Synthesis of Aziridine-2,2-dicarboxylates via 1,4-Addition of *N,O*-(Bistrimethylsilyl)hydroxylamine to α,*β*-Unsaturated Malonates

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Introduction

Aziridines[1] are important heterocyclic compounds present in unusual natural products that display strong biological activity. Azinomycines A and B, for instance, isolated from the fermentation broth of *Streptomyces griseofuscus*, and (+)-FR900482 from the culture broth of *Streptomyces sandaensis* are potent antitumor antibiotics that exhibit exceptional activity against various types of mammalian solid tumors. Mitomycin C is an aziridine-containing antibiotic, produced by *Streptomyces caespitosus*, whose antineoplastic activity is associated with the high reactivity of the strained aziridine ring.[2] Recently novel types of peptidic cysteine protease inhibitors containing aziridine-2,3-dicarboxylic acid have been designed and synthesized.[3] Moreover the synthesis has been reported of a new peptidelike structure containing an aziridine ring, to introduce a rigid core inside an oligopeptide frame.[4]

One of the most important features in aziridine chemistry is their use as starting material for further transformations. Aziridines are indeed useful intermediates in organic synthesis affording, through S_N2 ring-opening reactions, substituted α- or *β*-amino acids,[5] and through ring expansion of the amido derivatives, oxazolines as a protected form of hydroxyamino compounds. Recently we have utilized chiral aziridines in the synthesis of antibiotic Lysobactin fragments,[6] containing hydroxyamino acids in *syn* and *anti* configurations. In this context we reported a new synthesis of chiral *trans* aziridines in two steps, addition of *O*-benzylhydroxylamine to unsaturated imides and cyclization through the formation of an intermediate enolate.[7] We wish now to report the synthesis of aziridine-2,2-dicarboxylates via the conjugate addition of *N,O*-bis(trimethylsilyl)hydroxylamine (TMSNHOTMS) to alkylidene malonates, to give adducts **2** followed by cyclization (Scheme 1).

The procedure, exemplified by the reactions outlined in Scheme 1, affords aziridine **4** in good yields. The overall process shows that TMSNHOTMS behaves as a nitrenoidic polisynthon "(−)NH(+)", reacting as an equivalent of "$HN^{(-)}$-OTMS" during the nucleophilic addition to give adduct **2**, and like "$HN^{(+)}$" electrophilic synthon during the cyclization to aziridine with the displacement of the $^{(-)}$OTMS group.[8]

Results and Discussion

Conjugate addition is an important bond-forming strategy utilized in organic synthesis. In this field, one of the most straightforward routes for the carbon−nitrogen bond formation is the 1,4-addition of nitrogen nucleophiles to electrophilic olefines.[9] Recently Reetz and co-workers[10] reported the enhanced reactivity of substituted alkylidene malonates toward nucleophilic attack of silylated hydroxylamine simply by stirring the components in CH_2Cl_2 for 18 h at room temperature and in the absence of catalyst. Under these simple conditions we carried out the 1,4-addition of *N,O*-bis(trimethylsilyl)-hydroxylamine to a variety of dimethyl malonate olefines. The electrophilic substrates **1a**−**e** have been prepared by condensation of dimethyl malonate with aliphatic and aromatic aldehydes in the presence of $TiCl_4$ and pyridine in THF.[11] After workup in water and extraction with organic solvent, the α,*β*-unsaturated products were isolated and purified by distillation or chromatography on silica gel, in yields ranging from 50% to 75% (Scheme 2).

The subsequent 1,4-addition of *N,O*-bis(trimethylsilyl)-hydroxylamine to the olefins **1** was performed in CH_2Cl_2 with a 2:1 ratio of nucleophile in respect to electrophile. Compound **2** was obtained exclusively in good yield, with removal of the *N*-silyl protection during workup from the disilylated intermediate (Scheme 3). The results of the addition reaction of the silylated hydroxylamine to compounds **1a**−**e** are reported in Table 1.

