Thiadiazoles and Thiadiazolines. Part 4.[1] Acetylation, Hydrolysis, and Cyclocondensations of Δ^2-1,3,4-Thiadiazoline-α-carboxamidines

By **Stephen F. Moss** and **David R. Taylor,*** Chemistry Department, University of Manchester Institute of Science and Technology, Manchester M60 1QD

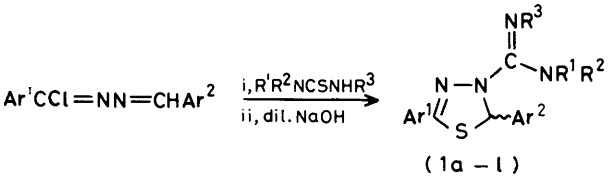
The thiadiazolinecarboxamidine (1a) forms a stable acetate in glacial acetic acid but is diacetylated to give the thiadiazoline (3) using acetic anhydride and mineral acid. Similar treatment of (1c) and (1d) gives, at 60 °C or below, the monoacetyl derivatives (10) and (6) respectively. The acetylthiadiazolinecarboxamidine (6) decomposes at 60—140 °C yielding the 4-acetylthiadiazoline (7), which may also be obtained by acetylation of an oil produced by basic hydrolysis of (1a). Neutral hydrolysis in aqueous methanol converts (1a) and (1b) into the carbamoylthiadiazoline (11), the trimethylthiadiazolinecarboxamidine (1e) into the *N*-methylcarbamoylthiadiazoline (12), and the diacetylthiadiazolinecarboxamidine (3) into the *N*-acetylcarbamoylthiadiazoline (5). The thiadiazolinecarboxamidine (1a) reacts with 1,3-dicarbonyl compounds to give 4-pyrimidin-2-ylthiadiazolines (15)—(17), and decomposes in refluxing mesitylene to give, amongst other products, *trans*-stilbene and 2,5-diphenyl-1,3,4-thiadiazole.

FOLLOWING the discovery of two easily accessible routes (Scheme 1) to Δ^2-1,3,4-thiadiazolin-4-carboxamidines (1a—l) [2-3] and 4-unsubstituted Δ^2-1,3,4-thiadiazolines (2a—k) [4] it is our intention to explore the synthetic possibilities of these two classes of compounds. Since almost all of the previously published work in this area deals with 4-aryl-Δ^2-1,3,4-thiadiazolines (3),[5-7] we have given priority to useful transformations of the 4-function, and here report the results of an investigation of the chemistry of the 4-amidino-residue in (1a—e), the structure of which is initially pre-determined by the choice of thiourea used in their synthesis. Several of the characteristic properties of amidines and guanidines are found in these compounds, including hydrolysis, acetylation, and condensation with 1,3-dicarbonyl compounds. The Δ^2-1,3,4-thiadiazoline ring system thus appears to be relatively stable, at least under non-oxidising conditions.

Acetylation of Δ^2-1,3,4-*Thiadiazoline-4-carboxamidines*.—The basic strength of the 4-amidino-moiety is illustrated by the conversion of (1a) into a stable acetate salt $C_{15}H_{14}N_4S$·AcOH (84%) on treatment with acetic anhydride in glacial acetic acid. This salt is comparable with the stable hydrochlorides and hydrobromides which are easily prepared from any of these thiadiazolines.[2,8]

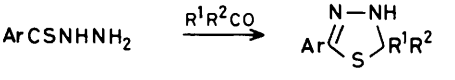
Acetylation of (1a) was achieved by treatment with acetic anhydride containing concentrated sulphuric acid, yielding a diacetyl derivative for which two isomeric structures (3) and (4) were considered. The presence of a strongly deshielded exchangeable proton was indicated by ^{1}H n.m.r. (δ 9.55), assigned to NHAc, so that although the two acetyl groups display a single ^{1}H resonance at 100 MHz, the former isomer (3) is preferred. The equivalence of the two acetyl groups may be satisfactorily explained by rapid tautomerism of the NH proton, which was not investigated but would be comparable to that shown previously to occur in N^1,N^2-disubstituted amidines of this type.[2,9]

The diacetylamidine (3) proved to be relatively unstable, and a 6 h reflux in aqueous ethanol was adequate to achieve its complete hydrolysis. The product isolated from the complex mixture was identified spectroscopically as the 4-(*N*-acetyl-carbamoyl)thiadiazoline (5) (34%) (NHAc δ_H 8.90), the structure of which also tends to confirm the deintification of (3) (Scheme 2).



(1a – l)

a; $Ar^1 = Ar^2 = Ph$, $R^1 = R^2 = R^3 = H$
b; $Ar^1 = Ar^2 = Ph$, $R^1 = Me$, $R^2 = R^3 = H$
c; $Ar^1 = Ar^2 = Ph$, $R^1 = R^3 = Me$, $R^2 = H$
d; $Ar^1 = Ar^2 = Ph$, $R^1R^3 = CH_2CH_2$, $R^2 = H$
e; $Ar^1 = Ar^2 = Ph$, $R^1 = R^2 = R^3 = Me$
f; $Ar^1 = Ar^2 = Ph$, R^1 = allyl, $R^2 = R^3 = H$
g; $Ar^1 = Ar^2 = Ph$, $R^1 = R^2 = H$, $R^3 = Ph$
h; $Ar^1 = 4ClC_6H_4$, $Ar^2 = Ph$, $R^1 = R^2 = R^3 = H$
i; $Ar^1 = 4MeOC_6H_4$, $Ar^2 = Ph$, $R^1 = R^2 = R^3 = H$
j; $Ar^1 = 4ClC_6H_4$, $Ar^2 = Ph$, $R^1R^3 = CH_2CH_2$, $R^2 = H$
k; $Ar^1 = Ar^2 = Ph$, $R^1 = R^3 = H$, $R^2 = NHAc$
l; $Ar^1 = Ar^2 = Ph$, $R^1 = R^3 = H$, $R^2 = NHBz$



