Chemistry of Heterocyclic Compounds, Vol. 44, No. 2, 2008

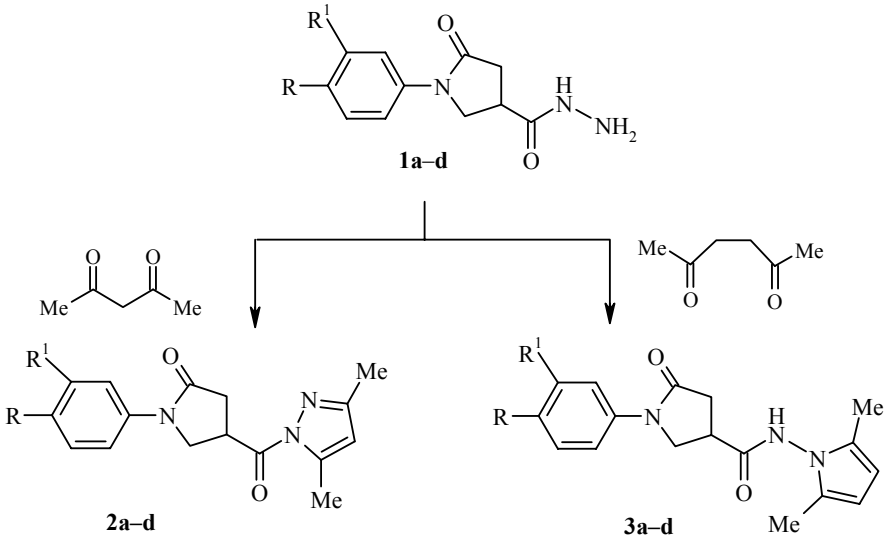
CONDENSATION PRODUCTS OF 1-ARYL-4-HYDRAZINOCARBONYL-2-PYRROLIDINONES WITH DIKETONES

V. Mickevičius and R. Vaickelionienė

The reactions of 1-aryl-4-hydrazinocarbonyl-2-pyrrolidinones with 2,4-pentanedione and 2,5-hexanedione have been studied. It was found that heating the hydrazinocarbonyl compounds with 2,4-pentanedione gave 3,5-dimethylpyrazole compounds and with 2,5-hexanedione gave 1-substituted 2,5-dimethylpyrroles.

Keywords: 1-aryl-4-hydrazinocarbonyl-2-pyrrolidinones, N-(2,5-dimethylpyrrol-1-yl)-1-aryl-5-oxo-3-pyrrolidinecarboxamides, 1-aryl-4-(3,5-dimethyl-1-pyrazolylcarbonyl)-2-pyrrolidinones, 2,5-hexanedione, 2,4-pentanedione, condensation.

The reaction route for carbonyl compounds with hydrazine derivatives and the structure of the products formed frequently depend on the condensation conditions. The formation of cyclic products instead of hydrazones is especially characteristic of the reactions of hydrazines with dicarbonyl compounds [1-3].



1–3 a R = H, R^1 = H; **b** R = Br, R^1 = H; **c** R = H, R^1 = F; **d** R = F, R^1 = H

Kaunas University of Technology, Kaunas LT-50254, Lithuania; e-mail: Vytautas.Mickevicius@ktu.lt.
Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 2, pp. 229-232, February, 2008. Original article submitted July 4, 2007.

 0009-3122/08/4402-0170

In this work we have studied the reactions of the 1-aryl-4-hydrazinocarbonyl-2-pyrrolidinones **1a-d** with 2,4-pentanedione and 2,5-hexanedione. It was found that refluxing in 2-propanol in the presence of a catalytic amount of hydrochloric acid gave good yields of the 1-aryl-4-(3,5-dimethyl-1-pyrazolylcarbonyl)-2-pyrrolidinones **2a-d**. The use of glacial acetic acid as catalyst in this reaction lengthens the ring formation by 3-5 times. The ^{1}H NMR spectra of these compounds (in $(CD_3)_2CO$, DMSO-d_6, or $CDCl_3$) showed characteristic methyl group singlets in the range 2.20-2.55 ppm and methine proton singlets at 6.01-6.31 ppm from the pyrazole ring. The IR spectra of the pyrazolylcarbonylpyrrolidinones **2a-b** show clearly marked absorption bands in the region 1719-1701 cm^{-1} for the carbonyl groups.

