

SAMARIUM IODIDE PROMOTED COUPLING OF *N*-SUBSTITUTED AZETIDIN-3-ONES. A NOVEL ROUTE TO SPIROANNULATED HETEROCYCLIC OXIRANES[†]

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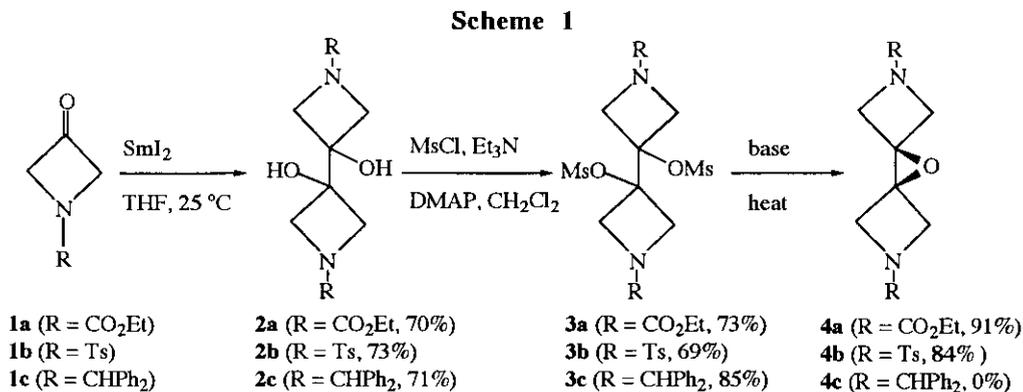
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Abstract- Samarium iodide promoted reductive coupling of *N*-ethoxycarbonylazetidine-3-one (**1a**), *N*-*p*-toluenesulfonylazetidine-3-one (**1b**), and *N*-benzhydrylazetidine-3-one (**1c**) each afforded the corresponding pinacol (**2a-2c**, respectively). Each pinacol was converted into the corresponding dimesylate (**3a-3c**, respectively). When heated in the presence of base, **3a** and **3b** each afforded the corresponding spirocyclic oxirane (**4a** and **4b**, respectively). In contrast to the behavior of **3a** and **3b**, **3c** proved to be inert under these conditions. Structure **4b** was established unequivocally *via* application of X-Ray crystallographic methods.

INTRODUCTION

The chemistry of *N*-substituted azetidin-3-ones has received considerable attention in recent years.¹⁻⁸ In particular, functionalized azetidin-3-ones have been used as intermediates in the synthesis of new energetic materials, e.g., 1,3,3-trinitroazetidine ("TNAZ").⁴⁻⁸ In the present study, samarium iodide promoted reductive coupling of *N*-substituted azetidin-3-ones have been investigated, and some aspects of the chemistry of the resulting "pinacols" have been explored.

Samarium iodide promoted reductive coupling was performed by using three *N*-substituted azetidin-3-ones, i.e., **1a-1c** as substrates (Scheme 1). In our hands, each of the three reductive coupling reactions proceeded smoothly to afford the corresponding pinacol (**2a-2c**, respectively). Each of the pinacols, in turn, could be converted into the corresponding dimesylate (**3a-3c**, respectively) *via* reaction with MsCl-Et₃N in the presence of dimethylaminopyridine (DMAP).

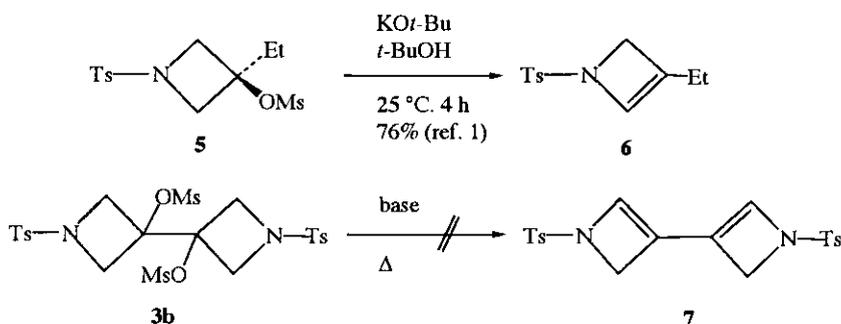


[†]Dedicated to Dr. Bernhard Witkop on the occasion of his 80th birthday.