(2a – k)

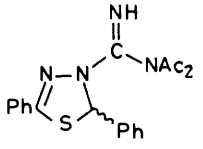
a; Ar = Ph, $R^1 = H$, $R^2 = Ph$
b; Ar = Ph, $R^1 = H$, $R^2 = 4ClC_6H_4$
c; Ar = Ph, $R^1 = H$, $R^2 = 4MeOC_6H_4$
d; Ar = Ph, $R^1 = H$, $R^2 = 4MeC_6H_4$
e; Ar = Ph, $R^1 = R^2 = Me$
f; Ar = Ph, R^1, $R^2 = -[CH_2]_5-$
g; $Ar = 4MeOC_6H_4$, $R^1 = H$, $R^2 = Ph$
h; $Ar = 4MeOC_6H_4$, $R^1 = H$, $R^2 = 4MeOC_6H_4$
j; $Ar = 4MeOC_6H_4$, $R^1 = R^2 = Me$
k; $Ar = 4MeOC_6H_4$, R^1, $R^2 = -[CH_2]_5-$

SCHEME 1

N^1,N^2-Diacetylation of an amidine or guanidine is an expected type of behaviour, since monoacetylation of such a species (best achieved using phenyl acetate [10]) occurs preferentially at the imine =NH. The synthesis and structure of acetylguanidines and acetylamidines have recently been re-investigated by Rapoport and co-

workers,[11] but their findings were not published until after our investigation was complete.

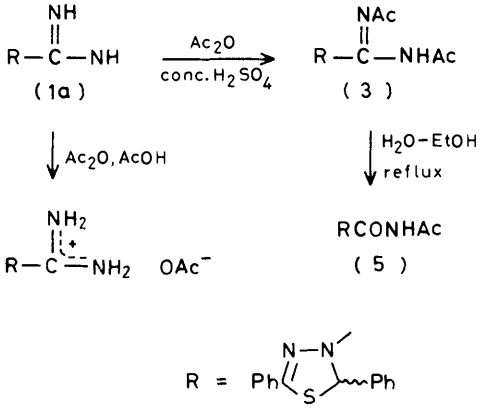
Acetylation of the imidazolinylthiadiazoline (1d) was accomplished under acidic conditions with gentle heating (50—60 °C). The monoacetyl derivative (6) cannot react further in this case and was isolated in good yield. Its ^{1}H n.m.r. spectrum shows no sign of the NH proton tautomerism which, in (1d) at room temperature and above, renders the two methylene groups equivalent,



(4)

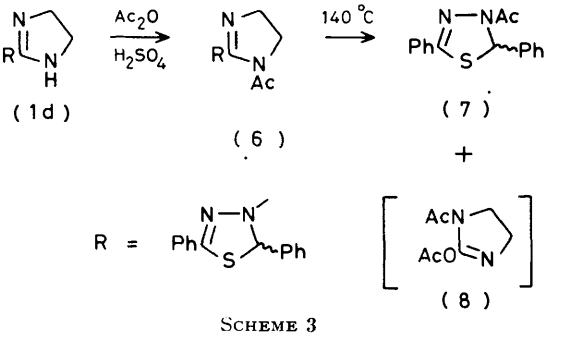
and in (6) a complex multiplet results (δ 4.3—3.0) which resembles that produced by (1d) at low temperature.[2]

When acetylation of (1d) was first attempted the temperature was allowed to rise to reflux (*ca.* 140 °C). The reaction was monitored by t.l.c. and it was noted that the initial product (R_F 0.5), later to be identified as (6), rapidly became superceded by a new product (R_F 0.7). The latter product was isolated and identified spectroscopically as the 4-acetylthiadiazoline (7) (71%) (Scheme 3). The fate of the imidazoline portion of the starting material was not established; in the presence of an



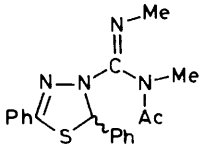
SCHEME 2

excess of acetic anhydride and the acetic acid formed as co-product in the acetylation of (1d), it is most probably converted into an amidinyl ester such as (8), though this was not detected. The mechanism of the facile decomposition of (6) most probably resembles that of the dealkylation–acetylation of tertiary amines by acetic anhydride,[12,13] and commences by quaternisation of the nitrogen at the 4-position of the 1,3,4-thiadiazoline ring. Intramolecular *N*,*N*′-acyl migrations are known to occur in acylguanidines,[11] but proceed *via* cyclic intermediates which seem unlikely to arise in this instance; 1,3-*O*,*N*-acyl migrations are also well known [14,15] but do not usually lead to fragmentation such as is observed here.

