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SYNTHESIS OF ALL FOUR HOMOCHIRAL STEREOISOMERS OF METHYL 3-PHENYL-1H-AZIRIDINE-2-CARBOXYLATE

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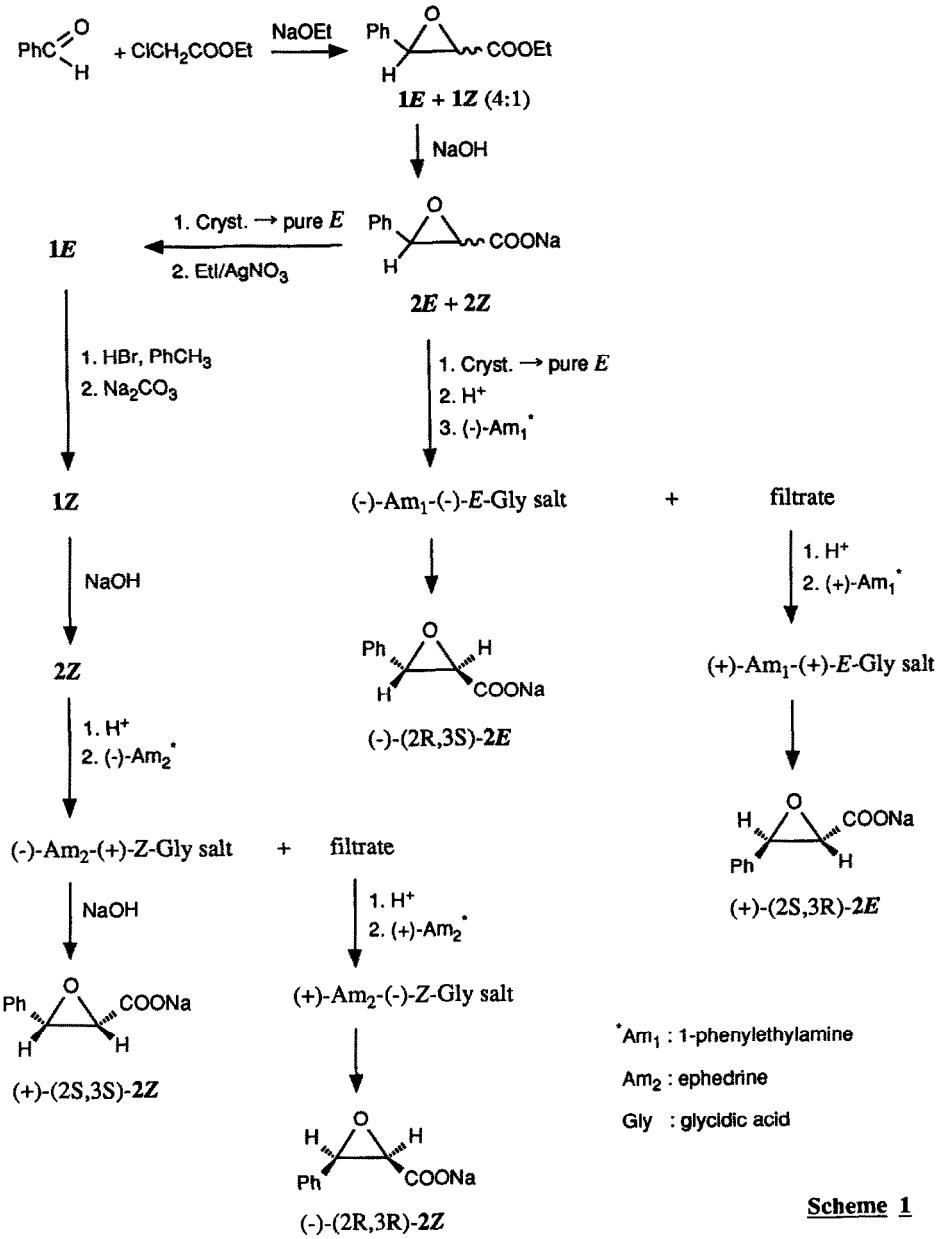
Summary: Sodium *E*-3-phenylglycidate (±)-**2*E*** was prepared using the Darzens' procedure. Classical resolution with 1-phenylethylamine afforded optically pure salts (+)-(2S,3R)-**2*E*** and (-)-(2R,3S)-**2*E***. Alternatively, (±)-**2*E*** was converted into (±)-**2*Z*** by ring opening of ethyl ester (±)-**1*E*** with hydrogen bromide, followed by recyclization and saponification. Classical resolution of (±)-**2*Z*** with ephedrine afforded optically pure salts (+)-(2S,3S)-**2*Z*** and (-)-(2R,3R)-**2*Z***. Treatment of the four sodium salts with sodium azide followed by esterification gave hydroxy azido esters **3**, which were finally converted into the four homochiral stereoisomers of methyl 3-phenyl-1H-aziridine-2-carboxylate **5** in a reaction with triphenylphosphine and subsequent heating of the initially formed oxazaphospholidines **4**.

