Journal of Molecular Structure 1089 (2015) 170–177

Contents lists available at ScienceDirect

Journal of Molecular Structure

journal homepage: www.elsevier.com/locate/molstruc

Structures, spectroscopic analysis, herbicidal activities and enamine–aminone tautomerism of new β-diketone derivatives modified with glycylglycine methyl ester

Hualing Zhu *, Jun Shi, Zhiqiang Huang *, Lijuan Lv, Jiawei Duan

College of Basic Science, Tianjin Agricultural University, Tianjin 300384, China

HIGHLIGHTS

- New β-diketone derivatives modified by glycylglycine ester are synthesized.
- Optimized geometries and theoretical vibrational frequencies can well reproduce the experimental data.
- The enamine–aminone tautomerism is caused by proton transfer.
- The tested compounds own higher inhibition ability to monocotyledon than to dicotyledon.

ARTICLE INFO

Article history:
Received 18 November 2014
Received in revised form 13 February 2015
Accepted 13 February 2015
Available online 21 February 2015

Keywords:
β-diketone
Glycylglycine ester
Spectroscopic analysis
Herbicidal activity
Enamine–aminone tautomerism

ABSTRACT

New β-diketone derivatives modified with glycylglycine methyl ester have been synthesized and characterized by IR, UV, ^{1}H NMR, ^{13}C NMR, Elemental analysis and single-crystal X-ray diffraction, the analytical results show that compound 1 and compound 2a exist in enamine form while compound 2b exists in aminone form. The optimized geometries and theoretical vibrational frequencies of the compounds calculated by using DFT/B3LYP with 6-31g (d, p) basis set in the ground state can well reproduce the experimental data. The results of herbicidal activity tests indicate that all the tested compounds own higher inhibition ability to monocotyledon than to dicotyledon, especially to green-bristlegrass with the inhibitory rates about 100%. Theoretical enamine–aminone tautomerism study at DFT/B3LYP/6-31g (d, p) shows that tautomerism between compound 2a and 2b is mainly caused by the proton transfer.

Introduction

The functionalized derivatives of beta-diketone are clinically important molecules and widely used for their antibacterial [1–3], antiviral [4], insecticidal [5], antioxidant [6], potential prophylactic antitumor [7], anti-sunscreen [8] and anti-HIV-1 activities [9]. Compared with the free amino acid, glycylglycine is widely studied for its lower transport energy, faster transport speed and its not easily saturated transport carrier. At the same time, glycylglycine has the absorption superiority because of its being absorbed completely into blood circulation in the form of peptide [10,11]; it is helpful for the protein synthesis and deposition to add a proper amount of glycylglycine in the animal feed. The derivatives of glycylglycine have some special biological functions such as growth-promoting [12], anti-cancer [13], antibacterial activity [14], anti-oxidation, immune regulation [15,16] and are widely used in medicine, cosmetics, health products, spices, animal feed additive [17]. So it is meaningful to modify β-diketone molecule with glycylglycine by using the superposition principle of reactive group.

Modifying the chemical structure of a drug by synthesis of dipeptide prodrugs is the possible way to minimize side effects and toxicity [18,19]. A good example of such approach is the synthesis of dipeptide ester prodrugs of acyclovir [20].

The aim of this study was to synthesize glycylglycine esters containing β-diketone and to evaluate their herbicidal activities. The synthesis routes and structures of the title compounds are shown in Fig. 1.

Experimental and theoretical methods

General remarks

Compound glycylglycine methyl ester was synthesized according to the literature [21]. Other reagents obtained from commercial

* Corresponding authors.
E-mail address: zhuhualing2004@126.com (H. Zhu).

