ХИМИЯ ГЕТЕРОЦИКЛИЧЕСКИХ СОЕДИНЕНИЙ. — 2012. — № 11. — С. 1767—1773

Z. Ghasemi*, M. Eshtad, F. Poorhossain Mejarshin

SYNTHESIS OF NEW *N*-HETEROARYL DERIVATIVES OF 4-PYRONES FROM KOJIC ACID BASED BAYLIS–HILLMAN ACETATES

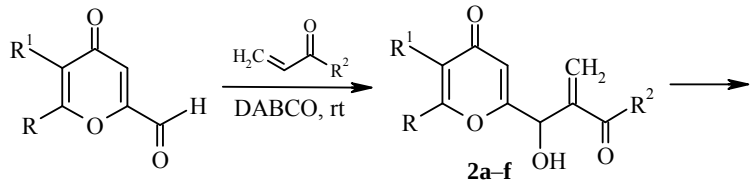
A series of kojic acid benzyl ether derivatives possesing imidazole, benzimidazole, and pyrazole rings were synthesized by S_N2'-substitution of these heterocycles using prepared Baylis–Hillman acetates.

Keywords: *N*-alkylbenzimidazoles, *N*-alkylimidazoles, *N*-alkylpyrazoles, kojic acid, Baylis–Hillman reaction.

Nucleophilic displacement of Baylis–Hillman acetates to obtain a variety of multifunctional allylic derivatives is one of the most straightforward reactions in organic synthesis [1, 2]. These derivatives which are accessible by two possible mechanisms (S_N2 or S_N2'), depending on the reaction conditions, can be used for various further transformations [3–8]. Arylation and heteroarylation of Baylis–Hillman acetates by two above mechanisms or by cross-coupling reactions make them valuable candidates for construction of polycyclic natural, unnatural, and bioactive molecules [9–14].

Kojic acid (5-hydroxy-2-hydroxymethyl-4-pyrone), a natural antioxidant and potent tyrosine inhibitor, has been the subject of several synthetic studies, owing to their various biological properties [15–19]. Benzimidazole, imidazole, and pyrazole are also frequently found in diverse compounds, including biologically and therapeutically active agents, natural products, and functional materials [20–25]. Following upon our recent work on the synthesis of new functional 4-pyrones based on Baylis–Hillman chemistry [26] or cross coupling reactions [27] we report here the synthesis of imidazolyl, benzimidazolyl, and pyrazolyl derivatives of kojic acid by *N*-substitution of these heterocycles with corresponding Baylis–Hillman acetates with a hope that combining the structural properties of these azaaryls with kojic acid backbone will result in the new products with interesting properties.

In this work we firstly report the new Baylis–Hillman reactions of 2-formyl-4-pyrones **1a**,**b**. Reactions of aldehydes **1a**,**b** with alkyl vinyl ketones such as methyl vinyl ketone and ethyl vinyl ketone in THF in the presence of a stoichiometric amount of DABCO at room temperature for 1 h, afforded the adducts **2a**–**d** in good yields (Table 1). In contrast to similar reactions with alkyl acrylates which were carried out in aqueous media [26], reactions of these vinylic ketones were optimized in absolute THF. Treatment of aldehydes **1a**,**b** with butyl acrylate in 1,4-dioxane−water (1:1, v/v) medium gave the alcohols **2e**,**f** in excellent yields (Table 1) as already reported for methyl and ethyl acrylates [26]. Alcohol **2a**, obtained from kojic acid derived aldehyde **1a**, was acetylated with acetyl chloride in dry CH_2Cl_2 in the presence of pyridine to afford acetate **3a**. This product, as well as the acetates **3b**–**d**, resulting from reactions of **1a** with alkyl acrylates (Table 1),



1a (R = H, R^1 = OBn)
1b (R = Ph, R^1 = H)

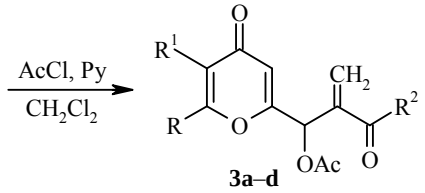


Table 1

Synthesis of Baylis–Hillman alcohols 2a–f and acetates 3a–d

Entry	R	R^1	R^2	Alcohols **2*** (yield, %)	Acetates **3**** (yield, %)
1	H	OBn	Me	**2a** (70)	**3a** (61)
2	Ph	H	Me	**2b** (69)	
3	H	OBn	Et	**2c** (72)	
4	Ph	H	Et	**2d** (74)	
5	H	OBn	OBu	**2e** (80)	**3b** (56)
6	Ph	H	OBu	**2f** (78)	
7	H	OBn	OMe	**2g** (75) [26]	**3c** (67) [26]
8	H	OBn	OEt	**2h** (85) [26]	**3d** (55)

* Conditions of entries 1–4: aldehyde **1a** or **1b** (2 mmol), alkyl vinyl ketone (4 mmol), DABCO (2 mmol), THF (20 ml), rt, 1 h; conditions of entries 5–6: aldehyde **1a** or **1b** (2 mmol), butyl acrylate (6 mmol), DABCO (2 mmol), H_2O–dioxane (1:1, 10 ml), rt, 45 min.

