Electron Deficient Heteroaromatic Ammonioamidates. Part 25.[1] *N*-(Quinazolin-3-io)amidates. Part 12.[1] The Synthesis of *N*-(6,7-Dimethoxy-2-methylquinazolin-3-io)ethoxythioformamidate and of 2-(3,4-Dimethoxyphenyl)-8,9-dimethoxy-5-methyl-10b*H*-[1,3,4]-thiadiazolo[3,2-*c*]quinazoline, the Ring Isomer of *N*-(6,7-Dimethoxy-2-methylquinazolin-3-io)-3,4-dimethoxy(thiobenzamidate)

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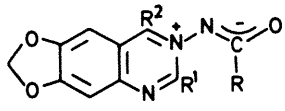
The synthesis of *N*-(6,7-dimethoxy-2-methylquinazolin-3-io)ethoxythioformamidate (7a) has been carried out starting with the thioacylhydrazone (5a) *via* cyclization of the acetylamino thioacylhydrazone (6a). An analogous attempt to synthesize the related thiobenzamidate (7b) failed and furnished instead the cyclic form of the desired product, the [1,3,4]thiadiazolo[3,2-*c*]quinazoline (12b). In contrast to the thioacylhydrazones (5a) and (6a) the related thiobenzoylhydrazones (5b) and (6b) are shown to exist as their cyclic isomers, the thiadiazolines (8b) and (9b) respectively, under the conditions studied. Cyclization of (9b) furnished the thiadiazoloquinazoline (12b). The existence of this cyclic form (12b), and the absence of the dimer (17) of the quinazolinio(thioamidate) (7b) are in sharp contrast to the case of the related quinazolinioamidates (1).

The chemistry of *N*-(6,7-methylenedioxyquinazolin-3-io)-amidates (1) † has been studied extensively,[2] but much less is known about their thioamidate counterparts or about heteroaromatic ammonio(thioamidates) in general. The synthesis and some photochemistry of the only quinazolinio(thioamidate) so far studied, *viz.* *N*-(6,7-dimethoxy-2-methylquinazolin-3-io)ethoxythioformamidate (7a) have been briefly mentioned in a preliminary communication.[3] Here we present the experimental details of the synthesis of compound (7a) and of the attempted synthesis of its 3,4-dimethoxythiobenzamidate analogue (7b) which, instead of the desired compound, furnished the isomeric 2-(3,4-dimethoxyphenyl)-8,9-dimethoxy-5-methyl-10b*H*-[1,3,4]thiadiazolo[3.2-*c*]quinazoline (12b). The photochemistry of compounds (7a) and (12b) will be reported later.

The syntheses of compounds (7a) and (12b) are outlined in the Scheme. While condensation of the 2-nitrobenzaldehyde (2) [4] with the thiocarbazate (4a) [5] furnished the thioacylhydrazone (5a), reaction of aldehyde (2) with the 3,4-dimethoxythiobenzohydrazide (4b) [6] furnished the thiadiazoline (8b), the cyclic form of the expected thioacylhydrazone (5b).

The cyclic structure (at least in chloroform solution) of the latter condensation product follows from its ^{1}H and ^{13}C n.m.r. spectra: the singlet at δ 6.92 ‡ and the doublet at 70.3 p.p.m., respectively, establish the presence of the thiadiazoline ring, while the complete absence of azomethine proton and thiocarbonyl carbon signals, respectively, indicate that no detectable amounts of the open-chain form (5b) are present.§ On the other hand, as shown by its ^{1}H n.m.r. spectrum, the condensation product of the aldehyde (2) and the thiocarbazate (4a) exists in chloroform solution in the open-chain form (5a). No signals corresponding to the cyclic form (8a) could be detected although the broadening of the azomethine proton and of the 6-H signals (at δ 8.50 and 7.48, respectively) in the ^{1}H n.m.r. spectrum indicated the occurrence of an exchange process which could be partial tautomerization to (8a). [Acetylation of the thiocylhydrazone (5a) furnished compound (10a), *i.e.* a fixed derivative of the unstable cyclic tautomer (8a).]



