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LETTERS TO THE EDITOR

Unexpected Formation of Tris(*tert*-butyl)-4a,8a,12a-trihydroxydecahydro-2,6,10-triazatriphenylene-2,6,10-triscarboxylate via the Reaction of *tert*-Butylpiperidin-4-one-1-carboxylate with Sodium Bis(trimethylsilyl)amide

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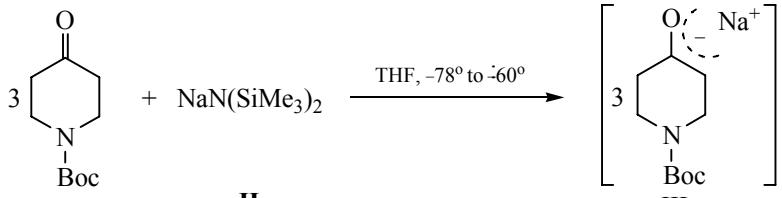
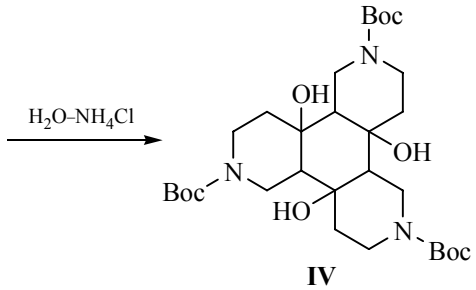
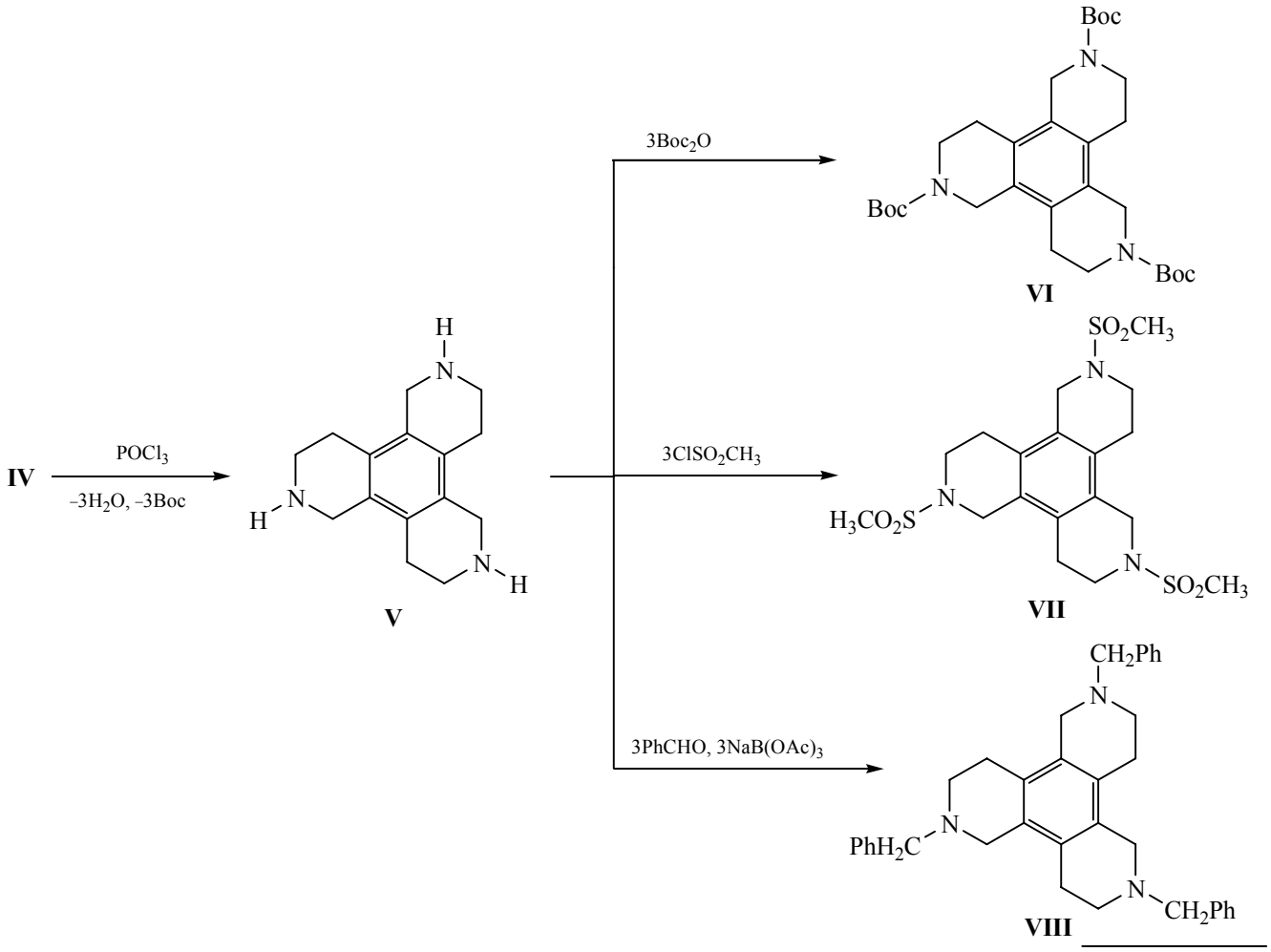
The piperidine derivatives are of interest as biologically active compounds with a diverse range of activity [1, 2]. One of the key substrates to prepare such derivatives is the commercially available *tert*-butylpiperidin-4-one-1-carboxylate **I**. In this work we first tried to perform the metallation of ketone **I** with sodium bis(trimethylsilyl)amide **II** solution in order to functionalize the resulting sodium salt **III** by treating with a variety of the electrophilic reagents. However, in the case of the reaction between reagents **I** and **II** the usual [3] treatment of the reaction mixture yields new substance **IV** (along with the unreacted ketone **I**) whose structure was established by the elemental analysis, IR, ^{1}H NMR spectroscopy, and GC-MS method. The formation of this compound is likely to occur as a result of the regioselective intermolecular interaction of three molecules of the ambidentate sodium anion **III**.