** Conditions: Baylis–Hillman alcohol (2 mmol), acetyl chloride (0.6 ml), pyridine (0.12 ml), abs. CH_2Cl_2 (6 ml), rt, 4 h.

were treated with imidazole, benzimidazole, and 3-methylpyrazole in H_2O–THF to give *N*-allylated compounds containing imidazole **4a**–**c**, benzimidazole **5a**–**c**, and pyrazole **6a**,**b** moieties (Table 2). The nucleophilic attack of imidazole were completed in milder conditions than in the case of benzimidazole and pyrazole rings. Furthermore, reactivity of 3-methylpyrazole at the N-1 position has been observed in other similar conjugative reactions of this reagent [28]. Moreover, all the reactions exhibit excellent *E*/*Z*-selectivity, because no isomeric vinyl and allylic methylene protons in the ^{1}H NMR spectra of the products were observed. The obtained compounds **4a**–**c**, **5a**–**c** and **6a**,**b** have *E* configuration, as it could be expected for *N*-functionalized azaaryls [14].

In summary, some new Baylis–Hillman derivatives of 2-carboxaldehyde-4-pyrones were synthesized. Modification of some Baylis–Hillman acetates containing kojic acid scaffold, by reactions with imidazole, benzimidazole, and 3-methylpyrazole, afforded the *N*-allylated compounds in good yields. Biological activity studies of these compounds are in program.

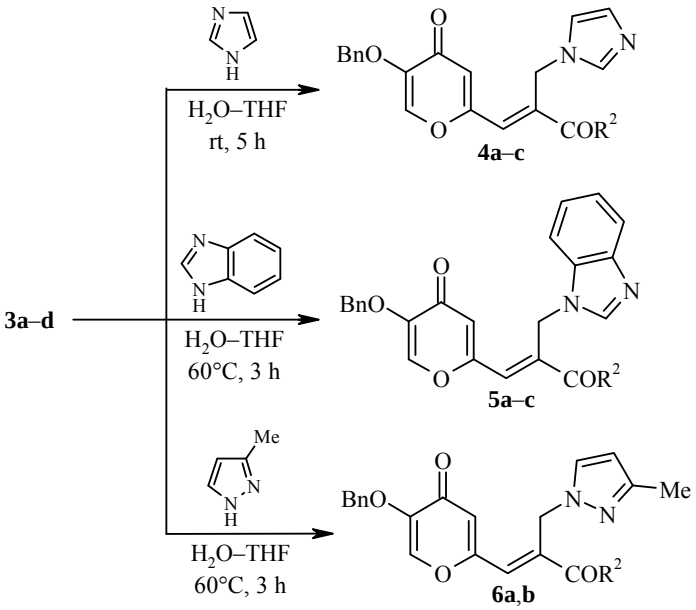


Table 2

Synthesis of *N*-substituted azaaryls 4a–c, 5a–c, and 6a,b

Entry*	R^2	Products (yield, %)
1	OMe	**4a** (73)
2	OEt	**4b** (75)
3	OBu	**4c** (80)
4	OMe	**5a** (85)
5	OEt	**5b** (79)
6	OBu	**5c** (88)
7	Me	**6a** (77)
8	OEt	**6b** (76)

* Conditions: acetate **3a–d** (1 mmol), hetarene (1.2 mmol), H_2O (2 ml), THF (10 ml), rt, 5 h (entries 1–3) or 60°C, 3 h (entries 4–8).

EXPERIMENTAL

FT-IR spectra were obtained on a Bruker Tensor 27 spectrometer. ^1H and ^{13}C NMR spectra were recorded on a Bruker Spectrospin Avance 400 spectrometer (400 and 100 MHz respectively) in $CDCl_3$, residual solvent peaks were used as standard (7.26 ppm for ^1H, 76.0 ppm for ^{13}C). Elemental analyses were performed on Vario EL III apparatus (Elementar Co.). Melting points were determined on a Electrothermal MEL-TEMP apparatus (model 1202D) and are uncorrected. Preparative thin layer chromatographies were done with prepared glass-backed plates (20 × 20 cm, 500 μ) using silica gel (Merk Kieselgel 60 $PF_{254+366}$). All reagents were purchased from Merck organics. The solvents were purified and dried according to the literature [29].

Synthesis of Baylis–Hillman adducts 2a–d (General Method). To a solution of aldehyde **1a**,**b** (2 mmol) and DABCO (0.224 g, 2 mmol) in THF (20 ml), alkyl vinyl ketones (4 mmol) are added, and the solution is stirred at room temperature for 1 h. The mixture is concentrated by a rotary evaporator, and the crude residue is purified by preparative TLC (CH_2Cl_2–MeOH, 30:1) to give pure products **2a**–**d**.

