Studies of Heterocyclic Compounds. Part 26.[1] Synthesis of 1,6,6aλ⁴-Triheterapentalenes from Isothiazole-5-carbaldehyde

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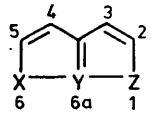
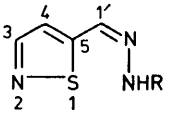
1,6,6aλ⁴-Triheterapentalenes have been synthesised from isothiazole-5-carbaldehyde. Methylation of isothiazole-5-carbaldehyde phenylhydrazone, *p*-nitrophenylhydrazone, and methylhydrazone with methyl fluorosulphonate, and treatment of the resulting 2-methylisothiazolium-5-carbaldehyde hydrazone fluorosulphonates with aqueous sodium carbonate gave 6-methyl-1-phenyl-, 6-methyl-1-*p*-nitrophenyl-, and 1,6-dimethyl-6aλ⁴-thia-1,2,6-triazapentalene, respectively. Methylation of isothiazole-5-carbaldehyde oxime with methyl toluene-*p*-sulphonate gave a mixture of 5-hydroxyiminomethyl-2-methylisothiazolium toluene-*p*-sulphonate and 5-(2-hydroxy-2-methyliminiomethyl)isothiazole toluene-*p*-sulphonate. Deprotonation of 5-hydroxyiminomethyl-2-methylisothiazolium toluene-*p*-sulphonate with aqueous sodium carbonate gave 6-methyl-1-oxa-6aλ⁴-thia-2,6-diazapentalene, the first derivative of the 1-oxa-6aλ⁴-thia-2,6-diazapentalene system to be reported. Deprotonation of 5-(2-hydroxy-2-methyliminiomethyl)isothiazole toluene-*p*-sulphonate gave 5-[methyl(oxido)iminiomethyl]isothiazole, which was also obtained by the reaction of isothiazole-5-carbaldehyde with *N*-methylhydroxylamine. Methylation of 5-[methyl(oxido)iminiomethyl]isothiazole with methyl fluorosulphonate gave 2-methyl-5-[methyl(oxido)iminiomethyl]isothiazolium fluorosulphonate, for which an alternative four-electron three-centre bonded structure is considered. The Wittig reaction of isothiazole-5-carbaldehyde with methoxymethylenetriphenylphosphorane gave a mixture of (*E*)- and (*Z*)-5-(2-methoxyvinyl)isothiazole which, when methylated with methyl fluorosulphonate, gave a mixture of (*E*)- and (*Z*)-2-methyl-5-(2-methoxyvinyl)isothiazolium fluorosulphonate. The fluorosulphonate reacted with methylamine to give 1,6-dimethyl-6aλ⁴-thia-1,6-diazapentalene, with sodium hydrogen sulphide to give mainly 6-methyl-1,6aλ⁴-dithia-6-azapentalene, and with sodium hydroxide to give 6-methyl-1-oxa-6aλ⁴-thia-6-azapentalene.

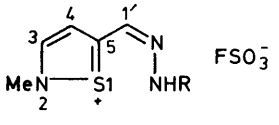
ALTHOUGH many types of five-membered heterocyclic compound containing two adjacent ring heteroatoms have been employed for the synthesis of 1,6,6aλ⁴-triheterapentalenes (1) and their aza-analogues, simple



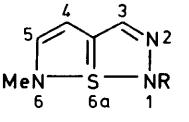
(1)



(2) R = Ph
(3) R = *p*-NO_2·C_6H_4
(4) R = Me



(5) R = Ph
(6) R = *p*-NO_2·C_6H_4
(7) R = Me



(8) R = Ph
(9) R = *p*-NO_2·C_6H_4
(10) R = Me

isothiazoles have not hitherto been used for this purpose. Here we describe the synthesis of several types of 1,6,6aλ⁴-triheterapentalene from isothiazole-5-carbaldehyde.

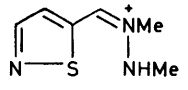
6aλ⁴-*Thia*-1,2,6-*triazapentalenes*.—The hydrazones (2)—(4) were obtained from isothiazole-5-carbaldehyde in high yield by standard methods. Methylation of the arylhydrazones (2) and (3) with methyl fluorosulphonate gave the isothiazolium salts (5) and (6) in nearly quantitative yield. Deprotonation of these salts with aqueous sodium carbonate afforded the corresponding 6aλ⁴-thia-1,2,6-triazapentalenes (8) and (9) in excellent yield. Methylation of the methylhydrazone (4) gave an oil which consisted of the desired isothiazolium salt (7) and an unidentified salt, believed to be (11). Treatment of this oil with aqueous sodium carbonate gave the dimethylthiatriazapentalene (10) in modest yield (19%).

Previous routes [2] to 6aλ⁴-thia-1,2,6-triazapentalenes have led to 1-aryl derivatives, among them compound (8). The synthesis described here allows a greater variety of substituents to be introduced into position 1 of the 6aλ⁴-thia-1,2,6-triazapentalene system.

Stable 1 : 1 charge-transfer complexes were obtained from compounds (8) and (10) with 1,3,5-trinitrobenzene. The only other classes of 1,6,6aλ⁴-triheterapentalenes which have been found to form charge-transfer complexes are the 1,6aλ⁴-dithia-6-azapentalenes [3] and the 6aλ⁴-thia-1,6-diazapentalenes; [4] these also contain one ring nitrogen atom at position 1 (6).

6-*Methyl*-1-*oxa*-6aλ⁴-*thia*-2,6-*diazapentalene and Related Compounds*.—While studying new reactivators of acetylcholinesterase that has been inhibited by organophosphorus nerve poisons, Benschop and his co-workers [5] methylated isothiazole-3- (12) and isothiazole-5-carbaldehyde oxime (13) with methyl toluene-*p*-sulphonate and obtained in low yield the corresponding 2-methylisothiazolium toluene-*p*-sulphonates (14) (9.5%) and (15) (8.6%). They noted that the acid strengths of the oximes (12) (pK_a 9.8), (13) (pK_a 8.6), and (14) (pK_a 7.6) are normal for compounds of these types, but that the oxime (15) (pK_a 2.6) is very much more acidic than compounds (12)—(14); indeed compound (15) appears to be the most acidic oxime hitherto to have been reported. The conjugate base of the oxime (15) must therefore be abnormally weakly basic. To account for this we propose that the conjugate base of the oxime (15) has the bicyclic oxathiadiazapentalene structure (17) rather than the monocyclic structure (18a) or (18b).

