1,3-Oxazolidin-2-ones from 1*H*-Aziridines by a Novel Stratagem which Mimics the Direct Insertion of CO_2

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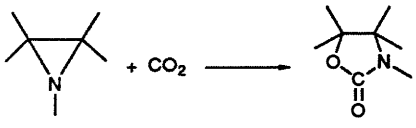
N-Ethoxycarbonylaziridines **2** undergo smooth thermal transformation into 1,3-oxazolidin-2-ones **3** on flash pyrolysis by a tandem reaction sequence equivalent to direct insertion of CO_2 into the parent 1*H*-aziridine.

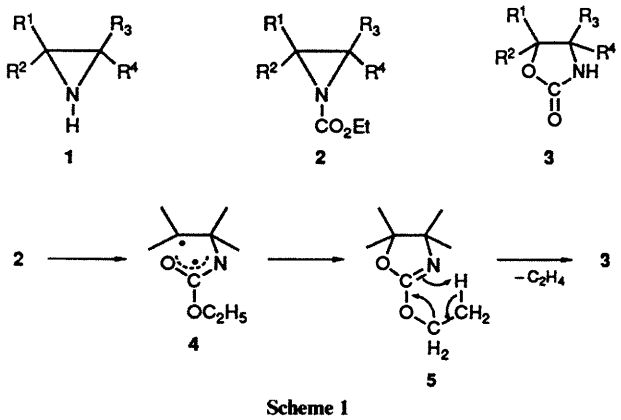
Although insertion of CO_2 into aziridines adumbrates a direct method for obtaining the industrially and pharmaceutically important 1,3-oxazolidin-2-ones[1] (eqn. 1), in practice this approach is blighted by the formation of large amounts of



(1)

polyurethane co-polymers, and requires high pressure.[2] This communication reports a much simpler and more efficient stratagem,[3] one which proceeds without recourse to CO_2 by the initial conversion of the aziridines into their *N*-ethoxycarbonyl derivatives **2**, whereupon in a single thermal step, these produce 1,3-oxazolidin-2-ones **3** in excellent yields.

The starting *N*-ethoxycarbonyl compounds **2** are obtained almost quantitatively from the parent aziridine **1** by reaction with ethyl chloroformate in the presence of Et_3N.[4] Their clean transformation into oxazolidin-2-ones **3** is effected readily in yields in the range 47–88% by flash vacuum pyrolysis (FVP).[5] In a specific example under typical conditions (inlet temperature 100 °C), slow volatilisation of the aziridine **2b** through the furnace at 650 °C and 0.001 mmHg produced in one pass a 88% yield of analytically pure 5-phenyl-1,3-oxazolidin-2-one **3b** after recrystallisation from ethyl acetate–hexane (m.p. 88–89 °C; lit.,[6] 89–90 °C). Other 1,3-oxazolidin-2-ones obtained by analogous pyrolyses are listed in Table 1 with their yields.



Scheme 1

The reactions were totally regiospecific with the exception of the *tert*-butyl derivative **2e** which afforded an isomeric mixture of products containing 79% of 5-*tert*-butyl-1,3-oxazolidin-2-one **3e** along with 21% of its 4-substituted isomer. In the case of the 2,3-disubstituted aziridine **2d**, the thermal transformation occurred with a loss of *cis*-stereospecificity to give a 86% yield of oxazolidin-2-one **3d** as a 1:3 mixture of *cis* and *trans* isomers whose stereostructures were assigned on the basis of ^1H NMR coupling constants $J_{4,5cis}$ 8.5 Hz and $J_{4,5trans}$ 7.3 Hz.[7]

The mechanism for these novel transformations is presented in Scheme 1 and is notable for its unique tandem sequence of thermal reactions, whose combined effect mimics the normally difficult process of direct insertion of CO_2 into a 1*H*-aziridine, *i.e.* **1**→**3**. The first step involves the thermal isomerisation of **2**, presumably *via* the diradical species **4**, to the isomeric 2-ethoxy-4,5-dihydrooxazole **5*** which can be isolated from the pyrolysates at temperatures below 600 °C. In the second step,

Table 1 1,3-Oxazolidin-2-ones **3** from *N*-ethoxycarbonylaziridines **2**

Starting material	R^1	R^2	R^3	R^4	Product (Yield[a,b] %) m.p. (lit) (°C)	
2a	H	H	H	H	(**3a**) 56	85–86 (85–86[13])
2b	Ph	H	H	H	(**3b**) 88	88–89 (89–90[6])
2c	Ph	Ph	H	H	(**3c**) 78	200–201 (200[14])
2d[c]	Ph	H	Ph	H	(**3d**) 86	*d*
2e	Bu^t	H	H	H	(**3e**) 47	*e*

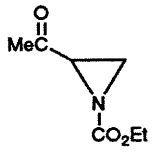
[a] Yields of isolated products purified by recrystallisation. [b] All compounds gave spectral data (^1H and ^{13}C NMR, IR and mass) in agreement with their structures and satisfactory analytical data. [c] *cis*-Isomer. [d] A 1:3 mixture of *cis*- and *trans*-isomers. [e] Contains 12% of 4-substituted isomer.

* Formation of *N*-allylcarbamates is usually encountered on thermolysis in the condensed phase,[8] but see M. L. Graziano and R. Scarpati, *J. Heterocycl. Chem.*, 1976, **13**, 205, for an isolated example of the thermal isomerisation (90 °C, 4 d) of an *N*-ethoxycarbonylaziridine, albeit as part of a mixture, to a dihydrooxazole.

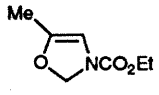
the dihydrooxazole **5** is converted into an oxazolidin-2-one **3** by thermal elimination of ethylene *via* a 6-centred cyclic reaction which is a rare nitrogen analogue of carboxylate ester pyrolysis.[9] This was confirmed by independent synthesis of **5b** [from **3b** and triethyloxonium tetrafluoroborate (Meerwein's reagent); 94% yield] and its pyrolysis which proceeded cleanly and rapidly at 600 °C to give a virtually quantitative yield of oxazolidin-2-one **3b** and ethylene. By virtue of this second step, oxazolidin-2-one formation from the pyrolysis of the corresponding *N*-methoxycarbonylaziridines is blocked, and the only products from their pyrolyses are 2-methoxy-2-oxazolines (*via* step 1) and their decomposition products.

Compared to insertion of CO_2 into aziridines, the present method provides an operationally much simpler route to oxazolidin-2-ones more so since the precursor *N*-ethoxycarbonyl derivatives **2** are accessible directly by the addition of ethoxycarbonylnitrene (EtO_2C–N:) to the appropriate alkene,[10] thus representing a considerable saving in time.

Current studies are focussed on extending the methodology to other heterocyclic systems. In the present context, it is found that use of the SEt analogue of **2a** provides a new method of preparing 1,3-oxazolidin-2-thione, whilst the corresponding *N*-thiocarbonyl derivative of **2a** gives rise to the isomeric thiazolidin-2-one in good yields. In a further development, we have found that incorporation of an acyl group into the 2-position of the aziridine **2** provokes a different rearrangement without loss of CO_2 that is a heterocyclic analogue of the vinylcyclopropane rearrangement.[11] For example, the acetyl derivative **2f** is converted directly into the 2,3-dihydrooxazole **6**, a novel representative from a virtually neglected class of heterocycles.[12]



2f



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