Synthesis of Cycl[3.2.2]azine and Benzo[*g*]cycl[3.2.2]azine Derivatives by Use of the [2 + 8] Cycloaddition Reaction of Indolizines and Dimethyl Acetylenedicarboxylate

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The reaction of 1-ethoxycarbonylmethylpyridinium bromides **5a-k** with nitro ketene dithioacetal, 1,1-bis(methylthio)-2-nitroethylene (**2**), in the presence of triethylamine in ethanol gave the desired ethyl 2-methylthioindolizine-3-carboxylates **3a-k** in good yields, along with ethyl 2-methylthio-1-nitroindolizine-3-carboxylates **4a-d**. Deesterification of **3** using sodium hydroxide in methanol followed by treatment with polyphosphoric acid gave the corresponding 2-methylthioindolizines **5a-d** in good yields. The desulfurization of **5** with Raney-nickel in ethanol occurs smoothly to give the 1,2,3-unsubstituted indolizines **6a-c** (**a**, parent indolizine; **b**, 8-methylindolzine; **c**, 6,8-dimethylindolizine). Similarly, pyrrolo[2,1-*a*]isoquinoline (**19**) was also synthesized.

These indolizine and pyrrolo[1,2-*a*]isoquinoline derivatives were allowed to react with dimethyl acetylene to give the corresponding cycl[3.2.2]azine and benzo[*g*]cycl[3.2.2]azine derivatives in good results.

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Indolizines are key intermediates for the synthesis of cycl[3.2.2]azine [1-4]. At present the most general method for the synthesis of indolizines and their related compounds is still the Tschitschibabin reaction because the modified synthesis of a variety of substituted indolizines can be easily attained [5]. However, this method is inconvenient for the synthesis of 1,2,3-unsubstituted indolizines. We attempted to solve this problem by use of ketene dithioacetals. It has been reported that ethyl 8-methyl-2-methylthioindolizine-3-carboxylate (**3b**) was prepared by the reaction of methylated pyridinium salts with 1,1-bis(methylthio)-2-nitroethylene (**2**) [6] in the presence of triethylamine as a base in good yields [7]. However, unsubstituted indolizines on the pyridine ring was not obtained. For the synthesis of the parent indolizine (**6a**), at first, we attempted the synthesis of ethyl 2-methylthioindolizine-3-carboxylate which is useful as a key intermediate of cycl[3.2.2]azines.

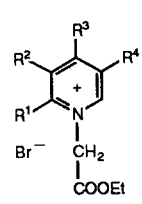
The reaction of 1-ethoxycarbonylmethylpyridinium bromide (**1a**) with **2** in the presence of triethylamine in ethanol gave the desired ethyl 2-methylthioindolizine-3-carboxylate (**3a**) in 93% yield, along with ethyl 2-methylthio-1-nitroindolizine-3-carboxylate (**4a**) in 5% yield. Similarly 1-ethoxycarbonylmethyl-3-methylpyridinium bromide (**1b**) reacted with **2** to give two products, ethyl 8-methyl-2-methylthioindolizine-3-carboxylate (**3b**), ethyl 6-methyl-2-methylthioindolizine-3-carboxylate (**3c**) in 82 and 5% yields, respectively. 1-Nitroindolizine derivative could not be detected in the reaction mixture. In the reaction of 3- and 4-ethyl-1-ethoxycarbonylmethylpyridinium bromides **1c,d** with **2** under the same condition, **3d** and **3e** were obtained in 46 and 28% yields. 4-Benzyl-1-ethoxycarbonylmethylpyridinium bromide (**1e**) was allowed to react with **2** to give ethyl 7-benzyl-2-methylthioindolizine-3-carboxylate (**3f**) in 48% yield. Moreover, 3,5-dimethyl-1-ethoxycarbonylmethylpyridinium bromide (**1f**) reacted with **2** to give ethyl 6,8-dimethylthioindolizine-3-carboxylate (**3g**) in 92% yield.

The reaction of **1g**, bearing a carbamoyl group as the electron-withdrawing group, with **2** under the same condition gave ethyl 6-carbamoyl-2-methylthio-1-nitroindolizine-3-carboxylate (**4b**) and ethyl 8-carbamoyl-2-methylthioindolizine-3-carboxylate (**3h**) in 73 and 8% yields, respectively. 3-*N*,*N*-Diethylcarbamoyl-1-ethoxycarbonylmethylpyridinium bromide (**1h**) was allowed to react with **22** to give **3i** and **4c** in **4** and 45% yields, respectively. When 4-acetyl-1-ethoxycarbonylmethylpridinium bromide (**1i**) reacted with **2** under the same condition, ethyl 7-acetyl-2-methylthio-1-nitroindolizine-3-carboxylate (**4d**) was obtained in only 21% yield. In these reactions, 1-nitroindolizine derivatives were obtained as major products (Scheme 1).

Deesterification of **3a** using sodium hydroxide in methanol followed by treatment with polyphosphoric acid (PPA) gave the corresponding 2-methylthioindolizine (**5a**) in 92% yield. The desulfurization of **5a** with Raney-nickel in ethanol solution occurred smoothly to give the parent indolizine (**6a**) in 58% yield [9]. 8-Methylindolizine (**6b**) and 6,8-dimethylindolizine (**6c**) were prepared from **5b** and **5e** in good yield in a manner similar to that described for **6a** (Scheme 3).

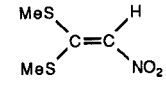
In 1961, Boekelheide reported the synthesis of dimethyl cycl[3.2.2]azine-1,2-dicarboxylate (**7a**) from 1,3-unsubstituted indolizine (**6a**) with DMAD in good yield [9]. However, alkyl and aryl substituted cyclazines on pyridine ring were not prepared because it was difficult to get starting alkylated indolizines [10]. 5,7-Dimethylcycl[3.2.2]azine de-

Scheme 1

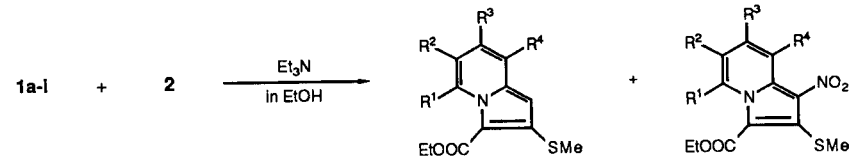


1a-l

1a: $R^1 = R^2 = R^3 = R^4 = H$
b: $R^1 = R^3 = R^4 = H$, $R^2 = Me$
c: $R^1 = R^3 = R^4 = H$, $R^2 = Et$
d: $R^1 = R^2 = R^4 = H$, $R^3 = Et$
e: $R^1 = R^2 = R^4 = H$, $R^3 = Bn$
f: $R^1 = R^3 = H$, $R^2 = R^4 = Me$
g: $R^1 = R^3 = R^4 = H$, $R^2 = CONH_2$
h: $R^1 = R^3 = R^4 = H$, $R^2 = CONEt_2$
i: $R^1 = R^2 = R^4 = H$, $R^3 = COMe$



2



3a-i **4a-d**

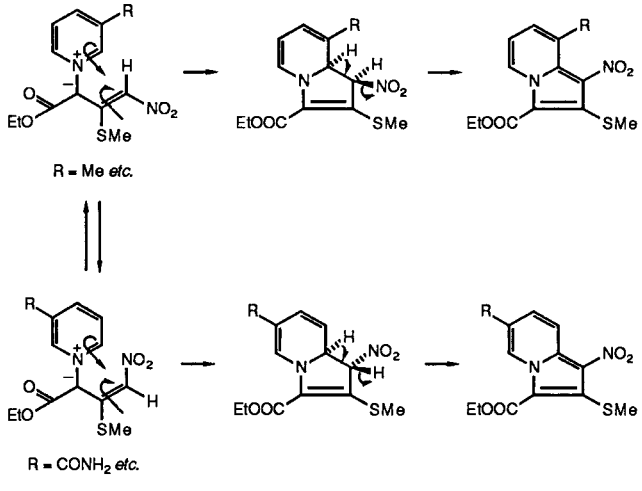
No.	R^1	R^2	R^3	R^4	mp (°C)	Yield (%)
3a	H	H	H	H	46	93
b	H	H	H	Me	87	82
c	H	Me	H	H	38	5
d	H	H	H	Et	70	46
e	H	H	Et	H	58	28
f	H	H	Bn	H	75	48
g	H	Me	H	Me	97	92
h	H	H	H	Ca	238 dec	8
i	H	NEt	H	H	111	4

No.	R^1	R^2	R^3	R^4	mp (°C)	Yield (%)
4a	H	H	H	H	105	5
b	H	Ca	H	H	222	73
c	H	NEt	H	H	111	45
d	H	H	Ac	H	159	21

Me = methyl, Et = ethyl, Bn = benzyl, Ph = phenyl, NEt = *N,N*-diethylcarbamoyl, Ca = carbamoy, Ac = acetyl.

Scheme 2

Reaction Mechanism of the Formation of 3 and 4



R = Me *etc.*

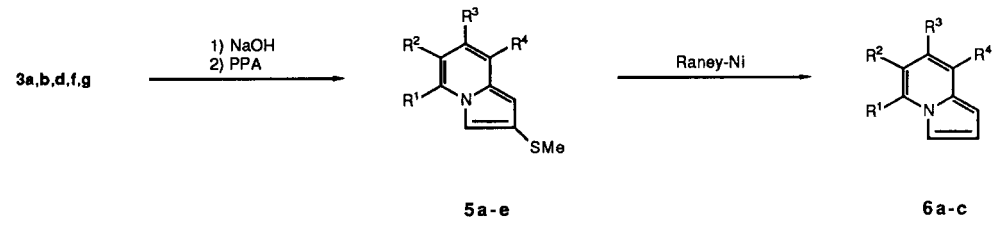
R = $CONH_2$ *etc.*

rivatives may be interesting intermediate for the synthesis of meta cyclophane derivatives of cyclazine [11]. So we attempted the synthesis of 5,7-dimethylcycl[3.2.2]azine (**9b**). The reaction of 6,8-dimethylindolizine (**6c**) with DMAD in the presence of 5% palladium on charcoal in boiling toluene gave a desired cyclized product, dimethyl 5,7-dimethylcycl[3.2.2]azine-1,2-dicarboxylate (**7c**) in 25% yield. 5-Methylcycl[3.2.2]azine-1,2-dicarboxylate (**7b**) was also prepared from **6b** in a similar manner to that described for **7c** in 34% yield.

Hydrolysis of diesters **7a,c** with 10% sodium hydroxide proceeded essentially quantitatively. Decarboxylation of the diacids **8a,b** using copper chromate in quinoline occurred to produce the desired cycl[3.2.2]azines **9a,b** in 30% and 27% yields, respectively (Scheme 4).

