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8,9-Methylenedioxy-3,4-dihydro-1,4,5-benzotriazocin-2(1*H*)-ones

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The title compounds are obtained directly on reaction of 6-chloroacetamidopiperonal with substituted phenylhydrazines. Piperonal was used as starting material.

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8,9-Methylendioxy-3,4-dihydro-1,4,5-benzotriazocin-2(1H)-one

Die Titelverbindungen werden in direkter Reaktion von 6-Chloroacetamidopiperonal mit substituierten Phenylhydrazinen erhalten. Dabei wird Piperonal als Ausgangsverbindung eingesetzt.

In connection with 1,4-benzodiazepin-2-ones chemistry considerable attention has been directed toward eight-membered ring systems such as 1,4,5-benzotriazocine[1,2] and 1,5-benzodiazocine[3]. This paper deals with a facile synthesis of new 8,9-methylenedioxy-3,4-dihydro-1,4,5-benzotriazocin-2(1*H*)-ones.

Nitration of piperonal in nitric acid-acetic acid solution gave 6-nitropiperonal (**2**) in good yield. **2** was reduced with ferrous sulfate-ammonium hydroxide to give 6-aminopiperonal (**3**). Condensation of **3** with chloroacetyl chloride in dry benzene afforded 6-chloroacetamidopiperonal (**4**). Reaction of **4** with different hydrazines led directly to cyclized products **6** (Table 1), none of the intermediates **5** were isolated. The nmr spectra of benzotriazocines **6** showed that the methylene group, —NCH_2CO—, shifts from 4.30 ppm in *DMSO*-d_6 to 5.10 in CF_3COOH. This agrees with the observation concerning ethyl glycinate

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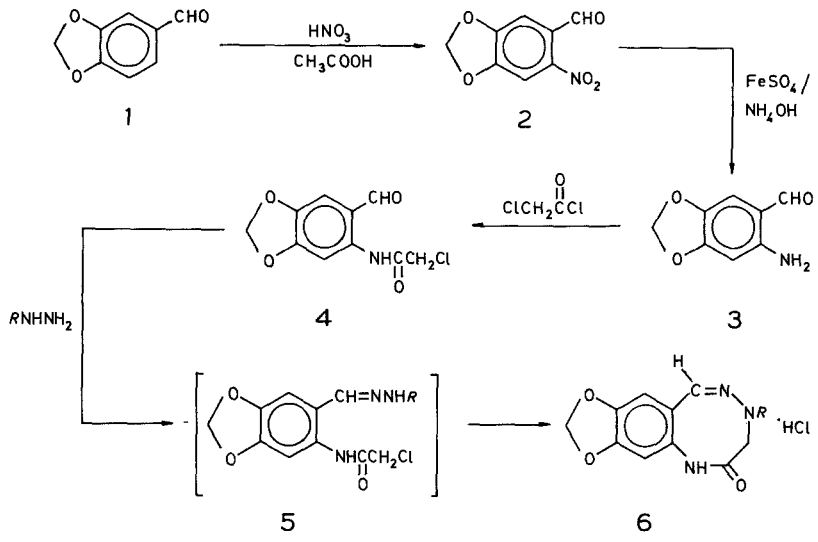
hydrochloride. The methylene group type XCH_2CO— like in 6-chloroacetamidopiperonal (**4**) stayed at the same position 4.42 in both solvents. The elemental analysis of the obtained compounds were consistent with structures **6**.



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Experimental

Infrared spectra were taken on a Perkin-Elmer model 180/spectrophotometer and the nuclear magnetic resonance spectra were measured with a Hitachi Perkin-Elmer R 20 B spectrometer, *TMS* was used as internal reference. Elemental analyses were obtained on a Perkin-Elmer model 240 elemental analyzer. The C,H,N values were in excellent agreement with the given elementary formulas. All the solvents used were distilled and if necessary they were purified by following the procedure metioned in Ref.[4].

6-Nitropiperonal (**2**)[5]

Piperonal (1 mol) was dissolved in an minimum quantity of glacial acetic acid and nitric acid (11 mol) was added dropwise at room temperature. At the end of addition the mixture was further stirred at room temperature for 30 min. This mixture was then mixed with 1000 ml ice-water, yellow crystals were isolated; m.p. 92 °C, 85% yield[5].

Table 1. *NMR data (δ, ppm) for 8,9-Methylenedioxy-3,4-dihydro-1,4,5-benzotriazocin-2(1H)one hydrochlorides* **6** *(Solvents:* A CF_3COOH; B *DMSO-*d_6*)*

No.	*R*-	Solvent	$-NCH_2C(=O)-$	$-OCH_2O-$	$-HC=N-$	$-NHC(=O)-$	$-ArH$
6a	C_6H_5-	A	5.10	6.45	7.66	9.43	6.78–6.90 (m, 2 H) 7.21–7.42 (m, 5 H)
		B	4.38	6.00	7.82	—	6.60–7.28 (m, 8 H)
6b	*p*-*Me*C_6H_5-	A	5.15	6.45	7.73	9.50	6.77, 7.23 (AB qu, $J = 8$ Hz, 4 H) 7.50 (s, 1 H)
		B	4.31	6.07	7.82	—	6.98 (s, 4 H) 7.20, 7.30 (s, 2 H)
6c	*m*-*Me*C_6H_5-	A	5.06	6.43	7.57	9.50	6.88–7.38 (m, 6 H)
6d	*o*-*Me*C_6H_5-	A	5.04	6.38	7.56	9.30	7.10–7.30 (m, 6 H)
6e	*o*-ClC_6H_5-	A	5.20	6.48	8.57	9.37	6.70–6.85 (m, 1 H) 7.20–7.50 (m, 4 H) 7.68 (s, 1 H)
		B	4.30	6.03	8.20	—	7.15–7.45 (m, 6 H)
6f	*p*-BrC_6H_5-	A	5.10	6.43	7.63	9.40	7.42, 7.58 (s, 2 H) 6.72, 7.50 (AB qu, $J = 9$ Hz, 4 H)
6g	2,4-di$NO_2C_6H_4$-	A	5.38	6.50	8.60	—	7.50, 7.70 (s, 2 H) 8.00–8.35 (m, 2 H) 8.80 (s, 1 H)
		B	4.33	6.08	8.58	—	7.05, 7.41, 8.82 (s, 3 H) 8.10–8.25 (m, 2 H)

