

2-Azabicyclo[2.2.0]hexane-3,5-dione, a New Building Block for Carbapenem Nuclei

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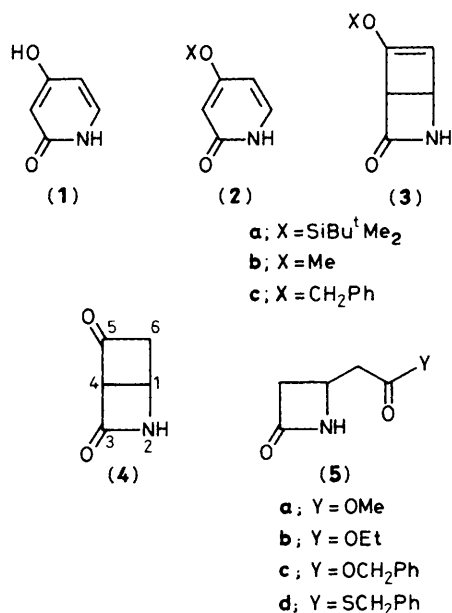
2-Azabicyclo[2.2.0]hexane-3,5-dione is synthesized *via* photopyridone formation from 4-(*t*-butyldimethylsilyloxy)- or 4-alkoxy-2-pyridone followed by mild acid hydrolysis and reacts with a variety of alcohols or thiols to give 4-alkoxycarbonyl- or 4-alkylthiocarbonyl-methylazetidino-2-ones.

Our previous studies have shown that 2-pyridones having an appropriately protected oxygen function at the 4-position do not dimerize *via* the S_1 state; hence irradiation of 4-alkoxy-¹ and 4-acetoxy-2-pyridones² (**2**) at ≥ 300 nm afforded the corresponding photopyridones (**3**) in high yields. We now report the synthesis of 2-azabicyclo[2.2.0]hexane-3,5-dione (**4**) which serves as a new building block for carbapenem nuclei, using the photopyridones (**3**) as the starting materials.

The dione (**4**) was synthesised as follows. Silylation [$\text{Bu}^t\text{Me}_2\text{SiCl}$ (1 equiv.) and imidazole (2.5 equiv.) in *N,N*-dimethylformamide, room temp.] of 4-hydroxy-2-pyridone,

(**1**), gave the 4-silyl ether (**2a**)[†] which was readily soluble in ether. The silyl ether (**2a**), without purification, was irradiated in ether at ≥ 300 nm (high-pressure mercury lamp with Pyrex filter) to give after chromatography (silica; hexane-ethyl

[†] M.p. 114 °C, softened at 105 °C, λ (Et₂O) 295 nm. Though (**2a**) could be recrystallized from hexane, the ether extract of the silylation mixture was immediately used for further photolysis, in order to attain high-yields of the photopyridone (**3a**). All new compounds gave satisfactory microanalytical and/or accurate mass spectral data and were adequately identified by i.r. and n.m.r. spectroscopy.



acetate, 3:1) the photopyridone (**3a**)‡ in 51% overall yield from (**1**). Treatment of the photopyridone (**3a**) with a small amount of trifluoroacetic acid in tetrahydrofuran (THF)–H₂O (*ca.* 7:3) at room temperature followed by neutralization with pyridine gave after chromatography (silica; ethyl acetate–hexane, 1:1) the azabicyclohexanedione (**4**), m.p. 70°C; ν (CHCl₃) 1800 and 1760 cm⁻¹; δ (CDCl₃) 3.20 (d, *J* 3.0 Hz, CH₂), 4.48 (q, *J* 3.0 Hz, H-1), 4.68 (t, *J* 3.0 Hz, H-4), and 6.70 (br. s, NH), in 62% yield. Similar removal of the silyl group from (**3a**) also proceeded in the presence of *p*-MeC₆H₄SO₃H,

‡ M.p. 65°C; ν (CHCl₃) 3425 and 1750 cm⁻¹; δ_{H} (CDCl₃) 0.22 (s, 2 × Me), 0.93 (s, 3 × Me), 4.20 (br. s, H-1 and H-4), 5.08 (br. s, H-6), and 6.15 (br. s, NH).

Dowex 50W (H⁺-form), or even 10% HCl instead of trifluoroacetic acid. This stability under acidic conditions led us to a simpler synthesis of (**4**). Thus, treatment of the photopyridones (**3b**) and (**3c**)¹ with aqueous THF containing a small amount of 10% HCl gave (**4**) in 51 and 72% yields, respectively.

Reaction between (**4**) and methyl, ethyl, and benzyl alcohols as solvent in the presence of a few drops of pyridine or triethylamine at room temperature gave the corresponding 4-alkoxycarbonylmethylazetidines (**5a**),³ (**5b**),⁴ and (**5c**)⁵ as the sole products in good yields (50–75%). A similar reaction of (**4**) with benzyl hydrosulphide afforded 4-benzylthiocarbonylmethylazetidines (**5d**) in 51% yield; m.p. 95–96°C; ν (CHCl₃) 1755 and 1675 cm⁻¹; δ (CDCl₃) 2.5–3.5 (m, 2 × H-3 and 2 × H-1'), 4.05 (m, H-4), 4.20 (s, CH₂Ph), 6.25 (br. s, NH), and 7.40 (br. s, Ph).

Similar reactions also proceeded with the *N*-methyl derivatives of (**2**)–(**4**), indicating that the present method for the synthesis of compounds of type (**5**) should have a wide applicability. Since cleavage of the C(4)–C(5) bond in (**4**) takes place under very mild conditions, we believe that (**4**) can serve as an equivalent of (**5**) and provide a new building block for carbapenem nuclei.

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