Unexpected Formation of Amidino-thiadiazolines by Reaction of a Chlorodiazabutadiene with Thioureas

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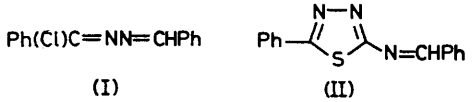
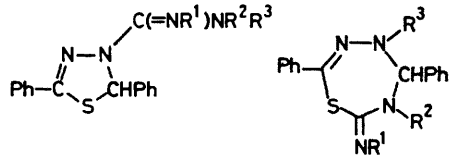
Summary Treatment of Ph(Cl)C : NN : CHPh with thioureas affords hydrochlorides which, on basification, liberate novel amidines in which the amidine function is attached to the 4-position of Δ^2-1,3,4-thiadiazolines.

FOLLOWING an earlier observation[1] that the chlorodiazabutadiene (I) reacts with potassium thiocyanate to give the corresponding thiocyanatodiazabutadiene which, in an unusual thermal rearrangement, is convertible into the Schiff's base (II) of a 2-amino-1,3,4-thiadiazole, we have investigated reactions between (I) and other *S*-nucleophiles. Treatment of (I) with thiourea or its *N*-alkyl derivatives has been found to initiate another unexpected rearrangement by which the sulphur atom becomes separated by two atoms from the rest of the thiourea residue. The products are novel 4-amidino-Δ^2-1,3,4-thiadiazolines (III), obtained initially as hydrochlorides from which the free bases are readily liberated. The unforeseen structure of these products required elucidation by a combination of spectroscopic analysis, degradation, and *X*-ray crystallography.

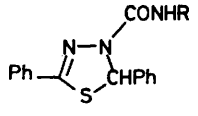


(I) (II)



(III) (IV)

a, $R^1 = R^2 = R^3 = H$
b, $R^1 = R^3 = H, R^2 = Me$
or $R^1 = Me, R^2 = R^3 = H$
(tautomeric equilibrium)
c, $R^1 = R^2 = Me, R^3 = H$
d, $R^1 = R^2 = R^3 = Me$



(V)

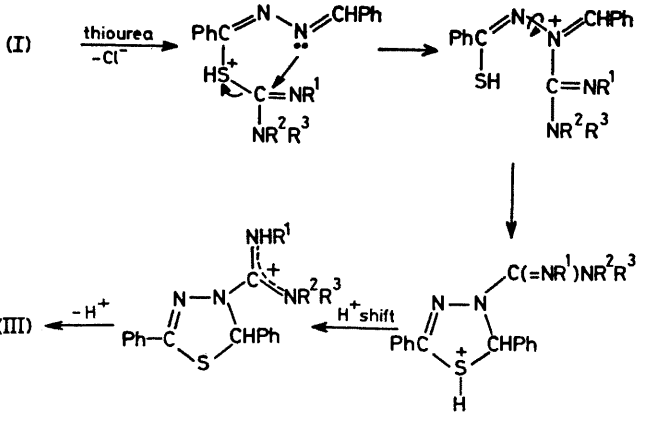
a, R = H
b, R = Me

In a typical reaction, an anhydrous ethanolic solution of (I) was added to a suspension of thiourea in ethanol and, after 1 h at ambient temperature, the solution was concentrated and chilled. The precipitated hydrochloride, m.p. (after removal of tenaciously retained ethanol of crystallization) 172—175 °C, was treated with cold ethanolic aqueous sodium hydroxide until the pH attained 9·5, the crystalline base (IIIa), m.p. 164—165 °C (decomp.) forming immediately in 71% overall yield. The corresponding *N*-methyl derivatives (IIIb—d) were obtained similarly in 70—80% overall yields; all new compounds gave satisfactory analyses.

The absence of aldehyde-like proton resonances in the n.m.r. spectra of (III) ruled out straightforward *S*-alkylation of the thioureas, and ring closure was suggested by the presence of ^{1}H n.m.r. singlets (δ 7·02—7·15) and ^{13}C n.m.r. doublets [in the off-resonance spectra, $\delta(Me_4Si)$ 70·5—72·6 p.p.m.] compatible with SC*H*PhN or NC*H*PhN groupings. Although the spectroscopic properties of (IIIa, b) are also compatible with novel thiatriazepines (IV), the formation of an analogous product from trimethylthiourea makes such a structure seem unreasonable, since it would require a methyl migration. Furthermore, tautomerism in the product (IIIc) obtained from *NN'*-dimethylthiourea readily explains the n.m.r. equivalence [^{1}H: δ 2·93, 6H, s; ^{13}C: δ (Me_4Si) 32·6 p.p.m., quartet in the off-resonance spectrum] of the *N*-methyl groups, whereas such equivalence would be most unlikely in the corresponding thiatriazepine (IVc).

