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Full Paper

# Selective Cleavage of Carbamate Protecting Groups from Aziridines with Otera's Catalyst

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Otera's distannoxane catalyst was found to promote the cleavage of carbamate groups from *N*-protected aziridines. This method enables the chemoselective cleavage of an aziridinyl *N*-carbobenzyloxy (Cbz) group in the presence of other *N*-Cbz groups. The selectivity is due to the longer, weaker N–C bond of aziridinyl carbamates, as inferred through IR and crystallographic analyses.

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## Introduction

Protecting group chemistry is central to virtually all facets of organic synthesis, and is of prime importance in peptide chemistry where orthogonal protecting groups are crucial to chemoselective reactions at numerous amine and carboxylate functional groups. Carbamate protection of amines is extremely versatile due to the variety of carbamate groups that have been developed and the consequent ability to selectively cleave these protecting groups under a range of conditions,[1] leaving other groups such as amides intact. The cleavage of carbamate protecting groups is normally determined by the nature of the *O*-alkyl group as the O–C bond is generally the initial bond cleaved during deprotection. Herein we describe the selective removal of carbamates based instead on the nature of the *N*-alkyl group. Specifically, we demonstrate that aziridinyl-based carbamates are uniquely susceptible to cleavage with Otera's catalyst.

Otera and co-workers showed that 1,3-disubstituted tetraorganodistannoxanes **1** are efficient transesterification catalysts.[2] Several of these distannoxanes have been made commercially available at times, and are collectively referred to as Otera's catalyst. These species are actually pre-catalysts, being converted to the active catalyst **2** in presence of the alcohol involved in the transesterification reaction (Scheme 1).

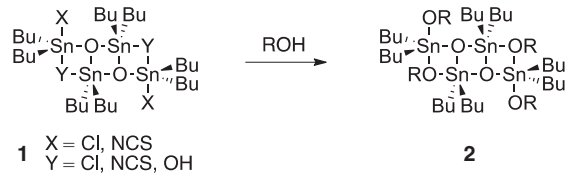
During the course of our studies on aziridine ring-opening reactions[3] we were surprised to find that treatment of Cbz-protected aziridine-2-carboxylate methyl ester **3a** with benzyl alcohol in the presence of Otera's catalyst not only resulted in transesterification to the benzyl ester, but also the cleavage of the Cbz group, generating aziridine **4**. Benzyl carbonate was isolated as a by-product, confirming that benzyl alcohol attacks the carbamate carbonyl group, displacing the aziridine. We therefore set out to explore the scope and limitations of carbamate deprotection reactions with Otera's catalyst.

Initial studies focussed on treatment of several carbamate-protected aziridine-2-carboxylates to investigate whether this reaction was general across a variety of carbamate protecting groups. Cleavage of the methyl carbamate (Moc) group of **3c** was successful, generating unprotected aziridine **4** (albeit in low isolated yield[4]; Scheme 2). However, the *tert*-butyloxycarbonyl (Boc)-protected compound **3b** underwent only transesterification to **5b**, with no Boc cleavage occurring. Presumably, sterically hindered carbamates are less prone to cleavage, in line with Otera's findings that sterically hindered esters are not effectively transesterified under such conditions.[2b]

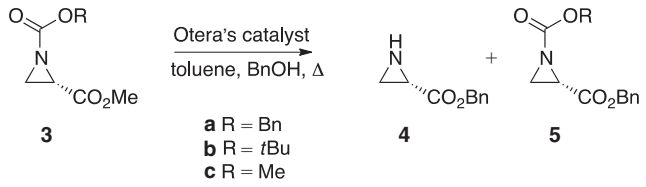
Acyclic carbamates were next investigated. Upon treatment of the Boc/Moc-protected diaminobutane **6** with Otera's catalyst and benzyl alcohol in toluene, no reaction was observed. Similarly, when differentially protected diaminopimelate derivative **7a** was treated under identical conditions no carbamate cleavage was observed, only transesterification of the methyl ester to the corresponding benzyl ester **7b**. Further, the carbamate-protected anilines **8a**–**c** were also unreactive under these conditions. Thus, it is apparent that the cleavage of carbamate groups under these conditions does not extend to acyclic systems (Chart 1).

