Synthesis of 3-Bromo-2-ethoxy-3,4-dihydro-2H-pyran-6-amide

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Scheme

The amide \(2\) \[1\] was prepared by hydrolysis of the nitrile \(1\) according to the reported procedure \[2\].

To a cooled (0deg.C) solution of \(1\) (232 mg, 1 mmol) in \(\text{CH}_2\text{Cl}_2\) (1 ml) was added successively hydrogen peroxide (30%, 0.5 ml), tetra-(n-butyl)ammonium hydrogen sulfate (70 mg) and an aqueous solution of sodium hydroxide (20%, 0.38 ml). The reaction mixture was allowed to warm to room temperature. Methylenechloride (15 ml) was added after 1 h. The organic layer was separated, washed with brine, dried (\(\text{Na}_2\text{SO}_4\)) and concentrated in vacuo. The residue (0.25 g) was flash chromatographed (AcOEt/Hexane = 3:1) to afford 200 mg (80%) of \(2\).

\(R_f\) (AcOEt): 0.50.

M. p. 141-142 deg.C.

IR (cm\(^{-1}\), KBr): 3400vs, 3260vs, 1674vs, 1635vs, 1610vs, 975vs, 847s, 810s, 765s.

\(^1\)H-NMR (CDCl\(_3\)): 6.33 (br, 1H, NH); 6.26 (br, 1H, NH); 6.06 (dd, \(J = 5.2, 3.0, 1H, H-5\)); 5.16 (d, \(J = 2.1, 1H, H-2\)); 4.12 (ddd, \(J = 10.4, 6.3, 2.1, 1H, H-3\)); 3.87 and 3.71 (2x dq, \(J = 9.7, 7.1, \text{OCH}_2\text{Me}\)); 2.77 (ddd, \(J = 18.2, 10.4, 3.0, 1H, H-4\)); 2.63 (ddd, \(J = 18.2, 6.3, 5.2, 1H, H-4\)); 1.26 (t, \(J = 7.1, 3H, \text{Me}\)).

\(^13\)C-NMR (CDCl\(_3\)): 163.9 (CONH\(_2\)), 141.5 (C-6), 107.5 (C-5), 97.6 (C-2), 65.2 (OCH\(_2\text{Me}\)), 43.1 (C-3), 27.8 (C-4), 14.8 (OCH\(_2\text{CH}_3\)).

CI-MS: 269/267 (M+NH\(_4^+\), 82/74), 253/251 (M+2, 9/9), 252/250 (M+H\(^+\), 87/87), 170 (M-Br, 100), 152/150 (7/7), 125 (31), 124 (41), 99 (9), 97 (21), 85 (11), 77 (31).

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References


Sample Availability: Available from MDPI, 0.1g, MDPI 12539.