Carbonylation of Silylated Hydroxymethyl Aziridines to β-Lactams

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Functionalized β-lactams are synthesized by carbonylative ring expansion of silylated hydroxymethyl aziridines catalyzed by dicobalt octacarbonyl, a process that proceeds with inversion of configuration. Ring opening and elimination occurs on attempted carbonylation of aziridine carboxylates.

Introduction

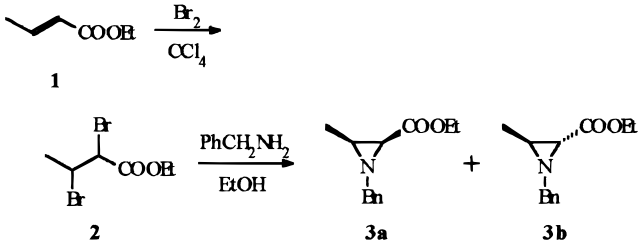
Carbonylative ring expansion using carbon monoxide in the presence of a transition-metal catalyst is a useful reaction for the synthesis of a variety of heterocyclic compounds.[1] In this process, carbon monoxide is inserted into a ring carbon−heteroatom bond, thus affording a carbonyl-containing ring-expanded product. For instance, β-lactams can be obtained by this methodology from aziridines.

N-alkyl phenylaziridines give β-lactams in quantitative yields using $[Rh(CO)_2Cl]_2$ and CO pressure by regiospecific insertion into the most substituted ring carbon−nitrogen bond.[2] This reaction is limited to aziridines bearing an activating group at the 2-position, such as a phenyl or vinyl. Carbonylation of alkylaziridines has been also performed, in moderate yields, using excess quantities of the highly toxic $Ni(CO)_4$, with CO insertion occurring into the less substituted ring C−N bond with net retention of configuration.[3] A significant advance in the carbonylation of simple *N*-alkylaziridines resulted when catalytic amounts of $Co_2(CO)_8$ were used:[4] the reaction proceeded in excellent yields and CO insertion occured into the less substituted carbon−nitrogen bond by a S_N2 like mechanism (inversion of configuration).

The application of the $Co_2(CO)_8$-catalyzed reaction to the synthesis of more functionalized β-lactams by the carbonylative ring expansion of aziridines was a desirable goal: our attention was focused on *cis*- and *trans*-2-alkoxycarbonyl- and silylated 2-hydroxymethyl-3-alkylaziridines as possible substrates for carbonylation. In fact, the presence of a carboxylic ester group may be of use in a subsequent step of an extended synthesis, since it can be easily transformed into different functionalities. An alternative ring substituent can be a hydroxymethyl group, acting as a "masked" ester function. Therefore, aziridinecarboxylates and hydroxy-methylated aziridines represent interesting substrates for carbonylation, taking into account the fact that they can be obtained in optically active form by several methods.[5]

We now wish to report that the cobalt-catalyzed carbonylation is applicable to different carbon-ring functionalized aziridines. In particular, silylated hydroxymethyl aziridines can be successfully carbonylated to β-lactams in excellent yields.

Scheme 1



Results and Discussion

Synthesis and Attempted Carbonylation of Aziridinecarboxylates 3a,b. Addition of bromine to commercial ethyl crotonate (**1**) in carbon tetrachloride readily afforded ethyl 2,3-dibromobutanoate (**2**) (98% yield) (Scheme 1). Cyclization of **2** with benzylamine in absolute ethanol gave a mixture of *cis*- and *trans*-1-benzyl-2-ethoxycarbonyl-3-methylaziridines, **3a** and **3b**, respectively, in a 73:27 ratio and in 86% total yield.[6,7a] On the basis of ^{1}H NMR spectral analysis ($^3J_{H-Hcis} > {}^3J_{H-Htrans}$), the cis stereochemistry was assigned to aziridine **3a** ($^3J_{2,3}$ 6.8 Hz) and trans stereochemistry to **3b** ($^3J_{2,3}$ 2.6−2.9 Hz).