We have repeated Benschop's methylation of isothiazole-5-carbaldehyde oxime (13) on a larger scale, in order to isolate the oxathiadiazapentalene (17). We obtained a two-component crystalline solid (18.6%) which, when fractionally crystallised from acetonitrile, yielded the toluene-*p*-sulphonate (15) (9.1%) and a previously un-



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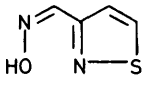

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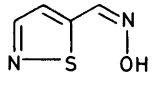

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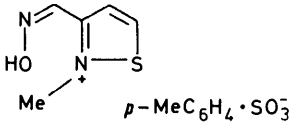
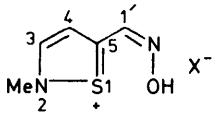
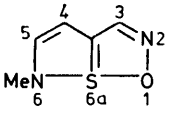


(14)

reported isomeric toluene-*p*-sulphonate (19) (4.8%). ^{1}H N.m.r. spectral data (see Experimental section) confirmed the structure of the toluene-*p*-sulphonate (15). In particular, the 3-H signal centred at δ 9.09 is a double quartet ($J_{3.4}$ 3.1, $J_{3,NMe}$ 0.7 Hz) which establishes the presence of the ring *N*-methyl group. The magnitude of $J_{3.4}$ * also confirms the presence of the isothiazolium ring



(15) X = *p*-$MeC_6H_4 \cdot SO_3$
(16) $X = ClO_4$



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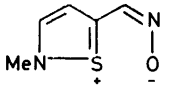
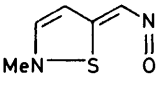


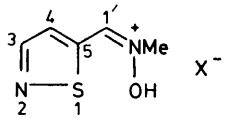
(18a)



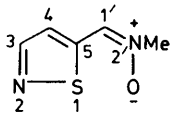
(18b)

in the salt (15). Deprotonation of the toluene-*p*-sulphonate (15) with aqueous sodium carbonate gave the oxathiadiazapentalene (17) as a stable, sublimable, pale yellow solid. Compound (17) is the first derivative of the 1-oxa-6aλ^4-thia-2,6-diazapentalene system hitherto to have been prepared. When treated with perchloric acid in methanol, compound (17) underwent *O*-protonation and gave the perchlorate (16) nearly quantitatively. The patterns of the ^{1}H n.m.r. spectra of the toluene-*p*-sulphonate (15) and the perchlorate (16) in [$^2H_6$]dimethyl sulphoxide were identical, save for the presence of the additional toluene-*p*-sulphonate anion signals of (15) and the variable position of the OH signals; the chemical shifts of corresponding protons in the two salts differed only slightly (≤0.06 p.p.m.). U.v. spectral studies (see Experimental section) showed that the salts (15) and (16) are virtually completely solvolysed in methanol to the oxathiadiazapentalene (17).

The second toluene-*p*-sulphonate (19), when deprotonated with aqueous sodium carbonate, gave the methylimine *N*-oxide (21), which was subsequently obtained more readily by the reaction of isothiazole-5-carbaldehyde with *N*-methylhydroxylamine. Treatment of compound (21) with perchloric acid in methanol gave the perchlorate (20). The patterns of the ^{1}H n.m.r. spectra of the toluene-*p*-sulphonate (19) and the perchlorate (20) in [$^2H_6$]dimethyl sulphoxide were identical, save for the presence of the additional toluene-*p*-sulphonate anion signals from the salt (19) and the variable position of the OH signal; $J_{3.4}$ for the salts (19) and (20) was 2.0 Hz. The spectrum of the perchlorate (20) in trifluoroacetic acid showed a downfield



(19) X = *p*-$MeC_6H_4 \cdot SO_3$
(20) $X = ClO_4$



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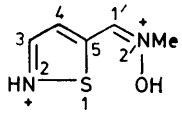


(22)

shift of all proton signals, with $J_{3.4}$ (3.1 Hz) indicative of an isothiazolium structure. The ^{1}H n.m.r. spectral data thus establish that the toluene-*p*-sulphonate and the perchlorate are the *O*-protonated salts (19) and (20), and that further protonation of the perchlorate (20) in trifluoroacetic acid gives the dication (22).

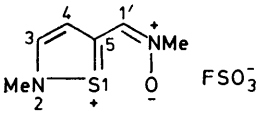
In contrast to the course of protonation, methylation of compound (21) took place at the ring nitrogen atom, as evidenced by the double quartet pattern of the 3-H signal ($J_{3.4}$ 3.2, $J_{3,NMe}$ 0.6 Hz) in the ^{1}H n.m.r. spectrum of the resulting salt (23). A possible alternative formulation of the methylation product is the four-electron three-centre bonded structure (24). The magnitude of $J_{3.4}$ is consistent with the isothiazolium structure (23) but does not exclude structure (24).

1,6-Dimethyl-6aλ^4-thia-1,6-diazapentalene, 6-Methyl-1,6aλ^4-dithia-6-azapentalene, and 6-Methyl-1-oxa-6aλ^4-thia-6-azapentalene.—The Wittig reaction between isothiazole-5-carbaldehyde and methoxymethylenetriphenylphosphorane readily gave 5-(2-methoxyvinyl)-isothiazole (25) [2 : 1 mixture of (*E*)- and (*Z*)-isomers]. The product contained a small quantity of biphenyl as a persistent impurity which, in preparative scale experiments, could not be removed without extensive loss of material. However, methylation of the product (25) (*ca.* 98% purity) with methyl fluorosulphonate gave the crystalline isothiazolium fluorosulphonate (26) [5 : 2 mixture of (*E*)- and (*Z*)-isomers] which was free from biphenyl.

* The magnitude of $J_{3.4}$ distinguishes an isothiazole (*J ca.* 2.0 Hz) from an isothiazolium compound (*J ca.* 3.0 Hz).

The salt (26) was converted into derivatives of several classes of 1,6,6aλ⁴-triheterapentalene by reaction with suitable nucleophiles. With aqueous methylamine it gave 1,6-dimethyl-6aλ⁴-thia-1,6-diazapentalene (27) in a yield (61%) which makes this route to compound (27) a good alternative to the synthesis[4] from 6-methyl-1,6aλ⁴-dithia-6-azapentalene (28).

