ISSN 1070-3632, Russian Journal of General Chemistry, 2014, Vol. 84, No. 4, pp. 629–631. © Pleiades Publishing, Ltd., 2014.
Original Russian Text © V.L. Gein, O.V. Bobrovskaya, A.A. Sitnikova, 2014, published in Zhurnal Obshchei Khimii, 2014, Vol. 84, No. 4, pp. 548–551.

Synthesis of 4-Aryl-2-hydroxy-4-oxo-2-butenoic (Aroylpyruvic) Acids *N*-(4-Acetylaminosulfonylphenyl)amides

V. L. Gein, O. V. Bobrovskaya, and A. A. Sitnikova

Perm State Pharmaceutical Academy, ul. Polevaya 2, Perm, 614990 Russia
e-mail: geinvl48@mail.ru

Received July 8, 2014

Abstract—Methyl aroylpyruvates react with sodium 4-aminobenzenesulfonylacetamide in acetic acid to afford 4-aryl-2-hydroxy-4-oxo-2-butenoic acids *N*-(4-acetylaminosulfonylphenyl)amides. The latter were studied in reactions with hydrazine hydrate.

Keywords: aroylpyruvic acids amides, diketones, hydrazine hydrate

DOI: 10.1134/S1070363214040045

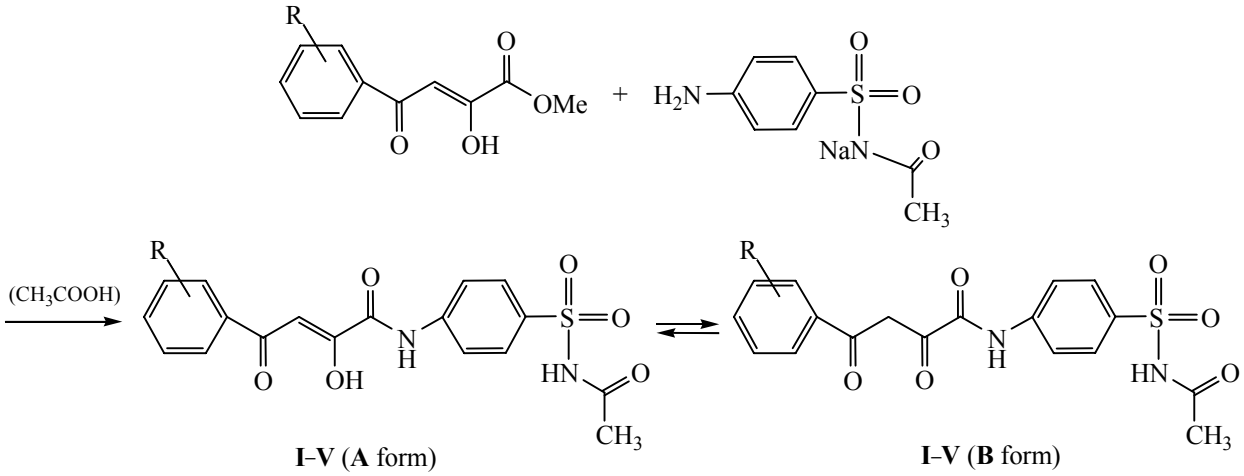
Amides of 4-aryl-2-hydroxy-4-oxo-2-butenoic acids are polycarbonyl compounds which may be used for the preparation of various heterocyclic compounds [1, 2], and some amides possess various biological activity [3].

Reaction of 5-aryl-2,3-dihydrofuran-2,3-diones with amines in anhydrous dioxane, toluene and other inert solvents is the most frequently used approach to the synthesis of these amides [3–5]. It should be noted that the direct interaction between arylamines and aroylpyruvic acids [6] or their esters [7, 8] leads to the formation of the corresponding aniles involving α-carbonyl group; amides formed as a byproduct with low yields or were not formed at all.

We have found that 4-aryl-2-hydroxy-4-oxo-2-butenoic acids *N*-(4-acetylaminosulfonylphenyl)amides **I–V** can be readily obtained in good yields (76–95%) when boiling aroylpyruvic acids methyl esters with sodium 4-aminobenzenesulfonylacetamide (sodium sulfacetamide) in glacial acetic acid for 5–10 min (Scheme 1).

Compounds **I–V** were fine crystalline yellow, light yellow, or cream-colored substances, soluble in DMF, DMSO, dioxane and acetic acid under heating, and insoluble in water.