With the conclusion that acyclic carbamate systems were not reactive towards Otera's catalyst, cyclic systems were explored. Cbz-proline benzyl ester **9** was unreactive to standard conditions, and similarly the Cbz-azetidine-2-carboxylate methyl ester **10a** did not undergo carbamate cleavage, only transesterification to **10b** (Chart 2).

Given the apparent selectivity for cleavage of aziridine-based carbamate groups, we sought to exploit this selectivity through the chemoselective removal of one of the two Cbz-protecting groups in dipeptide **14**. Dipeptide **14** was prepared from *N*-tritylaziridine carboxylate **11**. Hydrolysis of *N*-tritylaziridine carboxylate **11**[5] gave the corresponding acid, which was coupled to $N^{\varepsilon}$-Cbz lysine methyl ester to give dipeptide **13**. Trityl deprotection and Cbz-reprotection gave dipeptide **14**. Treatment of aziridine-containing dipeptide **14** with Otera's catalyst under the standard transesterification/deprotection conditions yielded the singly Cbz-deprotected, transesterified dipeptide **15** (Scheme 3), highlighting the




**Scheme 1.** Conversion of Otera's (pre)catalyst into active catalyst.




**Scheme 2.** Treatment of carbamate-protected aziridines with Otera's catalyst.

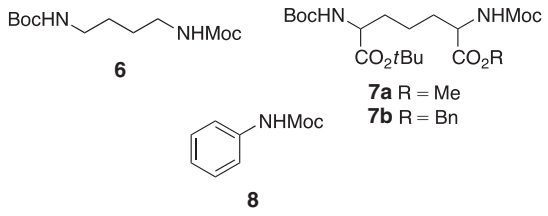



**Chart 1.**

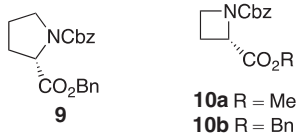
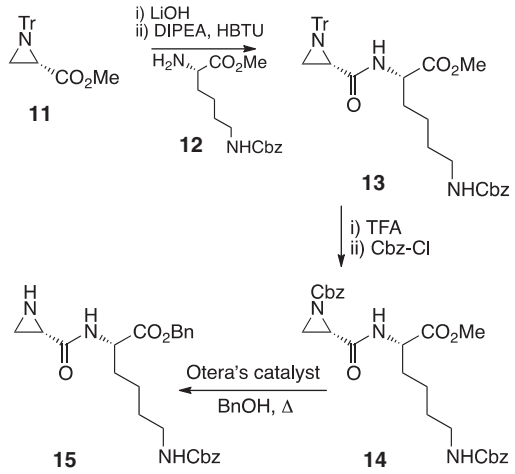



**Chart 2.**




**Scheme 3.** Chemoselective cleavage of aziridinyl-Cbz group.

chemoselective cleavage of carbamate protecting groups based on the nature of the nitrogen.

We postulate that the chemoselectivity for cleavage of aziridinyl-based carbamate groups is due to the highly strained nature of the three-membered ring. Aziridines possess bond angles of ~60°, much lower than a tetrahedral bond angle of 109.5°, which results in the nitrogen lone pair possessing more 's'-character and being less delocalized into the carbonyl group; such changes in the hybridization of the aziridinyl nitrogen render the $-CO_2R$ part of the carbamate more 'ester-like'. Analysis of the IR spectra of these and related carbamate-protected heterocycles reveals distinct differences between aziridinyl and other carbamates. While carbamates typically show carbonyl IR absorbances at ~1700 $cm^{-1}$,[6–8] the corresponding IR absorbances for the aziridinyl carbamates **3a**–**c** and others[9,10] occur at 1720–1735 $cm^{-1}$, closer to a typical ester C=O absorbance.[11] Further, an inspection of the Cambridge Structural Database (CSD) reveals a related effect where the N–C(O) bond of aziridinyl-carbamates is significantly longer than those of other carbamates. The N–C(O) bond of carbamate-protected aziridines is on average 1.40 Å (16 hits), whereas non-aziridinyl compounds average ~1.34 Å (azetidines, 1.33 Å (13 hits); pyrrolidines, 1.34 Å (620 hits); piperidines, 1.34 Å (304 hits).[12] The longer, weaker aziridinyl N–C(O) bonds are consequently more prone to cleavage under the described reaction conditions.