Treatment of **3a** with carbon monoxide and $Co_2(CO)_8$ in 1,2-dimethoxyethane (DME) for 18 h at 110 °C and 500 psi of CO gave only the elimination product, ethyl 3-benzylamino-2-butenoate (**3e**), in 73% yield (Scheme 2). The ^{1}H NMR spectrum shows two singlets, one for the methyl group and the other for the proton attached to the double bond, and ^{13}C NMR spectroscopy confirms the presence of two unsaturated carbons. This result indicates that the aziridine **3a** undergoes nucleophilic ring opening by the in situ-generated tetracarbonylcobaltate anion $[Co(CO)_4]^-$ with attack at the C_2 ring carbon atom. Formation of the four-membered β-lactam ring requires CO insertion into the C−Co bond and subsequent ring closure by nucleophilic attack on the new carbonyl by the

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(1) Khumtaveeporn K.; Alper H. *Acc. Chem. Res.* **1995**, *28*, 414.
(2) Calet S.; Urso F.; Alper H. *J. Am. Chem. Soc.* **1989**, *111*, 931.
(3) Chamchaang W.; Pinhas A. R. *J. Org. Chem.* **1990**, *55*, 2943.
(4) Piotti M. E.; Alper H. *J. Am. Chem. Soc.* **1996**, *118*, 111.
(5) Tanner D. *Angew. Chem., Int. Ed. Engl.* **1994**, *33*, 599 and references therein. Bucciarelli M.; Forni A.; Moretti I.; Prati F.; Torre G. *J. Chem Soc., Perkin Trans. 1* **1993**, 3041.
(6) (a) Stolberg M. A.; O'Neill J. J.; Wagner-Jauregg T. *J. Am. Chem. Soc.* **1953**, *75*, 5045. (b) v. Capeller R.; Griot R.; Häring M.; Wagner-Jauregg T. *Helv. Chim. Acta* **1957**, *40*, 1652.
(7) (a) Andersson P. H.; Guijarro D.; Tanner D. *J. Org. Chem.* **1997**, *62*, 7364. (b) Deyrup J. A.; Moyer C. L. *J. Org. Chem.* **1970**, *35*, 3424. A slightly modified procedure was adopted, using THF instead of ether as solvent.

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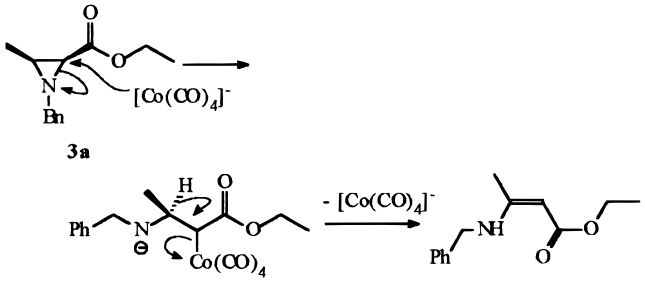
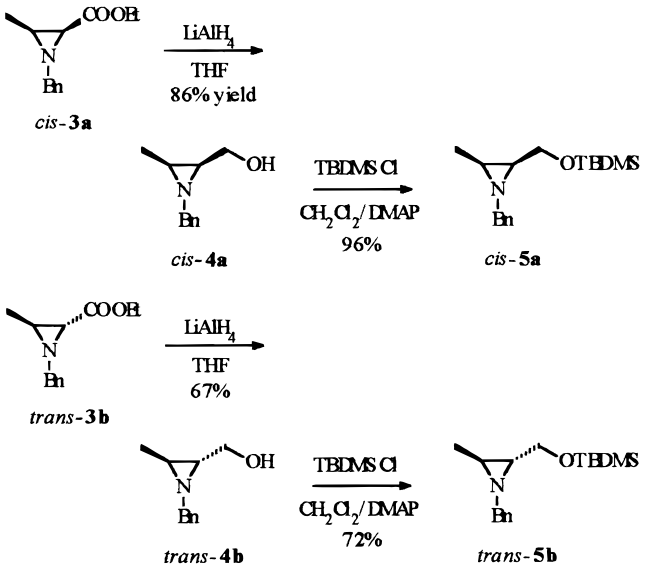
Scheme 2



Scheme 3



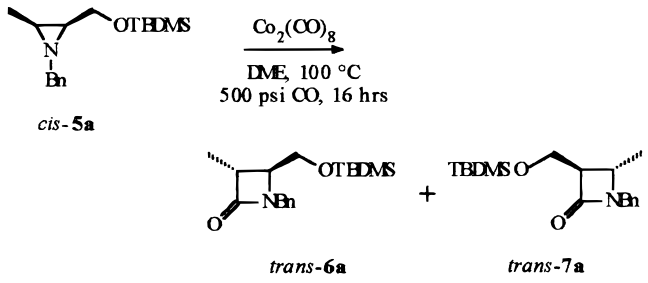
negative charged nitrogen: in this case, however, elimination to **3e** is favored possibly because of the formation of a conjugated system. Therefore, the presence of an ester group on the aziridine ring is detrimental for the carbonylation reaction. The synthetic strategy was then to reduce the ester function and to perform the carbonylation on the corresponding aziridino alcohol, after protection as a *tert*-butyldimethylsilyl ether.