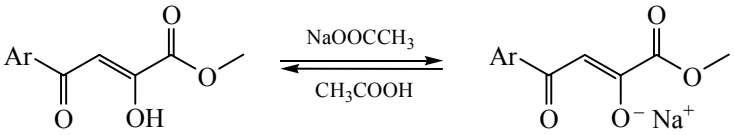
Scheme 1.



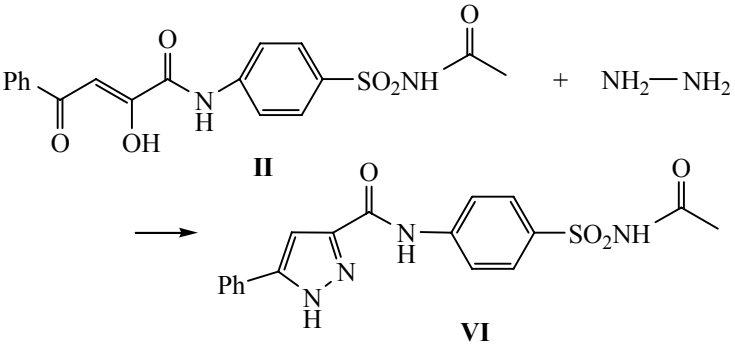
I–V (**A** form) **I–V** (**B** form)

4-Cl (**I**); H (**II**); 4-F (**III**); 3-CH_3O (**IV**); 2,4-Cl_2 (**V**).

Scheme 2.



Scheme 3.



^{1}H NMR spectra of compounds **I–V** contained singlet signals of methine proton at 6.76–7.15 ppm, methyl group CH_3CO at 1.90–1.92 ppm, amino moieties $CONHC_6H_4$ and SO_2NHCO at 10.83–10.94 and 11.80–11.90 ppm, respectively, along with the signals of aromatic protons. In addition, in the ^{1}H NMR spectra of **I–V** a low intensity signal appeared at 4.60–4.61 ppm corresponding to methylene group of the β-diketone form. The integral intensities ratio of the signals of β-methylene group and the CH= proton indicates that the compounds obtained exist predominantly in the enol form **A** (~90%). The absence of the proton signals of the enol hydroxy group is apparently due to their significant broadening as a result of exchange processes that was observed for other derivatives of aroylpyruvic acids [9]. All the obtained compounds gave an intense cherry coloring when mixed with an alcohol solution of iron(III) chloride.

In the IR spectra of compounds **I–V** there were absorption bands of the stretching vibrations of NH-amide groups (3568–3240 cm^{-1}), hydroxy (3150–3120 cm^{-1}), two amide carbonyl (1728–1720 and 1710–1688 cm^{-1}), ketone carbonyl (1620–1610 cm^{-1}), and SO_2 groups (1380–1368 and 1160–1152 cm^{-1}).

Mass spectrum of **II** contained peaks of the molecular ion $[M]^+$ of *m/z* 388 and fragment ions $[Ph]^+$ (*m/z* 77), $[C_6H_5CO]^+$ (*m/z* 105), $[C_6H_5COCH{=}C(OH)]^+$ (*m/z* 147), $[H_2NC_6H_4SO_2NHCOCH_3]^+$ (*m/z* 214) confirming its structure.

The exclusive formation of amides **I–V** is apparently due to the intermediate formation of sodium acetate, which reacts with aroylpyruvic acids esters to give the sodium derivative followed by deactivation of α-located carbonyl group (Scheme 2).

Aiming to confirm the presence of β-dicarbonyl moiety in amides **I–V** obtained, we performed a reaction with hydrazine hydrate. Boiling 2-hydroxy-4-oxo-4-phenyl-2-butenoic acids *N*-(4-acetylaminosulfonylphenyl)amides **II** with an excess of 20% hydrazine hydrate in glacial acetic acid for 2 h afforded as a result 5-phenylpyrazole-3-carboxylic acid *N*-(4-acetylaminosulfonylphenyl)amide **VI** (Scheme 3).

Compound **VI** was a white crystalline substance, soluble in DMF, DMSO, in ethanol, dioxane, glacial acetic acid under heating, and insoluble in water. In contrast to the starting amide **II** the synthesized compound **VI** gives no coloring when mixed with an alcohol solution of iron(III) chloride. The structure of **VI** was proved by ^{1}H NMR and IR spectroscopy.

