

N-Alkylation of 2- and 4-Carbamoylpyridine

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A number of new N-alkylated carbamoylpyridines required for a series of pharmacological investigations¹ have been prepared. Since adaptation of the usual alkylation methods to the carbamoylpyridines presented some difficulties, inasmuch as, *e.g.*, all attempts to use alkyl chlorides as alkylating agents were unsuccessful, the synthetic procedures finally adopted are reported in the following.

1,1'-Trimethylene-bis-(4-carbamoylpyridinium bromide). A solution of 30.5 g (0.25 mole) of isonicotinamide (prepared according to Prijs, Lutz and Erlenmeyer²) and 20 g (0.09 mole) of 1,3-dibromopropane in 200 ml of ethanol was heated in a stainless steel autoclave at 120° for one hour. After cooling the crystals were filtered by suction, washed with ether and dried at room temperature. Yield 26 g. After recrystallisation from 50 % ethanol, 18.7 g (43 %) of a dihydrate was obtained as small, colourless crystals, m.p. 256–257° (decomp.). (Found after drying at 50°/2 mm: N 11.81; Br 33.79; H₂O (Karl Fischer titration) 7.96. Calc. for C₁₅H₁₈N₄O₂Br₂ · 2H₂O: N 11.62; Br 33.19; H₂O 7.47).

1,1'-Trimethylene-bis-(4-carbamoylpyridinium chloride). To a solution of 48.2 g (0.10 mole) of 1,1'-trimethylene-bis-(4-carbamoylpyridinium bromide) dihydrate in 200 ml of water was added freshly precipitated silver chloride, prepared from 68 g (0.40 mole) of silver nitrate. The suspension was stirred for 10 min at 100°, the precipitate removed by filtration, and the filtrate evaporated. The crude product was recrystallised from 90 % methanol to give a dihydrate in very small, colourless crystals. Yield 25 g (64 %) m.p. 263–264° (decomp.). (Found after drying in the air: H₂O (Karl Fischer titration) 8.83. Calc. for C₁₅H₁₈N₄O₂Cl₂ · 2H₂O: 9.16. Found after drying at 50°/2 mm: C 50.24; H 5.19; N 16.22; Cl 19.62. Calc. for C₁₅H₁₈N₄O₂Cl₂: C 50.43; H 5.08; N 15.68; Cl 19.85).

2-Carbamoyl-1-methylpyridinium iodide. 12.1 g (0.10 mole) of α-picolinamide (prepared according to Engler³) and 28.4 g

(0.20 mole) of methyl iodide were heated at 85° for 3 h in a 250 ml Duran glass autoclave. The excessive methyl iodide was distilled off and the residue washed with ether and dried at room temperature. Yield 22.5 g. After recrystallisation from methanol, 15.8 g (60 %) of small, yellow crystals were obtained, m.p. 171–172° (decomp.). (Found after drying at 50°/2 mm: N 10.51; I 48.20. Calc. for C₇H₉N₂OI: N 10.61; I 48.06).

2-Carbamoyl-1-methylpyridinium chloride. To a solution of 13.2 g (0.05 mole) of 2-carbamoyl-1-methylpyridinium iodide in 100 ml of water was added freshly precipitated silver chloride, prepared from 17 g (0.10 mole) of silver nitrate, and the suspension was treated as described above. After recrystallisation from 90 % ethanol, 6 g (63 %) of a monohydrate was obtained as small, colourless crystals, m.p. 223–224° (decomp.). (Found after drying in the air: H₂O (Karl Fischer titration) 9.43. Calc. for C₇H₉N₂OCl · H₂O: 9.45. Found after drying at 50°/2 mm: C 48.63; H 5.43; N 15.98; Cl 20.38. Calc. for C₇H₉N₂OCl: C 48.71; H 5.26; N 16.23; Cl 20.54).

The elementary analyses were performed by Dr. A. Bernhardt, Max-Planck-Institut, Mülheim.

1. Karlog, O. *Private communication*.
2. Prijs, B., Lutz, A. H. and Erlenmeyer, H. *Helv. Chim. Acta* **31** (1948) 573.
3. Engler, C. *Ber.* **27** (1894) 1786.

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α-Longipinene, A Sesquiterpene with A New Carbon Skeleton*,**

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Longicyclene¹ and β-bergamotene² have recently been isolated from Indian turpentine oil (from *Pinus longifolia*) and

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** In view of our widening interest in the order Pinaceae the general title "Constituents of Pine Heartwoods" has been changed. Part 31, *Svensk Papperstidn.* **55** (1952) 605; the paper published in this journal, **17** (1963) 1826 is regarded as part 32.