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SUBSTITUTION REACTIONS ON PYRROLO[2,1-b]THIAZOLES

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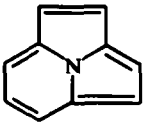
Abstract—2,6-Dimethylpyrrolo[2,1-b)]thiazole, **8**, undergoes electrophilic substitution with dimethyl acetylenedicarboxylate to form the *cis*- and *trans*-5-dicarbomethoxyvinyl derivatives of **8**. With tetracyanoethylene as electrophile, 5- and 7-tricyanovinyl derivatives of **8** are formed. Butyllithium metalates **8** in position 3, whereas 3-methyl-6-phenylpyrrolo[2,1-b]thiazole, **18**, is metalated in position 2. Reaction of the metalated compounds with dimethylformamide and carbon dioxide gives the corresponding formyl and carboxy derivatives. These reactions were carried out in attempts to synthesize the thiacycl[2.2.2]azine system **3**.

THE recent interest in the synthesis and behaviour of cyclazines, tricyclic systems with a central N atom common to all three rings and containing a periphery of completely conjugated sp^2 hybridized *C* or *N* atoms,[1] *e.g.* the cycl[3.2.2]azine, **1**,[2] and attempts to correlate their properties with theoretically obtained predictions have resulted in approximately a dozen systems of this general type containing either carbon atoms or carbon and nitrogen atoms in the periphery.[1, 3, 4] Since all these systems, with the possible exception of the cycl[3.3.3]azine, **2**,[5, 6] display aromatic properties, it would be of interest to prepare cyclazines with other heteroatoms in the periphery, *e.g.*, sulphur leading to thiacyclazines, and to determine if these also possess aromaticity.

In this communication we present preliminary, and unsuccessful, experiments directed towards the synthesis of a thiacyclazine of type **3**. The only compound of this



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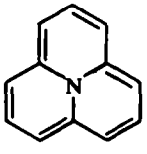

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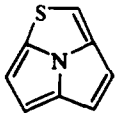


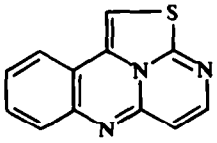
3

general type reported, but with another ring-size combination than in **3**, seems to be the benzodiazathiacycl[3.3.2]azine, **4**, which was isolated as an unexpected product during attempts to prepare thiazolo[5,4-*c*]quinoline, **5**.[7]

An obvious starting material for the synthesis of system **3** seemed to be pyrrolo-[2,1-b]thiazole, **6**, and this communication describes the introduction of different

groups in the 3 or 5 position of system **6**. The substituents chosen should be of a type suitable for ring closure to a tricyclic structure of type **3**.

The unsubstituted compound, **6**, seems to be unknown,[8] but homologs with a phenyl, or an alkyl group, in position 6 and alkyl groups in positions 2, 3, 5, and/or 7 have been described.[10,11,12] NMR studies on the pyrrolo[2,1-b]thiazolium ion, **7**,



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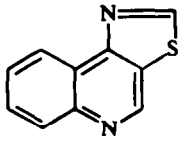

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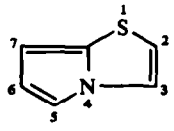
show that in acidic solution C-5 is protonated,[13] and in agreement with this observation electrophilic substitution has been found to occur when this position is unsubstituted.[14]

Our first approach to ring system **3** visualized the introduction of a C_2 unit in position 5, followed by ring closure. Dimethyl acetylenedicarboxylate and tetracyanoethylene were chosen as electrophilic agents.



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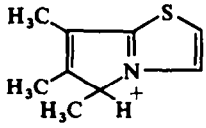

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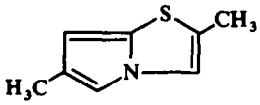


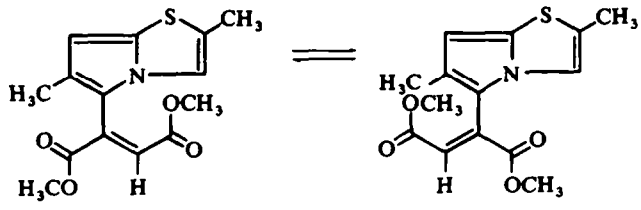
8

When 2,6-dimethylpyrrolo[2,1-b]thiazole, **8**,[10] was reacted with dimethyl acetylenedicarboxylate in a 1 :1 ratio, all starting materials were consumed and a mixture of a yellow (yield 70%) and a red (yield 5%) product was obtained. The two compounds gave identical mass spectra with a molecular ion at $m/e = 293$, which is in accordance with 1 :1 molar adducts.

