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BRIEF COMMUNICATIONS

Synthesis of Hydroxystyrylquinolines and Hydroxystyryl-2,2'-bipyridine under Uncatalyzed and Solvent-Free Conditions Using Microwave Irradiation

T. N. Gavrishova, V. M. Lee, K. V. Gor'kov, and M. F. Budyka

Institute of Chemical Physics Problems, Russian Academy of Sciences, Chernogolovka, Moscow oblast, Russia

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Abstarct—The possibility was explored of synthesizing *trans*-isomers of 2-(4-hydroxystyryl)quinoline, 2-(4-hydroxystyryl)-7-chloroquinoline, 3-(4-hydroxystyryl)benzo[*f*]quinoline, and 6-(4-hydroxystyryl)-2,2'-bipyridine under uncatalyzed and solvent-free conditions using microwave irradiation.

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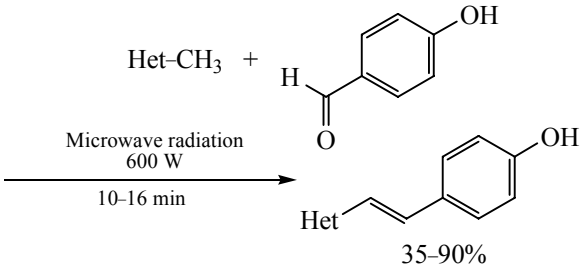
4-Hydroxystyrylquinolines and 4-hydroxystyrylpyridines serve as reactants in synthesis of supramolecular systems and compounds characterized by a broad spectrum of biological activities [1–6]; styryl-2,2'-bipyridine derivatives are used for preparation of materials with nonlinear optical properties [7]. A typical route for synthesis of 2-(4-hydroxystyryl)aza heterocycles is via condensation of the appropriate methyl heterocycle with 4-hydroxybenzaldehyde in the presence of acetic acid anhydride or zinc chloride under 12–30-h heating [1–5]. When acetic acid anhydride is used, the formed acetate needs to be hydrolyzed to the target hydroxy product, and in the case of zinc chloride the target product needs to be separated from zinc compounds. Since recently, broad prospects offered by conducting reactions in microwave ovens have attracted the attention of numerous researchers [8–11]. Of special interest is solvent-free synthesis route [11], which reduces the time and energy consumption, costs of chemicals, and amount of waste and also avoids laborious isolation of the products. There exist only three publications dedicated to the use of microwave irradiation for synthesis of styrylquinolines [8–10]. Li et al. carried out the reaction in acetic acid anhydride, and we [9] used zinc chloride as catalyst. Misiol et al. [10] were the first to demonstrate the possibility of uncatalyzed and solvent-free synthesis of styrylquinolines in a microwave oven, though by the example of 2-methylquinoline containing a carboxy group in the benzene ring. As to styryl-2,2-bipyridines, microwave irradiation was not previously applied in their synthesis.

Here, we developed a convenient procedure for uncatalyzed and solvent-free synthesis of 2-(4-hydroxystyryl)quinoline (**I**), 2-(4-hydroxystyryl)-7-chloroquinoline (**II**), 3-(4-hydroxystyryl)benzo[*f*]-quinoline (**III**), and 6-(4-hydroxystyryl)-2,2'-bipyridine (**IV**) by condensation of appropriate heterocyclic compounds with 4-hydroxybenzaldehyde using microwave irradiation. We showed that this is a stereoselective reaction which yields compounds **I–IV** with the double bond in the *trans* configuration. Compound **I** was described in literature, but it can be prepared by a laborious procedure via 12-h heating in acetic anhydride, purification of the resultant 2-(4-acetoxystyryl)quinoline on a silica gel column, recrystallization, and hydrolysis of 2-(4-acetoxystyryl)quino-line [1, 4]. Compounds **II–IV** were synthesized for the first time:



Here Het is quinolin-2-yl (**I**), 7-chloroquinolin-2-yl (**II**), benzo[*f*]quinolin-3-yl (**III**), and 2,2'-bipyridin-6-yl (**IV**).

