Monatshefte für Chemie 137, 339–345 (2006)
DOI 10.1007/s00706-006-0437-9

Monatshefte für Chemie
Chemical Monthly
Printed in Austria

Synthesis of 1,5-Disubstituted 3-(4-Hydroxy-6-methyl-2-oxo-2*H*-pyran-3-yl)-2-pyrazolines#

Albert Lévai[1,*] and **József Jekő**[2]

[1] Department of Organic Chemistry, University of Debrecen, P.O. Box 20, H-4010 Debrecen, Hungary
[2] ICN Hungary Co. Ltd., H-4440 Tiszavasvári, Hungary

Received July 21, 2005; accepted August 4, 2005
Published online February 27, 2006

Summary. A series of 1,5-disubstituted 3-(4-hydroxy-6-methyl-2-oxo-2*H*-pyran-3-yl)-2-pyrazolines were synthesized by the reaction of α,β-unsaturated ketones derived from dehydroacetic acid and hydrazine in hot acetic acid or propionic acid. The structures of all new compounds were elucidated by microanalyses, ^{1}H and ^{13}C NMR, IR, and mass spectroscopic measurements.

Keywords. α,β-Unsaturated ketones; Hydrazine; 2-Pyrazolines.

Introduction

3-Acetyl-4-hydroxy-6-methyl-2-oxo-2*H*-pyran (dehydroacetic acid) is a versatile starting material for the synthesis of a wide variety of heterocyclic ring systems [1]. Its reactions providing heterocyclic compounds can be divided into two major categories. In one case the pyrone moiety of the molecule is retained [2], whereas in the other group the pyrone ring is also involved in the reaction [3]. In some cases, the involvement of the pyrone unit in the reaction can be controlled by the reaction conditions [1]. Various derivatives of dehydroacetic acid are also useful substances for synthetic purposes. Among others, α,β-unsaturated ketones derived from dehydroacetic acid [4] are especially convenient intermediates for the preparation of heterocyclic compounds with different ring sizes. The most frequent representatives comprise 2-pyrazolines [4c–f, 5], 2-aryl-7-methylpyrano[4,3-b]pyran-4*H*,5*H*-diones (flavone analogues) [6], benzothiazepines [7], and benzodiazepines [8].

* Corresponding author. E-mail: alevai@puma.unideb.hu
# Dedicated to Prof. Dr. *W. Fleischhacker* on the occasion of his 75th birthday

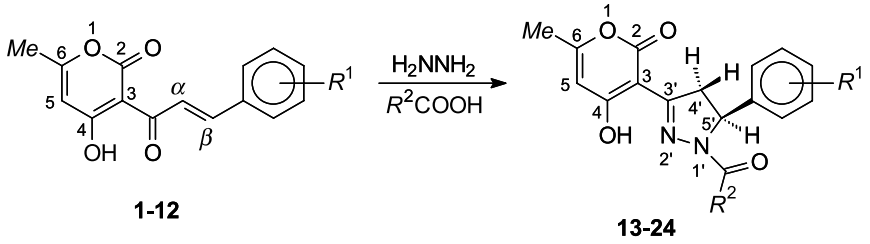
Pyrazolines have been found to possess important bioactivities, *e.g.* antibacterial [9], antiviral [10], antifungal [11], molluscicidal [12], *etc*. activities. Recently, 1-acetyl-3,5-diaryl-2-pyrazolines have been shown to inhibit the monoamine oxidases [13]. All their known pharmaceutical activities rendered them important compounds in drug research. In particular, the 2-pyrazolines proved to be useful pyrazoline type compounds and various methods have been developed for their synthesis [14].

We have been engaged in the synthesis of pyrazolines by the reaction of α,β-unsaturated ketones with diazomethane [15] or hydrazines [16] and prepared numerous 1-pyrazolines and 2-pyrazolines in this way. As a continuation of previous studies, the aim of our present work was to investigate the preparation of 2-pyrazolines bearing a pyrone moiety by the reaction of α,β-unsaturated ketones derived from dehydroacetic acid and hydrazine.