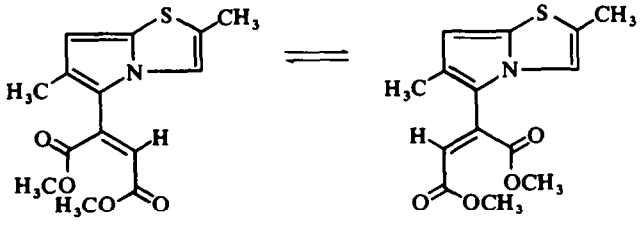
Desulfurization of the two isomers with Raney nickel gave one and the same product. Its molecular weight is 267 (mass spectrometry) and the UV spectrum (end absorption, shoulder at 210 nm) is in agreement with the *N*-propylpyrrol structure **9**. The NMR spectrum is in accord with the proposed formula (*cf* Fig 1 for structure and assignments). Of particular value is the AB type absorption, centered at 6·20 ppm, which should not be present, had the substitution occurred at position 7 in **8**.

Heating the red compound in biphenyl-diphenyl ether (200°) converted it to the yellow one. Irradiation of the yellow compound in benzene solution with a medium-pressure mercury lamp ($\lambda_{max} = 366$ nm) gave the red isomer in quantitative yield. We therefore believe that the two compounds are geometrical isomers* with structure

* Geometrical isomers have been observed in a number of cases where various heterocyclic compounds were reacted with acetylenedicarboxylic acid and its dimethyl ester.[15] The structures of the isomers were mainly determined by chemical methods only, and physical methods were not extensively used to confirm the structures.



10a 10b



11a 11b

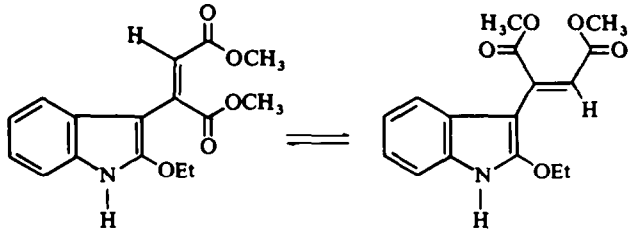
TABLE 1. ELECTRONIC SPECTRAL DATA FOR 10 AND 11

10		11	
λ_{max} (nm)	ε	λ_{max} (nm)	ε
218	15200	219	15500
279	4300	282	4000
		318	4700
432	3300	392	21500

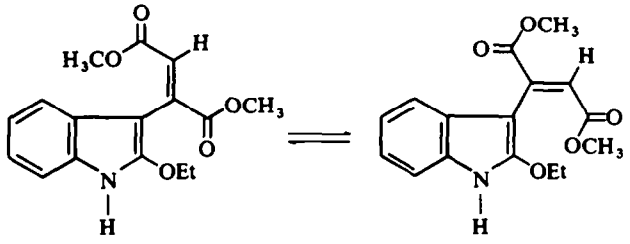
10 and **11**. Molecular models indicate that the unsaturated side chain in the **E** isomer, depending on the rotational angle around the exocyclic single bond, would be either out of plane of the bicyclic system or sterically hindered, while on the other hand the **Z** isomer would be less hindered in a co-planar conformation. The band in the electronic spectrum, associated with the whole chromophore, which appears at highest wave length, would therefore be expected to be more intense in the **Z** than in the **E** isomer.[16] The electronic spectral data for our two isomers are summarized in Table 1. The long-wave length absorption band is about six times as intense in the yellow isomer as in the red one. This implies that the yellow isomer possesses **Z**, and the red, **E** configuration. Plieninger and Wild[17] have described an analogous pair of red and yellow *cis* and *trans* compounds, **12** and **13**, obtained from dimethyl acetylenedicarboxylate and 2-ethoxyindole. Their spectral data, summarized in Table 2, indicate, with the same argument as used above, that **12** would represent the yellow and **13** the red isomer. The ratio between the extinction coefficients for the full chromophore is here *ca* 4, indicating strong disturbance of the co-planarity of the unsaturated side chain and the indole system in the red isomer. Plieninger and

Wild have arrived at the same conclusion based on a comparison of IR and NMR data for **12**, **13**, diethyl maleate, and diethyl fumarate.

The NMR spectra of our yellow and red adducts show the same number and types of protons. The correlations of the signals and protons, based on a comparison with similar chemical shifts and coupling constants observed in the starting material **8** (*cf* Ref 14), are summarized in Table 3.



12a **12b**



13a **13b**

TABLE 2. ELECTRONIC SPECTRAL DATA FOR **12** AND **13**

Yellow isomer (**12**)		Red isomer (**13**)	
λ_{max} (nm)	ε	λ_{max} (nm)	ε
225	36300	223	37200
267	12000	267	8300
280	10000	283	6500
356	18600	367	4600

TABLE 3. NMR SPECTRAL DATA FOR **8**, **10**, **11**, DIMETHYL MALEATE, AND DIMETHYL FUMARATE

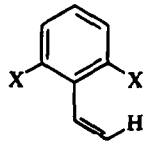
Compound	CH_3-2	CH_3-6	ester-CH_3	H-3	H-5	H-7	olefin
yellow (**11**)	2·30	2·21	3·74 : 3·91	7·27	—	6·08	5·84
red (**10**)	2·28	2·04	3·66 : 3·88	6·68	—	6·04	6·79
8	2·23	2·15	—	6·80	6·73	5·87	—
dimethyl maleate	—	—	3·80	—	—	—	6·28
dimethyl fumarate	—	—	3·80	—	—	—	6·83

