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SYNTHESIS OF NATURALLY OCCURRING (2*S*,3*S*)-(+)-AZIRIDINE-2,3-DICARBOXYLIC ACID.

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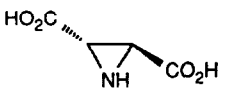
Summary: Diethyl (2*R*,3*R*)-(−)-oxirane-2,3-dicarboxylate was converted into diethyl (2*S*,3*S*)-(+)-aziridine-2,3-dicarboxylate in two steps, *viz.* ring opening with trimethylsilyl azide in *N*,*N*-dimethylformamide containing one equivalent of ethanol, followed by treatment with triphenylphosphine in *N*,*N*-dimethylformamide. Subsequent hydrolysis with lithium hydroxide and acidification with Dowex 50W-X2 (H^+) afforded (2*S*,3*S*)-(+)-aziridine-2,3-dicarboxylic acid, which was identical in all respects to the natural product.

In 1975 Naganawa and coworkers[1] reported the isolation and characterization of (2*S*,3*S*)-(+)-aziridine-2,3-dicarboxylic acid[2] **1** as a metabolite of *Streptomyces* MD398-A1. To the best of our knowledge this is the only example of a naturally occurring aziridinecarboxylic acid.

In view of our recent reports on the preparation of 3-alkyl- and 3-aryl-aziridine-2-carboxylic esters in high enantiomeric purity[3], natural product **1** is an interesting target molecule to demonstrate the utility of our method of synthesis of this type of compounds. Thus far, aziridine **1** has only been prepared as its racemic diethyl ester[4,5,6]. When our study was in progress, Tanner *et al.*[7] reported the synthesis of both enantiomers of diethyl *N*-tosyl-*trans*-aziridine-2,3-dicarboxylate using an approach which bears some resemblance with the one presented in this paper; however, the actual natural product has not been prepared.



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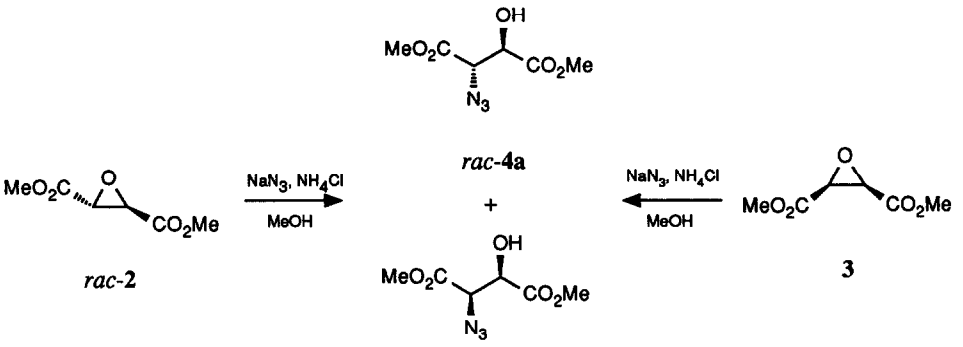
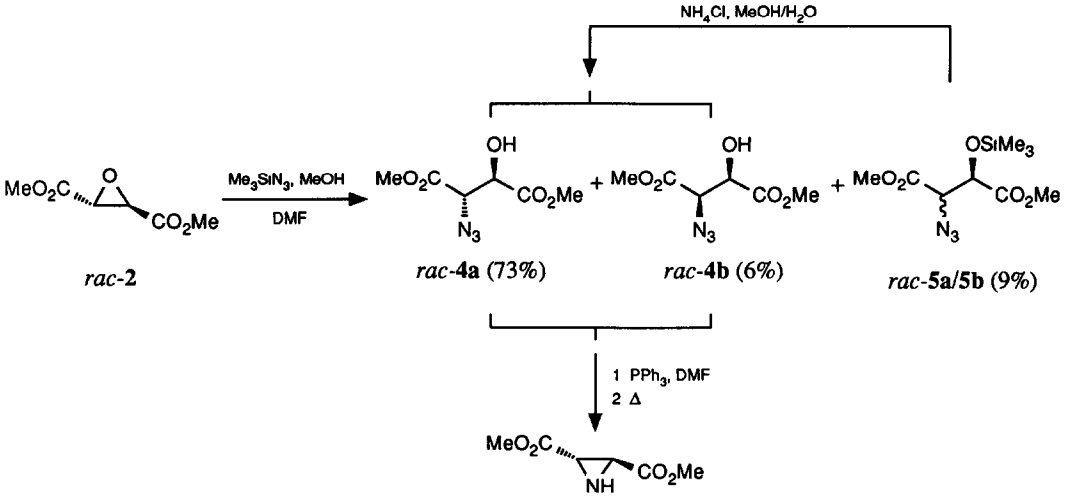
In essence, our method involves ring opening of an oxiranecarboxylic ester with sodium azide, followed by ring closure to the corresponding aziridinecarboxylate by treatment with triphenylphosphine. Accordingly, racemic dimethyl *trans*-oxiranedicarboxylate **2**[8] was treated with sodium azide in methanol in the presence of ammonium chloride[3a] to accomplish the desired epoxide opening. Unexpectedly, this reaction afforded a mixture of the diastereomeric azido alcohols **4a** and **4b** in the ratio of approximately 1:1. The same mixture of diastereomers was obtained when dimethyl *cis*-oxiranedicarboxylate **3** was treated with sodium azide under the same conditions. By closely monitoring the reaction of *rac*-**2** with sodium azide, it was found that initially one diastereomer was predominantly formed. However, before completion of the reaction a considerable amount of the other diastereomer already had appeared in the reaction mixture, with the ultimate ratio of diastereomers of