DISCUSSION

Initially, our interest in systems of the type (**3**) (Scheme 1) was to perform base-promoted E2 elimination of two equivalents of MsOH, thereby producing an unusual, conjugated bis(enamine). However, despite several attempts, we were unable to promote elimination in this system (e.g., note our inability to convert **3b** into **7**; see Scheme 2). This result is particularly vexing, since we have shown previously that *N*-tosyl-3-ethyl-3-mesyloxyazetidone (**5**) undergoes smooth base-promoted elimination of the elements of MsOH to afford the corresponding, substituted 2-azetine (**6**, Scheme 2).¹

Scheme 2



Instead, under the basic conditions employed (see the Experimental Section), competing nucleophilic displacement of one of the OMs groups in **3a** and **3b** by hydroxide ion (presumably either from water or from KOH that might have been present in KO*t*-Bu) occurred with concomitant intramolecular nucleophilic displacement of the remaining OMs group by -O^- . In this way, two novel, spiroannulated oxiranes (i.e., **4a** and **4b**) were prepared in excellent yield (91% and 84% from **3a** and **3b**, respectively, see Scheme 1). The structures of three compounds that are involved in the reaction sequence shown in Scheme 1, i.e., **2a**, **2b**, and **4b**, were established unequivocally *via* application of X-Ray crystallographic methods.

Interestingly, **3c** proved to be inert toward base under the same conditions that had been used previously to convert **3a** and **3b** into the corresponding oxiranes (i.e., **4a** and **4b**, respectively). The reasons for the failure of **3c** to undergo base-promoted conversion into the corresponding spirocyclic oxirane (**4c**) are not apparent to us and are being investigated further in our laboratory.

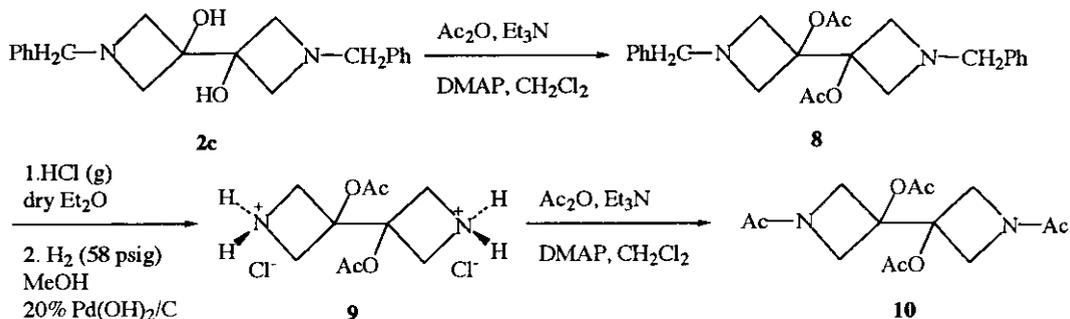
In the course of this study, some additional reactions of **2a** were investigated; the results thereby obtained are summarized in Scheme 3. Thus, **2a** was converted into the corresponding bis(*O*-acetyl) derivative (**8**). The structure of **8** was established unequivocally *via* application of X-Ray crystallographic methods. Subsequently, the *N*-benzyl groups in **8** were removed *via* hydrogenolysis, and the resulting product (**9**) was converted into the corresponding bis(*N*-acetyl) derivative (**10**).

EXPERIMENTAL

Melting points are uncorrected. Elemental microanalytical data was obtained by personnel at M-H-W Laboratories, Phoenix, AZ.

***N,N'*-Bis(ethoxycarbonyl)-3-hydroxy-3-(3'-hydroxy-3'-azetidynyl)azetidone (2a)**. To a solution of 0.1 M solution of SmI₂ in THF (100 mL, 10 mmol) under argon was added *N*-ethoxycarbonylazetidone-3-one⁹ (**1a**, 1.43 g, 10 mmol), and the resulting mixture was stirred at ambient temperature for 8 h.