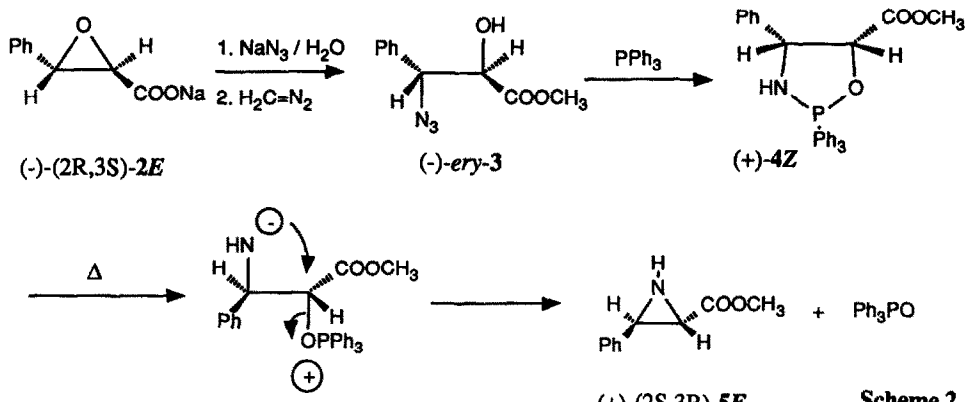
Aziridine-2-carboxylates are interesting compounds in view of their structural relationship with α- as well as β-amino acids and the intrinsic high reactivity of the three-membered ring. Although there is an extensive literature on aziridines in general[1], their carboxylic acids received limited attention[2]. Most of the reported syntheses of aziridine-2-carboxylates lead to N-substituted compounds; only scarce mention is made of N-unsubstituted examples[3].

In this paper we wish to report the preparation of all four enantiomers of methyl 3-phenyl-1H-aziridine-2-carboxylates, the formal analogs of phenylalanine, from the corresponding oxiranecarboxylates. In essence, the method of synthesis is adopted from the conversion of non-functionalized epoxides into the corresponding aziridines, *viz.* nucleophilic opening of the oxirane by azide ions to produce azido alcohols and subsequent ring closure by treatment with triphenylphosphine (the Staudinger reaction[4]).

Ethyl phenylglycidate **1** was prepared using the Darzens' procedure. The product obtained consisted of a mixture of isomers (**1*E*** : **1*Z*** = 4 : 1). After saponification, one crystallization of the sodium salt gave pure *E* derivative **2*E***. Classical resolution of **2*E*** was performed according to Harada[5] using 1-phenylethylamine as resolving agent (Scheme 1). The optically pure salts (+)-(2S,3R)-**2*E*** and (-)-(2R,3S)-**2*E*** were obtained in good


PhC(=O)H + ClCH2COOEt
NaOEt
Ph
COOEt
1E + 1Z (4:1)
NaOH
1. Cryst. → pure E
2. EtI/AgNO3
1E
Ph
COONa
2E + 2Z
1. HBr, PhCH3
2. Na2CO3
1. Cryst. → pure E
2. H+
3. (-)-Am1*
1Z
(-)-Am1-(-)-E-Gly salt
+
filtrate
NaOH
1. H+
2. (+)-Am1*
2Z
(+)-Am1-(+)-E-Gly salt
1. H+
2. (-)-Am2*
(-)-(2R,3S)-2E
(-)-Am2-(+)-Z-Gly salt
+
filtrate
NaOH
1. H+
2. (+)-Am2*
(+)-(2S,3S)-2Z
(+)-Am2-(-)-Z-Gly salt
(+)-(2S,3R)-2E
(-)-(2R,3R)-2Z
*Am1 : 1-phenylethylamine
Am2 : ephedrine
Gly : glycidic acid

Scheme 1



Scheme 2

yields.

Transformation of the *E*-isomer into the *Z*-isomer was accomplished as reported by Harada[6]. The sodium salts **2Z** were resolved using ephedrine as the resolving agent[6], furnishing the optically pure salts (-)-(2R,3R)-**2Z** and (+)-(2S,3S)-**2Z** (Scheme 1).

The respective homochiral sodium phenylglycidates were treated with an aqueous solution of sodium azide which resulted in the exclusive opening of the epoxide at the 3-position in high yield. The thus obtained hydroxy azido carboxylic acids were converted into the corresponding methyl esters **3** by treatment with diazomethane.

The hydroxy azido esters **3** smoothly reacted with triphenylphosphine in acetonitrile under evolution of nitrogen. The thus formed oxazaphospholidines **4** precipitated in most cases from the reaction mixture (Scheme 2). These products **4** were sufficiently pure for further conversions. A small amount of (±)-**4Z** was recrystallized for X-ray analysis (see experimental). Heating of the compounds **4** in a short-path distillation apparatus (Kugelrohr) at low pressure gave the methyl aziridinecarboxylates **5** in satisfactory to moderate yields[7] (Table 1). The optical purity of the aziridine esters **5** was determined by ^{19}F-NMR of the Mosher derivatives. The e.e. values exceed 95% in all cases[8].

The absolute configuration of the thus produced optically active aziridine esters **5** is opposite to that of the corresponding oxiranecarboxylates because an inversion has taken place at each carbon atom of the three-membered ring. During the ring opening of the oxirane with the azide ion an inversion takes place at the site of attack, *i.e.* the 3-position[9]. This stereochemical course was unambiguously proven by the X-ray diffraction analysis of oxazaphospholidine (±)-**4Z**[10] (figure 1), which revealed that the phenyl group and the methoxycarbonyl group have a *cis* relationship, whilst in the starting material for this compound, *i.e.* sodium *E*-phenylglycidate (±)-**2E**, these substituents are in a *trans* position. This particular oxazaphospholidine gave on heating the *trans* aziridine ester (±)-**5E**, implying that during this ring closure a second inversion has taken place.