Scheme 1

ca 1:1 at the end of the reaction. For the explanation of this unexpected isomerization some possibilities can be envisaged. An S_N2-type azide exchange reaction would explain the reaction; however, such a reaction is unprecedented in the literature. Another possibility is the formation of an α-(methoxycarbonyl) carbocation by a slow release of azide, followed by a fast recombination, thus causing a scrambling of stereochemical information. A third possibility, *viz.* the formation of an α-azido-α-(methoxycarbonyl) carbanion, as was reported by *Bruce* et al[9] in their explanation of the isomerization of α-azido lactones, does not seem very likely, because the reaction medium is slightly acidic due to the presence of ammonium chloride. An elimination of hydrazoic acid to give the enol of dimethyl α-oxosuccinate, followed by readdition of azide, is feasible, but rather unlikely under the slightly acidic conditions applied. The true nature of the equilibration remains unclear at this stage.



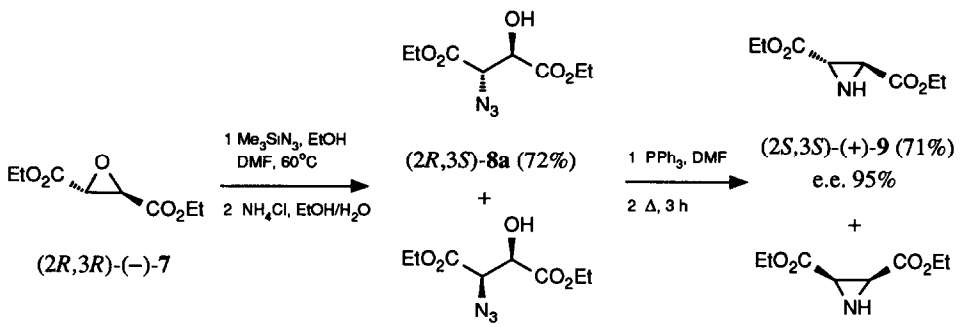
Scheme 2

Attempts to avoid this equilibration of **4a** and **4b** by modifying the reaction conditions (concentration, amount of azide, temperature) were unsuccessful. Therefore, an alternative manner for the introduction of the

azide function was needed. A reaction with hydrazoic acid seemed to be appropriate. Treatment of *rac*-**2** with hydrazoic acid in toluene[10,11], however, did not result in an epoxide opening. The method described by Saito *et al.*,[12] involving the *in situ* generation of hydrazoic acid from trimethylsilyl azide in *N,N*-dimethylformamide (DMF) containing one equivalent of alcohol, gave the desired reaction. Azido alcohol **4a** was obtained from *rac*-**2**, together with the corresponding trimethylsilyl ether **5a** and only a small amount of diastereomers **4b** and **5b** (ratio **4a**:**4b** = **5a**:**5b** = 92:8). The mixture of silyl ethers **5** was quantitatively converted into **4** by treatment with ammonium chloride in aqueous methanol (Scheme 2).

