Synthesis and crystal structure of enantiopure *N*-tritylaziridin-2-yl-methanols from L-serine and L-threonine

Johannes G. H. Willems,[a] Marco C. Hersmis,[a] René de Gelder,[b] Jan M. M. Smits,[b] Jeannet B. Hammink,[a] F. Jan Dommerholt,[a] Lambertus Thijs[a] and Binne Zwanenburg*[,a]

[a] *NSR Center for Molecular Structure, Design and Synthesis, Department of Organic Chemistry, University of Nijmegen, Toernooiveld, 6525 ED Nijmegen, The Netherlands*

[b] *NSR Center for Molecular Structure, Design and Synthesis, Department of Inorganic Chemistry, University of Nijmegen,Toernooiveld, 6525 ED Nijmegen, The Netherlands*

A convenient multigram 'one pot procedure' for the synthesis of methyl *N*-tritylaziridine-2-carboxylates 1 and 2, starting from the *N*-tritylmethyl esters of L-serine 9 and L-threonine 10 and using methanesulfonyl chloride and triethylamine, is described. The *N*-tritylaziridin-2-ylmethanols 3 and 4 are prepared from the corresponding methyl *N*-tritylaziridine-2-carboxylates 1 and 2 using a Grignard reaction. ^{1}H and ^{13}C NMR spectral and HPLC chromatographic analysis of aziridine alcohols 3 and 4 have been performed. The crystal structures of compounds 3 and 4 reveal that the aziridine ring substituents have the diphenylmethanol and the trityl groups in a *trans* relationship and show an intramolecular hydrogen bond between the aziridine nitrogen and the hydroxy group. According to temperature dependent ^{1}H NMR spectral analysis, a hydrogen bond is also present in solution. The enantiomeric purity of the *N*-tritylaziridin-2-ylmethanols 3 and 4 has been determined using HPLC techniques.

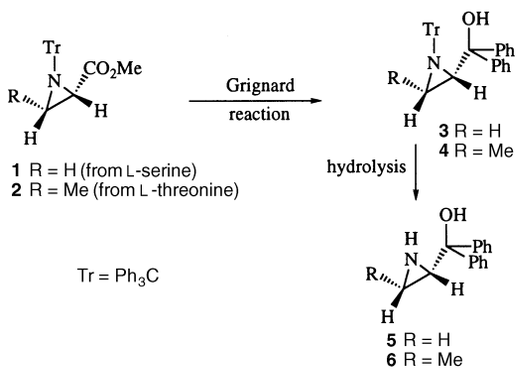
Introduction

During the last two decades the synthesis of enantiomerically pure compounds has become an important issue in organic chemistry and much attention has been devoted to the application of naturally occurring enantiopure starting materials in the synthesis of chiral compounds. In this respect chiral aziridines and aziridine-2-carboxylic esters form an attractive class of compounds, since they are available in enantiopure form from natural compounds by various routes.[1] Using enantiopure aziridines and aziridine-2-carboxylic esters, a wide range of chiral compounds, such as anomalous α-amino acids,[2] antibiotics[3] and selective enzyme inhibitors,[4] can be prepared.

Another strategy to obtain chiral compounds is the asymmetric conversion of prochiral substrates employing chiral catalysts. Recently, aziridines and derivatives thereof have been applied as new synthetic chiral catalysts in several asymmetric reactions.[5] This report deals with the synthesis and characterisation of new potential chiral catalysts derived from simple aziridine-2-carboxylic esters.

Our interest in chiral small-ring heterocycles, especially functionalised epoxides[6] and aziridines,[7] prompted us to investigate derivatives of aziridine-2-carboxylic esters **1** and **2** as new chiral catalysts in asymmetric reactions. *N*-Tritylaziridin-2-yl(diphenyl)methanols **3** and **4**, and the corresponding detritylated aziridine alcohols **5** and **6** (Scheme 1), were prepared and applied as catalysts in asymmetric imine isomerisation reactions[5b] and asymmetric reduction reactions,[5c] respectively.

A variety of routes to chiral nonracemic aziridine-2-carboxylic acid derivatives have been reported,[8] most of which rely either on the availability of enantiomerically pure starting materials from natural sources or on asymmetric transformations of C=C or C=N double bonds. The ring closure of 1,2-amino alcohols or suitable derivatives thereof[9] provides a convenient and efficient synthesis of aziridines and aziridine-2-carboxylic esters. In this context amino acids are widely used as chiral starting materials. A general method for the synthesis of