The olefinic proton in the **E** isomer will be fairly unaffected by the bicyclic system, regardless of the rotational angle around the exocyclic single bond. One would therefore expect, as was argued by Plieninger and Wild, the olefinic proton to have a chemical shift (6·79 ppm) close to the same proton in dimethyl fumarate (6·83 ppm). Since the electronic spectra indicate that the chromophore in the yellow isomer possesses a higher degree of planarity and since molecular models show that of the two planar rotational isomers **11a** and **11b**, the former seems to be the less sterically hindered, one would expect H-3 and the olefinic proton to be close enough to affect each other's chemical shifts. Table 3 shows change in chemical shifts of both protons in comparison to those of the corresponding protons in **8**, in dimethyl maleate, and in the red isomer.

The application of Simon's rule[18] to the two isomers, and to dimethyl maleate and fumarate gives the calculated values summarized in Table 4. The agreement with Simon's rule for the **E** isomer is to be expected, since, as is argued above, the olefinic proton is fairly unaffected by the aromatic ring system. The **Z** isomer shows a large upfield deviation from the calculated value. This has been observed[19] for compounds of type **14** and was thought to be due to the deshielding region of the aromatic ring.

TABLE 4. CALCULATED δ AND $\Delta\delta$-VALUES FOR THE OLEFINIC PROTONS IN **10**, **11**, DIMETHYL MALEATE, AND DIMETHYL FUMARATE

Compound	Obs	Calc	$\Delta\delta$
E isomer (**10**)	6·79	7·13	−0·34
Z isomer (**11**)	5·84	6·68	−0·84
Dimethyl maleate	6·28	6·49	−0·21
Dimethyl fumarate	6·83	7·04	−0·21



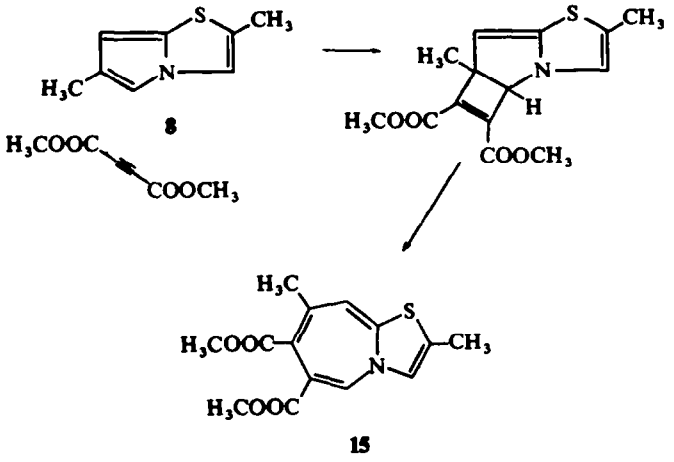
14

We believe these arguments to be sufficient support for assigning the red isomer structure **10** and the yellow isomer structure **11**.

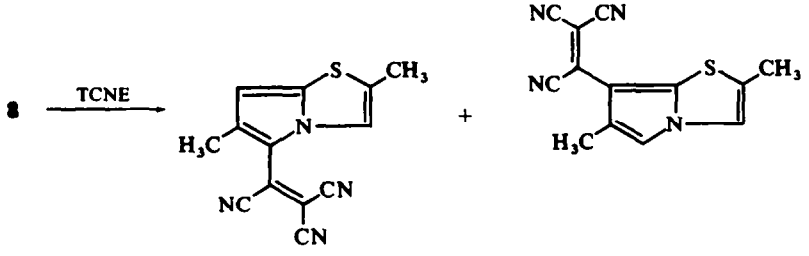
The formation of **9** excludes that **8** has added dimethyl acetylenedicarboxylate to form a fused 5- and 7-membered ring system like **15**. An analogous compound was formed from ethoxyindole and dimethyl acetylenedicarboxylate.[17]

The ring closure of **10** and **11** to system **3** was attempted by heating in biphenyl-diphenyl ether at 250°, by sulfur and selenium dehydrogenation at 220°, and by photolysis. None of these attempts lead to the desired compound.

Since tetracyanoethylene (TCNE) is more reactive than are acetylenedicarboxylates, we reacted equimolecular amounts of **8** and TCNE. Two compounds, one red (68%) and one violet (5%), resulted, both with a molecular weight of 252 (mass



spectrometry), corresponding to monotricyanovinylation. Their mass spectrometrical fragmentation patterns were fairly similar, but not identical. The compounds were not interconvertible, which was expected, since no geometrical isomerism exists in the tricyanovinyl group. Since in the NMR spectra of both compounds the two methyl signals appear as doublets, one is a 5 and the other a 7-substituted derivative.