The *anti* azido alcohol *rac*-**4a** obtained thus, was then treated with triphenylphosphine in the manner described previously[3a]. Accordingly, reaction with triphenylphosphine in either dimethylformamide or acetonitrile gave racemic dimethyl *trans*-aziridine-2,3-dicarboxylate *rac*-**6** in an acceptable yield (56%)[13,14]. When a mixture of **4a** and **4b**, obtained by ring-opening of either **2** or **3** with sodium azide, was subjected to these conditions, a mixture of *trans*- and *cis*-aziridine was formed (ratio 3:5).

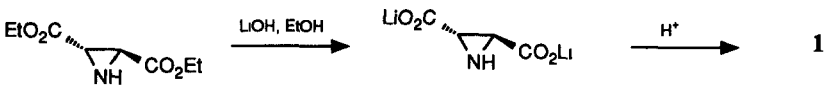
For the synthesis of the natural product **1** the required starting material is (2*R*,3*R*)-**7**, which could readily be prepared from L(+) diethyl tartrate, as described by Mori *et al.*[15] (reaction of diethyl (2*S*,3*S*)-(+)-tartrate with hydrogen bromide in acetic acid and subsequent acid-induced transesterification with ethanol gave diethyl (2*S*,3*R*)-2-bromo-3-hydroxysuccinate, which on treatment with sodium ethoxide in ethanol produced (2*R*,3*R*)-(−)-**7**). Treatment of (−)-**7** with trimethylsilyl azide in dimethylformamide in the presence of an equimolar amount of ethanol afforded the desired azido alcohol **8** in 80% yield as a 9:1 mixture of (2*R*,3*S*)-**8a** and (2*R*,3*R*)-**8b**, after hydrolysis of the corresponding silyl ethers which were formed as a side product[16]. The aziridinedicarboxylate (2*S*,3*S*)-(+)-**9** was obtained from this almost pure azido alcohol **8a** by treatment with triphenylphosphine in DMF. In addition to the main product, *i.e.* (2*S*,3*S*)-(+)-**9** (yield 71%), *ca.* 4% of achiral diethyl *cis*-aziridine-2-3-dicarboxylate **10**, formed from the azido alcohol (2*R*,3*R*)-**8b**, and *ca.* 10% of a 2:1 mixture of the products (2*S*,3*S*)-**9** and **10** was obtained after careful chromatography (Scheme 3).



Scheme 3

The spectral data of (2*S*,3*S*)-(+)-**9** obtained thus, were in full agreement with those previously reported for the racemic material. The enantiomeric purity of the product (e.e. ≥ 95%) was determined by a ^{19}F-NMR analysis of its Mosher derivative. Correct elemental analyses were obtained for *N*-(3,5-dinitrobenzoyl)- and *N*-(4-phenylbenzoyl) derivatives of (+)-**9**.

The almost enantiomerically pure diester (+)-**9** was converted into the free acid as follows (Scheme 4).



(2*S*,3*S*)-(+)-**9** **11**

Scheme 4

Hydrolysis of the diester with lithium hydroxide in ethanol afforded the dilithio salt **11** in high yield. The subsequent acidification could best be accomplished with the strongly acidic ion exchange resin Dowex 50W-X2. The diacid **1** produced in this manner was difficult to handle because of its insolubility in non-aqueous solvents. The crude diacid was crystallized from water by keeping the temperature below 40°C[17]. The pure crystalline material was characterized by its physical and spectral data. The optical rotation ($[\alpha]_D^{20}$ = +51.4° (c = 0.5, H_2O)) is in good agreement with that of the natural product[1] ($[\alpha]_D^{24}$ = +54° (c = 0.5, H_2O)).