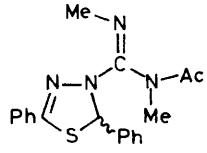


SCHEME 3

Acetylation of the comparably substituted N^1,N^2-dimethylthiadiazolinecarboxamidine (1c) was next investigated and found to proceed normally at room temperature. The *N*-acetylthiadiazolinecarboxamidine obtained (42% yield) displayed interesting spectroscopic properties, the ^{1}H and ^{13}C n.m.r. spectra both suggesting that although tautomerism was no longer possible there were two isomers present. Thus, there were two 5-methine groups (δ_H 7.0 and 6.9; δ_C 70.9 and 70.5 p.p.m., both doublets in the off-resonance spectrum) and two NAcMe groups (δ_H 2.94 and 2.91 for NMe, and 1.85 and 1.68 for Ac; δ_C 32.6 and 21.1 p.p.m., both quartets in the off-resonance spectrum, for NMe). Only a single iminomethyl group (δ_H 2.85, δ_C 35.5 p.p.m.) appeared, however, which rules out an explanation based upon geometrical isomerism in this unit, *i.e.* leading to isomers (9) and (10).



(9)



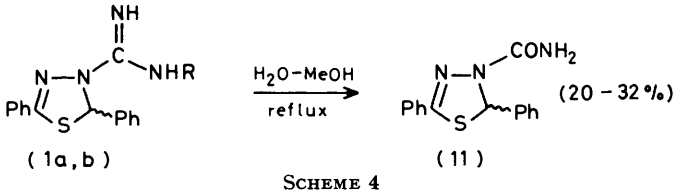
(10)

Believing that the n.m.r. data were due to restricted rotation in the NAcMe group, the proton spectra were re-run at 110 °C in tetrachloroethylene, and the duplicated signals were found to have coalesced. We accordingly prefer structure (10), though (9) cannot be ruled out. Restricted rotation about the amide C–N bond in *N*-methylacetamides is by no means unusual,[16,17] but its effect upon the 5-methine CH nuclei shows that the rotational restriction must also lie in close proximity to the thiadiazoline ring.

Hydrolysis of Δ^2-1,3,4-*Thiadiazoline*-4-*carboxamidines*.—These thiadiazolines (1a—l) are sufficiently stable in dilute aqueous alkali to permit their isolation by basification of their hydrochlorides,[3,4] but they are decomposed by hot aqueous alkali. The outcome of their hydrolysis was therefore investigated at first in neutral solution.

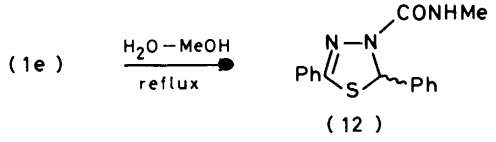
When either of the amidinothiadiazolines (1a) or (1b) was heated under reflux in aqueous methanol, slow decomposition occurred and after 100—140 h a common

product could be isolated (20—32%). It was identified spectroscopically as the 4-carbamoylthiadiazoline (11), the low yield being partly at least attributable to low conversion (Scheme 4). The amide (11) is a crystalline solid, m.p. 194—196 °C, and proved to be a critically useful product, since it was the first derivative of (1a) which could be analysed easily by *X*-ray crystallography. Earlier attempts with the hydrogen halide salts had failed owing to twinning in the crystal lattice. The crystallographic data for (11), already published,[9] provide a firm basis for the structural identification not only of (11), but also for the whole series of Δ^2-1,3,4-thiadiazolines (1) and (2), because their similarity to the amidothiadiazoline (11) is demonstrated by the characteristic n.m.r. parameters of their 5-CH or 5-CR^1R^2 groups, apparent in the spectra of (11) at δ_H 7.02 and δ_C 69.3 p.p.m. (doublet in the off-resonance spectrum), as well as in their i.r., u.v., and mass spectra.



SCHEME 4

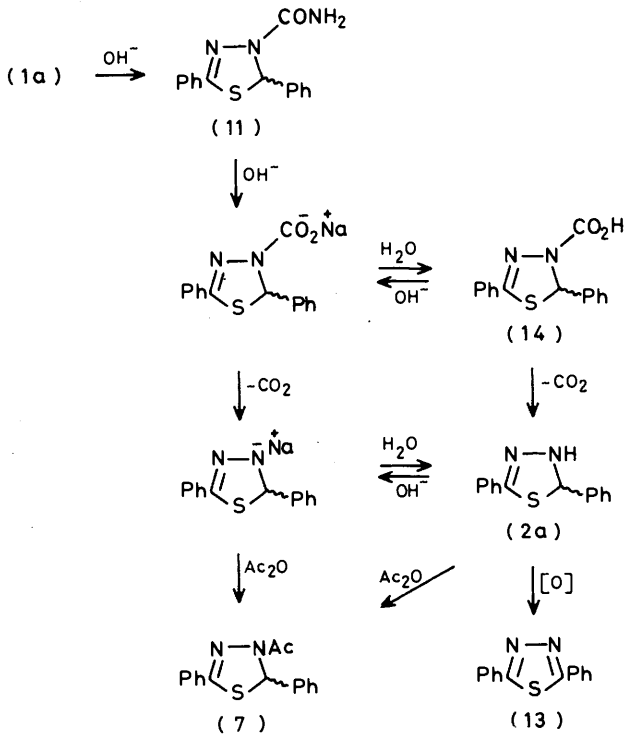
Neutral hydrolysis of the trimethylthiadiazolinecarboxamidine (1e) gave the *N*-methylcarbamoylthiadiazoline (12) (20%). The analogous hydrolysis of the diacetylthiadiazolinecarboxamidine (3) to the acetamide (5) has been described above.