In an alternative way the conjugate addition reaction was carried out in 30 min in CH_2Cl_2 at −40 °C in the presence of 3% of $Yb(OTf)_3$. In the presence of a greater amount of catalyst or when the temperature exceeds 0 °C, decomposition of the adduct takes place, affording the silyl oxime and dimethylmalonate.

During the step of trimethylsilyl deprotection by treatment of **2** with TBAF (1.1 equiv) in THF at room temperature, the isoxazolidin-5-one[12] **3** was isolated (Scheme 4). The attack of fluoride on silicon indeed induces the formation of tetrabutylammonium hydroxy-

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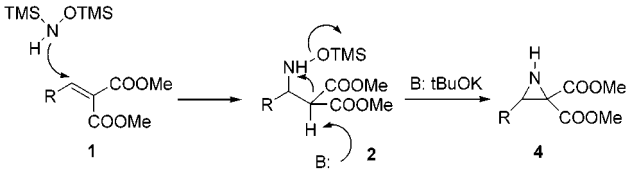
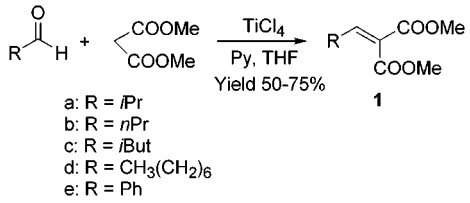
Scheme 1



Scheme 2



Scheme 3

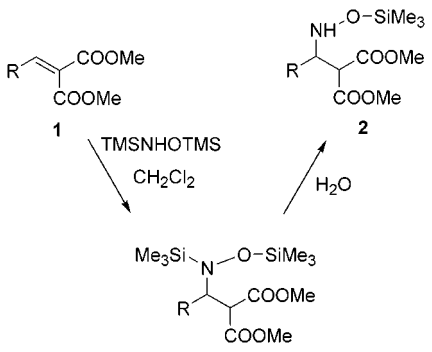
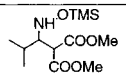
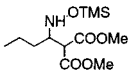
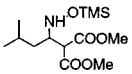
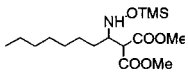
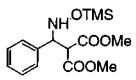


Table 1

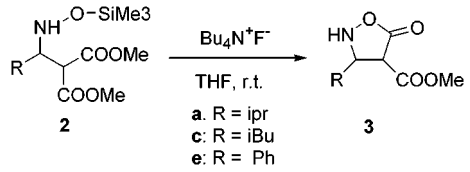
Entry	Reactant	Product **2**	Yield (%)[a]
1	**1a**		69
2	**1b**		57
3	**1c**		75
4	**1d**		68
5	**1e**		71

[a] Calculated on isolated product, after flash chromatography on silica gel.

lamino salt, which easily promotes the transesterification.

The reaction was performed successfully on derivatives **2a**, **2c**, and **2e**, giving the corresponding isooxazolidin-5-ones in 40−60% yield after purification by flash chromatography on silica gel. On the other hand, compound **3** may be easily obtained by refluxing the α,β-unsaturated derivative **1** and *N*,*O*-bis(trimethylsilyl)hydroxylamine in methanol.[13]

Scheme 4



Scheme 5

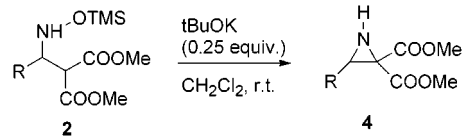
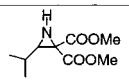
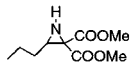
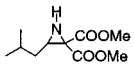
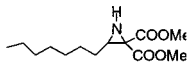


Table 2

Entry	Reactant	Product **4**	Yield (%)[a]
1	**2a**		78
2	**2b**		57
3	**2c**		65
4	**2d**		54

[a] Calculated on isolated product, after flash chromatography on silica gel.