Boc = COOBu^t.

The proposed structure of **IV** was also confirmed by chemical transformations. Thus, the heating with $POCl_3$ leads to the simultaneous dehydration and decarboxylation to form an aromatic secondary amine **V**. Under the suitable reaction conditions [4–6], the latter reacts readily with the electrophilic reagents like Boc_2O, $ClSO_2CH_3$, and PhCHO in the presence of sodium triacetoxyborohydride to give the corresponding products **VI–VIII** by substituting the NH-hydrogen atoms.



Tris(*tert*-butyl)-4a,8a,12a-trihydroxydecahydro-2,6,10-triazatriphenylene-2,6,10-triscarboxylate (IV). To a 2 M. solution (7 ml) of compound **II** in anhydrous THF was added 1.99 g of ketone **I** in 12 ml of anhydrous THF under argon within 40 min at a temperature not higher than –60°C. After completing the addition, the reaction mixture was stirred for 4 h in the temperature range of –78°C to –60°C and kept overnight at room temperature. Then to the mixture 100 ml of the saturated aqueous ammonium chloride solution was added and the product was extracted with ethyl acetate (2×50 ml). The organic layer was washed with the brine and dried over anhydrous sodium sulfate. After the solvent removal in a vacuum the residue was dissolved in an ethyl acetate–hexane mixture (1:3) and chromatographed on a silica gel column to yield in succession the unreacted ketone **I** (0.623 g), and then compound **IV**. Yield 1.099 g (80%) relative to the reacted ketone **I**, mp 132–134°C. IR spectrum, ν, cm^{-1}: 3491, 3428, 3405 (OH), 1692 (C=O). ^{1}H NMR spectrum, δ, ppm: 3.72–4.14 m (9H, CH_2N, OH), 2.94–3.25 m (6H, CH_2N), 1.46–1.95 m (6H, CH_2), 1.41 s [27H, $C(CH_3)_3$], 1.12–1.37 m (3H, CH). Mass spectrum, *m/z:* 596 $[M - H]^-$, 580 $[M + H - 18]^+$, 563 $[M + 2H - 36]^+$, 524 $[M + 2H - 75]^+$, 468 $[M + 3H - 132]^+$, 424 $[M + 3H - 176]^+$, 367 $[M + 3H - 233]^+$. Found, %: C 60.17; H 8.43; N 6.89. $C_{30}H_{51}N_3O_9$. Calculated, %: C 60.30; H 8.54; N 7.04. *M* 597.

1,2,3,4,5,6,7,8,9,10,11,12-Dodecahydro-2,6,11-triazatriphenylene (V). To 5 ml of the freshly distilled phosphorus oxychloride was added 0.6 g of compound **IV** under cooling with ice. The mixture was stirred at 80°C for 6 h, then cooled to room temperature and poured on 100 g of ice. The resulting solution was neutralized with 20% aqueous solution of sodium carbonate to pH 10–11 and extracted with ethyl acetate (3×50 ml). The organic solution was washed with brine and dried with the anhydrous sodium sulfate.

After the solvent removal in a vacuum, the residue was purified by the recrystallization from ethanol. Yield 0.156 g (64%), mp 189–191°C. IR spectrum, ν, cm^{-1}: 3280–3342 (NH), 1518, 1461, 1406 (Ph). ^1H NMR spectrum, δ, ppm: 5.08 5.08 br. s (3H, NH), 3.84–3.93 m (6H, CH_2N), 2.87–3.12 m (6H, CH_2N), 2.18–2.49 m (6H, CH_2). Mass spectr, *m*/*z:* $[M + H]^+$ 244. Found, %: C 73.83; H 8.54; N 17.09. $C_{15}H_{21}N_3$. Calculated, %: C 74.07; H 8.64; N 17.28. *M* 243.

The synthesis of compounds **VI–VIII** was performed according to procedures similar to those described in [4–6]. The composition and structure of compounds **VI–VIII** were confirmed by the elemental analysis, IR and ^1H NMR spectroscopy, and GC-MS method.

The IR spectra were recorded on a Specord 75 IR spectrometer from KBr pellets. The ^1H NMR spectra were registered on a Varian Mercury Plus-400 spectrometer (400 MHz) relative to internal HMDS using $CDCl_3$ as a solvent. The GC-MS spectra were taken on a Surveyor MSQ Thermo Finnigan instrument (USA) by the chemical ionization at atmospheric pressure.

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