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LETTERS
TO THE EDITOR

Microwave-Assisted Synthesis of Biphenyl-4,4'-dicarboxylic Acid Arylhydrazones in Water Medium

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Arylhydrazones like semicarbazones, thiosemicarbazones, and guanylhydrazones are used in the preparation of pharmaceuticals [1], metal complexes [2] and bioactive heterocyclic compounds [3].

Most of the known methods for arylhydrazones synthesis include refluxing the reaction mixture in methanol or ethanol for 16–24 h. In the case of carbonyl compounds containing electron-withdrawing groups the synthesis was performed under acid catalysis conditions [4].

At the same time many condensation and addition reactions (for example, the Barbier and the Mannich types reactions, Diels–Alder cycloaddition and Knoevenagel condensation) occur also in aqueous media [5]. However, efficient performance of organic reactions in an aqueous media often requires complete dissolution of the reagents. For this purpose organic solvents are often added to the reaction mixture or the reactions are carried out at heating [6]. It is known [7] that the presence of water in the condensation of amines with carbonyl-containing organic compounds decreases the imines yield. Meanwhile, it has been shown [8] that the reaction of aromatic aldehydes and aliphatic amines in aqueous medium at 100°C afford the corresponding imine with a yield of 65–90%.

In many cases the use of microwave irradiation in organic synthesis allows considerable reduction of the reaction time, increase in the yields of the desired products and minimization of the byproducts formation.

Aryl and heterocyclic hydrazones can be synthesized starting from arylhydrazine, aldehydes or ketones with yields up to 90% under microwave irradiation in an aqueous medium when using polystyrenesulfonic acid as a catalyst [9]. At the same time, the data on the synthesis of substituted arylhydrazones of aromatic dicarboxylic acids are absent in the literature.

In this work, we obtained the substituted arylhydrazones of biphenyl-4,4'-dicarboxylic acid, the potential biologically active compounds, in an aqueous medium under microwave irradiation.

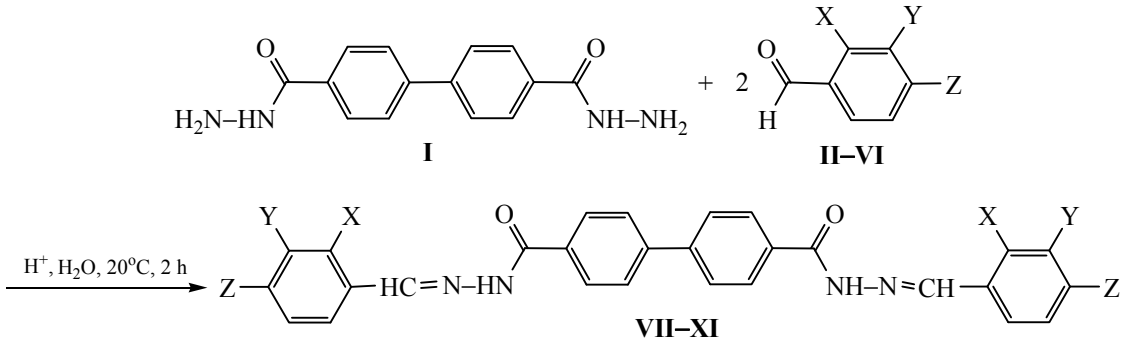
The reaction proceeded via protonation of the carbonyl group followed by condensation with hydrazide to form hydrazinocarbinol. The addition of acid affects the reaction rate and causes an increase in the yield of the desired products [7]. Further protonation of the carbonyl group improves the solubility of some carbonyl compounds in water.

Spectral data of the compounds obtained under microwave-assisted synthesis completely corresponded to those of arylhydrazones synthesized according to standard procedure [10].

The reaction products (yield 69–77%) are high-melting (T_{decomp} > 320°C) crystalline substances, poorly soluble in organic solvents. All the obtained arylhydrazones are soluble in dimethyl sulfoxide and dimethylformamide.

In conclusion, the developed by us enviromentally friendly microwave-assisted synthesis of the substituted arylhydrazones of biphenyl-4,4'-dicarboxylic acid in an aqueous medium in the presence of an acid significantly reduces the reaction time (to 120 min) and provides good yields of the obtained compounds. Furthermore, carrying out the reaction in

Scheme 1.



X = Y = H, Z = OH (**II, VII**); X = H, Y = OH, Z = OCH_3 (**III, VIII**); X = Z = OCH_3, Y = H (**IV, IX**); X = Y = H, Z = Cl (**V, X**); X = Z = H, Z = NO_2 (**VI, XI**).

an aqueous medium facilitates isolation of the reaction products (see Scheme 1).