The hydrolysis of (1a) under basic conditions was next investigated. Strong aqueous base (10M-NaOH) at reflux degrades the side-chain completely, but at first only 2,5-diphenyl-1,3,4-thiadiazole (13) could be obtained from the hydrolysis. Reasoning that its formation must involve an intermediate stage such as the carbamic acid (14), its sodium salt, or the 4*H*-thiadiazoline (2a) or its sodium salt (Scheme 5), attempts were made to isolate or trap such an intermediate. All efforts to isolate a pure sample of the intermediate from the coloured oils obtained, before substantial amounts of the thiadiazole (13) were detected, proved unsuccessful. However, immediate acetylation of the purest sample of the intermediate oil with acetic anhydride gave the 4-acetylthiadiazoline (7). In view of our more recent experiments with the 4*H*-thiadiazoline (2a), a comparatively stable solid, we consider that the intermediate present in the oil is the sodium salt of (2a) formed by decarboxylation of the salt of the carbamic acid (14). Nevertheless, our subsequent work[4] has shown that a better route to 4-acetylthiadiazolines is by the acetylation of thiadiazolines (2) prepared as shown in Scheme 1. 4-Acyl-2-amino-Δ^2-1,3,4-thiadiazolines have also been reported recently by Kubota and co-workers.[18]

Dicarbonyl Condensation of Δ^2-1,3,4-*Thiadiazolinecarboxamidines.*—When the structure of (1a) was first established[2] a limited programme of dicarbonyl condensation reactions was undertaken to confirm the presence of the amidine function by this characteristic type of cyclization.[19] The three dicarbonyl reagents selected were acetylacetone, ethyl acetoacetate, and diethyl malonate, and (1a) was indeed found to react with all three. The expected cyclization to pyrimidinylthiadiazolines occurred very readily with acetylacetone and ethyl acetoacetate, the former at reflux in a Dean-Stark water separator, the latter at room temperature. The products, identified as (15) and (16) respectively, were obtained in good yield and their spectra confirmed that the thiadiazoline ring had remained unaffected by the aromatization of the 4-substituent [δ(C-5) 70.6 and 70.0 p.p.m., respectively].

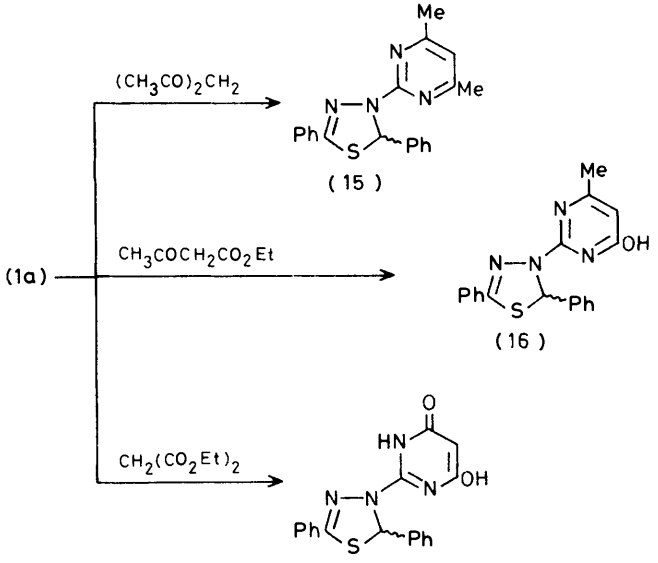
The cyclization of (1a) with diethyl malonate was slower and remained incomplete (37% recovery) after 95 h. Nevertheless, the expected dihydroxypyrimidine



SCHEME 5

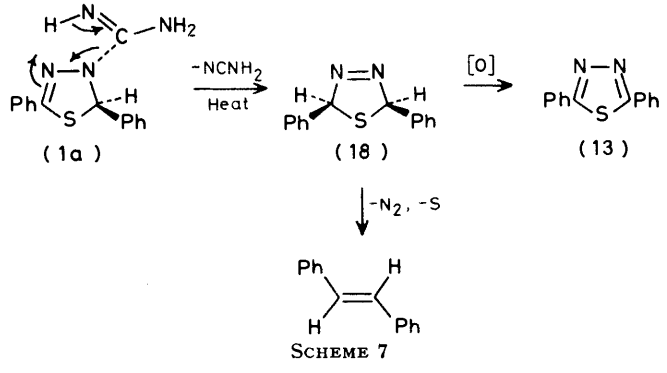
(17) (34%) was isolated [δ(C-5) 69.5 p.p.m.] (Scheme 6).

Thermal Decomposition of Δ²-1,3,4-*Thiadiazolinecarboxamidine* (1a).—An obvious limitation to the usefulness of thiadiazolines of the type discussed here and in



SCHEME 6

previous Parts is their thermal stability. The thiadiazoline (1a) was found to decompose in refluxing mesitylene (b.p. 163 °C); no starting material could be detected after 90 min, and a complex mixture of at least eight products was formed. Two of these were isolated and identified as *trans*-stilbene (10%) and 2,5-diphenyl-1,3,4-thiadiazole (6%). The formation of *trans*-stilbene indicates that a possible intermediate in the decomposition is the Δ³-1,3,4-thiadiazoline (18), a type of intermediate which has been shown to be useful in the synthesis of olefins by thermal extrusion of nitrogen and sulphur.[20,21] A possible mechanism is shown in Scheme 7.