The most interesting features of the silylated adducts **2a**−**d** is the conversion to iridine-2,2-dimethyl ester **4**. Compound **2** can be considered a precursor of aziridine because, close to an easily enolizable position, it presents a nitrogen carrying a O-SiMe$_3$ function, which was already observed by Ricci et al.[14] to be a good leaving group (Scheme 5). In this work we developed a new mild method to prepare aziridine-2,2-dicarboxylate simply by treatment of adduct **2** with a catalytic amount of potassium tertbutoxide[15] (0.25 equiv) in CH_2Cl_2 at room temperature for 4 h. The Me_3SiOK formed acts as base to complete the cyclization. When a larger amount of base was added, a mixture of byproducts was observed. The results obtained in the cyclization reaction are reported in Table 2.

All substrates (**2a**−**d**) gave good results and easy formation of aziridines **4a**−**d**. On the contrary, any attempt to convert **2e** to the corresponding aziridine

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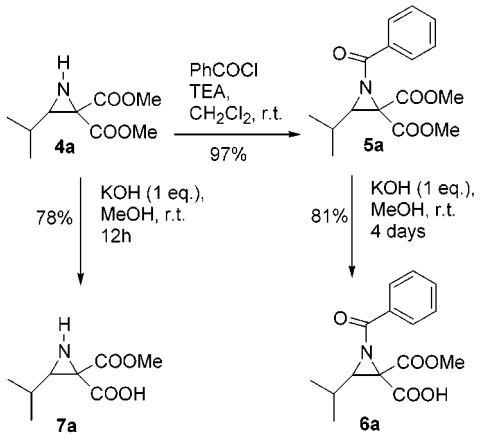
Scheme 6



failed, although different conditions and several bases were tested to induce cyclization. In contrast, the decomposition prevails to give the corresponding phenyl *O*-silyl oxime and malonate.

The nitrogen group protection of aziridine **4a** was performed by treatment with benzoyl chloride in CH_2Cl_2 in the presence of TEA and DMAP. The benzamide **5a**, obtained in quantitative yield, was analyzed by ^{1}H NMR and showed a methyl ester resonance at 4.0 ppm and another one shielded at 3.5 ppm. The amide **5a** is a very stable molecule whose regioselective hydrolysis of the more shielded methyl ester was achieved by treatment with 1 equiv of KOH in methanol for 4 days at room temperature. In the similar way the partial hydrolysis of **4a** was performed by treatment of the unprotected aziridine in methanol for 12 h in the presence of 1 equiv of KOH (Scheme 6). The reaction furnished a 1:1 mixture of monocarboxylic acids.

In conclusion, in this work we have reported the synthesis of aziridine-2,2-dicarboxylates, which are a new class of unusual amino acids that can be utilized in the synthesis of biologically active polipeptides. The design of receptor-selective peptide containing unusual amino acids and peptidomimetic ligands with highly potent and specific biological properties has become indeed one of the most important areas in bioorganic and medicinal chemistry.

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Experimental Section

General Procedure for the Synthesis of 1. To a chilled solution (0 °C) of $TiCl_4$ (20 mmol, 2.2. mL) in THF (15 mL) under nitrogen atmosphere were added dimethylmalonate (10 mmol, 1.14 mL) and aldehyde (10 mmol). After 40 min of stirring, pyridine (40 mmol, 3.23 mL) was added, and the reaction mixture was allowed to stir overnight, slowly warming to room temperature. The reaction was then quenched with a saturated solution of $NaHCO_3$ (2 mL), and after removal of THF under reduced pressure, the residue was extracted twice with ethyl acetate. The organic layers were washed with brine, dried over Na_2SO_4, and concentrated under reduced pressure. Compound **1** was isolated by flash chromatography on silica gel (cyclohexane/ethyl acetate, 9/1) or distilled from the crude reaction mixture by bulb to bulb distillation.