(1)

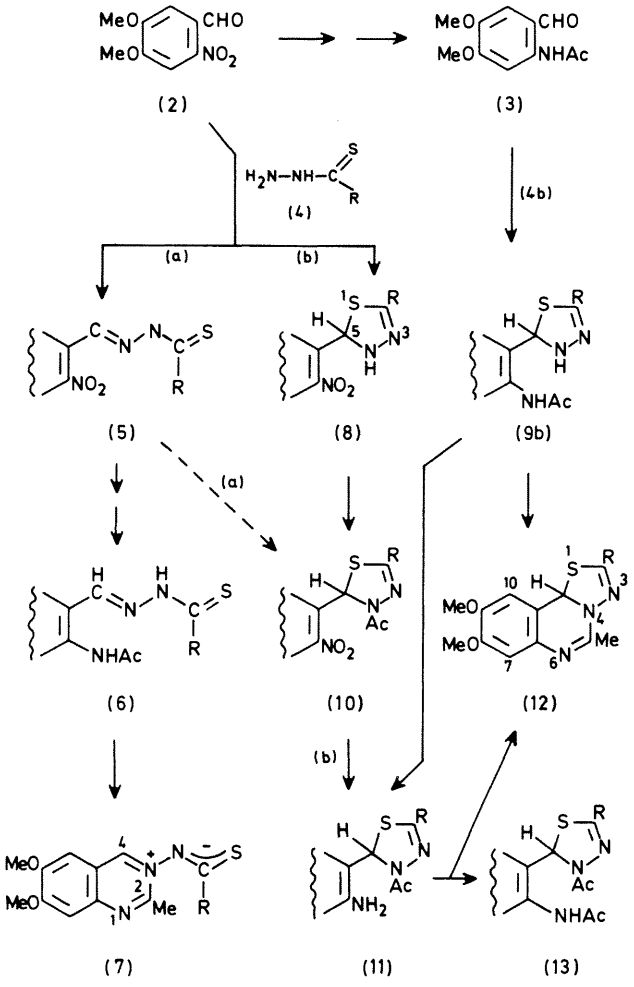
R^1, R^2 = H, Me
R = OEt, OCH_2Ph, Me, Ph

Conversion of the thioacylhydrazone (5a) *via* (6a) into the quinazolinio(thioamidate) (7a) was carried out as described [10] for the synthesis of quinazolinioamidates of type (1).

The best route to the ring isomer (12b) of the quinazolinio-(thioamidate) (7b) was by condensing the 2-acetylamino-benzaldehyde (3) [11] with the thiobenzohydrazide (4b), and refluxing the resulting crude thiadiazoline (9b) with ethanolic hydrogen chloride. When the condensation of compounds (3) and (4b) was carried out in the presence of hydrogen chloride, compound (12b) was obtained directly. Alternatively, the thiadiazoline (8b) was acetylated and reduced to furnish, *via* (10b), the acetylthiadiazoline (11b) which, when treated with a mixture of perchloric acid and acetic anhydride, furnished a mixture of the diacetyl derivative (13b) (main product) and the perchlorate of compound (12b) (minor product). Compound (11b) was also obtained by rearrangement of its isomer (9b) induced by perchloric acid–acetic anhydride.

The open-chain forms (7) and the cyclic forms (12) may be differentiated on the basis of their n.m.r. spectra. Diagnostic

† Compounds of this type are correctly called ' amidides '; they are so named in the Experimental section.
‡ *Cf.* the singlet at δ 6.80 in the ^{1}H n.m.r. spectrum ($CDCl_3$) of 5-(2-nitrophenyl)-2-phenyl-Δ^2-1,3,4-thiadiazoline.[7]
§ For other *N'*-thioacylhydrazones which exist exclusively in the cyclic thiadiazoline form, see refs. 7—9.