Results and Discussion

1,5-Diphenyl-3-(4-hydroxy-6-methyl-2-oxo-2*H*-pyran-3-yl)-2-pyrazolines were obtained by the reaction of 3-cinnamoyl-4-hydroxy-6-methyl-2-oxo-2*H*-pyrans and arylhydrazines in a mixture of hot ethanol and acetic acid [4c–f, 5]. The pyrone moiety of the starting materials was not involved in the reaction under these conditions. To our knowledge, the reaction of such α,β-unsaturated ketones and hydrazine has not hitherto been investigated. For this reason, we have synthesized the related 2-pyrazolines by reaction of 3-cinnamoyl-4-hydroxy-6-methyl-2-oxo-2*H*-pyrans **1**–**12** with hydrazine. Since the hydrazine may split the pyrone ring [3], we were looking for reaction conditions leaving the pyrone moiety intact. Formation of 2-pyrazolines by the reaction of α,β-unsaturated ketones and hydrazines may take place under various reaction conditions using ethanol [17], acetic acid [18], or pyridine [16d, e] as solvent. According to our preliminary experiments, acetic acid and propionic acid proved to be convenient solvents for this purpose.

3-Cinnamoyl-4-hydroxy-6-methyl-2-oxo-2*H*-pyrans **1**–**12** were allowed to react with hydrazine hydrate in hot acetic acid or propionic acid to yield 2-pyr-



1-12 **13-24**

1,**13:** R^1 = H, R^2 = *Me*
2,**14:** R^1 = 3-*Me*O, R^2 = *Me*
3,**15:** R^1 = 4-*Me*O, R^2 = *Me*
4,**16:** R^1 = 3-Cl, R^2 = *Me*
5,**17:** R^1 = 4-Cl, R^2 = *Me*
6,**18:** R^1 = 4-Br, R^2 = *Me*

7,**19:** R^1 = H, R^2 = *Et*
8,**20:** R^1 = 3-*Me*O, R^2 = *Et*
9,**21:** R^1 = 4-*Me*O, R^2 = *Et*
10,**22:** R^1 = 3-Cl, R^2 = *Et*
11,**23:** R^1 = 4-Cl, R^2 = *Et*
12,**24:** R^1 = 4-Br, R^2 = *Et*

Scheme 1

azolines **13**–**24** in good yields (72–83%) (Scheme 1). It is worth mentioning that under these reaction conditions only one product *viz.* the 1-acylated-2-pyrazoline could be detected by thin layer chromatography. The substitution pattern of the aromatic ring was without influence on the course of the reaction and on the yields of the isolated products.

The structures of all new compounds were elucidated by elemental analyses and combined spectroscopic techniques. The EI 70 eV mass spectra of compounds **13**–**24** are characterized by intense molecular ions. The most important fragmentation process is the loss of *Me*CO (**13**–**18**) or *Et*CO (**19**–**24**) from the molecular ion. This is followed by loss of the *Ph-R* unit resulting in the formation of the $m/z = 193$ ion, which is the base peak in each case. In their IR spectra, a characteristic lactone carbonyl band at around $\bar{\nu} = 1720\,\mathrm{cm}^{-1}$ proves that the pyrone moiety was retained in the course of the reaction. The presence of an amide carbonyl band at about $\bar{\nu} = 1660\,\mathrm{cm}^{-1}$ refers to an *N*-acyl group. A C=N band between $\bar{\nu} = 1570$ and $1580\,\mathrm{cm}^{-1}$ is in harmony with the 2-pyrazoline skeleton. In the ^{1}H NMR spectra of **13**–**24** the protons attached to the C-4′ and C-5′ carbon atoms of the 2-pyrazoline unit (Scheme 1) gave an ABX spin system. Chemical shifts and the coupling constant values (*cf.* Experimental) unambiguously prove the 2-pyrazoline structure. In the ^{1}H NMR spectra of **13**–**18** a singlet signal between $\delta = 2.3$ and 2.4 ppm indicates the presence of an *N*-acetyl group. On the other hand, a triplet (around 1.2 ppm) and a doublet–doublet (approx. 2.7 ppm), signals belonging to an *N*-propionyl unit, were assigned in the ^{1}H NMR spectra of **19**–**24**. In their ^{13}C NMR spectra the chemical shifts of carbon atoms C-3′ (156–157 ppm), C-4′ (about 45 ppm), and C-5′ (57–59 ppm) corroborate the 2-pyrazoline structure deduced from the ^{1}H NMR data. ^{13}C NMR chemical shifts of the carbon atoms of the pyrone unit and the *N*-acetyl or *N*-propionyl groups have also been observed in the ^{13}C NMR spectra of **13**–**24** (*cf.* Experimental). All these methods unequivocally prove the formation of 2-pyrazolines in which the pyrone moiety of the starting material is retained.