General procedure of the synthesis. The appropriate benzaldehyde derivative (2.2 mmol), 1 drop of conc. sulfuric acid, and 20 mL of water were added to the finely ground dihydrazide of biphenyl-4,4'-dicarboxylic acid (1.0 mmol, 0.27 g) obtained by hydrazinolysis of its dimethyl ester [10]. The reaction mixture was stirred at 120°C for 120 min. Microwave power was varied from 850 W at the start of the reaction to 4.3 W when temperature rises to 120°C (7–10 s). After the reaction completion, the product was filtered off, dried and recrystallized from ethanol–benzene mixture (1 : 2).

Biphenyl-4,4'-dicarboxylic acid dihydrazide (I). IR spectrum (KBr), ν, cm^{-1}: 3403, 3360, 3307, 3080, 3057, 3030, 3017, 1650, 1620, 1530, 1483, 1453, 1440, 1370, 1340, 1317, 1287, 1223, 1167, 1100, 1003, 980, 927, 907, 900, 843, 817, 750, 737, 710. ^{1}H NMR spectrum, δ, ppm: 9.83 s (2H, NH), 7.89 d (4H, H^{meta}, J_{HH} 8.3 Hz), 7.78 d (4H, H^{para}, J_{HH} 8.3 Hz), 4.52 s (4H, NH_2). Found, %: C 61.71; H 4.98; N 20.47. $C_{14}H_{14}N_4O_2$. Calculated, %: C 62.22; H 5.19; N 20.74.

***N,N'*-Bis[4-hydroxybenzylidene]biphenyl-4,4'-dicarbohydrazide (VII).** Yield 75%. IR spectrum (KBr), ν, cm^{-1}: 3357, 3240, 3059, 1649, 1607, 1587, 1543, 1511, 1492, 1367, 1289, 1238, 1169, 1147, 1064, 1004, 965, 936, 840, 751. ^{1}H NMR spectrum, δ, ppm: 11.63 s (2H, >NH), 9.94 s (2H, OH), 8.36 s (2H, =CH), 8.02 d (4H, H^{meta}, J_{HH} 7.5 Hz), 7.91 d (4H, H^{ortho}, J_{HH} 6.5 Hz), 7.53 d (4H, H^{ortho}, J_{HH} 6.5 Hz), 6.81 d (4H, H^{meta}, J_{HH} 7.5 Hz). Found, %: C 69.86; H 4.42; N 11.53. $C_{28}H_{22}N_4O_4$. Calculated, %: C 70.29; H 4.60; N 11.72.

***N,N'*-Bis[3-hydroxy-4-methoxybenzylidene]biphenyl-4,4'- dicarbohydrazide (VIII).** Yield 77%. IR spectrum (KBr), ν, cm^{-1}: 3425–3099, 1645, 1612, 1583, 1525, 1444, 1297, 1278, 1252, 1221, 1174, 1135, 1063, 1014, 901, 877, 837, 753. ^{1}H NMR spectrum, δ, ppm: 11.73 s (2H, >NH), 9.86 s (2H, OH), 8.29 s (2H, =CH), 8.00 d (4H, H^{meta}, J_{HH} 8.2 Hz), 7.89 d (4H, H^{ortho}, J_{HH} 8.1 Hz), 7.25 s (2H, 2,2'-Bn), 7.03 d (2H, 6,6'-Bn, J_{HH} 7.9 Hz), 6.95 d (2H, 5,5'-Bn, J_{HH} 7.9 Hz), 3.77 s (6H, OCH_3). Found, %: C 66.09; H 4.68; N 9.93. $C_{30}H_{26}N_4O_6$. Calculated, %: C 66.91; H 4.83; N 10.41.

***N,N'*-Bis[2,4-dimethoxybenzylidene]biphenyl-4,4'-dicarbohydrazide (IX).** Yield 77%. IR spectrum (KBr), ν, cm^{-1}: 1344, 1212, 1839, 1649, 1610, 1540, 1503, 1459, 1418, 1356, 1286, 1208, 1160, 1121, 1038, 905, 835, 752. ^{1}H NMR spectrum, δ, ppm: 11.76 s (2H, >NH), 8.71 s (2H, =CH), 8.01 d (4H, H^{meta}, J_{HH} 8.3 Hz), 7.88 d (4H, H^{ortho}, J_{HH} 8.3 Hz), 7.79 d (2H, 6,6'-Bn, J_{HH} 9.2 Hz), 6.63–6.61 m (4H, 3,3',5,5'-Bn), 3.83 s (6H, 4,4'-OCH_3), 3.79 s (6H, 2,2'-OCH_3). Found, %: C 66.97; H 5.11; N 9.52. $C_{32}H_{30}N_4O_6$. Calculated, %: C 67.84; H 5.3; N 9.89.

