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CYCLIC STRUCTURE OF N-METHYL-2-AMINOBENZOYL- AND 2-MERCAPTO-BENZOYLHYDRAZONES OF FATTY-AROMATIC ALDEHYDES

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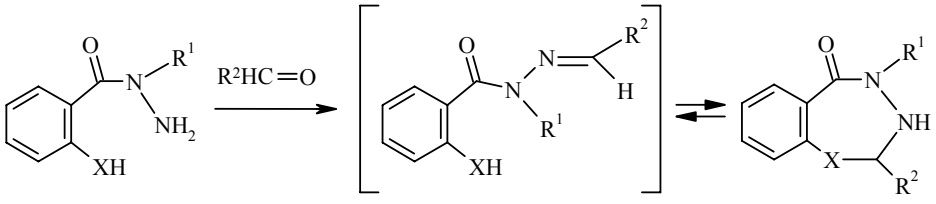
It has been shown by ^{1}H NMR spectroscopic methods that the previously unknown N-methyl-2-amino-benzoyl- and 2-mercaptobenzoylhydrazones of phenylacetic and 3-phenylpropionic aldehydes have cyclic benzo-1,2,4-triazepine and benzo-1,3,4-thiadiazepine structures respectively.

Keywords: benzo-1,3,4-thiadiazepines, benzo-1,3,4-triazepines, N-methyl-2-aminobenzoylhydrazones, 2-mercaptobenzoylhydrazones.

The products of condensation of carbonyl compounds with N-methyl-N′-(2-aminobenzoyl)hydrazine have a cyclic benzo-1,3,4-triazepine structure [1, 2]. On interacting 2-mercaptobenzoylhydrazine with carbonyl compounds derivatives of benzo-1,3,4-thiadiazepine are formed [3, 4]. In both cases the formation of cyclic reaction products assumes the intramolecular nucleophilic addition of NH_2 or SH groups of the aromatic ring to the C=N bond of the hydrazone fragment.



1 **A** **2a–d** **B**

a, **b** X = NH, R^1 = Me, **a** R^2 = CH_2Ph, **b** R^2 = CH_2CH_2Ph; **c**, **d** X = S, R^1 = H, **c** R^2 = CH_2Ph, **d** R^2 = CH_2CH_2Ph

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The aim of the present work was to study the structure of N-methyl-N′-(2-aminobenzoyl)hydrazones and (2-mercaptobenzoyl)hydrazones of phenylacetic and 3-phenylpropionic aldehydes, and also their inclination towards different variants of cyclization in solution leading to the formation of cyclic forms.

Compounds **2a-d** were obtained in 60-85% yield after briefly maintaining hydrazides **1** and the appropriate aldehyde in aqueous alcoholic solution at 25°C (EXPERIMENTAL).

The cyclic benzo-1,3,4-triazepine (or benzo-1,3,4-thiadiazepine) structure **B** is without doubt the structure of compounds **2a-d**, as may be judged by analysis of the ^{1}H NMR spectra. The formation of a typical ABX system was observed in the spectra of compounds **2a,c,** being derivatives of phenylacetic aldehyde, caused by the stereoisomerism of the methylene protons of the benzyl group at 2.8-3.0 ppm (AB portion of the ABX system), and the appearance of the H-2 signal at 4.5 ppm (X part of the ABX system). Furthermore, in the ^{1}H NMR spectra of compounds **2a,b** two signals of equal intensity were observed at 6.0 and 6.3 ppm for the NH protons of the benzo-1,3,4-triazepine ring, and signals of NH protons at 5.9 and 9.5 ppm were observed in the ^{1}H NMR spectra of compounds **2c,d** indicating the cyclic benzo-1,3,4-thiadiazepine form.

It is known that the phenomenon of ring–chain tautomerism of the **A** ↔ **B** type is characteristic of N-methyl-N′-(2-aminobenzoyl)- and (2-mercaptobenzoyl)hydrazones of carbonyl compounds [4-6]. However in the case of compounds **2a-d** we did not observe even trace amounts of the linear hydrazone form **A**, which was checked by plotting the ^{1}H NMR spectra in different solvents and by varying the time parameters.

The obtained data on the cyclic structure of the condensation products of hydrazones of N-methyl-2-aminobenzoic and -2-mercaptobenzoic acids with phenylacetic and 3-phenylpropionic aldehydes open certain prospects for predicting condensations with more complex derivatives of carbonyl compounds containing additional functions, such as with 1,3-dioxo compounds or monosaccharides, which will be the subject of our future investigations.