Conclusions

We synthesized a series of new 1,5-disubstituted 3-(4-hydroxy-6-methyl-2-oxo-2*H*-pyran-3-yl)-2-pyrazolines by the reaction of 3-cinnamoyl-4-hydroxy-6-methyl-2-oxo-2*H*-pyrans with hydrazine under simple and convenient reaction conditions. These conditions made possible to retain the pyrone moiety of these α,β-unsaturated ketones, which was an aim of our present study. These new 2-pyrazolines are stable compounds which may be benefiacially utilized in drug research.

Experimental

Melting points were determined on a *Kofler* hot-stage apparatus and are uncorrected. ^{1}H and ^{13}C NMR spectra were measured with a Varian Gemini 200 spectrometer at 200/50 MHz in $CDCl_3$ (internal standard *TMS*, $\delta = 0.0$ ppm) at ambient temperature. The IR spectra were obtained with a Perkin-Elmer 16 PC instrument. Mass spectra were recorded on a VG Trio-2 apparatus. Elemental analyses (C, H, N) were measured in-house with a Carlo Erba 1106 EA instrument and were in good agreement ($\pm 0.2\%$) with the calculated values. TLC was performed on Kieselgel 60 F_{254} (Merck) layer using

n-hexane:acetone (7:3, *v*/*v*) or toluene: ethyl acetate (4:1, *v*/*v*) as eluents. Starting materials **1**–**12** were synthesized according to known procedures [4].

*General Method for the Preparation of 2-Pyrazolines **13**–**24***

A mixture of α,β-unsaturated ketone (**1**–**12**, 5.0 mmol), hydrazine hydrate (10.0 mmol), and acetic acid (30 cm^3, in the case of 2-pyrazolines **13**–**18**) or propionic acid (30 cm^3, in the case of 2-pyrazolines **19**–**24**) was refluxed for 3 h, then poured into H_2O. The precipitate was separated by filtration, washed with H_2O, and crystallized from methanol to afford the 2-pyrazolines **13**–**24** (Scheme 1).

3-(1-Acetyl-5-phenyl-4,5-dihydro-1H-pyrazol-3-yl)-4-hydroxy-6-methyl-2H-pyran-2-one (**13**, $C_{17}H_{16}N_2O_4$)

Yield 80%; mp 183–184°C; ^{1}H NMR (200 MHz, $CDCl_3$): $\delta = 2.24$ (s, Me), 2.37 (s, Me), 3.67 (dd, $J = 4.7$, 19.6 Hz, 4′-H_{trans}), 4.01 (dd, $J = 11.8$, 19.6 Hz, 4′-H_{cis}), 5.54 (dd, $J = 4.7$, 11.8 Hz, 5′-H), 6.04 (s, 5-H), 7.19–7.40 (m, 5 arom H), 12.80 (s, OH) ppm; ^{13}C NMR (50 MHz, $CDCl_3$): $\delta = 20.3$, 22.0, 45.2, 58.1, 94.1, 100.8, 125.5, 127.8, 128.9, 141.0, 156.5, 161.9, 165.0, 167.1, 171.9 ppm; IR (KBr): $\bar{\nu} = 1722$, 1669, 1573, 1448, 1425, 1386, 1295, 1232, 1151, 1033, 989, 959, 830, 768, 703 cm^{-1}; MS (EI 70 eV): m/z (%) = 312 (M^+, 28), 269 (23), 235 (20), 193 (100).

3-[1-Acetyl-5-(3-methoxyphenyl)-4,5-dihydro-1H-pyrazol-3-yl]-4-hydroxy-6-methyl-2H-pyran-2-one (**14**, $C_{18}H_{18}N_2O_5$)

Yield 78%; mp 137–138°C; ^{1}H NMR (200 MHz, $CDCl_3$): $\delta = 2.29$ (s, Me), 2.34 (s, Me), 3.61 (dd, $J = 4.8$, 19.6 Hz, 4′-H_{trans}), 3.80 (s, MeO), 4.01 (dd, $J = 11.7$, 19.6 Hz, 4′-H_{cis}), 5.51 (dd, $J = 4.8$, 11.7 Hz, 5′-H), 6.04 (s, 5-H), 6.80–7.27 (m, 4 arom H), 12.74 (s, OH) ppm; ^{13}C NMR (50 MHz, $CDCl_3$): $\delta = 20.2$, 21.9, 45.2, 55.2, 57.9, 94.0, 100.8, 111.5, 112.7, 117.6, 129.9, 142.6, 156.5, 159.9, 161.8, 165.0, 167.0, 171.9 ppm; IR (KBr): $\bar{\nu} = 1718$, 1672, 1575, 1491, 1451, 1428, 1383, 1343, 1297, 1272, 1234, 1041, 991, 862, 818, 779, 695 cm^{-1}; MS (EI 70 eV): m/z (%) = 342 (M^+, 25), 299 (19), 235 (19), 193 (100).