The [2 + 8] cycloaddition reaction 2-methylthioindolizine (**5a**) with DMAD also proceeded to give the corresponding dimethyl 3-methylthiocycl[3.2.2]azine-1,2-dicarboxylate (**10a**) in 38% yield. Dimethyl 5,7-dimethyl-3-methylthiocycl[3.2.2]azine-1,2-dicarboxylate (**10b**) and dimethyl 5-methyl-3-methylthiocycl[3.2.2]azine-1,2-dicarboxylate (**10c**) were prepared in a manner similar to that described for **10a** in 40% and 49% yields, respectively. Hydrolysis of **10a** using sodium hydroxide in methanol followed by acidification with 10% hydrogen chloride gave the corresponding diacid. Decarboxylation of the

Scheme 3



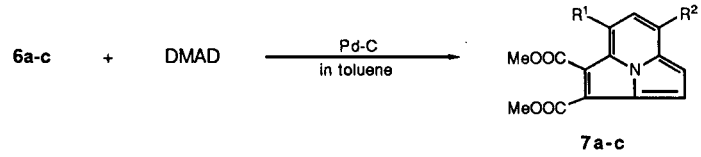
5a-e 6a-c

No.	R^1	R^2	R^3	R^4	mp (°C)	Yield (%)
5a	H	H	H	H	67	92
b	H	H	H	Me	36	94
c	H	H	H	Et	oil	99
d	H	H	Bn	H	58	90
e	H	Me	H	Me	66	92

No.	R^1	R^2	R^3	R^4	mp (°C)	Yield (%)
6a	H	H	H	H	73	58
b	H	H	H	Me	oil	75
c	H	Me	H	Me	oil	90

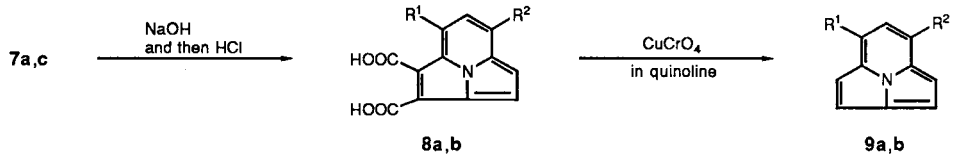
Me = methyl, Et = ethyl, Bn = benzyl.

Scheme 4



7a-c

No.	R^1	R^2	mp (°C)	Yield (%)
7a	H	H	91	33
b	H	Me	93	34
c	Me	Me	60	25



8a,b 9a,b

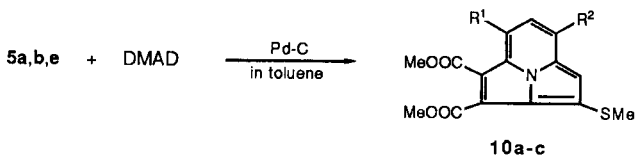
No.	R^1	R^2	mp (°C)	Yield (%)
9a	H	H	64	30
b	Me	Me	48	27

diacid with copper chromate was conducted in boiling quinoline to afford 2-methylthiocycl[3.2.2]azine (**11a**) in 56% yield. The desulfurization of **11a** with Raney-nickel in ethanol occurred to give a desired parent cycl[3.2.2]-azine (**9a**) in 25% yield. 5,6-Dimethyl-3-methylthiocycl-[3.2.2]azine (**11b**) was also prepared in good yield from **10c** in a manner similar to that described for **11a** (Scheme 5).

Recently there has been considerable effort to examine the effect of benzo-fusion on aromatic annulenes [12-17]. It is generally recognized that benzannelation reduces the diatropicity or paratropicity of the macrocyclic system and this reason is explained by the increasing bond localization in the macrocyclic ring. Therefore it seems worthwhile to prepare some benzo-fused compounds of cycl-[3.2.2]azine (**9a**). There are two isomers of benzannelated cycl[3.2.2]azine derivatives, benzo[*g*]cycl[3.2.2]azine (**12**) and benzo[*a*]cycl[3.2.2]azine (**13**) (Scheme 6).

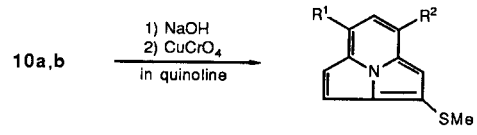
Tominaga *et al.* have reported a facile synthesis of ethyl 1-cycano-2-methylthiopyrrolo[2,1-*a*]isoquinoline-3-carboxylates by use of isoquinolinium *N*-ylides with sulfonyl ketene dithioacetals [18]. This method can be applied to the synthesis of pyrrolo[2,1-*a*]isoquinolines in a manner similar to that described for the synthesis of indolizine derivatives using nitroketene dithioacetal [19]. At first, we attempted the reaction of 2-ethoxycarbonylmethylisoquinolinium bromide (**14**) with 1,1-bis(methylthio)-2-nitroethylene (**2** in the presence of triethylamine in ethanol. Unfor-

Scheme 5



10a-c

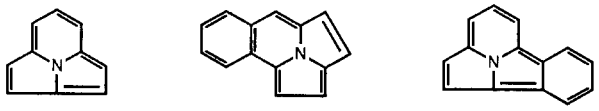
No.	R^1	R^2	mp (°C)	Yield (%)
10a	H	H	113	38
b	Me	Me	138	40
c	H	Me	131	49



11a,b

No.	R^1	R^2	mp (°C)	Yield (%)
11a	H	H	oil	56
b	Me	Me	oil	25

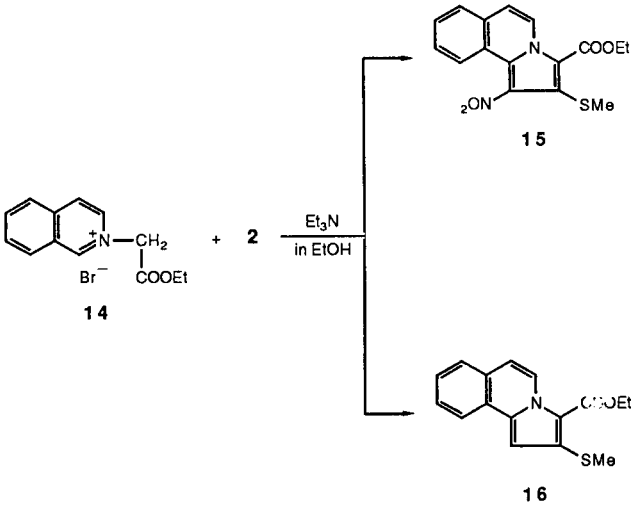
Scheme 6



9a 12 13

tunately, this reaction gave a mixture of ethyl 2-methylthio-1-nitropyrrolo[2,1-*a*]isoquinoline-3-carboxylate (**15**) and ethyl 2-methylthiopyrrolo[2,1-*a*]isoquinoline-3-carboxylate (**16**) in a ratio of 1:1 in 94% yield (Scheme 7).

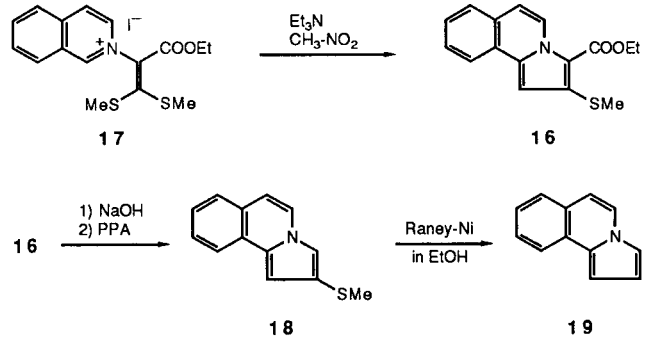
Scheme 7



It has been reported that pyridinium ketene dithioacetals are allowed to react with active methylene compounds to yield the corresponding displacement product of methylthio group of ketene dithioacetals in good yields [19]. We applied the above reaction to the synthesis of the parent pyrrolo[2,1-*a*]isoquinoline (**19**), otherwise inaccessible [19]. The reaction of the isoquinolinium ketene dithioacetal, 2-[1-ethoxycarbonyl-2,2-bis(methylthio)vinyl]isoquinolinium iodide (**17**) [20], with nitromethane in the presence of triethylamine as a base in ethanol gave the corresponding ethyl 2-methylthiopyrrolo[2,1-*a*]isoquinoline-3-carboxylate (**16**) in 56% yield. This method is much better than the reaction of **14** with **2**, since it is not necessary to separate **15** and **16**. Hydrolysis and subsequent decarboxylation of **16** occurred smoothly to give 2-methylthiopyrrolo[2,1-*a*]-isoquinoline (**18**), a key intermediate for the synthesis of **12**, in 91% yield.

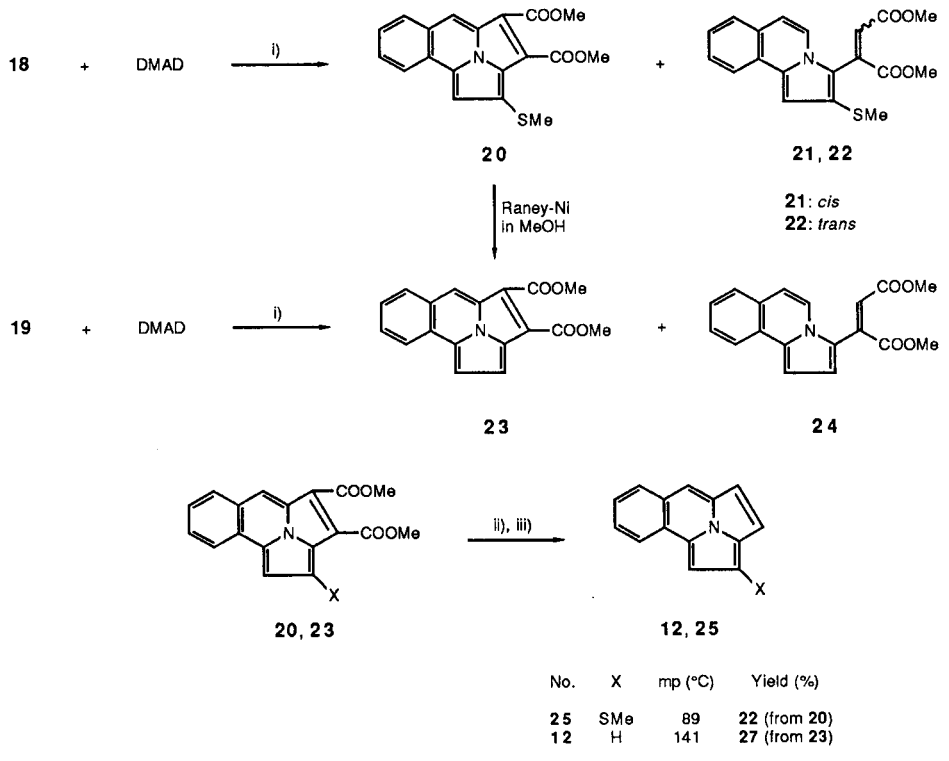
Desulfurization of **18** with Raney-nickel in ethanol gave a parent pyrrolo[2,1-*a*]isoquinoline (**19**) in 88% yield. This compound was not so stable and turned to dark brown solid soon after isolation (Scheme 8).

Scheme 8



The cycloaddition reaction of **19** with DMAD in presence of 5% palladium on charcoal at reflux for 30 hours in toluene gave three products. One of these compounds was an expected cycloaddition product, dimethyl 2-methylthiobenzo[*g*]cycl[3.2.2]azine-3,4-dicarboxylate (**20**) (27% yield). Other two products showed the same molecular formula $C_{19}H_{17}NO_4S$ (MW = 255) by the mass spectrum and were characterized as Michael addition products, **21** and **22** of **18** by the spectrum analysis. The desulfurization of **20** with Raney-nickel occurred easily to give dimethyl benzo-[*g*]cycl[3.2.2]azine-3,4-dicarboxylate (**23**) in 44% yield. Hydrolysis of the diester **23** with 10% sodium hydroxide proceeded essentially quantitatively to give the diacid. Finally, decarboxylation of the diacid by use of copper chromate in quinoline proceeded to give the desired benzo[*g*]-cycl[3.2.2]azine (**12**). The yield of **12** was 22% from **23**. Alternatively **23** was obtained from the parent pyrrolo[2,1-*a*]isoquinoline (**19**) by the reaction with DMAD in 33% yield, together with the Michael addition product

Scheme 9



No.	X	mp (°C)	Yield (%)
25	SMe	89	22 (from 20)
12	H	141	27 (from 23)

i) Pd-C in toluene. ii) NaOH and then ^{1}HCl. iii) $CuCrO_4$ in quinoline.