## Conclusion

In conclusion, we have unearthed a novel method for the selective deprotection of aziridines. We demonstrate that Otera's catalyst is able to perform a chemoselective transformation at aziridinyl-carbamate. Using this method two Cbz-protecting groups in a single molecule can be differentiated and made 'orthogonal' when one is on an aziridinyl nitrogen. The use of Otera's catalyst to cleave carbamates is unprecedented.

## Experimental

### *(S)*-N-*Benzyloxycarbonyl aziridine-2-carboxylate methyl ester* ***3a***

*N*-Trityl aziridine-2-carboxylate methyl ester[5] (1.00 g, 2.92 mmol) was dissolved in a solution of methanol (5 mL) and chloroform (5 mL), and the solution was cooled to 0°C. Trifluoroacetic acid (4 mL) was added and the resulting solution was stirred for 3 h. The solvent was removed under vacuum, and dried azeotropically with the addition of diethyl ether. The dried material was dissolved in dichloromethane (20 mL) and cooled to 0°C. Triethylamine (2 mL) and a 50 % benzyl chloroformate solution in toluene (1.2 mL, 3.5 mmol) were added, and the resulting solution was warmed to room temperature and stirred for 16 h. The solution was then evaporated under vacuum, and the crude residue was purified by flash chromatography (10–20 % ethyl acetate/hexanes) to yield the title compound as a pale amber oil (305 mg, 44 % yield). $\nu_{max}$ (neat)/$cm^{-1}$ 2957, 1729, 1441, 1379, 1323, 1294, 1224, 1192, 1025, 753, 699. $\delta_H$ (500 MHz, $CDCl_3$) 7.37–7.33 (m, 5H), 5.17–5.11 (m, 2H), 3.70 (s, 3H), 3.10 (dd, *J* 5.5, 3.0, 1H), 2.59 (dd, *J* 3.0, 1.5, 1H), 2.47 (dd, *J* 5.5, 1.5, 1H). Data in accordance with literature values.[9,13]

### *(S)*-N-tert-*Butoxycarbonyl aziridine-2-carboxylate methyl ester* ***3b***

*N*-Trityl aziridine-2-carboxylate methyl ester[5] (1.00 g, 2.92 mmol) was dissolved in a solution of methanol (5 mL) and chloroform (5 mL), and the solution was cooled to 0°C. Trifluoroacetic acid (4 mL) was added and the resulting solution was stirred for 3 h. The solvent was removed under vacuum, and dried azeotropically with the addition of diethyl ether. The dried material was dissolved in dichloromethane (20 mL) and

cooled to 0°C. Triethylamine (2 mL) and di-*tert*-butyl dicarbonate (764 mg, 3.5 mmol) were added, and the resulting solution was warmed to room temperature and stirred for 16 h. The solution was then evaporated under vacuum, and the crude residue was purified by flash chromatography (10–20 % ethyl acetate/hexanes) to yield the title compound as a pale amber oil (411 mg, 70 % yield); $\nu_{max}$ (neat)/$cm^{-1}$ 2980, 1745, 1722, 1440, 1392, 1369, 1327, 1306, 1233, 1203, 1150, 1087, 1021, 968, 852, 800. $\delta_H$ (600 MHz, $CDCl_3$) 3.63 (s, 3H), 2.89 (dd, *J* 5.3, 3.1, 1H), 2.37 (dd, *J* 3.1, 1.3, 1H), 2.27 (dd, *J* 5.3, 1.3, 1H), 1.31 (s, 9H); $\delta_C$ (150 MHz, $CDCl_3$) 168.7, 159.4, 81.8, 52.3, 34.6, 31.1, 27.7. Data in accordance with literature values.[14]