Experimental section:

General remarks: ^{1}H-NMR spectra were recorded on a Varian EM 390 (90 MHz, CW), a Bruker WH 90 (90 MHz, FT), a Bruker WM-200 (200 MHz, FT) or a Bruker AM-400 (400 MHz, FT) spectrometer with TMS as internal standard. ^{13}C-NMR spectra were recorded on a Bruker WM-200 (50.3 MHz) spectrometer with TMS as internal standard. ^{19}F-NMR spectra were recorded on a Bruker AM-400 spectrometer. IR spectra were run on a Perkin-Elmer 298 spectrophotometer. For mass spectroscopy a double focussing VG 7070E was used. Melting points were determined on a Reichert Thermopan microscope and are uncorrected. Gas chromatographic analyses were performed on a Hewlett-Packard 5790A or 5890 instrument equipped with a capillary cross-linked methyl silicone column (25 m). Optical rotations were measured on a Perkin-Elmer 241 polarimeter. For preparative chromatography the "flash"-chromatography technique as described by Still *et al.*[18] was used, with silicagel 60H (Merck, art. nr. 7736) as the stationary phase. Hexane was distilled from calcium hydride. Dichloromethane was distilled from phosphorus pentoxide. Diethyl ether was predried on calcium chloride and then distilled from calcium hydride and once more from sodium hydride. Acetonitrile was distilled from phosphorus pentoxide. DMF was initially purified by azeotropic distillation with benzene, and, after treatment with barium oxide, it was distilled at reduced pressure under nitrogen. Ethyl acetate p.a. (Janssen Chimica or Merck) was used as such. Triphenylphosphine was purchased from Janssen Chimica; it was recrystallized from ether. L(+)-diethyl tartrate and azidotrimethylsilane were purchased from Janssen Chimica.

Rac *dimethyl* anti/syn-*3-azido-2-hydroxysuccinate* **4a/4b**·

From rac *oxirane* **2***:* A solution of *rac*-**2** (1.00 g, 6.25 mmol), sodium azide (1.22 g, 18.8 mmol, 3 equiv.) and ammonium chloride (1.00 g, 18.8 mmol, 3 equiv.) in methanol (15 ml) was stirred at room temperature for 18 h. The solvent was then evaporated *in vacuo*. The residue was taken up in water (20 ml) and extracted with ether (3 x 20 ml). The combined extracts were dried on $MgSO_4$ and concentrated, affording 0.96 g (76%) of a mixture of **4a** and **4b** (ratio *ca* 1:1) as a slightly yellow oil (ratio determined by capillary gas chromatography). IR (CCl_4): ν 3520 (OH), 3400, 3000, 2950, 2120 (N_3), 1745 (C=O), 1435, 1260 (br), 1200, 1175, 1110, 1015 cm^{-1}. ^{1}H-NMR ($CDCl_3$): δ 3.4 (br s, 1H, O<u>H</u>), 3.75/3.80 (s + s, 6H, CO_2Me), 4.2/4.3 (d + d, 1H, C<u>H</u>N_3), 4.6/4.7

(d + d, 1H, CHOH) ppm.
From cis-*oxirane* **3***:* From **3** (1.00 g, 6.25 mmol), sodium azide (1.23 g, 18.8 mmol) and ammonium chloride (1.00 g, 18.8 mmol) in methanol (15 ml) a *ca.* 1:1 mixture of **4a** and **4b** (0.95 g, 75%) was obtained after 2 h of heating at reflux. IR and NMR, as above.

Rac *dimethyl* anti-*3-azido-2-hydroxysuccinate* **4a***:* A solution of **2** (603 mg, 3.77 mmol) in DMF (20 ml) was, after successive addition of azidotrimethylsilane (1.000 ml, 868 mg, 7.53 mmol, 2.0 equiv.) and methanol (0.305 ml, 241 mg, 7.53 mmol, 2.0 equiv.), stirred at 60°C (external temperature) for 24 h. After 7 h another 2 equivalents of azidotrimethylsilane and methanol were added. After cooling to room temperature the mixture was concentrated *in vacuo* and purified by chromatography (hexane/ethyl acetate 1:1 (v/v)). Yield 608 mg (79%) of a 92:8 mixture of **4a** and **4b** and 89 mg (9%) of a mixture of the corresponding silyl ethers **5** (which can be hydrolyzed in high yield with ammonium chloride in aqueous methanol, if desired *(vide infra)*). Azido alcohol **4a**: IR (CCl_4): ν 3520 (OH), 3030, 3000, 2950, 2120 (N_3), 1750 (C=O), 1435, 1275 (br), 1235 br), 1110, 1020 cm^{-1}. ^{1}H-NMR ($CDCl_3$): δ 3.35 (m, 1H, OH), 3.8 (s, 6H, CO_2Me), 4.35 (d, 1H, CHN_3), 4.65 (d, 1H, CHOH) ppm. Azido trimethylsilyl ether **5**: IR (CCl_4): ν 3000, 2955, 2120 (N_3), 1760/1745 (C=O), 1435, 1300, 1250 (br), 1200, 1155, 1025, 925, 850 cm^{-1}. ^{1}H-NMR (CCl_4): δ 0.15 (s, 9H, $OSiMe_3$), 3.7 (s + s, 6H, CO_2Me), 4.0 (d, 1H), 4.4 (d, 1H) ppm.