1a: IR (film) 2959, 2866, 1734, 1437 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.08 (d, 6H, J = 6.6 Hz), 2.60−2.73 (m, 1H), 3.76 (s, 3H), 3.80 (s, 3H), 6.85 (d, 1H, J = 10.8 Hz); ^{13}C NMR ($CDCl_3$) δ 21.7, 29.5, 52.1, 52.2, 125.7, 155.7, 164.3; MS *m*/*z* 186 (2), 171 (5), 155 (11), 122 (100), 111 (6), 94 (18), 67 (19), 59 (14). Anal. Calcd: C, 58.05; H, 7.58. Found: C, 58.03; H, 7.59.

1b: IR (film) 2959, 2853, 1739, 1440, 1241 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.95 (t, 3H, J = 7.5 Hz), 1.52 (sext, 2H, J = 7.5 Hz), 2.28 (q, 2H, J = 7.5 Hz), 3.78 (s, 3H), 3.83 (s, 3H), 7.04 (t, 1H, J = 7.5 Hz); ^{13}C NMR ($CDCl_3$) δ 13.5, 21.5, 31.6, 51.9, 52.0, 127.8, 149.9, 164.0, 165.6; MS *m*/*z* 186 (2), 155 (21), 122 (100), 113 (53), 94 (33), 59 (28). Anal. Calcd: C, 58.05; H, 7.58. Found: C, 58.07; H, 7.61.

1c: IR (film) 2965, 2866, 1746, 1646, 1434 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.88 (d, 6H, J = 6.6 Hz), 1.20−1.41 (m, 8H), 1.42−1.55 (m, 2H), 2.29 (q, 2H, J = 4.6 Hz), 3.78 (s, 3H), 3.83 (s, 3H), 7.04 (t, 1H, J = 4.9 Hz); ^{13}C NMR ($CDCl_3$) δ 22.2, 28.0, 38.5, 52.0, 52.1, 128.4, 149.1, 164.1, 165.7; MS *m*/*z* 200 (2), 169 (14), 158 (13), 136 (58), 126 (100), 113 (33), 98 (47), 68 (40), 59 (24). Anal. Calcd: C, 59.98; H, 8.05. Found: C, 59.95; H, 8.08.

1d: IR (film) 2926, 2952, 1739, 1646, 1428 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.94 (t, 3H, J = 6.9 Hz), 1.77−1.86 (m, 1H), 2.19 (dd, 2H, J = 6.9, 7.8 Hz), 3.79 (s, 3H), 3.83 (s, 3H), 7.06 (t, 1H, J = 7.8 Hz); ^{13}C NMR ($CDCl_3$) δ 13.9, 22.5, 28.1, 28.8, 29.0, 29.7, 31.5, 52.0, 52.1, 127.7, 150.3, 164.1, 165.6; MS *m*/*z* 201 (3), 186 (11), 169 (30), 141 (100), 126 (45), 112 (38), 99 (69), 68 (60), 55 (34). Anal. Calcd: C, 64.44; H, 9.15. Found: C, 64.41; H, 9.18.

1e: IR (film) 2998, 2946, 1732, 1620, 1427 cm^{-1}; ^{1}H NMR ($CDCl_3$) 3.86 (s, 6H), 7.38−7.45 (m, 5H), 7.79 (s, 1H); ^{13}C NMR ($CDCl_3$) δ 52.7, 125.4, 128.8, 129.3, 130.6, 132.6, 142.8, 164.3, 167.0; MS *m*/*z* 220 (56), 189 (54), 160 (83), 129 (39), 121 (100), 102 (72), 91 (22), 59 (27). Anal. Calcd: C, 65.45; H, 5.49. Found: C, 65.46; H, 5.47.