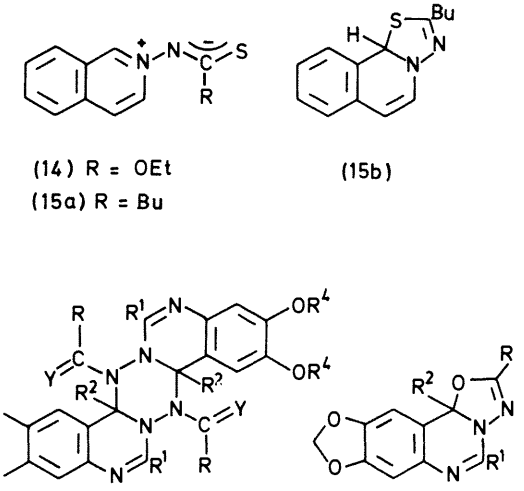


Scheme.

for the open-chain form are the low-field signals of 4-H and 2-Me at δ *ca.* 9 and 2.8 respectively, in the ^{1}H n.m.r. spectrum as well as that of the central carbon atom of the amidate side chain which appears at 195.1 p.p.m. in the ^{13}C n.m.r. spectrum of the related compound (14) [12] measured in $CDCl_3$. Ring closure effects upfield shifts of the signals due to 4-H and 2-Me (which become 10b-H and 5-Me, respectively) to δ *ca.* 6.8 and 2.45, respectively, and of the signal of the central atom of the side chain (which becomes C-2 of the ring system) to *ca.* 152 p.p.m.

The open-chain forms (7) and the cyclic forms (12) having identical groups R might be expected to be tautomeric. The related isoquinolinio(thioamidate) (15) is known to exist in both tautomeric forms (15a) and (15b), the latter being favoured in less polar solvents (*e.g.* chloroform) and the former in more polar ones (*e.g.* methanol).[12] It is therefore surprising that, as shown by their n.m.r. spectra, the chloroform solution of compound (7a) contains no detectable amounts of the ring form (12a) while neither the chloroform solution nor the chloroform–methanol (1 : 1) solution of compound (12b) contains detectable amounts of the open-chain form (7b).

A striking difference between the quinazolinio(thioamidates) and their amidate counterparts (1) should also be pointed out. While the latter exist in non-protic (*e.g.* chloroform) solutions as equilibrium mixtures of the amidate (1) and the dimeric form (16) (the position of equilibria depending on the nature of the groups R, R^1, and R^2, and no trace of the cyclic monomeric form (18) being detectable [1,10]) the two quinazolinio(thioamidates) described here (which are the only ones known so far) appear to exist either exclusively as the open-chain monomer (7a) or exclusively as the cyclic monomer (12b) without appreciable amounts of the dimer (17) being detectable. Since the ^{1}H n.m.r. spectra corresponding to the cyclic monomer (12b) and the dimer (17) should be quite similar, and, moreover, their mass spectra may be expected to be identical because of thermal decomposition of the dimer (*cf.* ref. 10), the obvious means of differentiating between the two structures was by examination of the ^{13}C n.m.r. spectrum. The lowest field signal in the ^{13}C n.m.r. spectrum appears at 152.9 p.p.m. while the thiocarbonyl carbon of 3,4-dimethoxy(thiobenzohydrazide) (4b) resonate at 191.6 p.p.m., and the dimeric structure (17) is therefore clearly ruled out.



Experimental

I.r. spectra were recorded with a Specord IR 75, u.v. spectra with a Specord UV-VIS (Carl Zeiss, Jena, GDR), 60 MHz ^{1}H n.m.r. spectra with a Varian A60D, and 100 MHz ^{1}H and ^{13}C n.m.r. spectra with a JEOL FX-100 spectrometer. Mass spectra were obtained at 70 eV with a Varian MAT 311A spectrometer, using the direct insertion system. Multiplicities given for ^{13}C n.m.r. data are from the off-resonance spectra throughout.

3,4-Dimethoxy(thiobenzohydrazide) (4b) in deuteriochloroform gave the following ^{13}C n.m.r. spectrum: δ 56.0 (2 MeO), 110.8 (d), 111.1 (d), 119.6 (d), 131.1 (s), 148.5 (s), and 151.6 (s) (ArC), and 191.6 p.p.m. (thiocarbonyl).

