resulting precipitate was collected by filtration. After drying, this compound was recrystallized from ethanol to give orange needles, mp 197°, in 79% yield. This compound was a stable methyl dithiocarboxylate derivative; ir (potassium bromide): $\nu$ max $cm^{-1}$ 1638 (C=O); $^1H$ nmr (deuteriochloroform): $\delta$ 1.18 (3H, t, J = 7.0 Hz, O-$CH_2$-$CH_3$), 2.65 (3H, s, SMe), 4.18 (2H, q, J = 7.0 Hz, O-$CH_2$-), 7.78-8.25 (6H, m, 3, 4, 5, 6, 7, 8-H), 9.28 (1H, s, 1-H).

*Anal.* Calcd. for $C_{15}H_{15}NO_2S_2$: C, 58.99; H, 4.95; N, 4.59; S, 21.00; Found: C, 58.76; H, 4.82; N, 4.64; S, 20.90.

2-[1-Ethoxycarbonyl-2,2-bis(methylthio)ethenyl]isoquinolinium Iodide (**2a**).

A solution of 3.05 g (10 mmoles) of the above methyl dithiocarboxylate derivatives and 2.83 g (20 mmoles) of methyl iodide in 100 ml of ethanol was refluxed for 30 minutes. After removal of the solvent and excess methyl iodide by rotary evaporator, the residue was recrystallized from ethanol to give yellow prisms, **2a**, mp 138°, in 70% yield (from isoquinolinium salt); ir (potassium bromide): $\nu$ max $cm^{-1}$ 1690 (C=O); $^1H$ nmr (deuteriochloroform): $\delta$ 1.12 (3H, t, J = 7 Hz, O-$CH_2$-$CH_3$), 2.37 (3H, s, SMe), 2.72 (3H, s, SMe), 4.19 (2H, q, J = 7.0 Hz, O-$CH_2$-), 8.10-8.61 (4H, m, 5, 6, 7, 8-H), 8.73 (1H, d, J = 7.9 Hz, 4-H), 8.96 (1H, dd, J = 1.5, 7.8 Hz, 3-H), 10.31 (1H, s, 1-H).

*Anal.* Calcd. for $C_{16}H_{18}INO_2S_2$: C, 42.96; H, 4.06; N, 3.13; S, 14.34. Found: C, 42.62; H, 4.04; N, 3.05; S, 14.59.

(Ethoxycarbonyl)(3-methyl-1-isoquinolinio)[(methylthio)thiocarbonyl]-methylide (Intermediate of **2b**).

This compound was synthesized in 60% yield from 2-ethoxycarbonylmethyl-3-methylisoquinolinium bromide in a manner similar to that described for the preparation of **2a**. The intermediate of this reaction which is the corresponding methyl dithiocarboxylate, and orange needles, mp 251°; ir (potassium bromide): $\nu$ max $cm^{-1}$ 1645 (C=O); $^1H$ nmr (deuteriochloroform): $\delta$ 1.15 (3H, t, J = 7.0 Hz, O-$CH_2$-$CH_3$), 2.65 (3H, s, SMe), 2.67 (3H, s, 3-Me), 3.96-4.34 (2H, m, O-$CH_2$-), 7.68-8.18 (5H, m, 4, 5, 6, 7, 8-H), 9.16 (1H, s, 1-H).

*Anal.* Calcd. for $C_{16}H_{17}NO_2S_2$: C, 60.16; H, 5.36; N, 4.38; S, 20.08. Found: C, 59.95; H, 5.38; N, 4.30; S, 20.10.

2-[1-Ethoxycarbonyl-2,2-bis(methylthio)ethenyl]-3-methylisoquinolinium Iodide (**2b**).

An analytical sample was prepared by recrystallization from ethanol to give yellow needles, mp 118°, in 90% yield; ir (potassium bromide): $\nu$ max $cm^{-1}$ 1700 (C=O); $^1H$ nmr (deuteriodimethylsulfoxide): $\delta$ 1.11 (3H, t, J = 7.0 Hz, O-$CH_2$-$CH_3$), 2.45 (3H, s, SMe), 2.67 (3H, s, 3-Me), 2.73 (3H, s, SMe), 4.09-4.32 (2H, m, O-$CH_2$-), 8.02-8.53 (4H, m, 5, 6, 7, 8-H), 8.68 (1H, s, 4-H), 10.29 (1H, s, 1-H).