24 in 11% yield. 2-Methylthiobenzocycl[3.2.2]azine (**25**) was also prepared from **20** in 27% yield in a manner similar to that described for the synthesis of **12** (Scheme 9).

The benzocyclazine (**12**) has an odor like naphthalene and the analytically pure sample was obtained as a stable crystalline solid of bright yellow leaflets after recrystallization from methanol, mp 141°. In the ^{1}H-nmr spectrum the chemical shifts of the peripheral protons are shown in the range of δ 7.37-8.23 ppm for the protons of the cyclazine ring and δ 7.62-8.67 ppm for the benzene ring protons. Thus due to the benzo-fusion, the peripheral protons displayed downfield shifts relative to those of the cycl[3.2.2]-azine (**9a**) [21], implying no reduction in ring current as expected.

Conclusion.

It has been proved that nitro ketene dithioacetal, 1,1-bis(methylthio)-2-nitroethylene (**2**), is a very useful electrophilic reagent for the synthesis of indolizine derivatives. This access to indolizine derivatives is the most useful and convenient method for the preparation of 1,2,3-unsubstituted indolizines and benzoindolizine, pyrrolo[2,1-*a*]isoquinolines which are the key intermediates for the synthesis of cycl[3.2.2]azine derivatives. It is important to note that the ring protons of cycl[3.2.2]azines **9a,b** appears at lower field than the corresponding ring protons of indolizines, since the ring current increases as is seen in polynuclear aromatic hydrocarbons (PAH). Methyl protons

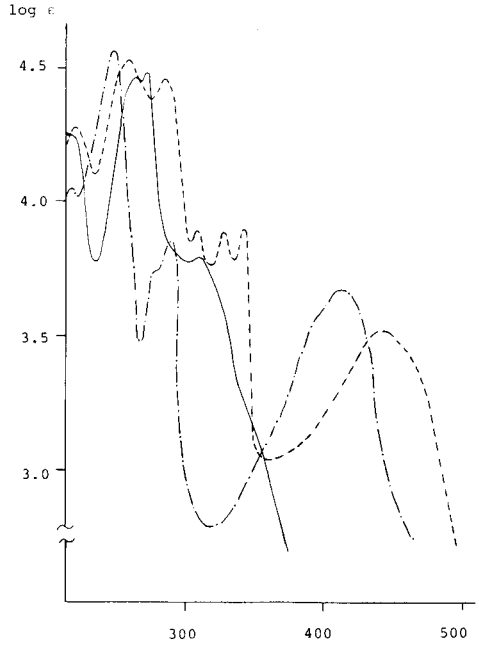


Figure 1. The uv spectra of **9a**, **12**, and **19**.

9a; - - - - - -, **12**; · · · · · ·, **19**; ——

both of the methyl group on the cyclazine ring and the methylthio group are also shown at lower field, compared with those of the corresponding indolizine derivatives. In generally, it is shown that the benzannelation toward the macrocyclic compound reduces the diatropicity. Although the cycl[3.2.2]azine derivatives are little different from benzannelated annulenes prepared by MaCague [16], Mitchell [15], Nakagawa [22], and Ojima [23] *et al.* In the case of PAH, the ring protons display downfield shift with increasing numbers of aromatic rings. So cycl[3.2.2]azine (**9a**) is the intermediary aromaticity between PAH and peripheral conjugated aromatic compounds involving delocalized 10π or 14π electrons. The resulting cycl[3.2.2]-azines and benzocycl[3.2.2]azines are strongly diatropic.

EXPERIMENTAL

All melting points were determined in a capillary tube and uncorrected. Infrared (ir) spectra were recorded in potassium bromide pellets on JASCO IRA-2 spectrometer and Shimadsu IR-460 and ultraviolet (uv) absorption spectra were determined in 95% ethanol on a Hitachi EP-S2 spectrometer. Nuclear magnetic resonance (nmr) spectra were obtained on JNM-PS-100(100 MHz), JNM-FX-90Q(90 MHz), JNM-GX-270(270 MHz), and JNM-GX-400(400 MHz) spectrometers with tetramethylsilane as an internal standard. Mass (ms) spectra were recorded on a JEOL JMS-01SG and JMS-303D mass spectrometers.

Ethyl 2-Methylthioindolizine-3-carboxylate (**3a**) and Ethyl 2-Methylthio-1-nitroindolizine-3-carboxylate (**4a**).

A solution of 12.3 g (50 mmoles) of 1-ethoxymethylcarbonylpyridinium bromide (**1a**), 50 g (100 mmoles) of **2**, and 50 g of triethylamine in 300 ml of ethanol was refluxed for 20 hours. After removal of the solvent and excess of triethylamine, 300 ml of water was added to the residue and extracted benzene (100 ml x 3). The combined extracts were dried over anhydrous sodium sulfate and evaporated *in vacuo*. The residue was chromatographed on neutral alumina column using hexane as an eluent to give 10.85 g (46 mmoles, 93%) of **3a** as colorless crystals. An analytical sample was recrytallized from ethanol to give colorless prisms, mp 46°; ir (potassium bromide): ν max cm^{-1} 1655 (C=O); uv (ethanol): λ max nm (log ϵ) 234 (3.98), 238 (3.97), 274 (4.44), 325 (3.65, shoulder), 340 (3.69), 350 (3.65); ^{1}H-nmr (deuteriochloroform): δ 1.49 (3H, t, J = 7.1 Hz, O-CH_2-CH_3), 4.42 (2H, q, J = 7.1 Hz, O-CH_2-), 6.29 (1H, s, 1-H), 6.70 (1H, dt, J = 1.5, 10.2 Hz, 7 or 6-H), 6.99 (1H, dt, J = 1.3, 12 Hz, 6 or 7-H), 7.35 (1H, near d, 8-H), 9.38 (1H, near d, 5-H).

Anal. Calcd. for $C_{12}H_{13}NO_2S$: C, 61.25; H, 5.57; N, 5.95; S, 13.65. Found: C, 61.02; H, 5.53; N, 6.05; S, 13.81.

Subsequent elusion using a mixture of hexane-benzene (4:1) as an eluent gave 0.66 g (2.5 mmoles, 5%) of **4a** as yellow crystals. An analytical sample was recrystallized from ethanol to give yellow leaflets, mp 105°; ir (potassium bromide): ν max cm^{-1} 1682 (C=O); uv (ethanol): λ max nm (log ϵ) 264 (4.09), 297 (4.05), 368 (4.15); ^{1}H-nmr (deuteriochloroform): δ 1.48 (3H, t, J = 7.5 Hz, O-CH_2-CH_3), 2.56 (3H, s, SCH_3), 4.05 (2H, q, J = 7.5 Hz, O-CH_2-), 7.02-7.19 (1H, m, 6-H), 7.44-7.63 (1H, m, 7-H), 8.46-8.58 (1H, m, 8-H), 9.45-9.56 (1H, m, 5-H).

Anal. Calcd. $C_{12}H_{12}N_2O_4S$: C, 51.42; H, 4.32; N, 10.00; S, 11.44. Found: C, 51.42; H, 4.28; N, 9.93; S, 11.52.

Ethyl 8-Methyl-2-methylthioindolizine-3-carboxylate (**3b**) and Ethyl 6-Methyl-2-methylthioindolizine-3-carboxylate (**3c**).

These compounds were prepared from 22.1 g (85 mmoles) of 1-ethoxycarbonylmethyl-3-methylpyridinium bromide (**1b**) and 14 g (85 mmoles) of **2** in a manner similar to that described for synthesis of **3a** and **4a**. The products were recrystallized from ethanol to give 17.3 g (70 mmoles, 82%) of **3b** as colorless needles, mp 87° (lit [23] mp 87°).

The above mother liquid was chromatographed over alumina column with hexane as an eluent to give 1.1 g (4.4 mmoles, 5%) of **3c** as colorless crystal. An analytical sample was recrystallized from ethanol to give colorless prisms, mp 38°; ir (potassium bromide): ν max cm^{-1} 1679 (C=O); uv (ethanol): λ max nm (log ϵ) 239 (4.16), 274 (4.50), 340 (3.88), 350 (3.86, shoulder); ^{1}H-nmr (deuteriochloroform): δ 1.43 (3H, t, J = 7.0 Hz, O-CH_2-CH_3), 2.20 (3H, s, 6-CH_3), 2.43 (3H, s, SCH_3), 4.41 (1H, d, J = 7.0 Hz, O-CH_2-), 6.08 (1H, near s, 1-H), 6.69 (1H, dd, J = 2.0, 9.3 Hz, 7-H), 7.10 (1H, d, J = 9.3 Hz, 8-H), 9.1 (1H, near s, 5-H).

Anal. Calcd. for $C_{13}H_{15}NO_2S$: C, 62.67; H, 6.06; N, 5.62; S, 12.86. Found: C, 62.58; H, 6.09; N, 5.68; S, 13.07.

Ethyl 8-Ethyl-2-methylthioindolizine-3-carboxylate (**3d**).

This compound was prepared from 13.4 g (49 mmoles) of 1-ethoxycarbonylmethyl-3-ethylpyridinium bromide (**1c**) and 8 g (49 mmoles) of **2** in a manner similar to that described for synthesis of **3a** and **4a**. The reaction product was recrystallized from ethanol to give 5.9 g (22 mmoles, 46%) of **3d** as colorless leaflets, mp 70°; ir (potassium bromide): ν max cm^{-1} 1670 (C=O); uv (ethanol): λ max nm (log ϵ) 235 (4.13, shoulder), 240 (4.14), 338 (3.90), 353 (3.92); ^{1}H-nmr (deuteriochloroform): δ 1.33 (3H, t, J = 7.5 Hz, 8-CH_2-CH_3), 1.45 (3H, t, J = 7.1 Hz, O-CH_2-CH_3), 2.53 (3H, s, SCH_3), 2.80 (2H, q, J = 7.5 Hz, 8-CH_2-), 4.42 (2H, q, 7.1 Hz, O-CH_2-), 6.28 (1H, near s, 1-H), 6.67 (1H, d, J = 7.0 Hz, 6-H), 6.84 (1H, near d, 7-H), 9.82 (1H, near d, 5-H), ms: m/z 264 (M^+ + 1, 16), 263 (M^+, 100), 218 (14), 191 (34), 172 (16).

Anal. Calcd. for $C_{14}H_{17}NO_2S$: C, 63.85; H, 6.51; N, 5.32; S, 12.17. Found: C, 63.98; H, 6.52; N, 5.63; S, 12.14.

Ethyl 7-Ethyl-2-methylthioindolizine-3-carboxylate (**3e**).

