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

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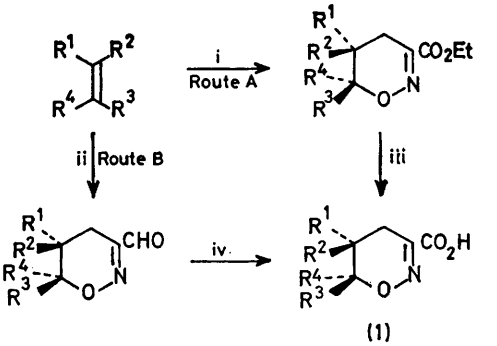
Summary The title compounds, which are derived from the cycloaddition of α-nitroso-acrylic esters or of α-nitrosoacrolein to olefins, are thermally decarboxylated to give γ-hydroxynitriles in a stereoselective process.

IN the preceding communication[1] we have described the preparation of several 3-ethoxycarbonyl-dihydro-oxazines from substrates containing a nucleophilic double bond. 3-Chloro-2-hydroxyiminopropanal[2] 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.



(**1**)

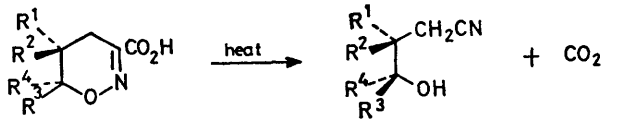
SCHEME 1. Reagents: i, $BrCH_2C(=NOH)CO_2Et$, Na_2CO_3; ii, $ClCH_2C(=NOH)CHO$, Na_2CO_3; iii, NaOH aq., 20 °C; iv, Ag_2O, 20 °C.

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./°C
α-Methylstyrene	A	H	H	Me	Ph	43	106—108
	B					49	
Cyclopentadiene	A	H	$-CH_2CH=CH-$		H	72	Unstable oil
	B					56	
Indene	A	H	$-CH_2{\cdot}C_6H_4$-*o*		H	42	101—102
Cyclo-octene	B	H	$-[CH_2]_6-$		H	42	77—79
trans-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



(2)

SCHEME 2

high yields, are γ-hydroxy-butanonitriles (**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.

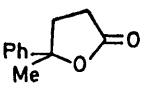
TABLE 2. γ-Hydroxybutanonitriles (**2**).

R^1	R^2	R^3	R^4	Yield[a]/%	B.p./°C (mm Hg)
H	H	Me	Ph	99	160 (0·5)
H	$-CH_2\cdot CH{=}CH-$		H	73	105 (0·1)
H	$-CH_2C_6H_4\cdot o-$		H	83	140 (0·1)[b]
H	$-[CH_2]_6-$		H	91	135—140 (0·1)

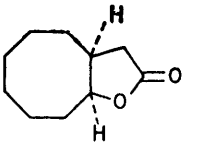
[a] Yields are based on the acids (**1**). New compounds are fully characterised. [b] M.p. 51—53 °C.

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



(3)



(4)

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 chloronitrones, as a^2-type synthetic reagents.[8]

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