3-[1-Acetyl-5-(4-methoxyphenyl)-4,5-dihydro-1H-pyrazol-3-yl]-4-hydroxy-6-methyl-2H-pyran-2-one (**15**, $C_{18}H_{18}N_2O_5$)

Yield 72%, mp 149–150°C; ^{1}H NMR (200 MHz, $CDCl_3$): $\delta = 2.24$ (s, Me), 2.36 (s, Me), 3.61 (dd, $J = 4.8$, 19.6 Hz, 4′-H_{trans}), 3.80 (s, MeO), 3.98 (dd, $J = 11.6$, 19.6 Hz, 4′-H_{cis}), 5.50 (dd, $J = 4.8$, 11.6 Hz, 5′-H), 6.02 (s, 5-H), 6.86–7.19 (m, 4 arom H), 12.80 (s, OH) ppm; ^{13}C NMR (50 MHz, $CDCl_3$): $\delta = 20.3$, 22.0, 45.0, 55.3, 57.6, 94.1, 100.8, 114.2, 126.9, 133.2, 156.5, 159.1, 164.9, 167.0, 171.9 ppm; IR (KBr): $\bar{\nu} = 1723$, 1664, 1584, 1451, 1422, 1385, 1295, 1251, 1031, 992, 847, 811 cm^{-1}; MS (EI 70 eV): m/z (%) = 342 (M^+, 26), 299 (43), 235 (17), 193 (100).

3-[1-Acetyl-5-(3-chlorophenyl)-4,5-dihydro-1H-pyrazol-3-yl]-4-hydroxy-6-methyl-2H-pyran-2-one (**16**, $C_{17}H_{15}ClN_2O_4$)

Yield 81%, mp 161–162°C; ^{1}H NMR (200 MHz, $CDCl_3$): $\delta = 2.26$ (s, Me), 2.37 (s, Me), 3.59 (dd, $J = 4.9$, 19.6 Hz, 4′-H_{trans}), 4.01 (dd, $J = 11.9$, 19.6 Hz, 4′-H_{cis}), 5.41 (dd, $J = 4.9$, 11.9 Hz, 5′-H), 6.08 (s, 5-H), 7.09–7.20 (m, 4 arom H), 12.69 (s, OH) ppm; ^{13}C NMR (50 MHz, $CDCl_3$): $\delta = 20.2$, 21.9, 45.1, 57.6, 93.9, 100.8, 123.9, 125.6, 128.0, 130.2, 134.7, 143.0, 156.3, 161.8, 165.2, 167.1, 171.9 ppm; IR (KBr): $\bar{\nu} = 1723$, 1667, 1575, 1450, 1421, 1384, 1344, 1297, 1230, 991, 951, 814, 696 cm^{-1}; MS (EI 70 eV): m/z (%) = 346 (M^+, 19), 303 (13), 235 (20), 193 (100).

3-[1-Acetyl-5-(4-chlorophenyl)-4,5-dihydro-1H-pyrazol-3-yl]-4-hydroxy-6-methyl-2H-pyran-2-one (**17**, $C_{17}H_{15}ClN_2O_4$)

Yield 76%; mp 176–177°C; ^{1}H NMR (200 MHz, $CDCl_3$): $\delta = 2.30$ (s, Me), 2.38 (s, Me), 3.62 (dd, $J = 4.9$, 19.6 Hz, 4′-H_{trans}), 4.01 (dd, $J = 11.8$, 19.6 Hz, 4′-H_{cis}), 5.52 (dd, $J = 4.9$, 11.8 Hz, 5′-H), 6.09 (s, 5-H), 7.12–7.38 (m, 4 arom H), 12.70 (s, OH) ppm; ^{13}C NMR (50 MHz, $CDCl_3$): $\delta = 20.3$, 21.9,

45.0, 57.5, 93.9, 100.8, 127.1, 129.1, 133.6, 139.5, 156.4, 161.9, 165.2, 167.0, 172.0 ppm; IR (KBr): $\bar{\nu} = 1724$, 1661, 1578, 1493, 1454, 1421, 1385, 1347, 1297, 1232, 1089, 1038, 990, 960, 830, 696 cm^{-1}; MS (EI 70 eV): m/z (%) = 346 (M^+, 26), 303 (25), 235 (22), 193 (100).