The stereochemical relationship of the hydrogen atoms at the three-membered ring could not easily be deduced from the ^{1}H-NMR spectra because almost no splitting pattern was observed. However, the

Table 1

5	m.p. (°C)	$[\alpha]_D^{20}$ (c=1, EtOH)	e.e. (%)	Yield (%)
rac. *E*	oil			65
rac. *Z*	65-76[11]			60
(+) *E* (2S,3R)	oil	+262.1	>95	63
(-) *E*	oil	-263.4	>95	66
(+) *Z*	51-57	+21.9	>95	26
(-) *Z*	50-56	-21.1	>95	20

N-*p*-phenylbenzoyl derivatives of (±)-**5*Z***, (-)-**5*E***, and (+)-**5*E*** showed a much better resolved ^{1}H-NMR spectrum for these vicinal protons. The coupling constants (^{3}J) of 6.0 Hz and 2.2 Hz for the *Z* and *E* derivatives, respectively, are in excellent agreement with assigned stereochemical structures. The Mosher derivatives used for e.e. determination also allowed the determination of the coupling constants, *viz.* 6.3 Hz and 1.8 Hz for the *Z* and *E* compounds, respectively.

It is of interest to note that the (+)-*E* oxirane ester is converted into the (-)-*E* aziridine ester and that the (+)-*Z* epoxy ester gives the (-)-*Z* aziridine. The same inversion of sign of optical rotation was observed for the conversion of the (-)-*E* and (-)-*Z* oxirane esters into the corresponding aziridine esters. This is an additional support of a two-fold inversion process.

Experimental

^{1}H-NMR spectra were recorded on a Varian EM-390 spectrometer with tetramethylsilane as internal standard. ^{19}F-NMR spectra were taken on a Nicolet NT 200 spectrometer by Mr. A. Wagenaar (University of Groningen, The Netherlands), with $CFCl_3$ as internal standard. IR spectra were run on a Perkin-Elmer 257 grating spectrometer. Mass spectra were measured on a double-focussing VG 7070E spectrometer by P. M. van Galen, M.M.M. Broekman and P.W.M. Wijers. Reaction products were checked for purity with a Hewlett-Packard 5790 or 5890 gas chromatograph on capillary cross-linked methyl silicone columns (25 m). Flash chromatography using Kieselgel 60H (Merck) was applied for the purification of the products. Microanalyses were performed by Mr. P.M. van Galen.

Ethyl 3-phenyl-oxirane-2-carboxylate (±)-**1** (***E*** + ***Z***).

Freshly prepared sodium ethoxide (107 g, 1.57 mol) was added to a cooled solution (ice-salt) of freshly distilled benzaldehyde (166 g, 1.57 mol) and ethyl chloroacetate (192 g, 1.57 mol) in dry diethyl ether (1200 ml) in such portions that the temperature did not exceed 0°C. During the reaction the mixture was kept under nitrogen. After the addition was completed the reaction mixture was stirred at room temperature for 18 h. The

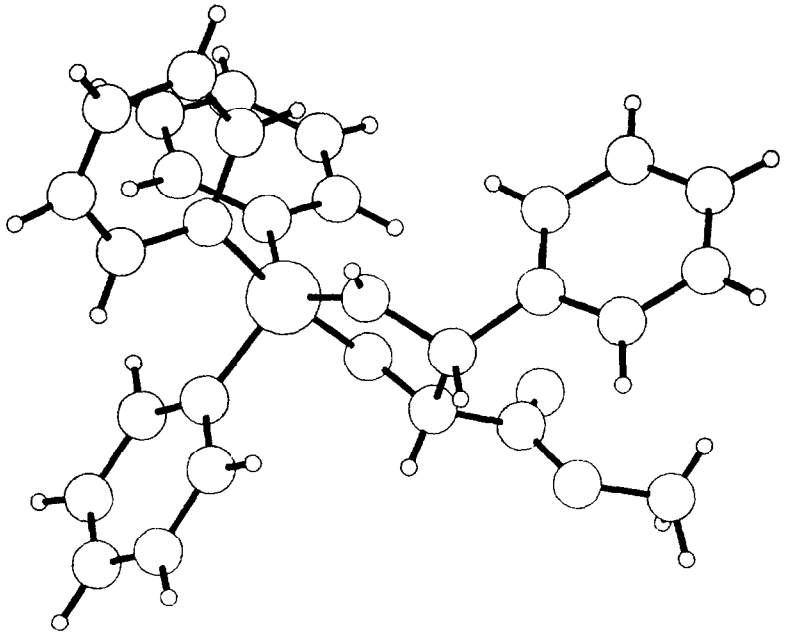


Figure 1: X-ray minimum overlap view of oxazaphospholidine (±)-4Z[10].

solvent was then removed in vacuo, the residue was suspended in ether and then poured into ice-water containing a few ml of acetic acid. The organic layer was separated and the aqueous layer was twice extracted with ether. The combined organic layers were washed with saturated bicarbonate soln (2x) followed by water. After drying ($MgSO_4$) and evaporation of the solvent distillation gave the glycidic ester (217 g, 72% yield, bp 102-103°C/0.9 torr). According to GLC this was a mixture of **1*E*** and **1*Z*** in the ratio of 4:1.

Sodium E-*3-phenyl oxirane-2-carboxylate* (±)-**2*E***.

The *E* + *Z* mixture from the aforementioned experiment (215 g, 1.12 mol) was added to a "solution" of sodium (26.1 g, 1.12 mol) in abs. ethanol (900 ml). After 5 min. water (20.2 g, 1.12 mol) was added. A white solid precipitated immediately. Diethyl ether (500 ml) was added and the mixture was stirred overnight. Filtration and washing with ether gave the sodium salt (208 g, 84%). Recrystallization from EtOH/H_2O with work-up of the mother liquor gave the sodium salt (79%) containing a minor amount of water that could be removed by drying in a vacuum-oven. For further experimentation the undried material was used.