5-Benzyloxy-2-[(1-hydroxy-2-methylidene-3-oxo)butyl]-4*H*-pyran-4-one (2a). Yield 0.42 g (70%). White solid. Mp 99–100°C. IR spectrum, ν, cm^{-1}: 3321 (br, OH), 3095, 3012, 2930, 1698, 1642, 1205. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 2.48 (3H, s, CH_3); 4.54 (1H, d, *J* = 6.7, OH); 5.46 (1H, d, *J* = 6.7, C<u>H</u>OH); 5.13 (2H, s, PhC<u>H</u>$_2$O); 6.33 (1H, s) and 6.44 (1H, s, =CH_2); 6.62 (1H, s, H-3); 7.40–7.51 (5H, m, H Ph); 7.61 (1H, s, H-6). ^{13}C NMR spectrum, δ, ppm: 25.1; 68.9; 70.9; 111.8; 126.7; 127.4; 127.7; 128.2; 134.6; 140.2; 144.5; 146.1; 165.6; 173.7; 198.4. Found, %: C 67.71; H 5.62. $C_{17}H_{16}O_5$. Calculated, %: C 67.99; H 5.37.

2-[(1-Hydroxy-2-methylidene-3-oxo)butyl]-6-phenyl-4*H*-pyran-4-one (2b). Yield 0.37 g (69%). White solid. Mp 94–96°C. IR spectrum, ν, cm^{-1}: 3244 (br, OH), 3094, 2925, 1697, 1653, 1403. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 2.40 (3H, s, CH_3); 4.54 (1H, d, *J* = 6.7, OH); 5.50 (1H, d, *J* = 6.7, C<u>H</u>OH); 6.34 (1H, d, *J* = 0.6) and 6.39 (1H, s, =CH_2); 6.48 (1H, d, *J* = 1.9, H-5); 6.65 (1H, d, *J* = 1.9, H-3); 7.41–7.49 (3H, m, H Ph); 7.65–7.67 (2H, m, H Ph). ^{13}C NMR spectrum, δ, ppm: 25.2; 68.6; 109.9; 111.7; 124.8; 127.9; 128.0; 129.9; 130.5; 145.1; 162.5; 166.8; 179.5; 198.1. Found, %: C 71.38; H 5.43. $C_{16}H_{14}O_4$. Calculated, %: C 71.10; H 5.22.

5-Benzyloxy-2-[(1-hydroxy-2-methylidene-3-oxo)pentyl]-4*H*-pyran-4-one (2c). Yield 0.45 g (72%). White solid. Mp 58–60°C. IR spectrum, ν, cm^{-1}: 3328 (br, OH), 3096, 3012, 2980, 1689, 1642, 1452, 1253. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.03 (3H, t, *J* = 7.2, CH_2C<u>H</u>$_3$); 2.73 (2H, q, *J* = 7.2, C<u>H</u>$_2$$CH_3$); 4.31 (1H, br. s, OH); 4.99 (2H, s, PhC<u>H</u>$_2$O); 5.30 (1H, d, *J* = 5.8, C<u>H</u>OH); 6.13 (1H, s) and 6.28 (1H, s, =CH_2); 6.48 (1H, s, H-3); 7.29–7.35 (5H, m, H Ph); 7.47 (1H, s, H-6). ^{13}C NMR spectrum, δ, ppm: 6.8; 30.1; 68.8; 70.8; 111.6; 126.6; 126.7; 127.3; 127.6; 134.6; 140.2; 144.1; 146.0; 166.2; 173.9; 200.9. Found, %: C 68.57; H 6.05. $C_{18}H_{18}O_5$. Calculated, %: C 68.78; H 5.77.

2-[(1-Hydroxy-2-methylidene-3-oxo)pentyl]-6-phenyl-4*H*-pyran-4-one (2d). Yield 0.42 g (74%). White solid. Mp 70–72°C. IR spectrum, ν, cm^{-1}: 3338 (br, OH), 3033, 2960, 1699, 1644, 1202. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.09 (3H, t, *J* = 7.2, CH_2C<u>H</u>$_3$); 2.78 (2H, q, *J* = 7.2, C<u>H</u>$_2$$CH_3$); 4.32 (1H, br. s, OH); 5.50 (1H, s, C<u>H</u>OH); 6.26 (1H, d, *J* = 0.4) and 6.37 (1H, s, =CH_2); 6.50 (1H, d, *J* = 1.9, H-5); 6.68 (1H, d, *J* = 1.9, H-3); 7.44–7.49 (3H, m, H Ph); 7.65–7.68 (2H, m, H Ph). ^{13}C NMR spectrum, δ, ppm: 6.9; 30.3; 69.3; 110.1; 111.7; 124.8; 126.7; 128.0; 129.9; 130.5; 144.4, 162.4; 166.7; 179.4; 201.1. Found, %: C 71.59; H 5.38. $C_{17}H_{16}O_4$. Calculated, %: C 71.82; H 5.67.

Synthesis of Baylis–Hillman adducts 2e,f (General Method). To a solution of aldehydes **1a**,**b** (2 mmol) and DABCO (0.224 g, 2 mmol) in dioxane−H_2O (1:1, 10 ml), butyl acrylate (6 mmol) is added and the solution is stirred at room temperature for 45 min. After adding water (100 ml), the mixture is extracted with EtOAc (4 × 30 ml). The combined organic extract is washed with H_2O (100 ml), dried over Na_2SO_4, and concentrated to dryness. The crude residue is purified by preparative TLC (acetone−$CHCl_3$−*n*-hexane, 1:1:2) to give products **2e**,**f**.