Scheme 3



To the reaction mixture was added 0.1 N aqueous HCl (20 mL, excess), and the resulting aqueous suspension was extracted with EtOAc (3 x 50 mL). The combined organic extracts were washed sequentially with saturated aqueous NaHCO₃ (2 x 20 mL), water (30 mL), and brine (2 x 20 mL). The organic layer was dried (MgSO₄) and filtered, and the filtrate was concentrated *in vacuo*. The residue was purified *via* column chromatography on silica gel by eluting with 60% EtOAc-hexane. The eluate was recrystallized from EtOAc-hexane, thereby affording pure **2a** (1.0 g, 70%) as a colorless microcrystalline solid: mp 230 °C (decomp); IR (KBr) 3418 (vs), 2980 (s), 2532 (vs), 1700 (vs), 1471 (vs), 777 cm⁻¹ (s); ¹H NMR (DMSO-*d*₆) δ 1.22 (t, *J* = 7.3 Hz, 6 H), 3.80 (d, *J* = 9.4 Hz, 4 H), 3.96-4.13 (m, 8 H), 6.25 (br s, 2 H); ¹³C NMR (DMSO-*d*₆) δ 13.3 (q), 57.0 (t), 57.1 (t), 57.2 (t), 57.5 (t), 60.6 (t), 70.5 (s), 156.6 (s). Anal. Calcd for C₁₂H₂₀N₂O₆: C, 49.99; H, 6.99. Found: C, 49.78; H, 6.92. The structure of **2a** was established unequivocally *via* application of X-Ray crystallographic methods (*vide infra*).

N,N'-Bis(ethoxycarbonyl)-3-mesyloxy-3-(3'-mesyloxy-3'-azetidiny)azetidine (3a). A solution of **2a** (810 mg, 2.8 mmol) in CH₂Cl₂ (15 mL) under argon was cooled to 0 °C *via* application of an external ice-water bath. To this cooled solution was added MsCl (958 mg, 8.4 mmol). To the resulting solution under argon was added dropwise with stirring a solution of Et₃N (2.83 g, 28 mmol) and 4-dimethylaminopyridine (DMAP, 100 mg, 0.82 mmol) in CH₂Cl₂ (5 mL), and the reaction mixture was stirred at 0-10 °C for 3 h. The external ice-water bath was removed, and the reaction mixture was allowed to warm gradually to ambient temperature with stirring during 3 h. To the reaction mixture was added CH₂Cl₂ (80 mL), and the resulting mixture was washed sequentially with water (20 mL), saturated aqueous NaHCO₃ (20 mL), and brine (20 mL). The organic layer was dried (Na₂SO₄) and filtered, and the filtrate was concentrated *in vacuo*. The residue was purified *via* column chromatography on acid-free silica gel that had been pre-treated with Et₃N by eluting with 40% EtOAc-hexane. The eluate was recrystallized from EtOAc-hexane, thereby affording pure **3a** (900 mg, 73%) as a colorless microcrystalline solid: mp 124-125 °C; IR (KBr) 3022 (s), 1715 (vs), 1346 (vs), 1159 (vs), 885 cm⁻¹ (s); ¹H NMR (CDCl₃) δ 1.21 (t, *J* = 7.1 Hz, 6 H), 3.10 (s, 6 H), 4.05-4.26 (m, 8 H), 4.61 (d, *J* = 11.2 Hz, 4H); ¹³C NMR (CDCl₃) δ 14.4 (q), 40.3 (q), 56.3 (t), 61.8 (t), 81.2 (s), 156.2 (s). Anal. Calcd for C₁₄H₂₄N₂O₁₀S₂: C, 37.83; H, 5.44. Found: C, 38.09; H, 5.70.

Reaction of 3a with Aqueous KOH. To a solution of dimesylate (**3a**) (200 mg, 0.46 mmol) in *t*-BuOH (5 mL), H₂O (18 mg, 1 mmol) and KOH (26 mg, 0.46 mmol) were added and the mixture was stir-

red at 40 °C for 3 h. The reaction mixture was extracted with Et₂O (2 x 50 mL) and the combined organic extracts were washed sequentially with water (2 x 50 mL) and brine (2 x 25 mL). The organic layer was dried (MgSO₄) and filtered, and the filtrate was concentrated *in vacuo*. The residue was purified *via* column chromatography on silica gel by eluting with 25% EtOAc-hexane. The eluate was recrystallized from EtOAc-hexane, thereby affording pure **4a** (113 mg, 91%) as a colorless microcrystalline solid: mp: 126-127 °C; IR (KBr) 2991 (m), 1713 (vs), 1441 (vs), 1049 (s), 775 cm⁻¹ (s); ¹H NMR (CDCl₃) δ 1.22 (t, *J* = 7.2 Hz, 6 H), 4.02-4.20 (m, 12 H); ¹³C NMR (CDCl₃) δ 14.6 (t), 55.4 (t), 61.3 (s), 61.5 (t), 156.5 (s). Anal. Calcd for C₁₂H₁₈N₂O₅: C, 53.33; H, 6.70. Found: C, 52.96; H, 6.86.