3-[1-Acetyl-5-(4-bromophenyl)-4,5-dihydro-1H-pyrazol-3-yl]-4-hydroxy-6-methyl-2H-pyran-2-one (**18**, $C_{17}H_{15}BrN_2O_4$)
Yield 83%; mp 197–198°C; ^{1}H NMR (200 MHz, $CDCl_3$): $\delta = 2.28$ (s, Me), 2.32 (s, Me), 3.59 (dd, $J = 4.9$, 19.6 Hz, 4′-H_{trans}), 4.00 (dd, $J = 11.8$, 19.6 Hz, 4′-H_{cis}), 5.48 (dd, $J = 4.9$, 11.8 Hz, 5′-H), 6.02 (s, 5-H), 7.10–7.50 (m, 4 arom H), 12.70 (s, OH) ppm; ^{13}C NMR (50 MHz, $CDCl_3$): $\delta = 20.3$, 21.9, 44.9, 57.6, 93.9, 100.8, 121.7, 127.4, 132.0, 140.0, 156.4, 161.9, 165.2, 167.2, 172.0 ppm; IR (KBr): $\bar{\nu} = 1724$, 1662, 1578, 1455, 1420, 1385, 1346, 1297, 1232, 1038, 989, 960, 827, 530 cm^{-1}; MS (EI 70 eV): m/z (%) = 390/392 (M^+, 15/15), 347/349 (8/8), 235 (22), 193 (100).

4-Hydroxy-6-methyl-3-(5-phenyl-1-propionyl-4,5-dihydro-1H-pyrazol-3-yl)-2H-pyran-2-one (**19**, $C_{18}H_{18}N_2O_4$)
Yield 73%; mp 143–144°C; ^{1}H NMR (200 MHz, $CDCl_3$): $\delta = 1.24$ (t, $J = 7.5$ Hz, $CH_2C\underline{H}_3$), 2.22 (s, Me), 2.70 (dd, $J = 7.5$, 14.9 Hz, $C\underline{H}_2CH_3$), 3.62 (dd, $J = 4.9$, 19.5 Hz, 4′-H_{trans}), 4.01 (dd, $J = 11.8$, 19.5 Hz, 4′-H_{cis}), 5.50 (dd, $J = 4.9$, 11.8 Hz, 5′-H), 6.06 (s, 5-H), 7.20–7.41 (m, 5 arom H), 12.81 (s, OH) ppm; ^{13}C NMR (50 MHz, $CDCl_3$): $\delta = 8.5$, 20.3, 27.5, 44.9, 58.3, 94.1, 100.8, 125.5, 127.8, 128.9, 141.2, 156.2, 161.9, 164.9, 170.2, 171.9 ppm; IR (KBr): $\bar{\nu} = 1720$, 1673, 1580, 1452, 1382, 1291, 1230, 1041, 991, 883, 822, 767, 704 cm^{-1}; MS (EI 70 eV): m/z (%) = 326 (M^+, 23), 269 (29), 249 (9), 193 (100).

4-Hydroxy-3-[5-(3-methoxyphenyl)-1-propionyl-4,5-dihydro-1H-pyrazol-3-yl]-6-methyl-2H-pyran-2-one (**20**, $C_{19}H_{20}N_2O_5$)
Yield 78%; mp 126–127°C; ^{1}H NMR (200 MHz, $CDCl_3$): $\delta = 1.26$ (t, $J = 7.5$ Hz, $CH_2C\underline{H}_3$), 2.26 (s, Me), 2.69 (dd, $J = 7.5$, 14.9 Hz, $C\underline{H}_2CH_3$), 3.60 (dd, $J = 4.8$, 19.5 Hz, 4′-H_{trans}), 3.79 (s, MeO), 3.99 (dd, $J = 11.7$, 19.5 Hz, 4′-H_{cis}), 5.49 (dd, $J = 4.8$, 11.7 Hz, 5′-H), 6.04 (s, 5-H), 6.70–7.28 (m, 4 arom H), 12.80 (s, OH) ppm; ^{13}C NMR (50 MHz, $CDCl_3$): $\delta = 8.5$, 20.2, 27.5, 44.9, 55.2, 58.1, 94.1, 100.8, 111.5, 112.7, 117.6, 130.0, 142.8, 156.2, 159.9, 161.9, 164.9, 170.5, 171.9 ppm; IR (KBr): $\bar{\nu} = 1718$, 1671, 1575, 1488, 1448, 1272, 1229, 1137, 1043, 992, 862, 807, 779, 699 cm^{-1}; MS (EI 70 eV): m/z (%) = 356 (M^+, 22), 299 (23), 249 (9), 193 (100).

