Russian Journal of Organic Chemistry, Vol. 40, No. 11, 2004, pp. 1644–1646. Translated from Zhurnal Organicheskoi Khimii, Vol. 40, No. 11, 2004, pp. 1692–1694.

Derivatives of α,β-Dehydro Amino acids: I. Synthesis of 1-Aryl-2,4-disubstituted Imidazol-5-ones from Arylamides of *N*-Benzoyl-α,β-dehydrophenylalanine and Trimethylchlorosilane

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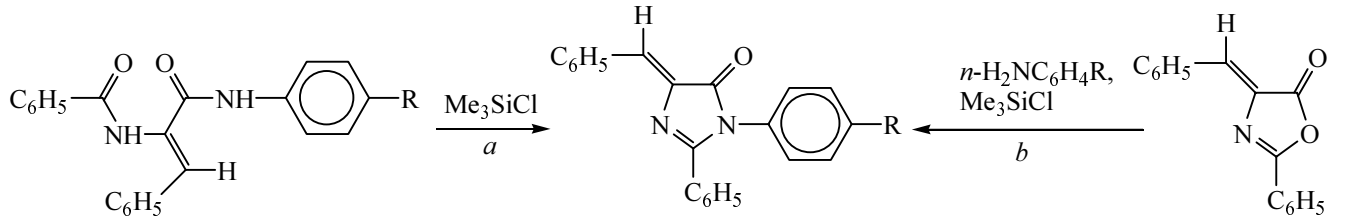
Received September 10, 2003

Abstract—A preparation method was developed for 1-aryl-2,4-disubstituted imidazol-5-ones from N-benzoyl-α,β-dehydrophenylalanine anilides or 2-phenyl-4-benzylidene-5-oxazolone and arylamine in the presence of trimethylchlorosilane.

Dehydration of amides of N-substituted α,β-dehydro amino acids can result in 2-imidazolin-5-ones formation [1], and the trimethylchlorosilane can be used as dehydrating agent [2–5].

This paper concerns the study of a reaction between N-substituted α,β-dehydrophenylalanine arylamides (**I–V**) and trimethylchlorosilane.

The reaction of arylamides **I–V** with Me_3SiCl was carried out by heating in DMF. The reaction gave rise to the corresponding 1-aryl-2-phenyl-4-benzylideneoxazol-5-ones (**VI–X**). The effect of temperature and of heating time on the yield of the target product was studied by an example of the synthesis of 1-(4-carboxyphenyl)-2-phenyl-4-benzylideneimidazol-5-one (**VII**) (see table). As show the



I–V **VI–X** **XI**

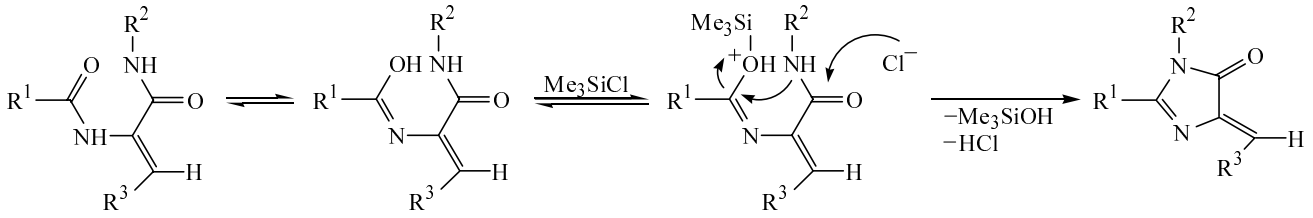
data in the table the best result at heating on the water bath (about 90°C) was obtained in 3 h (70%). The yield of compound **VII** obtained at boiling the reaction mixture (about 125°C) for 1 h was 84%.

Boiling of arylamide **II** in DMF for 1 h without Me_3SiCl did not affect its structure.

It should be mentioned that reaction of oxazolone **XI** with arylamines in DMF afforded arylamides **I** and **II**. This result suggests that the synthesis of 2-phenylimidazol-5-ones may be carried out from oxazolone **XI** and arylamine in the presence of Me_3SiCl (*b*). Method *b* actually afforded the target imidazol-5-ones **VI–X** but in relatively low yields (see table).

Imidazol-5-one (**VI**) was obtained in a 60% yield at boiling for 4 h aniline with oxazolone **XI** in acetic acid in the presence of sodium acetate [6]. The similar process in the presence of Me_3SiCl afforded compound **VI** in a 64% yield within 1 h.

Scheme.



The formation of imidazol-5-one from arylamides of N-substituted α,β-dehydro amino acids in the presence of Me_3SiCl can be rationalized by the scheme.

The IR spectra of compounds **VI–X** contain absorption bands at 1700–1710, 1645–1655, and 1615–1630 cm^{-1} corresponding to C=O, C=C, and C=N bonds respectively.

In the ^1H NMR spectra of compounds **VI–X** the singlet from the exocyclic CH=C group appeared at 7.20–7.25 ppm evidencing the *Z*-configuration of these products. In the UV spectra of compounds **VI–X** absorption was observed at 230–240, 290–310, and 377–400 nm.

EXPERIMENTAL

IR spectra were recorded on spectrophotometer Specord M-40. NMR spectra were registered on spectrimeter Varian Mercury 300. UV spectra were measured on spectrophotometer Specord UV-VIS. The purity of compounds obtained was checked by TLC on Silufol UV-254 plates, eluents toluene–hexane, 1:1 (**A**) and propanol–water, 7:3 (**B**); the spots were visualized by UV irradiation and iodine vapour.