Synthesis and Carbonylation of Silylated Hydroxymethyl Aziridines 5a,b. Reduction of isomeric aziridine carboxylic esters **3a**,**b** with $LiAlH_4$ in tetrahydrofuran (THF) at room temperature [6b,7] gave the corresponding hydroxymethyl aziridines, *cis*- and *trans*-1-benzyl-2-hydroxymethyl-3-methylaziridine (**4a** and **4b**) (Scheme 3). The latter were protected as TBDMS-ethers **5a**,**b** by treatment with *tert*-butyldimethylsilyl chloride (TBDMSCl) and 4-(dimethylamino)pyridine (DMAP) in dichloromethane at room temperature, in 83% and 48% overall yields, respectively.

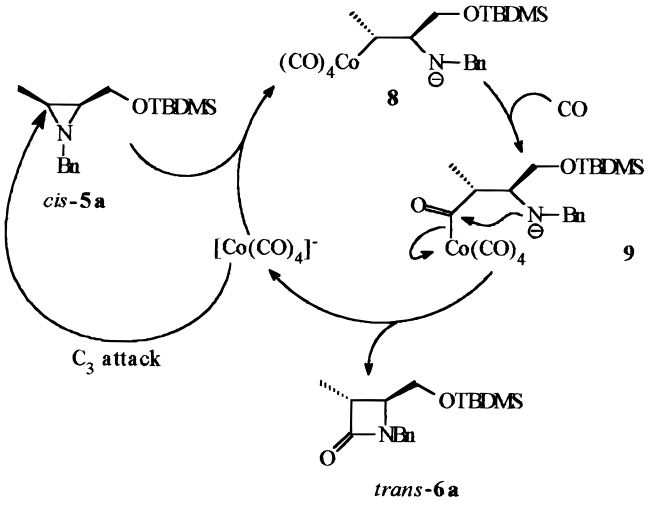
Treatment of *cis*-aziridine **5a** with carbon monoxide and $Co_2(CO)_8$ in DME for 16 h at 100 °C and 500 psi of CO using a 12:1 ratio of aziridine/catalyst gave a 92:8 mixture of *trans*-*β*-lactams 1-benzyl-3-methyl-4-((*tert*-butyldimethylsilyloxy)methyl)azetidin-2-one (**6a**) and 1-benzyl-4-methyl-3-((*tert*-butyldimethylsilyloxy)methyl)-azetidin-2-one (**7a**) in a total 99.8% isolated yield (Scheme 4).

Carbonyl insertion was confirmed by ^{13}C NMR spectroscopy, with the carbonyl carbon occurring at 170.8 ppm for **6a**. The relative trans stereochemistry of the *β*-lactam ring of regioisomers **6a** and **7a** was assigned

Scheme 4



Scheme 5



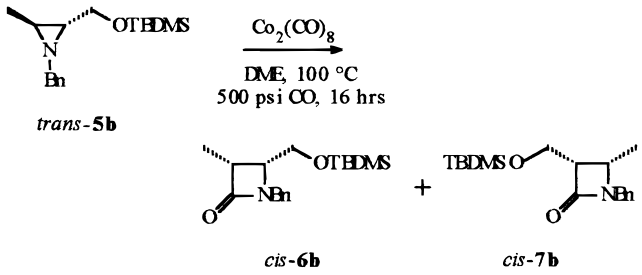
from the ring proton coupling constants ($^3J_{3,4}$ 1.9−2.1 Hz), whereas the ring substitution pattern was determined according to the MS fragmentation. From a vertical *cross-cleavage* of the azetidinone ring, a base fragment at *m*/*z* 206 was observed for **6a** but not for **7a**, and therefore, the $TBDMSOCH_2-$ side chain was assigned at position 4 for **6a** and at position 3 for **7a**.

The trans ring substitution of both **6a** and **7a** suggests an S_N2-like mechanism with inversion of configuration as previously reported,[4] with nucleophilic ring opening of the aziridine by the in situ-generated tetracarbonylcobaltate anion (Scheme 5). Moreover, the isomeric ratio indicates preferential nucleophilic attack by $[Co(CO)_4]^-$ at the alkyl-bearing ring carbon atom (C_3) rather than at the *O*-protected hydroxymethyl-bearing carbon atom (C_2) of the aziridinic ring in **5a**. After initial nucleophilic attack by tetracarbonylcobaltate at C_3 with inversion of configuration, giving **8**, subsequent CO insertion into the C−Co bond should proceed with retention of configuration to form **9**.[4] Finally, ring closure by intramolecular nucleophilic attack provides the *β*-lactam **6a** and regenerates the catalyst. Therefore, the cobalt carbonyl catalyzed carbonylation of the protected hydroxymethyl aziridine *cis*-**5a** is quantitative and highly regioselective.