4-Hydroxy-3-[5-(4-methoxyphenyl)-1-propionyl-4,5-dihydro-1H-pyrazol-3-yl]-6-methyl-2H-pyran-2-one (**21**, $C_{19}H_{20}N_2O_5$)
Yield 82%; mp 173–174°C; ^{1}H NMR (200 MHz, $CDCl_3$): $\delta = 1.20$ (t, $J = 7.5$ Hz, $CH_2C\underline{H}_3$), 2.30 (s, Me), 2.70 (dd, $J = 7.5$, 14.9 Hz, $C\underline{H}_2CH_3$), 3.61 (dd, $J = 4.8$, 19.5 Hz, 4′-H_{trans}), 3.70 (s, MeO), 4.01 (dd, $J = 11.4$, 19.5 Hz, 4′-H_{cis}), 5.49 (dd, $J = 4.8$, 11.4 Hz, 5′-H), 6.07 (s, 5-H), 6.89–7.20 (m, 4 arom H), 12.82 (s, OH) ppm; ^{13}C NMR (50 MHz, $CDCl_3$): $\delta = 8.5$, 20.3, 27.5, 44.8, 55.2, 57.8, 94.1, 100.9, 126.9, 133.4, 156.3, 159.1, 161.9, 164.9, 170.4, 171.9 ppm; IR (KBr): $\bar{\nu} = 1718$, 1665, 1575, 1514, 1452, 1285, 1243, 1183, 1034, 992, 851, 805 cm^{-1}; MS (EI 70 eV): m/z (%) = 356 (M^+, 18), 299 (44), 249 (6), 193 (100).

3-[5-(3-Chlorophenyl-1-propionyl-4,5-dihydro-1H-pyrazol-3-yl]-4-hydroxy-6-methyl-2H-pyran-2-one (**22**, $C_{18}H_{17}ClN_2O_4$)
Yield 81%; mp 161–162°C; ^{1}H NMR (200 MHz, $CDCl_3$): $\delta = 1.22$ (t, $J = 7.5$ Hz, $CH_2C\underline{H}_3$), 2.28 (s, Me), 2.71 (dd, $J = 7.5$, 15.1 Hz, $C\underline{H}_2CH_3$), 3.60 (dd, $J = 5.0$, 19.6 Hz, 4′-H_{trans}), 4.01 (dd, $J = 11.9$, 19.6 Hz, 4′-H_{cis}), 5.47 (dd, $J = 5.0$, 11.9 Hz, 5′-H), 6.07 (s, 5-H), 7.09-7.20 (m, 4 arom H), 11.79 (s, OH) ppm; ^{13}C NMR (50 MHz, $CDCl_3$): $\delta = 8.5$, 20.3, 27.5, 44.9, 57.8, 94.0, 100.9, 123.9, 125.6, 128.0, 130.2, 134.8, 143.3, 156.1, 161.9, 165.1, 170.6, 172.0 ppm; IR (KBr): $\bar{\nu} = 1722$, 1665, 1576, 1447,

1290, 1229, 1201, 1077, 991, 881, 793, 693 cm^{-1}; MS (EI 70 eV): m/z (%) = 360 (M^+, 12), 303 (18), 249 (6), 193 (100).

3-[5-(4-Chlorophenyl)-1-propionyl-4,5-dihydro-1H-pyrazol-3-yl]-4-hydroxy-6-methyl-2H-pyran-2-one (**23**, $C_{18}H_{17}ClN_2O_4$)
Yield 74%; mp 190–191°C; ^{1}H NMR (200 MHz, $CDCl_3$): $\delta = 1.20$ (t, $J = 7.5$ Hz, $CH_2C\underline{H}_3$), 2.30 (s, Me), 2.69 (dd, $J = 7.5$, 14.9 Hz, $C\underline{H}_2CH_3$), 3.59 (dd, $J = 5.1$, 19.6 Hz, 4′-H_{trans}), 4.01 (dd, $J = 11.9$, 19.6 Hz, 4′-H_{cis}), 5.58 (dd, $J = 5.1$, 11.9 Hz, 5′-H), 6.09 (s, 5-H), 7.06–7.38 (m, 4 arom H), 12.69 (s, OH) ppm; ^{13}C NMR (50 MHz, $CDCl_3$): $\delta = 8.4$, 20.3, 27.5, 44.8, 57.7, 93.9, 100.8, 127.0, 129.0, 133.5, 139.7, 156.1, 161.9, 165.1, 170.6, 171.9 ppm; IR (KBr): $\bar{\nu} = 1721$, 1664, 1577, 1556, 1446, 1377, 1292, 1230, 1087, 1040, 991, 832, 802, 693 cm^{-1}; MS (EI 70 eV): m/z (%) = 360 (M^+, 15), 303 (23), 249 (6), 193 (100).

