ISSN 1070-4280, Russian Journal of Organic Chemistry, 2008, Vol. 44, No. 4, pp. 621–623. © Pleiades Publishing, Ltd., 2008.
Original Russian Text © S.I. Yakimovich, I.V. Zerova, V.V. Pakal'nis, 2008, published in Zhurnal Organicheskoi Khimii, 2008, Vol. 44, No. 4, pp. 625–627.

SHORT COMMUNICATIONS

Reactions of 3-Ethoxymethylidenepentane-2,4-dione and Ethyl 2-Ethoxymethylidene-3-oxobutanoate with Benzohydrazide

S. I. Yakimovich, I. V. Zerova, and V. V. Pakal'nis

St. Petersburg State Institute of Technology, Moskovskii pr. 26, St. Petersburg, 190013 Russia
e-mail: viktoriapakalnis@mail.ru

Received November 7, 2007

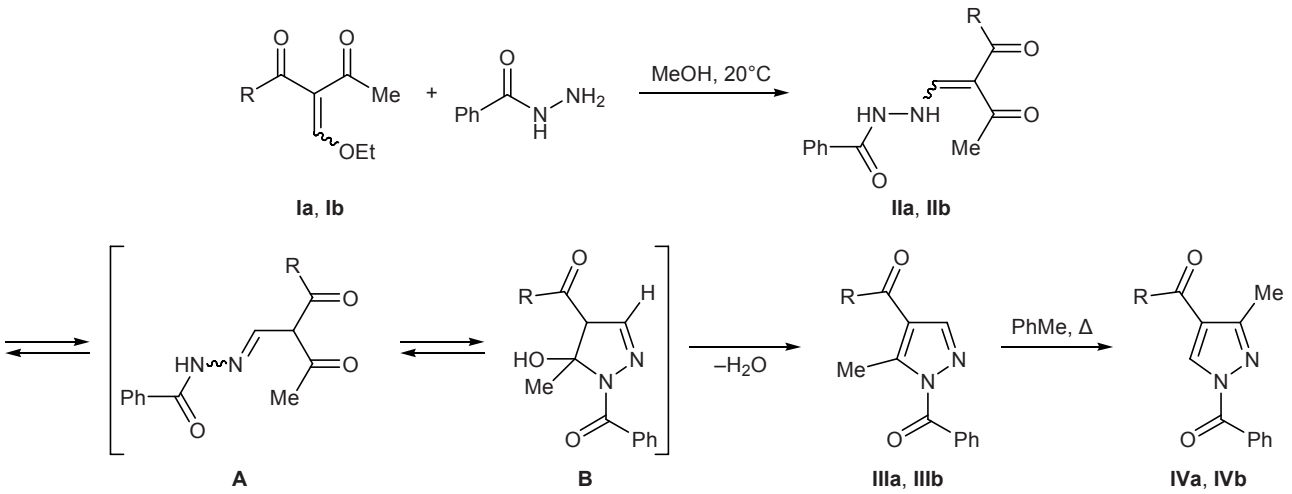
DOI: 10.1134/S1070428008040271

It is known that alkoxymethylidene derivatives of 1,3-dicarbonyl compounds react with acylhydrazines at elevated temperature to give the corresponding 3,4-disubstituted *N*-acylpyrazoles [1, 2]. Using the reaction of 3-ethoxymethylidenepentane-2,4-dione (**Ia**) with benzohydrazide as an example, we have demonstrated that the primary condensation product, conjugated enehydrazine **IIa**, can be isolated and characterized when the reaction is performed in methanol at room temperature in the absence of a catalyst. Enehydrazine **IIa** in methanol is gradually converted into 4,5-disubstituted *N*-benzoylpyrazole **IIIa** which can be isolated by careful removal of the solvent under reduced pressure. Most probably, compound **IIIa** is formed through intermediate hydrazone **A** (it cannot be detected) and 5-hydroxy-4,5-dihydro-1*H*-pyrazole structure **B** [3].

