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Aziridination of α,β-Unsaturated Esters by (Ethoxycarbonyl)nitrene

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Abstract: The reaction of α , β -unsaturated esters with (ethoxycarbonyl)nitrene, generated by α elimination of NsONHCO₂Et using CaO as a base in heterogeneous phase, allowed the preparation of aziridine-1,2-dicarboxylates (2a-e) in good isolated yields (57-72%). The same reaction does not take place using triethylamine instead of CaO, in homogeneous conditions. Copyright © 1996 Elsevier Science Ltd

Aziridine-2-carboxylates are versatile building blocks for organic synthesis;¹ they may be considered as precursors of a variety of functionalised α - or β -amino esters owing to the known high reactivity of the three-membered ring.² Nitrenes can convert suitably substituted alkenes to aziridines.³

(Ethoxycarbonyl)nitrene (NCO₂Et) reacts readily with electron-rich alkenes, while toward the double bond of allylic ethers and acetals it shows a lower reactivity.⁴ Only two cases are known in which NCO₂Et, generated by photolysis of ethyl azidoformate, reacts with α , β -unsaturated esters.⁵

Recently we introduced inorganic solid bases, such as CaO or K_2CO_3 , to induce the α -elimination of ethyl N-[(4-nitrobenzenesulphonyl)oxy]carbamate (NsONHCO₂Et).⁶

In this communication we report the results obtained by this procedure in the aziridination of α , β -unsaturated esters.



In the reaction of α , β -unsaturated esters carrying two methyl groups (1a and 1b) the corresponding aziridine-1,2-dicarboxylates were isolated by flash-chromatography in good yields as reported in Table. From monosubtituted unsaturated esters having only one methyl group (1d and 1e) lower yields of products were registered. With a phenyl group (1c) the yield rises again. It is noteworthy that the reaction does not occur when performed using triethylamine as the base under homogeneous conditions.

substrate	R ₁	R ₂	R ₃	molar ratio 1 : reagents	product (yield, %)
1a	Н	CH ₃	CH ₃	1:7	2a (70)
1b	CH ₃	CH ₃	Н	1:7	2b (72)
1c	Н	Ph	н	1:7	2c (70)
1 d	Н	CH ₃	н	1 : 5	2d (58)
1e	Н	н	CH ₃	1:5	2e (57)

Table. Reactions of NsONHCO₂Et and CaO with α , β -Unsaturated Esters.

The present method allows the synthesis of *N*-protected aziridine-2-carboxylates in one step from α,β unsaturated esters under mild conditions, by an easy procedure, without using a UV apparatus and hazardous precursors (azides). This kind of aziridines is known to be activated toward nucleophilic ring-opening reactions, moreover it is possible to deprotect them to the *N*-unsubstituted aziridine-2-carboxylates.⁷ Actually **2b** and **2c** were converted into **3b** and **3c**,⁸ upon treatment with three equivalents of 1.5 M MeONa in MeOH, at room temperature for 48 h and 10 h respectively.



As the development of simple routes to optically active aziridines is a goal of undoubted interest, we tried to extend the reported α -elimination procedure using a chiral carbamate as a precursor of a chiral nitrene. A preliminary reaction with the ester **1a** was performed using CaO and (1R, 2S, 5R)-menthyl N-[(4-nitrobenzenesulphonyl)oxy]carbamate prepared from the corresponding commercial chloroformate. A 1:1 mixture⁹ of the two diastereometric aziridine-2-carboxylates was obtained in the yield of 64%.

Efforts to extend the scope of this process to other useful substrates are currently in progress.

General procedure. To 4 mmol of the ester 1 at room temperature NsONHCO₂Et, CaO and CH₂Cl₂ were added, under stirring, portion wise in 1.5 h, reaching the molar ratios reported in Table and a total of 8 ml of solvent. After 12 h of stirring, 15 ml of CH₂Cl₂ and 200 ml of hexane were added to the mixture. After filtration and concentration *in vacuo*, the crude reaction mixture was purified by flash-chromatography on silica gel (hexane/ethyl acetate/triethylamine, 88:10:2), to obtain the aziridine-1,2-dicarboxylates **2a-e** in the yields reported in Table. Spectral data are in agreement with the reported structures.¹⁰

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- 10. For example 2a: ¹H NMR (200 MHz, CDCl₃) δ 1.18 (t, 3H, CH₂CH₃); 1.23 (d, 3H, CHCH₃); 1.40 (s, 3H, CCH₃); 2.93 (q, 1H, CHCH₃); 3.68 (s, 3H, OCH₃); 4.09 (q, 2H, CH₂CH₃). ¹³C NMR (200 MHz, CDCl₃) δ 12.97 (CH₃); 13.43 (CH₃); 14.07 (CH₃); 42.79 (CH); 44.55 (CCO); 52.45 (OCH₃); 62.08 (OCH₂); 160.77 (NCO); 170.83 (CO₂CH₃). IR (CCl₄) 1707, 1746 cm⁻¹. GC-MS *m*/z (%) 201 (M⁺, 1), 128 (18), 70 (10), 69 (38), 68 (22), 59 (100).