Synthesis of New 2,3-Dihydrofuran-3-one Derivative and its Reactions with Some Primary Amines

Ş. H. Üngören* [a], M. Saçmacı [a], Y. Akçamur [a],
C. Arıcı [b], D. Ülkü [b]
e-mail: hungoren@erciyes.edu.tr

[a] Erciyes University, Yozgat Faculty of Arts and Sciences, Department of Chemistry, 66200, Yozgat-Turkey
[b] Hacettepe University, Department of Engineering Physics, 06532 Beytepe, Ankara- Turkey
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The Wittig reaction of 2,3-dihydro-4-(4-methoxybenzoyl)-5-(4-methoxyphenyl)-furan-2,3-dione (1) with methyl (triphenylphosphoranylidene)acetate (2) stereo- and regioselectively afforded methyl (*Z*)-[2,3-dihydro-4-(4-methoxybenzoyl)-5-(4-methoxyphenyl)-3-oxofuran-2-ylidene]acetate (3) in good yield. The reactions of **3** with primary amines (**4a-k**) gave corresponding 1-substituted 2,3-dihydro-1*H*-pyrrol-3-ones (**5a-k**).

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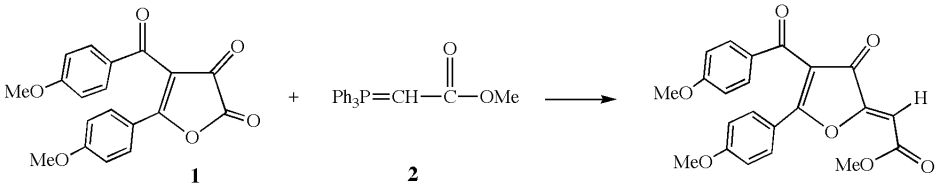
Recently, a novel class of furan-3-one derivatives has been reported with strong anti-inflammatory activites [1]. Some 2-alkoxy carbonylmethylene-2,3-dihydrofuran-3-ones [2] also show remarkable anti-microbial and anti-convulsant activites [2c], and also these reactive compounds might be useful synthons for heterocyclic compounds [3]. Some pyrrolone structures are interesting [4], because the lactam rings are present in some antibiotics, bile pigments [5], and the natural alkaloid jatropham (showing inhibitation against P-388 Lympocytic leukemia [6]).

In this paper, we report the Wittig reaction of 2,3-dihydro-4-(4-methoxybenzoyl)-5-(4-methoxyphenyl)-furan-2,3-dione (**1**) with methyl (triphenylphosphoranylidene)-acetate (**2**) giving methyl (*Z*)-[2,3-dihydro-4-(4-methoxybenzoyl)-5-(4-methoxyphenyl)-3-oxofuran-2-ylidene]-acetate (**3**), and the following reaction with some primary amines (**4a-k**) giving corresponding 1-substituted 2,3-dihydro-1*H*-pyrrol-3-ones (**5a-k**). The starting material, 2,3-dihydro-4-(4-methoxybenzoyl)-5-(4-methoxyphenyl)-furan-2,3-dione, **1** was prepared by cyclization of 1,3-bis(4-methoxybenzoyl)-propane-1,3-dione with oxalyl chloride [7]. Few Wittig reactions with furan-2,3-dione have been reported [2,8]. The Wittig reaction of furan-2,3-dione (**1**) with **2** was performed in refluxing benzene to give **3** as shown in Scheme 1. Very interestingly, a similar Wittig reaction of 4-acetyl-2,3-dihydro-5-methyl-furan-2,3-dione [9] with **2** did not give an isolable product.

The structure of **3** was determined by ir, ^{1}H nmr, and ^{13}C nmr, and finally by X-ray analysis. The ir spectrum showed three carbonyl bands, 1717, 1705, and 1644 cm^{-1}, and did not show a band corresponding to the lactone carbonyl. The ^{1}H nmr spectrum showed an olefinic proton at δ 6.01 ppm, and three methoxy protons at δ 3.84, 3.81 and 3.81 ppm, and the ^{13}C nmr showed three carbonyl carbons at δ 190.44, 186.18, and 179.35 ppm, and three methoxy carbons at δ 57.68, 57.58, 54.33 ppm. Also, to confirm compound **3**, the additive scheme for calculation of the methine proton H chemical shift was applied to **3** using the known values of Pascal *et al*. [10]. The chemical shift of the olefinic proton shows the *Z* structure by comparions (Δδ 0.29 ppm for a *E* isomer, Δδ 0.05 ppm for a *Z* isomer) with the each calcd values for *E* and *Z* isomers. The ORTEP of **3**, shown in Figure 1, showed the methoxymethylene group connected at the position 2 of the furan ring, and also showed a *Z* structure. These showed the Wittig reaction to be regio- and stereoselective.