In all derivatives of **6** thus far investigated,[14] the H-7 absorptions appear at a significantly higher field (1·1–2·5 ppm) than those of H-3 and H-5, which are both adjacent to a nitrogen atom. Introduction of a tricyanovinyl group seems to cause a general downfield shift for all aromatic protons (*cf* Table 5).

TABLE 5. NMR SPECTRAL DATA FOR THE RED AND VIOLET ISOMER

Compound	CH_3-2	CH_3-6	H-3	H-5	H-7
Red isomer	2·55	2·45	7·40	7·16	—
Violet isomer	2·50	2·45	7·53	—	6·48

It therefore seems reasonable to assume that in the spectrum of the red isomer the two signals at $\delta = 7{\cdot}40$ and 7·16 ($\Delta\delta = 0{\cdot}24$ ppm) should represent H-3 and H-5

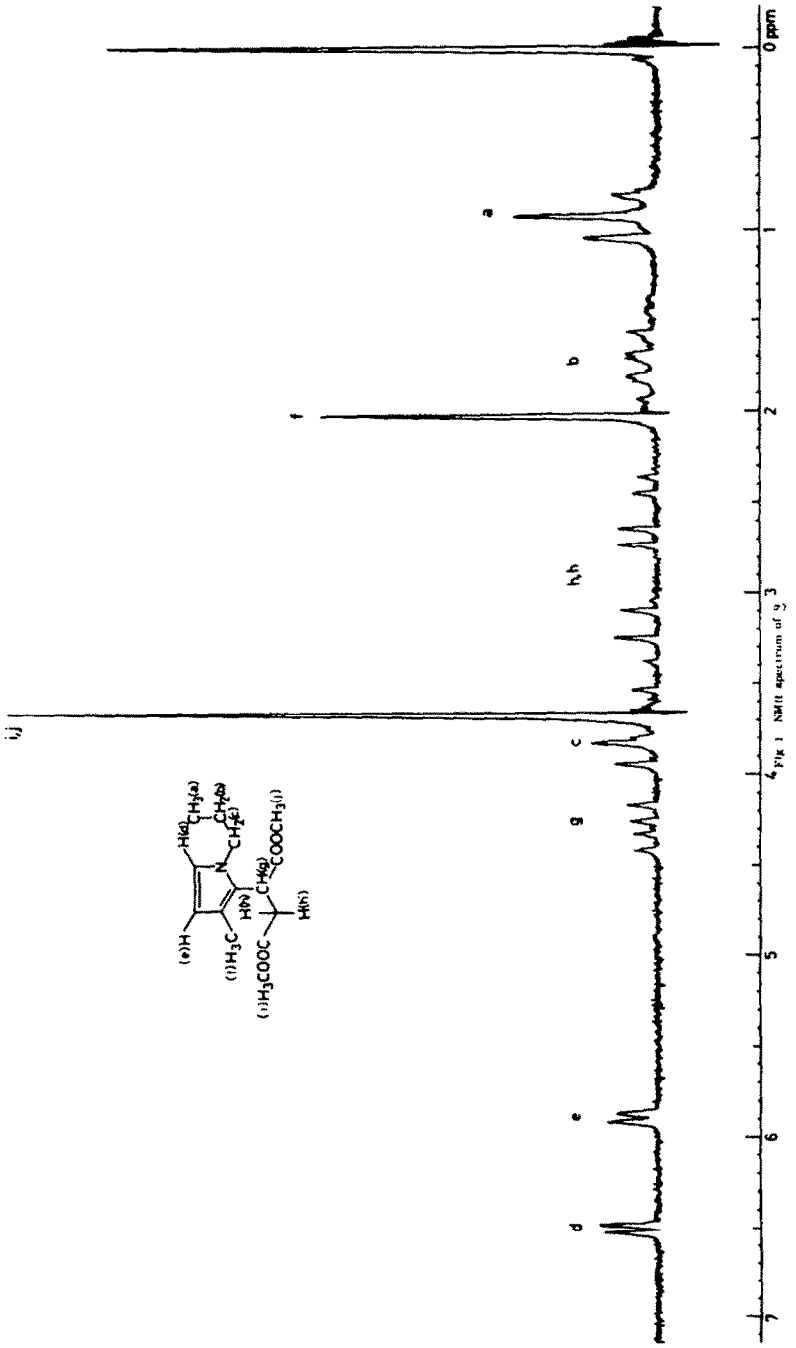


Fig 1. NMR spectrum of 9

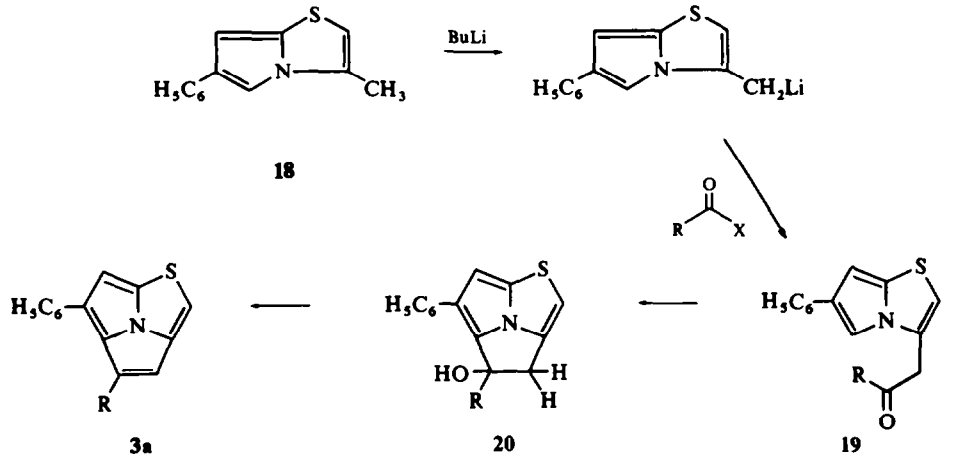
(or H-5 and H-3), respectively, and that in the spectrum of the violet isomer the signals at $\delta = 7{\cdot}53$ and $6{\cdot}48$ ($\Delta\delta = 1{\cdot}05$ ppm) should represent H-3 and H-7, respectively. We thus assign the violet isomer structure **16** and the red isomer structure **17**.

Tricyanovinylation is known to occur in the position with the highest electron density,[20] which in **8** probably is C-5.[13] It has been observed, however, that with bulky electrophiles mixtures of 5- and 7-substituted (and also 5,7-disubstituted) products of 6-methylpyrrolo[2,1-b]thiazole were obtained.[14]

The electronic spectra of **16** and **17** are fairly similar (*cf* Experimental) which would be expected for positional isomers, while geometrical isomers (**10** and **11**) give rise to considerable spectral differences (*cf* Table 1).