### (*S*)-N-*Methoxycarbonyl aziridine-2-carboxylate methyl ester* ***3c***

*N*-Trityl aziridine-2-carboxylate methyl ester[5] (1.06 g, 3.09 mmol) was dissolved in a solution of methanol (5 mL) and chloroform (5 mL), and the solution was cooled to 0°C. Trifluoroacetic acid (4 mL) was added and the resulting solution was stirred for 3 h. The solvent was removed under vacuum, and dried azeotropically with the addition of diethyl ether. The dried material was dissolved in dichloromethane (20 mL) and cooled to 0°C. Triethylamine (2 mL) and methyl chloroformate (290 µL, 3.7 mmol) were added, and the resulting solution was warmed to room temperature and stirred for 16 h. The solution was then evaporated under vacuum, and the crude residue was purified by flash chromatography (10–25 % ethyl acetate/hexanes) to yield the title compound as a pale amber oil (158 mg, 32 % yield); $\nu_{max}$ (neat)/$cm^{-1}$ 2923, 1735, 1464, 1378, 772. $\delta_H$ (600 MHz, $CDCl_3$) 3.72 (s, 3H), 3.68 (s, 3H), 3.04 (dd, *J* 5.4, 3.2, 1H), 2.49 (dd, *J* 3.2, 1.3, 1H), 2.42 (dd, *J* 5.4, 1.3, 1H). $\delta_C$ (150 MHz, $CDCl_3$) 168.7, 161.4, 53.8, 52.7, 34.7, 31.3. Data in accordance with literature values.[9]

### (*S*)-*Aziridine-2-carboxylate benzyl ester* ***4***

From **3a**: To (*S*)-*N*-benzyloxycarbonyl aziridine-2-carboxylate methyl ester **3a** (103 mg, 0.44 mmol) and Otera's catalyst (50 mg, 0.044 mmol) in toluene (2 mL) was added benzyl alcohol (450 µL, 4.4 mmol), and the solution was heated at 100°C overnight. The solution was diluted with ethyl acetate (20 mL) and extracted with 1 M hydrochloric acid solution (20 mL). The aqueous phase was basified with saturated sodium bicarbonate solution (10 mL), and extracted with ethyl acetate (20 mL). The organic phase was dried (magnesium sulfate) and reduced under vacuum to yield the title compound as a yellow oil (15 mg, 19 % yield).[4] $\delta_H$ (500 MHz, $CDCl_3$) 7.41–7.28 (m, 5H), 5.23–5.17 (m, 2H), 2.57 (br s, 1H), 2.04 (d, *J* 3.5, 1H), 1.88 (br s, 1H). $^1$H NMR data in accordance with literature values.[10]

From **3c**: To (*S*)-*N*-methoxycarbonyl aziridine-2-carboxylate methyl ester **3c** (70 mg, 0.44 mmol) and Otera's catalyst (50 mg, 0.044 mmol) in toluene (2 mL) was added benzyl alcohol (450 µL, 4.4 mmol), and the solution was heated at 100°C overnight. The solution was diluted with ethyl acetate (20 mL) and extracted with 1 M hydrochloric acid solution (20 mL). The aqueous phase was basified with saturated sodium bicarbonate solution (10 mL), and extracted with ethyl acetate (20 mL). The organic phase was dried (magnesium sulfate) and reduced under vacuum to yield the title compound as a yellow oil (8 mg, 10 % yield).[4]

### *1*-tert-*Butoxycarbonylamino-4-methoxycarbonylaminobutane* ***6***

To a solution of 1,4-diaminobutane (4.03 g, 45.7 mmol) in dichloromethane (60 mL) at 0°C was added a solution of di-*tert*-butyl dicarbonate (1.00 g, 4.58 mmol) in dichloromethane (20 mL) dropwise over 2 h, whereupon the solution was brought to room temperature and stirred for 20 h. The solution was washed with water (30 mL), brine (30 mL), dried (magnesium sulfate), and reduced under vacuum. The crude residue was purified by flash chromatography to yield *N*-Boc-diaminobutane as a yellow powder (0.815 g, 95 % yield); $\delta_H$ (400 MHz, $CDCl_3$) 4.70 (br s, 1H), 3.11 (m, 2H), 2.73 (m, 2H), 1.81 (m, 2H), 1.46 (m, 2H), 1.43 (s, 9H). *m/z* (ESI-MS) 189.1659; $[M+H]^+$ requires 189.1598.[15]

To a solution of *N*-Boc-1,4-diaminobutane (0.500 g, 2.66 mmol) and pyridine (0.26 mL, 3.2 mmol) in dichloromethane (20 mL) at 0°C was added methyl chloroformate (0.27 mL, 3.5 mmol). The solution was stirred overnight, quenched with ice/water (20 mL), and the organic phase was washed with water (3 × 20 mL), brine (20 mL), dried (magnesium sulfate), and reduced under vacuum. The crude residue was purified by flash chromatography to afford the title compound as an off-white powder (0.20 g, 30 % yield), mp 85–87°C. $\delta_H$ (400 MHz, $CDCl_3$) 4.84 (br s, 1H), 4.61 (br s, 1H), 3.77 (s, 3H), 3.17 (br s, 1H), 3.11 (m, 2H), 1.49 (m, 2H), 1.46 (m, 2H), 1.44 (s, 9H). $\delta_C$ (100 MHz, $CDCl_3$) 157.3, 156.2, 79.1, 52.0, 40.7, 40.2, 28.4, 27.4, 27.3. *m/z* (ESI-MS) 247.1653; $[M+H]^+$ requires 247.1652.