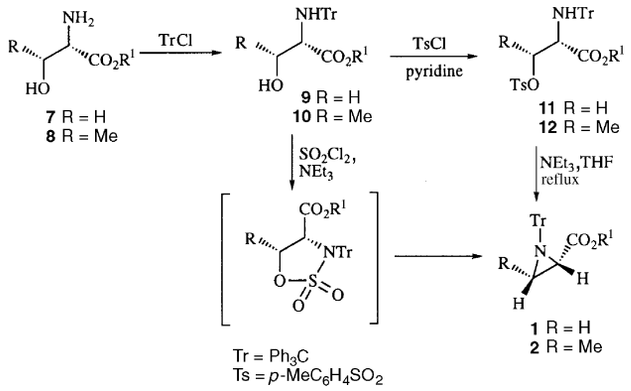


Scheme 1

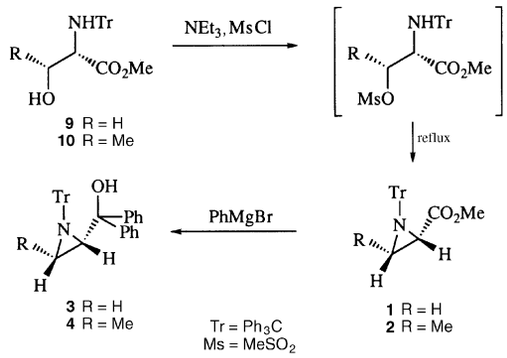
enantiopure *N*-unsubstituted aziridine-2-carboxylic esters from the corresponding oxirane-2-carboxylic esters in a two step procedure was described by Legters *et al.*[7a,c] For the purpose of this study the readily available amino acids serine **7** and threonine **8** were selected as the starting material.

In 1972, the synthesis of *N*-substituted aziridine-2-carboxylic esters was reported by Nakagawa *et al.*[10] These authors made use of a modified Wenker[11] aziridine synthesis starting from serine **7** and threonine **8** (Scheme 2). In the first step the hydroxy group in *N*-tritylated α-amino acid esters **9** and **10** was converted into the corresponding toluene-*p*-sulfonate using pyridine as the solvent. The second step was performed using triethylamine as the base, which resulted in an intramolecular cyclization reaction[12] to give the *N*-tritylaziridine-2-carboxylic esters **1** and **2**, as depicted in Scheme 2. In a following report,[13] Wakamiya *et al.* replaced toluene-*p*-sulfonyl chloride by methanesulfonyl chloride.

Van Boom[14] described a 2 mmol 'one-pot one-step' procedure for the conversion of *N*-trityl-L-serine **9** and -L-threonine esters **10** into the corresponding *N*-tritylaziridine-2-car-



Scheme 2



Scheme 3

boxylic esters **1** and **2**, respectively, using sulfuryl chloride and an excess of triethylamine, as shown in Scheme 2. Korn *et al.*[15] applied the procedure for the synthesis of aziridines as described by van Boom on a 100 g scale. It was found that during this multigram operation a by-product, *viz*. *N*-trityl-β-chloroalanine benzyl ester, was formed in *ca*. 30% yield, arising from an aziridine ring-opening by chloride ions. Separation of the desired *N*-tritylaziridine-2-carboxylic esters **1** and **2** and the by-product turned out to be a laborious process involving column chromatography, followed by crystallisation. In another study, Korn *et al.*[16] compared the efficiency of the one-step preparation of enantiopure *N*-tritylaziridine-2-carboxylic esters as described by van Boom[14] with that originally proposed by Nakajima.[10,12–13] Both procedures (Scheme 2) led to the desired aziridine compound in nearly identical yields (50–60%). X-Ray diffraction analysis of methyl (−)-(2*S*)-*N*-tritylaziridine-2-carboxylate was performed by Mishnev *et al.*[17] in 1983 and of benzyl (−)-(2*S*)-*N*-tritylaziridine-2-carboxylate by Korn *et al.*[15] in 1993.

Results and discussion

The aziridine-2-carboxylic esters **1** and **2** were used for the preparation of *N*-trityl alcohols **3** and **4** and the corresponding detritylated aziridine alcohols **5** and **6** (Scheme 1). It was important to have access to a convenient multigram scale synthesis of *N*-tritylaziridine esters **1** and **2**, the precursors of **3**–**6**. The literature reports on this synthesis indicated (*vide supra*) that improvements were needed. To this end, a convenient multigram 'one-pot procedure' for the preparation of **1** and **2** from the corresponding *N*-trityl amino esters **9** and **10** was developed (Scheme 3). The desired conversion was performed in THF using triethylamine (2.1 equiv.) and methanesulfonyl chloride (1.01 equiv.) at reflux temperature† for 48 h. Product **1** was isolated in almost quantitative yield with a purity of at least 95% according to GLC and NMR spectral analysis, and was used as such in further reactions. After recrystallisation from MeOH–NEt_3 the optical rotation of **1** {$[a]_D^{22}$ −96.8 (*c* 1.1, in MeOH)} was in good agreement with the reported value‡ {$[a]_D^{22}$ −95.4 (*c* 1.1, in MeOH)} for this aziridine derivative. This method was also successfully applied to the synthesis of methyl (2*S*,3*S*)-1-trityl-3-methylaziridine-2-carboxylate **2** from L-threonine. The optical rotation of **2** {$[a]_D^{22}$ −97.1 (*c* 1.0, in $CHCl_3$)} has a similar value but opposite sign as reported§ {$[a]_D^{22}$ +98.0 (*c* 1.0, in $CHCl_3$)} for the aziridine derived from D-threonine.

The essential difference between the procedure described here and those reported previously is that the mesylation of the hydroxy group and the aziridine ring closure can be carried out in one step on a multi-gram scale.