Hydrolysis of dimethyl 3-azido-2-trimethylsilyloxysuccinate **5***:* A solution of **5** (180 mg, 0.65 mmol) and ammonium chloride (70 mg, 1.31 mmol) in methanol/water (10:1) was heated under reflux for 4 h. After cooling to room temperature methanol was evaporated *in vacuo*. The aqueous residue was extracted with ether (3 x 15 ml). The combined extracts were dried on $MgSO_4$ and concentrated, affording 123 mg (92%) of **4**. IR and NMR as above.

Dimethyl trans- *and* cis-*aziridine-2,3-dicarboxylate*· To a solution of **4a** and **4b** (1:1, 107 mg, 0.53 mmol) in DMF (10 ml), triphenylphosphine (145 mg, 0.55 mmol) was added. The reaction mixture was stirred at room temperature for 1 h and then heated at 100°C for 8 h. The solvent was evaporated *in vacuo*. The residue was chromatographed (hexane/ethyl acetate 1:1), affording 26 mg (31%) of *trans*-aziridine **6** and 42 mg (50%) of *cis*-aziridine. trans-*Aziridine* **6**: IR (CCl_4): ν 3280, 3030, 3000, 2950, 2840, 1735 (C=O), 1435, 1405, 1340, 1285, 1205, 1175, 1125, 1085, 1025, 1015, 910, 890, 860, 675 cm^{-1}. ^{1}H-NMR ($CDCl_3$): δ 1.75 (br s, 1H, NH), 2.85 (s, 2H, $CHCO_2Me$), 3.75 (s, 6H, CO_2Me) ppm. cis-*Aziridine*: IR (CCl_4): ν 3280/3260 (NH), 3030, 3000, 2950, 1740 (C=O), 1440, 1365, 1265, 1205 (br), 1160, 1095, 1035 cm^{-1}. ^{1}H-NMR ($CDCl_3$): δ 2.0 (s, 1H, NH), 2.85 (s, 2H, $CHCO_2Me$), 3.7 (s, 6H, CO_2Me) ppm. The IR spectra are characteristic for the *cis* and *trans* compounds (comparison with authentic *trans* compound, *vide infra*).

Dimethyl trans-*aziridine-2,3-dicarboxylate* **6***:* Triphenylphosphine (130 mg, 0.50 mmol, 1.01 equiv.) was added to a solution of **4** (100 mg, 0.49 mmol, **4a**:**4b** = 93:7) in DMF (3 ml). The reaction mixture was stirred at room temperature for 1 h and then at 90°C for 3 days. After evaporation of the solvent *in vacuo* and chromatographic purification of the residue (hexane/ethyl acetate 1:1) 44 mg (56%) of *trans*-aziridine **6** was obtained as a yellowish oil. IR and NMR as described above. MS (CI): *m/e* (%) 160 (100, M + 1^+), 128 (57, - OMe), 114 (12), 100 (100, - CO_2Me), 71 (7). *Mosher's derivative:* Prepared following the procedure as described for the

Mosher's derivative of **9** *(vide infra).* ^{19}F-NMR ($CDCl_3$): 2 signals, $\Delta\delta$ = 0.40 ppm, ratio 0.941:1.000.