2-[(5-Benzyloxy-4-oxo-4*H*-pyran-2-yl)hydroxymethyl]acrylic acid butyl ester (2e). Yield 0.57 g (80%). White solid. Mp 80–84°C. IR spectrum, ν, cm^{-1}: 3415 (br, OH), 3093, 2959, 1715 (ester C=O), 1643 (pyrone C=O), 1202. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 0.91 (3H, t, *J* = 7.1, $(CH_2)_3C$<u>H</u>$_3$); 1.31–1.40 (2H, m, CH_2CH_2C<u>H</u>$_2CH_3$); 1.58–1.65 (2H, m, CH_2C<u>H</u>$_2CH_2CH_3$); 3.92 (1H, d, *J* = 7.3, OH); 4.16 (2H, t, *J* = 6.6, $COOCH_2$); 5.03 (2H, s, PhC<u>H</u>$_2$O); 5.25 (1H, d, *J* = 7.3, C<u>H</u>OH); 5.97 (1H, s, H-3); 6.43 (1H, s) and 6.54 (1H, s, =CH_2); 7.31–7.38 (5H, m, H Ph); 7.49 (1H, s, H-6). ^{13}C NMR spectrum, δ, ppm: 12.6; 18.1; 29.4; 64.3; 69.5; 70.8; 111.8; 126.7; 127.4; 127.6; 127.7; 134.6; 136.7; 140.2; 146.12, 164.5; 165.4; 173.7. Found, %: C 67.14; H 6.13. $C_{20}H_{22}O_6$. Calculated, %: C 67.03; H 6.19.

2-[Hydroxy(4-oxo-6-phenyl-4*H*-pyran-2-yl)methyl]acrylic acid butyl ester (2f). Yield 0.51 g (78%). White solid. Mp 92–94°C. IR spectrum, ν, cm^{-1}: 3296 (br, OH), 2960, 1715 (ester C=O), 1655 (pyrone C=O), 1452, 1329, 1219. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 0.85 (3H, t, *J* = 7.3, $(CH_2)_3C$<u>H</u>$_3$); 1.30–1.39 (2H, m, CH_2CH_2C<u>H</u>$_2CH_3$); 1.57–1.54 (2H, m, CH_2C<u>H</u>$_2CH_2CH_3$); 4.14 (2H, t, *J* = 6.6, $COOCH_2$); 5.13 (1H, br. s, OH); 5.47 (1H, s, C<u>H</u>OH); 6.15 (1H, s, H-5); 6.51 (2H, s, =CH_2); 6.64 (1H, d, *J* = 2.1, H-3); 7.39–7.47 (3H, m, H Ph); 7.64–7.66 (2H, m, H Ph). ^{13}C NMR spectrum, δ, ppm: 12.5; 18.0; 29.4; 64.1; 68.8; 109.8; 111.7; 124.8; 126.3; 127.9; 129.7; 130.4; 137.5; 162.7; 164.5; 167.0; 179.6. Found, %: C 69.25; H 6.26. $C_{19}H_{20}O_5$. Calculated, %: C 69.50; H 6.14.

Synthesis of Baylis–Hillman acetates 3a–d (General Method). The crude alcohols **2a**,**e**,**g**,**h** (2.0 mmol) are dissolved in dry CH_2Cl_2 (6 ml). Acetyl chloride (0.6 ml, 8.4 mmol) and pyridine (0.12 ml, 1.5 mmol) are added, and the solution is stirred at room temperature for 4 h. The mixture is concentrated by a rotary evaporator, and the residue is purified by preparative TLC (acetone–*n*-hexane, 1:3) to give acetates **3a**–**d**.

1-(5-Benzyloxy-4-oxo-4*H*-pyran-2-yl)-2-methylidene-3-oxobutyl acetate (3a) obtained from alcohol **2a**. Yield 0.42 g (61%). Colorless liquid. IR spectrum, ν, cm^{-1}: 3090, 2928, 1752, 1679, 1652, 1594. ^{1}H NMR spectrum, δ, ppm: 2.11 (3H, s, CH_3); 2.35 (3H, s, CH_3); 5.01 (2H, s, PhC$\underline{H}_2$O); 6.13 (1H, s, C$\underline{H}$OAc); 6.34 (1H, s) and 6.39 (1H, s, =CH_2); 6.46 (1H, s, H-3); 7.29–7.37 (5H, m, H Ph); 7.50 (1H, s, H-6). ^{13}C NMR spectrum, δ, ppm: 19.6; 24.6; 67.1; 70.8; 112.9; 126.6; 126.7; 127.3; 127.6; 134.5; 140.1; 142.3; 146.2; 161.8; 167.7; 173.2; 195.4. Found, %: C 66.34; H 5.41. $C_{19}H_{18}O_6$. Calculated, %: C 66.66; H 5.30.