SCHEME 7

EXPERIMENTAL

General spectroscopic and chromatographic techniques have been described previously.[2] N.m.r. spectra were obtained using $CDCl_3$ solutions unless otherwise stated. The Δ²-1,3,4-thiadiazoline-4-carboxamidines (1a—e) were prepared by the reaction of 1-chloro-1,4-diphenyl-2,3-diazabutadiene with thioureas.[2,3]

Reactions of 2,5-*Diphenyl*-Δ²-1,3,4-*thiadiazoline*-4-*carboxamidine* (1a).—(a) *Acetylation.* Attempted acetylation of (1a) (2.0 g, 7.1 mmol) with acetic anhydride in glacial acetic acid gave only the white crystalline 2,5-*diphenyl*-Δ²-1,3,4-*thiadiazoline*-4-*carboxamidinium acetate* (2.04 g, 6.0 mmol, 84%) (Found: C, 59.3; H, 5.6; N, 16.4%. $C_{17}H_{18}N_4O_3S$ requires C, 59.6; H, 5.3; N, 16.4%), m.p. 185—187 °C. When the thiadiazoline (1a) (1.50 g, 8.9 mmol) was treated with redistilled acetic anhydride (25 cm³) containing two drops of concentrated sulphuric acid (*d* 1.84) for 12 h, N¹,N²-*diacetyl*-2,5-*diphenyl*-Δ²-1,3,4-*thiadiazoline*-4-*carboxamidine* (3) (2.72 g, 7.4 mmol, 84%) (Found: C, 61.8; H, 5.0; N, 15.3; S, 8.8%; M^+, 366. $C_{19}H_{18}N_4O_2S$ requires C, 62.3; H, 4.9; N, 15.3; S, 8.7%; *M*, 366), m.p. 190—192 °C (with decomp.) was obtained; δ_H (100 MHz) 9.55 (br D_2O-labile, NHAc), 7.7—7.1 (10 H, Ph × 2), 6.94 (s, CHPh), and 2.02 (s, Me × 2); $\lambda_{max.}$ (ε) (EtOH) 323 (12 000) and 253 nm (14 300); $\lambda_{min.}$ 290 (9 200) and 239.5 nm (12 600); λ_{infl} 334 (11 400), 295 (9 400), and 283 nm (9 450).

Recrystallization of this compound must be performed carefully in dry ethanol, since when the diacetylthiazolinecarboxamidine (3) (4.29 g, 11.7 mmol) was heated under reflux in 95% ethanol (100 cm³) for 6 h, no starting material was detectable by t.l.c. ($CHCl_3$) and four products (R_F 0.92, 0.84, 0.70 and 0.32) were apparent. The major component (R_F 0.92) was isolated by column chromatography (toluene) and identified as 4-(N-*acetylcarbamoyl*)-2,5-*diphenyl*-Δ²-1,3,4-*thiadiazoline* (5) (1.30 g, 4.0 mmol, 34%) (Found: C, 62.8; H, 4.6; N, 12.8; S, 9.8%; M^+, 325. $C_{17}H_{15}N_3O_2S$ requires C, 62.8; H, 4.7; N, 12.9; S, 9.9%; *M*, 325), m.p. 169—170 °C; δ_H (60 MHz) 8.90 (br D_2O-labile, NHAc), 8.05—7.25 (10 H, m, Ph × 2), 7.00 (s, CHPh), and 2.47 (s, Me); $\lambda_{max.}$ (ε) (EtOH) 318 (8 950), 253 (17 400), and 223 nm (17 800); $\lambda_{min.}$ 289 (5 550) and 240 nm (14 950); λ_{infl} 296 nm (5 950).

(b) *Neutral hydrolysis.* A solution of compound (1a) (3.0 g, 10.6 mmol) in a methanol (80 cm³)–water (50 cm³) mixture was heated under reflux for 100 h, when t.l.c. ($CHCl_3$) indicated starting material (R_F 0) and two other components (R_F 0.3 and 0.6). The R_F 0.3 component was crystallized by cooling and identified as 4-carbamoyl-2,5-diphenyl-Δ²-1,3,4-thiadiazoline (11) (600 mg, 2.1 mmol, 20%) by mixed m.p. (194—196 °C) with an authentic sample (below).

(c) *Base hydrolysis.* A solution of compound (1a) (2.78 g, 9.9 mmol) in a mixture of ethanol (50 cm³) and aqueous sodium hydroxide (10M; 5 cm³) was heated under reflux for 20 h when t.l.c. ($CHCl_3$) indicated a new major component (R_F 0.64). The solution was evaporated to 20 cm³, diluted with water (100 cm³), and extracted with chloroform (4 × 50 cm³). The organic extract was dried and evaporated under reduced pressure, leaving an oil (1.46 g) which was further purified by rapid (flash) chromatography ($CHCl_3$) to give after evaporation an orange oil shown by t.l.c. ($CHCl_3$) to contain two components (R_F 0.64 and 0.76). Crystallization could not be induced to occur, even in ethanolic hydrogen chloride; the oil decomposed in solution, and after 48 h a large amount of 2,5-diphenyl-1,3,4-thiadiazole (13) was detected by t.l.c. A freshly prepared sample of the oil (800 mg) was dissolved in acetic anhydride