The *N*-tritylaziridine-2-carboxylic esters **1** and **2** were converted into the corresponding *N*-tritylaziridin-2-ylmethanols **3** and **4** using phenylmagnesium bromide (4 equiv.) in diethyl ether or THF at room temperature for 2 h (Scheme 1). After purification of the crude products by chromatography, followed by crystallisation from hexane–diethyl ether, the *N*-tritylaziridin-2-ylmethanols **3** and **4** were isolated in good yield (70%). The optical rotations of **3** {$[a]_D^{22}$ −78.8 (*c* 1.0, in $CHCl_3$)} and **4** {$[a]_D^{22}$ +22.5 (*c* 1.0, in $CHCl_3$)} have opposite signs, although the configuration at carbon C-2 of the aziridine ring is *S* in both cases. The ees of the protected aziridine alcohols **3** and **4** were determined by HPLC analysis using a chiral column (Chiralcel OD) and were greater than 99%.

The *N*-tritylaziridin-2-yl(diphenyl)methanols **3** and **4** were further characterised by X-ray diffraction and NMR spectroscopic analysis. Large cubic-shaped colourless and transparent crystals of **3** and **4** were obtained by slow recrystallisation from hexane–diethyl ether (2:1) over a period of 64 h. The X-ray structure analysis (Fig. 1) reveals that the *N*-trityl group is positioned *anti* to the methanol group in both **3** and **4**.

Comparison of the structures of **3** and **4** shows that the relative positions of the phenyl rings in the diphenylmethanol unit are very similar in both compounds, whereas the orientation of the phenyl rings of the trityl groups are slightly different (Table 1). The dihedral angles between the phenyl rings of the diphenylmethanol moiety and the aziridine ring are 94.0 and −142.6° in **3** and 93.0 and −146.2° in **4**. The dihedral angles between the aziridine ring and the phenyl rings of the trityl groups in **3** are −162.0, 84.7 and −40.1° and for aziridine alcohol **4** the values of the corresponding dihedral angles are −144.4, 101.5 and −18.3°, respectively. This difference in the spatial orientation of the phenyl rings in the trityl groups is due to the presence of the *cis*-methyl group in aziridine alcohol **4**. Inspection of space filling models of **3** and **4** confirms this observation. For the OH group in the aziridine alcohols one can envisage an intramolecular hydrogen bond with the nitrogen of the three-membered ring. It is of interest therefore to determine the orientation of the OH group in these alcohols more precisely. From the X-ray studies it was deduced that a hydrogen bond is present in the *N*-trityl alcohols **3** and **4**. The N–H distances in **3** and **4** were determined from the X-ray diffraction data and were shown to be 2.01 and 2.14 Å, respectively. These

† Note: When the reaction was performed at 50 °C instead of reflux temperature, *N*-tritylaziridine-2-carboxylic ester **1** and several reaction intermediates were formed according to GLC. After 48 h of additional heating of the reaction mixture at reflux temperature the product **1** could be isolated in almost quantitative yield.

‡ Reported value of methyl (2*S*)-1-tritylaziridine-2-carboxylate **1**: $[a]_D^{22}$ −95.4 (*c* 1.1, in MeOH). See K. Nakajima, T. Tanaka, M. Neya and K. Okawa, *Bull. Chem. Soc. Jpn.*, 1982, **55**, 3237.

§ Reported value of methyl (2*R*,3*R*)-1-trityl-3-methylaziridine-2-carboxylate **2**: $[a]_D^{22}$ +98.0 (*c* 1.0 in $CHCl_3$), the optical antipode of the synthesized methyl (2*S*,3*S*)-1-trityl-3-methylaziridine-2-carboxylate (see footnote ‡).

Table 1 Bond lengths, bond angles and dihedral angles of *N*-trityl-aziridin-2-yl(diphenyl)methanols **3** and **4**

	3	**4**
Bond lengths (Å)		
N(1)–C(5)	1.497	1.505
N(1)–C(3)	1.458	1.475
C(3)–C(2)	1.472	1.488
N(1)–C(2)	1.460	1.461
C(2)–C(4)	1.537	1.525
C(4)–O(1)	1.429	1.431
O(1)–H(1)	0.826	0.830
N(1)–H(1)	2.013	2.140
N(1)–O(1)	2.638	2.702
Bond angles (°)		
C(3)–N(1)–C(5)	122.1	119.2
C(2)–N(1)–C(5)	123.4	121.9
C(2)–N(1)–C(3)	60.58	60.9
N(1)–C(2)–C(4)	113.6	115.6
C(3)–C(2)–C(4)	123.9	126.1
N(1)–C(3)–C(2)	59.81	59.1
N(1)–C(2)–C(4)	113.6	115.6
O(1)–C(4)–C(2)	108.3	109.4
C(2)–C(4)–C(50)	114.0	112.7
C(2)–C(4)–C(40)	107.6	108.8
C(4)–O(1)–H(1)	102.7	106.3
N(1)–H(1)–O(1)	131.97	125.01
Dihedral angles (°)		
C(3)–N(1)–C(5)–C(10)	−88.36	−72.35
C(3)–N(1)–C(5)–C(20)	158.36	173.59
C(3)–N(1)–C(5)–C(30)	33.57	53.71
C(2)–N(1)–C(5)–C(10)	−162.0	−144.40
C(2)–N(1)–C(5)–C(20)	84.7	101.54
C(2)–N(1)–C(5)–C(30)	−40.1	−18.33
C(4)–C(2)–C(3)–N(1)	−99.5	−101.29
C(4)–C(2)–N(1)–C(5)	−132.32	−133.38
C(3)–C(2)–C(4)–C(40)	162.19	163.29
C(3)–C(2)–C(4)–C(50)	−74.42	−75.89
N(1)–C(2)–C(4)–C(40)	94.02	93.03
N(1)–C(2)–C(4)–C(50)	−142.6	−146.15
H(1)–O(1)–C(4)–C(2)	21.05	25.18
C(3)–C(2)–C(4)–C(50)	−74.42	−75.89
C(3)–C(2)–C(4)–C(40)	162.19	163.29
C(4)–O(1)–H(1)–N(1)	−12.32	−16.33

