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A New Route to the Metacyclophane System

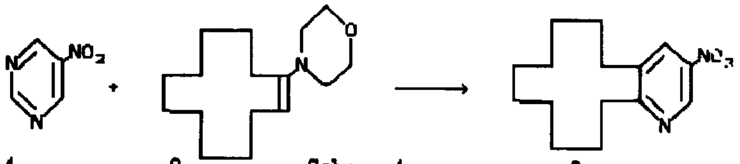
Galina P. Shkil and Reva S. Sagitullin

Department of Organic Chemistry, Omsk State University,
Omsk 644077, Russia

Abstract: Reaction of 5-nitropyrimidine with enamine of cyclododecanone provides 5,6,7,8,9,10,11,12,13,14-decahydro-3-nitrocyclododeca[b]pyridine. Ring-opening and recyclization of the quaternary salt of this on treatment with alkylamine leads to a substituted metacyclophane in high yield.

Metacyclophanes have been the subject of many investigations.[1,2] We have found a new route to metacyclophanes via a transformation of pyridinium salts to nitroanilines that we have previously described.[3-5]

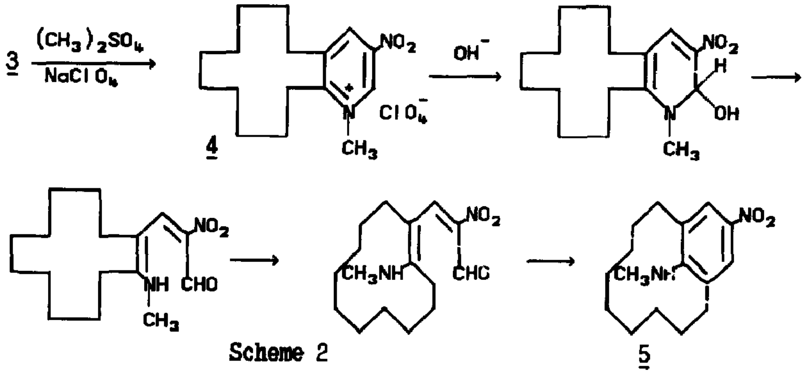
We obtained the new 3-nitrocyclododecenopyridine 3 (Scheme 1) according to the van der Plas[6,7] procedure, i.e. reaction of 5-nitropyrimidine with the enamine of a cyclic ketone. Alkylation of this nitropyridine with dimethyl sulfate and ring-opening and recyclization of the formed quaternary salt yields metacyclophane 5 (Scheme 2).



1 2 Scheme 1 3

This transformation is a new metacyclophane synthesis which gives a new kind of sterically hindered aromatic amine.

5,6,7,8,9,10,11,12,13,14-Decahydro-3-nitrocyclododeca[b]pyridine 3 was obtained by heating of mixture of 0.125g (1mmol) 1 and 0.502g (2mmol) enamine 2 in abs. EtOH at 70 ^{0}C for 10 hr. in 27% yield (0.070g),m.p. 82-83^{0}C/EtOH. ^{1}H-NMR ($CDCl_3$, 80 MHz, ppm): 1.32-2.69 (m, 16H, CH_2), 3.29-3.64(m, 4H, CH_2), 8.83 (d, J=2.74 Hz, 1H), 9.79 (d, 1H).MS (m/z): 252 [M].



Scheme 2

Alkylation of 3 with excess dimethyl sulfate at 60-70°C and subsequent anion exchange yields the N-methylpyridinium perchlorate 4, m.p. 168-170°C (81%). ^{1}H-NMR (DMSO, 200 MHz, ppm): 1.43-1.95 (m, 16H, CH_2), 2.94-3.05 (m, 2H, CH_2), 3.20-3.35 (m, 2H, CH_2), 4.50 (s, 3H, CH_3), 9.22 (d, J=2.36 Hz, 1H), 9.93 (d, 1H).

The 12-nitro-15-methylamino-(9)-metacyclophane 5 was obtained in 66% yield after boiling an ethanol solution of 4 (0.100g, 0.27mmol) and morpholine (10mmol) for 5 hr. M.p. 173.5-174.5°C, IR ($CHCl_3$): 3460cm^{-1} (NH), 1525 and 1350 (NO_2). ^{1}H-NMR (DMSO, 200 MHz, ppm): 0.25-0.62 (m, 2H, CH_2), 0.72-1.10 (m, 4H, CH_2), 1.12-1.60 (m, 6H, CH_2), 1.75-2.00 (m, 4H, CH_2), 2.40- 2.60 (m, 2H, CH_2), 3.00 (d,J=8 Hz,3H,CH_3), 3.00-3.14 (m, 2H, CH_2), 4.50 (s, 1H, NH), 7.81 (s, 2H, ar.). MS (m/z): 276 [M].

Salt 4 on heating with ethanolic methylamine in a sealed tube (100°C, 4 hr) gives metacyclophane 5 in 90% yield.

All elemental analyses were consistent in the structures assigned.

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