Attempts to ring-close **16** by irradiation (Q-81) gave no stable products. Treatment of **16** with butyllithium did not lead to any recognizable products.

The second line of approach to obtain ring-system **3** consisted of attempts to metalate a 3-methyl substituted derivative, *e.g.* **18**, which, after conversion to **19**, would use the nucleophilicity of C-5 to ring-close to **20**.



Treatment of **18**[12] with butyllithium in ether, followed by addition of dimethylformamide, yielded the aldehyde **21**. The same sequence of reactions performed with the 2-methyl derivative **8**, analogously gave the aldehyde **22**. Treatment of metalated **8**, with carbon dioxide gave the carboxylic acid **23a**, isolated as the methyl ester **23b**. Metalation therefore takes place in the ring and not in the side chain. This is in analogy with the behaviour of thiophenes and thiazoles.[21, 22] The point of attack was proved by the NMR spectra of the deuterated compounds, where the methyl protons appear as singlets, while they are doublets in the corresponding proton compounds. These reactions are outlined in Charts 1 and 2.

EXPERIMENTAL

General: UV and visible spectra were measured in EtOH, when not otherwise stated, with a Cary Model 15 spectrophotometer. IR spectra were determined in KBr with a Beckman IR 9 spectrophotometer. NMR spectra were recorded in $CDCl_3$ soln with a Varian A-60 spectrometer, using TMS as internal reference. Chemical shifts are given in δ-values. Mass spectra (MS) were recorded with a LKB 900 and a GEC-AEI 902 mass spectrometer. Analytical and preparative TLC was performed on alumina GF_{254} (Merck)