http://dx.doi.org/10.1016/j.molstruc.2015.02.051
0022-2860/

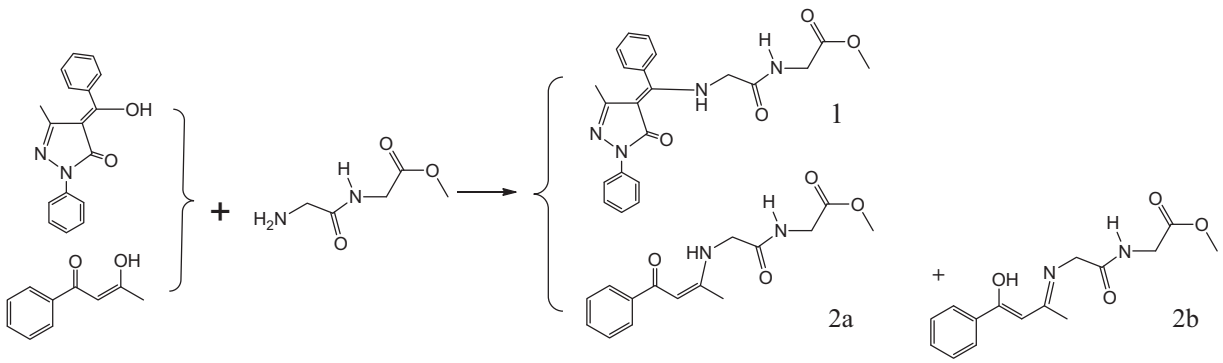

Fig. 1. Synthesis route and structures of the title compounds.

sources were of analytically pure grade. A Carlo-Erba 1106 Elemental Analyzer was utilized for elemental analysis. IR spectra were recorded (KBr disks) on a Perkin–Elmer FTIR spectrometer. Melting points were measured on a WRS-1B melting point apparatus and uncorrected. Crystal structure determination was carried out on a Rigaku Saturn724 CCD diffractometer. NMR spectra were recorded on a Bruker Avance 400 spectrometer with TMS as an internal standard in $CDCl_3$ (carbon frequency = 125 MHz). The UV absorption spectra were recorded on an UV-250IPC spectrometer in different solvents for the study of enamine–aminone tautomerism.

Synthesis of the title compounds

Compound 1: (Z)-methyl-2-(2-((3-methyl-5-oxo-1-phenyl-1H-pyrazol-4(5H)-ylidene) (phenyl) methyl) amino) acetamido) acetate

The compound was synthesized by refluxing the mixture of 1-phenyl-3-methyl-4-benzoyl-5-pyrazolone (15*m* mol) and glycylglycine methyl ester (15*m* mol) in ethanol (100 mL) over a steam bath for about 8 h, then the solutions were cooled down to room temperature. After about five days, blocks were obtained and dried in the air. The products were recrystallized from ethanol and pale yellow crystals were obtained suitable for X-ray analysis. Spectroscopic and some physical data are as follows: m.p = 533–534 K. Anal. Calc. For $C_{22}H_{22}N_4O_4$: C, 65.02; H, 5.42; N, 13.79%. Found: C, 64.98; H, 5.23; N, 13.83%. FT-IR (KBr, cm^{-1}) ν_{max}: 3348(m, NH), 3059(w, phenyl-H), 1745(s, COO), 1670(s, C═O), 1633(s, C═O of diketone), 1537(s, δ_{N-H}). 1219(s), 1159(s). UV (λ, nm): 216(1.3), 255(3.0), 276.0(2.4). ^{1}H NMR (DMF-$_{d7}$, 400 Hz) δ: 11.1 (t, *J* = 3.5 Hz, 1H), 8.5 (t, *J* = 3.3 Hz, 1H), 7.6–8.0 (m, 5H), 7.1–7.5 (m, 5H), 3.91 (d, *J* = 4.5 Hz, 2H), 3.85 (d, *J* = 4.7 Hz, 2H), 3.22 (s, 3H), 1.35 (s, 3H). ^{13}C NMR (DMSO-d, 400 Hz): 173.4, 172.2, 167.4, 161.1, 156.5, 137.8, 132.7, 130.1, 128.2, 125.6, 125.1, 120.4, 118.9, 98.5, 58.8, 43.7, 42.0, 17.5.

Compound 2a: (Z)-methyl-2-(2-((4-oxo-4-phenylbut-2-en-2-yl) amino)acetamido) acetate