*Anal.* Calcd. for $C_{17}H_{20}INO_2S_2$: C, 44.28; H, 4.37; N, 3.04; S, 13.91. Found: C, 44.15; H, 4.33; N, 3.00; S, 14.21.

Reaction of Pyridinium Ketene Dithioacetals with Aromatic *N*-Imines.

A solution of 10 mmoles of ketene dithioacetals **1a-r**, 10 mmoles of aromatic *N*-imines **3a-m,4,5**, 10 ml of triethylamine in 100 ml of ethanol was refluxed for 5 hours. After removal of the solvent and excess triethylamine, 200 ml of ice-water was added to the residue. The resulting precipitate was collected by filtration and recrystallized from an appropriate solvent such as ethanol to give the corresponding products. The main products were purified by either recrystallization or alumina column chromatography using hexane and hexane-benzene as the eluent. A mixture of **9i** and **9j** was readily separated by alumina column chromatography. Elution with hexane gave **9j** and continued elution with hexane-benzene (1:3) afforded **9i**. These compounds were purified by recrystallization from ethanol. Compound **11d** could not be separated from admixture with **11b** by tlc, alumina column chromatography, or recrystallization.

Reaction of Pyridinium Ketene Dithioacetals with *S*-Imines.

A solution of pyridinium ketene dithioacetals (10 mmoles). and either *S*-imines [*S*-aminotetrahydrothiophenium mesitylenesulfonates] **6** (50 mmoles), or diphenylsulfilimine **7** (20 mmoles), or dimethylsulfoximine **8**, (20 mmoles)], and 10 ml of triethylamine in 100 ml of ethanol was refluxed 5 hours. The solvent and excess triethylamine were removed by rotary evaporation and the residue was washed with water. The product was recrystallized from ethanol to give the corresponding imidazo[1,2-*a*]-pyridine derivatives **9a-k**. A mixture of **9c** and **9e** was separated by alumina column chromatography. Elution with hexane gave **9e** and further elution with hexane-benzene gave **9c**.

Ethyl 2-Methylthioimidazo[1,2-*a*]pyridine-3-carboxylate (**9a**).

This compound was obtained as colorless needles, mp 106° (lit mp 106° [10]).

Ethyl 5-Methyl-2-methylthioimidazo[1,2-*a*]pyridine-3-carboxylate (**9b**).

This compound was obtained as colorless needles, mp 80°; ir (potassium bromide): $\nu$ max $cm^{-1}$ 1685 (CO); uv (ethanol): $\lambda$ max nm (log $\epsilon$) 259 (4.29), 306 (3.66); $^1H$ nmr (deuteriochloroform): $\delta$ 1.45 (3H, t, O-$CH_2$-$CH_3$), 2.66 (6H, s, 5-Me and SMe), 4.38 (2H, q, O-$CH_2$-), 6.70 (1H, d, J = 8.0 Hz, 6-H or 8-H), 7.28 (1H, t, J = 8.0 Hz, 7-H), 7.46 (1H, d, J = 8.0 Hz, 6-H or 8-H).

*Anal.* Calcd. for $C_{12}H_{14}N_2O_2S$: C, 57.58; H, 5.64; N, 11.19; S, 12.81. Found: C, 57.52; H, 5.60; N, 11.51; S, 12.79.

Ethyl 6-Methyl-2-methylthioimidazo[1,2-*a*]pyridine-3-carboxylate (**9c**).

This compound was obtained as colorless needles, mp 113° (lit mp 113° [9]).

Ethyl 7-Methyl-2-methylthioimidazo[1,2-*a*]pyridine-3-carboxylate (**9d**).

This compound was obtained as colorless needles, mp 89°; ir (potassium bromide): $\nu$ max $cm^{-1}$ 1668 (CO); uv (ethanol): $\lambda$ max nm (log $\epsilon$) 260 (4.60), 305 (4.12); $^1H$ nmr (deuteriochloroform): $\delta$ 1.45 (3H, t, J = 7.0 Hz, O-$CH_2$-$CH_3$), 2.44 (1H, d, J = 0.9 Hz, 7-Me), 2.70 (3H, s, SMe), 4.43 (2H, q, J = 7.0 Hz, O-$CH_2$-), 6.81 (1H, dd, J = 1.8, 6.8 Hz, 6-H), 7.41 (1H, bs, 8-H), 9.10 (1H, d, J = 6.8 Hz, 5-H).