The reaction was run in a DAEWOO-KOR-4115SA domestic microwave oven (power 600 W). In synthesis of **I** we used different amounts of 2-methylquinoline (from 0.286 to 1.43 g) and different 2-methylquinoline to 4-hydroxybenzaldehyde ratios. This compound was obtained in a maximal (90%) yield under twofold excess of the aldehyde, which avoids its secondary reaction with two 2-methylquinoline molecules.

In the ^{1}H NMR spectra of **I–IV** the signals from the olefin protons of the styryl moiety at 7–8 ppm take the form of doublets with the vicinal coupling constant of 16–18 Hz, indicating the *trans* configuration of the double bond. The IR spectra of these compounds exhibit absorption bands at 968–982 cm^{-1}, associated with out-of-plane bending vibrations of C–H bonds attached to the C=C bond, which confirms the *trans* configuration of the double bond. Also, the IR spectra contain characteristic absorption bands of the –OH groups at 2430–3090 cm^{-1}, indicating strong hydrogen bonding between the hydroxy group and the nitrogen atom of the heterocycle.

EXPERIMENTAL

The ^{1}H NMR spectra were recorded on Bruker Avance III spectrometers (500 MHz; DMSO-d_6; internal standard TMS; chemical shifts reported using δ values). The IR absorpion spectra (KBr pellets) were taken on a Fourier-transform Spectrum BX-2 spectrometer. The melting points of the compounds synthesized were determined using a Koffler apparatus at the heating rate of 4 deg min^{-1}. The TLC analyses were carried out with ALUGRAM SIL G/UV$_{254}$ plates (visualization with UV light).

A test tube containing 2.0 mmol of methylquinoline, benzo[*f*]quinoline, or bipyridyl, and 4 mmol of 4-hydroxybenzaldehyde was placed into a glass beaker filled with water and irradiated in a domestic microwave oven (power 600 Wt) 3–5 times for 3 min at 30-s intervals (total irradiation time 9–15 min). The course of the reaction was monitored by the TLC technique (eluent acetone–hexane 1 : 1). We used different procedures for isolation of 4-hydroxystyrylquinolines and bipyridines. In the case of 2-(4-hydroxystyryl)quinoline, 2-(4-hydroxystyryl)-7-chloroquinoline, and 3-(4-hydroxystyryl)benzo[*f*]quinoline the reaction mixture was treated with aqueous ethanol, after which the undissolved residue was filtered off and washed with acetone (3 ml) and ethanol (3 × 5 ml).

For isolation of 6-(4-hydroxystyryl)-2,2'-bipyridine the reaction mixture was extracted with a hot diethyl ether–heptane mixture. The precipitate obtained upon cooling of the extract was recrystallized from a diethyl ether–heptane mixture (1 : 5).

2-(4-Hydroxystyryl)quinoline (I). Yield 90%, light-yellow crystals, mp 268°C (from isopropanol) (mp 268–270°C according to [4]). ^{1}H NMR spectrum, δ, ppm: 6.76 d (2H, J = 8.4 Hz, *o*-C_6H_4), 7.18 d (1H, J = 16.2 Hz, =CH–), 7.47–7.55 m (3H, *m*-C_6H_4, quinoline-6), 7.66–7.72 m (2H, –CH=, quinoline-7), 7.78 d (1H, J = 8.6 Hz, quinoline-3), 7.88 d (1H, J = 8.0 Hz, quinoline-5), 7.92 d (1H, J = 8.4 Hz, quinoline-8), 8.26 d (1H, J = 8.6 Hz, quinoline-4), 10.25 br. s (1H, OH). IR spectrum, ν, cm^{-1}: 1636 ($\nu_{C=C}$), 968 (out-of-plane δ *trans*-HC=C–H), 2430–3090 (OH). UV spectrum (in ethanol), λ_{max}, nm: 293, 359.