The reaction of the salt (26) with aqueous sodium hydrogen sulphide proceeded less satisfactorily. It gave the desired dithia-azapentalene (28) in modest yield (23%), together with 1,6,6aλ⁴-trithiapentalene (6aλ⁴-thiathiophthen) (29) (2.7%) and the thione (30) (8.5%). The thione (30) is formed by reductive cleavage of the S–N bond in the isothiazolium salt (26).



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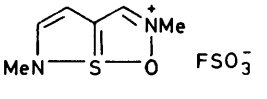

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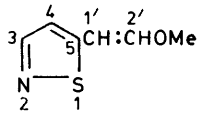

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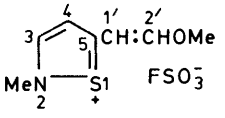

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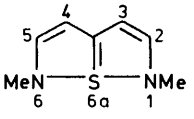

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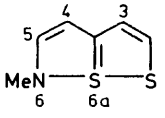

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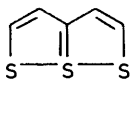

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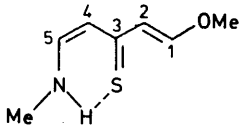

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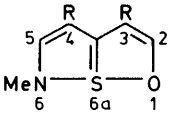

(31) R = H
(32) R = Br
(33) R = I

The salt (26) also reacted with aqueous sodium hydroxide to give 6-methyl-1-oxa-6aλ⁴-thia-6-azapentalene (31) in low yield (11%). Two 3,4-dihalogeno-derivatives [(32) and (33)] of compound (31) have recently been described.[6]

EXPERIMENTAL

M.p.s were determined with a Kofler hot-stage apparatus. Electronic absorption spectral data refer to solutions in methanol, unless otherwise stated. MeOH–$HClO_4$ denotes a 1% (v/v) solution of perchloric acid in methanol; throughout ether denotes diethyl ether. I.r. spectra refer to solids dispersed in KBr discs. ^1H N.m.r. spectra were determined at 100 MHz for 0.4M-solutions in deuteriochloroform, unless otherwise indicated, with tetramethylsilane as internal reference. Unless otherwise stated δ values imply singlet absorptions. *J* Values were measured on the 100-Hz scale. Signals assigned to the pairs of *o*- and *m*-protons of the *p*-nitrophenyl group in compounds (3), (6), and (9) and of the toluene-*p*-sulphonate ion in the salts (15) and (19) are the four most intense signals in the AA′BB′ pattern. Solutions were dried over sodium sulphate and evaporated at reduced pressure. Column chromatography was carried out with alumina (activity II, pH *ca.* 9.5, 100—250 mesh). Solvent mixtures are described in ratios by volume. Petroleum was of boiling range 40—60 °C. Aqueous methylamine was a 25—30% (w/v) solution. Perchloric acid refers to 70—72% (w/w) perchloric acid. Isothiazole-5-carbaldehyde was obtained from Raylo Chemicals Limited; b.p. 74 °C at 15 mmHg; δ 7.78 (1 H, d, $J_{4,3}$ 1.8 Hz, 4-H), 8.65 (1 H, d, $J_{3,4}$ 1.8 Hz, 3-H), and 10.14 (1 H, CHO).

Synthesis of 6aλ⁴-*Thia*-1,2,6-*triazapentalenes*.—Charge-transfer complexes of 6aλ⁴-thia-1,2,6-triazapentalenes with 1,3,5-trinitrobenzene were prepared from the base (1 mmol) and 1,3,5-trinitrobenzene (1 mmol) in boiling ethanol (10 ml, unless otherwise stated). The composition was obtained by elemental analysis and checked by integration of the ^1H n.m.r. spectrum (solvent $CDCl_3$).

6-*Methyl*-1-*phenyl*-6aλ⁴-*thia*-1,2,6-*triazapentalene* (8). A solution of isothiazole-5-carbaldehyde (1.13 g, 10 mmol), phenylhydrazine (1.19 g, 1.08 ml, 11 mmol), water (0.5 ml), and concentrated hydrochloric acid (0.2 ml) in methanol (10 ml) was boiled for 10 min. The ice-cooled solution deposited *isothiazole-5-carbaldehyde phenylhydrazone* (2) (1.78 g, 88%), yellow prisms from ethanol, m.p. 135—137 °C (Found: C, 58.9; H, 4.3; N, 21.0. $C_{10}H_9N_3S$ requires C, 59.1; H, 4.5; N, 20.7%).

A solution of the phenylhydrazone (2) (1.015 g, 5 mmol) and methyl fluorosulphonate (0.80 ml, 10 mmol) in dichloromethane (50 ml) was stirred at room temperature for 15 h. Ether was added to precipitate completely the solid which had gradually formed. Filtration and washing with ether gave 2-*methyl*-5-(*phenylhydrazonomethyl*)*isothiazolium fluorosulphonate* (5) (1.545 g, 97%), orange needles from ethanol, m.p. 145—147 °C (Found: C, 41.6; H, 3.9; N, 13.4. $C_{11}H_{12}FN_3O_3S_2$ requires C, 41.6; H, 3.8; N, 13.2%); $\lambda_{max.}$(MeOH–$HClO_4$) 444 (log ε 4.41), 257 (4.11), and 244infl nm (4.07); δ(CF_3·CO_2H) 4.14 (3 H, NMe), 7.08—7.43 (6 H, m, 4-H and Ph), 7.91 (1 H, 1′-H), and 8.42 (1 H, d, $J_{3,4}$ 3.0 Hz, 3-H).

An excess of sodium carbonate was added to a solution of the fluorosulphonate (5) (1.585 g, 5 mmol) in water (750 ml) and methanol (250 ml). The mixture was extracted with benzene, and the extracts were washed with water (× 3), dried, and evaporated. Chromatography [alumina (30 × 3.2 cm)] of the residue with benzene gave orange eluates which afforded 6-methyl-1-phenyl-6aλ⁴-thia-1,2,6-triazapentalene (1.017 g. 94%), orange-red needles from petroleum, m.p. and mixed m.p. with an authentic sample 92—94 °C (lit.,[2] 92—94 °C), which had the same ^1H n.m.r. spectrum and showed the same t.l.c. behaviour on silica (benzene) as an authentic sample.[2] The 1,3,5-*trinitrobenzene complex* formed black needles (73%) from ethanol

(15 ml), m.p. 140—141 °C (Found: C, 47.3; H, 3.2; N, 19.8. $C_{17}H_{14}N_6O_6S$ requires C, 47.4; H, 3.3; N, 19.5%).