This compound was prepared from 2.2 g (8 mmoles) of 1-ethoxycarbonylmethyl-4-ethylpyridinium bromide (**1d**) and 1.3 g (8 mmoles) of **2** in a manner similar to that described for synthesis of **3a** and **4a**. The reaction product was recrystallized from ethanol to give 0.74 g (3 mmoles, 28%) of **3e** as colorless needles, mp 58°; ir (potassium bromide): ν max cm^{-1} 1656 (C=O); uv (ethanol): λ max nm (log ϵ) 236 (4.18, shoulder), 241 (4.19), 257 (4.59), 339 (3.99), 352 (4.00); ^{1}H-nmr (deuteriochloroform): δ 1.25 (3H, t, J = 7.5 Hz, 7-CH_2-CH_3), 1.44 (3H, t, J = 7.1 Hz, O-CH_2-CH_2), 2.49 (3H, s, SCH_3), 2.63 (2H, q, J = 7.5 Hz, 7-CH_2-CH_3), 4.41 (2H, q, J = 7.1 Hz, O-CH_2-), 6.18 (1H, s, 1-H), 6.59 (1H, dd, J = 2.0, 7.3 Hz, 6-H), 7.12 (1H, m, 8-H), 9.28 (1H, d, J = 7.5 Hz, 5-H); ms: m/z 264 (M^+ + 1, 17), 263 (M^+, 100), 191 (54), 172 (31), 158 (25).

Anal. Calcd. for $C_{14}H_{17}NO_2S$: C, 63.85; H, 6.51; N, 5.32; S, 12.17. Found: C, 63.84; H, 6.51; N, 5.36; S, 12.05.

Ethyl 7-Benzyl-2-methylthioindolizine-3-carboxylate (**3f**).

This compound was prepared from 16.8 g (50 mmoles) of 4-benzyl-1-ethoxycarbonylmethylpyridinium bromide (**1e**) and 88.3 g (50 mmoles) of **2** in a manner similar to that described for synthesis of **3a** and **4a**. The reaction product was recrystallized from ethanol to give 7.8 g (24 mmoles, 48%) of **3f** as colorless needles, mp 75°; ir (potassium bromide): ν max cm^{-1} 1680 (C=O); uv (ethanol): λ max nm (log ϵ) 238 (4.13, shoulder), 243 (4.14), 278 (4.65), 340 (4.00), 353 (3.98); ^{1}H-nmr (deuteriochloroform): δ 1.34 (3H, t, J = 7.0 Hz, O-CH_2-CH_3), 2.48 (3H, s, SCH_3), 3.95 (2H, s, 7-CH_2-), 4.40 (2H, q, J = 7.0 Hz, O-CH_2-CH_3), 6.19 (1H, s, 1-H), 6.55 (1H, dd, J = 2.0, 7.25 Hz, 6-H), 7.09 (1H, near s, 8-H), 7.17-7.30 (5H, m, Ph), 9.27 (1H, d, J = 7.25 Hz, 5-H).

Anal. Calcd. for $C_{19}H_{19}NO_2S$: C, 70.13; H, 5.88; N, 4.30; S, 9.85. Found: C, 70.35; H, 5.96; N, 4.27; S, 9.81.

Ethyl 6,8-Dimethylindolizine-3-carboxylate (**3g**).

This compound was prepared from 29.8 g (80 mmoles) of 3,5-dimethyl-1-ethoxycarbonylmethylpyridinium bromide (**1f**) and 13.2 g (80 mmoles) of **2** in a manner similar to that described for synthesis of **3a** and **4a**. The reaction product was recrystallized from ethanol to give 14 g (74 mmoles, 92%) of **3g** as colorless needles, mp 97°; ir (potassium bromide): ν max cm^{-1} 1660 (C=O); uv (ethanol): λ max nm (log ϵ) 242 (4.13), 275 (4.59), 358 (3.87); ^{1}H-nmr (deuteriochloroform): δ 1.44 (3H, t, J = 7.0 Hz, O-CH_2-

CH_3), 2.26 (3H, s, 6 or 8-CH_3), 2.37 (3H, s, 6 or 8-CH_3), 2.49 (3H, s, SCH_3), 4.40 (2H, q, J = 7.0 Hz, O-CH_2-CH_3), 6.18 (1H, s, 1-H), 6.71 (1H, s, 7-H), 9.20 (1H, s, 5-H).

Anal. Calcd. for $C_{15}H_{17}NO_2S$: C, 63.80; H, 6.51; N, 5.32. Found: C, 63.88; H, 6.63; N, 5.30.

Ethyl 8-Carbamoyl-2-methylthioindolizine-3-carboxylate (**3h**) and Ethyl 6-Carbamoyl-2-methylthio-1-nitroindolizine-3-carboxylate (**4b**).

These compounds were prepared from 10.2 g (35 mmoles) of 3-carbamoyl-1-ethoxycarbonylmethylpyridinium bromide (**1g**), 5.8 g (35 mmoles) of **2**, 20 ml of triethylamine, and 200 ml of ethanol in a manner similar to that described for synthesis of **3a** and **4a**. After the reaction and cooling at room temperature, the crystals were collected by filtration and recrystallized from ethanol to give 4.9 g (15 mmoles, 73%) of **4b** as tan needles, mp 222°; ir (potassium bromide): ν max cm^{-1} 3150, 3220 (NH_2), 1665 (C=O), 1495 (NO_2); uv (ethanol): λ max nm (log ϵ) 220 (4.25), 281 (4.33), 380 (4.11); ms: m/z 323 (M^+, 15), 249 (21), 232 (33), 91 (100); ^{1}H-nmr (deuteriodimethyl sulfoxide): δ 1.41 (3H, t, J = 7.0 Hz, O-CH_2-CH_3), 2.52 (3H, s, SCH_3), 4.47 (2H, q, J = 7.0 Hz, O-CH_2-), 7.60-8.20 (2H, bs, NH_2), 8.10 (1H, dd, J = 1.5, 9.2 Hz, 7-H), 8.37 (1H, dd, J = 1.1, 9.3 Hz, 8-H), 9.82 (1H, near s, 5-H).

Anal. Calcd. for $C_{13}H_{13}N_3O_5S$: C, 48.29; H, 4.05; N, 13.00; S, 9.92. Found: C, 48.41; H, 4.15; N, 12.88; S, 9.82.

The filtrate was washed with water and dried over sodium sulfate anhydrous. After evaporation, the residue was purified by preparative tlc (silica gel using chloroform as an eluent) to give 0.48 g (1.7 mmoles, 8%) of **3h** and 2.4 g of **2**. An analytical sample of **3h** was recrystallized from ethanol to give pale yellow needles, mp 236° (brake point); ir (potassium bromide): ν max cm^{-1} 3375, 3185 (NH_2), 1664 (C=O); uv (ethanol): λ max nm (log ϵ) 218 (4.15), 234 (4.07), 295 (4.63), 344 (3.67); ms: m/z 278 (M^+, 100), 206 (23), 173 (16); ^{1}H-nmr (deuteriochloroform): δ 1.46 (3H, t, J = 7.1 Hz, O-CH_2-CH_3), 2.54 (3H, s, SCH_3), 4.44 (2H, q, J = 7.1 Hz, O-CH_2-), 5.91 (2H, bs, NH_2), 6.75 (1H, dd, J = 1.0, 7.0 Hz, 6-H), 6.89 (1H, near s, 1-H), 7.38 (1H, dd, J = 1.0, 7.1 Hz, 7.H), 9.58 (1H, near d, 5-H).

Anal. Calcd. for $C_{13}H_{14}N_2O_3S$: C, 56.10; H, 5.07; N, 10.07; S, 11.52. Found: C, 56.18; H, 5.17; N, 9.87; S, 11.08.

Ethyl 6-*N*,*N*-Diethylcarbamoyl-2-methylthioindolizine-3-carboxylate (**3i**) and Ethyl 6-*N*,*N*-Diethylcarbamoyl-2-methylthio-1-nitroindolizine-3-carboxylate (**4c**).

These compounds were prepared from 2 g (10 mmoles) of *N*,*N*-diethylnicotinamide, 1.7 g (10 mmoles) of ethyl bromoacetate, 1.7 g (12 mmoles) of **2** in a manner similar to that described for synthesis of **3a** and **4a**. The reaction product was recrystallized from ethanol. The yellow crystals that appeared were collected by filtrate to give 0.82 g (2.2 mmoles) of **4c** as yellow needles. The mother liquid was purified by preparative tlc (silica gel using benzene as an eluent) to give 0.61 g (1.6 mmoles, 45%) of **4c**, 0.11 g (0.3 mmole, 4%) of **3i**, and 0.27 g of **2**. Compound **4c** had mp 111°; ir (potassium bromide): ν max cm^{-1} 2975, 2930 (N-CH_2-), 1685 (C=O), 1487 (NO_2); uv (ethanol): λ max nm (log ϵ) 275 (4.34), 380 (4.15); ms: m/z 379 (M^+, 37), 362 (31), 305 (21), 288 (100); ^{1}H-nmr (deuteriochloroform): δ 1.26 (6H, t, J = 7.0 Hz, 2 x N-CH_2-CH_3), 1.48 (3H, t, J = 7.0 Hz, O-CH_2-CH_3), 2.57 (3H, s, SCH_3), 3.45 (4H, q, J = 7.0 Hz, N-CH_2 x 2), 4.50 (2H, q, J = 7.0 Hz, O-CH_2-), 7.54 (1H, dd, J = 1.5, 9.2 Hz, 7-H), 8.52 (1H, dd, J = 1.1, 9.2 Hz, 8-H), 9.63 (1H, dd, J = 1.5, 1.1 Hz, 5-H).

Anal. Calcd. for $C_{17}H_{21}N_3O_5S$: C, 53.85; H, 5.58; N, 11.08; S, 8.45. Found: C, 53.76; H, 5.53; N, 10.96; S, 8.52.

Compound **3i** was obtained as colorless needles, mp 111°; ir (potassium bromide): ν max cm^{-1} 2970, 2930 (NH_2), 1680 (C=O); uv (ethanol): λ max nm (log ϵ) 242 (4.19), 285 (4.65), 345 (3.82); ms: m/z 334 (M^+, 35), 262 (21), 165 (38), 104 (52), 86 (85), 72 (100); ^{1}H-nmr (deuteriochloroform): δ 1.24 (6H, t, J = 7.1 Hz, N-CH_2-CH_3 x 2), 1.45 (3H, t, J = 7.1 Hz, O-CH_2-CH_3), 2.51 (3H, s, SCH_3), 3.47 (4H, q, J = 7.1 Hz, N-CH_2- x 2), 4.42 (2H, q, J = 7.1 Hz, O-CH_2-), 6.35 (1H, s, 1-H), 7.07 (1H, dd, J = 1.3, 9.0 Hz, 7-H), 7.39 (1H, dd, J = 1.1, 9.0 Hz, 8-H), 9.55 (1H, m, 5-H).

Anal. Calcd. for $C_{17}H_{22}N_2O_3S$: C, 61.05; H, 6.63; N, 8.42; S, 9.59. Found: C, 60.92; H, 6.61; N, 8.28; S, 9.51.

Ethyl 7-Acetyl-2-methylthio-1-nitroindolizine-3-carboxylate (**4d**).

