

Synthesis and Behaviour of 4-Alkyl-5-acyl-1,3,4-thiadiazolines

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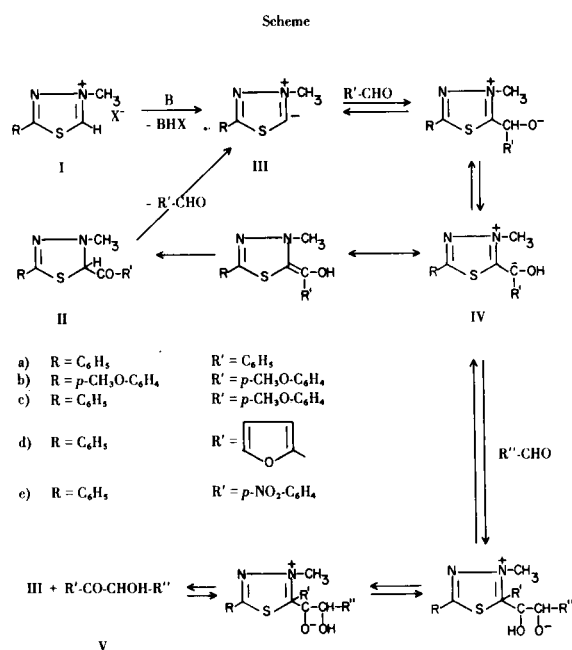
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The synthesis of the title compounds from thiadiazolium salts and aldehydes, and their behaviour towards some nucleophiles and aldehydes are described.

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In a previous note (1) we described the reaction between aldehydes and catalytic amounts of 1,3,4-thiadiazolium salts (I), leading to acyloins. We wish now to report that aldehydes react with equivalent amounts of I and bases to give the 4-alkyl-5-acyl- Δ 2-1,3,4-thiadiazolines (II) as the main product.



EXPERIMENTAL

General Procedure for the Preparation of 4-Alkyl-5-acyl- Δ 2-1,3,4-thiadiazolines.

A solution of aldehyde (0.01 mole) and triethylamine (0.01 mole) in ethanol (10 ml.) was added under nitrogen, at room temperature, to a solution of thiadiazolium salt (iodide, methanesulphate) (2) (0.01 mole) in ethanol (10 ml.). After 2 hours ethyl ether was added. The precipitated triethylammonium salt was filtered off and the solution concentrated *in vacuo* to 15-20 ml. On cooling the acylthiadiazoline precipitated and could be crystallized from ethanol. The reaction mixture contained variable amounts of unreacted aldehyde, benzonitrile (isonitrile in case b) and methyl isothiocyanate. No acyloin could ever be detected.

2-Phenyl-4-methyl-5-benzoyl- Δ 2-1,3,4-thiadiazoline (IIa).

From 2-phenyl-4-methyl-1,3,4-thiadiazolium iodide and benz-

aldehyde, IIa, m.p. 107-108°, was obtained in 64% yield; pmr (deuteriochloroform): τ 1.9-2 (multiplet, 10 H), 3.71 (singlet, 1H), 6.85 (singlet, 3 H); ir: ν 1680 cm⁻¹ (C=O).

Anal. Calcd. for C₁₆H₁₄N₂O₃S: C, 68.06; H, 5.00; N, 9.92. Found: C, 68.31; H, 4.95; N, 9.85.

2-*p*-Methoxyphenyl-4-methyl-5-anisoyl- Δ 2-1,3,4-thiadiazoline (IIb).

From 2-*p*-methoxyphenyl-4-methyl-1,3,4-thiadiazolium methanesulphate and anisaldehyde, IIb, m.p. 139°, was obtained in 14.4% yield; ir: ν 1670 cm⁻¹ (C=O).

Anal. Calcd. for C₁₈H₁₈N₂O₃S: C, 63.15; H, 5.30; N, 8.18. Found: C, 62.59; H, 5.25; N, 8.10.

2-Phenyl-4-methyl-5-anisoyl- Δ 2-1,3,4-thiadiazoline (IIc).

From 2-phenyl-4-methyl-1,3,4-thiadiazolium iodide and anisaldehyde, IIc, m.p. 118°, was obtained in 11% yield; ir: ν 1670 (C=O).

Anal. Calcd. for C₁₇H₁₆N₂O₂S: C, 65.35; H, 5.12; N, 8.99. Found: C, 65.13; H, 5.06; N, 8.92.

2-Phenyl-4-methyl-5-furoyl- Δ 2-1,3,4-thiadiazoline (IId).

Compound IId, obtained from 2-phenyl-4-methyl-1,3,4-thiadiazolium iodide and furfural in good yield, is unstable and could not be purified and characterized; ir and pmr spectra of the crude product are consistent with the assigned structure, however the compound was too unstable for element analysis.

2-Phenyl-4-methyl-5-*p*-nitrobenzoyl- Δ 2-1,3,4-thiadiazoline (IIe).