2-Acetylamino-4,5-dimethoxybenzaldehyde (3).—A solution of 4,5-dimethoxy-2-nitrobenzaldehyde (2) [4] (2.1 g, 10 mmol) in a mixture of acetic acid (50 cm^3) and acetic anhydride (10 cm^3) was reduced in the presence of an 8% Pd-on-charcoal catalyst at room temperature and normal pressure to give, after conventional work-up, the title compound (1.2 g, 50%), m.p. 178—179 °C (from MeOH) (lit.,[11] m.p. 176 °C); $\nu_{max.}$ (KBr) 1 680 and 1 650 cm^{-1}.

O-Ethyl Thiocarbazate (4a).[5]—98% Hydrazine hydrate (0.5 cm^3) was added to an ice-cold ethanolic (2 cm^3) solution of *O*-ethyl *S*-methyl dithiocarbonate [13] (*1* cm^3). The mixture was stirred for 30 min at 0 °C, diluted with water and extracted with diethyl ether. The crude product (93%), obtained after the ethereal solution had been dried ($MgSO_4$) and the solvent evaporated under reduced pressure, was used without further purification in the following step because attempted purification by distillation under reduced pressure caused extensive decomposition.

4,5-*Dimethoxy*-2-*nitrobenzaldehyde Ethoxy*(*thiocarbonyl*)*hydrazone* (5a).—A mixture of compounds (2) [4] (1.06 g, 5 mmol), crude thiocarbazate (4a) (0.1 cm^3), and ethanol (10 cm^3) was heated on a water-bath. From the resulting clear solution the product soon started to precipitate. The mixture was allowed to cool after 10 min to give the title compound (1.42 g, 90%), m.p. 200—201 °C (from BuOH) [Found: C, 45.85; H, 5.4; N, 13.1; O, 25.55; S, 9.85 Calc for $C_{12}H_{15}N_3O_5S$ (*M*, 313.3): C, 46.00; H, 4.83; N, 13.41; O, 25.53; S, 10.24%]; δ($CDCl_3$) 1.44 (t) and 4.65 (q) (OEt), 3.95 (MeO), 4.01 (MeO), 7.48 (bs, 6-H), 7.53 (s, 3-H), 8.50 (bs, CH=N), and 9.63 (bs, NH; exchangeable).

Acetylation of the Hydrazone (5a).—Acetyl chloride (0.7 cm^3, 10 mmol) was added dropwise with continuous stirring and cooling to a mixture of the hydrazone (0.3 g, 1 mmol), dry benzene (10 cm^3), and dry pyridine (2 cm^3). The mixture was kept overnight at room temperature and evaporated to dryness. The residue was taken up in CH_2Cl_2 and water, the organic phase was separated, the solvent was distilled off, and the residue was taken up in hot ethanol (2 cm^3) to yield, after cooling, crude 4-*acetyl*-5-(4,5-*dimethoxy*-2-*nitrophenyl*)-2-*ethoxy*-Δ^2-1,3,4-*thiadiazoline* (10a) (0.2 g) which was recrystallized from acetic acid–water to give pure material (0.18 g, 53%), m.p. 124—125 °C [Found: N, 11.95. $C_{14}H_{17}N_3O_6S$ (*M*, 355.4) requires N, 11.82%]; δ($CDCl_3$) * δ 1.37 (t) and 4.32 (q) (OEt), 2.32 (s, Ac), 3.92 (s) (2 MeO), 6.67 (s, 5-H), 7.50 (s, 6′-H) and 7.67 (s, 3′-H); δ(^{13}C) ($CDCl_3$) 14.3 and 68.3 (OEt), 21.7 (*C*Me), 56.3 (MeO), 56.5 (MeO), 68.5 (d, C-5), 107.6 (d), 108.7 (d), 131.1 (s), 137.7 (s), 148.3 (s), and 154.3 (s) (Ar C), 162.0 (C-2), and 169.0 p.p.m. (C=O).