3-[5-(4-Bromophenyl)-1-propionyl-4,5-dihydro-1H-pyrazol-3-yl]-4-hydroxy-6-methyl-2H-pyran-2-one (**24**, $C_{18}H_{17}BrN_2O_4$)
Yield 79%; mp 186–187°C, ^{1}H NMR (200 MHz, $CDCl_3$): $\delta = 1.21$ (t, $J = 7.5$ Hz, $CH_2C\underline{H}_3$), 2.30 (s, Me), 2.68 (dd, $J = 7.5$, 14.9 Hz, $C\underline{H}_2CH_3$), 3.58 (dd, $J = 5.1$, 19.6 Hz, 4′-H_{trans}), 3.99 (dd, $J = 11.9$, 19.6 Hz, 4′-H_{cis}), 5.42 (dd, $J = 5.1$, 11.9 Hz, 5′-H), 6.09 (s, 5-H), 7.10–7.49 (m, 4 arom H), 12.71 (s, OH) ppm; ^{13}H NMR (50 MHz, $CDCl_3$): $\delta = 8.5$, 20.3, 27.5, 44.7, 57.8, 94.0, 100.8, 121.7, 127.4, 132.0, 140.3, 156.1, 161.9, 165.1, 170.6, 171.9 ppm; IR (KBr): $\bar{\nu} = 1721$, 1662, 1579, 1448, 1291, 1229, 1072, 1041, 991, 828, 529 cm^{-1}; MS (EI 70 eV): m/z (%) = 404/406 (M^+, 7/7), 347/349 (12/12), 249 (8), 193 (100).

Acknowledgements

The present study was sponsored by the Hungarian National Research Foundation (Grant No. T 049468) for which our gratitude is expressed. Technical assistance of Mrs. *M. Nagy* is highly appreciated.

References

[1] Prakash O, Kumar A, Singh SP (2004) Heterocycles **63**: 1193
[2] a) Hassan MA, El-Kady M, Abd El-Mohay AA (1982) Ind J Chem **21B**: 372; b) Deshmukh MB, Shinde BS (1995) Ind J Heterocycl Chem **4**: 233; c) Cantos A, De March P, Manas MM, Pla A, Fernando FS, Virgili A (1986) Chem Lett **3**: 295; d) Cantos A, De March P, Manas MM, Pla A, Fernando FS (1987) Bull Chem Soc Jpn **60**: 4425; e) Lowe W (1977) J Heterocycl Chem **14**: 931; f) Siddiq M, Khan AW, Praill PF (1985) J Chem Soc Pak **7**: 59; g) Sosnovskikh VY, Usachev BI, Blinov AG, Kodess MI (2001) Mendeleev Commun **1**: 36; h) Mahesh VK, Gupta RS, Sharma R (1979) Ind J Chem **17B**: 513
[3] a) Gelin S, Chantegrel B, Nadi AI (1983) J Org Chem **48**: 4078; b) Singh SP, Tarar LS, Kumar D (1993) Synth Commun **23**: 1855; c) Inoue A, Iguchi S (1964) Chem Pharm Bull **12**: 381; d) Qayyoom MA, Hanumanthu P, Ratnam CY (1982) Ind J Chem **21B**: 883; e) El-Abbassi M, Djerrari B, Essassi B, Fifani J (1989) Tetrahedron Lett **30**: 7069
[4] a) Wiley RH, Hussung KH, Moffat J (1955) J Am Chem Soc **77**: 5102; b) Birch AJ, Cameron DW, Richards RW (1960) J Chem Soc: 4395; c) Mahesh VK, Gupta RS (1974) Indian J Chem **12B**: 956; d) Mahesh WK, Sharma CL, Washistha S, Sharma R (1979) J Indian Chem Soc **56**: 718; e) Takeuchi N, Nakagawa H, Tobinaga S (1980) Chem Pharm Bull **28**: 3002; f) Hassan MA, El-Kady M, El-Borai M, Zbd El-Moaty AA (1984) Rev Roum Chim **29**: 769
[5] a) Baboulene M, Lattes VSA (1986) J Heterocycl Chem **23**: 1721; b) Mittra AS, Mohanty SK, Sridhar R, Padmanavan SY, Rao S (1977) Ind J Chem **15B**: 1146