The molecule involves two 4-methoxyphenyl rings A (C8-C13) and B (C16-C21) connected to the 2,3-dihydrofuran-3-one ring C (C1-C4, O1), see Figure 1. The methoxycarbonylmethylene group also connected to C ring. The C ring with methoxycarbonylmethylene group bond distances and angles are very close to a similar compound [2c]. A least square plane analysis shows that all rings are fairly planar. The dihedral angles between the planes are as follows: A/B = 67.67(9), A/C = 5.99(8) and B/C = 70.48(7)°. The molecules in the crystal structure are connected by van der Waals interaction. There is one intermolecular hydrogen bond in the unit cell. The hydrogen bond between O4

Scheme 1



atom and hydrogen of C21 of the 4-methoxyphenyl ring shows with a D...A distance of 3.3456(2) Å and a D-H...A angle of 141.1(1)°.

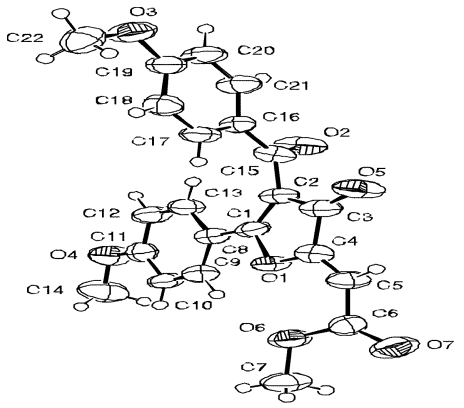


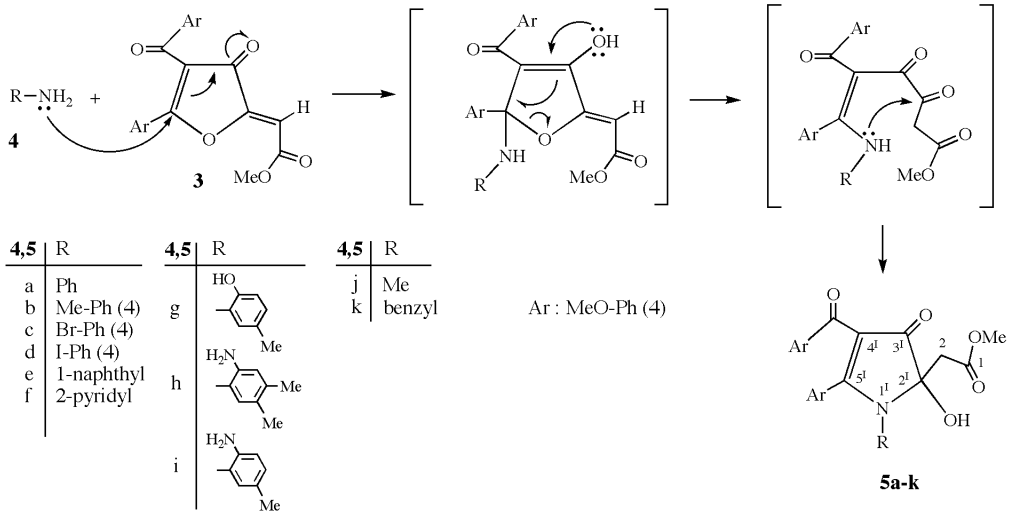
Figure 1. ORTEP drawing of **3** with the atom numbering scheme. Displacement ellipsoids are drawn at the 50% probability level.

of aliphatic and aromatic amines **4** to **3** give the corresponding intermediates. An attempt to isolate these intermediates by reacting at various temperatures failed and the corresponding 1-substituted 2,3-dihydro-1*H*-pyrrol-3-ones **5** were isolated instead. Ring closure of methyl 6-(aryl or alkylamino)-3,4-dioxo-5-hexenoate intermediates to rasemic mixtures of 1-substituted 2,3-dihydro-1*H*-pyrrol-3-ones **5** takes place *via* symmetrical addition of the NH group to the C=O moiety.