Compound IIe was prepared in chloroform from 2-phenyl-4-methyl-1,3,4-thiadiazolium iodide and *p*-nitrobenzaldehyde, and isolated, in rather poor yield, by column chromatography (silica gel-benzene). m.p. 157° (ethanol); ir: ν 1650 cm⁻¹ (C=O); pmr (deuteriochloroform): τ 1.82 (doublet, J = 15 ppm, 2 H), 2.47 (doublet J = 15 ppm, 2 H), 2.52 (multiplet, 5 H), 5.18 (singlet, 1 H), 6.38 (singlet, 3 H).

Anal. Calcd. for C₁₆H₁₃N₃O₃S: C, 58.71; H, 3.97; N, 12.84. Found: C, 58.28; H, 4.07; N, 12.74.

Conclusions.

Chemical Behaviour of 4-Alkyl-5-acyl- Δ 2-1,3,4-thiadiazolines.

The 4-alkyl-5-acyl-thiadiazolines (II) showed an interesting and somewhat unexpected reactivity. Thus, a solution of 2-phenyl-4-methyl-5-benzoyl- Δ 2-1,3,4-thiadiazoline (IIa) (50 mg.) in ethanol (1 ml.) + chloroform (1 ml.), after four days at room temperature revealed the presence (gas-chromatography) of ethyl benzoate. Analogously, with methanol one obtains methyl benzoate. Compound IIa (282 mg.) and aniline (100 mg.) in chloro-

form (2 ml.), refluxed 10 minutes and left 5 days at room temperature, on treatment with light petroleum gave benzanilide (170 mg). Thermal decomposition (250°, gas-chromatography) of IIa gave benzaldehyde, benzonitrile and methyl isothiocyanate. A solution of IIa in ethyl ether, on treatment with an ethereal solution of hydrobromic acid gave the corresponding hydrobromide, m.p. 122°; ir: ν 1680 cm^{-1} (C=O), 2350 ($\overset{\dagger}{\text{N}}\text{-H}$). This hydrobromide is isomeric with the conjugated acid of the so called "active aldehyde" (3) IV. It is reconverted to IIa in quantitative yield when treated with triethylamine.

According to the Breslow (3) scheme for benzoin condensation, the thiadiazolines II (4) represent the stable compounds to which the intermediate IV can evolve in the absence of the necessary excess of aldehyde. Therefore, we focused our attention on the reaction of II with aldehydes.

From 1.5 g. of benzaldehyde and 44 mg. of IIa in ethanol (1 ml.), after 3 days at room temperature, one could isolate 1.2 g. of benzoin; analogously, 2.5 g. of furfural gave 2.1 g. of furoin, while with anisaldehyde only a small amount of anisoin could be detected (gas-chromatography). When anisaldehyde and IIa were made to react in a 2:1 ratio, anisoin could be detected (gas-chromatography) only after a week, together with unreacted anisaldehyde, benzaldehyde and ethyl benzoate; with furfural, under the same conditions, furoin was isolated in good yield, but no benzoin or benzofuroin could be revealed. Analogous reaction carried out with IIc and benzaldehyde or furfural, either in a 1:2 or 1:20 ratio gave benzoin and furoin, respectively, in good yield, while with anisaldehyde only a little anisoin was formed. The presence of furoanisoin or furobenzoin could never

be detected.

Therefore, it seems likely that the acylthiadiazolines II, in their reaction with aldehydes to give acyloins, do not revert to the "active aldehyde" (IV), but rather undergo α -elimination (5) to the parent ylide (III) and aldehyde. Compound III should then react with the aldehyde present in the mixture in major concentration, in a kinetically controlled process, to give only acyloins with $R' = R''$ (6).

REFERENCES AND NOTES

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- (4) Compounds of analogous structure have sometimes been found starting from thiazolium salts; (B. Lächmann, H. Steinmaus and H. W. Wanzlick, *Tetrahedron*, **27**, 4085 (1971); J. Metzger, H. Larive, R. Dennilauler, R. Baralle and G. Gaurat, *Bull. Soc. Chim. France*, 2857 (1964); A. Takamizawa, K. Hirai, Y. Hamashima and S. Matsumoto, *Tetrahedron Letters*, 5071 (1967); A. Takamizawa, S. Matsumoto and S. Sakai, *ibid.*, 2189 (1968).
- (5) G. Scherowsky, K. Dünnebier, G. Höfle, *ibid.*, 2095 (1977).
- (6) The reaction between anisaldehyde, benzaldehyde, thiadiazolium salt and triethylamine in 2:1:1:1 ratio gave some anisoin together with unreacted aldehyde and minor amounts of unidentified products, but no benzoin or unsymmetrical acyloins (V , $R' \neq R''$). The latter instead were obtained under different reaction conditions: for instance, a 1:1 mixture of benzaldehyde and anisaldehyde, in the presence of a catalytic amount of thiadiazolium salt, gave some anisobenzoin (V , $R' = p$ -methoxyphenyl, $R'' = \text{phenyl}$), together with a larger amount of benzoin and a smaller one of anisoin (A. Alemagna and T. Bacchetti, unpublished results).