6-Methyl-1-p-nitrophenyl-6aλ⁴-thia-1,2,6-triazapentalene (9). A solution of isothiazole-5-carbaldehyde (1.13 g, 5 mmol), *p*-nitrophenylhydrazine (1.65 g, 11 mmol), water (2 ml), and concentrated hydrochloric acid (0.2 ml) in methanol (30 ml) was boiled for 10 min. The cooled solution deposited *isothiazole-5-carbaldehyde p-nitrophenylhydrazone* (3) (2.16 g, 87%), golden-yellow needles from ethanol, m.p. 209—211 °C (Found: C, 48.4; H, 3.3; N, 22.8. $C_{10}H_8N_4O_2S$ requires C, 48.4; H, 3.3; N, 22.6%).

Methyl fluorosulphonate (0.8 ml, 10 mmol) was added to a suspension of the *p*-nitrophenylhydrazone (3) (1.24 g, 5 mmol) in dichloromethane (50 ml), and the mixture was stirred at room temperature for 15 h. Addition of ether and filtration gave *2-methyl 5-(p-nitrophenylhydrazonomethyl)-isothiazolium fluorosulphonate* (6) (1.69 g, 93%), orange prisms from methanol, m.p. 226 °C (decomp.) (Found: C, 36.8; H, 3.5; N, 15.7. $C_{11}H_{11}FN_4O_5S_3$ requires C, 36.5; H, 3.1; N, 15.5%); $\lambda_{max.}$(MeOH–$HClO_4$) 432 (log ε 4.59), 322br (3.88), and 245br nm plateau (4.03); δ(CF_3·CO_2H) 4.36 (3 H, NMe), 7.28 and 7.37 (2 H, 2 *o*-protons of 1-Ar), 7.53 (1 H, d, $J_{4.3}$ 2.8 Hz, 4-H), 8.18 (1 H, 1′-H), 8.25 and 8.34 (2 H, 2 *m*-protons of 1-Ar), and 8.75 (1 H, d, $J_{3.4}$ 2.8 Hz, 3-H).

An excess of sodium carbonate was added to a solution of the fluorosulphonate (6) (1.81 g, 5 mmol) in methanol (750 ml) and water (250 ml). Dichloromethane (750 ml) was added, and the resulting mixture was stirred vigorously for 30 min. The aqueous layer was extracted with more dichloromethane, and the combined dichloromethane extracts were washed with water (× 3), dried, and evaporated. Chromatography [alumina (30 × 3.2 cm)] of the residue with benzene–ether (4 : 1) gave red eluates which afforded *6-methyl-1-p-nitrophenyl-6aλ⁴-thia-1,2,6-triazapentalene* (1.281 g, 97.7%), dark red spars from cyclohexane–benzene, m.p. 185—187 °C (Found: C, 50.3; H, 3.8; N, 21.5. $C_{11}H_{10}N_4O_2S$ requires C, 50.4; H, 3.8; N, 21.4%); $\lambda_{max.}$ (cyclohexane) 456 (log ε 4.55), 344br (3.78), and 236 nm (3.99); δ 3.72 (3 H, d, $J_{NMe.5}$ 0.7 Hz, NMe), 7.01 (1 H, d, $J_{4.5}$ 3.6 Hz, 4-H), 7.72 and 7.81 (2 H, 2 *o*-protons of 1-Ar), 8.09 (1 H, dq, $J_{5.4}$ 3.6 Hz, $J_{5.NMe}$ 0.7 Hz, 5-H), 8.18 and 8.27 (2 H, 2 *m*-protons of 1-Ar), and 8.26 (1 H, 3-H).

1,6-Dimethyl-6aλ⁴-thia-1,2,6-triazapentalene (10). A solution of isothiazole-5-carbaldehyde (1.13 g, 10 mmol), methylhydrazine (920 mg, 20 mmol), and acetic acid (0.5 ml) in methanol (20 ml) was boiled for 10 min, cooled, and poured into water. The mixture was basified with sodium carbonate and extracted with ether. Distillation of the residue from the dried and evaporated extracts gave *isothiazole-5-carbaldehyde methylhydrazone* (4) (1.31 g, 93%) as a yellow oil, b.p. 135 °C at 0.1 mmHg (Found: C, 42.7; H, 5.1; N, 29.8. $C_5H_7N_3S$ requires C, 42.5; H, 5.0; N, 29.8%); δ 2.94 (3 H, d, $J_{NMe.1'-H}$ 0.8 Hz, NMe), 6.28 (1 H, vbr, NH), 7.09 (1 H, dd, $J_{4.3}$ 1.8 Hz, $J_{4.1'}$ 0.4 Hz, 4-H), 7.56 (1 H, m, 1′-H), and 8.38 (1 H, d, $J_{3.4}$ 1.8 Hz, 3-H).

Methyl fluorosulphonate (0.8 ml, 10 mmol) was added to a solution of the methylhydrazone (4) (905 mg, 5 mmol) in dichloromethane (10 ml). A red oil began to separate from the solution, and after 10 min water was added. The mixture was thoroughly shaken, and the aqueous layer was washed with ether (× 2), basified with sodium carbonate, and extracted with benzene. The extracts were washed with water, dried, and evaporated, and the residue was chromatographed [alumina (30 × 3.2 cm)] with benzene. Evaporation of the yellow eluates and distillation of the residual oil at 65 °C and 1 mmHg (block) gave *1,6-dimethyl-6aλ⁴-thia-1,2,6-triazapentalene* (145 mg, 19%) as a pale yellow oil which on cooling crystallised as pale yellow prisms, m.p. 42—44 °C (Found: C, 46.7; H, 5.7; N, 27.1. $C_6H_9N_3S$ requires C, 46.4; H, 5.8; N, 27.1%); $\lambda_{max.}$ (cyclohexane) 386 (log ε 4.11), 283 (2.41), and 223 nm (4.01); δ 3.53 (3 H, d, $J_{6\text{-}Me.5}$ 0.7 Hz, 6-Me), 3.70 (3 H, 1-Me), 6.64 (1 H, d, $J_{4.5}$ 4.0 Hz, 4-H), 7.90 (1 H, dq, $J_{5.4}$ 4.0 Hz, $J_{5.6\text{-}Me}$ 0.7 Hz, 5-H), and 8.02 (1 H, 3-H). The *1,3,5-trinitrobenzene complex* formed brown needles (69%), m.p. 129—132 °C (Found: C, 38.9; H, 3.2; N, 23.1. $C_{12}H_{13}N_6O_6S$ requires C, 39.1; H, 3.3; N, 22.8%).