This compound was prepared from 1 g (8.3 mmoles) of 4-acetylpyridine, 1.4 g (8.3 mmoles) of ethyl bromoacetate, 1.1 g (6.7 mmoles), 10 ml of triethylamine, and 100 ml of ethanol in a manner similar to that described for the synthesis of **3a** and **4a**. The reaction product was separated purified by the preparative tlc (silica gel) using benzene as an eluent to give 0.39 g (1.2 mmoles, 21%) of **4d** and 0.1 g of **2**. An analytical sample was recrystallized from ethanol to give yellow needles, mp 159°. Compound **8d** had ir (potassium bromide): ν max cm^{-1} 1691, 1680 (C=O), 1505 (NO_2); uv (ethanol): λ max nm (log ϵ) 268 (4.34), 310 (4.14), 394 (4.18); ms: m/z 322 (M^+, 53), 305 (39), 277 (26), 248 (45), 231 (100), 147 (35); ^{1}H-nmr (deuteriochloroform): δ 1.50 (3H, t, J = 7.0 Hz, O-CH_2-CH_3), 2.73 (3H, s, CO-CH_3), 7.61 (1H, dd, J = 2.0, 7.5 H, 6-H), 8.99 (1H, m, 8-H), 9.47 (1H, dd, J = 1.1, 7.5 Hz, 5-H).

Anal Calcd. for $C_{14}H_{14}N_2O_5S$: C, 52.17; H, 4.38; N, 8.69; S, 9.95. Found: C, 52.21; H, 4.44; N, 8.67; S, 9.50.

2-Methylthioindolizine (**5a**).

A solution of 1 g (4.2 mmoles) fo **3a** and 10% sodium hydroxide (sodium hydroxide 0.85 g, 21 mmoles) in 100 ml of methanol was refluxed for 3 hours. After removal of the solvent and water, 15 g of polyphosphoric acid (PPA) was added to the residue and the mixture was heated at 100° for 1 hour. The reaction mixture was poured into 250 ml of ice-water, neutralized with sodium hydroxide and extracted with benzene (100 ml x 3). The combined extracts were dried over anhydrous sodium sulfate and evaporated *in vacuo*. The residue was chromatographed on alumina column with hexane as eluent to give 0.64 g (3.9 mmoles, 92%) of **5a** as colorless needles, mp 67°; ir (potassium bromide): ν max cm^{-1} 3090 (CH_3), 760, 720, 618; uv (ethanol): λ max nm (log ϵ) 244 (4.05, shoulder), 253 (4.14), 257 (4.11), 298 (3.18), 343 (3.18); ^{1}H-nmr (deuteriochloroform): δ 2.48 (3H, s, SCH_3), 6.33-6.73 (3H, m, 1,6,7-H), 7.21-7.29 (2H, m, 3,8-H), 7.76-7.84 (1H, m, 5-H).

Anal. Calcd. for $C_{10}H_9NS$: C, 66.22; H, 5.56; N, 8.58; S, 19.64. Found: C, 66.41; H, 5.61; N, 8.44; S, 19.29.

8-Methyl-2-methylthioindolizine (**5b**).

This compound was prepared from 8.8 g (35 mmoles) of **3b**, 10% sodium hydroxide (sodium hydroxide, 6 g, 150 mmoles) in 400 ml of methanol, and 40 g of PPA in a manner similar to that described for synthesis of **5a**. The residue was chromatographed on alumina column using hexane as an eluent to give 5.9 g (33 moles, 94%) of **9b** as colorless needles, mp 36°; ir (potassium bromide): ν max cm^{-1} 2980, 1360, 751; uv (ethanol): λ max nm (log ϵ) 222 (4.21), 239 (4.33, shoulder), 252 (4.40), 257 (4.38, shoulder), 287 (3.38, shoulder), 297 (3.47), 335 (3.47); ms: m/z 178 (M^+ +1, 13), 177 (M^+, 100), 176 (M^+ −1, 7), 162 (14), 144 (62), 130 (15), 118 (15); ^{1}H-nmr (deuteriochloroform): δ 2.33 (3H, s, 8-CH_3), 2.45 (3H, s, SCH_3), 6.13-6.35 (3H, m, 1,6,7-H), 7.14 (1H, s, 3-H), 7.57 (1H, near d, 5-H).

Anal. Calcd. for $C_{10}H_{11}NS$: C, 67.76; H, 6.25; N, 7.90; S, 18.09. Found: C, 67.92; H, 6.27; N, 7.96; S, 18.06.

8-Ethyl-2-methylthioindolizine (**5c**).

This compound was prepared from 0.42 g (1.6 mmoles) of **3d**, 10% sodium hydroxide (sodium hydroxide, 0.38 g, 9.6 mmoles) in 100 ml of methanol, and 10 g of PPA in a manner similar to that described for synthesis for **5a**. The residue was chromatographed on alumina column using hexane as eluent to give 0.3 g (1.6 mmoles, 100%) of **5c** as colorless viscous oil; ir (potassium bromide): ν max cm^{-1} 2960, 2930; uv (ethanol): λ max nm (log ϵ) 257 (4.39), 288 (3.38), 300 (3.41), 345 (3.29); ms: m/z 192 (M^+ +1, 14), 191 (M^+, 100), 176 (28), 158 (58); ^{1}H-nmr (deuteriochloroform): δ 1.31 (3H, t, J = 7.5 Hz, CH_2-CH_3), 2.48 (3H, s, SCH_3), 2.73 (2H, q, J = 7.5 Hz, CH_2-CH_3), 6.30-6.52 (2H, m, 6,7-H), 6.44 (1H, s, 1-H), 7.21 (1H, d, J = 1.5 Hz, 3-H), 7.68 (1H, near d, 5-H).

Anal. Calcd. for $C_{11}H_{13}NS$: C, 69.55; H, 6.85; N, 7.32; S, 16.76. Found: C, 69.05; H, 6.91; N, 7.27; S, 16.50.

The picrate was obtained as light yellow needles, mp 128°.

Anal. Calcd. for $C_{17}H_{16}N_4O_7S$: C, 48.57; H, 3.84; N, 13.33; S, 7.63. Found: C, 48.65; H, 3.84; N, 13.22; S, 7.62.

7-Benzyl-2-methylthioindolizine (**5d**).

This compound was prepared from 7.7 g (24 mmoles) of **3f**, 10% sodium hydroxide (sodium hydroxide 5.7 g, 144 mmoles) in 400 ml of methanol, and 25 g of PPA in a manner similar to that described for synthesis for **5a**. The residue was chromatographed on alumina column using hexane as eluent to give 6 g (22 mmoles, 90%) of **5d** as colorless needles, mp 58°; ir (potassium bromide): ν max cm^{-1} 1634, 1600, 1516, 1492, 1349, 1314; uv (ethanol): λ max nm (log ϵ) 222 (4.31), 243 (4.47, shoulder), 253 (4.55), 258 (4.52, shoulder), 288 (3.53, shoulder), 299 (3.58), 337 (3.58); ms: m/z 255 ($M^+ + 2$, 6), 254 ($M^+ + 1$, 19), 253 (M^+, 100), 252 ($M^+ - 1$, 9), 220 (55), 204 (20), 176 (10), 91 (11); ^{1}H-nmr (deuteriochloroform): δ 2.45 (3H, s, SCH_3), 3.85 (2H, s, CH_2-), 6.24 (1H, dd, J = 1.8, 7.0 Hz, 6-H), 6.28 (1H, s, 1-H), 7.01 (1H, s, 3-H), 7.13 (1H, near s, 8-H), 7.22-7.35 (5H, m, C_6H_5), 7.68 (1H, d, J = 7.0 Hz, 5-H).

Anal. Calcd. for $C_{16}H_{15}NS$: C, 75.85; H, 5.97; N, 5.53; S, 12.66. Found: C, 76.03; H, 6.06; N, 5.46; S, 12.66.

The picrate was obtained as yellow needles, mp 161°.

Anal. Calcd. for $C_{22}H_{18}N_4O_7S$: C, 54.77; H, 3.76; N, 11.61; S, 6.55. Found: C, 54.91; H, 3.86; N, 11.54; S, 6.55.

6,8-Dimethyl-2-methylthioindolizine (**5e**).

This compound was prepared from 5 g (19 mmoles) of **3g**, 10% sodium hydroxide (sodium hydroxide, 4.6 g, 114 mmoles) in 300 ml of methanol in a manner similar to described for synthesis of **5a**. The residue was chromatographed on alumina column using hexane as an eluent to give 3.5 g (17 mmoles, 92%) of **5e** as colorless needles, mp 66°; ir (potassium bromide): ν max cm^{-1} 2900, 1400, 810; uv (ethanol): λ max nm (log ϵ) 243 (4.34, shoulder), 252 (4.35), 302 (4.00), 334 (4.02); ms: m/z 191 (M^+, 100), 176 (20), 158 (50), 145 (12), 132 (10); ^{1}H-nmr (deuteriochloroform): δ 2.14 (3H, d, J = 1.1 Hz, 6-CH_3), 2.30 (3H, s, 8-CH_3), 2.45 (3H, s, SCH_3), 6.29 (1H, s, 1 or 3-H), 6.30 (1H, s, 1 or 3-H), 7.12 (1H, d, J = 1.8 Hz, 7-H), 7.45 (1H, bs, 5-H).

Anal. Calcd. for $C_{11}H_{13}NS$: C, 69.07; H, 6.85; N, 7.32; S, 16.76. Found: C, 69.45; H, 6.88; N, 7.22; S, 16.84.

An analytical sample of the picrate was recrystallized from methanol to give yellow needles, mp 140°.

Anal. Calcd. for $C_{17}H_{16}N_4O_7S$: C, 48.69; H, 3.85; N, 13.36; S, 7.65. Found: C, 48.64; H, 3.91; N, 13.27; S, 7.58.

Indolizine (**6a**).

A mixture of 0.63 g (3.9 mmoles) of **5a**, 1.4 g of Raney-nickel (W-2), and 30 ml of ethanol was refluxed for 20 hours. After removal of the Raney-nickel and the solvent, the residue was chromatographed on a alumina column using hexane as an eluent to give 0.26 g (2.3 mmoles, 58%) of **6a** as colorless needles, mp 73° (lit [9], mp 73°).

8-Methylindolizine (**6b**).

This compound was prepared from 3.95 g (22 mmoles) of **5b**, 7.9 g of Raney-nickel, and 200 ml of ethanol in a manner similar to that described for synthesis of **6a**. The product was purified by chromatograph on alumina column using hexane as an eluent to give 2.2 g (17 mmoles, 75%) of **6b** as colorless viscous oil; ir (sodium chloride): ν max cm^{-1} 2975, 1358, 1305, 747; uv (ethanol): λ max nm (log ϵ) 238 (4.42), 275 (3.24, shoulder), 286 (3.39), 299 (3.51), 335 (3.30); ms: m/z 132 ($M^+ + 1$, 11), 131 (M^+, 100), 130 ($M^+ - 1$, 80), 177 (19), 144 (34); ^{1}H-nmr (deuteriochloroform): δ 2.33 (3H, s, 8-CH_3), 6.07-6.47 (3H, m, 1,6,7-H), 7.68 (1-H, dd, J = 2.0, 4.0 Hz, 2-H), 7.10-7.20 (1H, m, 3-H), 7.47-7.73 (1H, m, 5-H).

Anal. Calcd. for $C_{10}H_{11}NS$: C, 67.76; H, 6.25; N, 7.90; S, 18.09. Found: 67.92; H, 6.27; N, 7.96; S, 18.06.

6,8-Dimethylindolizine (**6c**).