***N,N'*-Bis(toluenesulfonyl)-3-hydroxy-3-(3'-hydroxy-3'-azetidiny)azetidine (2b)**. To a solution of 0.1 M solution of SmI₂ in THF (115 mL, 11.5 mmol) under argon was added **1b**⁸ (2.54 g, 11.3 mmol), and the resulting mixture was stirred at ambient temperature for 8 h. To the reaction mixture was added 0.1 N aqueous HCl (5 mL, excess), and the resulting aqueous suspension was extracted with EtOAc (3 x 50 mL). The combined organic extracts were washed sequentially with saturated aqueous NaHCO₃ (2 x 20 mL), water (30 mL), and brine (2 x 20 mL). The organic layer was dried (MgSO₄) and filtered, and the filtrate was concentrated *in vacuo*. The residue was purified *via* column chromatography on silica gel by eluting with 10% CH₃OH-CH₂Cl₂. The eluate was recrystallized from CH₃OH-CH₂Cl₂, thereby affording pure **2b** (1.88 g, 73%) as a colorless microcrystalline solid: mp 260 °C (decomp.); IR (KBr) 3453 (vs), 3057 (w), 2949 (m), 1602 (m), 1153 (s), 670 cm⁻¹ (s); ¹H NMR (DMSO-*d*₆) δ 2.41 (s, 6 H), 3.33 (AB, *J*_{AB} = 7.7 Hz, 4 H), 3.51 (AB, *J*_{AB} = 7.7 Hz, 4 H), 5.87 (s, 2 H), 7.45 (AB, *J*_{AB} = 8.0 Hz, 4 H), 7.63 (AB, *J*_{AB} = 8.1 Hz, 4 H); ¹³C NMR (DMSO-*d*₆) δ 21.0 (q), 58.8 (t), 69.3 (s), 128.0 (d), 129.9 (d), 131.0 (s), 143.9 (s). Anal. Calcd for C₂₀H₂₄N₂O₆S₂: C, 53.08; H, 5.35. Found: C, 52.90; H, 5.33. The structure of **2b** was established unequivocally *via* application of X-Ray crystallographic methods (*vide infra*).

***N,N'*-Bis(toluenesulfonyl)-3-mesyloxy-3-(3'-mesyloxy-3'-azetidiny)azetidine (3b)**. A solution of **2b** (550 mg, 1.22 mmol) in CH₂Cl₂ (5 mL) under argon was cooled to 0 °C *via* application of an external ice-water bath. To this cooled solution was added MsCl (1.11 g, 9.76 mmol). To the resulting solution under argon was added dropwise with stirring a solution of pyridine (10 mL, excess) and DMAP (298 mg, 2.4 mmol) in CH₂Cl₂ (5 mL), and the reaction mixture was stirred at 0 °C for 10 h. The external ice-water bath was removed, and the reaction mixture was allowed to warm gradually to ambient temperature with stirring during 24 h. To the reaction mixture was added CH₂Cl₂ (80 mL), and the resulting mixture was washed sequentially with water (30 mL), saturated aqueous NaHCO₃ (30 mL), water (30 mL), and brine (30 mL). The organic layer was dried (MgSO₄) and filtered, and the filtrate was concentrated *in vacuo*. The residue was purified *via* column chromatography on acid-free silica gel that had been pre-treated with Et₃N by eluting with 20% EtOAc-CHCl₃. The eluate was recrystallized from EtOAc-hexane, thereby affording pure **3b** (510 mg, 69%) as a colorless microcrystalline solid: mp 180-181 °C; IR (KBr) 3032 (m), 2937 (m), 1605 (s), 1354 (vs), 1180 (vs), 842 cm⁻¹ (vs); ¹H NMR (CDCl₃) δ 2.43 (s, 6 H), 2.97 (s, 6 H), 3.96 (AB, *J*_{AB} = 11.0 Hz, 4 H), 4.21 (AB, *J*_{AB} = 11.1 Hz, 4 H), 7.40 (AB, *J*_{AB} = 8.1 Hz, 4 H), 7.70 (AB, *J*_{AB} = 8.0 Hz, 4 H); ¹³C NMR (CDCl₃) δ 21.7 (q), 40.3 (q), 56.9 (t), 128.5 (d), 130.2 (s), 130.3 (d), 145.3 (s). Anal. Calcd for C₂₂H₂₈N₂O₁₀S₄: C, 43.41; H, 4.64. Found: C, 43.41; H, 4.58.