Methylation of Isothiazole-5-carbaldehyde Oxime (13) *with Methyl Toluene-p-sulphonate* (cf. *ref.* 5).—A solution of hydroxyammonium chloride (8.34 g, 120 mmol) and sodium carbonate (7.42 g, 70 mmol) in water (30 ml) was added to a solution of isothiazole-5-carbaldehyde (11.31 g, 100 mmol) in methanol (65 ml), and the resulting solution was boiled for 30 min. The cooled mixture was neutralised by the dropwise addition of acetic acid, and the mixture was extracted with ether (× 4). Drying and evaporation of the extracts gave isothiazole-5-carbaldehyde oxime (13) (12.55 g, 98%) [(*Z*) : (*E*), *ca.* 7 : 1 (n.m.r.)]. Recrystallisation from benzene gave the oxime (13) (11.22 g, 88%) [(*Z*) : (*E*), *ca.* 10 : 1] as needles, m.p. 127—128 °C [lit., [5] (*Z*)-(13), 133—134 °C] (Found: C, 37.5; H, 3.1; N, 21.7. Calc. for $C_4H_4N_2OS$: C, 37.5; H, 3.2; N, 21.9%).

A solution of methyl toluene-*p*-sulphonate (14.90 g, 80 mmol) in benzene (25 ml) was added to a solution of the oxime (13) [(*Z*) : (*E*), *ca.* 10 : 1] (10.25 g, 80 mmol) in benzene (15 ml), and the mixture was boiled (oil-bath) for 1 h while a viscous oil separated from solution. The mixture was cooled, kept at room temperature for 2.5 h, and then ether (50 ml) was added to precipitate the oil completely. After 20 min the supernatant liquid was decanted, and the oil was washed twice by being swirled with 50-ml portions of ether. The oil was dissolved in acetone (20 ml), crystallisation began, and ether (5 ml) was added *gradually* during the next 4 h. The mixture was then kept overnight, filtered, and the solid was washed successively with ether–acetone (9 : 1; 2 × 50 ml) and ether (× 3). Recrystallisation of the solid (6.32 g, 25%) from ethanol gave a 6 : 5 mixture (n.m.r.) of the salts (15) and (19) (4.68 g, 14.9 mmol, 18.6%). Crystallisation of a portion (3.14 g, 10 mmol) of the mixture from acetonitrile gave *5-hydroxyiminomethyl-2-methylisothiazolium toluene-p-sulphonate* (15) (1.54 g, 4.9 mmol), pale beige prisms, m.p. 160.5—169 °C (decomp.) (lit.,[5] 174—176 °C) (Found: C, 45.9; H, 4.5; N, 8.9. Calc. for $C_{12}H_{14}N_2O_4S_2$: C, 45.8; H, 4.5; N, 8.9%); $\lambda_{max.}$ (MeOH–$HClO_4$) 333sh (log ε 3.47), 302br (3.96), 263sh (3.56), 219 (4.15), and 210sh nm (4.02); $\lambda_{max.}$ [MeOH: composite spectrum of the oxathiadiazapentalene (17) and toluene-*p*-sulphonic acid] 3.34 (log ε 3.89), 253 plateau (3.25), and 218 nm (4.24); δ[$(CD_3)_2SO$] 2.29 (3 H, *Me*·C_6H_4), 4.10 (3 H, d, $J_{NMe.3}$ 0.7 Hz, NMe), 7.10 and 7.18 (2 H, 2 *o*-protons of Me·C_6H_4), 7.50 and 7.58 (2 H, 2 *m*-protons of Me·C_6H_4), 7.88 (1 H, d, $J_{4.3}$ 3.1 Hz, 4-H), 8.97 (1 H, 1′-H), 9.09 (1 H, dq, $J_{3.4}$ 3.1 Hz, $J_{3.NMe}$ 0.7 Hz, 3-H), and 10.34 (*ca.* 1 H, br, OH). Concentration of the acetonitrile mother-liquors to the point of incipient crystallisation at the boiling point, cooling, and filtration, gave *5-[hydroxy(methyl)iminiomethyl]isothiazole toluene-p-sulphonate* (19) (808 mg, 2.57 mmol), straw-coloured prisms, m.p. 139.5—144.5 °C (Found: C, 45.8; H, 4.4; N, 9.0.

$C_{12}H_{14}N_2O_4S_2$ requires C, 45.8; H, 4.5; N, 8.9%); $\lambda_{max.}$ (MeOH–$HClO_4$) 327sh (log ε 3.93), 317 (3.99), 250 plateau (3.31), 227sh (3.96), and 217 nm (4.22); δ[$(CD_3)_2SO$] 2.30 (3 H, *Me*·C_6H_4), 3.94 (3 H, d, $J_{NMe,1'}$ 0.7 Hz, NMe), 7.14 and 7.22 (2 H, 2 *o*-protons of Me·C_6H_4), 7.55 and 7.63 (2 H, 2 *m*-protons of Me·C_6H_4), 7.77 (1 H, d, $J_{4.3}$ 2.0 Hz, 4-H), 8.60 (1 H, d, $J_{3.4}$ 2.0 Hz, 3-H), 8.81 (1 H, m, 1'-H), and 10.18 (*ca.* 1 H, OH).