EXPERIMENTAL

Solvents were dried by refluxing with the appropriate drying agent and distilled before use. Melting points were determined on an Electrothermal 9200 apparatus and are uncorrected. Elemental analysis was performed with a Carlo Erba Elemental Analyzer, 1108. FT-IR spectrum was measured on a Jasco Plus Model 460 spectrometer, using potassium bromide pellet. The ^{1}H and ^{13}C nmr spectra were obtained on a Gemini-Varian 200 MHz instrument. The chemical shifts were reported in ppm from tetramethylsilane and given in δ units. All experiments were followed by tlc using DC Alufolien Kieselgel 60 F 254 Merck and Camag TLC lamp (254/366 nm).

Scheme 2



4,5	R
a	Ph
b	Me-Ph (4)
c	Br-Ph (4)
d	I-Ph (4)
e	1-naphthyl
f	2-pyridyl

4,5	R
g	HO, Me
h	H2N, Me, Me
i	H2N, Me

4,5	R
j	Me
k	benzyl

Ar : MeO-Ph (4)

The reaction of **3** with some primaryl amine (**4a-k**) gave corresponding 1-substituted 2,3-dihydro-1*H*pyrrol-3-ones (**5a-k**) in 59-85% yield. The structures of compounds **5** are supported by elemental analyses and spectroscopic data. The ^{1}H nmr spectrum showed two AB type doublets, resulting from partial disturbance of free rotation of the methoxycarbonylmethyl causing the two methylene protons to be none-equivalent. The structure of **5a-k** were already determined by X-ray analysis, as reported previously [11].

A reasonable proposal for the reaction pathway from **3** to **5** is outlined briefly in Scheme 2. The Michael addition

Methyl (*Z*)-[2,3-Dihydro-4-(4-methoxybenzoyl)-5-(4-methoxyphenyl)-3-oxofuran-2-ylidene]acetate (**3**).

A solution of 2,3-dihydro-furan-2.3-dione **1** (3.38 g, 10 mmoles) and **2** (3.34 g, 10 mmoles) in dry benzene (60 ml) was refluxed for 30 min. After removal of the solvent, the residue was treated with cool methanol (20 ml, 0-5°) and crystallized to give pure **3**. The cool methanol washings were evaporated to dryness and the residue was recrystallized from cyclohexane to remove the byproduct triphenylphosphine oxide. The yield 2.96 g (75%), mp 162°; ir: 1717 (C1=O), 1705 (C'=O); 1687 (C=C, aliph.); 1644 (Ar-CO); 1598 cm^{-1} (C=C, aliph.); ^{1}H nmr (deuteriochloroform): δ 7.92-6.88 (m, 8H, Ar-H), 6.10 (s, 1H, C=CH), 3.84-3.81

Table 1

Final Atomic Coordinates and Equivalent Anisotropic Thermal Parameters for Non-hydrogen Atoms

Atom	x	y	z	Ueq*
O1	0.1848(2)	0.3055(4)	-0.1558(2)	0.0476(10)
O2	0.3241(2)	0.2428(5)	-0.3883(2)	0.0725(13)
O3	0.7076(3)	0.6017(5)	-0.2754(3)	0.0762(13)
O4	-0.0503(3)	0.7074(5)	-0.4463(2)	0.0729(12)
O5	0.4013(3)	0.1158(5)	-0.1448(2)	0.0710(12)
O6	0.1095(2)	0.2612(5)	-0.0046(2)	0.0630(11)
O7	0.1480(3)	0.0366(5)	0.0597(3)	0.0835(15)
C1	0.2139(4)	0.3493(6)	-0.2350(3)	0.0447(14)
C2	0.3012(3)	0.2887(6)	-0.2426(3)	0.0467(14)
C3	0.3312(4)	0.1959(7)	-0.1651(3)	0.0541(16)
C4	0.2518(3)	0.2096(7)	-0.1118(3)	0.0483(14)
C5	0.2443(3)	0.1363(7)	-0.0380(3)	0.0520(15)
C6	0.1627(4)	0.1366(8)	0.0108(4)	0.0495(15)
C7	0.0265(3)	0.2691(7)	0.0397(3)	0.0739(19)
C8	0.1472(3)	0.4450(6)	-0.2885(3)	0.0443(14)
C9	0.0591(4)	0.4731(6)	-0.2620(3)	0.0534(15)
C10	-0.0079(4)	0.5592(6)	-0.3132(3)	0.0518(15)
C11	0.0110(4)	0.6221(6)	-0.3898(4)	0.0514(15)
C12	0.0996(4)	0.5968(7)	-0.4166(3)	0.0607(17)
C13	0.1651(4)	0.5098(6)	-0.3672(3)	0.0518(15)
C14	-0.1447(4)	0.7276(8)	-0.4257(4)	0.089(2)
C15	0.3559(3)	0.3008(7)	-0.3180(3)	0.0508(15)
C16	0.4476(3)	0.3818(6)	-0.3039(3)	0.0431(14)
C17	0.4789(4)	0.4599(6)	-0.2279(3)	0.0524(16)
C18	0.5656(4)	0.5360(6)	-0.2148(3)	0.0544(16)
C19	0.6210(4)	0.5320(7)	-0.2809(4)	0.0544(16)
C20	0.5908(4)	0.4554(7)	-0.3580(4)	0.0640(17)
C21	0.5048(4)	0.3808(7)	-0.3701(3)	0.0596(17)
C22	0.7385(4)	0.6957(7)	-0.2020(4)	0.0732(18)

