

A Novel Synthesis of 4-Spirocyclopropyl β -Lactams

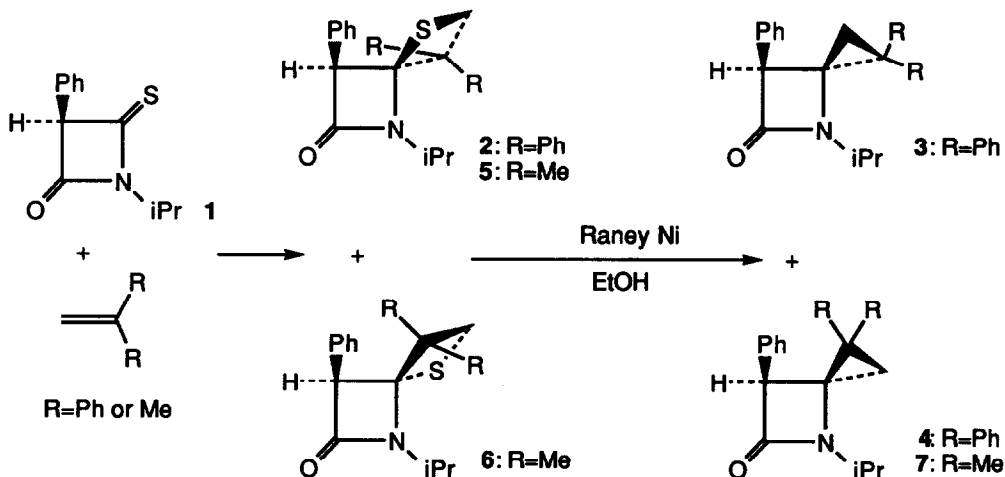
Hiromu Aoyama,* Hiroyuki Sagae, and Akira Hosomi

Department of Chemistry, University of Tsukuba, Tsukuba, Ibaraki, 305 Japan

Abstract: photochemical reaction of 4-thioxoazetidine-2-one with alkenes gave [2+2] adducts (thietane-fused β -lactams which were converted to 4-spirocyclopropyl β -lactams on desulfurization with Raney nickel.

The importance of β -lactams (azetidine-2-ones) has led to the development of many methods for their formation.¹ The synthesis of β -lactams having a small fused ring is of interest since the large strain of the ring should substantially alter the reactivities of the lactams. In relation to our studies on photochemical synthesis of β -lactams,² we report here the synthesis of 4-spirocyclopropyl-azetidin-2-ones³ via photocycloaddition of 4-thioxo-azetidine-2-ones to alkenes and subsequent desulfurization.

When a solution of 1-isopropyl-3-phenyl-4-thioxoazetidin-2-one (**1**) and 1,1-diphenylethylene in benzene was irradiated with a high pressure mercury lamp, an [2+2] adduct (**2**) was obtained in 67% yield.⁴ Desulfurization of **2** with Raney nickel⁵ in anhydrous ethanol gave two isomeric 4-spirocyclopropylazetidin-2-ones [**3** (42%) and **4** (18%)] which could be separated by column chromatography on silica gel. Meanwhile, photochemical reaction of **1** with 2-methylpropene yielded two thietanes [**5** (39%) and **6** (8%)], both of which produced the same β -lactam (**7**) on desulfurization with Raney nickel. The structures of these 4-spirocyclopropyl β -lactams were determined by means of spectral data⁶ and elemental analyses. The stereochemistry was



unambiguously determined as shown above on the basis of the difference NOE spectra: in the case of 4 and 7 strong NOE effects were observed between the methylene hydrogens and the C-3 methine hydrogen, whereas NOE effects were observed between the methine hydrogen and the aromatic hydrogens in the case of 3.

The starting materials, 4-thioxoazetidion-2-ones, are easily obtained by thionation of the corresponding azetidine-2,4-diones^{7a} which can be synthesized by various methods.⁸ Many other synthetic methods for the thioxoazetidionones have also been reported.⁷ The present reactions, therefore, provides a useful methods for the synthesis of these β -lactams bearing a spiro-fused small ring.

References and Notes

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6. 3: mp 173-174 °C; IR (CHCl₃) 1736 cm⁻¹; ¹H NMR (CDCl₃) δ 1.25 (d, 6H, *J* 6 Hz, CHMe₂), 1.46 and 1.66 (ABq, 2H, *J* 7 Hz, CH₂), 2.06 (sep, 1H, *J* 6Hz, CHMe₂), 4.26 (s, 1H, CH), 6.7-6.9 (m, 2H, Ph), 7.0-7.6 (m, 13H, Ph); ¹³C NMR (CDCl₃) δ 16.1, 20.8, 21.2, 35.5, 46.3, 57.2, 58.5, 126.4-130.1, 135.0, 140.5, 142.0, 168.7. 4: mp 172-173 °C; IR (CHCl₃) 1738 cm⁻¹; ¹H NMR (CDCl₃) δ 1.21 (d, 3H, *J* 7Hz, CHMe₂), 1.29 (d, 3H, *J* 7Hz, CHMe₂), 1.62 and 2.19 (ABq, 2H, *J* 8Hz, CH₂), 1.96 (sep, 1H, *J* 8Hz, CHMe₂), 4.30 (s, 1H, CH), 6.5-6.8 (m, 5H, Ph), 6.96 (s, 5H, Ph), 7.1-7.6 (m, 5H, Ph); ¹³C NMR (CDCl₃) δ 16.9, 20.2, 21.0, 34.7, 46.0, 56.4, 61.4, 125.2-130.6, 134.2, 138.8, 140.6, 169.3.
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