distances between the aziridine nitrogen and the hydroxy hydrogen atom are indicative of the presence of an intramolecular hydrogen bond in both aziridine alcohols **3** and **4**, as shown in Fig. 1. The N–H–O bond angles in **3** and **4** are 132 and 125°, respectively, which are close to the expected average value for a hydrogen bond present in a five-membered ring structure.

Evidence for the presence of a hydrogen bond in molecules **3** and **4** in solution was obtained from temperature dependent ^{1}H NMR experiments in deuteriochloroform. In the 400 MHz ^{1}H NMR spectrum of alcohol **3**, measured at 298 K, the OH hydrogen signal appears at δ 4.438. When the temperature was raised to 315 K this proton signal shifts upfield to δ 4.387 ($\Delta\delta$ = 0.051 ppm), which is an indication of the presence of an intramolecular hydrogen bond at ambient temperature. Similar behaviour was observed for alcohol **4**. When the temperature was raised from 298 K to 315 K the OH proton signal shifts from δ 4.919 to 4.858 ($\Delta\delta$ = 0.061 ppm), implying that an intramolecular hydrogen bond is present at ambient temperature. Saturation of the water signal present in the deuteriochloroform produced a reduction of the OH proton signal, which is indicative of a fast exchange of the hydroxy proton with water.

The results presented here show that the 'one-pot' synthesis of the enantiopure *N*-tritylaziridine esters **1** and **2** has been considerably improved in comparison with Nakajima's two step procedure[10,12–13] and van Boom's 'one-step'-process.[14] X-Ray

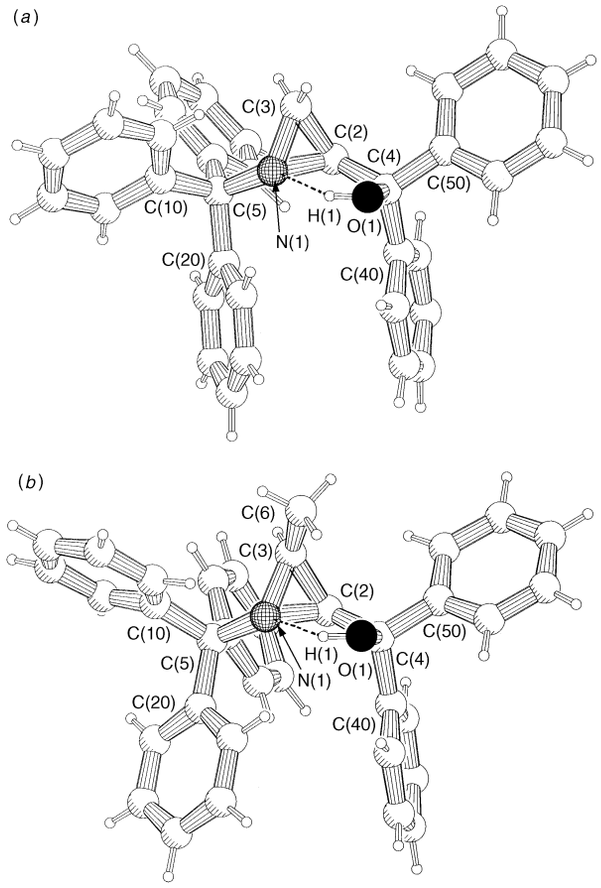


Fig. 1 PLUTON drawings[22] of *N*-trityaziridin-2-ylmethanols (*a*) **3** and (*b*) **4**

analysis reveals that the relative positions of the phenyl rings in the diphenylmethanol unit in **3** and **4** are very similar, whereas the orientation of the phenyl rings of the trityl groups are slightly different. The X-ray analysis, as well as ^{1}H NMR measurements, indicate that in aziridine alcohols **3** and **4** an intramolecular hydrogen bond is present in the crystalline state and in solution.