*Anal.* Calcd. for $C_{12}H_{14}N_2O_2S$: C, 57.59; H, 5.64; N, 11.19; S, 12.81. Found: C, 57.58; H, 5.64; N, 11.11; S, 12.71.

Ethyl 8-Methyl-2-methylthioimidazo[1,2-*a*]pyridine-3-carboxylate (**9e**).

This compound was obtained as colorless needles, mp 105° (lit mp 105° [9]).

Ethyl 6,8-Dimethyl-2-methylthioimidazo[1,2-*a*]pyridine-3-carboxylate (**9f**).

This compound was obtained as colorless needles, mp 89° (lit mp 89° [9]).

2-Methylthioimidazo[1,2-*a*]pyridine-3-carbonitrile (**9g**).

This compound was obtained as colorless needles, mp 134°; ir (potassium bromide): $\nu$ max $cm^{-1}$ 2200 (CN); uv (ethanol): $\lambda$ max nm (log $\epsilon$) 254 (4.54), 296 (3.90); $^1H$ nmr (deuteriochloroform): $\delta$ 2.75 (3H, s, SMe), 6.95-7.12 (1H, m, 6-H), 7.32-7.50 (1H, m, 7-H), 7.58-7.69 (1H, bd, J = 8.7 Hz, 8-H), 8.23 (1H, bd, J = 7.0 Hz, 5-H).

*Anal.* Calcd. for $C_9H_7N_3S$: C, 57.12; H, 3.73; N, 22.20; S, 16.94. Found: C, 56.91; H, 3.68; N, 22.43; S, 16.96.

3-Benzoyl-2-methylthioimidazo[1,2-*a*]pyridine (**9h**).

This compound was obtained as colorless needles, mp 158° (lit mp 157-158° [10]; $^1H$ nmr (deuteriochloroform): 2.51 (3H, s, SMe), 7.04 (1H, near dt, 6-H), 7.40-7.76 (6H, m, 7, 8, phenyl-H), 9.62 (1H, d, J = 8.0 Hz, 5-H).

3-Benzoyl-6-methyl-2-methylthioimidazo[1,2-*a*]pyridine (**9i**).

This compound was obtained as colorless needles, mp 146°; ir (potassium bromide): $\nu$ max $cm^{-1}$ 1590 (CO); uv (ethanol): $\lambda$ max nm (log $\epsilon$) 226 (4.28), 276 (4.43), 342 (4.13); $^1H$ nmr (deuteriochloroform): $\delta$ 2.40 (3H, s, 6-Me), 2.49 (3H, s, SMe), 7.08-7.76 (7H, m, phenyl-H), 9.45 (1H, bs, 5-H).

*Anal.* Calcd. for $C_{16}H_{14}N_2OS$: C, 68.06; H, 5.00; N, 9.92; S, 11.36. Found: C, 68.04; H, 4.95; N, 9.81; S, 11.21.

3-Benzoyl-8-methyl-2-methylthioimidazo[1,2-*a*]pyridine (**9j**).

This compound was obtained as colorless needles, mp 122°; ir (potassium bromide): $\nu$ max $cm^{-1}$ 1600 (CO); uv (ethanol): $\lambda$ max nm (log $\epsilon$) 225 (4.29), 272 (4.42), 345 (4.14); $^1H$ nmr (deuteriochloroform): $\delta$ 2.56 (3H, s, SMe), 2.63 (3H, s, 8-Me), 6.93 (1H, dd, J = 7.0, 7.0 Hz, 7.28 (1H, bd, J = 7.0 Hz, 7-H), 7.46-7.20 (5H, m, phenyl-H), 9.39 (1H, bd, J = 7.0 Hz, 5-H).

*Anal.* Calcd. for $C_{16}H_{14}N_2OS$: C, 68.06; H, 5.00; N, 9.92; S, 11.36. Found: C, 67.70; H, 4.94; N, 9.91; S, 11.61.

