Polyhedron 80 (2014) 193–197

Contents lists available at ScienceDirect

Polyhedron

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

4-[(Dimethylamino)methylene]-2-ferrocenyl-5-oxo-4,5-dihydrofuran-3-carboxaldehyde: Synthesis, spectral characterization and single crystal X-ray analysis

Zoran Ratković [a,*], Jovana Muškinja [a], Sladjana B. Novaković [b], Goran A. Bogdanović [b], Karoly Micskei [c], Rastko D. Vukićević [a]

[a] Department of Chemistry, Faculty of Science, University of Kragujevac, Radoja Domanovića 12, 34000 Kragujevac, Serbia
[b] Vinča Institute of Nuclear Sciences, Laboratory of Theoretical Physics and Condensed Matter Physics, University of Belgrade, P.O. Box 522, 11001 Belgrade, Serbia
[c] Department of Inorganic Chemistry, Faculty of Sciences, University of Debrecen, H-4010 Debrecen, Hungary

ARTICLE INFO

Article history:
Received 29 December 2013
Accepted 23 March 2014
Available online 2 April 2014

Dedicated to Professor Vukadin Leovac, on the happy occasion of his 70th birthday.

Keywords:
3-Aroylpropanoic acids
3-Ferocenoylpropanoic acid
Vilsmeier reagent
Furan derivatives
Crystal structure

ABSTRACT

The title compound 4-[(dimethylamino)methylene]-2-ferrocenyl-5-oxo-4,5-dihydrofuran-3-carboxaldehyde was synthesized by reacting 3-ferrocenoylpropionic acid with Vilsmeier reagent. This result is rather unexpected, since 3-aroylpropanoic acids under these conditions usually give the corresponding 2-aryl-4-chloro-3-formylfurans. 3-Ferrocenoylpropanoic acid is not the only 3-aroylpropanoic acid that exhibit an unusual behavior under the same conditions: 3-thenoylpropanoic acid gave 4-[(dimethylamino)-methylene]-2-(2-thienyl)-5-oxo-4,5-dihydrofuran-3-carboxaldehyde and 4-[(dimethylamino) methylene]-2-(2-thienyl-5-formyl)-5-oxo-4,5-dihydrofuran-3-carboxaldehyde, whereas 3-(4-methoxybenzoyl)propanoic acid yielded 4-[(dimethylamino)methylene]-2-(4-methoxyphenyl)-5-oxo-4,5-dihydrofuran-3-carboxaldehyde and 2-(4-methoxyphenyl)-5-chloro-furan-3,4-dicarboxaldehyde. Single crystal X-ray analysis was successfully performed for 4-[(dimethylamino)methylene]-2-ferrocenyl-5-oxo-4,5-dihydrofuran-3-carboxaldehyde and 4-[(dimethylamino)methylene]-2-(2-thienyl)-5-oxo-4,5-dihydrofuran-3-carboxaldehyde and their structures were compared.

1. Introduction

Furans are an important class of heterocyclic compounds, since they often represent core structure of many natural products and pharmaceuticals. Thus, different essential oils [1] and plant extracts [2] contain derivatives of this heterocycle. Also, many furans exhibit antiviral [3], antifungal [4], antibacterial [1,5] and anti-inflammatory activities [6].

Two important facts related to chemical properties of furan govern the scope and limitations of the use this heterocycle and its derivatives in organic synthesis: transformations involving the position 2 are easily achievable [7], whereas functionalization of the position 3 involves a multistep approach and lower yields [8,9]. On the other hand, furan derivatives functionalized in the position 3 are of a particular interest in organic synthesis. For example, 3-formylfurans are used in synthesis of pyrimidines [10], pyrazoles [11] and isoxazoles [12]. Recently, we required considerable amounts of 4-chloro-2-ferrocenyl-3-formylfuran as starting material in a more comprehensive synthetic project and carried out an extensive literature search. We found out that Perumal and co-workers [13] synthesized several 2-aryl-4-chloro-3-formylfurans in high yields starting from the corresponding 3-aroylpropanoic acids. However, in our hands the reaction did not work when 3-ferocenoylpropanoic acid (**1a**) was used as the substrate. Instead, we obtained the title compound in the crystal form. Herein, we describe the synthesis and the full characterization, including single crystal X-ray analysis, of this compound. Also, the behavior of some other 3-aroylpropanoic acids under the same reaction conditions was described.