The compound was synthesized by refluxing the mixture of benzoylacetone (15*m* mol) and glycylglycine methyl ester (15*m* mol) in ethanol (100 mL) over a steam bath for about 5 h, then the solutions were cooled down to room temperature. After about three days, white blocks were obtained and dried in the air. The products were recrystallized from ethanol which afforded pale crystals suitable for X-ray analysis. Spectroscopic and some physical data are as follows: m.p = 434–435 K. Anal. Calc. For $C_{15}H_{18}N_2O_4$: C, 62.07; H, 6.21; N, 9.66%. Found: C, 62.01; H, 6.24; N, 9.81%. FT-IR (KBr, cm^{-1}) ν_{max}: 3275(m, NH), 3085(w, phenyl-H), 1753(s, COO), 1662(s, C═O), 1600(s, C═O of diketone), 1543(s, δ_{N-H}), 1197(s), 1068(s). UV (λ, nm, methanol): 213(2.2), 241.0(1.75), 341.5(2.52). ^{1}H NMR (DMF-$_{d7}$, 400 Hz) δ: 10.70 (t, *J* = 3.8 Hz, 1H), 8.1 (t, *J* = 3.0 Hz, 1H), 7.00–8.00 (m, 5H), 6.86 (s, 1H), 3.68 (d, *J* = 3.4 Hz, 2H), 3.26 (d, *J* = 2.7 Hz, 2H), 3.86 (s, 3H), 2.15 (s, 3H). ^{13}C NMR (DMSO-d, 400 Hz): 186.4, 166.6, 165.4, 130.9, 128.7, 128.5, 127.1, 92.2, 52.2, 44.8, 41.1, 19.7.

Compound 2b: Methyl-2-(2-((E)-((Z)-4-hydroxy-4-phenylbut-3-en-2-ylidene)amino)acetamido) acetate

The synthesis way of this compound was the same as that of compound 2a, the only difference was that the products were recrystallized from dichloromethane and yellow solid was obtained. Spectroscopic and some physical data are as follows: m.p = 449–451 K. FT-IR (KBr, cm^{-1}) ν_{max}: 3495(w, OH), 3263(m, NH), 3082(w, phenyl-H), 1757(s, COO), 1659(s, C═O), 1599(s, C═N), 1546(s, δ_{N-H}), 1197(s), 1068(s). UV (λ, dichloromethane, nm): 213(0.72), 245.0(1.75), 338(3.55). ^{1}H NMR (DMF-$_{d7}$, 400 Hz) δ: 14.71 (s, 1H), 7.95 (t, *J* = 1.8 Hz, 1H), 7.00–8.00 (m, 5H), 5.64 (s, 1H), 4.16 (d, *J* = 2.9 Hz, 2H), 3.08 (d, *J* = 1.4 Hz, 2H), 2.98 (s, 3H), 2.35 (s, 3H). ^{13}C NMR (DMSO-d, 400 Hz): 170.6, 169.2, 165.7, 140.5, 128.7, 128.5, 127.1, 92.2, 52.2, 45.88, 41.1, 19.7.

X-ray crystallography

A pale yellow prism of compound 1 with dimensions of 0.18 mm × 0.14 mm × 0.12 mm and a colorless prism of compound 2a with dimensions of 0.14 mm × 0.13 mm × 0.12 mm were selected for X-ray analysis. All X-ray data were collected at 173(2) K on a Rigaku Saturn724 CCD diffractometer equipped with a multilayer-monochromatized Mo Kα radiation (λ = 0.71073 Å) by using a φ–ω scan mode in the range of $1.97 \leqslant \theta \leqslant 25.01°$ and $2.04 \leqslant \theta \leqslant 25.01°$, respectively. The data of compound 1 are as follows: triclinic system, $P-1$ space group, a = 9.239(3) Å, b = 10.468(3) Å, c = 10.8399(3) Å, α = 103.814(6)°, β = 96.902(6)°, γ = 101.572(6)°, V = 981.6(5) Å^3, Z = 2, D_C = 1.375 g/cm^3, μ(Mo Kα) = 0.097 mm^{-1}, $F(000)$ = 428, S = 1.004, the final R = 0.0552 and wR = 0.1149. The data of compound 2a are as follows: monoclinic system, $P2(1)/c$ space group, a = 14.830(4) Å, b = 9.478(3) Å, c = 19.999(5) Å, $\alpha = \beta = \gamma = 90(8)°$, V = 2811.0(4) Å^3, Z = 8, D_C = 1.372 g/cm^3, μ(MoKα) = 0.100 mm^{-1}, $F(000)$ = 1232, S = 1.103, the final R = 0.1257 and wR = 0.1463. The structures were solved by direct methods with SHELXS-97 [22] and further refined on F^2 by full-matrix least-squares methods with SHELXL-97 [23]. During refinement, all H atoms were geometrically positioned and treated as riding on their parent atoms, with C—H = 0.95 Å for the aromatic, 0.98 Å for the methyl and N—H = 0.88 Å with U_{iso} (H) = 1.2U_{eq}(C-aromatic, N) or 1.5U_{eq}(C-methyl).