[6] Siddiq M, Qamar Y (1988) Ind J Chem **27B**: 373
[7] a) Sucheta K, Prashant A, Rao NR (1995) Ind J Chem **34B**: 893; b) Naragapu L, Narendar R, Sucheta K (2003) Heterocycl Commun **9**: 35
[8] Fodili M, Amari M, Kolli B, Robet A, Baudy Floch M, La Grel P (1999) Synthesis: 811
[9] a) Dee HHO, Abd-El-Rahman AH, Kandeel EM, Ismail EM (1977) Arzneim-Forsch/Drug Res **27**: 2035; b) Khali HZ, Yanni SA (1981) J Ind Chem Soc **58**: 168
[10] Rawal AA, Thakor VM, Shah NM (1963) J Ind Chem Soc **40**: 323
[11] Dhal PN, Acharya TE, Nayak A (1975) J Ind Chem Soc **52**: 1196
[12] a) Mishriky N, Asaad FM, Ibrahim YA, Girgis AS (1996) Pharmazie **51**: 544; b) Mishriky N, Ibrahim YA, Girgis AS, Fawzy NG (1999) Pharmazie **54**: 738
[13] Manna F, Chimenti F, Bolasco A, Secci D, Bizzarri B, Befani O, Turini P, Mondovi B, Alcaro S, Tafi A (2002) Bioorg Med Chem Lett **12**: 3629
[14] a) In: Katritzky AR, Rees CW (eds) (1984) Comprehensive Heterocyclic Chemistry, vol. 5, Pergamon Press, Oxford, p. 167; b) Lévai A (1997) Khim Geterotsikl Soedin: 747; c) Lévai A (2002) J Heterocycl Chem **39**: 1
[15] a) Tőkés A, Szöllősy Á, Tóth G, Lévai A (1983) Acta Chim Hung **112**: 335; b) Tóth G, Szöllősy Á, Lévai A, Kotovych G (1986) J Chem Soc Perkin Trans 2: 1895; c) Tóth G, Lévai A, Duddeck H (1992) Magn Reson Chem **30**: 235; d) Tóth G, Lévai A, Szöllősy Á, Duddeck H (1993) Tetrahedron **49**: 863; e) Lévai A (1995) Monatsh Chem **126**: 1245; f) Lévai A, Cziáky Z, Jekő J, Szabó Z (1996) Ind J Chem **35B**: 1091; g) Lévai A, Patonay T (1999) J Heterocycl Chem **36**: 747; h) Lévai A, Silva AMS, Patonay T, Cavaleiro JAS (1999) J Heterocycl Chem **36**: 1215; i) Lévai A (2002) Org Prep Proced Int **34**: 425; j) Lévai A, Jekő J (2002) J Heterocycl Chem **39**: 1333
[16] a) Lévai A, Szöllősy Á, Tóth G (1985) J Chem Research (S): 392; b) Tóth G, Szöllősy Á, Lóránd T, Kónya T, Szabó D, Földesi A, Lévai A (1989) J Chem Soc Perkin Trans 2: 319; c) Szöllősy Á, Tóth G, Lóránd T, Kónya T, Aradi F, Lévai A (1991) J Chem Soc Perkin Trans 2: 489; d) Lévai A (1998) J Heterocycl Chem **35**: 13; e) Lévai A (1999) Heterocycl Commun **5**: 151; f) Lévai A (2003) Heterocycl Commun **9**: 287; g) Lévai A, Silva AMS, Pinto DCGA, Cavaleiro JAS, Alkorta I, Elguero J, Jekő J (2004) Eur J Org Chem: 4672; h) Lévai A (2005/IX) Arkivoc: 344; i) Lévai A, Jekő J (2005/X) Arkivoc: 199
[17] Sharma TC, Pawar SR, Reddy NJ (1983) Acta Chim Hung **112**: 159
[18] a) Raiford LC, Peterson WJ (1936) J Org Chem **1**: 544; b) Raiford LC, Gundy GV (1938) J Org Chem **3**: 265; c) Weber FG, Brosche K, Seedorf C, Rinow A (1969) Monatsh Chem **100**: 1924; d) Bilgin AA, Palaska E, Sunal R, Gümüsel B (1994) Pharmazie **49**: 67