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A Novel Approach to Chiral Spirodiaziridines

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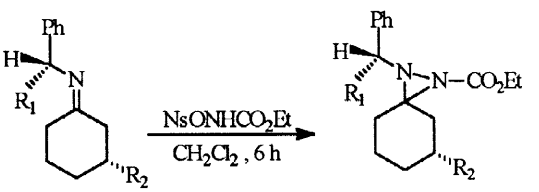
Abstract: Imines in the presence of $NsONHCO_2Et$ give diaziridines at room temperature in good yields and with good diastereoselectivity.

Keywords: Amination; diaziridines; strained compounds.

In the past we studied the amination reaction of enamines and were able to obtain regioselective attack on either carbon or nitrogen, depending on the reaction conditions.[1]

Recently we have extended our attention towards the formation of carbon-nitrogen bonds starting from azaallylic anions derived from imines at low temperatures or starting from imines at reflux in toluene. As aminating agents we considered two different [(arenesulphonyl)oxy]carbamates, namely ethyl *N*-[(4-nitrobenzenesulphonyl)oxy]carbamate ($NsONHCO_2Et$) and ethyl *N*-[(4-methylbenzenesulphonyl)oxy] carbamate ($TsONHCO_2Et$) or bis(*tert*-butoxycarbonyl)diazene [$N_2(CO_2t\text{-}Bu)_2$].[2]

We wish to report here the first results obtained in the amination reaction of imines[3] with $NsONHCO_2Et$ in CH_2Cl_2 in the absence of added base at room temperature to give diaziridines.[4]



1a-c **2a-c**

	Yield of **2**
a: $R_1 = R_2 = H$	31%
b: $R_1 = Me$; $R_2 = H$	46%
c: $R_1 = R_2 = Me$	42%

$TsONHCO_2Et$, under the same conditions, gives the diaziridines only in traces and over longer reaction times. As by-products, we obtained after work-up the corresponding nosylate salts, which after hydrolysis allowed us to recover the starting amine quantitatively.[5] The diastereomeric ratios (71:29 for **2b** and 68:32 for **2c**) were determined by ^1H and ^{13}C NMR spectra of crude reaction mixtures. The spirodiaziridines **2b** and **2c**[6] were easily separated by flash chromatography and obtained as pure diastereomers (≥ 95%).[7]

Surprisingly, all our attempts to obtain amination of **1** with $NsONHCO_2Et$ in the presence of an organic (Et_3N)[8] or inorganic (LiOH)[2] base failed. Attempted photolysis of N_3CO_2Et gave very complex reaction mixtures. Triaziridines were obtained from diazenes and (ethoxycarbonyl)nitrene (NCO_2Et) was claimed as reactive intermediate.[9] On the basis of our results we cannot exclude the involvement of NCO_2Et, but we think it is possible that an ionic pathway leading to diaziridines by addition of $NsON^-CO_2Et$ followed by the elimination of the good leaving group NsO^- might occur.[10]

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General Procedure. To a stirred solution of 10 mmol of imine in 20 ml of anhydrous CH_2Cl_2, under an atmosphere of N_2 10 mmol of $NsONHCO_2Et$ was added batchwise at room temperature. After 6 h of stirring, petroleum ether was added and nosylate salt was filtered. After evaporation of the solvent, the diaziridines were separated by flash chromatography on silica gel (hexane/diethyl ether, 8:2) and characterised.[11]