2-(3,4-*Dimethoxyphenyl*)-5-(4,5-*dimethoxy*-2-*nitrophenyl*)-Δ^2-1,3,4-*thiadiazoline* (8b).—A mixture of compounds (2) [4] (0.1 g, 0.5 mmol) and (4b) [6] (0.1 g, 0.5 mmol) and ethanol (2 cm^3) was refluxed for 10 min to give the title compound (0.17 g, 84%), m.p. 179—180 °C (from EtOAc) [Found: N, 10.3. Calc. for $C_{18}H_{19}N_3O_6S$ (*M*, 405.4): N, 10.35%]; $\lambda_{max.}$ (EtOH) 216 (4.45), 246sh (4.29), and 312 (4.23); δ ($CDCl_3$) † 3.86 (s, 2 MeO), 3.90 (s, MeO), 3.92 (s, MeO), 5.75 (bs, NH), 6.77 (d, *J* 8.5 Hz, 5′-H), 6.92 (s, 5-H), 7.07 (dd, *J* 8.5, 2.0 Hz, 6′-H), 7.24 (d, *J* 2.0 Hz, 2′-H), 7.43 (s, 6″-H), and 7.58 (s, 3″-H); δ(^{13}C) ($CDCl_3$) 55.9 (2 MeO), 56.4 (MeO), 56.5 (MeO), 70.3d (C-5), 108.1 (d), 109.1 (d), 109.9 (d), 110.7 (d), 120.8 (d), 123.8 (s), 131.9 (s), 138.7 (s), 148.5 (s), 148.9 (s), and 150.7(s) ‡ (ArC), and 153.9 (C-2).

2-*Acetylamino*-4,5-*dimethoxybenzaldehyde Ethoxy*(*thiocarbonyl*)*hydrazone* (6a).—(*a*) A mixture of compound (5a) (3.13 g, 10 mmol), 40% aqueous ethanol (140 cm^3), and $Na_2S_2O_4$ (5 1 g, 30 mmol) was stirred at 65—70 °C. After about 40—50 min a clear solution was obtained. If the mixture became acidic it was neutralized by the addition of Na_2CO_3. It was then filtered, diluted with water and extracted with CH_2Cl_2 The organic phase was dried and evaporated to dryness to give an oily product (1.95 g) which turned crystalline when left and which, according to t.l.c., proved to be homogeneous and was therefore used in the following step without further purification.

(*b*) Acetic anhydride (5 cm^3) was added in drops to the solution of the above crude product (1.95 g) in dichloromethane (20 cm^3) with continuous stirring Subsequently the mixture was refluxed for 15 min and allowed to cool to give the title compound (1.4 g, 43%), m.p. 230—231 °C (from BuOH) [Found: N, 12.65. Calc. for $C_{14}H_{19}N_3O_4S$ (*M*, 325.4): N, 12.91%]; $\nu_{max.}$ (KBr) 3 180 and 1 680 cm^{-1}.

N-(6,7-*Dimethoxy*-2-*methylquinazolin*-3-*io*)*ethoxythioformamidide* (7a).—(*a*) Thionyl chloride (0.1 cm^3) was added to a suspension of compound (6a) (0.32 g, 1 mmol) in dichloromethane (3 cm^3) with continuous stirring and cooling at such a rate that the temperature did not exceed 10 °C. A clear solution was formed from which the hydrochloride of the title compound (0.34 g, 99%), m.p. 118—119 °C, was precipitated by the addition of diethyl ether [Found: C, 49.05; H, 4.9; O, 13.65; S, 8.8. Calc. for $C_{14}H_{18}ClN_3O_3S$ (*M*, 343.8): C, 48.90; H, 5.28; O, 13.69; S, 8.78%].