***N,N'*-Bis[4-chlorobenzylidene]biphenyl-4,4'-dicarbohydrazide (X).** Yield 71%. IR spectrum (KBr), ν, cm^{-1}: 3441, 3223, 3058, 1649, 1609, 1544, 1489, 1365, 1293, 1146, 1090, 1060, 1114, 914, 838, 824, 751. ^{1}H NMR spectrum, δ, ppm: 11.99 s (2H, >NH), 8.44 s (2H, =CH), 8.03 d (4H, H^{meta}, J_{HH} 8.0 Hz), 7.91 d (4H, H^{ortho}, J_{HH} 8.3 Hz), 7.74 d (4H, 2,2',6,6'-Bn, J_{HH} 8.3 Hz), 7.51 d (4H, 3,3,5,5'-Bn, J_{HH} 8.2 Hz). Found, %: C 65.53; H 3.58; N 10.61. $C_{28}H_{20}N_4O_2Cl_2$. Calculated, %: C 65.24; H 3.88; N 10.87.

***N*,*N*'-Bis[3-nitrobenzylidene]biphenyl-4,4'-dicarbohydrazide (XI).** Yield 69%. IR spectrum (KBr), ν, cm^{-1}: 3441, 3212, 3052, 1653, 1607, 1527, 1345, 1289, 1148, 1071, 1004, 948, 895, 842, 750, 737, 694. ^{1}H NMR spectrum, δ, ppm: 12.19 s (2H, >NH), 8.56 d (2H, 2,2'-Bn, J_{HH} 13.7 Hz), 8.24 d (4H, 4,4',6,6'-Bn, J_{HH} 7.2 Hz), 8.15 s (2H, =CH), 8.04 d (4H, H^{meta}, J_{HH} 7.3 Hz), 7.92 d (4H, H^{ortho}, J_{HH} 7.8 Hz), 7.75–7.72 m (2H, 5,5'-Bn). Found, %: C 60.31; H 3.43; N 15.29. $C_{28}H_{20}N_6O_6$. Calculated, %: C 60.43; H 3.70; N 15.67.

Reactions were carried out in a Monowave 300 reactor for microwave synthesis (Anton Paar GmbH) with a maximum radiation power 850 W and a frequency 2455 MHz.

^{1}H NMR spectra (DMSO-d_6) were recorded on a Bruker Avance 500 spectrometer. IR spectra were registered on a Bruker TENSOR 27 spectrophotometer from a thin layer. Elemental analysis was performed on an Elementar Vario Micro Cube.

REFERENCES

1. Rollas, S. and Küçükgüzel, S.G., *Molecules*, 2007, no. 12, p. 1910.
2. Costa, R.F.F., Rebolledo, A.P., Matencio, T., Calado, H.D.R., Ardisson, J.D., Cortes, M.E., Rodrigues, B.L., and Beraldo, H., *J. Coord. Chem*., 2005, vol. 58, no. 15, p. 1307.
3. Salgin-Gökşen, U., Gökhan-Kelekçi, N., Göktaş, Ö., Köysal, Y., Kilıç, E., Işik, Ş., Aktay, G., and Özalp, M., *Bioorg. Med. Chem*., 2007, vol. 15, p. 5738.
4. Aguirre, G., Boiani, L., Cerecetto, H., Fernandez, M., Gonzalez, M., Denicola, A., Otero, L., Gambino, D., Rigol, C., Olea-Azar, C. and Faundez, M., *Bioorg. Med. Chem*., 2004, vol. 12, p. 4885.
5. Narayan, S., Muldoon, J., Finn, M.G., Fokin, V.V., Kolb, H.C. and Sharpless, K.B., *Angew. Chem. Int. Ed*., 2005, vol. 44, p. 3275.
6. Maya, V., Raj, M. and Singh, V.K., *Org. Lett*., 2007, vol. 9, p. 2593.
7. Kitaev, Yu.P. and Buzykin, Yu.P., *Gidrazony* (Hydrazones), Moscow: Nauka, 1974.
8. Simion, A., Simion, C., Kanda, T., Nagashima, S., Mitoma, Y., Yamada, T., Mimura, K., and Tashiro, M., *J. Chem. Soc. Perkin Trans. 1*, 2001, p. 2071.
9. Polshettiwar, V. and Varma, R.S., *Tetrahedron Lett*., 2007, vol. 48, p. 5649.
10. *Organic Reactions*, Adams, R., Ed., New-York: Wiley and Sons, 1948, vol. 3.