2-(4-Hydroxystyryl)-7-chloroquinoline (II). Yield 72%, yellow crystals, mp 266–267°C (from isopropanol). ^{1}H NMR spectrum, δ, ppm: 6.81 d (2H, J = 8.6 Hz, *o*-C_6H_4), 7.22 d (1H, J = 16.3 Hz, =CH–), 7.50–7.58 m (3H, *m*-C_6H_4, quinoline-3), 7.75 d (1H, J = 16.3 Hz, –CH=), 7.83 d (1H, J = 7.8 Hz, quinoline-6), 7.93–7.97 m (2H, quinoline-8,5), 8.32 d (1H, J = 8.6 Hz, quinoline-4), 9.85 br. s (1H, OH). IR spectrum, ν, cm^{-1}: 1636 ($\nu_{C=C}$), 968 (out-of-plane δ *trans*-HC=C–H), 2430–3090 (OH). UV spectrum (in ethanol), λ_{max}, nm: 218, 233, 287, 367. Found, %: C 72.28, H 4.18, N 4.81. Calculated %: C 72.47, H 4.29, N 4.97.

3-(4-Hydroxystyryl)benzo[*f*]quinoline (III). Yield 56%, light-yellow crystals, mp 299–300°C (from ethanol). ^{1}H NMR spectrum, δ, ppm: 6.84 d (2H, J = 8.4 Hz, *o*-C_6H_4), 7.31 d (1H, J = 16.1 Hz, =CH–), 7.59 d (2H, J = 8.4 Hz, *m*-C_6H_4), 7.68 t (1H, J = 7.6 Hz, benzoquinoline), 7.74 t (1H, J = 7.3 Hz, benzoquinoline), 7.79 d (1H, J = 16.1 Hz, –CH=), 7.89 d (1H, J = 9.1 Hz, benzoquinoline), 7.92 d (1H, J = 8.8 Hz, benzoquinoline), 8.04 d (1H, J = 7.7 Hz, benzoquinoline), 8.09 d (1H, J = 9.1 Hz, benzoquinoline), 8.82 d (1H, J = 7.7 Hz, benzoquinoline), 9.17 d (1H, J = 8.5 Hz, benzoquinoline), 9.78 s (1H, OH). IR spectrum, ν, cm^{-1}: 1638 ($\nu_{C=C}$), 982 (out-of-plane δ *trans*-HC=C–H), 2430–3090 (OH). UV spectrum (in ethanol), λ_{max}, nm: 240, 279, 296, 332, 344, 362, 379.

Found, %: C 84.65, H 5.18, N 4.55. Calculated, %: C 84.82, H 5.08, N 4.71.

6-(4-Hydroxystyryl)-2,2'-bipyridine (IV). Yield 35%, white powder, mp 222–223°C (from diethyl ether–heptane mixture). ^{1}H NMR spectrum, δ, ppm: 6.80 d (2H, C_6H_4), 7.16 d (1H, *J* = 16.0 Hz, =CH–), 7.46 d.d (1H, *J* = 5.5 Hz, *J* = 6.6 Hz, H-5'), 7.50–7.57 m (3H, C_6H_4, H-5), 7.73 d (1H, *J* = 16.0 Hz, =CH–), 7.88 t (1H, *J* = 7.7 Hz, H-4), 7.97 t (1H, *J* = 7.7 Hz, H-4'), 8.20 d (1H, *J* = 7.3 Hz, H-3), 8.53 d (1H, *J* = 7.9 Hz, H-3'), 8.70 d (1H, *J* = 4.3 Hz, H-6'), 9.73 s (1H, OH). IR spectrum, ν, cm^{-1}: 1636 ($\nu_{C=C}$), 968 (out-of-plane δ *trans*-HC=C–H), 2430–3090 (OH). UV spectrum (in ethanol), λ_{max}, nm: 225, 290, 328. Found, %: C 78.61, H 5.28, N 10.08.Calculated, %: C 78.81, H 5.14, N 10.21.

CONCLUSIONS

A convenient procedure was developed for synthesis of *trans*-isomers of 2-(4-hydroxystyryl)quinoline, 2-(4-hydroxystyryl)-7-chloroquinoline, 3-(4-hydroxystyryl)benzo[*f*]quinoline, and 6-(4-hydroxystyryl)-2,2'-bipyridine under uncatalyzed and solvent-free conditions using microwave irradiation.

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