2. Experimental

2.1. Chemistry

2.1.1. Materials and measurements

All starting chemicals were commercially available and used as received, except that the solvents were purified by distillation. 3-Aroylpropanoic acids were synthesized according to described procedures [14–17]. Chromatographic separations were carried

* Corresponding author. Tel.: +381 346362517; fax: +381 34335040.
E-mail address: wor@kg.ac.rs (Z. Ratković).

http://dx.doi.org/10.1016/j.poly.2014.03.038
0277-5387/

out using silica gel 60 (Merck, 230–400 mesh ASTM) whereas silica gel on Al plates, layer thickness 0.2 mm (Merck), was used for TLC. IR spectra were recorded on a Perkin-Elmer Spectrum One FT-IR spectrometer with a KBr disc. NMR spectra were recorded on a Varian Gemini (200 MHz) spectrometer, using $CDCl_3$ as the solvent and TMS as the internal standard.

Elemental microanalyses for C, H and N were performed by standard methods on a Vario III CHNS Elemental Analyzer, Elemental Analysensysteme GmbH.

2.2. General procedure for the reaction of 3-aroylpropanoic acids with Vilsmeier reagent

The corresponding 3-aroylpropanoic acid **1a–c** (10 mmol) was dissolved in 8 cm^3 of dry *N*,*N*-dimethylformamide and mixture was cooled to 0 °C, then 4 cm^3 of $POCl_3$ was dropwise added during period of 40 min. Reaction mixture was stirred 1 h at room temperature and 4 h at 65 °C. Crushed ice, 100 g, was added into beaker containing a solution of 5 g CH_3COONa in 30 cm^3 of water, and reaction mixture was poured onto with stirring. The product was extracted with toluene (3 × 60 cm^3). The organic layer was washed with water (2 × 80 cm^3), brine (2 × 80 cm^3) and dried over anhydrous sodium sulfate. Main part of solvent was evaporated at reduced pressure and crude concentrated solution was filtered through a short column of silica gel. Solvent was evaporated under reduced pressure and residue was chromatographed on silica gel column using toluene as eluent. Toluene and toluene-ethyl acetate 8:2 were used for separation of reaction products **2b** and **3b** (obtained from the acid **1b**). The compounds **2c** and **4c** were eluated with hexane-dichloromethane 9:1 mixture. Spectral data of the new compounds follows:

2.2.1. 4-[(Dimethylamino)methylene]-2-ferrocenyl-5-oxo-4,5-dihydrofuran-3-carboxaldehyde (**2a**)

Deep red crystals; mp 166–168 °C; Yield 60%; IR (cm^{-1}): 2854 (CH from CHO), 1717 and 1655 (CO); ^1H NMR: δ 3.28 (s, 3H), 3.54 (s, 3H), 4.23 (s, 5H), 4.48 (t, 2H), 4.74 (t, 2H), 8.27 (s, 1H), 10.01 (s, 1H); ^{13}C NMR: δ 42.5, 47.7, 68.5, 70.1, 70.8, 71.3, 88.7, 117.7, 152.6, 160.9, 164.1, 184.9 (CO). *Anal.* Calc. for $C_{18}H_{17}FeNO_3$ (351.171): N, 3.99; C, 61.56; H, 4.88. Found: N, 3.87; C, 61.06; H, 4.89%.

2.2.2. 4-[(Dimethylamino)methylene]-2-(2-thienyl)-5-oxo-4,5-dihydrofuran-3-carboxaldehyde (**2b**)

Yellow-orange solid; mp 158–160 °C; Yield 30%; IR (cm^{-1}): 2838 (CH from CHO), 1716 and 1646 (CO), ^1H NMR: δ 3.31 (s, 3H), 3.55 (s, 3H), 7.13 (m, 1H), 7.50 (m, 2H), 8.31 (s, 1H), 10.19 (s, 1H); ^{13}C NMR: δ 42.6, 47.8, 88.7, 117.9, 127.9, 129.2, 129.8, 152.1, 153.6, 163.4, 185.4 (CHO). *Anal.* Calc. for $C_{12}H_{11}NO_3S$ (249.278): N, 5.62; S, 12.86; C, 57.81; H, 4.45. Found: N, 5.33; S, 12.56; C, 57.79; H, 4.60%.

2.2.3. 4-[(Dimethylamino)methylene]-2-(4-methoxyphenyl)-5-oxo-4,5-dihydrofuran-3-carboxaldehyde (**2c**)

White solid; mp 113 °C; Yield 24%; IR (cm^{-1}): 2841 (CH from CHO), 1735 and 1643 (CO); ^1H NMR: δ 3.30 (s, 3H), 3.56 (s, 3H), 3.87 (s, 3H), 6.97 (d, 2H, J = 8.8 Hz), 7.59 (d, 2H, J = 8.8 Hz), 8.31 (s, 1H), 9.87 (s, 1H); ^{13}C NMR: δ 42.5, 47.7, 55.3, 88.8, 114.2, 117.8, 120.4, 130.1, 153.2, 158.7, 161.3, 163.9, 186.5 (CHO). *Anal.* Calc. for $C_{15}H_{15}NO_4$ (273.284): N, 5.12; C, 65.92; H, 5.53. Found: N, 5.11; C, 65.68; H, 5.50%.

