

SHORT COMMUNICATIONS

Derivatives of α,β -Dehydro Amino Acids: II. New Synthesis of 2,4-Disubstituted 1-Aminoimidazol-5-ones from *N*-Substituted α,β -Unsaturated α -Amino Acid Hydrazides

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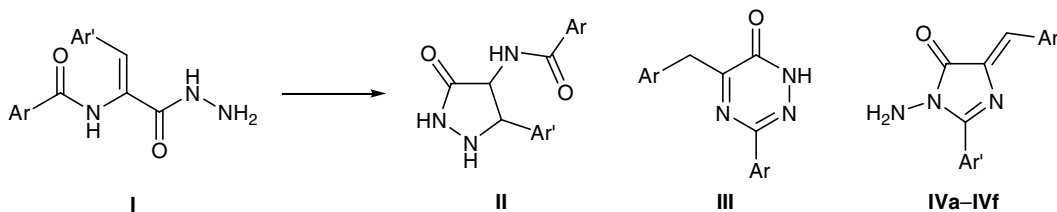
The direction of dehydration of *N*-substituted α,β -unsaturated amino acid hydrazides **I** is determined by reaction conditions. Compounds **I** on heating are converted into 4-acylaminopyrazolidin-3-ones **II** [1], while in the presence of alkali the corresponding 3,5-disubstituted 1,2,4-triazin-6(1*H*)-ones **III** are formed [2]. 2-Benzoylamino-3-phenylprop-2-enohydrazide (**Ia**) in boiling toluene (with simultaneous removal of water as azeotrope) gives rise to a mixture of compounds **II**, **III** (Ar = Ar' = Ph), and 1-amino-4-benzylidene-2-phenyl-4,5-dihydro-1*H*-imidazol-5-one (**IVa**), the yield of the latter being 11% [3].

We previously found [4] that *N*-substituted α,β -unsaturated amino acid *N*-arylamides undergo dehydration by the action of a silylating agent to give the corresponding imidazol-5-ones. In the present communication we report the results of our study on reactions of hydrazides **Ia–If** with hexamethyldisilazane (HMDS). The reactions were carried out at a reactant ratio of 1:3 in boiling DMF (reaction time 15–30 min), and the products were 1-amino-2-aryl-4-arylmethylidene-

dene-4,5-dihydro-1*H*-imidazol-5-ones **IVa–IVf** which were isolated in good yields. Increase of the reaction time from 15 to 30 min in the synthesis of compound **IVa** increases the yield of the latter to quantitative. We can conclude that the reaction of hydrazides **I** with HMDS in DMF is not accompanied by side formation of cyclization products like **II** or **III**. In the ¹H NMR spectra of **IVa–IVf**, the exocyclic vinyl proton appeared at δ 6.93–7.17 ppm, indicating *Z* configuration of these compounds.

Initial *N*-substituted α,β -unsaturated amino acid hydrazides were synthesized according to the procedure described in [2].

1-Amino-2-aryl-4-arylmethylidene-4,5-dihydro-1*H*-imidazol-5-ones IVa–IVf (general procedure). Hydrazide **Ia–If**, 0.01 mol, was dissolved in 10 ml of DMF, 1 ml (0.03 mol) of hexamethyldisilazane was added, and the mixture was heated under reflux over a period indicated below. During that time, the mixture turned brown. It was cooled to room temperature and diluted with 70 ml of water, and the yellow precipitate was filtered off and recrystallized from ethanol.



IV, Ar = Ar' = Ph (**a**); Ar = Ph, Ar' = 4-ClC₆H₄ (**b**); Ar = Ph, Ar' = 4-EtOC₆H₄ (**c**); Ar = 2,4-Cl₂C₆H₃, Ar' = Ph (**d**); Ar = 4-BuOC₆H₄, Ar' = 4-MeOC₆H₄ (**e**); Ar = 4-PrOC₆H₄, Ar' = 3,4-CH₂O₂C₆H₄ (**f**).

1-Amino-4-benzylidene-2-phenyl-4,5-dihydro-1H-imidazol-5-one (IVa). Yield 74% (reaction time 15 min), 99% (30 min), mp 206–208°C, R_f 0.79. IR spectrum, ν , cm^{-1} : 1630, 1700, 3275, 3338. ^1H NMR spectrum, δ , ppm: 5.10 s (2H, NH_2); 7.09 s (1H, $\text{CH}=\text{C}$); 7.33–7.57 m, 8.26 m, and 8.45 m (10H, H_{arom}). Found, %: C 72.98; H 4.97; N 15.19. $\text{C}_{16}\text{H}_{13}\text{N}_3\text{O}$. Calculated, %: C 73.21; H 4.73; N 15.70.

