

## 3-tert-butoxycarbonylamino-pyridine-2-carboxylic Acid Methyl Ester

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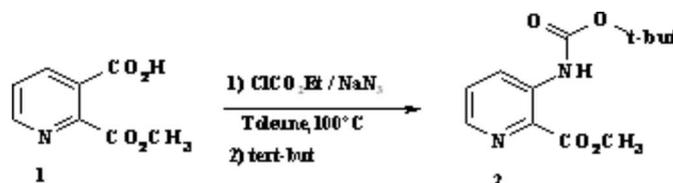
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The discussion and purpose for the synthesis of the 2, 3-pyridinecarboxylic acid-2-methyl ester 1 has been reported elsewhere [1]. To a solution of half-ester (1.0 g, 5.52 mmol) in dry tetrahydrofuran (15 ml) cooled at  $-10^\circ\text{C}$  was added drop-wise triethylamine (1.52 ml, 11.04 mmol) then ethyl chloroformate (0.79 ml, 8.28 mmol). The mixture was stirred for 30 minutes at  $-10^\circ\text{C}$ . Analysis by tlc showed complete conversion to a very non-polar product. A solution of sodium azide (0.61 g, 9.38 mmol) in water (4 ml) was then added drop wise continued stirring for 1h at  $-10^\circ\text{C}$ . The resulting mixture was filtered, evaporated and the aqueous phase was extracted with ethyl acetate (3 x 15 ml). The combined organic layer were washed with brine, dried ( $\text{MgSO}_4$ ), filtered and concentrated in vacuo. The acyl azide was slowly brought to reflux in toluene for 2h to give by Curtius rearrangement cleanly isocyanate. The subsequent reaction of isocyanate with 2-Methyl-2-propanol at  $100^\circ\text{C}$  for 3 hours. After evaporation in vacuo, the crude product was purified by chromatography on silica gel (9/1 : EtOAc/petroleum ether) to give 3-tert-Butoxycarbonylamino-pyridine-2-carboxylic acid methyl ester 2 (1.03 g, 80%).

$R_f$ : 0.36 (9:1, EtOAc/petroleum ether)

Melting point:  $94^\circ\text{C}$  (pale white crystals, from hexane)

IR (KBr,  $\nu$ ,  $\text{cm}^{-1}$ ): 3298, 3000 (NH), 1721, 1691 (CO).

$^1\text{H-NMR}$  (300 MHz,  $\text{DMSO-d}_6$ ,  $\delta$ , ppm): 1.47 (s, 9H,  $\text{CH}_3$ ), 3.85 (s, 3H,  $\text{CH}_3$ ), 7.55 (dd, 1H,  $J = 8.5, 4.3$  Hz, H-5), 8.32 (dd, 1H,  $J = 4.3, 1.3$  Hz, H-4), 8.41 (dd, 1H,  $J = 8.5, 1.3$ , H-6), 9.90 (s, 1H, NH).

$^{13}\text{C-NMR}$  (75 MHz,  $\text{DMSO-d}_6$ ,  $\delta$ , ppm): 27.82 ( $3\text{CH}_3$ ), 52.44 ( $\text{CH}_3\text{O}$ ), 80.62 ( $\text{C}(\text{CH}_3)_3$ ), 127.54, 127.71, 134.25, 137.28, 142.25, 152.17, 167.00 (CO).

MS  $m/z$ : 253 [ $\text{M}+1$ ], 197.5, 165.0, 153.0, 139.0, 121.5.

Elemental analysis: Calculated C<sub>12</sub>H<sub>16</sub> N<sub>2</sub>O<sub>4</sub>: C, 57.13; H, 6.39; N, 11.10 Found: C, 57.21; H, 6.45; N, 11.07.

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### References

1. Mamouni, R.; Aadil, M.; Akssira, M.; Lasri, J.; Sepulveda-Arques, J. *Tetrahedron Lett.* **2003**, *44*, 2745-2747.

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