(20 cm³) and a drop of concentrated sulphuric acid was added. After 24 h at 20—25 °C, t.l.c. ($CHCl_3$–MeOH, 20 : 1) showed that 2,5-diphenylthiadiazole (13) and a further major component were present. The mixture was worked up by neutralisation with 1M-NaOH, extraction with chloroform (2 × 30 cm³), and evaporation of the dried chloroform extract; elution of the residual oil by flash chromatography ($CHCl_3$) and addition of isopropyl alcohol (2 cm³) to the evaporated eluant (485 mg) gave the crystalline thiadiazole (13) (100 mg) which was identified by mixed m.p. [139—140 °C (lit.,[22] m.p. 141—142 °C)] with an authentic sample. The filtrate was evaporated, dissolved in diethyl ether (2 cm³), and cooled to −25 °C for 15 h to yield a solid (R_F 0.7, $CHCl_3$) identified as 4-acetyl-2,5-diphenyl Δ^2 1,3,4-thiadiazoline (7) (360 mg, 1.3 mmol) by mixed m.p. (116—117 °C) with an authentic sample (below).

(d) *Thermal decomposition.* A suspension of compound (1a) (8.0 g, 28.4 mmol) in mesitylene (50 cm³) was heated under reflux (163 °C) for 1.5 h, when t.l.c. ($CHCl_3$) indicated complete decomposition with the formation of at least eight new components. Two were isolated by evaporation and column chromatography ($CHCl_3$) of the residue and identified as *trans*-stilbene (510 mg, 2.8 mmol, 10%) (R_F 0.92) by mixed m.p. [125—126 °C (lit.,[23] m.p. 124 °C)] with an authentic sample (Aldrich) and 2,5-diphenyl-1,3,4-thiadiazole (13) (410 mg, 1.7 mmol, 6%) also by mixed m.p. [138—139 °C (lit.,[22] m.p. 141—142 °C)], R_F 0.6.

(e) *With acetylacetone.* A solution of compound (1a) (3.49 g, 12.4 mmol) and acetylacetone (3.4 g, 34 mmol) in toluene (80 cm³) was heated under reflux in a Dean-Stark water separator for 2 h. Evaporation of the mixture gave an oil which was stirred with diethyl ether (15 cm³) to give a solid identified spectroscopically as 4-(4,6-*dimethylpyrimidin*-2-*yl*)-2,5-*diphenyl*-Δ^2-1,3,4-*thiadiazoline* (15) (2.83 g, 8.2 mmol, 66% based on thiadiazoline) (Found: C, 69.6; H, 5.5; N, 16.2; S, 8.9%; M^+, 246. $C_{20}H_{18}N_4S$ requires C, 69.3; H, 5.2; N, 16.2; S, 9.3%; *M*, 346), m.p. 142—144 °C. δ_H (60 MHz) 8.0—7.15 (11 H m, Ph × 2 and C*H*Ph), 6.44 (s, =CH), and 2.31 (s, Me × 2); δ_C (20 MHz) 167.6 (MeC=N), 158.4 (N=*C*–N), 147.5 (C-2), 141.9—125.3 (Ar), 111.9 (CH=), 70.6 (C-5), and 23.5 p.p.m. (Me); $\lambda_{max.}$ (ε) (EtOH) 349 (14 050), 303 (8 921), and 244 nm (19 900); $\lambda_{min.}$ 314 (8 550), 300 (8 900), and 216 nm (13 300); λ_{infl} 360 (12 550), 294 (9 100), 277 (10 400), and 237 nm (19 350).

(f) *With ethyl acetoacetate.* The thiadiazoline (1a) (3.0 g, 10.6 mmol) and ethyl acetoacetate (1.38 g, 10.6 mmol) were stirred for 24 h at ambient temperature in a 1 : 1 ethanol–methanol mixture (50 cm³). Diethyl ether (25 cm³) was added, and the resulting precipitate was collected and identified as 4-(4-*hydroxy*-6-*methylpyrimidin*-2-*yl*)-2,5-*diphenyl*-Δ^2-1,3,4-*thiadiazoline* (16) (2.60 g, 7.5 mmol, 70%) (Found: C, 65.4; H, 4.8; N, 16.2; S, 9.1%; M^+, 348. $C_{19}H_{16}N_4OS$ requires C, 65.5; H, 4.6; N, 16.1; S, 9.2%; *M*, 348), m.p. (from EtOH) 264—265 °C (with decomp.); δ_H (60 MHz) 7.9—7.12 (12 H, m, 11 H after D_2O exchange, Ph × 2, OH, and C*H*Ph), 5.76 (s, =CH), and 2.08 (s, Me); δ_C (20 MHz) 166.2 (MeC=N), 162.8 (N=COH), 151.7 (NC=N), 149.2 (C-2), 140.3—125.6 (Ar), 104.0 (CH=), 70.0 (C-5), and 23.8 p.p.m. (Me); $\lambda_{max.}$ (ε) (EtOH) 347 (17 200), 235 (21 232), and 239 nm (21 232); $\lambda_{min.}$ 305 (6 250), 246 (20 579), and 219 nm (18 400); λ_{infl} 365 (10 900) and 295 nm (7 600).