6-*Methyl*-1-*oxa*-6aλ^4-*thia*-2,6-*diazapentalene* (17).—A solution of sodium carbonate (530 mg, 5 mmol) in water (15 ml) was added to a solution of the toluene-*p*-sulphonate (15) (1.57 g, 5 mmol) in water (25 ml), and the resulting solution was extracted with dichloromethane (× 4). The residue from the dried and evaporated extracts was sublimed at 130 °C and 0.5 mmHg. Crystallisation of the sublimate from benzene gave 6-*methyl*-1-*oxa*-6aλ^4-*thia*-2,6-*diazapentalene* (615 mg, 87%) as yellow plates, m.p. 91.5—92 °C (Found: C, 42.4; H, 4.3; N, 19.7. $C_5H_6N_2OS$ requires C, 42.2; H, 4.3; N, 19.7%); *m/e* 142.019 2 (M^+); $\lambda_{max.}$ 335 (log ε 4.00), 243 plateau (3.10), and 216 nm (4.03); δ 3.72 (3 H, d, $J_{NMe.5}$ 0.7 Hz, NMe), 7.20 (1 H, d, $J_{4.5}$ 3.6 Hz, 4-H), 8.15 (1 H, dq, $J_{5.4}$ 3.6 Hz, $J_{5.NMe}$ 0.7 Hz, 5-H), and 8.92 (1 H, 3-H); δ[$(CD_3)_2SO$] 3.74 (3 H, d, $J_{NMe.5}$ 0.7 Hz, NMe), 7.43 (1 H, d, $J_{4.5}$ 3.6 Hz, 4-H), 8.61 (1 H, d, $J_{5.4}$ 3.6 Hz, $J_{5,NMe}$ 0.7 Hz, 5-H), and 9.08 (1 H, 3-H).

Protonation of 6-*Methyl*-1-*oxa*-6aλ^4-*thia*-2,6-*diazapentalene* (17).—Perchloric acid (0.168 ml, 2 mmol) was added to a solution of 6-methyl-1-oxa-6aλ^4-thia-2,6-diazapentalene (142 mg, 1 mmol) in methanol (4 ml). Addition of ether (25 ml) precipitated 5-*hydroxyiminomethyl*-2-*methylisothiazolium perchlorate* (16) (225 mg, 93%) as needles, m.p. 113—122 °C (decomp.), which decompose upon attempted recrystallisation from acetonitrile (Found: C, 24.7; H, 3.0; N, 11.8. $C_5H_7ClN_2O_5S$ requires C, 24.8; H, 2.9; N, 11.6%); $\lambda_{max.}$ (MeOH–$HClO_4$) 332sh (log ε 3.45), 301br (3.96), 263sh (3.53), and 216sh nm (3.52); $\lambda_{max.}$[MeOH; spectrum of the oxathiadiazapentalene (17)] 334 (log ε 3.93), 249 plateau (3.15), and 216 nm (3.93); δ[$(CD_3)_2SO$] 4.10 (3 H, d, $J_{NMe.3}$ 0.7 Hz, NMe), 7.85 (1 H, d, $J_{4.3}$ 3.1 Hz, 4-H), 8.91 (1 H, 1'-H), 9.05 (1 H, dq, $J_{3.4}$ 3.1 Hz, $J_{3.NMe}$ 0.7 Hz, 3-H), and 10.84 (*ca.* 1 H, OH); δ(CF_3·CO_2H) 4.42 (3 H, d, $J_{NMe.3}$ 0.6 Hz, NMe), 8.16 (1 H, d, $J_{4.3}$ 3.0 Hz, 4-H), 8.97 (1 H, dq, $J_{3.4}$ 3.0 Hz, $J_{3.NMe}$ 0.6 Hz, 3-H), and 8.99 (1 H, 1'-H).

5-[*Methyl*(*oxido*)*iminiomethyl*]*isothiazole* (21).—(*a*) A solution of *N*-methylhydroxyammonium chloride (1.00 g, 12 mmol) and sodium carbonate (1.27 g, 12 mmol) in water (12 ml) was added to a solution of isothiazole-5-carbaldehyde (1.13 g, 10 mmol) in methanol (6.5 ml), and the mixture was boiled (oil-bath) for 30 min. The cooled mixture was diluted with water and extracted with dichloromethane (× 4), and the extracts were dried, and evaporated. Recrystallisation of the residue (1.39 g, 98%) from benzene afforded 5-[*methyl*(*oxido*)*iminiomethyl*]*isothiazole* as needles, m.p. 143.5—144 °C (Found: C, 42.3; H, 4.1; N, 19.8. $C_5H_6N_2OS$ requires C, 42.3; H, 4.3; N, 19.7%); *m/e* 142.019 4 (M^+); $\lambda_{max.}$ 312sh (log ε 4.05), 300 (4.10), 247 plateau (3.35), and 212 nm (3.80); δ 3.98 (3 H, d, $J_{NMe.1'}$ 0.8 Hz, NMe), 7.51 (1 H, d, $J_{4.3}$ 2.0 Hz, 4-H), 8.17 (1 H, br, 1'-H), and 8.52 (1 H, d, $J_{3.4}$ 2.0 Hz, 3-H); δ[$(CD_3)_2SO$] 3.94 (3 H, d, $J_{NMe.1'}$ 0.8 Hz, NMe), 7.76 (1 H, d, $J_{4.3}$ 2.0 Hz, 4-H), 8.58 (1 H, d, $J_{3.4}$ 2.0 Hz, 3-H), and 8.75 (1 H, br, 1'-H).

(*b*) A solution of sodium carbonate (106 mg, 1 mmol) in water (5 ml) was added to a solution of the toluene-*p*-sulphonate (19) (314 mg, 1 mmol) in water (5 ml). Work-up according to the procedure of the preceding experiment gave compound (21) (134 mg, 94%), which was shown to be identical with the product of the preceding experiment [m.p. and mixed m.p. 143—144 °C; identical ^1H n.m.r. spectra in $(CD_3)_2SO$; identical t.l.c. behaviour on silica (ether–acetonitrile, 2 : 1)].