Table 2

Selected Bond Lengths (Å)

C1	C2	1.373(6)
C1	O1	1.395(5)
C1	C8	1.429(6)
C2	C3	1.450(7)
C2	C15	1.494(6)
C3	O5	1.222(6)
C3	C4	1.497(6)
C4	C5	1.318(6)
C4	O1	1.369(5)
C5	C6	1.475(6)
C6	O7	1.186(6)
C6	O6	1.322(6)
C7	O6	1.451(5)
C11	O4	1.358(5)
C12	C13	1.347(6)
C14	O4	1.440(5)
C15	O2	1.218(5)
C19	O3	1.368(6)
C19	C20	1.372(7)
C22	O3	1.410(6)

(s, 9H, OCH_3); ^{13}C nmr (deuteriochloroform): δ 190.44 (Ar-*C*O), 186.18 (C3'=O), 179.34 (C1=O), 166.69, 166.64 165.97, 153.33, 134.27, 133.73, 131.65, 120.72, 116.79, 116.67, 116.03, 102.07 (C=C, arom. and aliph.), 57.68, 57.58, 54.33 ppm (OCH_3).

Table 3

Selected Bond Angles (°)

C2	C1	O1	111.1(5)
C2	C1	C8	135.2(5)
O1	C1	C8	113.7(4)
C1	C2	C3	107.7(4)
C1	C2	C15	128.6(5)
C3	C2	C15	123.5(5)
O5	C3	C2	131.2(5)
O5	C3	C4	124.3(5)
C2	C3	C4	104.5(5)
C5	C4	O1	125.4(4)
C5	C4	C3	126.6(5)
O1	C4	C3	107.9(5)
C4	C5	C6	127.4(5)
O7	C6	O6	124.1(5)
O7	C6	C5	123.2(6)
O6	C6	C5	112.7(5)
O4	C11	C10	125.5(5)
O4	C11	C12	114.9(5)
O2	C15	C16	122.4(4)
O2	C15	C2	119.3(5)
O3	C19	C20	115.7(5)
O3	C19	C18	123.7(5)
C20	C19	C18	120.6(5)
C4	O1	C1	108.7(4)
C19	O3	C22	118.6(4)
C11	O4	C14	117.6(4)
C6	O6	C7	116.2(4)

Anal. Calcd. for $C_{22}H_{18}O_7$: C, 67.00; H, 4.60. Found: C, 66.97; H, 4.69.

General Synthesis of **5**.

A solution of **3** (3.94 g, 10.0 mmoles) and primary amine (**4a-k**) (10.0 mmoles) in dry benzene was refluxed for 30 min. After the solvent was removed by evaporation, the oily residue was treated with dry diethyl ether to obtian the corresponding crude pyrrolone, which was purified by recrystallization.

Methyl (*RS*)-[2,3-Dihydro-2-hydroxy-4-(4-methoxybenzoyl)-5-(4-methoxyphenyl)-1-phenyl-3-oxo-1*H*-pyrrol-2-yl]acetate (**5a**).