Reaction of 3b with Aqueous KOH. To a solution of **3b** (304 mg, 0.50 mmol) in *t*-BuOH (5 mL) were added H₂O (18 mg, 1 mmol) and KOH (28 mg, 0.50 mmol), and the resulting mixture was stirred at

40 °C for 3 h. The reaction mixture was extracted with Et₂O (2 x 50 mL), and the combined organic extracts were washed sequentially with water (2 x 50 mL) and brine (2 x 25 mL). The organic layer was dried (MgSO₄) and filtered, and the filtrate was concentrated *in vacuo*. The residue was purified *via* column chromatography on silica gel by eluting with 25% EtOAc-hexane. The eluate was recrystallized from EtOAc-hexane, thereby affording pure **4b** (181 mg, 84%) as a colorless microcrystalline solid: mp: 219-220 °C; IR (KBr) 2961 (w), 2930 (m), 1609 (s), 1350 (vs), 1165 (vs), 679 cm⁻¹ (vs); ¹H NMR (CDCl₃) δ 2.47 (s, 6 H), 3.89 (dd, *J* = 10.7, 9.3 Hz, 8 H), 7.40 (d, 4 H, *J* = 8.2 Hz), 7.74 (d, 4 H, *J* = 8.3 Hz); ¹³C NMR (CDCl₃) δ 21.6 (q), 56.0 (t), 59.9 (s), 128.2 (d), 130.1 (d), 131.2 (s), 145.1 (s). Anal. Calcd for C₁₀H₂₂N₂O₅S₂: C, 55.28; H, 5.10. Found: C, 55.43; H, 5.04. The structure of **4b** was established unequivocally *via* application of X-Ray crystallographic methods (*vide infra*).

***N,N'*-Bis(benzhydryl)-3-hydroxy-3-(3'-hydroxy-3'-azetidiny)azetidone (2c)**. To a solution of 0.1 M solution of SmI₂ in THF (200 mL, 20 mmol) under argon was added *N*-benzhydrylazetidone⁸ (**1c**, 4.74 g, 20 mmol), and the resulting mixture was stirred at ambient temperature for 12 h. To the reaction mixture was added 0.1 N aqueous HCl (20 mL, excess), and the resulting aqueous suspension was extracted with EtOAc (3 x 50 mL). The combined organic extracts were washed sequentially with saturated aqueous NaHCO₃ (2 x 20 mL), water (30 mL), and brine (2 x 20 mL). The organic layer was dried (MgSO₄) and filtered, and the filtrate was concentrated *in vacuo*. The residue was purified *via* column chromatography on silica gel by eluting with 50% EtOAc-hexane. The eluate was recrystallized from EtOAc-hexane, thereby affording pure **2c** (3.4 g, 71%) as a colorless microcrystalline solid: mp 260 °C (decomp.); IR (KBr) 3041 (br, s), 2865 (vs), 1455 (vs), 749 vs), 701 cm⁻¹ (vs); ¹H NMR (CDCl₃) δ 3.09-3.16 (m, 4 H), 3.38-3.47 (m, 4 H), 4.44 (s, 2 H), 6.12 (br s, 2 H), 7.10-7.56 (m, 20 H); ¹³C NMR (CDCl₃) δ 127.1 (d), 127.4 (d), 128.6 (d), 141.1 (s). Anal. Calcd for C₃₂H₃₂N₂O₂: C, 80.64; H, 6.77. Found: C, 80.22; H, 6.72.

