A One-Pot Synthesis of Aziridines from 2-Aminoethanols[1]

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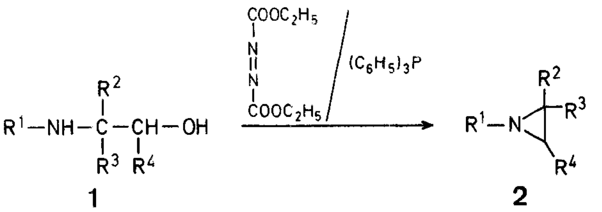
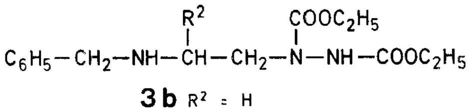
During the last two decades, the traditional two-step methods for converting 2-aminoethanols to aziridines[2,3] have been augmented by one-pot "redox-type" cyclizations employing triphenylphosphine/carbon tetrachloride/triethylamine[4] or triphenylphosphine dibromide/triethylamine[5]. Although the combination triphenylphosphine/diethyl azodicarboxylate (Mitsunobu reagent) has been used for intramolecular dehydrations[6], application of this reagent to the synthesis of aziridines has received only very scant attention. The only such report in the literature concerns the formation of 2,2-dimethylaziridine from 2-amino-2-methylpropan-1-ol in tetralin[7]. However, our treatment of 2-amino-1-phenylethan-1-ol (**1a**) with triphenylphosphine/diethyl azodicarboxylate in tetrahydrofuran did not produce any of the expected 2-phenylaziridine (**2a**).

In this communication, we report on the synthetic utility of this reaction, which is obviously not of a general nature. When a variety of 2-aminoethanols **1b–i** were treated with triphenylphosphine/diethyl azodicarboxylate in ether or tetrahydrofuran, good yields of aziridines **2b–i** were generally obtained if there was at least one substituent attached to either of the two carbon atoms between oxygen and nitrogen (Table). Treatment of the unsubstituted 2-benzylaminoethanol (**1b**) with triphenylphosphine dibromide/triethylamine has been reported to furnish only 1,4-dibenzylpiperazine[5]; under the present conditions, a low yield of 1-benzylaziridine **2b** was realized. The major side-products in this reaction and in the conversion of **1c** to **2c** were identified as the hydrazine derivatives **3b** (76%) and **3c** (32%), respectively. Similar adducts have recently been observed in the synthesis of azetidines from 3-aminopropanols[8].





$$C_6H_5-CH_2-NH-\overset{R^2}{CH}-CH_2-\overset{COOC_2H_5}{N}-NH-COOC_2H_5$$

3b R^2 = H
c R^2 = CH_3

The mildness of the procedure is documented by the fact that (−)-*erythro*-ephedrine (**1i**) gave a good yield of (+)-*trans*-1,2-dimethyl-3-phenylaziridine (**2i**), whereas use of the triphenylphosphine dibromide reagent resulted only in the formation of polymeric material[5].

In summary, this method provides a mild and convenient way of cyclizing appropriately substituted 2-aminoethanols **1b–i** to aziridines **2b–i**.

Cyclization of Aminoethanols 1 to Aziridines 2; General Procedure: To a solution of the aminoethanol **1** (30 mmol) and triphenylphosphine (11.8 g, 45 mmol) in ether or tetrahydrofuran (100 ml, choice of solvent depends on substrate solubility) stirred under nitrogen in an ice bath, is slowly added diethyl azodicarboxylate (95%, 7.5 ml, 45 mmol) via a syringe. The ice bath is removed, and the mixture is stirred at room temperature for the time indicated (Table). A crystalline precipitate (triphenylphosphine oxide/diethyl hydrazinedicarboxylate complex) is filtered off and washed with hexane/ether (1 : 1, 100 ml). The filtrate is evaporated on a rotary evaporator. Fairly volatile aziridines (entries **2b**, **2c**, **2d**, and **2i**) can be distilled from the residue using a Kugelrohr apparatus. Less volatile aziridines are purified by dissolution of the residue in ether (200 ml) and extraction into 0.5 normal hydrochloric acid (100 ml). The basified (potassium carbonate) aqueous phase is extracted with ether (2 × 100 ml) and the organic phase is dried with anhydrous potassium carbonate. Finally, remaining traces of diethyl hydrazinedicarboxylate (which has

Table. Aziridines **2** prepared.

Product No.	R_1	R_2	R_3	R_4	Reactions Conditions[a] time [h]/solvent	Yield[b] [%]	b.p. [°C]/torr found	reported
2a	H	H	H	C_6H_5	6/THF	[c]		
2b	$C_6H_5CH_2$	H	H	H	2/ether	18[d]	56–58°/2	69–71E/4.5[4]
2c	$C_6H_5CH_2$	CH_3	H	H	16/ether	59[e]	58–60°/2	57–58°/1.5[5]
2d	$C_6H_5CH_2$	H	H	CH_3	2/ether	90[f]	58–60°/2	57–58/1.5[5]
2e	$C_6H_5CH_2$	CH_3	CH_3	H	18/ether	89	54–56°/0.3	30–32°/0.05[9]
2f	$C_6H_5CH_2$	H	H	C_6H_5	16/THF	65	122–125°/0.25	138–139°/1[5]
2g	C_6H_{11}	H	H	C_6H_5	18/ether	86	94–96°/0.3	155–156°/16[5]
2h	t-C_4H_9	H	H	C_6H_5	18/ether	77	80–82°/0.25	50°/0.1[10]
2i	CH_3	CH_3	H	C_6H_5	2/ether	84	65–67°/1[g]	[h]

[a] All reactions were judged complete after 2 h (T.L.C.). Longer reaction times are not detrimental and allow formation of a crystalline triphenylphosphine oxide/diethyl hydrazinedicarboxylate complex in those instances in which it separates initially as a gum. No such precipitates were obtained when tetrahydrofuran was used as a solvent.

[b] Yield of isolated products of purity ≥ 95% by G.L.C. (conditions: Hewlett-Packard 402 instrument, glass column, 6 ft × 4 mm, 5% carbowax). ^{1}H-N.M.R. spectra (Varian EM 390 instrument, 90 MHz, $CDCl_3$/TMS) are consistent with the structures.

[c] No product was obtained.

[d] 76% of **3b** isolated.

[e] 32% of **3c** isolated.

[f] Products **2c** and **2d** are identical but derived from different starting materials (**1c** and **1d**).

[g] $[\alpha]_D^{25} = +51.8°$.

[h] Although this compound is known[11,12], no b.p. was given. The ^{1}H-N.M.R. spectrum of **2i** could be compared with that reported in Ref.[11].

appreciable solubility in ether and water) are removed by filtration of the crude product through a short column of alumina (Woelm, neutral, activity II), eluting with hexane/dichloromethane gradients (4:1 to 1:1).

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