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5. The same imine might behave like a base: therefore in these reaction conditions yields up to 50% can be obtained.
6. Only two of the possible diastereomers were isolated, owing to stereoselective attack on one face of **1c**.
7. GC-MS (50-250 °C, 14 °C/min, T (Injector) = 260 °C) of each pure diastereomer always gave a mixture of both diastereomers, due to thermal equilibration. The absolute configuration has not been determined yet. Probably inversion at the alkyl substituted nitrogen must be slower than that at the ethoxycarbonyl substituted nitrogen, see also ref 4 (pp 199-201).
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11. **2a**: IR (CCl_4) 1740 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.22 (*t*, 3 H, CH_3), 1.51-1.81 (*m*, 10 H, CH_2), 3.65 (*s*, 2 H, NCH_2), 4.16 (*m*, 2 H, OCH_2), 7.24-7.48 (*m*, 5 H, Ph); ^{13}C NMR ($CDCl_3$) δ 13.97 (CH_3), 24.09, 24.45, 24.89, 28.52, 34.28 (CH_2 ring), 56.51 (NCH_2), 62.62 (OCH_3), 68.35 (NCN), 127.24, 128.40, 128.60 (Ph), 137.79 (C), 162.78 (CO); GC-MS *m/z* 274 (M^+, 9), 201 (12), 140 (12), 111 (12), 106 (23), 96 (15), 92 (10), 91 (100), 81 (14), 79 (18), 77 (15), 67 (13), 65 (13), 53 (10).
2b, major diastereomer: $[\alpha]_D$ -7.66 (CH_2Cl_2); IR (CCl_4) 1736 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.00-1.96 (*m*, 10 H, CH_2), 1.36 (*t*, 3 H, OCH_2CH_3), 1.58 (*d*, 3 H, CH_3), 3.56 (*q*, 1 H, NCH), 4.29 (*m*, 2 H, OCH_2), 7.28-7.46 (*m*, 5 H, Ph); ^{13}C NMR ($CDCl_3$) δ 14.33 (OCH_2CH_3), 23.99 (CH_3), 24.13, 24.27, 24.98, 28.59, 34.78 (CH_2), 61.84 (OCH_2), 62.70 (NCH), 69.22 (NCN), 126.88, 127.13, 128.40 (Ph), 143.27 (C), 162.96 (CO); GC-MS *m/z* 288 (M^+, 12), 184 (21), 170 (21), 120 (25), 111 (45), 106 (11), 105 (100), 103 (12), 94 (14), 91 (10), 84 (12), 81 (15), 79 (31), 77 (29), 67 (20); minor diastereomer: $[\alpha]_D$ +24.77 (CH_2Cl_2); ^1H NMR ($CDCl_3$) δ 1.27-2.10 (*m*, 10 H, CH_2), 1.12 (*t*, 3 H, OCH_2CH_3), 1.44 (*d*, 3 H, CH_3), 3.59 (*q*, 1 H, NCH), 4.03 (*m*, 2 H, OCH_2), 7.25-7.51 (*m*, 5 H, Ph); ^{13}C NMR ($CDCl_3$) δ 14.02 (OCH_2CH_3), 21.33 (CH_3), 23.97, 24.81, 25.27, 28.71, 34.73 (CH_2), 60.48 (OCH_2), 62.45 (NCH), 69.39 (NCN), 127.11, 127.72, 128.02 (Ph), 143.19 (C), 162.43 (CO).
2c, major diastereomer: $[\alpha]_D$ -20.58 (CH_2Cl_2); IR (CCl_4) 1736 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.81 (*d*, 3 H CH_3); 1.02-1.81 (*m*, 9 H, CH_2, CH); 1.31 (*t*, 3 H, OCH_2CH_3); 1.54 (*d*, 3 H, CH_3CHN); 3.44 (*q*, 1 H, NCH); 4.24 (*m*, 2 H, OCH_2); 7.23-7.43 (*m*, 5 H, Ph); ^{13}C NMR ($CDCl_3$) δ 14.35 (OCH_2CH_3), 22.21, 23.30, (CH_3), 24.41, 27.23, 31.19, 33.48 (CH_2), 43.07 (CH), 62.51 (OCH_2), 62.71 (NCH), 69.13 (NCN), 127.05, 127.13, 128.42 (Ph), 143.23 (C), 162.91 (CO); GC-MS *m/z* 302 (M^+, 7), 184 (24), 183 (11), 125 (27), 120 (26), 108 (26), 106 (12), 105 (100), 103 (10), 95 (20), 93 (10), 91 (13), 81 (33), 79 (26), 77 (25), 67 (16), 55 (13); minor diastereomer: $[\alpha]_D$ +19.84 (CH_2Cl_2); ^1H NMR ($CDCl_3$) δ 1.04 (*d*, 3 H, CH_3), 1.21-2.00 (*m*, 9 H, CH_2, CH), 1.10 (*t*, 3 H, OCH_2CH_3), 1.49 (*d*, 3 H, CH_3CHN), 3.53 (*q*, 1 H, NCH), 4,03 (*m*, 2 H, OCH_2), 7.24-7.51 (*m*, 5 H, Ph); ^{13}C NMR ($CDCl_3$) δ 14.08 (OCH_2CH_3), 22.81, 22.16 (CH_3), 23.71, 31.20, 33.48, 34.16 (CH_2), 35 .99 (CH), 60.62 (OCH_2), 62.42 (NCH), 69.31 (NCN), 127.11, 127.80, 128.01 (Ph), 143.25 (C), 162.39 (CO).