***N,N'*-Bis(benzhydryl)-3-mesyloxy-3-(3'-mesyloxy-3'-azetidiny)azetidone (3c)**. A solution of **2c** (320 mg, 0.67 mmol) in CH₂Cl₂ (10 mL) under argon was cooled to 0 °C *via* application of an external ice-water bath. To this cooled solution was added MsCl (262 mg, 2.30 mmol). To the resulting solution under argon was added dropwise with stirring a solution of Et₃N (700 mg, 7.0 mmol) and DMAP (70 mg, 0.57 mmol) in CH₂Cl₂ (5 mL), and the reaction mixture was stirred at 0-10 °C for 3 h. The external ice-water bath was removed, and the reaction mixture was allowed to warm gradually to ambient temperature with stirring during 3 h. To the reaction mixture was added CH₂Cl₂ (100 mL), and the resulting mixture was washed sequentially with water (20 mL), saturated aqueous NaHCO₃ (20 mL), and brine (20 mL). The organic layer was dried (Na₂SO₄) and filtered, and the filtrate was concentrated *in vacuo*. The residue was purified *via* column chromatography on acid-free silica gel that had been pre-treated with Et₃N by eluting with 40% EtOAc-hexane. The eluate was recrystallized from EtOAc-hexane, thereby affording pure **3c** (360 mg, 85%) as a colorless microcrystalline solid: mp 88-89 °C; IR (KBr) 3032 (m), 2953 (w), 2855 (w), 1608 (m), 1346 (vs), 1176 (vs), 891 (s), 711 cm⁻¹ (vs); ¹H NMR (CDCl₃) δ 3.06 (s, 6 H), 3.84 (d, *J* = 9.8 Hz, 4 H), 4.11 (d, *J* = 9.1 Hz, 4 H), 4.6 (s, 2 H), 7.25-7.50 (m, 10 H); ¹³C NMR (CDCl₃) δ 40.2 (q), 59.9 (t), 77.6 (d), 82.1 (s), 127.2 (d), 127.4 (d), 128.6 (d), 141.4 (s). Anal. Calcd for C₃₄H₃₆N₂O₆S₂: C, 64.54; H, 5.73. Found: C, 64.73; H, 5.92.

Attempted Reaction of 3c with Base. A solution of **3c** (400 mg, 0.63 mmol) in *t*-BuOH (5 mL) was cooled to 0 °C *via* application of an external ice-water bath. To this cooled solution was added with stirring water (18 mg, 1 mmol) followed by portionwise addition of *t*-BuOK (292 mg, 2.60 mmol). After all of the base had been added, the external cold bath was removed, and the reaction mixture was allowed to warm slowly to ambient temperature with stirring during 3 h. The reaction mixture then was heated at 45 °C for 12 h. The reaction mixture was allowed to cool to ambient temperature and then was extracted with CH₂Cl₂ (2 x 50 mL). The combined extracts were washed sequentially with water (2 x 20 mL), saturated aqueous NaHCO₃ (2 x 20 mL), water (30 mL), and brine (2 x 30 mL). The organic layer was dried (MgSO₄) and filtered, and the filtrate was concentrated *in vacuo*. Analysis of the ¹H NMR spectrum of the crude product thereby obtained indicated only the presence of starting material (**3c**).

***N,N'*-Bis(benzhydryl)-3-acetoxy-3-(3'-acetoxy-3'-azetidiny)azetidene (**8**).** A solution of **2c** (1.9 g, 4.0 mmol) in CH₂Cl₂ (20 mL) under argon was cooled to 0 °C *via* application of external ice-water bath. To this cooled solution was added Ac₂O (920 mg, 9.0 mmol). To the resulting solution under argon was added dropwise with stirring a solution of Et₃N (1.21 mg, 12 mmol) and DMAP (200 mg, 1.64 mmol) in CH₂Cl₂ (5 mL), and the reaction mixture was stirred at 0-10 °C for 3 h. The external ice-water bath was removed, and the reaction mixture was allowed to warm gradually to ambient temperature with stirring during 12 h. To the reaction mixture was added CH₂Cl₂ (100 mL), and the resulting mixture was washed sequentially with water (20 mL), saturated aqueous NaHCO₃ (20 mL), and brine (20 mL). The organic layer was dried (MgSO₄) and filtered, and the filtrate was concentrated *in vacuo*. The residue was purified *via* column chromatography on silica gel by eluting with 50% EtOAc-hexane. The eluate was recrystallized from EtOAc-hexane, thereby affording pure **8** (1.96 g, 88%) as a colorless microcrystalline solid: mp 198-199 °C; IR (KBr) 2857 (w), 1743 (s), 1250 (s), 760 (s), 712 cm⁻¹ (s); ¹H NMR (CDCl₃) δ 1.78 (s, 6 H), 3.02-3.18 (m, 4 H), 3.92-4.02 (m, 4 H), 4.28 (s, 2 H), 6.92-7.40 (m, 20 H); ¹³C NMR (CDCl₃) δ 21.4 (q), 61.4 (t), 76.8 (s), 78.2 (d), 127.2 (d), 127.3 (d), 128.5 (d), 142.1 (s), 169.7 (s). Anal. Calcd for C₃₆H₃₆N₂O₄: C, 77.12; H, 6.47. Found: C, 77.19; H, 6.13. The structure of **5** was established unequivocally *via* application of X-Ray crystallographic methods (*vide infra*).