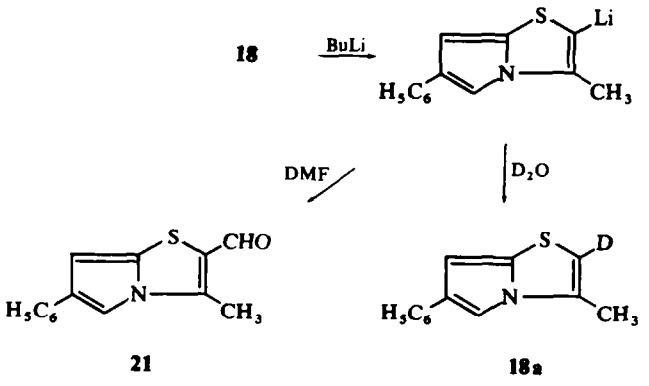


CHART 1

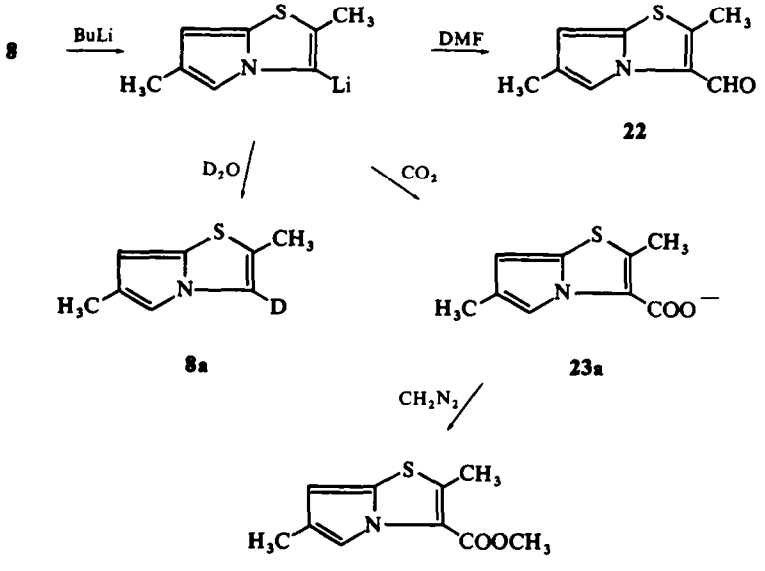


CHART 2

plates, with methylene chloride as the moving phase, when not otherwise stated, and visualized with short-wave UV light. The irradiations were carried out with a medium-pressure mercury arc (Hanau Q-81) placed in a pyrex container cooled with water.

Condensation of 2,6-*dimethylpyrrolo*[2,1-b]*thiazole*, **8**[10], *with dimethyl acetylenedicarboxylate*

To a solution of 5·0 g (33 mmoles) of **8** in 500 ml toluene, containing 500 mg of 30% Pd/C,* was added dropwise under argon and with stirring, a soln of 4·7 g (33 mmoles) dimethyl acetylenedicarboxylate in 100 ml toluene. The mixture, which immediately turned orange and gradually deepened in color, was either left overnight at room temp or refluxed for 1 hr. TLC of the soln showed a red (R_f = 0·43) and a yellow (R_f = 0·34) spot due to **10** and **11**, respectively. No trace of starting material could be detected. The toluene was removed under reduced pressure and the dark, oily residue was dissolved in 5 ml of chloroform. The

* Later observations showed that the reaction between **8** and dimethyl acetylenedicarboxylate in toluene solution takes place as readily in the absence of 30% Pd/C.

soln was allowed to stand overnight and 3·6 g of **11** precipitated as a yellow solid, which was removed by filtration and washed with ether to eliminate traces of **10**. After concentration of the mother liquor, the same procedure was repeated with 5 ml CCl_4 and yielded a second crop, 2·35 g, of **11**. The mother liquor from the last precipitation was passed through a 3 × 10 cm column of alumina (activity I) using 400 ml chloroform as the eluant. The solvent was removed under reduced pressure and the residue, containing a 1:2 mixture of **10** and **11**, was subjected to preparative TLC to give 500 mg (5%) of **10** and 1·0 g of **11**, thus giving **11** in a total yield of 6·95 g (72%). Crystallization of **11** from methanol gave, after drying at 40°/0·2 torr, yellow cubes, m.p. 147–148°. (Found for **11**: C, 57·23; H, 5·22; N, 4·69; S, 10·37. $C_{14}H_{15}NO_4S$ requires: C, 57·32; H, 5·15; N, 4·78; S, 10·93%). On standing, **10** which was obtained as a red oil, solidified, m.p. 109–111° MS for **10**: M^+ found 293·0739 ± 0·003. $C_{14}H_{15}NO_4S$ requires 293·0722. IR for **10**: 1700, 1725 cm^{-1} and for **11**: 1700, 1725 cm^{-1} (C=O).

Interconversions of **10** *and* **11**

1. *Photochemically* (**11** → **10**). A soln of 500 mg of **11** in 150 ml benzene was irradiated (Q-81) at room temp and samples were withdrawn every 10 min and analyzed by TLC. After about 1 hr, no starting material (R_f = 0·34) remained, and only **10** (R_f = 0·43), was present in the chromatogram. Evaporation of the solvent under reduced pressure gave 500 mg of a red oil identified as **10** by its NMR and IR spectra. No trace of **11** could be detected either by TLC or NMR.

2. *Thermally* (**10** → **11**). A soln of 500 mg of **10** in 2·5 g biphenyl and 2·5 g diphenyl ether was heated to 200° for 1 hr, during which time the color changed from red to orange. After being cooled to room temp, the mixture was diluted with 20 ml of light petroleum (bp. 40–60°) and passed over a 3 × 10 cm column of alumina (activity I). The biphenyl and diphenyl ether were washed through with 500 ml light petroleum (bp. 40–60°), while the orange product remained absorbed. Elution with 200 ml $CHCl_3$-MeOH (10:1) gave 400 mg of crude **11**, which was purified by preparative TLC.

After isolation, 300 mg of **11** remained, identified by its m.p., NMR, and IR spectra.

Desulfurization of **11**

A suspension of 2 g of freshly prepared W-4 Raney nickel[23] in 100 ml anhyd MeOH containing 200 mg of **11** was refluxed for 30 min. The soln was then colourless, and TLC showed only one major product (R_f = 0·43) and traces of starting material (R_f = 0·34). The soln was filtered, the solvent evaporated under reduced pressure, and the colourless oily residue, 250 mg, chromatographed on 15 g of silica gel. With CH_2Cl_2 125 mg (73%) of **9**, a colourless liquid was eluted. MS: M^+ found 267·1462 ± 0·003. $C_{14}H_{21}NO_4$ requires 267·1471. The NMR spectrum (*cf* Fig 1) shows an ABM spectrum for the protons g, h, and h', due to non-magnetic equivalence of the h-methylene protons.

