## Novel Ring Transformation of 1,3-Oxazines into Pyrroles by the Reaction with Soft Cyanide Anion

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Treatment of 2H-1,3-oxazine-2,4(3H)-diones (1) with potassium cyanide caused a ring transformation to afford 5-imino-1,5-dihydro-2H-pyrrol-2-ones (2).

The synthesis of a new heterocyclic ring by ring transformation is an important and intriguing topic in chemistry.<sup>1</sup> It is known that 2H-1,3-oxazine-2,4(3H)-diones undergo ring transformations into uracils,<sup>2,3</sup> pyrazol-3-ones,<sup>3</sup> 2-pyridones,<sup>3a</sup> or barbituric acids<sup>4</sup> on reaction with ammonia, primary aliphatic amines, hydroxylamine, hydrazine, OH<sup>-</sup>, or a carbanion. In all these ring transformations, an initial attack by the nucleophile takes place on the 2-position of the 1,3-oxazine ring, and, to our knowledge, no ring transformations caused *via* an initial attack on the 6-position have appeared in the literature. We report herein a novel type of ring transformation of 1,3-oxazines into pyrroles involving an initial attack of a soft nucleophile, the cyanide anion, on the 6-position.





 $Cy = cyclohexyl, Rf = \beta$ -D-ribofuranosyl

 $\mathbf{a}$ ;  $\mathbf{R}^1 = \mathbf{R}^2 = \mathbf{M}\mathbf{e}$ 

**b**;  $R^1 = Me$ ,  $R^2 = Cy$ 

3,6-Dimethyl-2H-1,3-oxazine-2,4(3H)-dione (1a)in dimethylformamide (DMF) was treated with an aqueous solution of potassium cyanide (1.2 equiv.) at room temperature for 2h. After extraction with chloroform followed by evaporation of the solvent in vacuo, trituration of the residue with hexane allowed isolation of 5-imino-1,4-dimethyl-1,5dihydro-2H-pyrrol-2-one (2a) (50%, m.p. 90-91°C), † along with 3-acetyl-4-amino-1-methyl-1H-pyrrole-2,5-dione (3a), (15%, m.p. 241-243 °C decomp.). The structure of the major product (2a) was confirmed by identification of its hydrolysis product, 1,3-dimethyl-1H-pyrrole-2,5-dione (4a), with an authentic sample.<sup>5</sup> The minor product (3a) was identical in every respect to an authentic sample which was prepared by the reaction of N-methylacetoacetamide with ethyl cyanoformate.6

Analogous treatment of the other 3-substituted compounds (1b) and (1c) with potassium cyanide gave the corresponding products (2b) (73%, m.p. 71.5—72.5 °C) and (2c) (71%, m.p. 150—151 °C decomp.) in good yields, accompanied by (3b) (20%, m.p. 236—238 °C decomp.) and (3a) (10%, m.p. 243—245 °C decomp.), respectively.

A reasonable mechanism for this conversion is as follows. An initial nucleophilic attack by a soft cyanide anion occurs on the soft 6-position rather than on the hard 2-position of compounds (1a-c) to give (Z)-3-cyanoacrylamide intermediates (A) which adopt a favourable configuration for the intramolecular cyclisation to give compounds (2a-c) (path a in Scheme 1). On the other hand, the minor product  $(3a<sup>±</sup>_{+} \text{ or } b)$ 



<sup>&</sup>lt;sup>†</sup> All new compounds gave satisfactory microanalytical results and spectral data consistent with the assigned structures.

<sup>‡</sup> A plausible mechanism for the formation of (3a) from (1c) remains equivocal and is now under investigation.

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is produced by nucleophilic attack by the cyanide anion on the 2-position, as is conventional<sup>2-4</sup> (path b in Scheme 1).

When the 6-unsubstituted compound (1d) similarly reacted with potassium cyanide, the expected product (2d) (13%, m.p. 58—59 °C) was obtained. No product formed via an attack on the 2-position was observed. In this case, however, (*E*)-3-cyano-*N*-methylmethacrylamide (5a) (m.p. 76—77 °C) was isolated in 73% yield. The (*E*)-methacrylamide (5a) was converted into the (*Z*)-methacrylamide (6) in 47% yield upon irradiation with a 400 W high-pressure mercury arc lamp through a Pyrex filter. On the other hand, analogous irradiation of (5a) in the presence of a catalytic amount of KCN resulted in the formation of the corresponding 5-imino-1,5-dihydro-2*H*-pyrrol-2-one (2d) in 30% yield. This fact is explained in terms of an initial photoisomerisation of the (*E*)-acrylamide (5a)§ to the corresponding (*Z*)-acrylamide (A) which cyclises to (2d) (see Scheme 1).

The reaction of the compound (1e), which possesses a structural similarity to a nucleoside antibiotic oxazinomycin (1f),<sup>7</sup> led to the formation of the 3-cyclohexyl-5-imino-1,5-dihydro-2*H*-pyrrol-2-one (2e) (57%, m.p. 68—70 °C) and the (*E*)-acrylamide (5b) (41%, m.p. 122—124 °C). Compound (2e) was smoothly hydrolysed to give the corresponding dione (4b) in 99% yield.

§ Nuclear Overhauser enhancement experiments also suggest that the acrylamide adopts the *E*-configuration.

Thus, the present ring transformation is of interest in connection with the possible transformation of oxazinomycin (**1f**) into a nucleoside antibiotic showdomycin (**4c**).<sup>8</sup>

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