Under the same reaction conditions, *trans*-**5b** gave a mixture of *cis*-*β*-lactams 1-benzyl-3-methyl-4-((*tert*-butyldimethylsilyloxy)methyl)-azetidin-2-one (**6b**) and 1-benzyl-4-methyl-3-((*tert*-butyldimethylsilyloxy)methyl)-azetidin-2-one (**7b**) in a 88:12 ratio and 63% overall isolated yield (Scheme 6).

The relative cis stereochemistry of regioisomers **6b** and **7b** was determined by ^1H NMR spectroscopy ($^3J_{3,4}$ 5.4 Hz), and the ring substitution pattern was assigned according to the MS fragmentation analogous to **6a** and **7a**. For the *trans*-aziridine **5b**, the carbonylation reaction

Scheme 6



proceeds with slightly lower regioselectivity and lower yield than for **5a**.

Conclusions. The well-established dicobalt octacarbonyl-catalyzed carbonylation described for alkylaziridines has been applied to 2-ethoxycarbonyl- and silylated 2-hydroxymethyl-3-methylaziridines. *N*-Benzyl TBDMSO-protected hydroxymethyl aziridines were successfully carbonylated to β-lactams using $Co_2(CO)_8$ as the catalyst: *trans*-β-lactams are obtained from a *cis*-aziridine in quantitative yields, whereas *cis*-β-lactams were isolated using a *trans*-aziridine. The reaction proceeds through nucleophilic ring opening of the aziridine by the in situ-generated tetracarbonylcobaltate anion and shows high regioselectivity, with preferential CO insertion into the alkyl-bearing ring carbon−nitrogen bond rather than into the O-protected hydroxymethyl-bearing ring carbon−nitrogen bond.

These results further expand the range of aziridines as useful substrates for the cobalt carbonyl catalyzed carbonylation, thus making easily available a variety of functionalized β-lactams, some of which can be used as suitable precursors for antibiotic drugs.

Experimental Section

Ethyl 2,3-Dibromobutanoate (2). Bromine (1.14 mL, 22.2 mmol) was slowly added dropwise at room temperature to a stirred solution of commercial ethyl crotonate (**1**) (2.51 g, 22 mmol) in carbon tetrachloride (100 mL). After gentle reflux for 2 h, the solution was cooled and rotary evaporated, affording ethyl 2,3-dibromobutanoate (**2**) (5.90 g, 98% yield) as an amber sweet-scented liquid that was used without further purification: ^{1}H NMR (200 MHz) δ 1.36 (3H, t, J = 7.1, $-CH_2CH_3$), 1.93 (3H, d, J = 6.3 Hz, CH_3CHBr-), 4.32 (2H, q, J = 7.1, $-CH_2CH_3$), 4.36 (1H, d, J = 11.0 Hz, $-CH$BrCOO−), 4.48 (1H, dq, J = 11.0, 6.3 Hz, CH_3CHBr−); MS m/z 248 − 246 − 244 ([M − 28]$^+$).

***cis*-1-Benzyl-2-ethoxycarbonyl-3-methylaziridine (3a) and *trans*-1-Benzyl-2-ethoxycarbonyl-3-methylaziridine (3b).**[6,7a] A solution of ethyl 2,3-dibromobutanoate (**2**) (5.299 g, 19.3 mmol) in 40 mL of absolute ethanol was slowly added dropwise at 0 °C, with magnetic stirring, to a solution of benzylamine (7.40 mL, 67.7 mmol) in anhydrous ethanol (100 mL). The reaction mixture was then left to warm to room temperature and stirred overnight. After evaporation of the solvent under reduced pressure, the residue was dissolved in ether (100 mL) and washed with water (200 mL), and the aqueous phase was extracted twice with ether (30 mL). The combined organic phases were dried ($MgSO_4$) and concentrated to give a crude dark yellow oil that was subjected to flash chromatography on SiO_2 (petroleum ether/ethyl ether 80:20 and finally 60:40), affording *cis*-aziridine **3a** (2.68 g) and *trans*-aziridine **3b** (0.97 g) as yellow oils in a 73:27 ratio and in 86% total yield. ^{1}H NMR spectroscopy showed compound **3b** as a 61:39 mixture of two invertomers at nitrogen, due to slow nitrogen inversion on the NMR scale.[7a,8]