EXPERIMENTAL

^{1}H NMR spectra in DMSO-d_6 were registered on a Bruker AM-300 (300 MHz) and Bruker DRX 500 (500.13 MHz) spectrometers, internal reference TMS. Mass spectra were taken on a Finnigan MAT INCOS-50 instrument (70 eV). IR spectra were recorded on a Specord M-80 from ulls in mineral oil. Elemental analysis was performed on a Perkin Elmer 2400 analyzer. Melting points were measured on a Melting Point M-565 instrument.

2-Hydroxy-4-oxo-4-(4-chlorophenyl)-2-butenoic acid *N*-(4-acetylaminosulfonylphenyl)amide (I). To

a solution of 0.01 mol of sodium 4-aminobenzenesulfonylacetamide in 15 mL of glacial acetic acid was added a solution of 0.01 mol of methyl 4-chlorobenzoylpyruvate in 10 mL of glacial acetic acid. The reaction mixture was refluxed for 5–10 min. After cooling, the precipitate formed was filtered off and recrystallized from an acetic acid–dioxane mixture (1 : 2). Yield 3.34 g (79%), mp 248–250°C. IR spectrum, ν, cm^{-1}: 3264 (CONH), 3125 (OH), 1724, 1696 (CONH), 1610 (C=O), 1376, 1152 (SO_2). ^1H NMR spectrum, δ, ppm: 1.92 s (3H, CH_3CO), 4.61 s (2H, $COCH_2CO$), 7.13 s (1H, CH=), 7.48–8.01 m (8H, CH_{Ar}), 10.91 s (1H, $CONHC_6H_4$), 11.90 s (1H, SO_2NHCO). Found, %: C 51.24, 51.01; H 3.65, 3.51; N 6.54, 6.71; S 7.49, 7.66. $C_{18}H_{15}ClN_2O_6S$. Calculated, %: C 51.13; H 3.58; N 6.62; S 7.58.

2-Hydroxy-4-oxo-4-phenyl-2-butenoic acid *N*-(4-acetylaminosulfonylphenyl)amide (II) was obtained similarly. Yield 2.95 g (76%), mp 232–234°C. IR spectrum, ν, cm^{-1}: 3240 (CONH), 3150 (OH), 1720, 1696 (CONH), 1610 (C=O), 1376, 1156 (SO_2). ^1H NMR spectrum, δ, ppm: 1.90 s (3H, CH_3CO), 4.61 s (2H, $COCH_2CO$), 7.15 s (1H, CH=), 7.43–8.03 m (9H, CH_{Ar}), 10.94 s (1H, $CONHC_6H_4$), 11.80 s (1H, SO_2NHCO). Found, %: C 55.52, 55.79; H 4.09, 4.22; N 7.12, 7.29; S 8.18, 8.34. $C_{18}H_{16}N_2O_6S$. Calculated, %: C 55.66; H 4.15; N 7.21; S 8.26.

2-Hydroxy-4-oxo-4-(4-fluorophenyl)-2-butenoic acid *N*-(4-acetylaminosulfonylphenyl)amide (III) was obtained similarly. Yield 3.86 g (95%), mp 258–260°C. IR spectrum, ν, cm^{-1}: 3240 (CONH), 3120 (OH), 1724, 1688 (CONH), 1620 (C=O), 1368, 1160 (SO_2). ^1H NMR spectrum, δ, ppm: 1.90 s (3H, CH_3CO), 4.60 s (2H, $COCH_2CO$), 7.13 s (1H, CH=), 7.23–8.15 m (8H, CH_{Ar}), 10.91 s (1H, $CONHC_6H_4$), 11.89 s (1H, SO_2NHCO). Found, %: C 53.08, 53.33; H 3.65, 3.77; N 6.81, 6.97; S 7.98, 7.80. $C_{18}H_{15}FN_2O_6S$. Calculated, %: C 53.20; H 3.72; N 6.89; S 7.89.

2-Hydroxy-4-(3-methoxyphenyl)-4-oxo-2-butenoic acid *N*-(4-acetylaminosulfonylphenyl)amide (IV) was obtained similarly. Yield 3.39 g (81%), mp 218–220°C. IR spectrum, ν, cm^{-1}: 3360, 3256 (CONH), 3130 (OH), 1728, 1710 (CONH), 1620 (C=O), 1380, 1160 (SO_2). ^1H NMR spectrum, δ, ppm: 1.90 s (3H, CH_3CO), 3.79 s (3H, 3-CH_3O), 4.60 s (2H, $COCH_2CO$), 7.13 s (1H, CH=), 7.20–8.02 m (8H, CH_{Ar}), 10.89 s (1H, $CONHC_6H_4$), 11.85 s (1H, SO_2NHCO). Found, %: C 54.41, 54.68; H 4.28, 4.41; N 6.61, 6.78; S 7.56, 7.74. $C_{19}H_{18}N_2O_7S$. Calculated, %: C 54.54; H 4.34; N 6.69; S 7.66.