General Procedure for the 1,4-Addition of *N*,*O*-Bis-(trimethylsilyl)hydroxylamine to 1. A stirred solution of **1** (2 mmol) in CH_2Cl_2 (10 mL) at −40 °C under inert atmosphere was treated with $Yb(Otf)_3$ (0.04 mmol, 21 mg). After 10 min *N*,*O*-bis(trimethylsilyl)hydroxylamine was added in one portion (4 mmol, 0.85 mL). The reaction was monitored by TLC and quenched with HCl 0.1 M (1 mL) after 30 min. The organic layer was diluted with 20 mL of CH_2Cl_2, washed with water, and dried over Na_2SO_4, and solvent was removed under reduced pressure. Compound **2** was purified by flash chromatography on silica gel (cyclohexane/ethyl acetate, 1:1 as eluant).

2a: IR (film) 3277, 2959, 1739, 1441 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.13 (s, 9H), 0.97 (d, 3H, J = 6.6 Hz), 1.03 (d, 3H, J = 6.6 Hz), 1.57−1.74 (m, 1H), 3.34 (dd, 1H, J = 4.2, 7.7 Hz), 3.61 (d, 1H, J = 4.2 Hz), 3.73 (s, 3H), 3.77 (s, 3H), 6.01−6.18 (bs, 1H); ^{13}C NMR ($CDCl_3$) δ −1.0, 19.7, 20.3, 29.2, 50.8, 52.1, 52.2, 68.3, 169.1, 169.6. Anal. Calcd: C, 49.46; H, 8.65; N, 4.81. Found: C, 49.48; H, 8.62; N, 4.79.

2b: IR (film) 3250, 2939, 1733, 1434, 1242 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.11 (s, 9H), 0.92 (t, 3H, J = 6.6 Hz), 1.26−1.58 (m, 4H), 3.36−3.47 (bm, 1H), 3.74 (s, 3H), 3.76 (s, 3H), 3.80 (d, 1H, J = 4.8 Hz), 5.66−5.80 (bs, 1H); ^{13}C NMR ($CDCl_3$) δ −0.9, 14.0, 20.0, 31.9, 52.0, 52.2, 62.1, 169.1. Anal. Calcd: C, 49.46; H, 8.65; N, 4.81. Found: C, 49.45; H, 8.63; N, 4.82.

2c: IR (film) 3283, 2959, 1745, 1447, 1241 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.12 (s, 9H), 0.91 (d, 3H, J = 6.6 Hz), 0.92 (d, 3H, J = 6.6 Hz), 1.17 (ddd, 1H, J = 4.2, 9.1, 13.7 Hz), 1.38 (ddd, 1H, J = 4.6, 9.1, 13.7 Hz), 1.73−1.87 (m, 1H), 3.50 (dt, 1H, J = 4.5, 9.1 Hz), 3.74 (s, 3H), 3.76 (s, 3H), 3.82 (d, 1H, J = 4.5 Hz), 5.50−5.90 (bs, 1H); ^{13}C NMR ($CDCl_3$) δ −0.9, 21.9, 23.3, 25.2, 38.9, 52.0, 52.2, 60.3, 169.0, 169.1. Anal. Calcd: C, 51.12; H, 8.91; N, 4.59. Found: C, 51.11; H, 8.93; N, 4.61.

2d: IR (film) 3462, 3277, 2959, 1739, 1427 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.11 (s, 9H), 0.88 (t, 3H, J = 6.8 Hz), 1.22−1.35 (m, 8H), 1.36−1.46 (m, 2H), 3.38−3.43 (m, 1H), 3.74 (s, 3H), 3.76 (s, 3H), 3.79 (d, 1H, J = 4.8 Hz), 5.71−5.79 (bs, 1H); ^{13}C NMR ($CDCl_3$) δ −0.9, 14.1, 22.6, 26.8, 29.2, 29.5, 29.7, 31.8, 52.0, 52.3, 62.3, 169.1. Anal. Calcd: C, 55.30; H, 9.57; N, 4.03. Found: C, 55.32; H, 9.60; N, 4.05.