EXPERIMENTAL

The ^{1}H NMR spectra were obtained on a Bruker AV 400 (400 MHz) spectrometer in DMSO-d_6, internal standard was HMDS. A check on the progress of reactions and the purity of the obtained compounds was effected by TLC on Silufol UV 254 plates in the system benzene–acetone, 4:1. The N-methylhydrazide of 2-aminobenzoic acid and the hydrazide of 2-mercaptobenzoic acid were obtained by known procedures [7, 8].

2-R-4-methyl-1,2,3,4-tetrahydro-5H-1,3,4-benzotriazepin-5-ones 2a,b and 2-R-1,2,3,4-tetrahydro-5H-1,3,4-benzothiadiazepin-5-ones 2c,d. A mixture of the N-methylhydrazide of 2-aminobenzoic acid (0.01 mol) or 2-mercaptobenzoic acid hydrazide (0.01 mol) and aldehyde (0.015 mol) in methanol (30 ml) and water (15 ml) was maintained at 25°C for 2 h. The precipitated crystals were filtered off, washed with ether, and dried.

2-Benzyl-4-methyl-1,2,3,4-tetrahydro-5H-1,3,4-benzotriazepin-5-one (2a). Yield 70%; mp 130-132°C. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 2.79; 2.91 (2H, ABX system, J_{AB} = 12.5, C<u>H</u>$_2$Ph); 2.93 (3H, s, CH_3N); 4.46 (1H, dd, ABX system, J_{AX} = 6.0, J_{BX} = 4.5, H-2); 5.98 (1H, br. s, NH); 6.31 (1H, br. s, NH); 6.60-7.65 (9H, m, Ar). Found, %: C 71.95; H 6.36; N 15.63. $C_{16}H_{17}N_3O$. Calculated, %: C 71.89; H 6.41; N 15.72.

4-Methyl-2-(2-phenylethyl)-1,2,3,4-tetrahydro-5H-1,3,4-benzotriazepin-5-one (2b). Yield 75%; mp 146-148°C. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.80 (2H, m, C<u>H</u>$_2$CH$_2$Ph); 2.74 (1H, m, CH$_2$C<u>H</u>$_2$Ph); 2.82 (1H, m, CH$_2$C<u>H</u>$_2$Ph); 3.11 (3H, s, CH_3N); 4.18 (1H, dd, *J* = 5.5, *J* = 4.0, H-2); 6.04 (1H, br. s, NH); 6.31 (1H, br. s, NH); 6.56-7.63 (9H, m, Ar). Found, %: C 72.63; H 6.77; N 15.05. $C_{17}H_{19}N_3O$. Calculated, %: C 72.57; H 6.81; N 14.94.

2-Benzyl-1,2,3,4-tetrahydro-5H-1,3,4-benzothiadiazepin-5-one (2c). Yield 60%; mp 178-180°C. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 2.83, 3.05 (2H, ABX system, J_{AB} = 13.6, C<u>H</u>$_2$Ph); 4.76 (1H, dd, ABX system, J_{AX} = 6.5, J_{BX} = 6.0, H-2); 5.90 (1H, br. s, NH); 7.21-7.63 (9H, m, Ar); 9.58 (1H, d, *J* = 4.0, NHCO). Found, %: C 66.59; H 5.17; N 10.41. $C_{15}H_{14}N_2OS$. Calculated, %: C 66.64; H 5.22; N 10.36.

2-(2-Phenylethyl)-1,2,3,4-tetrahydro-5H-1,3,4-benzothiadiazepin-5-one (2d). Yield 85%; mp 177-179°C. ^{1}H NMR spectrum (DMSO-d_6), δ, ppm (*J*, Hz): 1.79 (1H, m, C<u>H$_2$</u>CH$_2$Ph); 2.02 (1H, m, C<u>H$_2$</u>CH$_2$Ph); 2.66 (1H, m, CH$_2$C<u>H$_2$</u>Ph); 2.78 (1H, m, CH$_2$C<u>H$_2$</u>Ph); 4.52 (1H, dd, *J* = 6.0, *J* = 5.5, H-2); 5.88 (1H, br. s, NH); 7.22-7.63 (9H, m, Ar); 9.53 (1H, d, *J* = 4.0, NHCO). Found, %: C 67.63; H 5.74; N 9.77. $C_{16}H_{16}N_2OS$. Calculated, %: C 67.58; H 5.67; N 9.85.

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