3-Benzoyl-6,8-dimethyl-2-methylthioimidazo[1,2-*a*]pyridine (**9k**).

This compound was obtained as pale yellow prisms, mp 149°; ir (potassium bromide): $\nu$ max $cm^{-1}$ 1595 (CO); uv (ethanol): $\lambda$ max nm (log $\epsilon$) 232 (4.27), 277 (4.42), 347 (4.11); $^1H$ nmr (deuteriochloroform): $\delta$ 2.36 (3H, s, 6-Me), 2.52 (3H, s, SMe), 2.58 (3H, s, 8-Me), 7.15 (1H, bs, 7-H), 7.44-7.72 (5H, m, phenyl-H), 9.32 (1H, bs, 5-H).

*Anal.* Calcd. for $C_{17}H_{16}N_2OS$: C, 68.89; H, 5.44; N, 9.45; S, 10.82. Found: C, 68.92; H, 5.48; N, 9.23; S, 10.81.

Ethyl 2-Methylthioimidazo[2,1-*a*]isoquinoline-3-carboxylate (**10**).

This compound was obtained as colorless needles, mp 154° (lit mp 154° [9]).

Ethyl 2-Methylthiopyrazolo[1,5-*a*]pyridine-3-carboxylate (**11a**).

This compound was obtained as colorless needles, mp 106° (lit mp 103° [8]).

Ethyl 5-Methyl-2-methylthiopyrazolo[1,5-*a*]pyridine (**11c**).

This compound was obtained as colorless needles, mp 137°, ir (potassium bromide): $\nu$ max $cm^{-1}$ 1670 (CO); uv (ethanol): $\lambda$ max nm (log $\epsilon$) 249 (4.63), 317 (3.87); $^1H$ nmr (deuteriochloroform): $\delta$ 1.43 (3H, t, J = 7.0 Hz, O-$CH_2$-$CH_3$), 2.43 (3H, s, 7-Me), 2.62 (3H, s, SMe), 4.39 (2H, q, O-$CH_2$-), 6.66 (1H, dd, J = 1.6, 7.0 Hz, 6-H), 7.78 (1H, bs, 4-H), 8.26 (1H, d, J = 7.0 Hz, 7-H).

*Anal.* Calcd. for $C_{12}H_{14}N_2O_2S$: C, 57.58; H, 5.64; N, 11.19; S, 12.81. Found: C, 57.76; H, 5.82; N, 10.88; S, 12.78.

Ethyl 6-Methyl-2-methylthiopyrazolo[1,5-*a*]pyridine (**11d**).

This compound was obtained as colorless needles, mp 98°; ir (potassium bromide): $\nu$ max $cm^{-1}$ 1680 (CO); uv (ethanol): $\lambda$ max nm (log $\epsilon$) 249 (4.61), 300 (3.76), 334 (3.85); $^1H$ nmr (deuteriodimethyl sulfoxide): $\delta$ 1.31 (3H, t, J = 7 Hz, O-$CH_2$-$CH_3$), 2.30 (3H, s, SMe), 2.49 (3H, s, 6-Me), 4.24 (2H, q, J = 7.0 Hz, O-$CH_2$-), 7.43 (1H, d, J = 9.0 Hz, 5-H), 7.84 (1H, d, J = 9.0 Hz, 4-H), 4.67 (1H, s, 7-H).

*Anal.* Calcd. for $C_{12}H_{14}N_2O_2S$: C, 57.59; H, 5.64; N, 11.20; S, 12.81. Found: C, 57.18; H, 5.60; N, 11.01; S, 12.56.

Ethyl 7-Methyl-2-methylthiopyrazolo[1,5-*a*]pyridine-3-carboxylate (**11e**).

This compound was obtained as colorless needles, mp 118°; ir (potassium bromide): $\nu$ max $cm^{-1}$ 1670 (CO); uv (ethanol): $\lambda$ max nm (log $\epsilon$) 249 (4.57), 320 (3.98); $^1H$ nmr (deuteriochloroform): $\delta$ 1.41 (3H, t, J = 7.0 Hz, O-$CH_2$-$CH_3$), 2.65 (3H, s, SMe), 2.72 (3H, s, 7-Me), 4.37 (2H, q, O-$CH_2$-), 6.64 (1H, d, J = 7.0 Hz, 6-H), 7.29 (1H, m, 5-H), 7.93 (1H, d, J = 10.0 Hz, 4-H).