Desulfurization of **10**

A suspension of 5 g of freshly prepared W-4 Raney nickel[23] in 100 ml of abs MeOH containing 500 mg of **10** was stirred at room temp for 2 hr. The isolation procedure described above yielded 350 mg (81%) of a colourless liquid identified as **9** by R_f-values, NMR and UV spectra. To examine whether **10** is converted to **11** under the weak alkaline conditions of Raney nickel desulfurization, the following experiment was performed. A suspension of 10 g of W-4 Raney nickel in 100 ml of abs MeOH was filtered, and 100 mg of **10** was dissolved in the MeOH. After standing for 2 hr at room temp the MeOH was evaporated under reduced pressure. TLC and NMR showed that only **10** was present.

Reaction of **8** *with TCNE*

To a stirred soln of 0·9 g (6 mmoles) of **8** in 30 ml of anhyd THF was added over a period of a few min 0·77 g (6 mmoles) of TCNE, dissolved in 20 ml THF. The soln immediately turned blue on addition of TCNE, but the colour gradually changed to pale red. The mixture was stirred for a few min. and then poured into 150 ml NaCl aq. The organic layer was separated and the aqueous layer extracted with two 25 ml portions diethyl ether. The organic phases were combined, dried ($MgSO_4$) and evaporated under reduced pressure to give 1·7 g of a dark solid residue. TLC (benzene) showed two products, **16** (R_f = 0·34) and **17** (R_f = 0·19), and some probably polymeric material (R_f = 0). The crude mixture, dissolved in CH_2Cl_2, was passed through a 3 × 8 cm column of alumina (activity I) to free it of polymeric material, using 300 ml CH_2Cl_2 as eluant. The mixture obtained, 1·25 g, was chromatographed on a 7 × 25 cm column of Si-gel (ϕ < 0·08 mm) using 4·5 l benzene as the eluant. After combination of the fractions and evaporation of the benzene, 1·03 g (68%) of red crystalline **17**, m.p. 157–158°, and 80 mg (5%) of violet crystalline **16**,

m.p. 176–178°, were obtained. Sublimation of **16** at 100°/0·1 torr gave crystals of m.p. 179–180°. (Found for **16**: C, 61·90; H, 3·31; N, 21·93; S, 12·83. Found for **17**: C, 61·97; H, 3·38; N, 21·97; S, 12·65. $C_{13}H_8N_4S$ requires: C, 61·89; H, 3·20; N, 22·21; S, 12·71%). IR for **16**: 2235 cm^{-1} (C≡N) and for **17**: 2240 cm^{-1} (C≡N). UV for **16**: λ_{max} at 269 (ε = 7100), 292 (ε = 4300), 403 (ε = 7400), and 507 nm (ε = 20500). UV for **17**: λ_{max} at 256 (ε = 9100), 304 (ε = 3900), 382 (ε = 3900), and 486 nm (ε = 20000).

Preparation of 2-*formyl*-3-*methyl*-6-*phenylpyrrolo*[2,1-b]*thiazole*, **21**

To a stirred soln of 1·06 g (5 mmoles) of **18**[12] in 10 ml abs. ether was added under argon at − 30°, 3·5 ml of a 1·43 M etheral soln of BuLi (5 mmoles). The solution turned pale yellow and was left under stirring for 1·5 hr to attain room temp. This soln was then cooled to − 30° and 365 mg (5 mmoles) of DMF in 5 ml of abs ether was added dropwise. A white solid precipitated, and the mixture was stirred for 3 hr at room temp. When 2 ml of water was added the white ppt turned yellow. It was filtered off, washed with ether, and dried to give 880 mg (73%) of crystalline **21**, m.p. 171–172°. (Found: C, 69·45; H, 4·67; N, 5·80; S, 13·35. $C_{14}H_{11}NOS$ requires: C, 69·68; H, 4·56; N, 5·81; S, 13·29%). TLC shows only one spot (R_f = 0·39). UV (dioxan): λ_{max} = 325 (ε = 18000) and 239 nm (ε = 15000). IR: 1640 cm^{-1} (C=O). NMR spectrum *cf* Table 6. M^+ = 241.

Preparation of 3-*methyl*-6-*phenylpyrrolo*[2,1-b]*thiazole*-2-*d*, **18a**

A stirred soln of 213 mg (1 mmole) of **18** in 10 ml abs ether was treated under argon at − 30° with 0·85 ml of a 1·17 M etheral soln of BuLi (1 mmole). The soln was allowed to attain room temp and after 1 hr, 1 ml of D_2O was added. The ether layer was separated, dried ($MgSO_4$), and the solvent evaporated, yielding 200 mg of **18a**, as pale yellow crystals, mp. 71°. The NMR spectrum is reported in Table 6.

