Resolution of dl-Deoxynupharidine ; The Total Synthesis of Nupharidine

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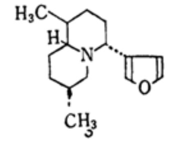
Recently we have suggested the absolute configuration of deoxynupharidine should be represented as the formula I on the bases of NMR spectroscopic evidences[1]. A chromatography of the diastereoisomeric mixtures of



I

deoxynupharidine (42 g.)[2] on alumina resulted in the separation of the fraction which showed the same infrared and NMR spectra with those of natural deoxynupharidine (10 g., eluted by peterolum-ether)[3]. This fraction was converted to *N*-oxide (hydrochloride, m. p. 193∼196°C, Found: C, 62.85; H, 8.29; N, 4.98. Calcd. for $C_{15}E_{23}O_2N$–HCl: C, 63.03; H, 8.46; N, 4.90%, infrared spectrum was found to be identical with that of nupharidine hydrochloride in Nujol), and then reduced with Pd–C to give *dl*-deoxynupharidine. Infrared spectrum of its hydrochloride (m. p. 224∼225°C, Found: C, 66.69; H, 8.84. Calcd. for $C_{15}H_{23}ON$–HCl; C, 66.77; H, 8.97; N, 5.19%) in Nujol and free base (liquid) were identical with that of natural deoxynupharidine. The treatment of *dl*-deoxynupharidine (1.5 g.) with *l*-tartaric acid afforded *l*-deoxynupharidine *l*-tartrate (0.6 g., m. p. 142∼144°C), which was recrystallized several times from ethyl methyl ketone, yielded 0.2 g., Found: C, 59.30; H, 7.64; N, 3.58. Calcd. for $C_{19}H_{29}O_7N$: C, 59.51; H, 7.62; N, 3.65%, $[\alpha]_D$ $-11.54°$ (*c* 1.00 in EtOH), m. p. 152∼153°C and mixed m. p. 152∼154°C with *l*-tartrate of natural *l*-deoxynupharidine (m. p. 154∼155°C,

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[1] Previous communication, This Bulletin, **35**, 697 (1962), presented at the 5th Meeting on Natural Organic Compounds of the Chemical Society of Japan, Sendai, October, 1961.

[2] M. Kotake, I. Kawasaki, T. Okamoto, S. Kusumoto and T. Kaneko, *Ann.*, **636**, 158 (1960).

[3] In the course of this resolution, we found the contribution of F. Bohlmann, E. Winterfeld, P. Studt, H. Laurent, G. Boroschewoki and K. M. Kleine, *Chem. Ber.*, **94**, 3151 (1961).

$[\alpha]_D$ −14.65° (*c* 1.11 in EtOH)), and regenerated *l*-deoxynupharidine showed $[\alpha]_D$ −68.82° (*c* 1.01, in EtOH), its hydrochloride, m. p. 258~260°C, $[\alpha]_D$ −17.03°, (*c* 1.02 in 1 N HCl), Found: C, 66.82; H, 8.96; N, 5.03%, (natural deoxynupharidine had $[\alpha]_D$ −93.5° (*c* 2.03 in EtOH), hydrochloride, m. p. 261~263°C, $[\alpha]_D$ −21.4° (*c* 0.98 in 1 N HCl)). Oxidation of *l*-deoxynupharidine (65 mg.) with hydrogenperoxide yielded *d*-nupharidine (68 mg.), which recrystallized from acetone yielding as white plates, m. p. 212°C (decomp.), $[\alpha]_D$ +13.00° (*c* 0.38 in EtOH), Found: C, 71.81; H, 9.57. Calcd. for $C_{15}H_{23}O_2N$: C, 72.25; H, 9.30%, was identical with natural *d*-nupharidine, ($[\alpha]_D$ +17.2° (*c* 1.10 in EtOH)).

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