Protonation of 5-[*Methyl*(*oxido*)*iminiomethyl*]*isothiazole* (21).—Perchloric acid (0.84 ml, 10 mmol) was added to a solution of compound (21) (711 mg, 5 mmol) in methanol (10 ml). Addition of ether (30 ml) precipitated 5-[*hydroxy*(*methyl*)*iminiomethyl*]*isothiazole perchlorate* (20) (1.11 g, 91%), prisms from methanol, m.p. 190.5—201.5 °C (Found: C, 24.6; H, 3.0; N, 11.7. $C_5H_7ClN_2O_5S$ requires C, 24.8; H, 2.9; N, 11.6%); $\lambda_{max.}$ (MeOH–$HClO_4$) 327sh (log ε 3.99), 317 (4.03), 248 (3.08), and 213 nm (3.91); δ[$(CD_3)_2SO$] 3.95 (3 H, d, $J_{NMe.1'}$ 0.7 Hz, NMe), 7.78 (1 H, d, $J_{4.3}$ 2.0 Hz, 4-H), 8.61 (1 H, d, $J_{3.4}$ 2.0 Hz, 3-H), 8.77 (1 H, br, 1'-H), and 11.13 (*ca.* 1 H, br, OH); δ[CF_3·CO_2H; spectrum of the cation (22)] 4.34 (3 H, d, $J_{NMe.1'}$ 0.8 Hz, NMe), 8.19 (1 H, d, $J_{4.3}$ 3.1 Hz, 4-H), 9.04 (1 H, d, $J_{3.4}$ 3.1 Hz, 3-H), and 9.10 (1 H, 1'-H).

Methylation of 5-[*Methyl*(*oxido*)*iminiomethyl*]*isothiazole* (21).—Methyl fluorosulphonate (0.8 ml, 10 mmol) was added to a solution of compound (21) (711 mg, 5 mmol) in dichloromethane (10 ml). A precipitate quickly formed, and after 15 min ether (15 ml) was added. Filtration and washing with ether gave 2-*methyl*-5-[*methyl*(*oxido*)*iminiomethyl*]*isothiazolium fluorosulphonate* (23) (1.22 g, 95%) as small prisms, m.p. 151.5—154.5 °C (Found: C, 28.3; H, 3.6; N, 10.9. $C_6H_9FN_2O_4S_2$ requires C, 28.1; H, 3.5; N, 10.9%); $\lambda_{max.}$ 331 (log ε 3.96), 260 (3.44), and 218 nm (3.95); δ[$(CD_3)_2SO$] 4.17 (3 H, 2'-Me), 4.19 (3 H, d, $J_{3.2-Me}$ 0.6 Hz, 2-Me), 8.16 (1 H, d, $J_{4.3}$ 3.2 Hz, 4-H), 9.17 (1 H, dq, $J_{3.4}$ 3.2 Hz, $J_{3.2-Me}$ 0.6 Hz, 3-H), and 9.40 (1 H, br, 1'-H).

(E)- *and* (Z)-2-*Methyl*-5-(2-*methoxyvinyl*)*isothiazolium Fluorosulphonate* (26).—A solution of phenyl-lithium (75 mmol) in ether (71 ml) was added to a suspension of methoxymethyltriphenylphosphonium chloride (34.28 g, 100 mmol) in tetrahydrofuran (200 ml) under nitrogen, and the mixture was stirred at room temperature for 30 min. A solution of isothiazole-5-carbaldehyde (5.65 g, 50 mmol) in tetrahydrofuran (25 ml) was added gradually, and the resulting mixture was stirred at room temperature under nitrogen for a further 1 h. The mixture was filtered, and the solid was washed thoroughly with ether before being discarded. The combined tetrahydrofuran–ether filtrates were evaporated, and the residual sticky oil was vigorously stirred with ether (250 ml) for 5 min. The ether solution was decanted from the oil, and the oil was extracted a further five times in the same manner. Evaporation of the combined ether extracts left a red oil. The reaction was repeated, and the red oils from the two reactions were combined. Distillation (Vigreux) at 72—74 °C and 0.1 mmHg gave an oil containing the product (25) [*ca.* 93% purity; biphenyl (*m/e* 154), triphenylphosphine (*m/e* 262), and triphenylphosphine oxide (*m/e* 278)]. The oil was redistilled through a column (6 × 1 cm) of Fenske helices, and the fraction (7.91 g) boiling at 68—70 °C and 0.1 mmHg was shown to be (*E*)- and (*Z*)-5-(2-methoxyvinyl)isothiazole (25) [(*E*) : (*Z*), 2 : 1], *m/e* 141, of *ca.* 98% purity (biphenyl impurity, *m/e* 154); (*E*)-(25): δ 3.68 (3 H, OMe), 5.95 (1 H, d, $J_{1'.2'}$ 13.2 Hz, 1'-H), 6.93 (1 H, d, $J_{4.3}$ 1.8 Hz, 4-H), 7.12 (1 H, d, $J_{2'.1'}$ 13.2 Hz, 2'-H), and 8.27 (1 H, d, $J_{3.4}$ 1.8 Hz, 3-H); (*Z*)-(25): δ 3.86 (3 H, OMe), 5.77 (1 H, d, $J_{1'.2'}$ 6.0

Hz, 1'-H), 6.38 (1 H, d, $J_{2'.1'}$ 6.0 Hz, 2'-H), 7.01 (1 H, d, $J_{4.3}$ 1.8 Hz, 4-H), and 8.30 (1 H, d, $J_{3.4}$ 1.8 Hz, 3-H).

A solution of methyl fluorosulphonate (8 ml, 100 mmol) in dichloromethane (25 ml) was added dropwise to a solution of the foregoing ether in dichloromethane (25 ml), and the solution was kept for 5 min. Gradual addition of ether precipitated a solid. The supernatant liquid was decanted, and the solid was washed with ether before being redissolved in acetonitrile (25 ml). Addition of ether gave (E)- and (Z)-2-*methyl*-5-(2-*methoxyvinyl*)*isothiazolium fluorosulphonate* (26) [(*E*) : (*Z*), 5 : 2] (13.58 g, 53% from isothiazole-5-carbaldehyde); (*E*)-(26): δ[$(CD_3)_2SO$] 3.82 (3 H, OMe), 4.15 (3 H, d, $J_{NMe.3}$ 0.6 Hz, NMe), 6.53 (1 H, d, $J_{1'.2'}$ 12.8 Hz, 1'-H), 7.62 (1 H, d, $J_{4.3}$ 3.0 Hz, 4-H), 8.00 (1 H, d, $J_{2'.1'}$ 12.8 Hz, 2'-H), and 8.93 (1 H, dq, $J_{3.4}$ 3.0 Hz, $J_{3.NMe}$ 0.6 Hz. 3-H); (*Z*)-(26): δ[$(CD_3)_2SO$] 4.17 (3 H, OMe), 4.20 (3 H, d, $J_{NMe.3}$ 0.6 Hz, NMe), 6.39 (1 H, d, $J_{1'.2'}$ 5.8 Hz, 1'-H), 7.42 (1 H, d, $J_{2'.1'}$ 5.8 Hz, 2'-H), 7.51 (1 H, d, $J_{4.3}$ 3.0 Hz, 4-H), and 9.01 (1 H, dq, $J_{3.4}$ 3.0 Hz, $J_{3.NMe}$ 0.6 Hz, 3-H). A sample, recrystallised from acetonitrile, formed prisms, m.p. 177—178 °C [(*E*)-isomer (n.m.r.)] (Found: C, 33.2; H, 4.5; N, 5.7. $C_7H_{10}FNO_4S_2$ requires C, 32.9; H, 4.0; N, 5.5%).