Compound **5a** was obtained from **3** and aniline **4a** (0.93 g, 0.91 ml, 10 mmoles). The yield 3.36 g (69%), mp 187° (chloroform/cyclohexane, 1:4); ir: 3231 (br, OH), 1728 (C1=O), 1657 (Ar-CO), 1629 (C3'=O), 1253 cm^{-1} (C1-O-CH_3); ^1H nmr (deuteriochloroform): δ 7.90-6.62 (m, 5H, Ar-H), 5.78 (s, 1H, OH), 3.82, 3.70, 3.56 (s, 9H, OCH_3), 3.13, 3.04, 2.74, 2.65 (q, J_{gem} = 16.9 Hz, 2H, CH_2); ^{13}C nmr (deuteriochloroform): δ 196.59 (C3'=O), 191.34 (Ar-*C*O), 180.22 (C1=O), 165.22, 163.47, 143.88, 138.89, 134.35, 133.57, 133.50, 130.95, 130.35, 128.57, 123.37, 115.65, 115.25, 112.92 (C=C, arom. and aliph.), 91.43 (C2_), 57.40, 57.21, 53.87 (OCH_3), 41.28 ppm (C2).

Anal. Calcd. for $C_{28}H_{25}NO_7$: C, 68.98; H, 5.17; N, 2.87; Found: C, 68.82; H, 5.14; N, 2.95.

Methyl (*RS*)-[2,3-Dihydro-2-hydroxy-4-(4-methoxybenzoyl)-5-(4-methoxyphenyl)-1-(4-methylphenyl)-3-oxo-1*H*-pyrrol-2-yl]-acetate (**5b**).

Compound **5b** was obtained from **3** and 4-methylaniline (**4b**) (1.07 g, 10 mmoles). The yield 2.86 g (57%), mp 188° (ethanol); ir: 3263 (br, OH), 1729 (C1=O), 1698 (Ar-CO), 1635 (C3'=O), 1255

cm^{-1} (C1-O-CH_3); ^1H nmr (deuteriochloroform): δ 7.90-6.63 (m, 12H, Ar-H), 5.73 (s, 1H, OH), 3.82, 3.71, 3.57 (s, 9H, OCH_3), 3.11, 3.02, 2.74, 2.65 (q, J_{gem} = 16.7 Hz, 2H, CH_2), 2.28 ppm (s, 3H, Ar-CH_3); ^{13}C nmr (deuteriochloroform): δ 196.52 (C3'=O), 191.24 (Ar-*C*O), 180.38 (C1=O), 165.14, 163.38, 139.52, 135.89, 134.32, 133.82, 133.46, 131.76, 131.82, 130.14, 123.49, 115.61, 115.40, 112.87 (C=C, arom. and aliph.), 91.38 (C2'), 57.38, 57.22, 53.88 (OCH_3), 41.29 (C2), 23.12 ppm (Ar-CH_3).

Anal. Calcd. for $C_{29}H_{27}NO_7$: C, 69.45; H, 5.43; N, 2.79; Found: C, 69.51; H, 5.49; N, 2.84.

Methyl (*RS*)-[1-(4-Bromophenyl)-2,3-dihydro-2-hydroxy-4-(4-methoxybenzoyl)-5-(4-methoxyphenyl)-3-oxo-1*H*pyrrol-2-yl]-acetate (**5c**).

Compound **5c** was obtained from **3** (10 mmoles) and 4-bromoaniline (**4c**) (1.72 g, 10 mmoles). The yield 3.06 g (54%), mp 182° (ethanol); ir: 3291 (br, OH), 1729 (C1=O), 1702 (Ar-CO), 1632 (C3'=O), 1251 cm^{-1} (C1-O-CH_3); ^1H nmr (deuteriochloroform): δ 7.86-6.84 (m, 12H, Ar-H), 6.07 (s, 1H, OH), 3.82, 3.72, 3.57 (s, 9H, OCH_3), 3.16, 3.07, 2.72, 2.64 ppm (q, J_{gem} = 16.8 Hz, 2H, CH_2); ^{13}C nmr (deuteriochloroform): δ 196.58 (C3'=O), 191.45 (Ar-*C*O), 178.73 (C1=O), 165.33, 163.82, 137.86, 134.37, 134.12, 133.43, 133.35, 131.83, 123.38, 123.08, 115.84, 115.30, 113.42 (C=C, arom. and aliph.), 91.47 (C2'), 57.42, 57.27, 53.90 (OCH_3), 41.28 ppm (C2).

Anal. Calcd. for $C_{28}H_{24}BrNO_7$: C, 59.38; H, 4.27; N, 2.47; Found: C, 59.29; H, 4.29; N, 2.36.

Methyl (*RS*)-[2,3-Dihydro-2-hydroxy-1-(4-iodophenyl)-4-(4-methoxybenzoyl)-5-(4-methoxyphenyl)-3-oxo-1*H*pyrrol-2-yl]-acetate (**5d**).