2-[Acetyloxy(5-benzyloxy-4-oxo-4*H*-pyran-2-yl)methyl]acrylic acid butyl ester (3b) obtained from alcohol **2e**. Yield 0.45 g (56%). White solid. Mp 110–112°C. IR spectrum, ν, cm^{-1}: 3088, 2915, 1748, 1720, 1649, 1570. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 0.87 (3H, t, *J* = 7.1, $(CH_2)_3C\underline{H}_3$); 1.27–1.38 (2H, m, $CH_2CH_2C\underline{H}_2CH_3$); 1.52–1.64 (2H, m, $CH_2C\underline{H}_2CH_2CH_3$); 2.12 (3H, s, $OCOCH_3$); 4.18 (2H, t, *J* = 6.6, $COOCH_2$); 5.04 (2H, s, PhC$\underline{H}_2$O); 5.78 (1H, s, C$\underline{H}$OAc); 6.39 (1H, s) and 6.45 (1H, s, =CH_2); 6.53 (1H, s, H-3); 7.28–7.36 (5H, m, H Ph); 7.49 (1H, s, H-6). ^{13}C NMR spectrum, δ, ppm: 12.5; 18.1; 19.6; 29.3; 64.4; 69.5; 70.8; 112.8; 126.6; 126.7; 127.4; 127.6; 134.5; 140.1; 142.3; 146.2; 161.5; 162.5; 168.4; 173.7. Found, %: C 65.65; H 6.13. $C_{22}H_{24}O_7$. Calculated, %: C 65.99; H 6.04.

2-[Acetyloxy(5-benzyloxy-4-oxo-4*H*-pyran-2-yl)methyl]acrylic acid ethyl ester (3d) obtained from alcohol **2h**. Yield 0.41 g (55%). Colorless liquid. IR spectrum, ν, cm^{-1}: 3084, 2982, 1752, 1722, 1650, 1445, 1219. ^{1}H NMR spectrum, δ, ppm (*J,* Hz): 1.23 (3H, t, *J* = 7.1, $CH_2C\underline{H}_3$); 2.12 (3H, s, $OCOCH_3$); 4.18 (2H, q, *J* = 7.1, $C\underline{H}_2CH_3$); 5.02 (2H, s, PhC$\underline{H}_2$O); 5.91 (1H, s, C$\underline{H}$OAc); 6.39 (1H, s) and 6.44 (1H, s, =CH_2); 6.50 (1H, s, H-3); 7.29–7.37 (5H, m, H Ph); 7.51 (1H, s, H-6). ^{13}C NMR spectrum, δ, ppm: 12.9; 19.5; 60.4; 67.9; 70.7; 113.0; 126.6; 127.3; 127.5; 127.6; 134.3; 134.4; 140.1; 146.2; 161.5; 162.9; 167.7; 173.2. Found, %: C 64.25; H 5.13. $C_{20}H_{20}O_7$. Calculated, %: C 64.51; H 5.41.

Synthesis of compounds 4a–c, 5a–c, 6a,b (General Method). To a solution of Baylis–Hillman acetate **3a**–**d** (1 mmol) in THF–H_2O (5:1, 12 ml), imidazole, benzimidazole or 3-methylpyrazole (1.2 mmol) are added. The resulting mixture is stirred (5 h at rt for imidazole and 3 h at 60°C for benzimidazole and 3-methylpyrazole). After concentration by removal of the THF, the reaction mixture is extracted with EtOAc (3 × 10 ml). The organic phase is washed with brine (10 ml) and dried over Na_2SO_4. The solvents are removed under reduced pressure to give the crude product which is purified by preparative TLC using *n*-hexane–acetone (2:1) as eluent.

(*E*)-3-[5-Benzyloxy-4-oxo-4*H*-pyran-2-yl]-2-[(imidazol-1-yl)methyl]acrylic acid methyl ester (4a). Yield 0.27 g (73%). White solid. Mp 116–118°C. IR spectrum, ν, cm^{-1}: 3070, 2926, 1720, 1641, 1443, 1091. ^{1}H NMR spectrum, δ, ppm: 3.84 (3H, s, CH_3); 5.12 (2H, s, PhC$\underline{H}_2$O); 5.20 (2H, s, CH_2N); 6.58 (1H, s, H-3); 6.93 (1H, br. s, H-4 Im); 7.06 (1H, br. s, H-5 Im); 7.27 (1H, s, –C$\underline{H}$=CCOOMe); 7.29–7.37 (5H, m, H Ph); 7.53 (1H, s, H-2 Im); 7.75 (1H, s, H-6). ^{13}C NMR spectrum, δ, ppm: 41.7; 52.2; 70.9; 118.2; 119.7; 126.8; 127.2; 127.5; 127.8; 129.9; 130.9; 131.6; 134.1; 139.6; 146.9; 156.9; 164.6; 172.8. Found, %: C 65.32; H 4.80; N 7.49. $C_{20}H_{18}N_2O_5$. Calculated, %: C 65.57; H 4.95; N 7.65.