***N,N'*-Bisacetyl-3-acetoxy-3-(3'-acetoxy-3'-azetidiny)azetidene (**10**).** A solution of **8** (1.96 g, 3.5 mmol) in Et₂O (50 mL) was cooled to 0 °C *via* application of an external ice-water bath. Dry HCl gas was passed through the solution for 5 min, during which time a precipitate formed. Argon then was bubbled through the reaction mixture to purge excess HCl (g), and the precipitate was collected subsequently *via* suction filtration. The residue was washed with Et₂O (2 x 20 mL) and then dried *in vacuo*. The dihydrochloride salt of **8** (i.e., **8**·2HCl, 2.2 g, 100%) was thereby obtained as a colorless microcrystalline solid. This material was used as obtained in the next synthetic step.

To a solution of **8**·2HCl (2.2 g, 3.5 mmol, *vide supra*) in dry MeOH (75 mL) was added 20% Pd(OH)₂ on powdered charcoal (700 mg, 1.0 mmol),¹⁰ and the resulting mixture was hydrogenated with H₂ at 58 psi at ambient temperature by using a Parr hydrogenation apparatus for 65 h. At that time, tlc analysis of the reaction mixture indicated the complete absence of **8** (or of **8**·2HCl). The reaction mixture was filtered to remove spent catalyst, and the filtrate was concentrated *in vacuo*. The residue was washed with Et₂O (3 x 30 mL); after each washing procedure, the organic layer was decanted carefully and discarded. The residue was

dried *in vacuo*, thereby affording **9** (780 mg, 74%) as a colorless microcrystalline solid. This material was used as obtained in the next synthetic step.

A solution of **9** (780 mg, 2.6 mmol, *vide supra*) in CH₂Cl₂ (10 mL) under argon was cooled to 0 °C *via* application of an external ice-water bath. To this cooled solution was added Ac₂O (2.04 g, 20 mmol). To the resulting solution under argon was added dropwise with stirring a solution of pyridine (5 mL) and DMAP (100 mg, 0.82 mmol) in CH₂Cl₂ (5 mL), and the reaction mixture was stirred at 0-10 °C for 3 h. The external ice-water bath was removed, and the reaction mixture was allowed to warm gradually to ambient temperature with stirring during 8 h. Dichloromethane (100 mL) was added, and the resulting mixture was washed sequentially with water (20 mL), saturated aqueous NaHCO₃ (20 mL), and brine (20 mL). The organic layer was dried (MgSO₄) and filtered, and the filtrate was concentrated *in vacuo*. The residue was purified *via* column chromatography on silica gel by eluting with 50% EtOAc-hexane. The eluate was recrystallized from EtOAc-hexane, thereby affording pure **10** (650 mg, 80%) as a colorless microcrystalline solid: mp 181-182 °C; IR (KBr) 2962 (m), 1750 (vs), 1670 (vs), 1468 (s), 1250 cm⁻¹ (s); ¹H NMR (CDCl₃) δ 1.80 (s, 6 H), 1.98 (s, 6 H), 3.98-4.57 (m, 8 H); ¹³C NMR (CDCl₃) δ 18.9 (q), 19.0 (q), 20.8 (q), 20.9 (q), 55.5 (t), 55.9 (t), 57.6 (t), 58.4 (t), 169.6 (s), 170.4 (s). Exact Mass (CI-HRMS) Calcd for C₁₄H₂₀N₂O₆: [M_r + H]⁺ 313.139962 Found: [M_r + H]⁺ 313.139176.