NMR (D_2O) δ 3.71 (d, 1H, J = 2 Hz), 4.13 (d, 1H, J = 2 Hz), 4.88 (H_2O), 7.52 (m, 5H) ppm.

IR (KBr) ν CO 1620 cm^{-1}.

Ethyl E-*3-phenyl oxirane-2-carboxylate* (±)-**1*E***.

A solution of silver nitrate (36.5 g, 215 mmol) in water (300 ml) was added to a soln of the sodium salt **2*E*** (40.0 g, 215 mmol) in water (300 ml). A white precipitate formed immediately which was filtered off after 15

min. The solid was washed with water, methanol and ether. The yield was 54 g, 93%, mp 182°C (dec). This salt was suspended in ether (200 ml), and then ethyl iodide (200 ml) was added and the mixture was heated under reflux for 3 h. After filtration of the silver iodide the filtrate was concentrated, giving (±)-**1*E*** (38.2 g, 93%) with a purity of >99%, according to GLC.
NMR (CCl_4) δ 1.28 (t, 3H, J = 7 Hz), 3.26 (d, 1H, J = 2 Hz), 3.94 (d, 1H, J = 2 Hz), 4.18 (q, 2H, J = 7 Hz), 7.21 (m, 5H) ppm.
IR (neat) ν CO 1740 cm^{-1}.

*Ethyl Z-3-phenyl oxirane-2-carboxylate (±)-***1Z**.
A stream of hydrogen bromide was passed through a soln of epoxy ester (±)-**1*E*** (38.2 g, 199 mmol) in toluene (200 ml) for 8 h. The solvent was evaporated and the solid residue was washed with hexane. Recrystallization (hexane/CCl_4) gave 32.6 g of ring-opened product (60%, mp 90-96°C, lit.[5] 96-97°C), NMR ($CDCl_3$) δ 1.34 (t, 3H, J = 7.5 Hz), 3.45 (s, 1H), 4.31 (q, 2H, J = 7.5 Hz), 4.46 (d, 1H, J = 3 Hz), 5.39 (d, 1H, J = 3 Hz), 7.34 (m, 3H), 7.58 (m, 2H) ppm, which was suspended in a mixture of water (170 ml), acetone (14 ml) and sodium carbonate (12.6 g, 119 mmol) and kept at 50°C. Some more acetone (15 ml) and sodium carbonate (2.0 g) were needed to dissolve all solid material. The *Z*-ester separated as an oil. After 3.5 h the mixture was extracted with ether (3x). Drying ($MgSO_4$) and evaporation of the solvent gave the *Z*-epoxy ester (±)-**1Z** as a light-yellow oil (20.1 g, 90%). The yield calculated on *E*-epoxy ester amounted to 54%.
NMR (CCl_4) δ 0.92 (t, 3H, J = 7.5 Hz), 3.58 (d, 1H, J = 5 Hz), 3.85 (q, 2H, J = 7.5 Hz), 4.06 (d, 1H, J = 5 Hz), 7.21 (m, 5H) ppm.
IR (neat) ν CO 1750 cm^{-1}.

Sodium Z-3-phenyl oxirane-2-carboxylate (±)-**2Z**.
The *Z*-ester (79.8 g, 0.416 mol) was added to a "solution" of sodium (9.56 g, 0.416 mol) in EtOH (500 ml). After adding water (7.48 g, 0.416 mol) the sodium salt soon separated. Ether was added (100 ml) and the salt was filtered off and washed with ether. Yield of (±)-**2Z** 71.2 g (92%).
NMR (D_2O) δ 3.77 (d, 1H, J = 5 Hz),4.24 (d, 1H, J = 5 Hz), 4.66 (H_2O), 7.34 (m, 5H) ppm.
IR (KBr) ν CO 1620 cm^{-1}.

Resolution of racemic sodium E-*3-phenyl-oxirane-2-carboxylate (±)-***2*E*** in (2R,3S)-(-)-**2*E*** and (2S,3R)-(+)-**2*E***.
Ether (160 ml) and hydrochloric acid soln (161 ml, 1.0 molar) were added to a solution of rac *E* sodium salt (±)-**2*E*** (30 g, 161 mmol) in water (400 ml). After brief shaking the ether layer was separated and the aqueous layer extracted two more times with ether (100 ml). After drying (Na_2SO_4) and filtration *l*-α-phenylethylamine (19.5 g, 161 mmol) was added. Soon an oil separated that was forced to crystallize by scratching with a glass rod. After standing for 2 h the precipitate was filtered off and the filtrate was used for the next separation *(vide infra)*. The precipitate was washed with acetone, leaving 23.0 g (80 mmol) of ammonium salt with $[\alpha]_D^{20}$ = -119° [c = 1, EtOH]. Recrystallization from acetone/EtOH (120/110 ml) gave, with work-up of the mother liquor, the ammonium salt (-)-Am_1-(-)-*E*-Gly salt (18.5 g, 40%), mp 154-157°C, $[\alpha]_D^{20}$ = -124.7° [c = 1, EtOH]. Lit.[5] mp 161-162°C (dec), $[\alpha]_D^{25}$ = -125.4° [c = 1, EtOH]
To the above mentioned filtrate ice-water (200 ml) and hydrochloric acid soln (80.5 ml, 1N) were added. After extraction with ether (3x100 ml) the soln was dried over Na_2SO_4, filtered and treated with

d-α-phenylethylamine (9.74 g, 80.5 mmol). Crystallization of the ammonium salt started immediately. Filtration and washing with acetone yielded 22.0 g of product. Recrystallization from acetone/EtOH (120/110 ml) gave the ammonium salt (+)-Am_1-(+)-*E*-Gly salt (17.5 g, 38%), mp 156-158°C, $[\alpha]_D^{20}$ = +125° [c = 1, EtOH]. Lit.[5] mp 161-162°C (dec), $[\alpha]_D^{25}$ = +125.5° [c = 0.96, EtOH].