2e: IR (film) 3277, 3032, 2959, 1746, 1434 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.04 (s, 9H), 3.52 (s, 3H), 3.76 (s, 3H), 3.99 (d, 1H, J = 8.6 Hz), 4.66 (d, 1H, J = 8.6 Hz), 5.87−5.98 (bs, 1H), 7.25−7.31 (m, 5H); ^{13}C NMR ($CDCl_3$) δ −1.1, 52.3, 52.5, 54.7, 65.8,

127.9, 128.1, 128.2, 137.4, 167.6, 168.4. Anal. Calcd: C, 55.36; H, 7.12; N, 4.30. Found: C, 55.38; H, 7.13; N, 4.26.

General Procedure for the Ring Closure of 2 to Isoxazolidin-5-one 3. Adduct **2** (1 mmol) was dissolved in dry THF (5 mL) under nitrogen atmosphere, and tetrabutylammonium fluoride (1.1 mmol, 0.287 g) was added in one portion at 0 °C. The reaction was vigorously stirred for 1 h and then quenched with water. After THF was removed under reduced pressure, the residue was diluted with Et_2O and washed twice with water. The organic layers were dried over Na_2SO_4, and solvent was removed under reduced pressure. Isoxazolidin-5-one **3** was isolated by flash chromatography on silica gel (cyclohexane/Et_2O, 7/3 as eluant).

3a: IR (film) 3244, 2964, 1786, 1741, 1438, 1270, 1164 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.98 (d, 3H, $J = 6.6$ Hz), 1.02 (d, 3H, $J = 6.6$ Hz), 1.80−1.93 (m, 1H), 3.52 (d, 1H, $J = 6.3$ Hz), 3.82−3.84(m, 1H), 3.83 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 18.6, 18.8, 31.0, 51.5, 53.3, 68.5, 167.1, 173.0; MS *m*/*z* 187 (2), 144 (100), 128 (11), 112 (41), 111 (44), 101 (31), 59 (44). Anal. Calcd: C, 51.33; H, 7.00; N, 7.48. Found: C, 51.35; H, 6.99; N, 7.49.

3c: IR (film) 3231, 2952, 2926, 1786, 1733, 1448 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.96 (d, 3H, $J = 6.6$ Hz), 0.97 (d, 3H, $J = 6.6$ Hz), 1.40−1.69 (m, 2H),1.70−1.81 (m, 1H), 3.41 (d, 1H, $J = 6.6$ Hz), 3.85 (s, 3H), 4.05−4.28 (m, 1H); ^{13}C NMR ($CDCl_3$) δ_22.3, 22.7, 25.1, 41.2, 53.4, 53.7, 61.5, 166.7, 173.0; MS *m*/*z* 201 (2), 169 (11), 144 (41), 116 (64), 101 (100), 69 (59), 59 (72). Anal. Calcd: C, 53.72; H, 7.51; N, 6.96. Found: C, 53.69; H, 7.52; N, 6.96.

3e: IR (film) 3244, 3025, 2946, 1786, 1733, 1282, 1143 cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.85 (s, 3H), 3.91 (d, 1H, $J = 8.4$ Hz), 5.28 (dd, 1H, $J = 8.4$, 8.8 Hz), 7.38−7.49 (m, 6H); ^{13}C NMR ($CDCl_3$) δ 53.5, 54.4, 65.7, 126.6, 129.2, 130.6, 166.1, 172.2; MS *m*/*z* 221 (1), 177 (71), 162 (6), 146 (100), 119 (36), 104 (41), 91 (24). Anal. Calcd: C, 59.73; H, 5.01; N, 6.33. Found: C, 59.75; H, 5.01; N, 6.34.