### *2*-tert-*Butoxycarbonylamino-6-methoxycarbonylaminopimelic acid 1*-tert-*butyl 7-methyl diester* ***7a***

To *N*-Cbz glycine methyl ester α-dimethyl phosphonate[16] (235 mg, 0.710 mmol) and DBU (100 µL, 0.68 mmol) in dichloromethane (4.5 mL) was added a solution of *N*-diBoc L-glutamate semialdehyde *tert*-butyl ester[17] (250 mg, 0.645 mmol) in dichloromethane (4.5 mL). The solution was stirred for 3 h, and then reduced under vacuum. The crude residue was purified by flash chromatography (10–20 % ethyl acetate/hexanes) to yield the corresponding alkene as a yellow oil (215 mg, 56 % yield). To the alkene (165 mg, 0.278 mmol) was added a solution of trifluoroacetic acid (64 µL, 0.835 mmol) in dichloromethane (1 mL), and the resulting solution was stirred for 3 h. The solution was washed with a solution of sodium carbonate (89 mg, 0.84 mmol) in water (1 mL), and the organic phase was dried (magnesium sulfate), and reduced under vacuum to yield the corresponding singly Boc-protected compound (134 mg, 98 % yield). This alkene (134 mg, 0.27 mmol) was dissolved in methanol, then $Pd(OH)_2$/C (13 mg) was added. The mixture was stirred under a hydrogen atmosphere for 16 h, filtered over Celite, and reduced under vacuum to yield 2-*tert*-butoxycarbonylamino-6-aminopimelic acid 1-*tert*-butyl ester 7-methyl ester (as a mixture of diastereomers). The residue was dissolved in dichloromethane (2 mL) and cooled to 0°C. Pyridine (29 µL, 0.35 mmol) and methyl chloroformate (25 µL, 0.33 mmol) were added and the resulting solution was stirred for 30 min at 0°C. The solution was then warmed to room temperature and then continued to stir 16 h. The solvent was removed under vacuum and the residue was diluted with dichloromethane (20 mL) and washed with water (3 × 10 mL), brine (10 mL), dried (magnesium sulfate), and evaporated. The crude residue was purified by flash chromatography (20 % ethyl acetate/hexanes)

to yield the title compound as a pale yellow oil (60 mg, 53 % yield over two steps). $\delta_H$ (500 MHz, $CDCl_3$) 5.29 (m, 1H), 5.05 (m, 1H), 4.33 (m, 1H), 4.12 (m, 1H), 1.83–1.58 (m, 6H), 1.45 (s, 9H), 1.44 (s, 9H). *m/z* (ESI-MS) 419.2383; $[M+H]^+$ requires 419.2388.

### *2*-tert-*Butoxycarbonylamino-6-methoxycarbonylaminopimelic acid 1*-tert-*butyl 7-benzyl diester* ***7b***

To **7a** (7.0 mg, 17 μmol) and Otera's catalyst (2.0 mg, 2 μmol) in toluene (0.4 mL) was added benzyl alcohol (18 μL, 0.17 mmol), and the solution was heated at 100°C for 40 h. The solvent was removed under a stream of nitrogen and the residue was purified by flash chromatography (15 % ethyl acetate/hexanes) to yield the title compound as an pale oil (6.0 mg, 71 % yield). $\delta_H$ (600 MHz, $CDCl_3$) 7.39–7.33 (m, 5H), 5.31 (m, 1H), 5.17 (m, 2H), 5.03 (m, 1H), 4.38 (m, 1H), 4.12 (m, 1H), 3.67 (s, 3H), 1.91–1.52 (m, 6H), 1.44 (s, 18H). *m/z* (ESI-MS) 495.2692; $[M+H]^+$ requires 495.2701.