The sodium glycidates were prepared from the above prepared ammonium salts by adding exactly one equivalent of sodium hydroxide to an aqueous soln of the ammonium glycidates. The amine was then extracted with ether and the aqueous soln was evaporated to dryness. The sodium salts were dried over P_2O_5 in a desiccator for three days but then still some traces of water remained. (-)-Am_1-(-)-*E*-Gly salt thus gave (-)-(2R,3S)-**2*E*** (13.2 g, 40% from (±)-**2*E***), $[\alpha]_D^{20}$ = -142.6° [c = 1, H_2O]. From (+)-Am_1-(+)-*E*-Gly salt (+)-(2S,3R)-**2*E*** (11.8 g, 35%) was obtained, $[\alpha]_D^{20}$ = +151.5° [c = 1, H_2O].

NMR as for (±)-2 E. IR (KBr) ν CO 1600 cm^{-1}.

Resolution of sodium Z-*3-phenyl-oxirane-2-carboxylate (±)-2Z* in *(2S,3S)*-(+)-**2Z** and *(2R,3R)*-(-)-**2Z**.

Ether (130 ml) and hydrochloric acid (134 ml, 1 molar) were added to a solution of rac Z sodium salt (±)-**2Z** (25.0 g, 134 mmol) in water (200 ml). After brief shaking the layers were separated and the aqueous layer was extracted with ether (2 x 130 ml). The combined ether extracts were dried (Na_2SO_4) at 4°C, filtered and treated with *l*-ephedrine (22.21 g, 134.4 mmol) in ether (66 ml). Crystallization commenced in 15 min. The mixture was left overnight and then the ether was evaporated. The residue was triturated with acetone (100 ml). Filtration gave 17.19 g (39%) of crude ammonium salt (mp 137-142°C). Recrystallization from EtOH resulted in pure (-)-Am_2-(+)-*Z*-Gly salt (12.70 g, 29%), mp 143-146°C, $[\alpha]_D^{20}$ = -28.3° [c = 1.5, EtOH], lit.[6] mp 145-146°C, $[\alpha]_D^{25}$ = -27.7° [c = 2.77, EtOH].

The filtrate of the crude ammonium salt was concentrated in vacuo to give a thick syrupy oil, containing a calculated amount of 82 mmoles of ammonium salt. Water (210 ml) and some ice were added followed by the calculated amount of sulfuric acid in water (75 ml) and ether (70 ml). After vigorous stirring for 10 min the oil had dissolved. The two-phase system was separated and the aqueous layer was extracted with ether (2 x 70 ml). The combined ether extracts were dried over Na_2SO_4 at 4°C, and after filtration *d*-ephedrine (13.56 g, 82 mmol) in ether (40 ml) was added. Crystallization started immediately. Standing overnight gave the crude ammonium salt (16.09 g, 36%). Recrystallization from EtOH gave pure (+)-Am_2-(-)-*Z*-Gly (13.13 g, 30%), mp 143-145°C, $[\alpha]_D^{20}$ = +27.9° [c = 1.5, EtOH].

The ammonium salts were converted into the sodium salts. A solution of the (-)-ammonium salt (12.55 g, 38 mmol) in water (130 ml) with some ice was stirred while adding ether (80 ml) and NaOH (38.12 ml, 1N). After 30 min the layers were separated and the aqueous layer was concentrated to give an oil consisting of some ephedrine and the desired sodium salt. This residue was triturated with acetone. Filtration and washing with acetone gave the sodium salt (+)-(2S,3S)-**2Z** (6.35 g, 90%), $[\alpha]_D^{20}$ = +5.7° [c = 1, EtOH]. NMR as for the racemic compound. IR (KBr) ν CO 1620 cm^{-1}.

The (+)-Am_2-(-)-*Z*-Gly salt (12.97 g, 39.39 mmol) gave in the same manner the sodium salt (-)-(2R,3R)-**2Z** (6.65 g, 91%). NMR as for the racemic salt. IR (KBr) ν CO 1620 cm^{-1}.

Methyl (2S,3S*)-2-hydroxy-3-azido-3-phenyl-propionate* (±)-*ery*-**3. General procedure.**

A soln of sodium glycidate (±)-**2*E*** (2.0 g, 11 mmol) and sodium azide (3.7 g, 56 mmol) in water (50 ml) was stirred at 70°C for 24 h. After cooling the reaction mixture was acidified to pH 4 and extracted with ether. The

pH was again adjusted to 4 and the extraction repeated. This procedure was continued until the pH remained constant. The ether extracts were dried over $MgSO_4$. After filtration and concentration of the filtrate diazomethane in ether was added. After 30 min excess diazomethane was removed with a stream of nitrogen. Removal of solvent gave a residue which was subjected to flash chromatography (EtOAc/hexane 1:3) to give the desired product as a colorless oil (2.0 g, 90%).
NMR ($CDCl_3$) δ 2.9 (br s, 1H), 3.66 (s, 3H), 4.50 (d, 1H, J = 4.5 Hz), 4.86 (d, 1H, J = 4,5 Hz), 7.33 (m, 5H) ppm.
IR (neat) ν OH 3520 cm^{-1}, ν N_3 2100 cm^{-1}, ν CO 1740 cm^{-1}.