Diethyl (2R,3R)-(−)-oxirane-2,3-dicarboxylate **7***:* Oxirane **7** was prepared in three steps from L(+) diethyl tartrate, as described by Mori *et al*[15]. Overall yield 38%. B.p. 100-110°C/1.9 mm Hg. According to GC it was 87% pure. A small amount was further purified by bulb-to-bulb distillation (130°C/17 mm Hg). $[\alpha]_D^{20}$ = −82.3° (c = 0.84, EtOH). Lit[15] $[\alpha]_D$ = −88.47° (c = 1.030, ether). IR (CCl_4): ν 2980, 2935, 2900, 1745 (C=O), 1445, 1370, 1325, 1310, 1250, 1195, 1095, 1035, 900 cm^{-1}. ^{1}H-NMR ($CDCl_3$): δ 1.3 (t, 6H, $C\underline{H}_3$), 3.65 (s, 2H, $C\underline{H}CO_2Et$), 4.3 (q, 4H, $OC\underline{H}_2CH_3$) ppm.

Diethyl (2R,3S)-(+)-3-azido-2-hydroxysuccinate **8a***:* To a cooled solution (0°C) of crude (−)-**7** (8.92 g, 47.4 mmol) in DMF (70 ml), azidotrimethylsilane (12.58 ml, 94.8 mmol, 2.0 equiv.) and absolute ethanol (5.60 ml, 94.8 mmol, 2.0 equiv.) were added sequentially. The reaction mixture was stirred at 65°C (external temperature). After 18 h an additional amount of ethanol (2.80 ml, 1.0 equiv.) was added and the mixture was heated for another 5 h. The solvents were then removed *in vacuo* and the crude product (12.18 g of a reddish brown oil) was purified by chromatography (hexane/ethyl acetate 3:1). Yield 7.96 g (73%) of the desired alcohol **8a** containing a small amount of **8b**, 1.04 g (7%) of the corresponding silyl ether and 1.47 g of an impurity (which appeared to be diethyl tartrate). The silyl ether was subsequently hydrolyzed. It was dissolved in ethanol (10 ml), to which an aqueous solution of ammonium chloride (370 mg, 6.9 mmol, 2 equiv.) was added. After stirring at room temperature for 65 h, 0.79 g (7%, 100% from silyl ether) of **8** was obtained (usual work-up). Total yield of **8** 80% (ratio **8a/8b** = 9:1). $[\alpha]_D^{20}$ = +31.9° (c = 1.25, EtOH). $[\alpha]_D^{20}$ = +17.5° (c = 1.48, CH_2Cl_2) (lit[12] $[\alpha]_D^{18}$ = +16.5° (c = 1.47, CH_2Cl_2)). IR (CCl_4): ν 3520 (br, OH), 2980, 2935, 2905, 2125 (N_3), 1745 (C=O), 1465, 1440, 1365, 1240 (br), 1110, 1030, 930, 860 cm^{-1}. ^{1}H-NMR (CCl_4): δ 1.3 (t, 6H, $C\underline{H}_3$), 3.4 (d, 1H, $O\underline{H}$, J = 6 Hz), 4.05-4.35 (m, 5H, $OC\underline{H}_2CH_3$, $C\underline{H}N_3$), 4.5 (m, 1H, $C\underline{H}OH$) ppm.

Diethyl (2S,3S)-(+)-aziridine-2,3-dicarboxylate **9***:* Triphenylphosphine (7.45 g, 28.4 mmol) was slowly added to a stirred ice-cooled solution of **8** (6.50 g, 28.1 mmol) (**8a**:**8b** = 9:1) in DMF (125 ml). After being stirred at room temperature for 1.5 h the reaction mixture was heated at 90°C for 3 h. The solvent was evaporated *in vacuo*. The residue was chromatographed (hexane/ethyl acetate 4:1 and then increasing the polarity by changing the solvent ratio), yielding 3.72 g (71%) of **9**, 0.19 g (4%) of the corresponding *cis*-aziridine **10** as a yellowish solid and 0.50 g (10%) of a mixture of both (*cis*/*trans* = 2:1).

