Chemistry of Heterocyclic Compounds, Vol. 40, No. 9, 2004

SYNTHESIS OF AMINO ACID ESTERS: DERIVATIVES OF 1,2,3,4-TETRAHYDROISOQUINOLINE

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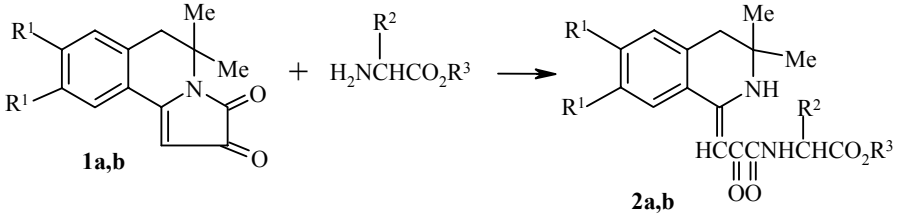
Keywords: amino acids, 2,3-dioxopyrrolo[2,1-*a*]isoquinolines, esters of N-[3-(3,3-dimethyl-1,2,3,4-tetrahydro-1-isoquinolinidene)-2-oxopropanoyl]glycine and -*L*-phenylalanine.

Isoquinoline derivatives that have an amino acid residue within their structure have not been well studied. One of the few examples of such compounds are amidines [1], which exhibit antiarrhythmic and antithrombotic activity. The goal of our studies was synthesis of compounds which would not only combine amino acid and isoquinoline moieties within their molecules but also would contain functional groups making possible further modification of the molecule, such as an ester group.

In continuing the study of reactions of derivatives of pyrrolo[2,1-*a*]isoquinoline with N-nucleophiles [2, 3], we observed that compounds **1a,b** at a temperature of 20°C readily undergo ring opening when treated with amino acid esters to form enaminoketo amides **2a,b**.



1, **2 a** R^1 = MeO, **b** R^1 = H, **2 a** R^2 = H, R^3 = Et, **b** R^2 = Bn, R^3 = Me

The amides obtained are synthons, including chiral synthons, containing an amino acid residue.

Ethyl Ester of N-[3-(3,3-Dimethyl-1,2,3,4-tetrahydro-1-isoquinolinidene)-2-oxopropanoyl]glycine (2a). Ethyl ester of glycine (1.54 g, 15 mmol) was added to compound **1a** (2.87 g, 10 mmol) in alcohol (20 ml). When the mixture was stirred for 20-30 min (20°C), the red color of the solution disappeared; after 3-4 h at a temperature of 5-10°C, a precipitate formed which was filtered off, dried, and recrystallized from ethanol. Yield 63%; mp 143-145°C. IR spectrum ($CHCl_3$, 0.01 mol/l), ν, cm^{-1}: 1605, 1630, 1690 (C=O); 3080, 3240 (NH). ^{1}H NMR spectrum (100 MHz, $CDCl_3$), δ, ppm: 1.15 (3H, t, CH_3CH_2O); 1.30 (6H, s, $2CH_3$); 2.75 (2H, s, 4-CH_2); 3.83 (3H, s, CH_3O); 3.85 (3H, s, CH_3O); 3.95-4.15 (2H, s, NCH_2 and 2H, q, OCH_2CH_3); 6.45 (1H, s, HC=); 6.60 (1H, s, 5-CH); 7.10 (1H, s, 8-CH); 7.80 (1H, s, NH); 11.50 (1H, s, NH). Found, %: C 61.38; H 6.52; N 7.34. $C_{20}H_{26}N_2O_6$. Calculated, %: C 61.52; H 6.71; N 7.18.

Methyl Ester of N-[3-(3,3-Dimethyl-1,2,3,4-tetrahydro-1-isoquinolinidene)-2-oxopropanoyl]-*L*-phenylalanine (2b) was obtained similarly from compound **1b** (2.27 g, 10 mmol) and methyl ester of *L*-phenylalanine (2.70 g, 15 mmol). Yield 61%; mp 135-137°C. IR spectrum ($CHCl_3$, 0.01 mol/l), ν, cm^{-1}: 1610,

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1630, 1685 (C=O); 3080 and 3240 (NH). ^{1}H NMR spectrum (100 MHz, $CDCl_3$), δ, ppm: 1.27 (6H, s, $2CH_3$); 2.80 (2H, s, 4-CH_2); 3.10 (2H, d, CH_2CH); 3.59 (3H, s, CH_3O); 4.80 (1H, t, $CH_2C\underline{H}$); 6.55 (1H, s, HC=); 7.03-7.90 (9H, m, Ar); 8.07 (1H, s, NH); 11.45 (1H, s, NH). Found, %: C 70.81; H 6.28; N 7.03. $C_{24}H_{26}N_2O_4$. Calculated, %: C 70.91; H 6.45; N 6.89.

REFERENCES

1. B. Ya. Syropyatov, A. A. Gorbunov, V. S. Shklyaev, Yu. V. Shklyaev, and E. S. Boronenkova, *Khim.-Farm. Zh.*, No. 11, 13 (1996).
2. A. G. Mikhailovskii and M. O. Dekaprilevich, *Khim. Geterotsikl. Soedin.*, 1111 (1998).
3. A. G. Mikhailovskii, M. O. Dekaprilevich, and V. S. Shklyaev, in: *Abstracts, Eighteenth Ukrainian Conference on Organic Chemistry* [in Russian], Dnepropetrovsk (1998), p. 265.