Methyl (2R,3S*)-2-hydroxy-3-azido-3-phenyl-propionate* (±)-*thr*-**3**.
Following the general procedure sodium glycidate (±)-**2Z** (5.0 g, 26.9 mmol) and sodium azide (8.74 g, 134 mmol) gave, after chromatography (EtOAc/hexane 4:1), 5.23 gr (88%) of compound (±)-*thr*-**3**, which slowly crystallized on standing at low temperature.
NMR (CCl_4) δ 3.2 (br s, 1H), 3.73 (s, 3H), 4.26 (d, 1H, J = 3 Hz), 4.66 (d, 1H, J = 3 Hz), 7.35 (m, 5H) ppm.
IR (CCl_4) ν OH 3520 cm^{-1}, ν N_3 2110 cm^{-1}, ν CO 1740 cm^{-1}.

Methyl (2S,3S)-(+)-2-hydroxy-3-azido-3-phenyl-propionate (+)-*ery*-**3**.
This compound was obtained from sodium glycidate (+)-**2*E*** in a yield of 89%, after chromatography; mp 42.5-44.5°C, $[\alpha]_D^{20}$ = +106° [c = 1, EtOH]. Found C 54.18, H 5.00, N 18.80 %, calc for $C_{10}H_{11}N_3O_3$ (221.217) C 54.30, H 5.01, N 18.99 %.
NMR (CCl_4) δ 3.13 (br s, 1H), 3.59 (s, 3H), 4.37 (d, 1H, J = 5 Hz), 4.72 (d, 1H, J = 5 Hz), 7.26 (m, 5H) ppm.
IR (KBr) ν OH 3360 cm^{-1},ν N_3 2110 cm^{-1}, ν CO 1730 cm^{-1}.

Methyl (2R,3R)-(-)-2-hydroxy-3-azido-3-phenyl-propionate (-)-*ery*-**3**.
This compound was obtained from sodium glycidate (-)-**2*E*** in a yield of 78%, after chromatography; mp 44-45°C, $[\alpha]_D^{20}$ = -106.7° [c = 1, EtOH]. Found C 54.26, H 5.02, N 18.78 %, calc for $C_{10}H_{11}N_3O_3$ (221.217) C 54.30, H 5.01, N 18.99 %.
NMR and IR as for (+)-*ery*-**3**.

Methyl (2S,3R)-(-)-2-hydroxy-3-azido-3-phenyl-propionate (-)-*thr*-**3**.
This compound was obtained from sodium glycidate (+)-**2Z** in a yield of 57%, after chromatography; mp 54-56°C, $[\alpha]_D^{20}$ = -113° [c = 1, EtOH].
NMR (CCl_4) δ 3.24 (br s, 1H), 3.76 (s, 3H), 4.33 (d, 1H, J = 3 Hz), 4.73 (d, 1H, J = 3 Hz), 7.39 (m, 5H) ppm.
IR (KBr) ν OH 3500 cm^{-1}, ν N_3 2100 cm^{-1}, ν CO 1730 cm^{-1}.

Methyl (2R,3S)-(+)-2-hydroxy-3-azido-3-phenyl-propionate (+)-*thr*-**3**[9].
This compound was obtained from sodium glycidate (-)-**2Z** in a yield of 84%, after chromatography, mp 55-56°C, $[\alpha]_D^{20}$ = +114.7° (c = 1, EtOH], $[\alpha]_D^{20}$ = +142.8° [c = 1, $CHCl_3$]. Found : C 53.82, H 4.99, N 18.45 %, calc for $C_{10}H_{11}N_3O_3$ (221.217) C 54.30, H 5.01, N 18.99 %.
NMR and IR as for (-)-*thr*-**3**.

Cis (4S,5S*)-2,2,2,4-tetraphenyl-5-methoxycarbonyl-1,3,2-oxazaphospholidine* (±)-**4Z**.
Triphenylphosphine (1.97 g, 7.5 mmol) was added to a solution of rac hydroxy azido propionate (±)-*ery*-**3** (1.12 g, 5 mmol) in ether. The crystallization of oxazaphospholidine started after 15 min. The mixture was stirred for 24 h at room temp, the precipitate was then filtered off and washed with ether (yield 1.89 g, 80%). A small amount was crystallized from acetonitrile to give an analytically pure sample (mp 169-170°C). Found : C 73.27, H 5.85, N 2.99 %, calc. for $C_{28}H_{26}NO_3P$ (455.494) C 73.83, H 5.75, N 3.08 %. Mass spectrum (CI), m/e 456 (M^+ + 1), 279 (Ph_3P=O + 1), 178 (aziridine + 1).
^{1}H-NMR gave only broad unresolved peaks. IR (KBr) ν NH 3440 cm^{-1}, ν CO 1760 cm^{-1}.

Trans (4S,5R*)-2,2,2,4-tetraphenyl-5-methoxycarbonyl-1,3,2-oxazaphospholidine* (±)-**4E**. **General procedure.**
Triphenylphosphine (4.49 g, 17.2 mmol) was added to a solution of rac hydroxy azido propionate (±)-*thr*-**3** (3.77 g, 17.1 mmol) in acetonitrile (17 ml), while cooling with ice-water. The evolution of nitrogen began immediately and a precipitate was formed after 30 min. After one hour the precipitate was filtered off and washed with ether. Yield 4.77 g (61%), mp 80-108°C. This material was sufficiently pure for further experiments.
IR (KBr) ν NH 3450 cm^{-1}, ν CO 1745 cm^{-1}.