***cis*-3a**: ^{1}H NMR (200 MHz) δ 1.27 (3H, t, J = 7.1 Hz, $-COOCH_2CH_3$), 1.30 (3H, d, J = 5.6 Hz, CH_3CH-), 2.01 (1H, dq, J = 6.8, 5.6 Hz, CH_3CH-), 2.22 (1H, d, J = 6.8 Hz, $-CH$COOEt), 3.56 (1H, d, J = 13.9 Hz, $-CH_2$Ph), 3.65 (1H, d, J = 13.9 Hz, $-CH_2$Ph), 4.21 (2H, dq, J = 1.4, 7.1 Hz, $-COOCH_2CH_3$), 7.24−7.34 (5H, m, aromatic); MS m/z 219 (M^+).

***trans*-3b**: major invertomer, ^{1}H NMR (400 MHz) δ 1.22 (3H, t, J = 7.1 Hz, $-COOCH_2CH_3$), 1.26 (3H, d, J = 5.4 Hz, CH_3CH-), 2.34 (1H, dq, J = 2.9, 5.4 Hz, CH_3CH-), 2.46 (1H, d, J = 2.9 Hz, $-CH$COOEt), 3.89 (1H, d, J = 13.8 Hz, $-CH_2$Ph), 4.06 (1H, d, J = 13.8 Hz, $-CH_2$Ph), 4.13 (2H, q, J = 7.1 Hz, $-COOCH_2CH_3$), 7.20−7.40 (5H, m, aromatic); minor invertomer, ^{1}H NMR (400 MHz) δ 1.27 (3H, t, J = 7.6 Hz, $-COOCH_2CH_3$), 1.39 (3H, d, J = 5.9 Hz, CH_3CH-), 2.02 (1H, d, J = 2.6 Hz, $-CH$COOEt), 2.62 (1H, dq, J = 2.6, 5.9 Hz, CH_3CH-),3.69 (1H, d, J = 14.3 Hz, $-CH_2$Ph), 3.86 (1H, d, J = 14.3, $-CH_2$Ph), 4.18 (2H, q, J = 7.6 Hz, $-COOCH_2CH_3$), 7.20−7.40 (5H, m, aromatic); MS m/z 219 (M^+).

***cis*-1-Benzyl-2-hydroxymethyl-3-methylaziridine (4a).**[6b,7] In a 250-mL two-necked round-bottom flask equipped with a condenser and a drierite drying tube was dissolved aziridine **3a** (1.25 g, 5.71 mmol) in freshly distilled anhydrous tetrahydrofuran (36 mL). At rt under magnetic stirring, 11.4 mL of a 1.0 M $LiAlH_4$ solution in THF was slowly added dropwise (syringe) through a rubber septum. After 30 min, TLC (ethyl ether/petroleum ether 50:50) showed total disappearance of the starting material: the reaction mixture was then cooled to 0 °C, and 0.55 mL of water was carefully added, followed by 0.55 mL of a 0.15 N KOH solution. The white precipitate was filtered off and washed with abundant ether, the filtrate was dried ($MgSO_4$), and the solvent was evaporated in vacuo. After flash chromatography on silica gel (ethyl ether/petroleum ether 80:20 and finally pure ethyl ether), **4a** was obtained as a colorless sticky oil (0.87 g, 86% yield): ^{1}H NMR (200 MHz) δ 1.24 (3H, d, J = 5.6 Hz, CH_3CH-), 1.78 (1H, dq, J = 6.6, 5.6 Hz, CH_3CH-) 1.85 (1H, m, $-CH$CH$_2$OH), 2.31 (1H, br, −OH), 3.56 (2H, s, $-CH_2$Ph), 3.57 (1H, dd, J = 11.4, 6.2 Hz, $-CH_2$OH), 3.75 (1H, dd, J = 11.4, 5.0 Hz, $-CH_2$OH), 7.24−7.40 (5H, m, aromatic); MS m/z 177 (M^+).