*Anal.* Calcd. for $C_{12}H_{14}N_2O_2S$: C, 57.58; H, 5.64; N, 11.19; S, 12.81. Found: C, 57.66; H, 5.70; N, 11.10; S, 12.79.

2-Methylthiopyrazolo[1,5-*a*]pyridine-3-carbonitrile (**11f**).

This compound could not be separated from a mixture of **9g** and **11f** by tlc, alumina column chromatography, and recrystallization. The existence of **11f** was confirmed by gc and $^1H$-nmr by comparison with an authentic sample [8].

5-Methyl-2-methylthiopyrazolo[1,5-*a*]pyridine-3-carbonitrile (**11g**).

This compound could not be separated from a mixture of **9g** and **11g** by tlc, alumina column chromatography, and recrystallization. The existence of **11g** was confirmed by gc and $^1H$-nmr by comparison with an authentic sample [8].

Ethyl 4-Amino-2-methylthiopyrazolo[1,5-*a*]pyridine-3-carboxylate (**11h**).

This compound was obtained as colorless needles, mp 125°; ir (potassium bromide): $\nu$ max $cm^{-1}$ 3340 (NH), 1662 (CO); uv (ethanol): max nm (log $\epsilon$) 238 (4.28), 265 (4.27), 295 (3.90), 347 (4.09); $^1H$ nmr (deuteriochloroform): $\delta$ 1.45 (3H, t, J = 7.0 Hz, O-$CH_2$-$CH_3$), 2.59 (3H, s, SMe), 4.36 (2H, q, J = 7.0 Hz, O-$CH_2$-), 6.40 (1H, J = 1.1, 7.7 Hz, 5-H), 6.50 (2H,

bs, $NH_2$), 6.68 (1H, J = 6.6, 7.7 Hz, 6-H), 7.89 (1H, dd, J = 1.1, 6.6 Hz, 7-H).

*Anal.* Calcd. for $C_{11}H_{13}N_3O_2S$: C, 52.57; H, 5.21; N, 16.79; S, 12.76. Found: C, 52.31; H, 5.23; N, 16.58; S, 12.72.

Ethyl 4-Hydroxy-2-methylthiopyrazolo[1,5-*a*]pyridine-3-carbonitrile (**11i**).

This compound was obtained as colorless leaflets, mp 157°; ir (potassium bromide): $\nu$ max $cm^{-1}$ 3400 (OH), 1642, 1616 (CO); uv (ethanol): $\lambda$ max nm (log $\epsilon$) 238 (4.39), 262 (4.31), 286 (3.85), 297 (3.86), 328 (4.18), 341 (4.19); $^1H$ nmr (deuteriochloroform): $\delta$ 1.42 (3H, t, J = 7.0 Hz, O-$CH_2$-$CH_3$), 2.57 (3H, s, SMe), 4.18 (2H, q, J = 7.0 Hz, O-$CH_2$-), 6.66-6.77 (2H, m, 5-H, 6-H), 7.92-8.00 (1H, m, 7-H).

*Anal.* Calcd. for $C_{11}H_{12}N_2O_3S$: C, 52.37; H, 4.79; N, 11.10; S, 12.71. Found: C, 52.27; H, 4.77; N, 11.01; S, 12.62.

Ethyl 5-Carbamoyl-2-methylthiopyrazolo[1,5-*a*]pyridine-3-carboxylate (**11j**).

This compound was obtained as colorless needles, mp 221°; ir (potassium bromide): $\nu$ max $cm^{-1}$ 3390, 3290 ($NH_2$), 1665, 1645 (CO); uv (ethanol): $\lambda$ max nm (log $\epsilon$) 219 (4.28), 255 (4.60), 315 (3.98), 344 (3.75); $^1H$ nmr (deuteriochloroform + deuteriodimethyl sulfoxide): $\delta$ 1.39 (3H, t, J = 7.0 Hz, O-$CH_2$-$CH_3$), 2.58 (3H, s, SMe), 4.32 (2H, q, J = 7.0 Hz, O-$CH_2$-), 7.42 (1H, dd, J = 1.0, 7.0 Hz, 6-H), 7.26 (2H, bs, $NH_2$), 8.49 (1H, d, J = 1.0 Hz, 5-H), 8.62 (1H, J = 7.0 Hz, 7-H).