Experimental

General

Optical rotations were determined with a Perkin-Elmer automatic polarimeter, model 241 MC, using 1% solutions at 20 °C in the solvents indicated. Melting points were determined using a Reichert thermopan microscope equipped with crossed polarisers, and are uncorrected. GLC was conducted with a Hewlett-Packard HP 5890A and HP 5790A gas chromatograph, using a capillary column (25 m) of HP-1 and PAS-1701, a temperature program from 100–250 °C at 10 °C min^{-1} followed by 10 min at 250 °C (isothermal), and nitrogen at 2 ml min^{-1} (0.5 atm) as the carrier gas. The instruments were connected to a HP 3396 or HP 3390 calculating integrator. The enantiomeric purity of aziridine alcohols **3** and **4** was determined by HPLC ¶ using a chiral column with hexane–propan-2-ol (ratio as indicated) as the eluent. The chromatographic system consisted of a Pharmacia LKB (Sweden) model 2150 HPLC pump, a LKB model 2152 HPLC controller and a Rheodyne injector. The injection loop had a 20 μl capacity. The column used was a Daicel Chiralcel OD (250 × 4.6 mm, i.d. 10 μm) from J. T. Baker (Deventer,

¶ The HPLC analysis was performed on the aziridine alcohols **3** and **4** using a Daicel Chiralcel OD column (eluent: hexane–propan-2-ol, 95:5).

The Netherlands). The flow rate was 1.0 ml min^{-1} and the column was operated at ambient temperature. The column effluent was monitored with a LKB model 2138 uvicord S absorbance detector at 254 nm. NMR Spectra (^1H and ^{13}C) were performed on a Bruker AC 100 (100 MHz) or a Bruker AM-400 (400 MHz) spectrometer using solutions in $CDCl_3$ (referenced internally to Me_4Si); *J* values are given in Hz. IR Spectra were determined on a Perkin-Elmer 298 spectrophotometer. FT-IR Spectra were determined on a Biorad WIN-IR FTS-25 spectrophotometer. Elemental analyses were performed on a Carlo Erba Instruments CHNS-O EA 1108 element analyser. Electron impact (EI) and chemical ionisation (CI) mass spectra, induced with methane gas at 200 °C and emission current 0.5 mA, were determined on a VG 7070E spectrometer.

Reagents and solvents. Diethyl ether was pre-dried over calcium chloride, then distilled from calcium hydride. Tetrahydrofuran (THF) was distilled from potassium–benzophenone under Schlenk conditions. Benzene and absolute ethanol (both Merck P.A. quality) were used without further purification. All other solvents were either P.A. or 'reinst' quality. All other reagents are commercially available and were used as received. Unless otherwise stated, yields refer to isolated yields of products of greater than 95% purity as estimated by capillary GC and/or ^1H NMR spectroscopy.

Preparation of methyl aziridine-2-carboxylates 1 and 2

(−)-(2*S*)-Methyl 1-tritylaziridine-2-carboxylate 1. Compound **9** (93.8 g, 259 mmol) was dissolved in THF (700 ml) at room temperature. Triethylamine (83.0 ml, 574 mmol, 2.2 equiv.) was added, followed by gradual addition of methanesulfonyl chloride (20.0 ml, 262 mmol, 1.01 equiv.) over a period of 15 min. The mixture was left for 30 min at 20 °C. The temperature was then raised to 66 °C and the reaction mixture was heated at reflux for 48 h. The reaction was monitored with capillary GLC. After 48 h the reaction mixture was cooled to room temperature and concentrated. Ethyl acetate (300 ml) was then added, followed by extraction with aqueous citric acid (10%) (3 × 100 ml) and saturated aqueous sodium hydrogen carbonate (3 × 50 ml). The combined organic layers were dried ($MgSO_4$) and concentrated to give the product (92.0 g, 100%), which was 95% pure according to capillary GLC [R_F 0.7 (CH_2Cl_2)]. For characterisation purposes, 1 g of this material was recrystallised from MeOH–NEt_3 (50 ml–15 drops) yielding material with a purity of 99.5% according to GLC (the NEt_3 was added to prevent detritylation of the product during the purification procedure); mp 127–129 °C (from MeOH–NEt_3) (Found: C, 80.11; H, 6.23; N, 4.07. Calc. for $C_{23}H_{21}O_2N$: C, 80.44; H, 6.16; N, 4.08%); $[\alpha]_D^{22}$ −86.2 (*c* 1.0, in $CHCl_3$); $[\alpha]_D^{22}$ −96.8 (*c* 1.1, in MeOH); ν_{max}(KBr)/cm^{-1} 3100–3000, 3000–2900, 1740 (C=O) and 1600; δ_H(100 MHz) 7.55–7.21 (15 H, m, Ph_3C), 3.76 (3 H, s, OCH_3), 2.24 (1 H, dd, *J* 1.6 and 2.7, H-3), 1.89 (1 H, dd, *J* 6.2 and 2.7, H-2), 1.40 (1 H, dd, *J* 1.6 and 6.2, H-3); δ_C(25.2 MHz) 171.9, 143.6–127.0, 74.4, 52.1, 31.7, 26.7.

(−)-(2*S*,3*S*)-Methyl 1-trityl-3-methylaziridine-2-carboxylate 2. Using the same procedure as described for **1**, compound **10** (23.4 g, 62.4 mmol) was converted into **2** (22.3 g, 100%) with a purity >95% according to NMR analysis. The reaction was monitored using TLC because the aziridine was not stable under capillary GLC conditions. For characterisation purposes, 1 g of the material thus obtained was recrystallised from MeOH–hexane yielding a clear crystalline compound, mp 112–113 °C (from MeOH–hexane) (Found: C, 80.56; H, 6.42; N, 3.96. Calc. for $C_{24}H_{23}O_2N$: C, 80.64; H, 6.48; N, 3.92%); $[\alpha]_D^{22}$ −97.1 (*c* 1.0, in $CHCl_3$); ν_{max}(KBr)/cm^{-1} 3100–3000 (arom.), 3000–2900 (alkyl), 1740 (C=O), 1600 (arom.); δ_H(100 MHz) 7.58–7.10 (15 H, m, Ph_3C), 3.74 (3 H, s, OCH_3), 1.88 (1 H, d, *J* 6.3, H-2), 1.69–1.56 (1 H, m, H-3), 1.36 (3 H, d, *J* 5.2, CH_3); δ_C(25.2 MHz) 170.7, 143.9, 129.4, 127.9, 127.7, 126.7, 75.1, 51.8, 35.9, 34.6, 13.4.