Synthesis of 1,6,6aλ⁴-*Triheterapentalenes from* 2-*Methyl*-5-(2-*methoxyvinyl*)*isothiazolium Fluorosulphonate* (26).—1,6-*Dimethyl*-6aλ⁴-*thia*-1,6-*diazapentalene* (27). Aqueous methylamine (25 ml) was added to a solution of the fluorosulphonate (26) (1.28 g, 5 mmol) in acetonitrile (50 ml), and the solution was kept at room temperature for 5 min. Water (250 ml) was then added, and the mixture was cooled in ice-cold water for 30 min. Filtration gave a brown solid which was dried *in vacuo*. The solid was extracted exhaustively with petroleum at room temperature, and the filtered extracts were evaporated to low volume at reduced pressure. (Heating the solution above room temperature must be avoided throughout the purification procedure.) 1,6-Dimethyl-6aλ⁴-thia-1,6-diazapentalene (496 mg, 61%) crystallised as yellow plates, m.p. 94—96 °C (lit.,[4] 82—84 °C) (Found: C, 54.2; H, 6.5; N, 18.2. Calc. for $C_7H_{10}N_2S$: C, 54.5; H, 6.5; N, 18.2%), *m/e* 154 (M^+). The ^1H n.m.r. spectrum was identical with that previously reported.[4]

6-*Methyl*-1,6aλ⁴-*dithia*-6-*azapentalene* (28). Ice-cold aqueous 1M-sodium hydrogen sulphide (50 ml) was added to an ice-cold solution of the fluorosulphonate (26) (1.28 g, 5 mmol) in acetonitrile (50 ml). The mixture was immediately extracted with benzene and the residue from the washed, dried, and evaporated extracts was chromatographed [alumina; activity II—III, pH *ca.* 9.5, 70—230 mesh (30 × 2.7 cm)]. Elution with benzene gave red eluates which yielded 1,6,6aλ⁴-trithiapentalene (6aλ⁴-thiathiophthen) (29) (22 mg, 2.7%) as red plates, m.p. and mixed m.p. with an authentic sample 112—113 °C (lit.,[7] 112—113 °C; lit.,[8] 113—114 °C), *m/e* 160 (M^+). Compound (29) had the same ^1H n.m.r. spectrum [7a] and showed the same t.l.c. behaviour on silica [petroleum–benzene (3 : 1)] as an authentic sample. Continued elution with benzene gave yellow eluates which afforded 6-methyl-1,6aλ⁴-dithia-6-azapentalene (28) (182 mg, 23%), yellow needles from hexane, m.p. and mixed m.p. with an authentic sample 107.5—108.5 °C (lit.,[3] 107—108 °C; 108—109 °C), *m/e* 157 (M^+). Compound (28) had the same ^1H n.m.r. spectrum [3] and showed the same t.l.c. behaviour on silica (benzene) as an authentic sample. Subsequent elution with ether gave a red oil which was extracted with petroleum, and the extracts were evaporated to low volume. (E,Z)-1-*Methoxy*-5-*methylaminopenta*-1,4-*diene*-3-*thione* (30) (67 mg, 8.5%) crystallised as red prisms, m.p. 53—55 °C (Found: C, 53.2; H, 7.0; N, 8.6. $C_7H_{11}NOS$ requires C, 53.5; H, 7.1; N, 8.9%); $\lambda_{max.}$ (cyclohexane) 406 (log ε 4.02), 349 (4.16), and 335sh nm (4.15); $\nu_{max.}$ 2 930 cm^{-1} (N–H); δ 3.13 (3 H, d, $J_{NMe.NH}$ 5.4 Hz, NMe), 3.74 (3 H, OMe), 5.85 (1 H, d, $J_{4.5}$ 7.8 Hz, 4-H), 6.04 (1 H, d. $J_{2.1}$ 12.0 Hz, 2-H), 7.09 (1 H, dd, $J_{5.4}$ 7.8 Hz, $J_{5.NH}$ 13.8 Hz, 5-H), 7.64 (1 H, d, $J_{1.2}$ 12.0 Hz, 1-H), and 12.94 (1 H, br, NH).

6-*Methyl*-1-*oxa*-6aλ⁴-*thia*-6-*azapentalene* (31). A solution of the fluorosulphonate (26) (1.28 g, 5 mmol) in acetonitrile (50 ml) was added to ice-cold aqueous 0.5M-sodium hydroxide (100 ml). The mixture was kept for 2 h, diluted with water, and extracted successively with petroleum (× 2) (extracts discarded) and ether (× 2). The residual oil from the washed, dried, and evaporated ether extracts was extracted with boiling petroleum, and the extracts were evaporated to low volume. 6-*Methyl*-1-*oxa*-6aλ⁴-*thia*-6-*azapentalene* (77 mg, 11%) crystallised as yellow prisms, m.p. 36—40 °C (Found: C, 51.3; H, 5.1; N, 9.9. C_6H_7NOS requires C, 51.0; H, 5.0; N, 9.9%); *m/e* 141 (M^+); $\lambda_{max.}$ (cyclohexane) 374 (log ε 4.13) and 235 nm (3.74); $\nu_{max.}$ 1 530 cm^{-1} (ring C···O); δ 3.61 (3 H, d, $J_{NMe.5}$ 0.4 Hz, NMe), 6.35 (1 H, d, $J_{3.2}$ 2.6 Hz, 3-H), 6.60 (1 H, d, $J_{4.5}$ 3.6 Hz, 4-H), 7.65 (1 H, dq, $J_{5.4}$ 3.6 Hz, $J_{5.NMe}$ 0.4 Hz, 5-H), and 8.86 (1 H, d, $J_{2.3}$ 2.6 Hz, 2-H).

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