***trans*-1-Benzyl-2-hydroxymethyl-3-methylaziridine (4b).**[6b,7] Following the above procedure for **4a**, 6.5 mL of a 1.0 M $LiAlH_4$ solution in THF was slowly added, at room temperature, to a stirred solution of aziridine **3b** (0.713 g, 3.25 mmol) in THF (21 mL). After 1 h 30 min, water (0.4 mL) was added dropwise at 0 °C, followed by 0.4 mL of a 0.15 N KOH solution. The inorganic salts were removed by filtration and washed with ether, the filtrate was dried ($MgSO_4$) and rotary evaporated, and the residue was flash chromatographed on silica gel (ethyl ether/petroleum ether 90:10 and finally pure ethyl ether) to give 0.39 g of **4b** as a pale light yellow oil (67% yield): ^{1}H NMR (200 MHz) δ 1.36 (3H, d, J = 6.1 Hz, CH_3CH-), 1.67 (1H, dt, J = 3.4, 5.2 Hz, $-CH$CH$_2$OH), 2.19 (1H, dq, J = 3.4, 6.1 Hz, CH_3CH-), 2.51 (1H, t, J = 5.8 Hz, −OH), 3.44 (1H, ddd, J = 11.2, 5.7, 5.3 Hz, $-CH_2$OH), 3.60 (1H, d, J = 13.8 Hz, $-CH_2$Ph), 3.77 (1H, m, $-CH_2$OH), 3.82 (1H, d, J = 13.8 Hz, $-CH_2$Ph), 7.24−7.42 (5H, m, aromatic); MS m/z 177 (M^+).

***cis*-1-Benzyl-2-((*tert*-butyldimethylsilyloxy)methyl)-3-methylaziridine (5a).** DMAP (1.319 g, 10.8 mmol) and TBDMSCl (0.781 g, 5.18 mmol) were added at room temperature to a stirred solution of **4a** (0.764 g, 4.32 mmol) in freshly distilled dichloromethane (25 mL) (nitrogen atmosphere). After 40 min, the reaction mixture was diluted with dichloromethane (30 mL), washed with water (2 × 50 mL) and with brine (50 mL), dried ($MgSO_4$), and rotary evaporated. Flash chromatography of the residue on silica gel (petroleum ether/ethyl ether 80:20) gave 1.12 g of **5a** as a pale yellow liquid (96% yield): ^{1}H NMR (200 MHz) δ 0.096 (6H, s, $-OSiMe_2$tBu), 0.94 (9H, s, $-OSiMe_2tBu$), 1.23 (3H, d, J = 5.5 Hz, CH_3CH-), 1.73 [2H, m, CH_3CH- and $-CH$CH$_2$O−; decoupled from $-CH_2O-$: 1.69 (1H, dq, J = 6.6, 5.5 Hz, CH_3CH-), 1.76 (1H, d, J = 6.6 Hz, $-CH$CH$_2$O−)], 3.55 (2H, s, $-CH_2$Ph), 3.61 (1H, dd, J = 10.9,

(8) Pierre, J.-L.; Baret, P.; Arnaud, P. *Bull. Soc. Chim. Fr.* **1971**, 3619.

6.2 Hz, $-CH_2O-$), 3.82 (1H, dd, J = 10.9, 5.5 Hz, $-CH_2O-$) 7.24−7.41 (5H, m, aromatic); MS m/z 291 (M^+). Anal. Calcd for $C_{17}H_{29}NOSi$: C, 70.05; H, 10.03; N, 4.80. Found: C, 69.84; H, 10.27; N, 4.82.

***trans*-1-Benzyl-2-((*tert*-butyldimethylsilyloxy)methyl)-3-methylaziridine (5b).** As for the procedure for **5a**, aziridine **4b** (0.326 g, 1.84 mmol) was dissolved in dichloromethane (15 mL): DMAP (0.563 g, 4.61 mmol) and finally TBDMSCl (0.335 g, 2.22 mmol) were added at room temperature under magnetic stirring (nitrogen atmosphere). After 35 min, TLC analysis showed disappearance of the starting material: the reaction mixture was then diluted with dichloromethane (25 mL), washed with water (2 × 30 mL) and brine (30 mL), dried ($MgSO_4$), and concentrated. After flash chromatography on SiO_2 (petroleum ether/ethyl ether 80:20), **5b** was obtained as a light yellow oil (0.39 g, 72% yield): ^{1}H NMR (200 MHz) δ 0.073 (6H, s, $-OSiMe_2tBu$), 0.92 (9H, s, $-OSiMe_2t\mathit{Bu}$), 1.37 (3H, d, J = 6.0 Hz, CH_3CH-), 1.61 (1H, dt, J = 3.2, 5.7 Hz, $-CHCH_2O-$), 2.05 (1H, dq, J = 3.2, 6.0 Hz, CH_3CH-), 3.58 (1H, dd, J = 11.0, 5.7 Hz, $-CHCH_2O-$), 3.59 (1H, d, J = 14.0 Hz, $-CH_2Ph$), 3.68 (1H, dd, J = 11.0, 5.7 Hz, $-CHCH_2O-$), 3.80 (1H, d, J = 14.0 Hz, $-CH_2Ph$), 7.22−7.45 (5H, m, aromatic); MS m/z 291 (M^+). Anal. Calcd for $C_{17}H_{29}NOSi$: C, 70.05; H, 10.03; N, 4.80. Found: C, 69.80; H, 10.29; N, 4.74.