*Anal.* Calcd. for $C_{12}H_{13}N_3O_3S$: C, 51.60; H, 4.69; N, 15.04; S, 11.48. Found: C, 51.61; H, 4.73; N, 15.00; S, 11.36.

Ethyl 5-Cyano-2-methylthiopyrazolo[1,5-*a*]pyridine-3-carboxylate (**11k**).

This compound was obtained as colorless needles, mp 159°; ir (potassium bromide): $\nu$ max $cm^{-1}$ 2220 (CN), 1675 (CO); uv (ethanol): $\lambda$ max nm (log $\epsilon$) 223 (4.31), 260 (4.60), 322 (4.03), 350 (3.75); $^1H$ nmr (deuteriochloroform): $\delta$ 1.45 (3H, t, J = 7.0 Hz, O-$CH_2$-$CH_3$), 2.64 (3H, s, SMe), 4.42 (2H, q, J = 7.0 Hz, O-$CH_2$-), 6.98 (1H, dd, J = 2.0, 8.0 Hz, 6-H), 4.44 (1H, bs, 5-H), 8.53 (1H, d, J = 8.0 Hz, 7-H).

*Anal.* Calcd. for $C_{12}H_{11}N_3O_2S$: C, 55.16; H, 4.24; N, 16.08; S, 12.27. Found: C, 55.11; H, 4.25; N, 16.29; S, 12.16.

Ethyl 3-Benzoyl-2-methylthiopyrazolo[1,5-*a*]pyridine-5-carboxylate (**11l**).

This compound was obtained as colorless needles, mp 154°; ir (potassium bromide): $\nu$ max $cm^{-1}$ 1715, 1618 (CO); uv (ethanol): $\lambda$ max nm (log $\epsilon$) 256 (4.56), 325 (4.06), 364 (3.94); $^1H$ nmr (deuteriochloroform): $\delta$ 1.33 (3H, t, J = 7.0 Hz, O-$CH_2$-$CH_3$), 2.59 (3H, s, SMe), 4.31 (2H, q, J = 7.0 Hz, O-$CH_2$-), 7.36-7.73 (6H, m, 6-H, phenyl-H), 8.04 (1H, bs, 5-H), 8.45 (1H, d, J = 7.0 Hz, 7-H).

*Anal.* Calcd. for $C_{18}H_{16}N_2O_3S$: C, 63.51; H, 4.74; N, 8.23; S, 9.42. Found: C, 63.46; H, 4.76; N, 8.30; S, 9.63.

Ethyl 6-*N*,*N*-Diethylcarbamoyl-2-methylthiopyrazolo[1,5-*a*]pyridine-3-carboxylate (**11m**).

This compound was obtained as colorless needles, mp 136°; ir (potassium bromide): $\nu$ max $cm^{-1}$ 1688, 1615 (CO); uv (ethanol): $\lambda$ max nm (log $\epsilon$) 265 (4.67), 310 (3.83); $^1H$ nmr (deuteriochloroform): $\delta$ 1.23 (6H, t, J = 7.0 Hz, N-$CH_2$-$CH_3$), 1.43 (3H, t, J = 7.0 Hz, O-$CH_2$-$CH_3$), 2.62 (3H, s, SMe), 3.46 (4H, q, J = 7.0 Hz, N-$CH_2$-), 4.39 (2H, q, J = 7.0 Hz, O-$CH_2$-), 7.38 (1H, d, J = 9.0 Hz, 5-H), 8.05 (1H, d, J = 9.0 Hz, 4-H), 8.57 (1H, s, 7-H).

*Anal.* Calcd. for $C_{16}H_{21}N_3O_3S$: C, 57.29; H, 6.31; N, 12.53; S, 9.56. Found: C, 57.00; H, 6.41; N, 12.52; S, 9.51.

3-Benzoyl-2-methylthiopyrazolo[1,5-*a*]pyridine-6-carboxamide (**11p**).