X-Ray Crystal Structures of 2a, 2b, 4b, and 8. All data were collected on an Enraf-Nonius CAD-4 diffractometer by using the ω-2θ scan technique, Mo Kα radiation (λ = 0.71073 Å), and a graphite monochromator. Standard procedures used in our laboratory for this purpose have been described previously.¹¹ Pertinent X-Ray data are given in Table 1. Data were corrected for Lorentz and polarization effects but not for absorption. The structures were solved by direct methods (**2a** and **4b** were solved by using SIR¹², while **2b** and **8** were solved by using SHELXS-86¹³), and the models were refined by using full-matrix least-squares techniques. All atoms in **2b** were refined with anisotropic thermal parameters, while those in **8** were refined by using isotropic thermal parameters. Sufficient data were available for the remaining two structures (i.e., **2a** and **4b**) to permit only some of the atoms to be refined anisotropically: i.e., (i) the oxygen atoms, nitrogen atoms, and the ethyl group carbon atoms in **2a** and (ii) the sulfur atoms, oxygen atoms, nitrogen atoms, and the methyl carbon atoms in **4b**. Hydrogen atoms were located on difference maps and then were included in the model in idealized positions [U(H) = 1.3 B_{eq}(C)] and were allowed to ride upon the attached carbon. All computations other than those specified were performed by using MolEN.¹⁴ Scattering factors were taken from the usual sources.¹⁵

ACKNOWLEDGMENT

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Table 1. X-Ray data collection and processing parameters for **2a**, **2b**, **4b**, and **8**.

| Compound | 2a | 2b | 4b | 8 |
|---|---|---|--|---|
| Elemental Formula | C ₁₂ H ₂₀ N ₂ O ₆ | C ₂₀ H ₂₄ N ₂ O ₆ S ₂ ·2(DMSO) (C ₂₄ H ₃₆ N ₂ O ₈ S ₄) | C ₂₀ H ₂₂ N ₂ O ₅ S ₂ | C ₃₆ H ₃₆ N ₂ O ₄ |
| Size (mm) | 0.07 x 0.22 x 0.24 | 0.11 x 0.22 x 0.29 | 0.09 x 0.10 x 0.42 | 0.06 x 0.07 x 0.08 |
| Space Group | P2 ₁ /n | P-1 bar | P2 ₁ /c | P2 ₁ /n |
| a (Å) | 10.251 (4) | 6.2973 (8) | 16.476 (2) | 9.054 (1) |
| b (Å) | 5.782 (2) | 8.4717 (6) | 7.5480 (5) | 15.426 (2) |
| c (Å) | 12.336 (3) | 14.023 (1) | 16.811 (1) | 10.619 (1) |
| α (°) | 90 | 95.400 (6) | 90 | 90 |
| β (°) | 105.05 (2) | 95.939 (9) | 99.195 (7) | 100.03 (1) |
| γ (°) | 90 | 97.494 (8) | 90 | 90 |
| V (Å ³) | 706.1 (4) | 738.3 (1) | 2063.8 (3) | 1460.5 (4) |
| Z-value | 2 | 1 | 4 | 2 |
| D _{calc} (g·cm ⁻³) | 1.356 | 1.379 | 1.398 | 1.275 |
| μ (cm ⁻¹) | 1.023 | 3.56 | 2.79 | 0.77 |
| T (K) | 293 | 295 | 293 | 295 |
| 2θ _{max} (°) | 45 | 44 | 44 | 44 |
| Total reflections | 1084 | 1787 | 2851 | 1998 |
| Unique reflections | 1030 | 1787 | 2755 | 1872 |
| R _{int} | 0.036 | - | 0.024 | 0.034 |
| I ≥ 3σ(I) | 410 | 1079 | 1440 | 493 |
| Parameters | 71 | 172 | 172 | 85 |
| R, R _w | 0.0673, 0.0708 | 0.050, 0.050 | 0.0497, 0.0550 | 0.0510, 0.0556 |
| (Δ/σ) _{max} | 0.03 | <0.01 | <0.01 | <0.01 |
| ρ _{max} ; ρ _{min} (eÅ ⁻³) | 0.22; -0.25 | 0.46; -0.33 | 0.32; -0.37 | 0.22; -0.19 |

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