***trans*-1-Benzyl-3-methyl-4-((*tert*-butyldimethylsilyloxy)-methyl)azetidin-2-one (6a) and *trans*-1-Benzyl-4-methyl-3-((*tert*-butyldimethylsilyloxy)methyl)azetidin-2-one (7a).** In a 45-mL stainless steel autoclave equipped with a glass liner and a stirring bar was dissolved *cis*-aziridine **5a** (531.1 mg, 1.82 mmol) in freshly distilled anhydrous and O_2-free DME (10 mL), and $Co_2(CO)_8$ (52 mg, 0.15 mmol) was added. The autoclave was purged four times with 300 psi of CO, charged with 500 psi of CO, and placed in an oil bath at 95 °C for 16 h. After release of CO, the autoclave was opened, and the brown clear solution was left in contact with air for some hours, adding ether to accelerate the decomposition of the catalyst. The reaction mixture was then filtered through a small SiO_2 column to remove the violet precipitate and then washed with abundant ether. After rotary evaporation, the crude yellow oil was flash chromatographed on a silica gel column (petroleum ether/ethyl ether 60:40), thus affording, as pale yellow oils, the two β-lactam regioisomers *trans*-**6a** (531.9 mg) and *trans*-**7a** (49.1 mg) in a 92:8 ratio in 99.8% total isolated yield.

***trans*-6a**: ^{1}H NMR (200 MHz) δ 0.028 (6H, s, $-OSiMe_2$-tBu), 0.88 (9H, s, $-OSiMe_2t\mathit{Bu}$), 1.27 (3H, d, J = 7.3 Hz, CH_3-$CH-$), 2.93 (1H, dq, J = 1.9, 7.3 Hz, CH_3CH-), 3.18 (1H, ddd, J = 5.2, 4.2, 1.9 Hz, $-CHCH_2O-$), 3.63 (1H, dd, J = 10.9, 5.2 Hz, $-CHCH_2O-$), 3.71 (1H, dd, J = 10.9, 4.2 Hz, $-CHCH_2O-$), 4.10 (1H, d, J = 15.1 Hz, $-CH_2Ph$), 4.70 (1H, d, J = 15.1 Hz, $-CH_2Ph$), 7.25−7.35 (5H, m, aromatic); ^{13}C NMR (200 MHz) δ −5.6, 12.7, 18.1, 22.6, 44.8, 46.6, 60.1, 63.1, 127.5, 128.1, 128.6, 136.4, 170.8; MS m/z 319 (M^+). Anal. Calcd for $C_{18}H_{29}NO_2Si$: C, 67.66; H, 9.15; N, 4.38. Found: C, 67.62; H, 9.23; N, 4.35.

***trans*-7a**: ^{1}H NMR (200 MHz) δ 0.051 (6H, s, $-OSiMe_2$-tBu), 0.86 (9H, s, $-OSiMe_2t\mathit{Bu}$), 1.22 (3H, d, J = 6.1 Hz, $-CHCH_3$), 2.87 (1H, m, $-OCH_2CH-$), 3.61 (1H, dq, J = 2.1, 6.1 Hz, $-CHCH_3$), 3.85 (1H, dd, J = 10.9, 3.7 Hz, $-OCH_2CH-$), 3.92 (1H, dd, J = 10.9, 5.2 Hz, $-OCH_2CH-$), 4.07 (1H, d, J = 15.4 Hz, $-CH_2Ph$), 4.66 (1H, d, J = 15.4 Hz, $-CH_2Ph$), 7.20−7.40 (5H, m, aromatic); MS m/z 319 (M^+). Anal. Calcd for $C_{18}H_{29}NO_2Si$: C, 67.66; H, 9.15; N, 4.38. Found: C, 67.58; H, 9.25; N, 4.33.