Compound **5d** was obtained from **3** and 4-iodoaniline (**4d**) (2.19 g, 10 mmoles). The yield 4.48 g (73%), mp 183-185° (1-butanol); ir: 3302 (br, OH), 1728 (C1=O), 1701 (Ar-CO), 1629 (C3'=O), 1251 cm^{-1} (C1-O-CH_3). ^1H nmr (deuteriochloroform): δ 7.86-6.64 (m, 12H, Ar-H), 6.06 (s, 1H, OH), 3.83, 3.72, 3.57 (s, 9H, OCH_3), 3.15, 3.09, 2.72, 2.64 ppm (q, J_{gem} = 17.0 Hz, 2H, CH_2); ^{13}C nmr (deuteriochloroform): δ 196.59 (C3'=O), 191.46 (Ar-*C*O), 178.67 (C1=O), 165.33, 163.82, 140.11, 138.58, 134.38, 133.44, 133.32, 131.99, 123.01, 115.88, 115.31, 113.45 (C=C, arom. and aliph.), 91.46 (C2'), 57.44, 57.29, 53.94 (OCH_3), 41.30 ppm (C2).

Anal. Calcd. for $C_{28}H_{24}INO_7$: C, 54.83; H, 3.94; N, 2.28; Found: C, 54.97; H, 4.10; N, 2.12.

Methyl (*RS*)-[2,3-Dihydro-2-hydroxy-4-(4-methoxybenzoyl)-5-(4-methoxyphenyl)-1-(4-methylphenyl)-1-(1-naphthyl)-3-oxo-1*H*-pyrrol-2-yl]acetate (**5e**).

Compound **5e** was obtained from **3** and 1-naphthylamine (**4e**) (1.43 g, 10 mmoles). The yield 3.23 g (60%), mp 117° (carbon tetrachloride); ir: 3427 (br, OH), 1737 (C1=O), 1693 (Ar-CO), 1632 (C3'=O), 1257 cm^{-1} (C1-O-CH_3); ^1H nmr (deuteriochloroform): δ 8.00-6.46 (m, 15H, Ar-H), 5.76 (s, 1H, OH), 3.86, 3.81, 3.58 ppm (s, 9H, OCH_3), 2.93, 2.91, 2.83, 2.82 ppm (q, J_{gem} = 3.7 Hz, 2H, CH_2).

Anal. Calcd. for $C_{32}H_{27}NO_7$: C, 71.50; H, 5.06; N, 2.61; Found: C, 71.20; H, 5.25; N, 2.47.

Methyl (*RS*)-[2,3-Dihydro-2-hydroxy-4-(4-methoxybenzoyl)-5-(4-methoxyphenyl)-1-(2-pyridyl)-3-oxo-1*H*pyrrol-2-yl]acetate (**5f**).

Compound **5f** was obtained from **3** and 2-aminopyridine (**4f**) (0.94 g, 10 mmoles). The yield 3.47 g (71%), mp 124-126° (benzene); ir: 3200 (br, OH), 1742 (C1=O), 1682 (Ar-CO), 1631 (C3'=O), 1255 cm^{-1} (C1-O-CH_3); ^1H nmr (deuteriochloroform): δ 8.30-6.57 (m, 12H, Ar-H), 6.28 (s, 1H, OH), 3.82, 3.73, 3.62 (s, 9H, OCH_3), 3.39, 3.31, 3.13, 3.05 ppm (q, J_{gem} = 16.4 Hz, 2H, CH_2); ^{13}C nmr (deuteriochloroform): δ 195.58 (C3'=O), 190.89 (Ar-*C*O), 177.84 (C1=O), 165.35, 163.74, 153.13, 150.59, 138.81, 134.24, 133.43, 132.84, 130.33, 123.67, 123.48, 118.94, 116.05, 115.33, 101.70 (C=C, arom. and aliph.), 91.28 (C2'), 57.40, 57.29, 53.96 (OCH_3), 42.42 ppm (C2).

Anal. Calcd. for $C_{27}H_{24}N_2O_7$: C, 66.39; H, 4.95; N, 5.73; Found: C, 66.20; H, 4.90; N, 5.54.

Methyl (*RS*)-[2,3-Dihydro-2-hydroxy-1-(2-hydroxy-5-methylphenyl)-4-(4-methoxybenzoyl)-5-(4-methoxyphenyl)-3-oxo-1*H*-pyrrol-2-yl]acetate (**5g**).