2-Hydroxy-4-(2,4-dichlorophenyl)-4-oxo-2-butenoic acid *N*-(4-acetylaminosulfonylphenyl)amide (V) was obtained similarly. Yield 3.79 g (83%), mp 206–208°C. IR spectrum, ν, cm^{-1}: 3568, 3500, 3344 (CONH), 3120 (OH), 1696 (CONH), 1620 (C=O), 1376, 1160 (SO_2). ^1H NMR spectrum, δ, ppm: 1.90 s (3H, CH_3CO), 4.60 s (2H, $COCH_2CO$), 6.76 s (1H, CH=), 7.43–7.99 m (7H, CH_{Ar}), 10.83 s (1H, $CONHC_6H_4$), 11.87 s (1H, SO_2NHCO). Found, %: C 47.39, 47.17; H 3.04, 3.15; N 6.04, 6.21; S 6.92, 7.11. $C_{18}H_{14}Cl_2N_2O_6S$. Calculated, %: C 47.28; H 3.09; N 6.13; S 7.01.

5-Phenylpyrazole-3-carboxylic acid *N*-(4-acetylaminosulfonylphenyl)amide (VI). To a suspension of 0.005 mol of compound **II** in 35 mL of glacial acetic acid was added 0.006 mol of hydrazine hydrate (20% excess). The reaction mixture was refluxed for 2 h. After cooling, the precipitate formed was filtered off and recrystallized from ethanol. Yield 1.25 g (65%), mp 283–285°C. IR spectrum, ν, cm^{-1}: 3344, 3190, 3128 (NH), 1724, 1664 (CON), 1376, 1160 (SO_2). ^1H NMR spectrum, δ, ppm: 1.91 s (3H, CH_3CO), 7.19 s (1H, CH-4), 7.34–8.03 m (9H, CH_{Ar}), 10.44 s (1H, $CONHC_6H_4$), 11.80 s (1H, SO_2NHCO), 13.69 s (1H, NH-1). Found, %: C 56.09, 56.38; H 4.15, 4.26; N 14.47, 14.66; S 8.43, 8.26. $C_{18}H_{16}N_4O_4S$. Calculated, %: C 56.24; H 4.20; N 14.57; S 8.34.

REFERENCES

1. Maslivets, A.N., Tarasova, O.P., and Andreichikov, Yu.S., *Zh. Org. Khim.*, 1992, vol. 28, no. 6, p. 1287.
2. Andreichikov, Yu.S., Kozlov, A.P., and Kurdina, L.N., *Zh. Org. Khim.*, 1984, vol. 20, no. 4, p. 826.
3. Andreichikov, Yu.S., Milyutin, A.V., Krylova, I.V., Saraeva, R.F., Dormidontova, E.V., Drovosekova, M.P., Nazmetdinov, F.Ya., and Kolla, V.E., *Pharm. Chem. J.*, 1990, vol. 24, no. 7, p. 33.
4. Andreichikov, Yu.S., Nalimova, Yu.A., Tandryakova, S.P., and Vilenchik, Ya.M., *Zh. Org. Khim.*, 1978, vol. 14, no. 1, p. 160.
5. Kozlov, A.P., Sazhnev, S.S., Kozlova, G.A., and Andreichikov, Yu.S., *Zh. Org. Khim.*, 1996, vol. 32, no. 10, p. 1573.
6. Kozlov, A.P., Ryabova, V.V., and Varkentin, L.I., Book of Abstracts, *Conference Dedicated to A. Butlerov "Chemistry of Unsaturated Compounds,"* Kazan, 1986, p. 120.
7. Kozlov, A.P., Varkentin, L.I., and Andreichikov, Yu.S., *Zh. Org. Khim.*, 1984, vol. 20, no. 10, p. 2198.
8. Kozlov, A.P., Varkentin, L.I., and Andreichikov, Yu.S., *Zh. Org. Khim.*, 1989, vol. 25, no. 9, p. 1991.
9. Andreichikov, Yu.S., Gein V.L., and Anikina I.N., *Zh. Org. Khim.*, 1986, vol. 22, no. 8, p. 1749.