N-Benzoylpyrazole **IIIa** in boiling toluene undergoes fairly fast and irreversible transformation into 4-acetyl-1-benzoyl-3-methyl-1*H*-pyrazole (**IVa**). The same process also occurs at room temperature but at a very low rate. Presumably, the driving force of this isomerization is considerably weaker steric interactions between the substituents in the pyrazole ring of **IVa** as compared to **IIIa**. Pyrazole **IVa** was also formed when enehydrazine **IIa** was heated in boiling toluene.

Analogous results were obtained in the reaction of ethyl 2-ethoxymethylidene-3-oxobutanoate (**Ib**) with benzohydrazide. Enehydrazine **IIb** in solution exists as a mixture of *Z* and and *E* isomers; on keeping in methanol, compound **IIb** is completely converted into pyrazole **IIIb**. The reaction is chemoselective: the ester group is not involved in the cyclization. Heating of pyrazole **IIIb** in boiling toluene gives 3,4-disubstituted *N*-benzoylpyrazole **IVb**.

Thus reactions of alkoxymethylidene derivatives of 1,3-dicarbonyl compounds with acylhydrazines can be used to synthesize not only previously known con-



Ia, **Ib** **IIa**, **IIb** **A** **B** **IIIa**, **IIIb** **IVa**, **IVb**

R = Me (**a**), EtO (**b**).

jugated enehydrazines and 3,4-disubstituted *N*-acylpyrazoles but also isomeric 4,5-disubstituted *N*-acylpyrazoles.

Initial 3-ethoxymethylidenepentane-2,4-dione (**Ia**) and ethyl 2-ethoxymethylidene-3-oxobutanoate (**Ib**) were synthesized according to the procedures reported in [4, 5].

***N′*-(2-Acetyl-3-oxobut-1-en-1-yl)benzohydrazide (IIa).** A solution of 0.340 g (2.5 mmol) of benzohydrazide in 5 ml of anhydrous methanol was added dropwise under stirring to a solution of 0.390 g (2.5 mmol) of compound **Ia** in 4 ml of anhydrous methanol on cooling to 3–5°C. The precipitate was filtered off and washed with cold anhydrous methanol. Yield 0.603 g (98%), mp 169–170°C. ^{1}H NMR spectrum (DMSO-d_6), δ, ppm: 2.23 s (3H, CH_3), 2.37 s (3H, CH_3), 7.54 t (2H, *m*-H, *J* = 7.3 Hz), 7.62 t (1H, *p*-H, *J* = 7.3 Hz), 7.90 d (2H, *o*-H, *J* = 7.3 Hz), 8.17 d (1H, HC=C, *J* = 10.2 Hz), 11.69 br.s (1H, NH), 12.28 br.d (1H, NH, *J* = 10.9 Hz). Found, %: C 63.35; H 5.68; N 11.30. $C_{13}H_{14}N_2O_3$. Calculated, %: C 63.41; H 5.69; N 11.38.