Preparation of aziridine alcohols 3 and 4 using Grignard reactions

For the Grignard reactions described below all glassware was dried at 140 °C for *ca.* 16 h and flame dried *in vacuo* using a Schlenk apparatus. The magnesium was activated by magnetic stirring overnight under an argon atmosphere.[18] All reactions were carried out under a static pressure of argon.

(−)-(2*S*)-1-Tritylaziridin-2-yl(diphenyl)methanol 3. To a stirred suspension of magnesium turnings (2.52 g, 104 mmol, 3.4 equiv.) in diethyl ether (20 ml) was gradually added bromobenzene (10.8 ml, 103 mmol, 3.4 equiv.) in diethyl ether (15 ml). After heating the Grignard reagent for 1.5 h, compound **1** (10.3 g, 29.9 mmol) in THF (20 ml) was added dropwise over a period of 20 min. The reaction was monitored with capillary GLC and TLC (CH_2Cl_2). After 1.5 h the reaction was quenched with saturated aqueous $(NH_4)_2SO_4$ (30 ml) followed by the evaporation of the organic solvents. The residue was extracted with diethyl ether (3 × 150 ml) and the combined organic layers were dried ($MgSO_4$) and concentrated to give the product (12.9 g, 92%) as a yellow crystalline compound. The crude product was purified by flash column chromatography (hexane–ethyl acetate, 12:1); NEt_3 (1 ml l^{-1}) was added to the eluent to prevent detritylation of the product during the purification procedure. Recrystallisation from MeOH–NEt_3 (50 ml–15 drops) afforded **3** (8.7 g, 62%), mp 133.5–134.5 °C (from MeOH–NEt_3) (Found: C, 87.22; H, 6.26; N, 2.96. Calc. for $C_{34}H_{29}NO$: C, 87.33; H, 6.25; N, 3.00%); $[\alpha]_D^{22}$ −78.8 (*c* 1.0, in $CHCl_3$); ν_{max}(KBr)/cm^{-1} 3500–3300 (OH), 3100–3000 (aromatic), 1600 (aromatic); δ_H(100 MHz) 7.40–7.02 (25 H, m, aromatic H), 4.36 (1 H, s, OH), 2.29 (1 H, dd, *J* 6.3 and 3.2, H-2), 2.00 (1 H, d, *J* 3.2, H-3), 1.25 (1 H, d, *J* 6.3, H-3); δ_C(25.2 MHz) 147.0–125.9, 74.0, 73.9, 41.5, 23.6; *m/z* 390 (0.5%, M − Ph), 243 (100, Ph_3C), 183 (30.4, Ph_2COH), 165 (53.5, Ph_2C), 105 (32.0, PhCO), 91 (8, C_7H_7), 77 (25.6, Ph).

(+)-(2*S*,3*S*)-1-Trityl-3-methylaziridin-2-yl(diphenyl)methanol 4. To a stirred suspension of magnesium turnings (1.49 g, 61.2 mmol, 4 equiv.) in THF (75 ml) was gradually added bromobenzene (6.5 ml, 61.2 mmol, 4 equiv.). After heating the Grignard reagent for 30 min, compound **2** (5.47 g, 15.3 mmol) in THF (25 ml) was added dropwise over a period of 20 min. The reaction was monitored with TLC (hexane–ethyl acetate, 3:1). After 1.5 h the reaction was quenched with saturated aqueous NH_4Cl (50 ml). The crude reaction mixture was extracted with diethyl ether (3 × 100 ml) and the combined organic layers were dried ($MgSO_4$) and concentrated. The crude product was purified by flash column chromatography (hexane–ethyl acetate, 3:1). Recrystallisation from hexane–diethyl ether afforded **4** (5.6 g, 76%), mp 174–175 °C (from hexane–diethyl ether) (Found: C, 87.31; H, 6.68; N, 2.96. Calc. for $C_{35}H_{31}NO$: C, 87.28; H, 6.49; N, 2.91%); $[\alpha]_D^{22}$ +22.5 (*c* 1.0, in $CHCl_3$); ν_{max}(KBr)/cm^{-1} 3500–3300 (OH), 3100–3000 (aromatic), 3000–2900 (alkyl), 1600 (aromatic); δ_H(100 MHz) 7.32–7.02 (25 H, m, aromatic H), 4.95 (1 H, s, OH), 2.22 (1 H, d, *J* 6.3, H-2), 1.68 (1 H, m, H-3), 1.19 (3 H, d, *J* 5.7, CH_3); δ_C(25.2 MHz) 148.6–125.7, 75.3, 73.6, 45.3, 32.0, 13.7; *m/z* 481 (M^+, 0.1%), 243 (100), 183 (37.2, Ph_2COH), 165 (39.8, Ph_2C), 105 (23.5, PhCO), 91 (5, C_7H_7), 77 (14.1, Ph).