6-Aminopiperonal (**3**)[6]

3 was prepared in 60% yield by reduction of 6-nitropiperonal (**2**) with ferrous sulfate heptahydrate-ammonium hydroxide. The crude product consisted of red crystal needles, recrystallization from 95% ethanol gave light yellow needles, m.p. 103-104 °C[6].

6-Chloro-acetamidopiperonal (**4**)

6-Aminopiperonal (0.78 g, 0.048 mol) and triethylamine (0.48 g, 0.048 mol) were dissolved in 10 ml of dry benzene and this solution was cooled in an ice bath, a solution of chloroacetyl chloride (0.5 g, 0.048 mol) in 5 ml dry benzene was added dropwise. After the addition, the mixture was kept stirring at room temperature for 30 min. At end of the reaction the solvent was removed to give a red residue. Crystallization from 95% ethanol gave light yellow needles, m.p. 145-146 °C, 88% yield; ir: 3120, 1680, 1660, 1640 cm^{-1}; nmr: (CF_3COOH) 6.05 (s, 2H, OCH_2O), 7.3 (s, 1H, *Ar*), 8.30 (s, 1H, *Ar*), 4.43 (s, 2H, $ClCH_2CO$); (*DMSO-d*$_6$) 4.42 (s, 2H $ClCH_2CO$), 6.18 (s, 2H, OCH_2OO), 7.42 (s, 1H, *Ar*), 7.86 (s, 1H, *Ar*). $C_{10}H_8NO_4Cl$.

Condensation of **4** *with Hydrazines, General Method*

Compound **4** (200 mg, 0.00082 mol) and 0.00082 mol of hydrazine in question were dissolved in 10 ml 95% ethanol and this solution was refluxed. The reaction mixture was cooled and crude product was isolated by filtration.

4-Phenyl-8,9-methylenedioxy-1,4,5-benzotriazocin-2(1H)one hydrochloride (**6a**)

Phenylhydrazine was used. The product (0.231 g, 85.3% yield) was recrystallized from benzene-ethanol mixture, m.p. 157-160 °C; ir: 3280, 1665, 1630, 1600 cm^{-1}. $C_{16}H_{15}N_3O_3Cl$.

4-(p-Methylphenyl)-8,9-methylenedioxy-1,4,5-benzotriazocin-2(1H)-one hydrochloride (**6b**)

p-Tolylhydrazine was used. The product (0.205 g, 72.2% yield) was recrystallized from ethanol, m.p. 176-178 °C; ir: 3278, 1665, 1633 cm^{-1}. $C_{17}H_{16}ClN_3O_3$.

4-(m-Methylphenyl)-8,9-methylenedioxy-1,4,5-benzotriazocin-2(1H)-one hydrochloride (**6c**)

m-Tolylhydrazine was used. The product (0.185 g, 65.6% yield) was recrystallized from ethanol, m.p. 165-166 °C, ir: 3270, 1670, 1620 cm^{-1}. $C_{17}H_{16}ClN_3O_3$.

4-(o-Methylphenyl)-8,9-methylenedioxy-1,4,5-benzotriazocin-2(1H) hydrochloride (**6d**)

o-Tolylhydrazine was used. The product (0.200, 70.9% yield) was recrystallized from ethanol to give a light yellow powder, m.p. 160-165 °C; ir: 3270, 1660, 1630 cm^{-1}. $C_{17}H_{16}ClN_3O_3$.

4-(o-Chlorophenyl)-8,9-methylenedioxy-1,4,5-benzotriazocin-2(1H)-one hydrochloride (**6e**)

o-Chlorophenylhydrazine was used. The product (0.208 g, 69.3% yield) was recrystallized from ethanol-water mixture (2:1), m.p. 232-234 °C; ir: 3300, 1680, 1640, 1600 cm^{-1}. $C_{16}H_{13}Cl_2N_3O_3$.

4-(p-Bromophenyl)-8,9-methylenedioxy-1,4,5-benzotriazocin-2(1H)-one hydrochloride (**6f**)

p-Bromophenylhydrazine was used. The product (0.193 g, 62.3% yield) was recrystallized from ethanol, m.p. 180-181 °C; ir: 3280, 1660, 1630 cm^{-1}. $C_{16}H_{13}BrClN_3O_3$.

4-(o,p-dinitrophenyl)-8,9-methylenedioxy-1,4,5-benzotriazocin-2-(1H)one hydrochloride (**6g**)

o,p-Dinitrophenylhydrazine was used. The product (0.150 g, 43.4% yield) was recrystallized from ethanol, m.p. 185-186 °C; ir: 3250, 1640, 1610 cm^{-1}. $C_{16}H_{12}ClN_5O_7$.

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