Cis (4S,5S)-2,2,2,4-tetraphenyl-5-methoxycarbonyl-1,3,2-oxazaphospholidine (-)-**4Z**.
Compound (-)-**4Z** was prepared from hydroxy azido propionate (+)-*ery*-**3** in a yield of 81 %, mp 120-145°C, $[\alpha]_D^{20}$ = -65° [c = 1, $CHCl_3$].
Mass spectrum m/e 456 (M^+ + 1), 279 (Ph_3P=O + 1), 178 (aziridine + 1). Found: C 74.78, H 5.82, N 2.67 %, calc for $C_{28}H_{26}NO_3P$ (455.490) C 73.83, H 5.75, N 3.08 %.

Cis (4R,5R)-2,2,2,4-tetraphenyl-5-methoxycarbonyl-1,3,2-oxazaphospholidine (+)-**4Z**.
Hydroxy azido propionate (-)-*ery*-**3** furnished (+)-**4Z** in a yield of 78 %, mp 120-145°C, $[\alpha]_D^{20}$ = +58° [c = 1, $CHCl_3$]. Found : C 73.82, H 5.85, N 3.01 %, calc for $C_{28}H_{26}NO_3P$ (455.490) C 73.83, H 5.75, N 3.08 %.

Trans (4S,5R)- 2,2,2,4-tetraphenyl-5-methoxycarbonyl-1,3,2-oxazaphospholidine $\mathbf{4E}_a$ and *trans (4R,5S)-2,2,2,4-tetraphenyl-5-methoxycarbonyl-1,3,2-oxazaphospholidine* $\mathbf{4E}_b$.
These compounds were prepared from hydroxy azido propionates (-)-*thr*-**3** and (+)-*thr*-**3**, respectively, following the general procedure. The oily products did not crystallize; the material obtained after evaporation of the solvent was used in the next step.

rac Methyl (2R,3S*)-3-phenyl-1H-aziridine-2-carboxylate* (±)-**5E**.
Compound (±)-**4Z** was heated at 100-110°C at 0.5 torr in a small distillation apparatus (Kugelrohr). This gave the aziridinecarboxylate as an oil. Purification by chromatography (EtOAc/hexane 1:4) gave a yield of 65 % calcd. on phospholidine. The oil solidified on standing in a refrigerator.
Mass spectrum m/e 178 (M^+ + 1), 146 (M^+ - OCH_3), 118 (M^+ - O=C-OCH_3), 117 (phenylazirine$^+$).
NMR ($CDCl_3$) δ 1.87 (br s, 1H), 2.53 (br s, 1H), 3.25 (br s, 1H), 3.80 (s, 3H), 7.25 (m, 5H) ppm.
IR (neat) ν NH 3280 cm^{-1}, ν CO 1725 cm^{-1}.

Methyl (2R,3S)-3-phenyl-1H-aziridine-2-carboxylate (-)-**5E**.
Compound (-)-**5E** was obtained from oxazaphospholidine (-)-**4Z** by heating in a small distillation apparatus (Kugelrohr) at 10^{-4}-10^{-5} torr. The initial temperature was 90°C, which was raised to 160°C to keep the contents of the flask oily. Addition of glass beats improved the result. The yield of aziridine ester, after chromatography (see above), was 517 mg (oil, 81%).
$[\alpha]_D^{20}$ = -263° [c = 1, EtOH]. Peak matching, found m/e M^++1 178.0871 calc for $C_{10}H_{11}NO_2$ + 1 178.0868.
Found C 66.39, H 6.05, N 7.67 %, calc. for $C_{10}H_{11}NO_2$ (177.087) C 67.78, H 6.26, N 7.90 %.
NMR (CCl_4) δ 1.82 (br s, 1H), 2.62 (br s, 1H), 3.25 (br s, 1H), 3.80 (s, 3H), 7.25 (m, 5H) ppm.
IR (neat) ν NH 3280 cm^{-1}, ν CO 1725 cm^{-1}.
N-p-Phenylbenzoyl derivative mp 175-182°C, $[\alpha]_D^{30}$ = -31.9° [c = 1, $CHCl_3$). Found C 76.66, H 5.49, N 4.05 %, calc for $C_{23}H_{19}NO_3$ (357.411) C 77.29, H 5.36, N 3.92 %.
NMR ($CDCl_3$) δ 3.40 (d, 1H, J = 2.2 Hz), 3.65 (s, 3H), 4.06 (d, 1H, J = 2.2 Hz), 7.3-8.1 (m+q, 14 H, J = 9 Hz) ppm.

Methyl (2S,3R)-3-phenyl-1H-aziridine-2-carboxylate (+)-**5E**.
From oxazaphospholidine (+)-**4Z** (2.33 g, 5.1 mmol) (+)-**5E** (730 mg, 81%) was obtained, after purification by chromatography, $[\alpha]_D^{20}$ = +262° [c = 1, EtOH]; MS, NMR, IR as for (-)-**5E**. Peak matching, found 178.0863, calc for M+1 178.0868. Found C 65.96, H 6.20, N 7.66 %, calc for $C_{10}H_{11}NO_2$ (177.086) C 67.78, H 6.26, N 7.90 %
N-p-Phenyl-benzoyl derivative mp 180-184°C, $[\alpha]_D^{30}$ = +31.5° [c = 1, $CHCl_3$] Found C 76.86, H 5.42, N 3.96 % calc for $C_{23}H_{19}NO_3$ (357.411) C 77.29, H 5.36, N 3.92 %.