X-Ray crystal structure analysis of 3 and 4

(−)-(2*S*)-1-Tritylaziridin-2-yl(diphenyl)methanol 3. $C_{34}H_{29}NO$, $M = 467.58$, orthorhombic, spacegroup $P2_12_12_1$, $a = 8.2743(7)$, $b = 14.9630(11)$, $c = 20.640(2)$ Å, $V = 2555.3$ Å^3, $\lambda = 0.710\,73$ Å, $Z = 4$, $D_x = 1.215\,g\,cm^{-3}$, μ(Mo-Kα) = 0.67 cm^{-1}. A transparent and colourless crystal of dimension 0.25 × 0.42 × 0.54 mm was mounted on a glass fibre and the structure of the aziridine alcohol **3** was determined at 284 K.

Data collection and processing.[19]—CAD4 diffractometer, ω-

mode with ω scan width = 1.5 °, ω scan speed 3.0° min^{-1}; graphite-monochromated Mo-Kα radiation; 29 646 reflections measured ($1.68 < \theta < 29.97°$), ($-11 < h < 11$, $-21 < k < 21$, $-28 < l < 28$), 7438 unique [$R = 0.0575$ after absorption correction (max. and min. transmission factors = 0.986 and 1.013)], giving 4228 with $I > 2\sigma(I)$. Crystal decay *ca.* 1%, corrected during processing. The crystal structure was determined using CRUNCH95.[20] The structure was refined by full-matrix least-squares on F_o^2 values using SHELXL[21] with anisotropic parameters for the non-hydrogen atoms. During the structure determination the configuration of the chiral aziridine carbon C-2 was assumed to be *S*. The hydrogen atoms of the phenyl rings were placed at calculated positions and were subsequently freely refined. All other hydrogen atoms were taken from a difference Fourier map.

(+)-(2*S*,3*S*)-1-Trityl-3-methylaziridin-2-yl(diphenyl)methanol 4. $C_{35}H_{31}NO$, $M = 481.61$, monoclinic, spacegroup $P2_1$, $a = 10.565(2)$, $b = 10.0123(11)$, $c = 12.8568(14)$ Å, $\beta = 97.56(2)$, $V = 1348.2$ Å^3, $\lambda = 0.710\ 73$ Å, $Z = 2$, $D_x = 1.186$ g cm^{-3}, μ(Mo-Kα) = 0.65 cm^{-1}. A transparent and colourless crystal of dimension 0.21 × 0.39 × 0.46 mm was mounted on a glass fibre and the structure of the aziridine alcohol **4** was determined at 208 K.

Data collection and processing.[19]—CAD4 diffractometer, ω-mode with ω scan width = 1.5 °, ω scan speed 3.0° min^{-1}; graphite-monochromated Mo-Kα radiation; 9452 reflections measured ($1.60 < \theta < 24.97°$), ($-12 < h < 12$, $-11 < k < 11$, $-15 < l < 15$), 4727 unique [$R = 0.0441$ after absorption correction (max. and min. transmission factors = 0.968 and 1.026)], giving 3369 with $I > 2\sigma(I)$. Crystal decay *ca.* 3%, corrected during processing. The crystal structure was determined using a similar procedure to that described for **3**. During the structure determination the configuration of the chiral aziridine carbons C-2 and C-3 were both assumed to be *S*. The hydrogen atoms of the methyl group were obtained by rotation of an idealised methyl group to match maximum electron density in a difference Fourier synthesis.

Atomic coordinates, thermal parameters and bond lengths and angles have been deposited at the Cambridge Crystallographic Data Centre (CCDC). See Instructions for Authors, *J. Chem. Soc., Perkin Trans. 1*, 1997, Issue 1. Any request to the CCDC for this material should quote the full literature citation and the reference number 207/87.

Acknowledgements

We are grateful to DSM Research (Geleen, the Netherlands) for their financial support.