Ethyl 2-acetyl-3-(2-benzoylhydrazino)prop-2-enoate (IIb) was synthesized in a similar way from 0.558 g (3 mmol) of compound **IIb** and 0.408 g (3 mmol) of benzohydrazide. Yield 0.695 g (84%), mp 109–110°C. ^{1}H NMR spectrum, δ, ppm: in $CDCl_3$: *E* isomer (82%): 1.28 t (3H, $CH_2C\mathbf{H}_3$, *J* = 7.3 Hz), 2.46 s (3H, $COCH_3$), 4.17 q (2H, OCH_2, *J* = 7.3 Hz), 7.45–7.89 m (5H, H_{arom}), 8.12 d (1H, HC=C, *J* = 10.9 Hz), 9.39 br.s (1H, NH), 12.02 d (1H, NH, *J* = 10.9 Hz); *Z* isomer (18%): 1.38 t (3H, $CH_2C\mathbf{H}_3$, *J* = 7.3 Hz), 2.43 s (3H, $COCH_3$), 4.31 q (2H, OCH_2, *J* = 7.3 Hz), 7.45–7.93 m (5H, H_{arom}), 8.53 d (1H, HC=C, *J* = 12.4 Hz), 10.83 br.s (1H, NH), 11.12 d (1H, NH, *J* = 12.4 Hz); in DMSO-d_6: *E* isomer (94%): 1.24 t (3H, $CH_2C\mathbf{H}_3$, *J* = 7.3 Hz), 2.40 s (3H, $COCH_3$), 4.13 q (2H, OCH_2, *J* = 7.3 Hz), 7.51–7.90 m (5H, H_{arom}), 8.16 d (1H, HC=C, *J* = 10.9 Hz), 11.77 br.s (1H, NH), 12.42 d (1H, NH, *J* = 10.9 Hz); *Z* isomer (6%): 1.29 t (3H, $CH_2C\mathbf{H}_3$, *J* = 7.3 Hz), 2.34 s (3H, $COCH_3$), 4.24 q (2H, OCH_2, *J* = 7.3 Hz), 7.45–7.90 m (5H, H_{arom}), 8.05 d (1H, HC=C, *J* = 12.4 Hz), 11.77 br.s (1H, NH), 10.50 d (1H, NH, *J* = 12.4 Hz). Found, %: C 60.80; H 5.69; N 10.11. $C_{14}H_{16}N_2O_4$. Calculated, %: C 60.87; H 5.80; N 10.14.

4-Acetyl-1-benzoyl-5-methyl-1*H*-pyrazole (IIIa). A mixture of 0.369 g (1.5 mmol) of hydrazide **IIa** and 6 ml of anhydrous methanol was kept at room temperature until complete dissolution. The solvent was removed under reduced pressure, and the precipitate was filtered off and washed with cold methanol. Yield 0.267 g (78%), mp 85–86°C. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 2.53 s (3H, $COCH_3$), 2.98 s (3H, 5-CH_3), 7.52 t (2H, *m*-H, *J* = 7.3 Hz), 7.65 t (1H, *p*-H, *J* = 7.3 Hz), 7.95 d (2H, *o*-H, *J* = 7.3 Hz), 7.99 s (1H, 3-H). ^{13}C NMR spectrum ($CDCl_3$), δ_C, ppm: 13.48 (5-CH_3); 29.88 ($CO\mathbf{C}H_3$); 122.98 (C^4); 128.58, 131.82, 132.20, 133.91 (C_{arom}); 143.22 (C^5); 148.59 (C^3); 169.07 (Ph**C**O); 194.03 ($CH_3\mathbf{C}O$). Found, %: C 68.36; H 5.21; N 12.17. $C_{13}H_{12}N_2O_2$. Calculated, %: C 68.42; H 5.26; N 12.28.

Ethyl 1-benzoyl-5-methyl-1*H*-pyrazole-4-carboxylate (IIIb) was synthesized in a similar way from 0.414 g (1.5 mol) of compound **IIb**. Yield 0.317 g (82%), mp 78–79°C. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 1.40 t (3H, $CH_2C\mathbf{H}_3$, *J* = 7.3 Hz), 2.97 s (3H, 5-CH_3), 4.37 q (2H, OCH_2, *J* = 7.3 Hz), 7.51 t (2H, *m*-H, *J* = 7.3 Hz), 7.64 t (1H, *p*-H, *J* = 7.3 Hz), 7.95 d (2H, *o*-H, *J* = 7.3 Hz), 8.01 s (1H, 3-H). ^{13}C NMR spectrum ($CDCl_3$), δ_C, ppm: 13.41 (5-CH_3); 14.22 ($CH_2\mathbf{C}H_3$); 61.05 (OCH_2); 116.23 (C^4); 128.62, 131.02, 132.17, 133.80 (C_{arom}); 142.17 (C^5); 148.89 (C^3); 163.71 (4-CO); 164.97 (Ph**C**O). Found, %: C 65.06; H 5.40; N 10.79. $C_{14}H_{14}N_2O_3$. Calculated, %: C 65.12; H 5.43; N 10.85.

