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SHORT COMMUNICATIONS

New Synthesis of Diphenylmethanamines

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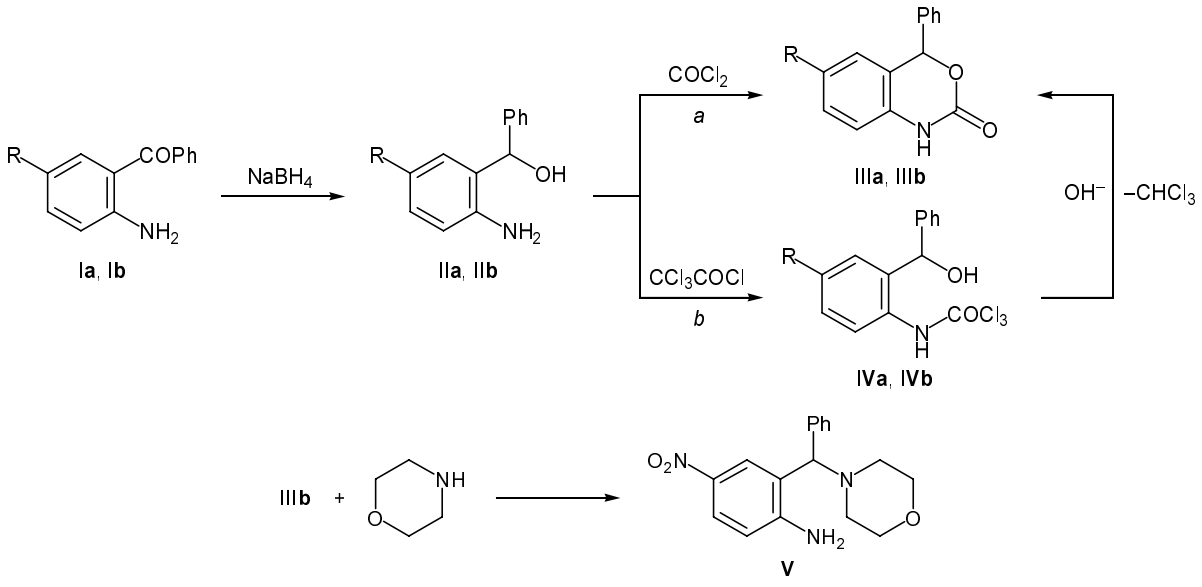
Diphenylmethyl derivatives of ethers and amines constitute structural fragments of drugs with a broad spectrum of activity, in particular antihistaminic drugs, mild tranquilizers, etc. [1]; diarylmethylidene fragment is a structural base of 1,4-benzodiazepine tranquilizers [2]. Bell et al. [3, 4] showed that *o*-aminophenyl (phenyl)methaneamines can be synthesized by reduction of diarylmethylidenamines obtained from *o*-aminobenzophenones. *N*,*N*-Dialkyl(*o*-aminophenyl)phenylmethanamines may be interesting from both practical and theoretical viewpoints; however, there are no reliable methods for their preparation. We have found that these compounds can be synthesized from 3,1-benzoxazines.

3,1-Benzoxazines **IIIa** and **IIIb** were obtained by cyclization of the corresponding diphenylmethanols **IIa** and **IIb** in two ways: (*a*) by the action of phosgene and (*b*) by treatment with trichloroacetyl chloride and subsequent cyclization of trichloroacetamides **IVa** and **IVb** in the presence of a base [5]. The second procedure is not advantageous, for the yields calculated on initial compounds **IIa** and **IIb** differ insignificantly. In addition, method *b* requires proper selection of solvent in the cyclization stage. For example, compound **IVb** (R = NO_2) in methanol undergoes hydrolysis at the amide bond, while in the presence of ethanol benzoxazine **IIIb** is formed; the reason is different basicities of the reagent in these alcohols. The amination of benzoxazine **IIIb** [6] with morpholine was performed under severe conditions (diethylene glycol, 6 h at 210°C). As a result, compound **V** was isolated in 30% yield.

It is known that benzophenones can be reduced under mild conditions to the corresponding diphenyl-



R = Cl (**a**), NO_2 (**b**).

methanols with complex metal hydrides [7, 8]. Compounds **IIa** and **IIb** were obtained in good yield by reduction of *o*-aminobenzophenones **Ia** and **Ib** with sodium tetrahydridoborate.

(2-Aminophenyl)phenylmethanols IIa and IIb (*general procedure***).** Sodium tetrahydridoborate, 2.85 g (0.075 mol), was added over a period of 30 min to a mixture of 0.05 mol of 2-aminobenzophenone **Ia** or **Ib** and 250 ml of isopropyl alcohol, heated to 60°C. The mixture was stirred for 3 h at that temperature and poured onto ice, and the precipitate was filtered off and recrystallized from methanol.