References

1 (*a*) J. A. Deyrup, in *Small Ring Heterocycles*, ed. A. Hassner, Wiley Interscience, New York, Part 1, 1983; (*b*) M. Bartok and K. L. Lang, in *Small Ring Heterocycles*, ed. A. Hassner, Wiley Interscience, New York, Part 3, 1985.
2 (*a*) K. Sato and A. P. Kozikowski, *Tetrahedron Lett.*, 1989, **30**, 4073; (*b*) J. E. Baldwin, R. M. Adlington and N. G. Robinson, *J. Chem. Soc., Chem. Commun.*, 1987, 153; (*c*) K. Okawa and K. Nakajima, *Biopolymers*, 1981, **20**, 1811.
3 (*a*) T. Tanaka, K. Nakajima and K. Okawa, *Bull. Chem. Soc. Jpn.*, 1980, **53**, 1352; (*b*) G. Cainelli and M. Panunzio, *Tetrahedron Lett.*, 1991, **32**, 121.
4 (*a*) F. Gerhart, W. Higgins, C. Tardif and J. B. Ducep, *J. Med. Chem.*, 1990, **33**, 2157; (*b*) D. Tanner, *Angew. Chem., Int. Ed. Engl.*, 1994, **33**, 599.
5 (*a*) P. G. Andersson, A. Harden, D. Tanner and P-O. Norrby, *Chem. Eur. J.*, 1995, **1**, 12; (*b*) J. G. H. Willems, J. G. de Vries, R. J. M. Nolte and B. Zwanenburg, *Tetrahedron Lett.*, 1995, **36**, 3917; (*c*) J. G. H. Willems, F. J. Dommerholt, J. B. Hamink, A. M. Vaarhorst, L. Thijs and B. Zwanenburg, *Tetrahedron Lett.*, 1995, **36**, 603; (*d*) D. Tanner, P. G. Andersson, A. Harden and P. Somfai, *Tetrahedron Lett.*, 1994, **35**, 4631.
6 (*a*) J. M. Lemmens, W. W. J. M. Blommerde, L. Thijs and B. Zwanenburg, *J. Org. Chem.*, 1984, **49**, 2231; (*b*) L. Thijs, F. J. Dommerholt, F. M. C. Leemhuis and B. Zwanenburg, *Tetrahedron Lett.*, 1990, **31**, 6589; (*c*) F. M. C. Leemhuis, L. Thijs and B. Zwanenburg, *J. Org. Chem.*, 1993, **58**, 7172.
7 (*a*) J. Legters, L. Thijs and B. Zwanenburg, *Tetrahedron Lett.*, 1989, **30**, 4881; (*b*) L. Thijs, J. J. M. Porskamp, A. A. W. M. van Loon, M. P. W. Derks, R. W. Feenstra, J. Legters and B. Zwanenburg, *Tetrahedron*, 1990, **46**, 2611; (*c*) J. Legters, L. Thijs and B. Zwanenburg, *Tetrahedron*, 1991, **47**, 5287; (*d*) J. Legters, L. Thijs and B. Zwanenburg, *Recl. Trav. Chim. Pays-Bas*, 1992, **111**, 16; (*e*) J. Legters, J. G. H. Willems, L. Thijs and B. Zwanenburg, *Recl. Trav. Chim. Pays-Bas*, 1992, **111**, 59; (*f*) J. Legters, L. Thijs and B. Zwanenburg, *Recl. Trav. Chim. Pays-Bas*, 1992, **111**, 75; (*g*) J. Legters, L. Thijs and B. Zwanenburg, *Recl. Trav. Chim. Pays-Bas*, 1992, **111**, 211.
8 (*a*) For a review, see K. Okawa, K. Nakajima and T. Tanaka, *J. Synth. Org. Chem. Jpn.*, 1984, **42**, 390; (*b*) J. E. G. Kemp, in *Comprehensive Organic Synthesis*, ed. B. M. Trost and I. Fleming, Pergamon, Oxford, 1991, vol 7, p. 469.
9 J. W. Kelly, N. L. Eskew and S. A. Evans, Jr., *J. Org. Chem.*, 1986, **51**, 95.
10 Y. Nakagawa, T. Tsuno, K. Nakajima, M. Iwai and H. Kawai, *Bull. Chem. Soc. Jpn.*, 1972, **45**, 1162.
11 H. Wenker, *J. Am. Chem. Soc.*, 1935, **57**, 2328.
12 K. Nakajima, F. Takai, T. Tanaka and K. Okawa, *Bull. Chem. Soc. Jpn.*, 1978, **51**, 1577.
13 T. Wakamiya, K. Shimbo, T. Shiba, K. Nakajima, M. Neya and K. Okawa, *Bull. Chem. Soc. Jpn.*, 1982, **55**, 3878.
14 E. Kuyl-Yeheskiely, M. Lodder, G. A. van der Marel and J. H. van Boom, *Tetrahedron Lett.*, 1992, **33**, 3013.
15 A. Korn, S. Rudolph-Böhner, L. Moroder and W. Hiller, *Z. Naturforsch., Teil B*, 1993, **48**, 1146.
16 A. Korn, S. Rudolph-Böhner and L. Moroder, *Tetrahedron*, 1994, **50**, 1717.
17 A. F. Mishnev, M. F. Bundule, Ya Ya. Bleidelis, A. V. Eremeev and F. D. Polyak, *Zh. Strukt. Khim.*, 1983, **26**, 159.
18 K. V. Baker, J. M. Brown, N. Hughes, A. J. Skarnulis and A. Sexton, *J. Org. Chem.*, 1991, **56**, 698.
19 J. M. M. Smits, H. Behm, W. P. Bosman and P. T. Beurskens, *J. Crystallogr. Spectrosc. Res.*, 1988, **18**, 447.
20 R. de Gelder, R. A. G. de Graaff and H. Schenk, *Acta Crystallogr., Sect. A*, 1993, **49**, 287.
21 G. M. Sheldrick, SHELXL93, A Program for the Refinement of Crystal Structures, University of Göttingen, Germany, 1993.
22 A. L. Spek, PLUTON, Department of Crystallography and Structural Chemistry, University of Utrecht, 1995.

Paper 6/03801H
Received 31*st May* 1996
Accepted 13*th November* 1996