TRANSFORMATIONS OF 2-TRIFLUOROMETHYLIMIDAZO[4,5-*b*]PYRIDINE

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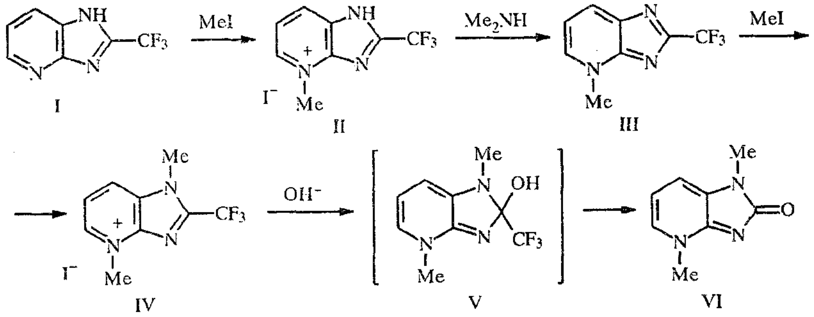
We have found that the reaction of 2-trifluoromethylimidazo[4,5-*b*]pyridine (I) with excess methyl iodide in DMF and subsequent treatment of the reaction product with alkali and, then, DMSO leads to the replacement of the trifluoromethyl group by a hydroxyl group to give 1,4-dimethylimidazo[4,5-*b*]pyridin-2-one (VI) in 18% yield.

The most likely pathway for this transformation involves the formation of iodomethylate II in the first step, which is converted into III by the action of dimethylamine present in DMF as its decomposition product. Subsequent quaternization of III leads to salt IV, which reacts with aqueous alkali apparently to give pseudobase V as a precipitate. Heating V with DMSO gives imidazolone VI. This pathway was supported by the transformations of monosalt II into disalt IV and of disalt IV into base VI.



A sample of 1.3 ml (1 mmole) methyl iodide was added to a solution of 2 g (1 mmole) 2-trifluoromethyl-1H-imidazo[4,5-*b*]pyridine in 6 ml DMF and heated at reflux for 2 h. The solvent was distilled off in vacuum using a water pump and the residue was washed with ether. The product was dissolved in 8 ml water and 9 ml concentrated aqueous sodium hydroxide was added. The precipitate was filtered off, washed with a small amount of cold water, and dried in a desiccator over calcium chloride. The dried product was dissolved in DMSO and maintained for 10-20 min at 50-60°C. The precipitate formed (0.3 g) was filtered off, washed with dimethylsulfoxide, and dried, mp 278°C. PMR spectrum in CF_3CO_2H: 3.26 and 3.99 (each 3H, s, CH_3), 7.35 (1H, q, 6-H), 7.62 (1H, d, 7-H), 7.72 ppm (1H, d, 5-H). No depression of the melting point was found for a mixed probe of this sample with authentic 1,4-dihydro-1,4-dimethylimidazo[4,5-*b*]pyridin-2-one [1].

Base III was also obtained upon the consecutive action of dimethyl sulfate in acetic acid and of aqueous alkali on imidazopyridine I. Salt IV was also obtained starting from 1-methyl-2-trifluoromethylimidazo[4,5-*b*]pyridine (VII).

4-Methyl-2-trifluoromethyl-1H-imidazo[4,5-*b*]pyridinium iodide (II, $C_8H_7N_3F_3I$) was obtained in 80% yield by the reaction of hydriodic acid and base III in acetic acid, mp 165-166°C (from acetonitrile—ether). PMR spectrum in CF_3CO_2H: 4.19 (3H, s, 4-CH_3), 7.52 (1H, q, 6-H), 8.29 (1H, d, 5-H, $J_{5,6}$ = 5.0 Hz), 8.46 (1H, d, 7-H, $J_{6,7}$ = 8.5 Hz).

4-Methyl-2-trifluoromethyl-4H-imidazo[4,5-*b*]pyridine (III, $C_8H_6F_3$) was obtained in 50% yield, mp 141-142°C (from benzene). PMR spectrum in D_2O: 4.02 (3H, s, 4-CH_3), 7.06 (1H, t, 6-H), 8.2 (2H, d, J = 7.0 Hz, 5-H, 7-H).

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1,4-Dimethyl-2-trifluoromethylimidazo[4,5-*b*]pyridinium iodide (IV, $C_3H_9N_3F_3I$). A. This compound was obtained in 35% yield by the reaction of methyl iodide and 1-methyl-2-trifluoromethylimidazo[4,5-*b*]pyridine (VII) in ethanol.

B. Iodide IV was obtained in 55% yield by heating salt II in DMF with a 1.5-fold excess of methyl iodide, mp 190-191°C (from ethanol). PMR spectrum in D_2O: 4.14 (3H, s, $1\text{-}CH_3$), 7.93 (1H, q, 6-H), 8.86 (2H, m, 5-H, 7-H, $J_{5,6}$ = 9.7 Hz). Imidazolone VI was also obtained in 61% yield upon the consecutive action of alkali and DMSO on salt IV.

The elemental analysis data for nitrogen were in accord with the calculated values.

REFERENCES

1. Yu. M. Yutilov and R. M. Bystrova, Khim. Geterotsikl. Soedin., No. 5, 859 (1972).