### N-*Benzyloxycarbonyl azetidine-2-carboxylate methyl ester* ***10a***

To a solution of *N*-Boc azetidine-2-carboxylate (1.00 g, 4.98 mmol) in methanol (10 mL) and benzene (15 mL) was added dropwise 2.0 M (trimethylsilyl)diazomethane solution in hexanes (4 mL, 8 mmol). Water (~10 mL) was added and the mixture was stirred for 1 h. The solvent was removed under vacuum to quantitatively yield *N*-Boc azetidine-2-carboxylate methyl ester. To the methyl ester (300 mg, 1.40 mmol) in dichloromethane (5 mL) was added trifluoroacetic acid (1 mL), and the resulting solution was stirred for 1 h. The solvent was azeotropically removed with dichloromethane under vacuum to yield the amine product. The residue was redissolved in anhydrous dichloromethane (5 mL), followed by the addition of triethylamine (1 mL). Upon cooling to 0°C, a 50 % benzyl chloroformate/toluene solution was added, and the solution was stirred overnight. The solvent was then removed and the crude residue was purified by flash chromatography (15–35 % ethyl acetate/hexanes) to yield the title compound as a pale yellow oil (277 mg, 80 % yield). $\delta_H$ (600 MHz, $CDCl_3$) 7.32–7.26 (m, 5H), 5.12–5.04 (m, 2H), 4.67 (m, 1H), 4.06 (m, 1H), 3.93 (m, 1H), 3.68 (s, 3H), 2.52 (m, 1H), 2.19 (m, 1H). $\delta_C$ (150 MHz, $CDCl_3$) 171.6, 155.8, 136.5, 128.5, 128.1, 128.0, 66.9, 60.4, 52.3, 47.7, 20.8. $^1H$ and $^{13}C$ NMR data in accordance with literature values.[18]

### N-*Benzyloxycarbonyl azetidine-2-carboxylate benzyl ester* ***10b***

To *N*-Cbz azetidine methyl ester **10a** (45 mg, 0.18 mmol) and Otera's catalyst (20 mg, 0.018 mmol) in toluene (1 mL) was added benzyl alcohol (190 μL, 1.8 mmol), and the solution was heated at 100°C overnight. The solution was diluted with ethyl acetate (20 mL) and this was washed with 10 % sodium bicarbonate solution (3 × 10 mL). The organic phase was dried (magnesium sulfate) and reduced under vacuum to yield the title compound as a pale oil (15 mg, 25 % yield) contaminated with benzyl alcohol. $\nu_{max}$ (neat)/$cm^{-1}$ 2955, 1743, 1705, 1408, 1347, 1286, 1207, 1125, 1064, 1024, 970, 917, 755, 738, 698. $\delta_H$ (600 MHz, $CDCl_3$) 7.37–7.35 (m, 10H), 5.16 (br s, 2H), 5.07 (br s, 2H), 4.74 (m, 1H), 4.10 (m, 1H), 3.97 (m, 1H), 2.56 (m, 1H), 2.22 (m, 1H). Data in accordance with literature values.[19]

### N-*Benzyloxycarbonyl aziridine-2-carboxyl-(*$N^{\varepsilon}$*-benzyloxycarbonyl)lysine methyl ester* ***14***

*N*-Trityl aziridine-2-carboxylate methyl ester[4] (500 mg, 1.46 mmol) was dissolved in a mixture of tetrahydrofuran (15 mL) and water (2 mL) at 0°C. Aqueous 1 M sodium hydroxide (20 mL) was added, followed by aqueous 1 M lithium hydroxide (10 mL) and the mixture was stirred for 2 h. The mixture was diluted with dichloromethane (50 mL) and 15 % w/v aqueous citric acid (40 mL), and the organic phase was further washed with citric acid solution (3 × 20 mL). The combined aqueous phases were extracted with dichloromethane (3 × 30 mL), and the combined organic phases were then dried (magnesium sulfate) and reduced under vacuum, giving *N*-tritylaziridine-2-carboxylate (quantitative). *N*-Tritylaziridine-2-carboxylate (500 mg, 1.52 mmol) was added to dimethylformamide (10 mL), followed by addition of diisopropylethylamine (2.8 mL, 15 mmol) and (benzotriazol-1-yloxy)tripyrrolidinophosphonium hexafluorophosphate (1.58 mg, 3.04 mmol). After standing for 15 min, lysine derivative **12**[20] (503 mg, 3.04 mmol) was added, and the solution was stirred for 16 h. The solution was diluted with dichloromethane (40 mL), washed with water (5 × 30 mL), dried (magnesium sulfate), and reduced under vacuum. The crude residue was purified by flash chromatography (20–35 % ethyl acetate/hexanes) to yield dipeptide **13** (0.46 g, 50 % yield).