This compound was prepared from 8.8 g (46 mmoles) of **5e**, 17 g of Raney-nickel, and 300 ml of ethanol in a manner similar to that described for the synthesis of **6a**. The product was purified by chromatography on alumina column using hexane as an eluent to give 5 g (34 mmoles, 90%) of **6c** as a colorless oil; ir (sodium chloride): ν max cm^{-1} 2975, 1349, 1306, 708; uv (ethanol): λ max nm (log ϵ) 231 (4.20, shoulder), 236 (4.32), 260 (3.65), 283 (3.31), 295 (3.40), 342 (3.13); ms: m/z 146 ($M^+ + 1$, 18), 145 (M^+, 100), 144 ($M^+ - 1$, 70), 130 (26); ^{1}H-nmr (deuteriochloroform): δ 2.17 (3H, d, J = 1.1 Hz, 6-CH_3), 2.36 (3H, s, 8-CH_3), 6.29-6.34 (2H, m, 1,3-H), 6.69 (1H, dd, J = 2.6, 4.0 Hz, 2-H), 7.17-7.23 (1H, m, 7-H), 7.58 (1H, bs, 5-H).

Anal. Calcd. for $C_{10}H_{11}N$: C, 82.72; H, 7.64; N, 9.65. Found: C, 82.06; H, 7.97; N, 9.52.

Dimethyl Cycl[3.2.2]azine-1,2-dicarboxylate (**7a**).

A mixture of 0.49 g (4.2 mmoles) of **6a**, 1.19 g (8.4 mmoles) of dimethyl acetylenedicarboxylate (DMAD), 1.2 g of 5% of palladium-on-charcoal (Pd-C), and 100 ml of toluene was refluxed for 30 hours. After removal of the solvent and Pd-C, the residue was taken up 20 ml of methanol. The yellow crystals that appeared were collected by filtration and recrystallized from methanol to give 0.36 g (1.4 mmoles, 33%) of **7a** as yellow needles, mp 91° (lit [9], mp 91°).

Dimethyl 5-Methyl-3-methylthiocycl[3.2.2]azine-1,2-dicarboxylate (**7b**).

This compound was prepared from 2.18 g (16.6 mmoles) of **6b**, 4.8 g (33.8 mmoles) of DMAD, 4.8 g of Pd-C, and 150 ml of toluene in a manner similar to that described for the synthesis of **7a**. The product was taken up 20 ml of methanol. The yellow crystal that appeared was collected by filtration and recrystallized from methanol to give 1.53 g (5.7 mmoles) of **7b** as yellow needles, mp 93°; ir (potassium bromide): ν max cm^{-1} 1728 (C=O); uv (ethanol): λ max nm (log ϵ) 220 (4.13), 253 (4.44), 265 (4.39, shoulder), 320 (3.95), 414 (4.02); ms: m/z 272 ($M^+ + 1$, 18), 271 (M^+, 100), 240 (94), 210 (14); ^{1}H-nmr (deuteriochlororform): δ 2.87 (3H, s, 5-CH_3), 4.02 (3H, s, O-CH_3), 4.06 (3H, s, O-CH_3), 7.44 (1H, d, J = 4.6 Hz, 3-H), 7.63-7.73 (2H, m, 1,6-H), 8.32 (1H, d, J = 8.4 Hz, 7-H).

Anal. Calcd. for $C_{15}H_{15}NO_4$: C, 66.41; H, 4.83; N, 5.16. Found: C, 65.81; H, 4.98; N, 5.12.

Dimethyl 5,7-Dimethylcycl[3.2.2]azine-1,2-dicarboxylate (**7c**).

This compound was prepared from 0.42 g (2.9 mmoles) of **6c**, 0.62 g (4.4 mmoles) of DMAD, 0.6 g of Pd-C, 100 ml of toluene in a manner similar to that described for synthesis of **7a**. The residue was chromatographed on alumina column using a mixture of benzene-hexane (1:5) as an eluent to give 0.21 g (0.725 mmole, 25%) of **7c** as yellow needles, mp 73°; ir (potassium bromide): ν max cm^{-1} 2960, 1720 (C=O); uv (ethanol): λ max nm (log ϵ) 258 (4.47), 322 (4.08), 410 (3.91), 420 (3.87); ms: m/z 286 ($M^+ + 1$, 12), 285 (M^+, 68), 253 (100), 195 (23); ^{1}H-nmr (deuteriochloroform): δ 2.81 (3H, s, 5 or 7-CH_3), 2.88 (3H, s, 5 or 7-CH_3), 4.01 (3H, s, O-CH_3), 4.02 (3H, s, O-CH_3), 7.36 (1H, d, J = 4.6 Hz, 2-H), 7.38 (1H, s, 6-H), 7.60 (1H, d, J = 4.6 Hz, 1-H).

Anal. Calcd. for $C_{16}H_{15}NO_4$: C, 67.36; H, 5.30; N, 4.91. Found: C, 67.33; H, 5.44; N, 4.63.

Cycl[3.2.2]azine (**9a**).

A solution of 1.09 g (4.2 mmoles) of **7a**, 10% sodium hydroxide (sodium hydroxide, 1.35 g, 34 mmoles) solution in 100 ml of methanol was refluxed for 4 hours. After removal of the methanol, the residual solid was dissolved in water. The aqueous solution was acidified with 10% hydrochloric acid. The solid that appeared was collected by filtration to give 0.95 g (4.1 mmoles, 98%) of diacid. This acid must be used after drying by the vacuum pump. A solution of 0.95 g of the crude diacid, 2.7 g of copper chromate, 1.35 g of copper powder, and 100 ml of quinoline was refluxed for 5 hours. After removal of the catalysts, a solution was acidified with 10% hydrochloric acid and extracted with benzene (100 ml x 3). After removal of the organic layer, the residue was chromatographed on alumina column using hexane as an eluent to give 0.18 g (1.3 mmoles, 30%) of **9a** as yellow prisms, mp 64° (lit [9], mp 64°).

5,7-Dimethylcycl[3.2.2]azine (**9b**).

This compound was prepared from 1.19 g (4.2 mmoles) of **7c**, a solution of 10% sodium hydroxide (sodium hydroxide, 1.3 g, 33 mmoles) in 100 ml of methanol, 1.5 g of copper chromate, 0.75 g of copper powder, and 100 ml of quinoline in a manner similar to that described for the synthesis of **9a**. The residue was chromatographed on alumina column using

hexane as eluent to give 0.19 g (1.1 mmoles, 27%) of **9b**. An analytical sample was recrystallized from methanol to give pale yellow needles, mp 48°; ir (potassium bromide): ν max cm^{-1} 3055, 2920, 1466, 1356, 1303, 785; uv (ethanol): λ max nm (log ε) 225 (4.14), 238 (4.39, shoulder), 248 (4.58), 252 (4.58), 255 (4.58), 283 (3.73, shoulder), 289 (3.87), 293 (4.15), 400 (3.75); ms: m/z 170 (M^+ + 1, 13), 169 (M^+, 100), 168 (M^+ − 1, 46), 167 (M^+ − 2, 17), 154 (24); ^{1}H-nmr (deuteriochloroform): δ 2.84 (6H, s, 2 x CH_3), 7.23 (2H, d, J = 4.4 Hz, 2,3-H), 7.29 (1H, bs, 6-H), 7.43 (2H, d, J = 4.4 Hz, 1,4-H); ^{13}C-nmr (400 MHz, deuteriochloroform): δ 128.81 (C-5, C-7), 127.01 (C-4a, C-9a), 123.62 (C-2a), 123.66 (C-6), 115.09 (C-2, C-3), 108.46 (C-1, C-4), 17.29 (Me).

Anal. Calcd. for $C_{12}H_{11}N$: C, 85.17; H, 6.55; N, 8.28. Found: C, 85.47; H, 6.70; N, 8.03.

The picrate had mp 177°.

Anal. Calcd. for $C_{18}H_{14}N_4O_7$: C, 54.28; H, 3.54; N, 14.07. Found: C, 54.38; H, 3.64; N, 14.08.

Dimethyl 3-Methylthiocycl[3.2.2]azine-1,2-dicarboxylate (**10a**).

A solution of 10 g (61 mmoles) of **5a**, 17 g (120 mmoles) of DMAD, 10 g of 5% of palladium-on-charcoal (Pd-C), and 400 ml of toluene was refluxed for 30 hours. After removal of the solvent and Pd-C, the residue was chromatographed on alumina column using benzene as an eluent to give yellow crystals. This compound was recrystallized from methanol to give 7.0 g (23 mmole, 38%) of **10a** as yellow needles, mp 113°; ir (potassium bromide): ν max cm^{-1} 1735, 1700 (C=O); uv (ethanol): λ max nm (log ε) 217 (4.45), 230 (4.34, shoulder), 263 (4.50), 290 (3.74), 370 (4.03), 405 (4.09); ms: m/z 304 (M^+ + 1, 18), 303 (M^+, 95), 271 (69), 239 (37), 136 (25), 81 (51), 69 (100); ^{1}H-nmr (dueteriochloroform): δ 2.69 (3H, s, SCH_3), 4.01 (3H, s, O-CH_3), 7.01 (1H, s, 4-H), 7.67-7.90 (2H, m, 5,6-H), 8.26 (1H, dd, J = 1.9, 6.9 Hz, 7-H).

Anal. Calcd. for $C_{15}H_{13}NO_4S$: C, 59.39; H, 4.32; N, 4.62; S, 10.57. Found: C, 59.65; H, 4.31; N, 4.41; S, 10.28.

Dimethyl 5,7-Dimethyl-2-methylthiocycl[3.2.2]azine-1,2-dicarboxylate (**10b**).

This compound was prepared from 8.9 g (46.6 mmoles) of **5e**, 10.9 g (76.8 mmoles) of DMAD, 10 g of Pd-C, and 300 ml of toluene in a manner similar to that described for the synthesis of **10a**. The residue was chromatographed on a alumina column using hexane as an eluent to give 6.17 g (18.6 mmoles, 40%) of **10b** as yellow prisms, mp 138°; ir (potassium bromide): ν max cm^{-1} 1710, 1700 (C=O); uv (ethanol): λ max nm (log ε) 220 (4.43), 266 (4.50), 380 (4.11, shoulder), 394 (4.14); ms: m/z 332 (M^+ + 1, 15), 331 (M^+, 73), 299 (100), 284 (18), 81 (48), 69 (84); ^{1}H-nmr (deuteriochloroform): δ 2.66 (3H, s, SCH_3), 2.72 (3H, s, 5 or 7-CH_3), 2.83 (3H, s, 5 or 7-CH_3), 3.99 (3H, s, O-CH_3), 4.03 (3H, s, O-CH_3), 6.93 (1H, s, 1-H), 7.29 (1H, s, 6-H).

Anal. Calcd. for $C_{17}H_{17}NO_4S$: C, 61.62; H, 5.17; N, 4.23; S, 9.68. Found: C, 61.53; H, 5.23; N, 4.19; S, 9.55.

Dimethyl 5-Methyl-3-methylthiocycl[3.2.2]azine-1,2-dicarboxylate (**10c**).