Compound **5g** was obtained from **3** and 2-hydroxy-5-methylaniline (**4g**) (1.23 g, 10 mmoles). The yield 3.52 g (68%), mp 186-188° (cyclohexane/methylene chloride, 2:1); ir: 3427 (br, OH), 1737 (C1=O), 1659 (Ar-CO), 1634 (C3'=O), 1260 cm^{-1} (C1-O-CH_3); ^1H nmr (deuteriochloroform): δ 7.85-6.52 (m, 11H, Ar-H), 6.52 (s, 1H, Ar-OH), 5.27 (s, 1H, OH), 3.81, 3.67, 3.59 (s, 9H, OCH_3), 3.23, 3.13, 2.75, 2.66 (q, J_{gem} = 17.2 Hz, 2H, CH_2), 2.10 ppm (s, 3H, Ar-CH_3); ^{13}C nmr (deuteriochloroform): δ 196.44 (C3'=O), 191.87 (Ar-*C*O), 181.86 (C1=O), 165.54, 165.18, 163.81, 153.88, 134.58, 134.22, 133.28, 132.85, 132.58, 132.07, 131.42, 125.26, 122.96, 118.67, 115.81, 113.82 (C=C, arom. and aliph.), 91.48 (C2'), 57.37, 57.20, 53.90 (OCH_3), 40.94 (C2), 22.15 ppm (Ar-CH_3).

Anal. Calcd. for $C_{29}H_{27}NO_8$: C, 67.30; H, 5.26; N, 2.71; Found: C, 67.48; H, 5.21; N, 2.85.

Methyl (*RS*)-[1-(2-Amino-4,5-dimethylphenyl)-2,3-dihydro-2-hydroxy-4-(4-methoxybenzoyl)-5-(4-methoxyphenyl)-3-oxopyrrol-2-yl]acetate (**5h**).

Compound **5h** was obtained from **3** (10 mmole) and 4,5-dimethyl-1,2-benzenediamine (**4h**) (1.36 g, 10 mmoles). The yield 4.51 g (85%), mp 196-198° (benzene/methylene chloride, 2:1); ir: 3500-3200 (br, OH), 3423 (NH_2), 1738 (C1=O), 1690 (Ar-CO), 1632 (C3'=O), 1255 cm^{-1} (C1-O-CH_3); ^1H nmr (deuteriochloroform): δ 7.92-6.62 (m, 10H, Ar-H), 6.26 (s, 1H, OH), 4.43 (br s, 2H, NH_2), 3.83, 3.71, 3.57 (s, 9H, OCH_3), 3.05, 2.97, 2.84, 2.76 (q, J_{gem} = 16.5 Hz, 2H, CH_2), 2.08, 1.90 ppm (s, 6H, Ar-CH_3).

Anal. Calcd. for $C_{30}H_{30}N_2O_7$: C, 67.91; H, 5.70; N, 5.28; Found: C, 67.86; H, 5.76; N, 5.20.

Methyl (*RS*)-[1-(2-Amino-5-methylphenyl)-2,3-dihydro-2-hydroxy-4-(4-methoxybenzoyl)-5-(4-methoxyphenyl)-3-oxo-1*H*-pyrrol-2-yl]acetate (**5i**).

Compound **5i** was obtained from **3** (10 mmoles) and 4-methyl-1,2-benzenediamine, (**4i**) (1.22 g, 10 mmoles). The yield 3.51 g (68%), mp 108-110° (benzene); ir: 3442 (NH_2), 3350-3100 (br, OH), 1735 (C1=O), 1690 (Ar-CO), 1631 (C3'=O), 1255 cm^{-1} (C1-O-CH_3); ^1H nmr (deuteriochloroform): δ 7.81-6.19 (m, 11H, Ar-H), 6.21 (s, 1H, OH), 4.50 (br s, 2H, NH_2), 3.81, 3.70, 3.59 (s, 9H, OCH_3), 3.16, 3.07, 2.81, 2.73 (q, J_{gem} = 16.9 Hz, 2H, CH_2), 1.99 ppm (s, 3H, Ar-CH_3).

Anal. Calcd. for $C_{29}H_{28}N_2O_7$: C, 67.43; H, 5.46; N, 5.42; Found: C, 67.28; H, 5.35; N, 5.32.

Methyl (*RS*)-[2,3-Dihydro-2-hydroxy-4-(4-methoxybenzoyl)-5-(4-methoxyphenyl)-1-methyl-3-oxo-1*H*-pyrrol-2-yl]acetate (**5j**).