1-Amino-4-(4-chlorobenzylidene)-2-phenyl-4,5-dihydro-1H-imidazol-5-one (IVb). Reaction time 15 min. Yield 86%, mp 257–259°C, R_f 0.80. IR spectrum, ν , cm^{-1} : 1625, 1702, 3255, 3294, 3325. ^1H NMR spectrum, δ , ppm: 5.12 s (2H, NH_2); 7.07 s (1H, $\text{CH}=\text{C}$); 7.41 m, 7.48–7.58 m, 8.27 m, and 8.44 m (9H, H_{arom}). Found, %: C 64.54; H 4.06; Cl 11.91; N 14.11. $\text{C}_{16}\text{H}_{12}\text{ClN}_3\text{O}$. Calculated, %: C 64.30; H 4.00; Cl 12.05; N 14.20.

1-Amino-4-(4-ethoxybenzylidene)-2-phenyl-4,5-dihydro-1H-imidazol-5-one (IVc). Reaction time 15 min. Yield 91%, mp 227–230°C, R_f 0.83. IR spectrum, ν , cm^{-1} : 1625, 1696, 3225, 3290, 3330. ^1H NMR spectrum, δ , ppm: 1.45 t (3H, CH_3 , $J = 7.0$ Hz); 4.11 q (2H, CH_2O , $J = 7.0$ Hz); 5.04 s (2H, NH_2); 7.04 s (1H, $\text{CH}=\text{C}$); 6.92 m, 7.45–7.52 m, 8.22 m, and 8.43 m (9H, H_{arom}). Found, %: C 70.34; H 5.57; N 13.67. $\text{C}_{18}\text{H}_{17}\text{N}_3\text{O}_2$. Calculated, %: C 70.02; H 5.19; N 13.44.

1-Amino-4-benzylidene-2-(2,4-dichlorophenyl)-4,5-dihydro-1H-imidazol-5-one (IVd). Reaction time 30 min. Yield 70%, mp 203–206°C, R_f 0.77. IR spectrum, ν , cm^{-1} : 1630, 1700, 3231, 3300, 3318. ^1H NMR spectrum, δ , ppm: 4.86 s (2H, NH_2); 7.17 s (1H, $\text{CH}=\text{C}$); 7.33–7.43 m, 7.48 m, 7.58 m, 7.69 m, and 8.20 m (8H, H_{arom}). Found, %: C 57.85; H 3.34; Cl 21.35; N 12.65. $\text{C}_{16}\text{H}_{11}\text{Cl}_2\text{N}_3\text{O}$. Calculated, %: C 57.49; H 3.21; Cl 21.50; N 12.78.

1-Amino-2-(4-butoxyphenyl)-4-(4-methoxybenzylidene)-4,5-dihydro-1H-imidazol-5-one (IVe). Reaction time 30 min. Yield 64%, mp 150–152°C,

R_f 0.83. IR spectrum, ν , cm^{-1} : 1625, 1700, 3219, 3295, 3331. ^1H NMR spectrum, δ , ppm: 1.02 t (3H, CH_3 , $J = 7.03$ Hz); 1.54 t.q (2H, CH_2 , $J = 7.5, 7.3$ Hz); 1.80 t.t (2H, CH_2 , $J = 7.5, 6.4$ Hz); 3.86 s (3H, OCH_3); 4.06 t (2H, OCH_2 , $J = 6.4$ Hz); 5.04 s (2H, NH_2); 6.97 s (1H, $\text{CH}=\text{C}$); 6.94 m, 6.97 m, 8.22 m, and 8.45 m (8H, H_{arom}). Found, %: C 69.02; H 6.34; N 11.50. $\text{C}_{21}\text{H}_{23}\text{N}_3\text{O}_3$. Calculated, %: C 68.91; H 6.11; N 11.70.

1-Amino-4-(3,4-methylenedioxybenzylidene)-2-(4-propoxyphenyl)-4,5-dihydro-1H-imidazol-5-one (IVf). Reaction time 30 min. Yield 80%, mp 204–206°C, R_f 0.84. IR spectrum, ν , cm^{-1} : 1618, 1710, 3230, 3280, 3330. ^1H NMR spectrum, δ , ppm: 1.08 t (3H, CH_3 , $J = 7.04$ Hz); 1.85 q.t (2H, CH_2 , $J = 7.4, 6.5$ Hz); 4.02 t (2H, OCH_2 , $J = 6.5$ Hz); 5.05 s (2H, NH_2); 6.06 s (2H, OCH_2O); 6.93 s (1H, $\text{CH}=\text{C}$); 6.86 m, 6.98 m, 7.51 m, 8.14 m, and 8.45 m (7H, H_{arom}). Found, %: C 65.74; H 5.24; N 11.50. $\text{C}_{20}\text{H}_{19}\text{N}_3\text{O}_4$. Calculated, %: C 65.56; H 5.40; N 11.32.

The IR spectra were recorded on a Specord M-80 spectrometer. The ^1H NMR spectra were measured on a Varian Mercury 300 instrument from solutions in $\text{DMSO}-d_6$. The purity of the products was checked by TLC on Silufol UV-254 plates using toluene–hexane–ethanol (1:1:1) as eluent; spots were visualized under UV light or by treatment with iodine vapor.

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