(*E*)-3-[5-Benzyloxy-4-oxo-4*H*-pyran-2-yl]-2-[(imidazol-1-yl)methyl]acrylic acid ethyl ester (4b). Yield 0.29 g (75%). White solid. Mp 107–109°C. IR spectrum, ν, cm^{-1}: 3072, 2930, 1722, 1644, 1450, 1089. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.25 (3H, t, *J* = 7.1, $CH_2C\underline{H}_3$); 4.23 (2H, q, *J* = 7.1, $C\underline{H}_2CH_3$); 5.09 (2H, s, PhC$\underline{H}_2$O); 5.23 (2H, s, CH_2N); 6.64 (1H, s, H-3); 6.92 (1H, br. s, H-4 Im); 7.03 (1H, s, H-5 Im); 7.25 (1H, s, –C$\underline{H}$=CCOOEt); 7.28–7.37 (5H, m, H Ph); 7.54 (1H, s, H-2 Im); 7.76 (1H, s, H-6). ^{13}C NMR spectrum, δ, ppm: 12.7; 40.3; 61.6; 70.8; 118.3; 119.6; 126.7; 127.0; 127.4; 127.9; 129.9; 130.9; 131.5; 134.0; 139.5; 146.8; 156.7; 164.7; 172.8. Found, %: C 66.02; H 5.13; N 7.09. $C_{21}H_{20}N_2O_5$. Calculated, %: C 66.31; H 5.30; N 7.36.

(*E*)-3-[(5-Benzyloxy-4-oxo-4*H*-pyran-2-yl)]-2-[(imidazol-1-yl)methyl]acrylic acid butyl ester (4c). Yield 0.33 g (80%). White solid. Mp 123–124°C. IR spectrum, ν, cm^{-1}: 3068, 2927, 2862, 1715, 1645, 1456, 1261, 1091. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 0.87 (3H, t, *J* = 7.4, $(CH_2)_3C\underline{H}_3$); 1.26–1.32 (2H, m, $CH_2CH_2C\underline{H}_2CH_3$); 1.56–1.63 (2H, m, $CH_2C\underline{H}_2CH_2CH_3$); 4.15 (2H, t, *J* = 6.7, $COOCH_2$); 5.04 (2H, s, $PhC\underline{H}_2O$); 5.11 (2H, s, CH_2N); 6.51 (1H, s, H-3); 6.85 (1H, br. s, H-4 Im); 6.98 (1H, br. s, H-5 Im); 7.20 (1H, s, –C<u>H</u>=CCOOBu); 7.26–7.38 (5H, m, H Ph); 7.60 (1H, s, H-2 Im); 7.65 (1H, s, H-6). ^{13}C NMR spectrum, δ, ppm: 12.6; 18.0; 29.4; 41.6; 65.4; 70.9; 118.3; 119.6; 126.8; 127.1; 127.6; 127.8; 129.8; 131.3; 131.4; 134.1; 139.5; 146.9; 157.0; 164.2; 172.8. Found, %: C 67.29; H 5.63; N 6.77. $C_{23}H_{24}N_2O_5$. Calculated, %: C 67.63; H 5.92; N 6.86.

(*E*)-2-[(Benzimidazol-1-yl)methyl]-3-[(5-benzyloxy-4-oxo-4*H*-pyran-2-yl)]acrylic acid methyl ester (5a). Yield 0.35 g (85%). White solid. Mp 120–122°C. IR spectrum, ν, cm^{-1}: 3070, 2859, 1719, 1640, 1444, 1264. ^{1}H NMR spectrum, δ, ppm: 3.78 (3H, s, $COOCH_3$); 5.09 (2H, s, $PhC\underline{H}_2O$); 5.43 (2H, s, CH_2N); 6.61 (1H, s, H-3); 7.29–7.34 (4H, m, H Ar); 7.35–7.41 (5H, m, H Ph); 7.60 (1H, s, H-6); 7.80 (1H, s, –C<u>H</u>=CCOOMe); 8.10 (1H, br. s, H-2'). ^{13}C NMR spectrum, δ, ppm: 40.1; 52.2; 70.9; 108.6; 119.2; 119.8; 121.7; 122.5; 126.8; 127.3; 127.6; 127.8; 130.8; 131.6; 132.9; 134.1; 139.5; 142.5; 146.9; 156.9; 164.6; 172.9. Found, %: C 68.98; H 4.53; N 6.97. $C_{24}H_{20}N_2O_5$. Calculated, %: C 69.22; H 4.84; N 6.73.