A 50 % v/v solution of trifluoroacetic acid/dichloromethane (0.2 mL) was added to a solution of dipeptide **13** (53 mg, 88 μmol) in 50 % v/v methanol/dichloromethane at 0°C. After stirring for 20 min, additional 50 % v/v trifluoroacetic acid/dichloromethane (0.2 mL) was added, and the solution stirred for a further 20 min. The solvent was then removed azeotropically with methanol under vacuum and the residue was redissolved in dichloromethane (2.5 mL). Upon cooling, triethylamine (40 μL, 0.26 mmol) and 50 % benzyl chloroformate/toluene (45 μL, 0.13 mmol) were added to the solution, which was then warmed to room temperature and stirred overnight. The solvent was removed under vacuum, and the crude residue was purified by flash chromatography (30–60 % ethyl acetate/hexanes) to yield the title compound as a yellow oil (30 mg, 68 % yield). $\delta_H$ (500 MHz, $CDCl_3$) 7.36–7.25 (m, 10H), 6.79 (d, *J* 7.5, 1H), 5.18–5.08 (m, 4H), 4.85 (m, 1H), 4.55 (m, 1H), 3.73 (s, 3H), 3.15 (m, 2H), 3.06 (dd, *J* 5.0, 2.5, 1H), 2.51 (d, *J* 5.5, 1H), 2.38 (d, *J* 1.0, 1H), 1.82 (m, 1H), 1.67 (m, 1H), 1.47 (m, 2H), 1.27 (m, 2H). $\delta_C$ (125 MHz, $CDCl_3$) 172.4, 167.2, 161.3, 156.7, 136.7, 135.4, 128.8, 128.7, 128.7, 128.6, 128.3, 69.0, 66.8, 52.7, 51.9, 40.6, 37.1, 32.2, 32.0, 29.5, 22.3. *m/z* (ESI-MS) 520.2051; $[M+H]^+$ requires 520.2054.

### *Aziridine-2-carboxyl-(*$N^{\varepsilon}$*-benzyloxycarbonyl)lysine benzyl ester* ***15***

To dipeptide **14** (34 mg, 68 μmol) and Otera's catalyst (8 mg, 7 μmol) in toluene (2 mL) was added benzyl alcohol (75 μL, 0.69 mmol), and the solution was heated at 100°C for 28 h. The solvent was removed under a stream of nitrogen and the residue was purified by flash chromatography (0–10 % methanol/dichloromethane) to yield the title compound as a pale yellow oil (5.0 mg, 17 % yield). [4]; $\delta_H$ (400 MHz, $CDCl_3$) 7.36–7.31 (m, 10H), 5.18–5.04 (m, 4H), 4.48–4.42 (m, 1H), 3.12–3.01 (m, 2H), 1.90–1.63 (m, 3H), 1.52–1.25 (m, 6H). $\delta_C$ (100 MHz, $CDCl_3$) 173.3, 158.9, 129.6, 129.6, 129.5, 129.4, 129.3, 128.9, 128.8, 67.9, 67.4, 54.0, 41.4, 32.1, 30.7, 30.4, 26.2, 23.9. *m/z* (ESI-MS) 440.2176; $[M+H]^+$ requires 440.2180. Purification

also yielded the transesterifed product (benzyl ester of **14**) as an oil (1.0 mg, 3 % yield). $\delta_H$ (500 MHz, $CDCl_3$) 7.38–7.30 (m, 15H), 6.78 (d, *J* 7.6, 1H), 5.21–5.07 (m, 6H), 4.75 (m, 1H), 4.59 (m, 1H), 3.11–3.08 (m, 2H), 3.06 (dd, *J* 6.4, 3.3, 1H), 2.50 (d, *J* 6.4, 1H), 2.38 (d, *J* 2.9, 1H), 1.86–1.80 (m, 2H), 1.67–1.18 (m, 4H). *m/z* (ESI-MS) 574.2556; $[M+H]^+$ requires 574.2548.

## Supplementary Material

NMR spectra for compounds **3**–**5**, **7**, **10**, **13**–**15** are available on the Journal's website.

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