2-Amino-5-chlorophenyl(phenyl)methanol (IIa). Yield 99%, mp 112–113°C; published data [7]: mp 111–112°C.

2-Amino-5-nitrophenyl(phenyl)methanol (IIb). Yield 98%, mp 116–117°C; published data [8]: mp 116–117°C).

N*-[2-(α-Hydroxybenzyl)phenyl]trichloroacetamides IVa and IVb (general procedure*).** A solution of 1.8 g (0.1 mol) of trichloroacetylchloride in benzene was added dropwise over a period of 30 min to a solution of 0.1 mol of compound **IIa** or **IIb** and 1 g (0.1 mol) of triethylamine in benzene, cooled to 5°C. After 2 h, the mixture was filtered, the filtrate was evaporated to dryness, and the residue was recrystallized from benzene.

***N*-[5-Chloro-2-(α-hydroxybenzyl)phenyl]trichloroacetamide (IVa).** Yield 80%, mp 130–131°C; published data [5]: mp 130–131°C.

***N*-[2-(α-Hydroxybenzyl)-5-nitrophenyl]trichloroacetamide (IVb).** Yield 76%, mp 113–114°C. IR spectrum: ν(C=O) 1705 cm^{-1}. ^{13}C NMR spectrum, δ_C, ppm: 66.97, 91.78, 120.32, 123.09, 125.67, 126.9, 127.93, 131.45, 136.52, 139.13, 142.88, 161.50. Found, %: C 46.15; H 2.78; Cl 27.33; N 7.22. $C_{15}H_{11}Cl_3N_2O_4$. Calculated, %: C 46.24; H 2.85; Cl 27.30; N 7.19.

3,1-Benzoxazines IIIa and IIIb (*general procedure*). *a*. A mixture of 0.012 mol of compound **IIa** or **IIb** and 2.6 ml (0.024 mol) of *N*-methylmorpholine in 60 ml of 1,4-dioxane was heated to 50°C and was treated with phosgene over a period of 5 h. The precipitate was filtered off and washed on a filter with 1,4-dioxane, the filtrate was evaporated to dryness, the residue was dissolved in methylene chloride, and the solution was washed with water. The solvent was distilled off, and the residue was recrystallized from benzene.

6-Chloro-4-phenyl-1,4-dihydro-2*H*-3,1-benzoxazin-2-one (IIIa). Yield 64%, mp 195–196°C; published data [5]: mp 191–193°C.

6-Nitro-4-phenyl-1,4-dihydro-2*H*-3,1-benzoxazin-2-one (IIIb). Yield 60%, mp 235–236°C. IR spectrum: ν(C=O) 1709 cm^{-1}. ^{13}C NMR spectrum, δ_C, ppm: 73.18, 107.22, 121.15, 125.40, 125.57, 125.86, 127.02, 129.14, 136.56, 142.13, 143.25, 156.24. Found, %: C 62.17; H 3.65; N 10.42. $C_{14}H_{10}N_2O_4$. Calculated, %: C 62.22; H 3.73; N 10.37.

b. A solution of 5.3 mmol of compound **IVa** or **IVb** and 0.9 g (15.9 mmol) of potassium hydroxide in 40 ml of anhydrous alcohol was heated for 4 h under reflux. The resulting suspension was evaporated to a volume of 10 ml and treated under stirring with 5 ml of 1 N hydrochloric acid and 50 ml of water. The precipitate was filtered off, washed on a filter with water, and recrystallized from alcohol. Yield 65% (**IIIa**), 55% (**IIIb**).

4-[(2-Amino-5-nitrophenyl)(phenyl)methyl]morpholine (V). A mixture of 1 g (3.7 mmol) of compound **IIIb** and 1.24 ml (14.2 mmol) of morpholine in 10 ml of diethylene glycol was stirred for 6 h at 210°C. The mixture was then poured onto ice and extracted with methylene chloride. The organic phase was evaporated, and the residue was recrystallized from 70% methanol. Yield 30%, mp 181–182°C. IR spectrum: ν(Ar_2CHN) 1310 cm^{-1}. ^{13}C NMR spectrum, δ_C, ppm: 50.73, 63.44, 67.63, 121.82, 122.97, 124.18, 125.11, 126.10, 126.35, 127.53, 139.14, 144.10, 156.21. Found, %: C 65.18; H 6.09; N 13.37. $C_{17}H_{19}N_3O_3$. Calculated, %: C 65.16; H 6.11; N 13.41.

The ^{13}C NMR spectra were recorded on a Bruker DRX-400 spectrometer (400 MHz) from solutions in $CDCl_3$ using TMS as internal reference. The IR spectra were obtained in KBr on a Shimadzu FTIR-8300 instrument.

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