General Procedure for the Ring Closure of 2 to Aziridine 4. To a stirred solution of **2** (1 mmol) in dry CH_2Cl_2 at room temperature under nitrogen atmosphere was added *t*BuOK (0.25 mmol, 0.25 mL, solution 1 M in THF) in one portion. After 4 h of stirring, the reaction was quenched with water, extracted twice with CH_2Cl_2, and dried over Na_2SO_4, and solvent was removed under reduced pressure. Aziridine **4** was isolated by flash chromatography on silica gel (cyclohexane/diethyl ether, 7:3 as eluant).

4a: IR (film) 3297, 2959, 2859, 1739, 1441 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.88−1.28 (m, 7H), 1.98 (d, 1H, $J = 9.6$ Hz), 2.28−2.37 (m, 1H), 3.82 (s, 6H); ^{13}C NMR ($CDCl_3$) δ 19.2, 20.7, 30.2, 45.9, 51.4, 52.5, 53.4, 166.3, 169.8; MS *m*/*z* 201 (7), 186 (6), 169 (1), 142 (100), 132 (36), 100 (19), 82 (94), 55 (52). Anal. Calcd: C, 53.72; H, 7.51; N, 6.96. Found: C, 53.70; H, 7.53; N, 6.97.

4b: IR (film) 3277, 2965, 2906, 1733, 1441 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.95 (t, 3H, $J = 7.1$ Hz), 1.49−1.57 (m, 4H), 2.02 (bd, 1H, $J = 9.0$ Hz), 2.52−2.68 (m, 1H), 3.81 (s, 3H), 3.82 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 13.8, 20.5, 29.7, 32.1, 44.8, 52.8, 53.4, 164.9, 166.7; MS *m*/*z* 201 (3), 186 (11), 169 (30), 141 (100), 126 (45), 112 (38), 99 (69), 68 (60), 55 (34). Anal. Calcd: C, 53.72; H, 7.51; N, 6.96. Found: C, 53.73; H, 7.52; N, 6.94.

4c: IR (film) 3291, 2952, 2873, 1726, 1434 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.96 (d, 3H, $J = 6.6$ Hz), 0.98 (d, 3H, $J = 6.6$ Hz), 0.98−1.20 (m, 1H), 1.52 (ddd, 1H, $J = 4.2$, 6.9, 13.8 Hz), 1.77−1.88 (m, 1H), 2.03 (bd, 1H, $J = 9.6$ Hz), 2.62 (dt, 1H, $J = 4.2$, 9.6 Hz), 3.81 (s, 3H), 3.82 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 22.3, 22.5, 27.1, 38.6, 43.7, 44.9, 52.8, 53.4, 166.8, 169.8; MS *m*/*z* 215(1), 200(93), 156(26), 140(67), 112(76), 96(100). Anal. Calcd: C, 55.80; H, 7.96; N, 6.51. Found: C, 55.82; H, 7.95; N, 6.50.

4d: IR (film) 3291, 2952, 2846, 1733, 1448 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.81−0.92 (m, 3H), 1.12−1.37 (m, 10H), 1.38−1.40 (m, 2H), 1.98 (d, 1H, $J = 9.6$ Hz), 2.51−2.59 (m, 1H), 3.79 (s, 6H); ^{13}C NMR ($CDCl_3$) δ 14.1, 22.7, 27.2, 29.2, 29.3, 30.5, 31.7, 45.0, 45.3, 52.8, 53.6, 167.1, 170.0; MS *m*/*z* 257 (2), 198(26), 173 (59), 138 (16), 114 (100), 69(23). Anal. Calcd: C, 60.68; H, 9.01; N, 5.44. Found: C, 60.64; H, 8.98; N, 5.47.