(*E*)-2-[(Benzimidazol-1-yl)methyl]-3-[(5-benzyloxy-4-oxo-4*H*-pyran-2-yl)]acrylic acid ethyl ester (5b). Yield 0.34 g (79%). White solid. Mp 118–120°C. IR spectrum, ν, cm^{-1}: 3063, 2963, 1714, 1644, 1454, 1251, 1204. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.26 (3H, t, *J* = 7.1, $CH_2C\underline{H}_3$); 4.22 (2H, q, *J* = 7.1, $C\underline{H}_2CH_3$); 5.09 (2H, s, $PhC\underline{H}_2O$); 5.44 (2H, s, CH_2N); 6.62 (1H, s, H-3); 7.26–7.28 (4H, m, H Ar); 7.32–7.39 (5H, m, H Ph); 7.62 (1H, s, H-6); 7.80 (1H, s, –C<u>H</u>=CCOOEt); 8.07 (1H, br. s, H-2'). ^{13}C NMR spectrum, δ, ppm: 12.9; 40.2; 61.5; 70.9; 108.7; 119.2; 119.7; 121.7; 122.5; 126.8; 127.2; 127.6; 127.8; 131.4; 131.6; 132.8; 134.1; 139.5; 142.4; 146.9; 156.0, 164.1; 172.9. Found, %: C 69.49; H 5.01; N 6.69. $C_{25}H_{22}N_2O_5$. Calculated, %: C 69.76; H 5.15; N 6.51.

(*E*)-2-[(Benzimidazol-1-yl)methyl]-3-[(5-benzyloxy-4-oxo-4*H*-pyran-2-yl)]acrylic acid butyl ester (5c). Yield 0.40 g (88%). White solid. Mp 126–128°C. IR spectrum, ν, cm^{-1}: 3065, 2958, 1714, 1644, 1455, 1252, 1204. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 0.78 (3H, t, *J* = 7.3, $(CH_2)_3C\underline{H}_3$); 1.12–1.21 (2H, m, $CH_2CH_2C\underline{H}_2CH_3$); 1.45–1.52 (2H, m, $CH_2C\underline{H}_2CH_2CH_3$); 4.07 (2H, t, *J* = 6.7, $COOCH_2$); 4.99 (2H, s, $PhC\underline{H}_2O$); 5.32 (2H, s, CH_2N); 6.51 (1H, s, H-3); 7.17–7.21 (4H, m, H Ar); 7.28–7.32 (5H, m, H Ph); 7.58 (1H, s, H-6); 7.82 (1H, s, –C<u>H</u>=CCOOBu); 7.98 (1H, br. s, H-2'). ^{13}C NMR spectrum, δ, ppm: 12.5; 17.9; 29.3; 39.9; 65.2; 70.8; 108.5; 119.3; 119.5; 121.3; 122.2; 126.7; 127.2; 127.5; 127.7; 131.1; 131.3; 132.6; 134.0; 139.4; 142.2; 146.7; 157.0; 164.1; 172.8. Found, %: C 70.38; H 5.89; N 6.45. $C_{27}H_{26}N_2O_5$. Calculated, %: C 70.73; H 5.72; N 6.11.

(*E*)-5-Benzyloxy-2-{2-[(3-methylpyrazol-1-yl)methyl]-3-oxobut-1-enyl}-4*H*-pyran-4-one (6a). White solid. Yield 0.28 g (77%). Mp 110–112°C. IR spectrum, ν, cm^{-1}: 3033, 2955, 1692, 1654, 1202. ^{1}H NMR, δ, ppm: 2.24 (3H, s, $ArC\underline{H}_3$); 2.40 (3H, s, $COCH_3$); 5.09 (2H, s, $PhC\underline{H}_2O$); 5.25 (2H, s, CH_2N); 5.96 (1H, br. s, H Ar); 6.72 (1H, s, H-3); 7.28–7.32 (2H, m, –C<u>H</u>=CCOMe, H Ar); 7.33–7.39 (5H, m, H Ph); 7.62 (1H, s, H-6). ^{13}C NMR spectrum, δ, ppm: 25.3; 42.5; 46.5; 70.7; 103.9; 118.1; 118.5; 126.6; 127.7; 127.9; 129.4; 130.6; 131.2; 137.5; 139.7; 146.4; 157.4; 164.5; 173.5. Found, %: C 68.86; H 5.66; N 7.53. $C_{21}H_{20}N_2O_4$. Calculated, %: C 69.22; H 5.53; N 7.69.

(*E*)-3-[(5-Benzyloxy-4-oxo-4*H*-pyran-2-yl)]-2-[(3-methylpyrazol-1-yl)methyl] acrylic acid ethyl ester (6b). Yield 0.30 g (76%). White solid. Mp 113–115°C. IR spectrum, ν, cm^{-1}: 3065, 2923, 1720, 1640, 1444, 1092. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.28 (3H, t, *J* = 7.1, $CH_2C\underline{H}_3$); 2.22 (3H, s, $ArC\underline{H}_3$); 4.24 (2H, q, *J* = 7.1, $C\underline{H}_2CH_3$); 5.09 (2H, s, $PhC\underline{H}_2O$); 5.27 (2H, s, CH_2N); 5.97 (1H, br. s, H Ar); 6.74 (1H, s, H-3); 7.26–7.30 (2H, m, –C<u>H</u>=CCOMe, H Ar); 7.31–7.39 (5H, m, H Ph); 7.60 (1H, s, H-6). ^{13}C NMR spectrum, δ, ppm: 13.0; 43.5; 46.4; 60.9; 70.9; 104.2; 118.3; 118.7; 126.7; 127.5; 127.7; 129.3; 130.4; 134.9; 137.9; 140.2; 146.6; 157.6; 164.5; 173.2. Found, %: C 66.76; H 5.76; N 7.33. $C_{22}H_{22}N_2O_5$. Calculated, %: C 66.99; H 5.62; N 7.10.