trans-*Aziridine* **9***:* $[\alpha]_D^{20}$ = +133.3° (c = 1, $CHCl_3$). IR (CCl_4): ν 3280 (NH), 2980, 2935, 2910, 1750/1730 (C=O), 1465, 1445, 1390, 1370, 1335, 1280, 1250, 1200, 1180, 1085, 1035, 855 cm^{-1}. ^{1}H-NMR ($CDCl_3$): δ 1.3 (t, 6H, $C\underline{H}_3$), 1.75 (br s, 1H, $N\underline{H}$), 2.85 (br s, 2H, $C\underline{H}CO_2Et$), 4.25 (q, 4H, $OC\underline{H}_2CH_3$, J = 8 Hz) ppm. ^{1}H-NMR ($CDCl_3$ + D_2O): δ 1.3 (t), 2.85 (s), 4.25 (q) ppm. N-*4-phenylbenzoyl derivative:* At 0°C to a solution of **9** (71 mg, 0.38 mmol) in dichloromethane (5 ml) pyridine (61.4 µl, 0.76 mmol), 4-phenylbenzoyl chloride (123 mg, 0.57 mmol) and a few crystals of DMAP were added sequentially. The reaction mixture was stirred at room temperature for 18 h. Water (10 ml) was added, layers were separated and the aqueous layer was extracted with dichloromethane (3 x 15 ml). The combined extracts were dried on $MgSO_4$ and concentrated. Purification of the crude product (153 mg) by chromatography afforded 133 mg (96%) of pure product, which was recrystallized from hexane. M.p. 69-73°C. IR (KBr): ν 2950, 1740 (OC=O), 1680 (NC=O), 1610, 1450, 1410, 1375, 1330, 1310, 1250, 1195, 1090, 1060, 1035, 1015, 1010, 870, 850, 745, 710, 695 cm^{-1} ^{1}H-NMR (CCl_4): δ

1.2 (t, 6H, $C\underline{H}_3$, J= 7.5 Hz), 3.5 (s, 2H, $C\underline{H}CO_2Et$), 4.15 (q, 4H, $OC\underline{H}_2CH_3$, J = 7.5 Hz), 7.25-7.6 (m, 7H, $C_6\underline{H}_5$, $C_6\underline{H}_2$), 7.95 (d, 2H, $C_6\underline{H}_2$, J = 8 Hz) ppm. Calc. for $C_{21}H_{21}NO_5$ (367.404): C 68.65, H 5.76, N 3.81 %, found C 68.91, H 5.77, N 3.57 %. *N-3,5-dinitrobenzoyl derivative:* A solution of **9** (50 mg, 0.27 mmol), triethylamine (55.8 µl, 0.40 mmol) and 3,5-dinitrobenzoyl chloride (62 mg, 0.27 mmol) in dichloromethane (5 ml) was stirred at room temperature for 3 days. Then water (10 ml) was added, layers were separated and the aqueous layer was extracted with dichloromethane (2 x 15 ml). The combined extracts were washed with 2N H_2SO_4 and satd. sodium bicarbonate solutions, dried on $MgSO_4$ and concentrated, affording 101 mg (99%) of crude product as a yellowish oil which slowly solidified. Recrystallization from diisopropyl ether gave 39 mg (38%) of nice yellowish crystals. M.p. 99-100°C. IR (KBr): ν 3130, 3100, 2990, 1755/1730 (OC=O), 1695 (NC=O), 1630, 1550, 1465, 1375, 1350, 1335, 1320, 1245, 1215, 1205, 1130, 1080, 1045, 1030, 955, 940, 925, 910, 870, 825, 780, 735, 730, 695, 660, 640 cm^{-1}. ^{1}H-NMR ($CDCl_3$): δ 1.3 (t, 6H, $C\underline{H}_3$, J= 7.5 Hz), 3.7 (s, 2H, $C\underline{H}CO_2Et$), 4.25 (q, 4H, $OC\underline{H}_2CH_3$, J = 7.5 Hz), 9.05 (d, 2H, $C_6\underline{H}_2$-*o*, J = 1.5 Hz), 9.2 (t, 1H, $C_6\underline{H}$-*p*) ppm. Calc. for $C_{15}H_{15}N_3O_9$ (381.300): C 47.25, H 3.96, N 11.02 %, found C 47.33, H 4.02, N 11.04 %. *Mosher's derivative:* To a stirred solution of **9** (37 mg, 0.20 mmol) in dichloromethane (1 ml) Mosher's acid chloride (57 mg, 0.23 mmol), pyridine (8 drops) and a few crystals of DMAP were added sequentially. The mixture was stirred at room temperature for 4 h. Water (10 ml) was added, layers were separated and the aqueous layer was extracted with dichloromethane (3 x 15 ml). The combined extracts were washed with 2N H_2SO_4 and satd. sodium bicarbonate solutions, dried on $MgSO_4$ and concentrated. The residue (69 mg, 87%) was subjected to NMR analysis. ^{19}F-NMR ($CDCl_3$): 2 signals, Δδ = 0.53 ppm, ratio 1.000:0.026, hence e.e. = 95%.