In view of the unusual course of these reactions, further confirmation of the structure of (III) was sought.† Whereas the amidines (III) resist hydrolysis in acid solution, their prolonged hydrolysis in refluxing neutral aqueous methanol gives moderate yields of the corresponding amido-thiadiazolines (V), one of which (Va) was unequivocally identified by *X*-ray crystallographic analysis. The similarities in the n.m.r. spectra of (IIIa) and (Va) [(Va), SC*H*PhN revealed by ^{1}H: δ 7·05, ^{13}C: $\delta(Me_4Si)$ 69·4 p.p.m. (d in off-resonance spectrum)] may reasonably be taken to exclude the occurrence of substantial skeletal re-organization during hydrolysis. The adoption of structure (III) also explains satisfactorily the chemical and spectroscopic properties of derivatives obtained from (III) by standard acetylation and benzoylation procedures.

We advance, without substantiating evidence, the mechanism in the Scheme as a possible explanation for the unexpected formation of the amidinothiadiazolines (III).



SCHEME

Crystal data: (Va), $C_{15}H_{13}N_3OS$, *M* 283·35, orthorhombic, space group $P2_12_12_1$, a = 7·9596(10), b = 27·7626(9), c = 6·4878(9) Å, D_c = 1·31 g cm^{-3} with Z = 4.

1126 Reflections for the ($h k l$) octant were measured in the range 1° ≤ θ ≤ 25° using a Hilger and Watts four-circle diffractometer with graphite-monochromated Mo-K_α radiation (λ = 0·7107 Å). The structure was solved directly with 150 *E*'s ≥ 1·43 and 17 of the 20 non-hydrogen atomic

† *X*-Ray crystallographic investigation of the hydrobromide of (IIIa) was exhaustively attempted but was prevented by awkward twinning.

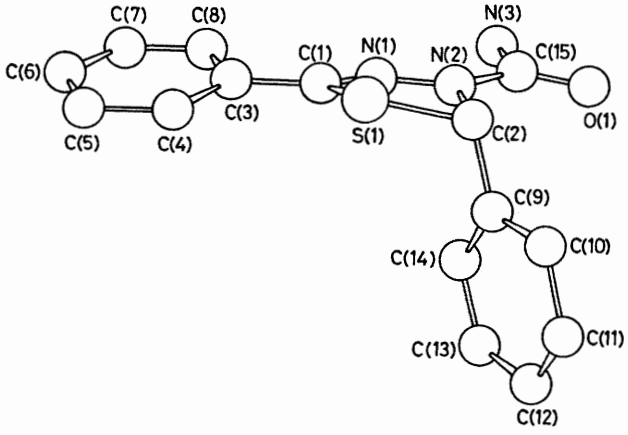


FIGURE. Molecular structure of (Va). The thiadiazoline ring parameters are as follows. Bond lengths: C(1)–N(1), 1·274(13); N(1)–N(2), 1·382(10); N(2)–C(2), 1·460(14); C(2)–S(1), 1·855(10); and S(1)–C(1), 1·760(11) Å. Bond angles: S(1)–C(1)–N(1), 115·88(73); C(1)–N(1)–N(2), 110·59(84); N(1)–N(2)–C(2), 119·30(80); N(2)–C(2)–S(1), 99·63(64); and C(2)–S(1)–C(1), 90·36(52)°.

positions were revealed in the best *E*-map. The remaining positions were located from a difference synthesis and the structure was refined using 792 independent, observed reflections to isotropic convergence followed by weighted, anisotropic least-squares. Phenyl hydrogen atoms were added by calculation but their positions were not refined. The final *R* value was 5·1%. The molecular structure of (Va) is illustrated in the Figure.‡

The thiadiazoline ring is in the form of an approximate plane from which the sulphur atom is appreciably displaced. The least-squares plane containing non-sulphur atoms shows the atomic deviations to be C(1), −0·038; N(1), 0·069; N(2), −0·067; and C(2), 0·035 Å, with sulphur −0·343 Å out of the plane.

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‡ The atomic co-ordinates for this work are available on request from the Director of the Cambridge Crystallographic Data Centre, University Chemical Laboratory, Lensfield Rd., Cambridge CB2 1EW. Any request should be accompanied by the full literature citation for this communication.

[1] W. T. Flowers, D. R. Taylor, A. E. Tipping, and C. N. Wright, *J. Chem. Soc.*, (*C*), 1971, 3097.