This paper reports a part of a research project entitled "Synthesis of new heterocyclic derivatives of 4-pyrones via nucleophilic substitution reactions". We thank the research affair of University of Tabriz for financial support.

REFERENCES

1. D. Basavaiah, B. S. Reddy, S. S. Badsara, *Chem. Rev.*, **110**, 5447 (2010).
2. V. Singh, S. Batra, *Tetrahedron*, **64**, 4511 (2008).
3. M. Baidya, G. Y. Remennikov, P. Mayer, H. Mayr, *Chem. Eur. J.*, **16**, 1365 (2010).
4. V. Declerck, J. Martinez, F. Lamaty, *Chem. Rev.*, **109**, 1 (2009).
5. D. Basavaiah, K. Aravindu, *Org. Lett*., **9**, 2453 (2007).
6. B. Sreedhar, P. S. Reddy, N. S. Kumar, *Tetrahedron Lett*., **47**, 3055 (2006).
7. C. G. Lee, S. Gowrisankar, J. N. Kim, *Bull. Korean Chem. Soc*., **26**, 481 (2005).
8. S. Gowrisankar, M. J. Lee, S. Lee, J. N. Kim, *Bull. Korean Chem. Soc*., **25**, 1963 (2004).
9. S. Kathiravan, E. Ramesh, R. Raghunathan, *Tetrahedron Lett*., **50**, 2389 (2009).
10. V. Singh, S. Hutait, S. Batra, *Eur. J. Org. Chem*., **2009**, 3454 (2009).
11. H. S. Lee, S. H. Kim, S. Gowrisankar, J. N. Kim, *Tetrahedron*, **64**, 7183 (2008).
12. G. W. Kabalka, G. Dong, B. Venkataiah, C. Chen, *J. Org. Chem*., **70**, 9207 (2005).
13. J. H. Gong, H. R. Kim, E. K. Ryu, J. N. Kim, *Bull. Korean Chem. Soc*., **23**, 789 (2002).
14. J. Li, X. Wang, Y. Zhang, *Tetrahedron Lett*., **46**, 5233 (2005).
15. J. Farard, C. Logé, B. Pfeiffer, B. Lesur, M. Duflos, *Tetrahedron Lett*., **50**, 5729 (2009).
16. T. Kamino, K. Kuramochi, S. Kobayashi, *Tetrahedron Lett*., **44**, 7349 (2003).
17. X. Xiong, M. C. Pirrung, *Org. Lett*., **10**, 1151 (2008).
18. B. V. S. Reddy, M. R. Reddy, C. Madan, K. P. Kumar, M. S. Rao, *Bioorg. Med. Chem. Lett*., **20**, 7507 (2010).
19. A. P. D. Rodrigues, A. S. C. Carvalho, A. S. Santos, C. N. Alves, J. L. de Nascimento, E. O. Silva, *Cell. Biol. Int*., **35**, 335 (2011).
20. J. P. Soni, D. J. Sen, K. M. Modh, *J. Appl. Pharm. Sci*., **1**, 115 (2011).
21. G. Yaseen, J. Sudhakar, *Int. J. Pharma Bio Sci*., **1**, 281 (2010).
22. L. M. Stanley, J. F. Hartwig, *J. Am. Chem. Soc*., **131**, 8971 (2009).
23. A. Figueiras, J. M. G. Sarraguça, R. A. Carvalho, A. A. C. C. Pais, F. J. B. Veiga, *Pharm. Res*., **24**, 377 (2007).
24. J. A. Asensio, P. Gómez-Romero, *Fuel Cells*, **5**, 336 (2005).
25. J. Qi, J. Zhu, X. Liu, L. Ding, C. Zhen, G. Han, J. Lv, Y. Zhou, *Bioorg. Med. Chem. Lett*., **21**, 5822 (2011).
26. A. Shahrisa, Z. Ghasemi, *Khim. Geterotsikl. Soedin.*, 37 (2010). [*Chem. Heterocycl. Compd.*, **46**, 30 (2010).]
27. Z. Ghasemi, V. Nazari-Belvirdi, M. Allahvirdinasab, A. Shahrisa, *Heterocycles*, **83**, 117 (2011).
28. M. S. Kabir, O. A. Namjoshi, R. Verma, M. Lorenz, V. V. N. P. B. Tiruveedhula, A. Monte, S. H. Bertz, A. W. Schwabacher, J. M. Cook, *J. Org. Chem*., **77**, 300 (2012).
29. B. S. Furniss, A. J. Hannaford, P. W. G. Smith, A. R. Tatchell, *Vogels Textbook of Practical Organic Chemistry*, 5th ed., 1989.

Department of Organic and Biochemistry,
Faculty of Chemistry, University of Tabriz,
5166616471, Tabriz, Iran
e-mail: z.ghasemi@tabrizu.ac.ir

Received 4.03.2012