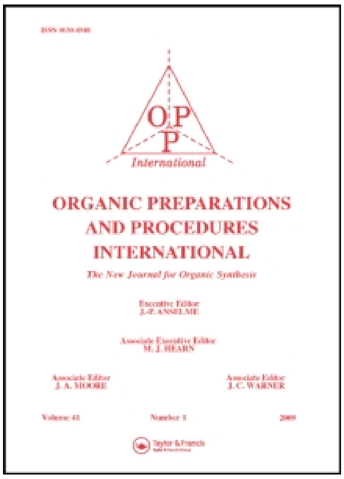

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# PREPARATION OF 1-(*o*-AMINOBENZOYL)-1-METHYLHYDRAZINES

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# PREPARATION OF 1-(*o*-AMINOBENZOYL)-1-METHYLHYDRAZINES

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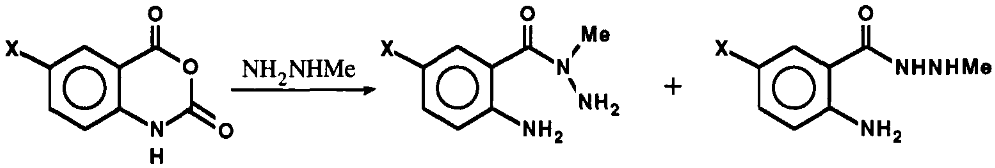
2-Aminobenzoylhydrazines are important starting compounds for the synthesis of various heterocycles. With oxo reagents for example, quinazolines, oxadiazoles or benzotriazepinones are formed depending on the reagent and conditions used.[1] The easiest method for the preparation of 2-aminobenzoylhydrazines is the treatment of isatoic anhydrides[2] with hydrazines. When monoaryl or acetylated hydrazines are used, 2-(*o*-aminobenzoyl)-1-substituted hydrazines (**3**) are formed.[2,3] With methylhydrazine, the main product is of type **2** since the methyl group increases the basicity of the substituted nitrogen. Sunder et al.[4] reported that the ring opening of isatoic anhydride with methylhydrazine in dry DMF resulted in an 85:15 mixture of **2a** and **3a**, whereas Leiby and Heindel[5] stated that the same reaction and the ring opening of 5-chloroisatoic anhydride (**1b**) in 95% ethanol resulted in **2b** and **3b**, respectively, as the sole products. Both groups of authors described the products as oils which were used in different reactions.[6] When these experiments were repeated under the reported conditions, the $^1$H NMR (400 MHz) spectra showed the distilled oily products to be 9:1 mixtures of **2**:**3**. When diethyl ether was added to these oils, **2** crystallized (**2b** rapidly and **2a** more slowly). After two recrystallizations, the isomer-free **2a** and **2b** were obtained. From the mother liquor of **2a**, the minor product **3a** was separated by means of TLC. The products were stable at room temperature.



1 2 3

a) X = H b) X = Cl

## EXPERIMENTAL SECTION

Melting points were determined in capillary tubes with an Electrothermal Digital Melting Point apparatus and are uncorrected. $^1$H NMR spectra were recorded on a JEOL GX 400 FT NMR spectrometer in $CDCl_3$ with TMS as internal standard. MS spectra were obtained on an MM 7070E mass spectrometer at 70 eV.

Reaction of Isatoic Anhydrides (**1a** or **1b**) with Methylhydrazine.- To a slurry of isatoic anhydride (0.1 mol) in ethanol (100 ml), methylhydrazine (6 g, 0.13 mol) was added over a 5 min period. A clear solution was obtained with concurrent evolution of carbon dioxide. After stirring for 4 hrs, the solvent was evaporated and the residue was distilled at 170-185° (1 mm) to afford a 9:1 mixture of **2**:**3**. The oily product was dissolved in ether (100 ml) and left to stand overnight at 4°. The isomer-free product (**2a** or **2b**) was collected and recrystallized.

**2a**: 10.0 g, (60%), mp. 71-73° (3:1 diisopropyl ether-ethanol). $^1$H NMR ($CDCl_3$): δ 3.24 (s, 3H, $CH_3$), 4.50 (s, 4H, 2 x $NH_2$), 6.70-6.74 (m, 2H, Ar), 7.13-7.20 (m, 2H, Ar). MS (EI): m/z(%) 165(22), 120(100), 92(32), 65(7).

Anal. Calcd for $C_8H_{11}N_3O$: C, 58.16; H, 6.71; N, 25.44. Found: C, 58.24; H, 6.86; N, 25.39

**2b**: 13.2 g (66%), mp. 82-84° (9:1 diisopropyl ether-ethanol). $^1$H NMR ($CDCl_3$): δ 3.25 (s, 3H, $CH_3$), 4.47 (s, 4H, 2 x $NH_2$), 6.65-6.67 (m, 1H, Ar), 7.13-7.20 (m, 2H, Ar). MS (EI): m/z (%) 199(24), 154(100), 126(26), 99(12).

Anal. Calcd for $C_8H_{10}ClN_3O$: C, 48.13; H, 5.05; N, 21.05. Found: C, 48.20; H, 5.12; N, 20.96

From the mother liquor obtained from the purification of **2a**, separation on a preparative TLC plate (Merck) with 4:1 benzene-ethanol gave small amounts of **3a** as white crystals, mp. 90-91° (hexane), lit.[6] mp. 90-91°. $^1$H NMR ($CDCl_3$): δ 2.71 (s, 3H, $CH_3$), 5.47 (s, 3H, NH and $NH_2$), 6.63-6.70 (m, 2H, Ar), 7.20-7.30 (m, 2H, Ar), 7.60 (s, 1H, N$\underline{H}$$CH_3$). MS(EI): m/z(%) 165(22), 136(5), 120(100), 92(37), 65(28).

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