***cis*-1-Benzyl-3-methyl-4-((*tert*-butyldimethylsilyloxy)-methyl)azetidin-2-one (6b) and *cis*-1-Benzyl-4-methyl-3-((*tert*-butyldimethylsilyloxy)methyl)azetidin-2-one (7b).** Following the same protocol as for **5a**, *trans*-aziridine **5b** (318.9 mg, 1.10 mmol) was dissolved in DME (10 mL), and the catalyst was added (31.2 mg, 0.019 mmol). After being purged with CO, the autoclave was filled with 500 psi of CO and kept in an oil bath for 16 h at 100 °C. An identical workup as above gave a crude dark brown-olive oil that was flash chromatographed on a SiO_2 column (petroleum ether/ethyl ether 60:40), affording the two β-lactam isomers *cis*-**6b** (192.8 mg) and *cis*-**7b** (26.3 mg) in a 88:12 ratio in 63% total isolated yield.

***cis*-6b**: ^{1}H NMR (400 MHz) δ 0.024 (3H, s, $-OSiMe_2tBu$), 0.030 (3H, s, $-OSiMe_2tBu$), 0.87 (9H, s, $-OSiMe_2t\mathit{Bu}$), 1.22 (3H, d, J = 7.6 Hz, CH_3CH-), 3.26 (1H, dq, J = 5.4, 7.6 Hz, CH_3CH-), 3.59 (1H, q, J = 5.6 Hz, $-CHCH_2O-$), 3.69 (1H, dd, J = 10.7, 5.8 Hz, $-CHCH_2O-$), 3.72 (1H, dd, J = 10.7, 5.7 Hz, $-CHCH_2O-$), 4.16 (1H, d, J = 15.0 Hz, $-CH_2Ph$), 4.65 (1H, d, J = 15.0, $-CH_2Ph$), 7.24−7.36 (5H, m, aromatic); ^{13}C NMR (200 MHz) δ −5.6, 8.7, 18.1, 25.8, 45.0, 46.1, 55.3, 62.3, 127.5, 128.2, 128.6, 136.4, 171.1; MS m/z 319 (M^+). Anal. Calcd for $C_{18}H_{29}NO_2Si$: C, 67.66; H, 9.15; N, 4.38. Found: C, 67.60; H, 9.24; N, 4.31.

***cis*-7b**: ^{1}H NMR (400 MHz) δ 0.057 (3H, s, $-OSiMe_2tBu$), 0.063 (3H, s, $-OSiMe_2tBu$), 0.88 (9H, s, $-OSiMe_2t\mathit{Bu}$), 1.22 (3H, d, J = 7.6 Hz, $-CHCH_3$), 3.36 (1H, dq, J = 5.4, 7.6 Hz, $-CHCH_3$), 3.70 (1H, m, $-OCH_2CH-$), 3.93 (2H, AB system, $-OCH_2CH-$), 4.15 (1H, d, J = 15.2 Hz, $-CH_2Ph$), 4.54 (1H, d, J = 15.2 Hz, $-CH_2Ph$), 7.24−7.36 (5H, m, aromatic); MS m/z 319 (M^+). Anal. Calcd for $C_{18}H_{29}NO_2Si$: C, 67.66; H, 9.15; N, 4.38. Found: C, 67.55; H, 9.25; N, 4.32.

Attempted Carbonylation of Aziridines 3a,b. Reaction of aziridinecarboxylate **3a** (265.3 mg, 1.21 mmol) with $Co_2(CO)_8$ (34.8 mg, 0.10 mmol) in DME (10 mL) under similar conditions (110 °C, 500 psi of CO, 18 h) and identical workup gave a crude oil that was flash chromatographed on SiO_2 (petroleum ether/ethyl ether 60:40), affording 195 mg of ethyl 3-benzylamino-2-butenoate (**3e**)[9] as a lemon yellow oil (73% yield): ^{1}H NMR (200 MHz) δ 1.26 (3H, t, J = 7.1 Hz, $-OCH_2CH_3$), 1.91 (3H, s, $-CH{=}CCH_3-$), 4.10 (2H, q, J = 7.1 Hz, $-OCH_2CH_3$), 4.41 (1H, s, $-CH_2Ph$), 4.44 (1H, s, $-CH_2Ph$), 4.53 (1H, s, $-CH{=}CCH_3-$), 7.24−7.34 (5H, m, aromatic), 8.95 (1H, br, $-NHCH_2Ph$); ^{13}C NMR (200 MHz) δ 14.6, 19.4, 46.8, 58.4, 83.1, 126.7, 127.3, 128.9, 138.7, 161.8, 170.6; MS m/z 219 (M^+).

Reaction of **3a** and **3b** at lower temperature (50−55 °C) and at higher CO pressure (1000 psi) gave only a complex mixture of unidentified products.

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