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Preliminary communication

ALKYL DICHLOROACETATES: A NOVEL APPLICATION IN THE PREPARATION OF HIGHLY FUNCTIONALISED AZIRIDINES FROM IMINES

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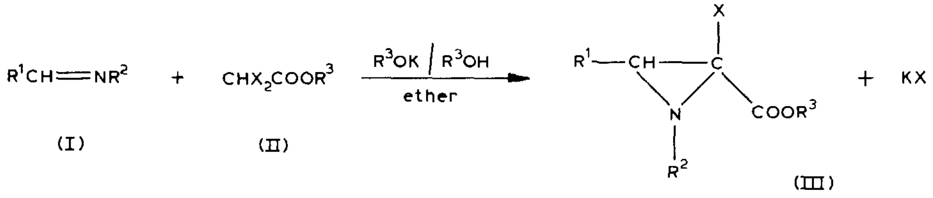
Summary

2-Aziridine-2-chlorocarboxylic acid alkyl esters have been prepared in basic alcoholic medium from alkyl dichloroacetate and aromatic imines by an extension of the Darzens reaction.

There is increasing use of substituted aziridines as synthons in organic chemistry [1] but the highly functionally substituted 1,3-diaryl aziridines III ($X = Cl$, $R^1 = Ar^1$, $R^2 = Ar^2$) where a halogen atom, a nitrogen atom and an ester function are present on the same carbon are practically unknown [2,3]. A recent publication deals with the analogous 2-halo-2-(phenylsulfonyl)aziridines [4].

Among the various approaches to functionally substituted aziridines described in the literature, attempts to extend the Darzens condensation by the action of stabilized α halo carbanions on imines have been limited [1,5]. The study reported here involves the reaction of the anions derived from alkyl dichloroacetate II with imines I, and is an extension of other work in this laboratory concerned with the preparation and the Darzens type reactions of various stabilized α,α'-dihalocarbanions [6]. A recent report on the reaction of imines with α-(monohalosulfonyl)carbanions [7] prompts us to disclose our preliminary results on the synthesis of aziridines III using a Darzens type approach.



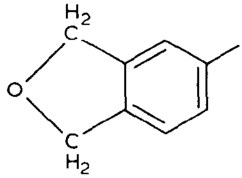
The reaction was carried out by adding a mixture of alkyl dichloroacetate II (2 equiv.) and imine I (1 equiv.) in ether solution to a potassium alcoholate (2 equiv.) in alcohol/ether solution (1/1) at room temperature. After the addition was complete the mixture was stirred for 15 h to 48 h. The reaction was quenched with water and the aziridine products III were extracted with ether. They were purified by chromatography on neutral alumina or by fractional crystallisation. Under these conditions 2-aziridine-2-chlorocarboxylic acid alkyl esters III (X = Cl) were obtained in excellent yields (Table 1).

Our preliminary findings have indicated that the reaction is limited to aromatic imines (R^1 = Ar^1 and R^2 = Ar^2). An attempt, in the case where R^1 = C_6H_5, R^2 = C_6H_{11}, R^3 = CH_3 gave III in only 57% yield after eight days at room temperature, and with R^1 = i-C_3H_7, R^2 = C_6H_{11} the method did not work*. Use of isopropyl dibromoacetate instead of the corresponding dichloroacetate, along with I (R^1 = R^2 = C_6H_5) gave only 50% yield of aziridine III (X = Br) under the same conditions (20 h).

It is noteworthy that the anion derived from II (X = Cl, Br) was generated in protic medium [6,8], whereas other preparations of functionalized aziridines which make use of an extension of the Darzens condensation on imines are carried out in aprotic medium and at low temperatures [5,7]. In the present reactions the protic medium probably stabilizes the various anionic intermediates and allows the reaction to take place at room temperature, which is more convenient. It is interesting to note that no nucleophilic attack of potas-

TABLE 1

YIELDS OF 2-AZIRIDINE-2-CHLOROCARBOXYLIC ACID ISOPROPYL ESTERS III (R^2 = Ph, R^3 = i-C_3H_7; X = Cl) FROM THE REACTIONS BETWEEN IMINES I AND ISOPROPYL DICHLOROACETATE II

R^1	Yield (%)[a]
Ph	84[b]
m$NO_2C_6H_4$	65[b]
p$NO_2C_6H_4$	77[b]
mClC_6H_4	89[b]
pClC_6H_4	85[b]
	96[c]
o$CH_3C_6H_4$	90[d]
p$CH_3C_6H_4$	75[c]
p$CH_3OC_6H_4$	85[c]

[a] Yield of aziridine III based on the starting imine I. The aziridines III were identified by ^{1}H NMR and IR spectroscopy. The microanalyses were in satisfactory agreement with the calculated values. [b] After fractional crystallisation. [c] Crude product. Difficulties are encountered in crystallisation, but the analysis of the crude product was correct. [d] After chromatography on alumina.

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*We have observed that whatever the nature of the imine, the reaction is clearly slower with imines than with carbonyl compounds [6,9]. Hence a regioselective preparation of mono-α-chloroglycidic esters from dicarbonyl compounds may be possible by using the imine function as a protective group for one carbonyl group. This point is under investigation.

sium alcoholate on the halogen atom was observed during the preparation of the aziridine III; such a reaction has been observed for 2-halo-2-(arylsulfonyl)-aziridines [4].

In all cases, only one stereoisomer III was obtained, and this is analogous to the observations encountered in the preparation of α-haloglycidic esters by reaction of dihaloacetate anions with carbonyl compounds [6,9]. However, the stereochemistry of aziridines III has not yet been determined, and is under investigation.

The extension of the Darzens reaction of dichloroacetate with aromatic imines in protic medium is very convenient and provides an attractive route to the interesting class of aziridines III, even on a large scale. The method requires only commercial available starting materials and imines. It should be applicable to the synthesis of various functionalized 2-haloaziridines. The scope and utility of the reaction with other stabilized α,α′-dihalocarbanions is under investigation.

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