Methyl (2R,3R*)-3-phenyl-1H-aziridine-2-carboxylate* (±)-**5Z**.
From oxazaphospholidine (±)-**4E** (1.04 g, 2.3 mmol) *cis* aziridinecarboxylate (±)-**5Z** (263 mg, 65 %) was obtained. Flash chromatography gave 228 mg (59%) of pure product mp 65-76°C (hexane/ether).
Mass spectrum (CI) m/e 178 (M^+ + 1), 146 (M^+ - OCH_3), 118 (M^+ - O=C-OCH_3), 117 (azirine$^+$).
NMR (CCl_4) δ 1.83 (br s, 1H), 2.75 (d, 1H, J = 6 Hz), 3.24 (d, 1H, J = 6 Hz), 3.40 (s, 3H), 7.16 (m, 5H) ppm.
IR (KBr) ν NH 3220 cm^{-1}, ν CO 1740 cm^{-1}.
N-p-phenyl-benzoyl derivative, mp 165-166°C, Found C 77.15, H 5.40, N 3.94 %, calc for $C_{23}H_{19}NO_3$ (357.411) C 77.29, H 5.36, N 3.92 %. NMR ($CDCl_3$) δ 3.48 (s, 3H), 3.61 (d, 1H, J = 6 Hz), 3.92 (d, 1H, J = 6 Hz), 7.3-8.2 (m+q, 14 H, J = 9 Hz).

Methyl (2R,3R)-3-phenyl-1H-aziridine-2-carboxylate (-)-**5Z**.
Oxazaphospholidine $\mathbf{4E}_a$ (4.1 gr, 9.0 mmol) gave, after chromatography, aziridinecarboxylate (-)-**5Z** (319 mg, 20%), mp 50-58°C, $[\alpha]_D^{20}$ = -21° [c = 1, EtOH], Found C 67.15, H 6.22, N 7.67 %, calc for $C_{10}H_{11}NO_2$ (177.086) C 67.78, H 6.26, N 7.90 %. MS, NMR, IR as for (±)-**5Z**.

Methyl (2S,3S)-3-phenyl-1H-aziridine-2-carboxylate (+)-**5Z**.
Oxazaphospholidine $\mathbf{4E}_b$ (4.31 g, 9.4 mmol) gave, after chromatography, aziridinecarboxylate (+)-**5Z** (416 mg, 26%), mp 51-57°C, $[\alpha]_D^{20}$ = +22° [c = 1, EtOH]. Found C 67.46, H 6.20, N 7.75 %, calc for $C_{10}H_{11}NO_2$ C 67.78, H 6.26, N 7.90%. MS, NMR, IR as for (±)-**5Z**.

Mosher-derivative of aziridine (±)-**5Z**. **General procedure.**
Dicyclohexyl carbodiimide (90 mg, 1.3 eq) was added to a soln of rac *cis* aziridinecarboxylate (61 mg, 0.345 mmol) and methoxy-trifluoromethyl-phenylacetic acid (96 mg, 1.3 eq) in dichloromethane (5 ml). 2 mg of *N,N*-dimethylaminopyridine was added as a catalyst. A precipitate immediately was formed. The reaction was monitored by TLC. After 3 h dicyclohexylurea was filtered off and the filtrate was concentrated. The residual oil (131 mg) was chromatographed (EtOAc/hexane 3:17) to give 80 mg of product (59 %).
^{19}F NMR δ -70.048 and -70.305 ppm, relative to $CFCl_3$, integration gave a ratio of 1:1 of both diastereomers.
Mosher-derivative of aziridine (+)-**5Z**.
An oil was obtained (yield 80%), which solidified on standing for a few days.
^{19}F NMR δ -70.279 ppm, relative to $CFCl_3$, with no other peaks present.
^{1}H NMR (CCl_4) δ 3.03 (d, 1H, J = 6.3 Hz), 3.36 (d, 1H, J = 6.3 Hz), 3.39 (s, 3H), 3.62 (two s of OCH_3) 7.1-7.5 (m, 10H) ppm.
Mosher-derivative of aziridine (-)-**5E**.
Yield 51 % of an oil which crystallized on standing for a few days.
^{19}F NMR δ -70.204 ppm, relative to $CFCl_3$, with no other peaks present.
^{1}H NMR δ 2.78 (d, 1H, J = 2 Hz), 3.05 (d, 1H, J = 2 Hz), 3.43 (two s, OCH_3), 3.69 (s, 3H), 7.0-7.5 (m, 10H) ppm.
Mosher-derivative of aziridine (+)-**5E**.
This component was obtained in a low yield. ^{19}F NMR showed an absorption only at -69.084 ppm.

References and notes

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7. A better procedure is described in ref. 3. The high temperature needed for the distillation of the *cis* aziridinecarboxylate caused considerable decomposition.
8. The Mosher derivatives were prepared from Mosher's acid using dicyclohexyl carbodiimide. The formation of the amide was not always complete (see experimental) and therefore a chromatographic purification was needed. There are no indications that a diastereomer was lost during this process.
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$CHCl_3$]), but is consistent with the fact that the e.e. of their product was 76-80%. Our product has an e.e. close to 100%.

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11. In spite of several crystallizations no sharp m.p. could be obtained, while the product was analytically pure. It is of interest to note that the *N-p*-phenylbenzoyl derivative, in contrast, has a sharp m.p.

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