Glacial acetic acid was used as catalyst in the condensation of the 4-hydrazinocarbonyl-2-pyrrolidinones **1a-d** with 2,5-hexanedione in 2-propanol. Reaction over 3-4 h gave compounds which spectroscopic analysis showed to have the corresponding N-(2,5-dimethylpyrrol-1-yl)-1-aryl-5-oxo-3-pyrrolidine carboxamide structures **3a-d**. The reaction of the above reagents in the presence of concentrated hydrochloric acid as catalyst led to tarring of the product. The ^{1}H NMR spectra of the substituted (2,5-dimethylpyrrol-1-yl)-5-oxo-3-pyrrolidine carboxamides **3** in DMSO-d_6 showed methyl group proton singlets at 1.99 and 2.00 ppm and signals for the CH groups (5.64 and 5.65 ppm) pointing to the presence of a substituted pyrrole ring. The structure of compounds **3a-d** was also confirmed by the characteristic absorption bands occurring for the NH and carbonyl groups.

EXPERIMENTAL

^{1}H and ^{13}C NMR spectra were obtained on a Varian Unity Inova spectrometer (300 and 75 MHz respectively) using TMS as internal standard. IR spectra were taken on a Perkin Elmer Bx FT-IR instrument using KBr and mass spectra on a Waters ZQ 2000 spectrometer with electrospray type ionization (ESI 20 eV). Monitoring of the reaction course and purity of the products obtained was carried out by TLC on Silicagel 60 F_{254} plates and revealed using UV light (λ =254 and 366 nm).

Preparation of 1-aryl-4-(3,5-dimethyl-1-pyrazolylcarbonyl)-2-pyrrolidinones 2a-d (General Method). A mixture of the corresponding 4-hydrazinocarbonyl-2-pyrrolidinone **1a-d** (1 mmol), 2,4-pentanedione (0.3 g, 3 mmol), 2-propanol (15 ml), and hydrochloric acid (0.5 ml) was refluxed for 4 h, cooled, and water (15 ml) added. The crystals of compounds **2a-d** were filtered off, washed with 2-propanol, and crystallized from the appropriate solvent.

4-(3,5-Dimethyl-1-pyrazolylcarbonyl)-1-phenyl-2-pyrrolidinone (2a). Yield 58%; mp 133-134ºC (hexane). IR spectrum, ν, cm^{-1}: 1719, 1705 (C=O). ^{1}H NMR spectrum ($(CD_3)_2CO$), δ, ppm: 2.26 and 2.55 (6H, s, $(CH_3)_2$); 2.83-3.02 (2H, m, H-3); 3.94-4.31 (2H, m, H-5); 4.34-4.71 (1H, m, H-4); 6.31 (1H, s, C=CH); 7.04-7.82 (5H, m, ArH). Mass spectrum, *m/z* (I_{rel}, %): 284 $[M+H]^+$ (100). Found, %: C 67.66; H 6.24; N 14.99. $C_{16}H_{17}N_3O_2$. Calculated, %: C 67.83; H 6.05; N 14.83.

1-(4-Bromophenyl)-4-(3,5-dimethyl-1-pyrazolylcarbonyl)-2-pyrrolidinone (2b). Yield 66%; mp 147-148ºC (hexane). ^{1}H NMR spectrum ($(CD_3)_2CO$), δ, ppm: 2.21 and 2.49 (6H, 2s, $(CH_3)_2$); 2.82-3.02 (2H, m, H-3); 3.93-4.32 (2H, m, H-5); 4.34-4.71 (1H, m, H-4); 6.22 (1H, s, C=CH); 7.44-7.75 (4H, m, ArH). Found, %: C 52.91; H 4.01; N 11.52. $C_{16}H_{16}BrN_3O_2$. Calculated, %: C 53.05; H 4.25; N 11.60.