(g) *With diethyl malonate.* Incomplete reaction occurred when the thiadiazoline (1a) (4.11 g, 14.6 mmol) and diethyl malonate (2.40 g, 15 mmol) were stirred in methanol (10 cm³) for 95 h at 20—25 °C. Evaporation under reduced pressure gave an oil which was dissolved in chloroform (60 cm³) and freed from starting material by extraction into 1M-aqueous NaOH (2 × 50 cm³). The thiadiazoline (1a) (37%) was recovered from the chloroform layer as its hydrochloride, m.p. 175—179 °C (lit.,[2] m.p. 175—179 °C) by recrystallization from ethanol 0.5M in HCl. The aqueous layer was acidified to pH 5 and extracted with chloroform (2 × 25 cm³) yielding an organic layer which was dried and evaporated under reduced pressure. The solid residue was purified by flash chromatography (35 mm o.d. column, 50 : 9 $CHCl_3$–MeOH) and identified as 4-(4,6-*dihydroxypyrimidin*-2-*yl*)-2,5-*diphenyl*-Δ^2-1,3,4-*thiadiazoline* (17) (1.08 g, 3.1 mmol, 34% based on thiadiazoline) (Found: C, 60.8; H, 3.9; N, 15.9; S, 9.0%; M^+ 350. $C_{18}H_{14}N_4O_2S$ requires C, 61.7; H, 4.0; N, 16.0; S, 9.2%; *M*, 350), m.p. 218—220 °C (decomp.); δ_H [60 MHz, $(CD_3)_2SO$] 8.18—7.35 (13 H m, 11 H after D_2O exchange; 2 × Ph, 2 × OH and C*H*Ph) and 4.94 (s, D_2O labile, =C*H*); δ_C [20 MHz, $(CD_3)_2SO$] 167.3 (2 × *C*OH), 150.9 (N=*C*–N), 150.2 (C-2), 140.8—125.4 (Ar), 82.0 (=*C*H), and 69.5 p.p.m. (C-5).

Hydrolysis of N¹-*Methyl*-2,5-*diphenyl*-Δ^2-1,3,4-*thiadiazoline*-4-*carboxamidine* (1b).—A solution of (1b) (2.75 g, 9.3 mmol) in a mixture of methanol (80 cm³) and water (50 cm³) was heated under reflux for 140 h to give, after cooling and recrystallization of the precipitate, 4-*carbamoyl*-2,5-*diphenyl*-Δ^2-1,3,4-*thiadiazoline* (11) (850 mg, 3.0 mmol, 32%) (Found: C, 63.8; H, 4.5; N, 15.1; S, 11.3%; M^+, 283. $C_{15}H_{13}N_3OS$ requires C, 63.6; H, 4.6; N, 14.8; S, 11.3%; *M*, 283), m.p. 194—196 °C (from EtOH); δ_H (60 MHz) 7.82—7.20 (10 H, m, Ph × 2), 7.02 (s, C*H*Ph), and 5.18 (br, D_2O-labile, $CONH_2$); δ_C (15 MHz) 154.8 (C=O), 148.9 (C=N), 141.2—125.5 (Ar), and 69.3 p.p.m. (C-5, d in off-res.); $\lambda_{max.}$ (ε) (EtOH) 321 (7 750), 251 (15 650), and 219 nm (16 222); $\lambda_{min.}$ 290 (4 650) and 240 nm (13 700); λ_{infl} 295 (4 750) and 235 nm (14 050).

Hydrolysis of N¹,N¹,N²-*Trimethyl*-2,5-*diphenyl*-Δ^2-1,3,4-*thiadiazoline*-4-*carboxamidine* (1e).—A solution of compound (1e) (4.80 g, 14.8 mmol) in a mixture of methanol (120 cm³) and water (75 cm³) was heated at reflux for 4 h, when t.l.c. ($CHCl_3$–CCl_4, 1 : 3) indicated the absence of starting material and three new components (R_F 0.3, 0.55, and 0.66). The solution was evaporated under reduced pressure and the oily residue subjected to flash chromatography (55 mm o.d. column, eluant as above). Fractions containing the R_F 0.30 component were combined and evaporated to give a solid which was recrystallized from ethanol and identified as 4-(N-*methylcarbamoyl*)-2,5-*diphenyl*-Δ^2-1,3,4-*thiadiazoline* (12) (900 mg, 3 mmol, 20%) (Found: C, 64.4; H, 4.9; N, 14.0; S, 10.8%; M^+, 297. $C_{16}H_{15}N_3OS$ requires C, 64.6; H, 5.1; N, 14.1; S, 10.8%; *M*, 297), m.p. 143—145 °C; δ_H (100 MHz) 7.80—7.05 (10 H, m, 2 × Ph), 6.95 (s, C*H*Ph), 5.95 (br D_2O-labile, NH), and 2.80 (d, s after D_2O exchange, $NHCH_3$); $\lambda_{max.}$ (ε) (EtOH) 325 (7 750), 251 (14 050), and 222 nm (16 600); $\lambda_{min.}$ 291 (4 000) and 243 nm (13 650); λ_{infl} 296 (4 200) and 235 nm (14 700).