Synthesis of *N*-Benzoyl-aziridine 5a. Benzoyl chloride (1.1. mmol, 0.127 mL) in CH_2Cl_2 (5 mL) was added dropwise to a stirred solution of aziridine **4a** (1 mmol) and TEA (1.2 mmol, 0.167 mL) in CH_2Cl_2 (5 mL). The reaction was left stirring for 2 h and then quenched with water. After diluting with 20 mL of CH_2Cl_2 and washing with water, the organic layer was dried over Na_2SO_4, and solvent was removed under reduced pressure. Compound **5a** was obtained in 97% yield after flash chromatography on silica gel as a white solid (cyclohexane/Et_2O, 8/2)

5a: mp 81−84 °C; IR (film) 3059, 2972, 1739, 1693, 1428, 1242 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.10 (d, 3H, $J = 6.6$ Hz), 1.23 (d, 3H, $J = 6.3$ Hz), 1.30−1.41 (m, 1H), 3.14 (d, 1H, $J = 9.6$ Hz), 3.34 (s, 3H), 3.94 (s, 3H), 7.38−7.60 (m, 3H), 8.10−8.14 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 18.8, 20.8, 29.7, 52.7, 52.9, 53.0, 128.3, 128.6, 130.0, 132.9, 165.0, 165.3, 175.6; MS *m*/*z* 305 (6), 290 (11), 200 (13), 105 (100), 77 (33). Anal. Calcd: C, 62.94; H, 6.27; N, 4.59. Found: C, 62.92; H, 6.26; N, 4.59.

Partial Hydrolysis of Aziridine 5a. To a stirred solution of aziridine **5a** (0.5 mmol, 150 mg) in MeOH (5 mL) at room temperature was added KOH (1 equiv, 2 mL of 0.25 M solution in MeOH) in one portion. The mixture was left stirring at room temperature for 4 days and quenched with diluted HCl, and then solvent was removed under reduced pressure. The residue was diluted with EtOAc and washed twice with water. The organic layer was dried over Na_2SO_4, and solvent was removed under reduced pressure to give aziridine **6a** in 81% yield.

6a: IR (film) 3131, 2965, 1752, 1706, 1283 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.09 (d, 3H, $J = 6.6$ Hz), 1.21 (d, 3H, $J = 6.6$ Hz), 1.31−1.51 (m, 1H), 3.07 (d, 1H, $J = 9.02$ Hz), 3.94 (s, 3H), 6.51−6.82 (bs, 1H), 7.35−7.51 (m, 3H), 8.04−8.11 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 18.6, 20.6, 29.7, 52.6, 52.9, 53.2, 128.2, 128.5, 132.7, 133.6, 165.6, 167.3, 175.8; MS *m*/*z* 291 (2), 248 (7), 142 (4), 105 (100), 77 (24). Anal. Calcd: C, 61.85; H, 5.88; N, 4.81. Found: C, 61.88; H, 5.86; N, 4.82.

Partial Hydrolysis of Aziridine 4a. To a stirred solution of aziridine **4a** (0.5 mmol, 100 mg) in MeOH (5 mL) at room temperature was added KOH (1 equiv, 2 mL of 0.25 M solution in MeOH) in one portion. The mixture was left stirring at room temperature for 12 h and quenched with diluted HCl, and then solvent was removed under reduced pressure. The residue was diluted with EtOAc and washed twice with water. The organic layer was dried over Na_2SO_4, and solvent was removed under reduced pressure to give aziridine **7a** in 78% yield as a white solid.

7a: mp 114−116 °C; IR (film) 3423, 2972, 1746, 1640, 1361 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.96 (d, 3H, $J = 6.8$ Hz), 1.15 (d, 3H, $J = 6.6$ Hz), 1.40−1.60 (m, 1H), 2.44 (d, 1H, $J = 9.4$ Hz), 3.92 (s, 3H), 5.35−5.81 (bs, 1H); ^{13}C NMR ($CDCl_3$) δ 19.4, 20.9, 29.2, 52.9, 53.4, 54.3, 170.1, 170.7. Anal. Calcd: C, 51.33; H, 7.00; N, 7.48. Found: C, 51.28; H, 6.98; N, 7.50.

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