TABLE 6. NMR SPECTRAL DATA FOR **18**, **18a**, and **21**

Compound	H-2	H-5	H-7	CH_3-3	Phenyl-6	CHO
18	6·15	7·20	6·45	2·27(d)	7·16–7·62	—
18a	—	7·20	6·45	2·14(s)	7·16–7·62	—
21	—	7·30	6·50	2·65(s)	7·16–7·62	9·93

Preparation of 3-*formyl*-2,6-*dimethylpyrrolo*[2,1-b]*thiazole*, **22**

To a stirred soln of 750 mg (5 mmoles) of **8**[10] in 10 ml abs ether was added dropwise under argon at − 30° 3·6 ml of 1·39 M (5 mmoles) of BuLi in ether. The yellow solution was left for 2 hr at room temp, then cooled to − 20°, whereafter 365 mg (5 mmoles) DMF in 5 ml of abs ether was added dropwise. The yellow colour disappeared, the soln was stirred for 1 hr at room temp, and then mixed with 20 ml of water. The now orange-yellow product was extracted with 5 × 25 ml of ether, the combined extracts were dried ($MgSO_4$), and the solvent evaporated under reduced pressure. TLC of the dark, unstable, oily residue showed a yellow component, **22**, (R_f = 0·44) to be the major component. Purification by preparative TLC gave 220 mg (25%) of **22** as a yellow solid, m.p. 97–98°, decomposing in air to a dark oil. MS: M^+ found 179·0394 ± 0·003. C_9H_9NOS requires 179·0405. M + 2 found 181·0358 ± 0·003. $C_9H_9NO^{34}S$ requires 181·0363. IR: 1650 cm^{-1} (C=O). UV: λ_{max} at 247 (ε = 10400), 254 (ε = 9900), 318 (ε = 3600), and 388 nm (ε = 2600). NMR spectrum *cf* Table 7.

Preparation of 2,6-*dimethylpyrrolo*[2, 1-b]*thiazole*-3-*d*, **8a**

To a stirred soln of 151 mg (1 mmole) of **8** in 10 ml abs ether was added under argon at − 30° 0·75 ml of a 1·34 M etheral soln of BuLi (1 mmole). The soln was allowed to attain room temp and after 3 hrs 1 ml of D_2O was added. The ether layer was separated, dried ($MgSO_4$), and the solvent evaporated, yielding 120 mg of **8a**, as white crystals, m.p. 80–81°. The NMR spectrum is reported in Table 7.

Preparation of **23a**

To a soln of 453 mg (3 mmoles) of **8** in 15 ml abs. diethyl ether under argon, 2.3 ml of a 1·31 M etheral soln of BuLi (3 mmoles) was added at − 30°. The soln, which turned yellow on addition of BuLi, was stirred at room temp for 3 hrs then cooled to − 30° and reacted with *ca* 2 g of dry ice. A light-yellow solid

precipitated and the mixture was stirred for 2 hr at room temp. After addition of a few drops water, separation of the solid by filtration, and washing with ether, 660 mg (110%) of **23a** remained as a pale yellow solid, m.p. > 300°.

Preparation of 3-*carbomethoxy*-2,6-*dimethylpyrrolo*[2,1-b]*thiazole*, **23b**

A 10 ml aqueous soln of 350 mg of the Li salt of **23a** was acidified with 5 ml 1 M HCl to pH ~ 1 and extracted with 3 × 15 ml of ether. The dried ($MgSO_4$) ether extract was stirred for 10 min at 0° with *ca* 15 ml of etheral diazomethane. The yellow (excess diazomethane) ether soln was acidified with 10 ml 1 M HCl and the organic layer was then immediately separated, washed with water, sat $NaHCO_3$ aq, and, again, with water. The ether soln was dried ($MgSO_4$), the solvent evaporated under reduced pressure, and the solid residue, 320 mg, was chromatographed on a 2 × 10 cm column of alumina (activity I), using benzene as the eluant. After evaporation of the solvent, 130 mg of **23b** (32%) remained as white crystals, m.p. 91–92°. MS: M^+ found 209·0486 ± 0·003. $C_{10}H_{11}NO_2S$ requires: 209·0511. M + 2 found 211·0477 ± 0·003. $C_{10}H_{11}NO_2{}^{34}S$ requires: 211·0468. The NMR spectrum is reported in Table 7.

TABLE 7. NMR SPECTRAL DATA FOR **8**, **8a**, **22**, AND **23b**

Compound	H-3	H-5	H-7	CH_3-2	CH_3-6	CHO	ester-CH_3
8	6·80	6·73	5·87	2·23(d)	2·15	—	—
8a	—	6·73	5·87	2·23(s)	2·15	—	—
22	—	7·22	5·98	2·57(s)	2·20	9·73	—
23b	—	7·50	6·00	2·63(s)	2·21	—	3·94

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