Acetylation of 4-(3,5-*Dihydroimidazolin*-2-*yl*)-2,5-*diphenyl*-Δ^2-1,3,4-*thiadiazoline* (1d).—(a) *At* 50—60 °C. A solution of (1d) (3.00 g, 9.7 mmol) and two drops of concentrated sulphuric acid in acetic anhydride (25 cm³) was stirred for 45 min at 50—60 °C, cooled to 20 °C, and made alkaline to pH 11 with 2M-NaOH. The mixture was stirred for 20 min and then extracted with carbon tetrachloride (2 × 50 cm³). The organic layer was dried and evaporated under reduced pressure to give an oil which was stirred with diethyl ether

(15 cm³). A precipitate was collected, recrystallized from ethanol, and identified as 4-(N-*acetylimidazolin-2-yl*)-2,5-*diphenyl*-Δ^2-1,3,4-*thiadiazoline* (6) (2.50 g, 7.1 mmol, 78%) (Found: C, 65.4; H, 5.3; N, 16.0; S, 9.2%; M^+, 350. $C_{19}H_{18}N_4OS$ requires C, 65.1; H, 5.2; N, 16.0; S, 9.2%; *M*, 350), m.p. 130—131 °C; δ_H (100 MHz) 7.75—7.15 (10 H m, 2 × Ph), 7.05 (s, C*H*Ph), 4.3—3.0 (4 H, m, NCH_2CH_2N), and 2.40 (Me); δ_H (20 MHz) 168.9 (C=O), 152.7 (imidazolinyl C=N), 147.1 (C-3 C=N), 138.0—126.8 (Ar), 73.5 (*C*HPh), 49.6 (imidazolinyl C-4), 48.4 (imid. C-5), and 24.2 (Me); $\lambda_{max.}$ (ε) (EtOH) 321 (8 150) and 223 nm (23 400); $\lambda_{min.}$ 287 (4 850); λ_{infl} 294 (5 154), 278 (5 175), and 245 nm (18 900).

(b) *At* 140 °C. In a similar experiment using (1d) (500 mg, 1.6 mmol) and acetic anhydride (7 cm³) the acetylation mixture was kept at reflux point for 45 min. The product isolated on dilution was identified as 4-*acetyl*-2,5-*diphenyl*-Δ^2-1,3,4-*thiadiazoline* (7) (320 mg, 1.1 mmol, 71%) (Found: C, 67.8; N, 5.0; N, 10.0; S, 11.6%; M^+, 282. $C_{16}H_{14}N_2OS$ requires C, 68.1; H, 5.0; N, 9.9; S, 11.4%; *M*, 282), m.p. (from isopropyl alcohol), 116—117 °C, δ_H (60 MHz) 7.95—7.25 (10 H, m, 2 × Ph), 7.12 (s, C*H*Ph), and 2.45 (Me); δ_C (15 MHz) 169.3 (C=O), 150.5 (C=N), 140.5—125.8 (Ar), 69.3 (d in off-res., *C*HPh), and 22.6 (Me); $\lambda_{max.}$ (ε) (EtOH) 317 (10 150), 253 (20 150), and 223 nm (19 400); $\lambda_{min.}$ 288.5 (6 200) and 239 nm (15 950); λ_{infl} 294 nm (6 700).

Acetylation of N^1,N^2-*Dimethyl*-2,5-*diphenyl*-Δ^2-1,3,4-*thiadiazoline*-4-*carboxamidine* (1c).—A mixture of compound (1c) (2.0 g, 6.5 mmol) and redistilled acetic anhydride (15 cm³) containing two drops of concentrated sulphuric acid was stirred for 23 h at room temperature. The solution was basified to pH 11 with 2M-NaOH, stirred for 20 min, and extracted with carbon tetrachloride (3 × 25 cm³); the extract was dried and evaporated, and the residue triturated with diethyl ether (15 cm³) for 30 min. The solid which formed was recrystallized from isopropyl alcohol and identified as N^2-*acetyl*-N^1,N^2-*dimethyl*-2,5-*diphenyl*-Δ^2-1,3,4-*thiadiazoline*-4-*carboxamidine* (10) (950 mg, 2.7 mmol, 42%) (Found: C, 64.8; H, 5.8; N, 15.9; S, 9.1%; M^+, 382. $C_{19}H_{20}N_4OS$ requires C, 64.8; H, 5.7; N, 15.9; S, 9.1%; *M*, 352), m.p. 106—109 °C; δ_H (100 MHz; C_2Cl_4, 35 °C; values in parentheses 90 MHz, C_2Cl_4, 110 °C) 7.70—7.05 (7.70—7.10) (10 H m, 2 × Ph) 7.00 and 6.92 (7.03) (s, C*H*Ph), 2.94 and 2.91 (2.99) (s, AcN*Me*), 2.85 (2.92) (s, =NMe), and 1.85 and 1.68 (1.88) (s, CO*Me*); δ_C (15 MHz, $CDCl_3$, 35 °C) 169.7 (C=O), 147.7 (imidazolinyl C=N), 146.3 (C-3 C=N), 140.8—126.0 (Ar), 70.9 and 70.5 (both d in off-res., CHPh) 35.5 (=N*Me*), 32.6 and 32.1 (both q in off-res., AcN*Me*), and 21.1 p.p.m. (COMe); $\lambda_{max.}$ (ε) (EtOH) 335 (11 100) and 241 nm (18 200); $\lambda_{min.}$ 299 (6 350) and 219 nm (15 500); λ_{infl} 304 (6 450), 294 (6 600), 280 (7 900), and 252 (15 950).

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