cis-*Aziridine* **10***:* IR (CCl_4): ν 3280/3260(br) (NH), 2980, 2935, 2900, 2870, 1735 (C=O), 1465, 1445, 1380, 1355, 1200, 1155, 1120, 1085, 1030, 915, 870 cm^{-1}. IR (KBr): ν 3220 (br, NH), 2990, 2945, 1750, 1675, 1450, 1405, 1385, 1220 (br), 1165, 1120, 1030, 895, 875, 865, 755, 750, 730, 690 cm^{-1}. ^{1}H-NMR ($CDCl_3$): δ 1.3 (t, 6H, $C\underline{H}_3$), 1.85 (br s, 1H, $N\underline{H}$), 2.8 (br s, 2H, $C\underline{H}CO_2Et$), 4.2 (q, 4H, $OC\underline{H}_2CH_3$, J = 8 Hz) ppm. *N-3,5-dinitrobenzoyl derivative:* From **10** (50 mg, 0.27 mmol) 86 mg (84%) of crude product was obtained as an off-white solid. Recrystallization from diisopropyl ether gave long needle-shaped crystals. M.p. 131.5-133.5°C. Calc. for $C_{15}H_{15}N_3O_9$ (381.300): C 47.25, H 3.96, N 11.02%, found C 47.25, H 4.00, N 11.09%.

Dilithio aziridine-2,3-dicarboxylate **11***:* Lithium hydroxide (400 mg, 16.8 mmol) was added to an ice-cooled solution of **9** (750 mg, 2.0 mmol) in ethanol (25 ml), which was then stirred at 0°C for 2 h. After evaporation of the solvent the residue was taken up in ether and stirred for 5 minutes. Ether was then evaporated, affording the crude lithium salt which was dried *in vacuo*. Yield 822 mg (>100%) of crude **11** as an off-white solid. IR (KBr): ν 3650-3100 (br), 1600 (C=O), 1410, 1350, 1295, 1200 cm^{-1}.

Aziridine-2,3-dicarboxylic acid **1***:* The crude lithium salt **11** as prepared above (807 mg) was dissolved in water (20 ml) and passed through a column of Dowex 50W-X2 (strongly acidic sulfonic acid ion exchange resin, H^+-form). Concentration of the eluate *in vacuo* afforded 471 mg (91%) of crude **1** as an off-white solid. Recrystallization from water (max. 40°C[17]) gave 357 mg (69%) of **1** as nice colorless plates. M.p. 171°C (dec.) (lit.[1a] 178°C (dec.)). $[\alpha]_D^{20}$ = +51.4° (c = 0.5, H_2O) (lit.[1a] $[\alpha]_D^{24}$ = +54° (c = 0.5, H_2O). IR (KBr): ν 3400 (br), 3300-2200 (br), 3100, 1680 (br, C=O), 1540, 1385, 1315, 1115, 890, 855, 765, 680 cm^{-1}. ^{1}H-NMR (DMSO-d_6): δ 2.57 (s, 2H, OOC-CHCH-COO), 4.50 (br s, 3H, NH_2^+, COOH) ppm (lit.[1a]: δ 2.59 (s), 7.8 (br s) ppm). ^{13}C-NMR (DMSO-d_6): δ 35.14 (C-2), 170.98 (COO) ppm (lit.[1a]: δ 35.9, 174.6 ppm). Calc. for $C_4H_5NO_4$

(131.088) C 36.65, H 3.84, N 10.68%, found C 36.41, H 3.89, N 10.45%.

References and notes:

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17. In a pilot experiment an aqueous solution of **1** was heated to 100°C, but this led to partial hydrolysis due to the acidity of the solution. This was reflected in a considerable decrease of the optical rotation.
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