2.2.4. 4-[(Dimethylamino)methylene]-2-(2-thienyl-5-formyl)-5-oxo-4,5-dihydrofuran-3-carboxaldehyde (**3b**)

Deep red powder, mp 168 °C; Yield 29%; IR (cm^{-1}): 2931, 2852 (CH from CHO), 1747 and 1648 (CO); ^1H NMR: δ 3.37 (s, 3H), 3.58 (s, 3H), 7.55 (d, 1H, J = 4 Hz), 7.76 (d, 1H, J = 4 Hz), 8.35 (s, 1H), 9.93 (s, 1H), 10.29 (s, 1H); ^{13}C NMR: δ 42.9, 48.2, 89.1, 120.6, 128.8, 136, 137.9, 144.9, 149.2, 154.5, 163.1, 182.6 (CHO from thiophene ring), 184.8 (CHO from furan ring). *Anal.* Calc. for $C_{13}H_{11}NO_4S$ (277.297): N, 5.05; C, 56.31; H, 4.00, S, 11.56. Found: N, 5.08; C, 56.02; H, 3.98, S, 11.51%.

2.2.5. 2-(4-Methoxyphenyl)-furan-5-chloro-3,4-dicarboxaldehyde (**4c**)

Pale yellow solid; mp 98–99 °C; Yield 29%; IR (cm^{-1}): 2973, 2834 (CH from CHO), 1690, 1675 and 1669 (CO); ^1H NMR: δ 3.88 (s, 3H), 3.56 (s, 3H), 7.0 (d, 2H, J = 9.2 Hz), 7.84 (d, 2H, J = 9 Hz), 10.25 (s, 1H), 10.27 (s, 1H); ^{13}C NMR: δ 55.4, 114.3, 119.3, 119.4, 119.8, 130, 144.1, 159.8, 162.1, 184.6 (CHO at C-4), 185.3 (CHO at C-3). *Anal.* Calc. for $C_{13}H_9O_4Cl$ (264.66): C, 58.99; H, 3.43. Found: C, 58.75; H, 3.41%.

2.3. X-ray crystallography

Single-crystal X-ray diffraction data for **2a** and **2b** were collected on an Enraf–Nonius CAD4 diffractometer [18] by using graphite-monochromated Mo Kα (0.71073 Å) radiation at 293(2) K. The data were corrected for Lorentz and polarization effects [19]. The crystal structure was solved by direct methods with the program SHELXS [20] and refined on the F^2 by full-matrix least-square method with SHELXL [20] both incorporated in WINGX [21] program package.

All non-H atoms were refined anisotropically to convergence. All H atoms were placed at geometrically calculated positions with the C–H distances fixed to 0.93 Å from C(sp^2) and 0.96 Å from methyl C(sp^3). Methyl-group H atoms were located from ΔF map, then geometrically idealized and refined as a rigid groups with U_{iso}(H) = 1.5 U_{eq}(C). The positions of all other H atoms were geometrically idealized and allowed to ride on their parents atoms with U_{iso}(H) = 1.2 U_{eq}(C).

A summary of crystallographic data is given in Table 1. Figures were produced using ORTEP-3 [22] and MERCURY, Version 2.4 [23]. The software used for the preparation of the materials for publication: WINGX [21], PLATON [24], PARST [25].

3. Results and discussion

3.1. Synthesis

As mentioned in the Section 1, our synthetic goal was 4-chloro-2-ferrocenyl-3-formylfuran. Following the literature procedure [13] we submitted 3-ferocenoylpropanoic acid (**1a**) to described reaction conditions with Vilsmeier reagents (DMF/$POCl_3$, 4 h at 85 °C) and obtained a deep-red crystalline product in 60% yield. However, to our surprise spectral data of this compound did not confirm the structure of expected 4-chloro-2-ferrocenyl-3-formylfuran. The detailed analysis of ^1H and ^{13}C NMR spectra (see below) pointed out to structure **2a** (Scheme 1), what has been unambiguously confirmed by single crystal X-ray analysis. Since we learned out from experience gained in ferrocene chemistry [26] that these compounds under the same conditions can behave quite differently from the corresponding compounds containing the phenyl group, we conducted several experiments with this substrate at different temperatures. However, in all cases the only reaction product was compound **2a**, not 4-chloro-2-ferrocenyl-3-formylfuran (the best condition being 65 °C/4 h).

In order to examine whether the ferrocene acid (**1a**) is an exception, we checked two additional starting compounds (**1b** and **1c**) under the same reaction conditions. Thus, 3-(2-thienoyl)propanoic acid **1b** gave two products in a ratio ~1:1 (see Scheme 1 and