(*b*) A methanolic (2 cm^3) solution of the above hydrochloride (0.5 g, 1.45 mmol) was treated with triethylamine (0.25 cm^3) to give the title compound (0.35 g, 82%), m.p. 136—137 °C, which was washed with methanol. This product was pure without further purification; recrystallization from benzene did not change the m.p. [Found: C, 55.1; H, 5.45; N, 13.8. Calc. for $C_{14}H_{17}N_3O_3S$ (*M*, 307.3): C, 54.89; H, 5.59; N, 13.71%]; δ($CDCl_3$) 1.42 (t) and 4.53 (q) (*J* 7.2 Hz, OEt), 2.84 (s, 2-Me), 3.98 (s) and 4.10 (s) (2 MeO), 7.22 (s) and 7.30 (s) (5- and 8-H), and 9.15 (s, 4-H); *m*/*z* (120 °C) (rel int., %) 307 (3.7, $M^{+\cdot}$), 246 (2.7), 204 (100), 189 (27), 161 (14), 136 (10), 134 (6.1), 120 (16), and 102 (8.8, 204^{2+}).

2-(3,4-*Dimethoxyphenyl*)-8,9-*dimethoxy*-5-*methyl*-10bH-[1,3,4]*thiadiazolo*[3,2-c]*quinazoline* (12b).—(*a*) A mixture of compounds (3) [11] (0.22 g, 1 mmol) and (4b) [6] (0.22 g, 1.1 mmol), in ethanol (8 cm^3) and 8% ethanolic HCl (0.5 cm^3) was refluxed for 3 h. A clear solution was first formed from which a crystalline hydrochloride soon started to separate. The mixture was allowed to cool and the salt was filtered off, suspended in dichloromethane and shaken with aqueous $NaHCO_3$ solution to give, after conventional work-up, the free base (12b) (0.29 g, 73%), m.p. 148—149 °C [Found: N, 10.3; S, 7.7. Calc. for $C_{20}H_{21}N_3O_4S$ (*M*, 399.5): N, 10.52; S, 7.70%; δ($CDCl_3$) § δ 2.45 (s, 5-Me), 3.86 (s, 2 MeO), 3.90 (s, MeO), 3.92 (s, MeO), 6.56 (s), 6.80 (s), and 6.93 (s) (7-, 10-, and 10b-H), 6.75—6.92 (m, 5′-H), 7.20—7.35 (m, 2′- and 6′-H); δ($CDCl_3$–CD_3OD, 1 : 1, v/v) § 2.45 (s, 5-Me), 3.87 (s), 3.89 (s), 3.91 (s), and 3.92 (s) (4 MeO), 6.63 (s), 6.80 (s), and 6.94 (s) (7-, 10-, and 10b-H), 6.82—6.98 (m, 5′-H), and 7.23—7.40 (m, 2′- and 6′-H); δ(^{13}C) ($CDCl_3$) 21.1 (5-Me), 56.0 (3 MeO), 56.3 (MeO), 70.9 (d, C-10b), 108.1 (d), 108.7 (d), 109.6 (d), 110.7 (d), 112.1 (s), 122.1 (d), 123.3 (s), 135.0 (s), 147.0 (s), 147.7 (s), 149.1 (s), and 150.3 (s) (12 ArC), and 152.0 and 152.9 p.p.m. (C-2 and -5); *m*/*z* (135 °C) (% rel. int.) 399 (4.1, $M^{+\cdot}$), 398 (4.2), 384 (4.3), 236 (40), 221 (6.6), 204 (100), 189 (28), 163 (89), 161 (16), 148 (32), 136 (12), 134 (7.0), 120 (35), and 102 (17).

(*b*) When compounds (3) [11] and (4b) [6] were allowed to react

* Unprimed locants refer to the thiadiazoline ring, while primed locants refer to the 5-aryl group.

† Unprimed locants refer to the thiadiazoline ring, primed locants to the 2-aryl group, and doubly primed locants to the 5-aryl group.

‡ Actually two very close signals.

§ Unprimed locants refer to the thiadiazoloquinazoline ring, and primed locants to the dimethoxyphenyl group.

in refluxing ethanol in the absence of hydrogen chloride, crude (9b) (84%), m.p. 195—196 °C, was obtained. This product analysed correctly (C, H, N) but several peaks in its mass spectrum appeared to originate from some contaminant (or from decomposition in the spectrometer prior to fragmentation). The extreme insolubility of compound (9b) made it impossible to check its purity by ^{1}H n.m.r. Recrystallization from butan-1-ol of the crude product furnished, owing to its thermal instability, a less pure product. The crude compound (9b) was therefore converted by refluxing with ethanolic hydrogen chloride into the hydrochloride of compound (12b) from which the free base was liberated as described in (*a*).