N-(N-Benzoyl-α,β-dehydrophenylalanine)-*p*-aminobenzoic acid (II). To a solution of 1 g (0.004 mol) of 2-phenyl-4-benzylidene-5-oxazolone (**XI**) in 10 ml of DMF was added 0.55 g (0.004 mol) of *p*-aminobenzoic acid, and the mixture was boiled for 1 h. To the reaction mixture 100 ml of water was added, the separated substance was filtered off, washed with the hot ethyl acetate (25 ml), and recrystallized from ethanol. Yield 0.55 g (35.7%). mp 240–242°C. IR spectrum, ν, cm^{-1}: 1583, 1645, 1666, 1705, 3208, 3240. UV spectrum, λ, nm (log ε): 294 (3.39). ^1H NMR spectrum, δ, ppm: 7.09 s (1H, C=CH), 7.29 t (1H, C_6H_5, *J* 7.2 Hz), 7.36 t (2H, C_6H_5, *J* 7.4 Hz), 7.47 t (2H, C_6H_5, *J* 7.4 Hz), 7.54 t (1H, $_6H_5$, *J* 7.0 Hz), 7.64 d (2H, C_6H_5, *J* 7.9 Hz), 7.86 and 7.90 m (4H, *p*-C_6H_4, *J* 8.9 Hz), 8.05 d (2H, C_6H_5, *J* 7.8 Hz), 10.01 s

Yields of 1-aryl-2,4-disubstituted imidazol-5-ones **VI-X** depending on the method and conditions of synthesis

Compd. no.	Reaction temperature, °C	Heating time, min	Method of synthesis	Yield, %	mp, °C	R_f
VI	125	60	*a*	80	180–181 [6]	0.58 (**A**)
VI	125	60	*b*	65	181–183	0.58 (**A**)
VII	125	30	*a*	45	283–286	0.82 (**B**)
VII	125	60	*a*	84	283–286	0.82 (**B**)
VII	90	180	*a*	68	283–286	0.82 (**B**)
VII	90	10	*b*	19	282–285	0.82 (**B**)
VII	90	120	*b*	37	282–285	0.82 (**B**)
VII	90	180	*b*	46	282–285	0.82 (**B**)
VIII	125	60	*a*	79	170–173	0.45 (**A**)
IX	125	60	*a*	73	198–200	0.47 (**A**)
IX	125	60	*b*	60	197–199	0.47 (**A**)
X	125	60	*a*	84	191–193	0.43 (**A**)
X	125	60	*b*	71	190–193	0.43 (**A**)

(1H, NH), 10.38 s (1H, NH), 12.2 br.s (1H, COOH). Calculated, %: C 71.52; H 4.69; N 7.25. $C_{23}H_{18}N_2O_4$. Found, %: C 71.20; H 5.00; N 7.09.

Likewise were synthesized compounds **I, III–V**.

1-Aryl-2-phenyl-4-benzylideneimidazol-5-ones (VI–X). (a) To a solution of 0.026 mol of *N*-benzoyl-α,β-dehydrophenylalanine arylamide (**I–V**) in 10 ml of DMF was added 1.1 ml of Me_3SiCl, and the mixture was heated as indicated in the table. Then the reaction mixture was cooled to room temperature, 100 ml of water was added, and the separated precipitate was filtered off. The recrystallization from ethanol furnished 2-phenyl-4-benzylideneimidazol-5-ones (**VI–X**).

(b) To a solution of 0.007 mol of 2-phenyl-4-benzylidene-5-oxazolone (**XI**) and 0.007 mol of arylamine in 10 ml of DMF was added 1.1 ml of Me_3SiCl and the mixture was heated as indicated in the table. Then the reaction mixture was cooled to room temperature. The reaction mixture was worked up as in the procedure (a).

^{1}H NMR spectra (DMSO-d_6–CCl_4, 1:3), δ, ppm: compound **VI**, 7.21 s (1H, CH=C), 7.29 d.d (2H, J_2 8.0, J_2 1.8 Hz), 7.34 t (2H, *J* 7.9 Hz), 7.38–7.48 m (7H), 7.55 d (2H, *J* 8.1 Hz), 8.30 d (2H, *J* 7.6 Hz); compound **VII**, 7.23 s (1H, CH=C), 7.26 d (2H, *J* 8.4 Hz), 7.33–7.50 m (6H), 7.54 d.d (2H, J_1 7.1, J_2 1.6 Hz), 8.03 d (2H, *J* 8.5 Hz), 8.30 d.d (2H, J_1 7.7, J_2 1.8 Hz), 12.75 br.s (1H, COOH); compound **VIII**, 1.40 t (3H, CH_3, *J* 7.1 Hz), 4.36 q (2H, OCH_2, *J* 7.1 Hz), 7.23 s (1H, CH=C), 7.28 d (2H, *J* 8.2 Hz), 7.33–7.50 m (6H), 7.54 m (2H), 8.05 d (2H, *J* 8.5 Hz), 8.30 d.d (2H, J_1 7.9, J_2 1.9 Hz); compound **IX**, 2.43 s (3H, CH_3), 7.05 d (2H, *J* 8.3 Hz), 7.18 s (1H, CH=C), 7.23 d (2H, *J* 8.3 Hz), 7.30–7.48 m (6H), 7.56 m (2H), 8.29 d.d (2H, J_1 7.9, J_2 1.8); compound **X**, 3.48 s (3H, OCH_3), 6.95 d (2H, *J* 8.8 Hz), 7.18 s (1H, CH=C), 7.09 d (2H, *J* 8.8 Hz), 7.31–7.49 m (6H), 7.58 d (DH, *J* 7.7 Hz), 8.29 d (2H, *J* 7.6 Hz).

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