This compound was prepared from 0.9 g (5 mmoles) of **5b**, 1.4 g (10 mmoles) of DMAD, 1.4 g of Pd-C, and 50 ml of toluene in a manner similar to that described for synthesis of **10a**. The residue was chromatographed on alumina column using benzene as an eluent to give 0.78 g (2.5 mmoles, 49%) of **10c** as yellow needles, mp 131°; ir (potassium bromide): ν max cm^{-1} 2900, 1743, 1709 (C=O); uv (ethanol): λ max nm (log ε) 219 (4.47), 233 (4.42, shoulder), 266 (4.64), 358 (4.38, shoulder), 400 (4.52); ms: m/z 318 (M^+ + 1, 19), 317 (M^+, 100), 285 (80), 271 (43), 253 (50), 240 (57); ^{1}H-nmr (deuteriochloroform): δ 2.61 (3H, s, SCH_3), 270 (3H, s, CH_3), 3.97 (3H, s, O-CH_3), 4.03 (3H, s, O-CH_3), 6.90 (1H, s, 4-H), 7.47 (1H, d, J = 8.0 Hz, 6-H), 8.03 (1H, d, J = 8.0 Hz, 7-H).

Anal. Calcd. for $C_{16}H_{15}NO_4S$: C, 60.55; H, 4.76; N, 4.41; S, 10.10. Found: C, 60.35; H, 4.78; N, 4.45; S, 10.03.

2-Methylthiocycl[3.2.2]azine (**11a**).

This compound was prepared from 2.5 g (8.2 mmoles) of **10a**, a solution of 10% sodium hydroxide (sodium hydroxide, 2.6 g, 66 mmoles) in 50 ml of methanol, 3.1 g of copper chromate, 1.5 g of copper powder, and 100 ml of quinoline in a manner similar to that described for the synthesis of **9a**. The residue was chromatographed on alumina column using hexane as eluent to give 0.95 g (5 mmoles, 56%) of **11a** as orange oil; ir (sodium chloride): ν max cm^{-1} 2944, 1612, 1513, 1440, 1386, 1305, 1232, 1033, 787; uv (ethanol): λ max nm (log ε) 225 (4.16), 245 (4.56), 265 (4.14, shoulder), 323 (4.17), 402 (3.74), 410 (3.68, shoulder); ms: m/z 188 (M^+ + 1, 15), 187 (M^+, 100), 141 (17); ^{1}H nmr (deuteriochloroform): δ 2.76 (3H, s, SCH_3), 7.02 (1H, d, J = 1.1 Hz, 1-H), 7.17 (1H, dd, J = 1.1, 4.4 Hz, 4-H), 7.56 (1H, d, J = 4.4 Hz, 3-H), 7.62 (1H, d, J = 7.0 Hz, 7-H), 7.73 (1H, d, J = 7.0 Hz, 5-H), 7.77 (1H, dt, J = 1.8, 7.3, 8.8 Hz, 6-H).

The picrate was obtained as red needles, mp 115°.

Anal. Calcd. for $C_{17}H_{12}N_4O_7S$: C, 49.04; H, 2.91; N, 13.46. Found: C, 49.13; H, 2.98; N, 13.45.

5,7-Dimethyl-2-methylthiocycl[3.2.2]azine (**11b**).

This compound was prepared from 1.17 g (3.5 mmoles) of **10b**, a solution of 10% sodium hydroxide (sodium hydroxide, 1.13 g, 28 mmoles) in 50 ml of methanol, 1.34 g of copper chromate, 0.67 g of copper powder, and 200 ml of quinoline in a manner similar to that described for the synthesis of **11a**. The reaction product was chromatographed on alumina column using hexane as an eluent to give 0.19 g (0.88 mmole, 25%) of **11b** as orange oil; ir (sodium chloride): ν max cm^{-1} 2930, 2860, 1505, 1463, 1440, 1400, 1385, 1325, 1300, 1040, 868, 768, 709; uv (ethanol): λ max nm (log ε) 251 (4.53), 325 (4.19), 394 (3.51); ms: m/z 216 (M^+ + 1, 15), 216 (M^+, 100), 229 (32), 200 (63), 182 (27), 62 (23); ^{1}H-nmr (deuteriochloroform): δ 2.72 (6H, s, 5, 7-CH_3), 2.74 (3H, s, SCH_3), 6.97 (1H, d, J = 1.1 Hz, 1-H), 7.10 (1H, dd, J = 0.9, 4.4 Hz, 4-H), 7.15-7.17 (1H, m, 6-H), 7.38 (1H, d, J = 4.4 Hz, 3-H).

The picrate had mp 150°.

Anal. Calcd. for $C_{13}H_{13}NS$: C, 51.35; H, 3.63; N, 12.96; S, 7.21. Found: C, 51.26; H, 3.66; N, 12.69; S, 6.63.

Reaction of **14** with **2**.

A solution 4.4 g (15 mmoles) of **14**, 1.7 g (10 mmoles) of **2** and 7.3 g (72 mmoles) of triethylamine in 200 ml of ethanol was refluxed for 20 hours. After removal of ethanol and excess triethylamine, the residue was diltued with 200 ml of water and the resulting precipitate was collected by filtration to give a mixture of **15** and **16**. The mixture was separated by functional recrystallization with ethanol to give **15** and **16**, respectively. The crystals that first appeared were collected by filtration to give 1.4 g (4.2 mmoles, 42%) of ethyl 2-methylthio-1-nitropyrrolo[2,1-*a*]isoquinoline-3-carboxylate (**15**) as yellow prisms, mp 116°; ir (potassium bromide): ν max cm^{-1} 1670 (C=O); uv (ethanol): λ max nm (log ε) 218 (4.43), 258 (4.47), 280 (4.57), 340 (3.93), 356 (3.88, shoulder), 388 (3.61, shoulder); ^{1}H-nmr (deuteriochloroform): δ 1.50 (3H, t, J = 7.0 Hz, O-CH_2-CH_3), 2.52 (3H, s, SCH_3), 4.51 (2H, q, J = 7.0 Hz, O-CH_2-), 7.16 (1H, dd, J = 0.7, 7.5 Hz, 6-H), 7.53-7.71 (3H, m, 7,8,9-H), 8.24 (1H, m, 10-H), 9.20 (1H, d, J = 7.5 Hz, 5-H); ms: m/z 331 (M^+ + 1, 19), 330 (M^+, 100), 313 (45), 239 (35), 194 (21), 154 (24).

Anal. Calcd. for $C_{16}H_{14}N_2O_4S$: C, 58.17; H, 4.27; N, 8.48; S, 9.71. Found: C, 58.05; H, 4.28; N, 8.30; S, 9.73.

The above filtrate was allowed to stand for 10 minutes. The colorless crystal that appeared was collected by filtration and recrystallized from ethanol to give 1.4 g (4.9 mmoles, 49%) of ethyl 2-methylthiopyrrolo-[2,1-*a*]isoquinoline-3-carboxylate (**16**) as colorless needles, mp 125° (lit [24], mp 125°); ir (potassium bromide): ν max cm^{-1} 1670 (C=O); uv (ethanol): λ max nm (log ε) 214 (4.20), 289 (4.40), 315 (3.93, shoulder), 328 (3.88, shoulder), 352 (3.73), 371 (3.77); ^{1}H-nmr (deuteriochloroform): δ 1.48 (3H, t, J = 7.0 Hz, O-CH_2-CH_3), 2.59 (3H, s, SCH_3), 4.45 (2H, q, J = 7.0 Hz, O-CH_2-), 6.84 (1H, d, J = 0.7 Hz, 1-H), 6.95 (1H, d, J = 7.7 Hz, 6-H), 7.45-7.66 (3H, m, 7,8,9-H), 8.04-8.15 (1H, m, 10-H), 9.20 (1H, d, J = 7.7 Hz, 5-H).

Ethyl 2-Methylthiopyrrolo[2,1-*a*]isoquinoline-3-carboxylate (**16**).

A solution of 4.0 g (10 moles) of **17**, 1.8 g (30 mmoles) of nitromethane and 10.1 g (100 mmoles) of triethylamine in 200 ml of ethanol was reflux-

ed for 36 hours. After removal of ethanol and excess triethylamine, the residue was washed with water, followed by extraction with benzene (100 ml x 3). The combined extracts was dried over anhydrous sodium sulfate and evaporated *in vacuo*. The residue was chromatographed on alumina column using a mixture of hexane-benzene (1:1) as an eluent to give 1.6 g (5.6 mmoles, 56%) of **16**, mp 125°.

2-Methylthiopyrrolo[2,1-*a*]isoquinoline (**18**).

A solution of 14 g (49 mmoles) of **16** and 20% sodium hydroxide (sodium hydroxide, 15 g, 375 mmoles) in 500 ml of methanol was refluxed for 3 hours. After removal of solvent and water, 50 g of PPA was added to the residue. This mixture was heated at 100° for 1 hour and was poured into 500 ml of ice-water, neutralized with sodium hydroxide. This reaction mixture was extracted with benzene (200 ml x 4). The combined extracts were dried over an hydrous sodium sulfate and evaporated *in vacuo*. The residue was chromatographed on alumina column using hexane as an eluent to give 9.5 g (44.5 mmoles, 91%) of **18**. An anlaytical sample was recrystallized from ethanol to give colorless prisms, mp 59°; ir (potassium bromide): ν max cm^{-1} 1355, 1305, 1139, 776, 743; uv (ethanol): λ max nm (log ϵ) 236 (5.20), 258 (4.50), 266 (4.42), 274 (4.44), 310 (3.87); ^{1}H-nmr (deuteriochloroform): δ 2.49 (3H, s, SCH_3), 6.69 (1H, d, J = 8.0 Hz, 6-H), 6.92 (1H, dd, J = 0.8, 1.5 Hz, 1-H), 7.20 (1H, d, J = 1.5 Hz, 3-H), 7.26-7.58 (3H, m, 7,8,9-H), 7.62 (1H, d, J = 8.0 Hz, 5-H), 7.89-8.00 (1H, m, 10-H).

Anal. Calcd. for $C_{13}H_{11}NS$: C, 73.20; H, 5.20; N, 6.57; S, 15.30. Found: C, 73.09; H, 5.16; N, 6.38; S, 15.08.

Pyrrolo[2,1-*a*]isoquinoline (**19**).

A mixture of 4.8 g (23 mmoles) of **18**, 16 g of Raney-nickel, and 300 ml of ethanol was refluxed for 10 hours. After removal of Raney-nickel and the solvent, the residue was chromatographed on alumina column using hexane as an eluent to give 3.3 g (20 mmoles, 88%) of **19** as colorless needles, mp 83° (lit [25], mp 83.5-84°); ir (potassium bromide): ν max cm^{-1} 1490, 1450, 1338, 1245, 1098, 1065, 783, 747, 690; uv (ethanol): λ max nm (log ϵ) 214 (4.25), 259 (4.44, shoulder), 263 (4.46), 271 (4.48), 295 (3.80, shoulder), 310 (3.79), 325 (3.66, shoulder); ^{1}H-nmr (deuteriochloroform): δ 6.69 (1H, d, J = 7.2 Hz, 5-H), 6.67-6.74 (1H, m, 1-H), 6.89-6.96 (1H, m, 3-H), 7.22-7.58 (4H, m, 2,6,7,8-H), 7.71 (1H, dd, J = 0.66, 7.2 Hz, 4-H), 7.95-8.05 (1H, m, 9-H).

Reaction of **18** with DMAD.