4-*Acetyl*-2-(3,4-*dimethoxyphenyl*)-5-(4,5-*dimethoxy*-2-*nitrophenyl*)-Δ^2-1,3,4-*thiadiazoline* (10b).—A mixture of compound (8b) (0.2 g, 0.05 mmol), acetic acid (2 cm^3), and acetic anhydride (0.5 cm^3) was refluxed for 1 h. The mixture was allowed to cool, diluted with water, and extracted with dichloromethane. The organic phase was washed with aqueous $NaHCO_3$, dried and evaporated to dryness. The residue was crystallized from methanol to give the title compound (0.21 g, 94%), m.p. 168—169 °C [Found: C, 53.65; H, 5.15; S, 7.15. Calc. for $C_{20}H_{21}N_3O_7S$ (*M*, 447.5): C, 53.67; H, 4.73; S, 7.17%]; $\nu_{max.}$ (KBr) 1 670 cm^{-1}; $\lambda_{max.}$ (EtOH) 226 (4.48), 267sh (4.24), and 316 (4.34); δ($CDCl_3$) * δ 2.52 (Ac), 3.88 (s, 2 MeO), 3.90 (s, 2 MeO), 6.76 (s, 5-H), 6.83 (d, *J* 8.5 Hz, 5′-H), 7.18 (dd, *J* 8, 5, and 2.0 Hz, 6′-H), 7.27 (d, *J* 2.0 Hz, 2′-H), and 7.60 (s) and 7.70 (s) (6″- and 3″-H); δ(^{13}C) ($CDCl_3$) 22.3 (CH_3CO), 56.1 (2 MeO), 56.4 (MeO), 56.5 (MeO), 67.0 (d, C-5), 107.6 (d), 108.7 (d), 109.4 (d), 110.9 (d), 121.4 (d), 122.7 (s), 131.3 (s), 137.9 (s), 148.6 (s), 149.1 (s), 151.9 (s), and 152.6 (s) (ArC), 154.4 (s, C-2), and 169.3 p.p.m. (CH_3CO); *m*/*z* (160 °C) (% rel. int.) 447 (6.0, $M^{+\cdot}$), 404 (5.4), 388 (74), 371 (6.8), 358 (36), 344 (9.6), 331 (5.9), 328 (5.8), 284 (5.3), 223 (8.3), 190 (11), 181 (100), 165 (10), 164 (16), and 163 (12).

4-*Acetyl*-5-(2-*amino*-4,5-*dimethoxyphenyl*)-2-(3,4-*dimethoxyphenyl*)-Δ^2-1,3,4-*thiadiazoline* (11b).—$Na_2S_2O_4$ (1.3 g, 7.5 mmol) was added with continuous stirring at room temperature in small portions to a suspension of compound (10b) (0.45 g, 1 mmol) in a mixture of ethanol (7 cm^3) and water (10 cm^3). After further stirring for 15 min the mixture was made alkaline by adding Na_2CO_3 and diluted with water to give crude (11b) (0.25 g, 61%) which was filtered off the following morning. This product was purified *via* its perchlorate: 70% aqueous $HClO_4$ (0.1 cm^3) was added to the solution of crude (11b) (0.1 g) in CH_2Cl_2 (1 cm^3), the mixture was stirred for a short time at room temperature, and the resulting perchlorate (0.1 g), m.p. 170—171 °C, was precipitated by adding diethyl ether to the solution. The suspension of the perchlorate in CH_2Cl_2 was then stirred with aqueous $NaHCO_3$ until the crystals completely disappeared. The base was isolated from the organic phase by conventional methods in the form of an oil which turned crystalline (m.p. 167—169 °C and, after resolidification, 180—181 °C) on addition of a small amount of methanol [Found: N, 10.15; S, 7.7. Calc. for $C_{20}H_{23}N_3O_5S$ (*M*, 417.5): N, 10.06; S, 7.68%]; $\nu_{max.}$ (KBr) 3 390, 3 320, 1 640, 1 550, and 1 515 cm^{-1}; *m*/*z* (160 °C) (% rel. int.) 417 (33, $M^{+\cdot}$), 374 (43), 358 (12), 254 (7.3), 239 (3.8), 236 (6.7), 223 (13), 221 (16), 212 (39), 204 (19), 197 (17), 181 (100), 179 (38), and 163 (27).