Compound **5j** was obtained from **3**, methylamine hydrochloride (**4j**) (0.68 g, 10 mmoles) and sodium hydroxide (0.4 g, 10 mmoles) in water (10 ml). The yield 2.68 g (63%), mp 184-186° (ethanol); ir: 3182 (br, OH), 1728 (C1=O), 1678 (Ar-CO), 1630 (C3'=O), 1255 cm^{-1} (C1-O-CH_3); ^1H nmr (deuteriochloroform): δ 7.62-6.88 (m, 8H, Ar-H), 6.40 (s, 1H, OH), 3.78, 3.74, 3.64 (s, 9H, OCH_3), 3.18, 3.09, 2.97, 2.89 (q, J_{gem} = 14.6 Hz; 2H, CH_2), 3.05 ppm (s, 3H, N-CH_3); ^{13}C nmr (deuteriochloroform): δ 196.25 (C3'=O), 190.53 (Ar-*C*O), 181.89 (C1=O), 164.63, 163.40, 133.85, 133.54, 132.19, 123.38, 115.89, 114.89, 111.49 (C=C, arom. and aliph.), 90.48 (C2_), 57.31, 54.13 (OCH_3), 41.97 (C2), 31.19 ppm (N-CH_3).

Anal. Calcd. for $C_{23}H_{23}NO_7$: C, 64.93; H, 5.45; N, 3.29; Found: C, 64.81; H, 5.41; N, 3.21.

Methyl (*RS*)-[1-Benzyl-2,3-dihydro-2-hydroxy-4-(4-methoxybenzoyl)-5-(4-methoxyphenyl)-3-oxo-1*H*-pyrrol-2-yl]acetate (**5k**).

Compound **5k** was obtained from **3** and benzylamine (**4k**) (1.07 g, 1.1 ml, 10 mmoles). The yield 2.96 g (59%), mp 101-103° (benzene); ir: 3173 (br, OH), 1738 (C1=O), 1687 (Ar-CO), 1632 (C3'=O), 1254 cm^{-1} (C1-O-CH_3); ^1H nmr (deuteriochloroform): δ 7.78-6.76 (m, 13H, Ar-H), 6.29 (s, 1H, OH), 4.77, 4.69, 4.64, 4.56 (q, 2H, Ar-CH_2), 3.77, 3.74, 3.52 (s, 9H, OCH_3), 3.01, 2.93, 2.77, 2.69 ppm (q, J_{gem} = 16.1 Hz, 2H, CH_2); ^{13}C nmr (deuteriochloroform): δ 196.35 (C3'=O), 190.64 (Ar-CO), 183.48 (C1=O), 164.87, 163.33, 138.79, 134.09, 133.53, 131.84, 130.55, 128.59, 116.01, 115.04, 112.97 (C=C, arom. and aliph.), 90.77 (C2'), 57.31, 54.01 (OCH_3), 48.63 (N-CH_2), 42.20 ppm (C2).

Anal. Calcd. for $C_{29}H_{27}NO_7$: C, 69.45; H, 5.43; N, 2.79; Found: C, 69.51; H, 5.37; N, 2.62.

Crystal Data of **3**.

The compound crystallizes in the monoclinic system with space group $P2_1/a$, a = 14.2770(12), b = 8.6646(13), c = 15.3807(14)Å, b = 98.394(4)°, V = 1882.3(4)$Å^3$, Z = 4. The intensity data were collected at room temperature using an Enraf-Nonius CAD 4 diffractometer [12] with MoK_α radiation using $\omega/2\theta$ scan mode. The cell parameters were determined from least-squares analysis using 25 centered reflections. Three standard reflections were periodically measured (every 120 minutes) during data collection and showed no significant intensity variations. The structure was solved by direct methods using the solution program SHELXS97 [13] in the WinGX package [14] and refined using SHELXL97 [13]. All non-hydrogen atoms were refined, first with isotropic and then with anisotropic thermal displacement parameters by full matrix least squares. All hydrogen atoms were placed geometrically and were refined as riding with $U_{iso}(H) = 1.2\ U_{eq}(C)$. The final cycle of the refinement included 263 variable parameters and gave R = 0.051, wR = 0.107, Goodness of fit = 0.97. The minimum and maximum residual elektron densities were -0.180 and 0.212 e$Å^{-3}$, repectively.

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