4-Acetyl-1-benzoyl-3-methyl-1*H*-pyrazole (IVa). A solution of 0.342 g (1.5 mmol) of pyrazole **IIIa** in 8 ml of anhydrous toluene was heated for 8 h under reflux. The solvent was distilled off under reduced pressure, and the residue was recrystallized from petroleum ether. Yield 0.291 g (85%), mp 110–111°C. ^{1}H NMR spectrum ($CDCl_3$), δ_C, ppm: 2.54 s (3H, CH_3), 2.55 s (3H, CH_3), 7.54 t (2H, *m*-H, *J* = 7.3 Hz), 7.66 t (1H, *p*-H, *J* = 7.3 Hz), 8.17 d (2H, *o*-H, *J* = 7.3 Hz), 8.84 s (1H, 5-H). ^{13}C NMR spectrum ($CDCl_3$), δ_C, ppm: 14.85 (3-CH_3); 28.95 ($CO\mathbf{C}H_3$); 123.73 (C^4); 128.67, 130.94, 132.21, 134.03 (C_{arom}); 135.19 (C^5); 154.79 (C^3); 166.38 (Ph**C**O); 193.37 ($CH_3\mathbf{C}O$). Found, %: C 68.40; H 5.26; N 12.23. $C_{13}H_{12}N_2O_2$. Calculated, %: C 68.42; H 5.26; N 12.28.

Ethyl 1-benzoyl-3-methyl-1*H*-pyrazole-4-carboxylate (IVb) was synthesized in a similar way from 0.387 g (1.5 mmol) of pyrazole **IIIb**; the product was recrystallized from hexane. Yield 0.310 g (80%), mp 36–37°C. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 1.39 t (3H, $CH_2C\mathbf{H}_3$, *J* = 7.3 Hz), 2.56 s (3H, 3-CH_3), 4.35 q (2H, OCH_2, *J* = 7.3 Hz), 7.53 t (2H, *m*-H, *J* = 7.3 Hz), 7.65 t (1H, *p*-H, *J* = 7.3 Hz), 8.16 d (2H, *o*-H,

J = 7.3 Hz). 8.82 s (1H, 5-H). ^{13}C NMR spectrum ($CDCl_3$), δ_C, ppm: 14.27 ($CH_2\mathbf{C}H_3$); 14.68 (3-CH_3); 61.00 (OCH_2); 116.65 (C^4); 128.61, 131.06, 132.14, 133.85 (C_{arom}); 135.51 (C^5); 154.93 (C^3); 163.23 (4-CO); 166.07 (Ph**C**O). Found, %: C 65.08; H 5.38; N 10.79. $C_{14}H_{14}N_2O_3$. Calculated, %: C 65.12; H 5.43; N 10.85.

The ^1H and ^{13}C NMR spectra were measured on a Bruker DX-300 spectrometer at 300 and 75 MHz, respectively. The *E*/*Z*-isomer ratios were determined from the intensity ratio of signals corresponding to particular isomers with an accuracy of ±2%.

REFERENCES

1. Mitkidou, S., Stephanidou-Stephanatou, J., and Stephopoulou, H., *J. Heterocycl. Chem*., 1993, vol. 30, p. 441.
2. Dyachenko, V.D. and Tkachev, R.P., *Russ. J. Org. Chem*., 2006, vol. 42, p. 149.
3. Emelina, E.E., Iz"yurov, A.L., Ermakov, N.V., and Ershov, B.A., *Russ. J. Org. Chem*., 1996, vol. 32, p. 430.
4. Dorofeenko, G.N., Mezheritskii, V.V., Ryabukhin, Yu.I., and Olekhnovich, E.P., *Khim. Geterotsikl. Soedin*., 1973, p. 1314.
5. Dorofeenko, G.N., Olekhnovich, E.P., and Laukhina, L.I., *Khim. Geterotsikl. Soedin*., 1971, p. 435.