4-*Acetyl*-5-(2-*acetylamino*-4,5-*dimethoxyphenyl*)-2-(3,4-*dimethoxyphenyl*)-Δ^2-1,3,4-*thiadiazoline* (13b) *and* 8,9-*Dimethoxy*-2-(3,4-*dimethoxyphenyl*)-5-*methyl*-10*b*H-[1,3,4]*thiadiazolo*[3,2-c]*quinazoline* (12b).—A mixture of acetic anhydride (3 cm^3) and 70% aqueous $HClO_4$ (1 cm^3) was added with ice-cooling and continuous stirring to the solution of compound (11b) (1.0 g, 2.4 mmol) in CH_2Cl_2 (20 cm^3). After being left overnight the solvent was distilled off. Addition of water furnished a solid (0.9 g) which was dried and triturated with $CHCl_2$ at room temperature. The insoluble residue (fraction A) was filtered off. The filtrate was evaporated to dryness and the residue was triturated with a small amount of ethanol to give compound (13b) (0.55 g, 50%), m.p. 208—210 °C (from a large volume of ethanol) [Found: C, 57.8; H, 5.65; N, 9.3. Calc. for $C_{22}H_{25}N_3O_6S$ (*M*, 459.5): C, 57.50; H, 5.48; N, 9.14%]; $\nu_{max.}$ (KBr) 1 690 and 1 650 cm^{-1}; δ($CDCl_3$) † δ 2.23 (s) and 2.40 (2 Ac), 3.71 (s, MeO), 3.84 (s, MeO), 3.91 (s, 2 MeO), 6.87 (d, *J* 9 Hz, 5′-H), 6.87 (s, 5-H), 7.17—7.35 (m, 4 H, other ArH), and 9.55 (bs, NH).

A suspension of fraction A [the perchlorate of compound (12b) (0.03 g, 25%)] in methanol was treated with aqueous $NaHCO_3$. The methanol was distilled off, and the residue was extracted with CH_2Cl_2 to give, after conventional work-up, a product which proved to be identical (i.r.) with an authentic sample (see above) of compound (12b).

Rearrangement of Compound (9b) *into Compound* (11b).—A mixture of acetic anhydride (0.2 cm^3) and 70% aqueous $HClO_4$ (0.2 cm^3) was added with stirring and ice-cooling to the suspension of crude (9b) (0.2 g, 0.48 mmol) in CH_2Cl_2 (6 cm^3). Stirring was continued for a further 30 min, and the solvent was poured off from the oily precipitate which became crystalline when treated with a small amount of methanol. The crystals were taken up in diether ether and filtered off to give a perchlorate (0.16 g), m.p. 265—310 °C. The perchlorate was stirred for 1 h at room temperature with a mixture of methanol (30 cm^3) and 3% aqueous $NaHCO_3$ (6 cm^3). The resulting mixture was evaporated to dryness and the residue was crystallized from methanol to give compound (11b) (0.14 g, 70%), m.p. 167—169 °C, which proved to be identical (mixed m.p., i.r.) with an authentic sample obtained as described above.

^{13}C *N.m.r. Spectrum of the Isoquinolinio*(*thioamidate*) (14) [12] *in* $CDCl_3$.—Compound (14) gave the following ^{13}C n.m.r. spectrum: δ 15.2 and 65.6 (EtO), 125.2 d (C-5), 127.5 (d, C-8), 128.2 (s, C-8a), 129.3 (d, C-7), 130.4 (d, C-6), 135.0 (d, C-4), 135.7 (s, C-4a), 136.6 (d, C-3), 146.5 (d, C-1), and 195.1 (s, thioamidate carbon).

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