1-(3-Fluorophenyl)-4-(3,5-dimethyl-1-pyrazolylcarbonyl)-2-pyrrolidinone (2c). Yield 60%; mp 133-134ºC (2-propanol). IR spectrum, ν, cm^{-1}: 1716, 1703 (C=O). ^{1}H NMR spectrum (DMSO-d_6), δ, ppm: 2.20 and 2.48 (6H, s, $(CH_3)_2$); 2.84-2.96 (2H, m, H-3); 4.05-4.27 (2H, m, H-5); 4.33-4.56 (1H, m, H-4); 6.23 (1H, s, C=CH); 6.95-7.94 (4H, m, ArH). ^{13}C NMR spectrum (DMSO-d_6), δ, ppm: 12.93, 13.40 ($(CH_3)_2$); 34.59 (C-4 and C-3); 49.46 (C-5); 105.52, 105.87 (C'-4); 114.27, 129.63, 129.76, 139.90, 143.25, 151.53 (C_6H_5); 159.80 (C'-5); 163.01 (C'-2); 171.40, 171.84 (C-2 and CO). Found, %: C 63.52; H 5.44; N 13.76. $C_{16}H_{16}FN_3O_2$. Calculated, %: C 63.78; H 5.35; N 13.95.

1-(4-Fluorophenyl)-4-(3,5-dimethyl-1-pyrazolylcarbonyl)-2-pyrrolidinone (2d). Yield 86%; mp 147-148ºC (hexane). IR spectrum, ν, cm^{-1}: 1719, 1701 (C=O). ^1H NMR spectrum ($CDCl_3$), δ, ppm: 2.22 and 2.55 (6H, s, $(CH_3)_2$); 2.92-3.13 (2H, m, H-3); 4.04-4.28 (3H, m, H-5 and H-4); 6.01 (1H, s, C=CH); 6.94-7.71 (4H, m, ArH). Mass spectrum, *m/z* (I_{rel}, %): 302 $[M+H]^+$ (100). Found, %: C 63.61; H 5.28; N 13.83. $C_{16}H_{16}FN_3O_2$. Calculated, %: C 63.78; H 5.35; N 13.95.

Preparation of N-(2,5-Dimethylpyrrol-1-yl-1-aryl-5-oxo-3-pyrrolidinecarboxamides (3a-d) (General Method). A mixture of the corresponding 4-hydrazinocarbonyl-2-pyrrolidinone **1a-d** (1 mmol), 2,5-hexanedione (0.23 g, 2 mmol), 2-propanol (25 ml), and acetic acid (0.5 ml) was refluxed for 3 h and water (25 ml) was added. The crystals of compounds **3a-d** formed on cooling were filtered off, washed with water and 2-propanol and crystallized from a mixture of 2-propanol and DMF.

N-(2,5-Dimethylpyrrol-1-yl)-5-oxo-1-phenyl-3-pyrrolidinecarboxamide (3a). Yield 72%; mp 150-151ºC. IR spectrum, ν, cm^{-1}: 3268 (NH), 1685, 1666 (C=O). ^1H NMR spectrum (DMSO-d_6), δ, ppm: 1.99 (6H, s, $(CH_3)_2$); 2.68-2.98 (2H, m, H-3); 3.40-3.52 (1H, m, H-4); 3.92-4.22 (2H, m, H-5); 5.65 (2H, s, $(CH)_2$); 7.10-7.73 (5H, m, ArH); 10.91 (1H, s, NH). ^{13}C NMR spectrum (DMSO-d_6), δ, ppm: 10.87 $(CH_3)_2$); 33.99 (C-4); 35.59 (C-3); 50.28 (C-5); 103.01 (C'-3 and C'-4); 119.43, 124.08, 126.66, 128.65, 139.01 (C_6H_5, C'-2 and C'-5); 171.50, 171.79 (C-2 and CO). Mass spectrum, *m/z* (I_{rel}, %): 298 $[M+H]^+$ (100). Found, %: C 68.43; H 6.51; N 14.03. $C_{17}H_{19}N_3O_2$. Calculated, %: C 68.67; H 6.44; N 14.13.

