

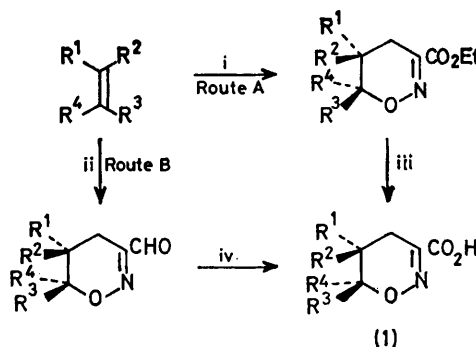
Decarboxylation and Fragmentation of 5,6-Dihydro-4*H*-1,2-oxazine-3-carboxylic Acids

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Summary The title compounds, which are derived from the cycloaddition of α -nitroso-acrylic esters or of α -nitrosoacrolein to olefins, are thermally decarboxylated to give γ -hydroxynitriles in a stereoselective process.

In the preceding communication¹ we have described the preparation of several 3-ethoxycarbonyl-dihydro-oxazines from substrates containing a nucleophilic double bond. 3-Chloro-2-hydroxyiminopropanal² also reacts with these substrates in a similar way, giving the corresponding dihydro-oxazine-3-carbaldehydes (Scheme 1). Both groups of compounds serve as convenient precursors for the 3-carboxylic acids (1). Table 1 shows a selection of the acids which we have prepared by these methods.



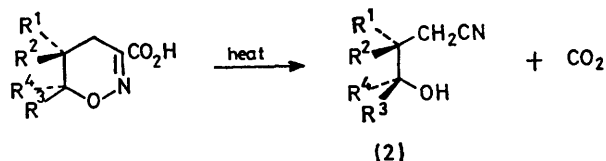
SCHEME 1. Reagents: i, $\text{BrCH}_2\text{C}(=\text{NOH})\text{CO}_2\text{Et}$, Na_2CO_3 ; ii, $\text{ClCH}_2\text{C}(=\text{NOH})\text{CHO}$, Na_2CO_3 ; iii, NaOH aq., 20°C ; iv, Ag_2O , 20°C .

TABLE 1. 5,6-Dihydro-4*H*-1,2-oxazine-3-carboxylic acids (1).

Substrate	Preparative route ^a	R ¹	R ²	R ³	R ⁴	Yield/% ^b	M.p./ $^\circ\text{C}$
α -Methylstyrene	A	H	H	Me	Ph	43	106—108
	B					49	
Cyclopentadiene	A	H	$-\text{CH}_2\text{CH}=\text{CH}-$		H	72	Unstable oil
	B					56	
Indene	A	H	$-\text{CH}_2\cdot\text{C}_6\text{H}_4\text{-}o$		H	42	101—102
Cyclo-octene	B	H	$-\text{[CH}_2\text{]}_6-$		H	42	77—79
<i>trans</i> -Stilbene	B	H	Ph	H	Ph	13	124—126

^a Route specified in Scheme 1. ^b Yields are for overall (two-step) processes from the substrate, and are for isolated compounds. New compounds are fully characterised.

The acids are decarboxylated when heated briefly above about 150 °C: the reaction is conveniently carried out under reduced pressure in a kugelrohr apparatus, when the products distil over. These products, which are isolated in



SCHEME 2

high yields, are γ -hydroxybutanonitriles (2) (Scheme 2 and Table 2). The reaction is highly stereoselective, and with adducts derived from cyclic olefins, the *cis* stereochemistry of the original oxazines is retained in the γ -hydroxy-nitriles.

TABLE 2. γ -Hydroxybutanonitriles (2).

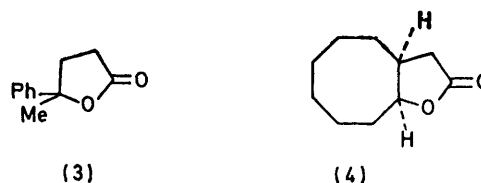
R ¹	R ²	R ³	R ⁴	Yield ^a /%	B.p./°C (mm Hg)
H	H	Me	Ph	99	160 (0.5)
H	-CH ₂ -CH=CH-	H	H	73	105 (0.1)
H	-CH ₂ C ₆ H ₄ o-	H	H	83	140 (0.1) ^b
H	-[CH ₂] ₆ -	H	H	91	135—140 (0.1)

^a Yields are based on the acids (1). New compounds are fully characterised. ^b M.p. 51—53 °C.

The decarboxylative fragmentation is in accord with earlier studies of the behaviour of related carboxylic acids.

Open-chain α -hydroxyimino acids are known to decarboxylate readily to give nitriles,³ and a similar fragmentation is observed with isoxazoline-3-carboxylic acids.⁴ The reactions described here provide a convenient method of *cis*-addition to nucleophilic double bonds.

In some cases the reactions also provide a route to γ -lactones, since it is known that γ -hydroxybutanonitriles can be cyclised to γ -lactones in acidic media.⁵ We carried out the preparation of the lactones (3)⁶ and (4) from the



corresponding hydroxynitriles (methanolic hydrochloric acid, reflux); both were formed in high yield (>95%) and in the case of the lactone (4), only the *cis* isomer was detected. The overall sequence, from olefins to γ -lactones, is similar in several respects to that based on α -chloronitrone addition,⁷ the nitroso-alkenes acting, like the chloronitrines, as a²-type synthetic reagents.⁸

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