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

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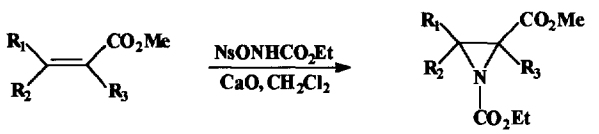
Abstract: The reaction of α,β-unsaturated esters with (ethoxycarbonyl)nitrene, generated by α-elimination of $NsONHCO_2Et$ using CaO as a base in heterogeneous phase, allowed the preparation of aziridine-1,2-dicarboxylates (**2a-e**) in good isolated yields (57-72%). The same reaction does not take place using triethylamine instead of CaO, in homogeneous conditions.

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 (NCO_2Et) 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 NCO_2Et, 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 ($NsONHCO_2Et$).[6]

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



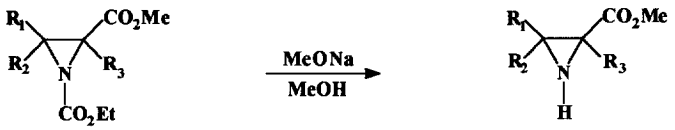
1 **2**

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 monosusbtituted 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.

Table. Reactions of $NsONHCO_2Et$ and CaO with α,β-Unsaturated Esters.

substrate	R_1	R_2	R_3	molar ratio **1** : reagents	product (yield, %)
1a	H	CH_3	CH_3	1 : 7	**2a** (70)
1b	CH_3	CH_3	H	1 : 7	**2b** (72)
1c	H	Ph	H	1 : 7	**2c** (70)
1d	H	CH_3	H	1 : 5	**2d** (58)
1e	H	H	CH_3	1 : 5	**2e** (57)

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.



2 **3**

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 (1*R*,2*S*,5*R*)-menthyl *N*-[(4-nitrobenzenesulphonyl)oxy]carbamate prepared from the corresponding commercial chloroformate. A 1:1 mixture[9] of the two diastereomeric 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 $NsONHCO_2Et$, CaO and CH_2Cl_2 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 CH_2Cl_2 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, $CDCl_3$) δ 1.18 (t, 3H, CH_2CH_3); 1.23 (d, 3H, $CHCH_3$); 1.40 (s, 3H, CCH_3); 2.93 (q, 1H, $CHCH_3$); 3.68 (s, 3H, OCH_3); 4.09 (q, 2H, CH_2CH_3). ^{13}C NMR (200 MHz, $CDCl_3$) δ 12.97 (CH_3); 13.43 (CH_3); 14.07 (CH_3); 42.79 (CH); 44.55 (*C*CO); 52.45 (OCH_3); 62.08 (OCH_2); 160.77 (NCO); 170.83 (CO_2CH_3). IR (CCl_4) 1707, 1746 cm^{-1}. GC-MS *m/z* (%) 201 (M^+, 1), 128 (18), 70 (10), 69 (38), 68 (22), 59 (100).

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