N-(2,5-dimethylpyrrol-1-yl)-1-(4-Bromophenyl)-5-oxo-3-pyrrolidinecarboxamide (3b). Yield 76%; mp 178-179ºC. IR spectrum, ν, cm^{-1}: 3275 (NH), 1702, 1698 (C=O). ^1H NMR spectrum (DMSO-d_6), δ, ppm (*J*, Hz): 1.99 (6H, s, $(CH_3)_2$); 2.72-2.94 (2H, m, H-3); 3.39-3.57 (1H, m, H-4); 3.89-4.19 (2H, m, H-5); 5.64 (2H, s, $(CH)_2$); 7.55 and 7.66 (4H, 2d, *J* = 9.0, ArH); 10.91 (1H, s, NH). ^{13}C NMR spectrum (DMSO-d_6), δ, ppm: 10.87 $((CH_3)_2)$; 33.89 (C-4); 35.57 (C-3); 50.14 (C-5); 103.01 (C'-3 and C'-4); 115.91, 121.19, 126.65, 131.41, 138.29 (C_6H_5, C'2 and C'-5); 171.67, 171.75 (C-2 and CO). Mass spectrum, *m/z* (I_{rel}, %): 376 $[M+H]^+$ (95), 378 $[M+H+1]^+$ (100). Found, %: C 54.01; H 4.84; N 11.22. $C_{17}H_{18}BrN_3O_2$. Calculated, C 54.27; H 4.82; N 11.17.

N-(2,5-Dimethylpyrrol-1-yl)-1-(3-fluorophenyl)-5-oxo-3-pyrrolidinecarboxamide (3c). Yield 65%; mp 176-177ºC (2-propanol). IR spectrum, ν, cm^{-1}: 3280 (NH), 1693 (C=O), 1671 (C=O). ^1H NMR spectrum (DMSO-d_6), δ, ppm: 2.00 (6H, s, $(CH_3)_2$); 2.73-2.92 (2H, m, H-3); 3.41-3.53 (1H, m, H-4), 3.94-4.16 (2H, m, H-5); 5.65 (2H, s, $(CH)_2$); 6.93-7.76 (4H, m, ArH); 10.93 (1H, s, NH). ^{13}C NMR spectrum (DMSO-d_6), δ, ppm: 10.87 $((CH_3)_2)$; 33.84 (C-4); 35.74 (C-3); 50.26 (C-5); 103.01, 105.99, 106.34 (C'-3 and C'-4); 114.74, 114.77, 126.66, 130.23, 130.36, 140.52, 140.66, 160.41, 163.61 (C_6H_5, C'-2 and C'-5); 171.69, 172.00 (C-2 and CO). Mass spectrum, *m/z* (I_{rel}, %): 316 $[M+H]^+$ (100). Found, %: C 65.45; H 5.95; N 13.36. $C_{17}H_{18}FN_3O_2$. Calculated, %: C 64.75, H 5.75; N 13.33.

N-(2,5-Dimethylpyrrol-1-yl)-1-(4-fluorophenyl)-5-oxo-3-pyrrolidinecarboxamide (3d). Yield 71%; mp 142-143ºC. IR spectrum, ν, cm^{-1}: 3239 (NH), 1707, 1681 (C=O). ^1H NMR spectrum (DMSO-d_6), δ, ppm: 2.00 (6H, s, $(CH_3)_2$); 2.70-2.98 (2H, m, H-3); 3.41-3.59 (1H, m, H-4); 3.90-4.22 (2H, m, H-5); 5.65 (2H, s, $(CH)_2$); 7.11-7.79 (4H, m, ArH); 10.92 (1H, s, NH). ^{13}C NMR spectrum (DMSO-d_6), δ, ppm: 10.72 $((CH_3)_2)$; 33.84 (C-4); 39.56 (C-3); 50.35 (C-5); 102.87 (C'-3 and C'-4); 114.95, 115.24, 121.28, 121.38, 126.52, 135.28, 156.75, 159.96 (C_6H_5, C'-2 and C'-5); 171.28, 171.60 (C-2 and CO). Mass spectrum, *m/z* (I_{rel}, %): 316 $[M+H]^+$ (100). Found, %: C 64.20; H 5.68; N 13.06. $C_{17}H_{18}FN_3O_2$. Calculated, %: C 64.75; H 5.75; N 13.33.

REFERENCES

1. Yu. P. Kitaev and B. I. Buzykin, *Hydrazones* [in Russian], Nauka, Moscow (1974).
2. S. P. Singh, L. S. Tarar, R. K. Vaid, J. Elguero, and A. Martinez, *J. Heterocycl. Chem.*, **26**, 733 (1989).
3. K. Brokaite, V. Mickevicius, and G. Mikulskiene, *ARKIVOC*, Ch. XII (2006), p. 61.