A mixture of 11.7 g (70 mmoles) of **18**, 15 g (106 mmoles) of DMAD, 8 g of palladium-on-charcoal, and 300 ml of toluene was refluxed for 30 hours. After removal of palladium on charcoal and the solvent, the residue was taken up in 20 ml of methanol. The orange crystals that appeared were collected by filtration and recrystallized from methanol to give 6.7 g (19 mmoles, 27%) of dimethyl 2-methylthiobenzo[*g*]cycl[3.2.2]-azine-3,4-dicarboxylate (**20**) as orange needles, mp 144°; ir (potassium bromide): ν max cm^{-1} 1728, 1692 (C=O); uv (ethanol): λ max nm (log ϵ) 275 (4.79), 320 (3.99, shoulder), 440 (4.01, shoulder), 435 (4.05, shoulder), 458 (4.18); ms: m/z 353 (M^+, 100), 340 (57), 320 (60), 308 (40), 296 (47), 281 (44), 249 (45), 245 (36), 222 (42); ^{1}H-nmr (deuteriochloroform): δ 2.76 (3H, s, SCH_3), 4.06 (3H, s, OCH_3), 4.13 (3H, s, OCH_3), 7.48 (1H, s, 1-H), 7.56-7.85 (2H, m, 7,8-H), 8.21-8.28 (1H, m, 6-H), 8.32-8.54 (1H, m, 9-H), 8.67 (1H, s, 5-H).

Anal. Calcd. for $C_{19}H_{15}NO_4S$: C, 64.58; H, 4.28; N, 3.96; S, 9.07. Found: C, 64.76; H, 4.33; N, 3.79; S, 9.01.

After removal of solvent from the filtrate, the residue was chromatographed on alumina column using hexane-benzene (3:1) as an eluent to give 6.6 g (19 mmoles, 26%) of methyl *cis*-(2-methylthiopyrrolo[2,1-*a*]isoquinolin-3-yl)-α-methoxycarbonylacrylate (**21**) as red needles, mp 106°; ir (potassium bromide): ν max cm^{-1} 1722, 1685 (C=O); uv (ethanol): λ max nm (log ϵ) 224 (4.28), 277 (4.49), 306 (4.07), 402 (4.24); ^{1}H-nmr (deuteriochloroform): δ 2.53 (3H, s, SCH_3), 3.82 (3H, s, OCH_3), 3.90 (3H, s, OCH_3), 6.24 (1H, s, vinyl-H), 6.80 (1H, d, J = 7.5 Hz, 6-H), 7.01 (1H, s, 1-H), 7.35-7.57 (3H, m, 7,8,9-H), 7.90 (1H, d, J = 7.5 Hz, 5-H), 7.96-8.07 (1H, m, 10-H); ms: m/z 355 (M^+, 95), 340 (100), 308 (23), 296 (27), 281 (94), 236 (32), 223 (36).

Anal. Calcd. for $C_{19}H_{17}O_4NS$: C, 64.21; H, 4.82; N, 3.94; S, 9.02. Found: C, 64.22; H, 4.87; N, 3.77; S, 9.00.

Subsequent elution using hexane-benzene (1:1) as an eluent gave 4.3 g (12 mmoles, 17) of methyl *trans*-(2-methylthiopyrrolo[2,1-*a*]isoquinolin-3-yl)-α-methoxycarbonylacrylate (**22**) as orange needles, mp 130°; ir (potassium bromide): ν max cm^{-1} 1715 (C=O), 1615 (vinyl); uv (ethanol): λ max nm (log ϵ) 271 (4.51), 308 (3.91), 324 (3.77), 414 (3.71); ^{1}H-nmr (deuteriochloroform): δ 2.41 (3H, s, SCH_3), 3.63 (3H, s, OCH_3), 3.80 (3H, s, OCH_3), 6.75 (1H, d, J = 7.9 Hz, 6-H), 7.70 (1H, d, J = 0.7 Hz, 1-H), 7.19 (1H, s, vinyl-H), 7.33 (1H, d, J = 7.9 Hz, 5-H), 7.41-7.57 (3H, m, 7,8,9-H), 9.97-8.04 (1H, m, 10-H).

Anal. Calcd. for $C_{19}H_{17}O_4NS$: C, 64.21; H, 4.82; N, 3.94; S, 9.07. Found: C, 64.19; H, 4.90; N, 3.81; S, 8.91.

Dimethyl Benzo[*g*]cycl[3.2.2]azine-3,4-carboxylate (**23**).

A mixture of 0.78 g (2.2 mmoles) of 20, 3.9 g of Raney-nickel, and 50 ml of methanol was refluxed for 10 hours. After removal of Raney-nickel and the solvent, the residue was recrystallized from methanol to give 0.3 g (1.0 mmole, 44%) of **23** as orange needles, mp 134°; ir (potassium bromide): ν max cm^{-1} 1735, 1695 (C=O); uv (ethanol): λ max nm (log ϵ) 260 (4.57), 368 (4.23), 464 (4.27); ^{1}H-nmr (deuteriochloroform): δ 4.10 (3H, s, OCH_3), 4.11 (3H, s, OCH_3), 7.67-7.94 (4H, m, 1,2,7,8-H), 8.23-8.39 (1H, m, 6-H), 8.56-8.66 (1H, m, 9-H), 8.85 (1H, s, 5-H); ms: m/z 307 (M^+, 100), 283 (21), 276 (50), 252 (19), 190 (28).

Anal. Calcd. for $C_{18}H_{13}O_4N$: C, 70.35; H, 4.26; N, 4.65. Found: C, 70.08; H, 4.20; N, 4.31.

Reaction of **19** with DMAD.

This compound was prepared from 1.2 g (7 mmoles) of **19**, 2 g (14 mmoles) of DMAD, 15 g of 5% of palladium on charcoal, and 200 ml of toluene in a manner similar to that described for the synthesis of **20**. The reaction product was recrystallized from methanol to give 0.24 g (0.8 mmole, 11%) of methyl *cis*-pyrrolo[2,1-*a*]isoquinolin-3-yl-α-methoxycarbonyl acrylate (**24**) as yellow leaflets, mp 179°; ir (potassium bromide): ν max cm^{-1} 1740, 1713 (C=O); uv (ethanol): λ max nm (log ϵ) 226 (4.26), 264 (4.45), 271 (4.47), 300 (4.07), 393 (4.30), 409 (4.29); ^{1}H-nmr (deuteriochloroform): δ 3.80 (3H, s, OCH_3), 3.98 (3H, s, OCH_3), 6.25 (1H, s, vinyl-H), 6.91 (1H, d, J = 7.5 Hz, 6-H), 6.95 (1H, d, J = 4.4 Hz, 1 or 2-H), 7.04 (1H, dd, J = 0.7, 4.4 Hz, 1 or 2-H), 7.41-7.60 (3H, m, 7,8,9-H), 8.02 (1H, near s, 10-H), 8.14 (1H, d, J = 7.5 Hz, 5-H).

Anal. Calcd. for $C_{18}H_{15}NO_4$: C, 69.89; H, 4.89; N, 4.53. Found: C, 70.24; H, 4.88; N, 4.31.

The above filtrate was allowed to stand for 10 minutes. The orange needles that appeared were collected by filtration and recrystallized from methanol to give 2.21 g (7 mmoles, 33%) of **20** as mp 134°.

Benzo[*g*]cycl[3.2.2]azine (**12**).

This compound was prepared from 0.25 g (0.8 mmole) of **23**, 100 ml of 10% methanolic sodium hydroxide (sodium hydroxide, 0.33 g, 8 mmoles) solution, 0.5 g of copper chromate, and 30 ml of quinoline in a manner similar to that described for the synthesis of **9a**. The residue was purified by alumina column chromatography using hexane as an eluent and was recrystallized from methanol to give 0.07 g (0.4 mmole, 22% from **23**) of **12** as bright yellow leaflets, mp 141°; ir (potassium bromide): ν max cm^{-1} 1485, 1400, 1375, 1208, 1130, 1020, 1010, 740; uv (ethanol): λ max nm (log ϵ) 218 (4.28), 258 (4.53), 283 (4.46), 308 (3.88), 316 (3.76), 329 (3.88), 343 (3.90), 440 (3.50), 456 (3.46, shoulder); ms: m/z 192 ($M^+ + 1$, 16), 191 (M^+, 16), 190 ($M^+ - 1$, 13), 96 (14), 95 (12); ^{1}H-nmr (400 MHz, deuteriochloroform): δ 7.38 (1H, d, J = 4.8 Hz, 4-H), 7.46 (1H, d, J = 4.4 Hz, 1-H), 7.62 (1H, d, J = 4.4 Hz, 2-H), 7.63 (1H, near t, 7-H), 7.73 (1H, d, J = 4.8 Hz, 3-H), 7.74 (1H, near t, 8-H), 8.21 (1H, s, 5-H), 8.24 (1H, d, J = 8.4 Hz, 6-H), 8.60 (1H, d, J = 8.6 Hz, 9-H); ^{13}C-nmr (400 MHz, deuteriochloroform): δ 130.71 (C-5a), 129.47 (C-6), 128.38 (C-9a), 127.19 (C-9b), 126.67 (C-8), 126.02 (C-4a), 124.70 (C-7), 123.13 (C-9), 122.56 (C-2a), 122.32 (C-3), 113.34 (C-4), 111.97 (C-2), 111.41 (C-5), 105.90 (C-1).

Anal. Calcd. for $C_{14}H_9N$: C, 87.93; H, 4.74; N, 7.32. Found: C, 88.02; H, 4.86; N, 6.95.

Complex of **12** with 2,4,7-trinitro-9-fluorenone complex was dark violet needles, mp 233°.

Anal. Calcd. for $C_{27}H_{14}N_4O_7$: C, 64.04; H, 2.79; N, 11.06. Found: C, 64.35; H, 2.70; N, 10.86.

2-Methylthiobenzo[*g*]cycl[3.2.2]azine (**25**).

This compound was prepared from 3.5 g (10 mmoles) of **20**, 100 ml of 10% methanolic sodium hydroxide solution (sodium hydroxide, 1.6 g, 40 mmoles), 0.6 g of copper chromate, and 50 ml of quinoline in a manner similar to that described for the synthesis of **9a**. The reaction product was purified by alumina column chromatography using hexane as an eluent and was recrystallized from methanol to give 0.52 g (2.2 mmoles, 22%, from 20) as greenish yellow leaflets, mp 89°; ir (potassium bromide): ν max cm^{-1} 1539, 1509, 1393, 1316, 866, 749; uv (ethanol): λ max nm (log ϵ) 252 (4.44, shoulder), 265 (4.53), 292 (4.36), 310 (4.14), 323 (4.10), 374 (4.03), 436 (3.65), 452 (3.64); ms: m/z 238 (M^+ + 1, 18), 237 (M^+, 100), 223 (16), 222 (91), 178 (13), 118 (12); ^{1}H-nmr (deuteriochloroform): δ 2.82 (3H, s, SCH_3), 7.33 (1H, dd, J = 0.9, 4.9 Hz, 4-H), 7.47 (1H, d, J = 0.9 Hz, 1-H), 7.60-7.70 (2H, m, 7,8-H), 7.74 (1H, d, J = 4.9 Hz, 3-H), 8.14 (1H, s, 5-H), 8.17-8.27 (1H, m, 6-H), 8.42-8.58 (1H, m, 9-H).

Anal. Calcd. for $C_{15}H_{11}NS$: C, 75.92; H, 4.67; N, 5.90; S, 13.51. Found: C, 76.01; H, 4.65; N, 5.72; S, 13.56.

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