This compound was obtained as colorless needles, mp 213°; ir (potassium bromide): $\nu$ max $cm^{-1}$ 3380 (NH), 1710, 1620 (CO); uv (ethanol): $\lambda$ max nm (log $\epsilon$) 220 (4.33), 272 (4.45), 343 (4.18); $^1H$ nmr (deuteriochloroform + deuteriodimethyl sulfoxide): $\delta$ 2.99 (3H, s, SMe), 7.19 (1H, d, J = 10.0 Hz, 4-H), 7.48-7.72 (7H, m, phenyl-H, $NH_2$), 7.83 (1H, d, J = 10.0 Hz, 5-H), 9.41 (1H, s, 7-H).

*Anal.* Calcd. for $C_{16}H_{13}N_3O_2S$: C, 61.72; H, 4.21; N, 13.50; S, 10.30. Found: C, 61.56; H, 4.25; N, 13.20; S, 10.29.

Methyl 2-Methylthiopyrazolo[1,5-*a*]pyridine-6-carboxylate (**11q**).

This compound was obtained as colorless needles, mp 92°; ir (potassium bromide): $\nu$ max $cm^{-1}$ 1720 (CO); uv (ethanol): $\lambda$ max nm (log $\epsilon$) 272 (4.46), 316 (3.93); $^1H$ nmr (deuteriochloroform): $\delta$ 2.63 (3H, s, SMe), 3.96 (3H, s, OMe), 6.41 (1H, s, 3-H), 7.37 (1H, d, J = 9.0 Hz, 4-H), 7.63 (1H, d, J = 9.0 Hz, 5-H), 9.14 (1H, s, 7-H).

*Anal.* Calcd. for $C_{10}H_{10}N_2O_2S$: C, 54.04; H, 4.54; N, 12.60; S, 14.42. Found: C, 54.10; H, 4.53; N, 12.62; S, 14.39.

Ethyl 2-Methylthiopyrazolo[1,5-*a*]quinoline-3-carboxylate (**12**).

This compound was obtained as colorless needles, mp 122°; ir (potassium bromide): $\nu$ max $cm^{-1}$ 1690 (CO); uv (ethanol): $\lambda$ max nm (log $\epsilon$) 232 (4.07), 263 (4.69), 318 (4.04), 344 (3.93), 360 (3.84); $^1H$ nmr (deuteriochloroform): $\delta$ 1.43 (3H, t, J = 7.0 Hz, O-$CH_2$-$CH_3$), 2.71 (3H, s, SMe), 4.41 (2H, q, J = 7.0 Hz, O-$CH_2$-), 7.48-7.92 (3H, m, 6, 7, 8-H), 7.68 (1H, d, J = 9.0 Hz, 5-H), 8.03 (1H, d, J = 9.0 Hz, 4-H), 8.63 (1H, d, J = 9.0 Hz, 9-H).

*Anal.* Calcd. for $C_{15}H_{14}N_2O_2S$: C, 62.92; H, 4.93; N, 9.78; S, 11.20. Found: C, 62.79; H, 4.93; N, 9.64; S, 11.05.

Ethyl 2-Methylthiopyrazolo[1,5-*a*]isoquinoline-1-carboxylate (**13**).

This compound was obtained as colorless needles, mp 97°; ir (potassium bromide): $\nu$ max $cm^{-1}$ 1700 (CO); uv (ethanol): $\lambda$ max nm (log $\epsilon$) 251 (4.44), 273 (4.66), 331 (3.80); $^1H$ nmr (deuteriochloroform): $\delta$ 1.48 (3H, s, O-$CH_2$-$CH_3$), 2.63 (3H, s, SMe), 4.45 (2H, d, J = 7.0 Hz, O-$CH_2$-), 7.09 (1H, d, J = 8.0 Hz, 5-H), 7.56-7.82 (3H, m, 7, 8, 9-H), 8.23 (1H, d, J = 8.0 Hz, 6-H), 9.78 (1H, m, 10-H).

*Anal.* Calcd. for $C_{15}H_{14}N_2O_2S$: C, 62.92; H, 4.93; N, 9.78; S, 11.20. Found: C, 62.80; H, 4.95; N, 9.74; S, 11.33.

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