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SYNTHESIS OF FUSED PYRIMIDONE DERIVATIVES OF 4-PYRONES FROM THE ACETATES OF BAYLIS–HILLMAN ADDUCTS

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A series of fused pyrimidone derivatives of 4-pyrones was synthesized by conversion of the acetates of Baylis–Hillman adducts obtained from 2-formyl-4-pyrones with 2-aminopyridine and 2-aminothiazole.

Keywords: fused pyrimidines, heteroaryl-substituted 4-pyrones, Baylis–Hillman reaction.

The fused pyrimidine derivatives are of interest not only for their rich and varied synthetic chemistry but also for their important medicinal and physiological properties [1-3]. Therefore the synthesis of such derivatives has been an attractive area of a focus for synthetic organic and bioorganic chemists as well as numerous methods for the preparation of these heterocyclic compounds have been developed [4-9].

The Baylis–Hillman reaction, a powerful tool for construction of a variety of cyclic and heterocyclic frameworks, has been used for the synthesis of various fused heterocyclic systems [10, 11] such as fused pyrimidines. The reaction of 2-aminopyridine with acetates of Baylis–Hillman adducts leading to the formation of substituted fused pyrimidones has been reported [12]. Later the Baylis–Hillman products of acrylonitrile were used for the synthesis of annelated pyrimidine derivatives [13]. The allyl amine derivatives generated from acetates of Baylis–Hillman adducts have been also used as viable precursors for several fused pyrimidine derivatives [14-17].

Heterocyclic substituted 4-pyrones have also been found in a variety of natural and synthetic biologically active compounds. Some of them are anticoagulants [18] or anti-HIV [19] agents. In continuation of our attempts in preparing various N-hetaryl-substituted 4-pyrones [20], we turned our attention to the synthesis of 4-pyrone derivatives containing a fused pyrimidone moiety. Since the Baylis–Hillman derivatives originating from substituted heterocyclic aldehydes have been known as excellent synthons for the synthesis of polycyclic ring systems, we first examined the Baylis–Hillman reactions of 2-formyl-4-pyrones that had not yet been reported. We describe in this report the results of these reactions and the reaction of acetates of these new adducts with 2-aminopyridine and 2-aminothiazole to afford fused pyrimidone derivatives in 4-pyrone structures.

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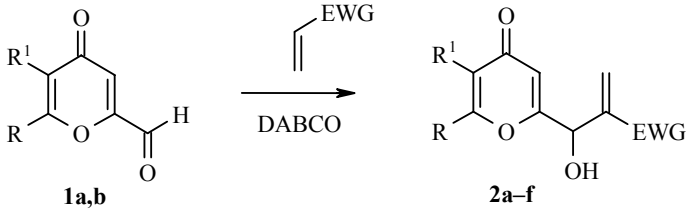
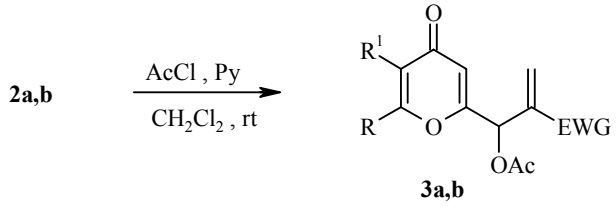
We initiated our studies from the Baylis–Hillman reaction of 2-formyl-4-pyrones **1a,b**. For Baylis–Hillman coupling of methyl and ethyl acrylates with aldehydes **1a,b**, we used a 1,4-dioxane–water (1:1, v/v) medium in the presence of a stoichiometric amount of 1,4-diazabicyclo[2.2.2]octane (DABCO) (100 mol/%), and products **2a**–**d** were obtained in short reaction times and excellent yields. These efficient conditions have been employed for converting a variety of aliphatic and aromatic aldehydes to their corresponding Baylis–Hillman products [21]. But the best results in the reaction of aldehydes **1a,b** with acrylonitrile were achieved when these reactions were carried out in THF as a solvent in the presence of 100 mol/% of DABCO. The use of aqueous medium in the reaction with acrylonitrile resulted in a complex mixture of products.



1a,b **2a–f**

1a, 2a,c,e R = H, R^1 = OCH_2Ph; **1b, 2b,d,f** R = Ph, R^1 = H;
2a,b EWG = CO_2Me, **c,d** EWG = CO_2Et, **e,f** EWG = CN

The Baylis–Hillman adducts **2a** and **2b** obtained by the reaction of aldehydes **1a** and **1b** with methyl acrylate were acetylated with acetyl chloride in the presence of pyridine in dichloromethane to yield acetates **3a** and **3b** in good yields.



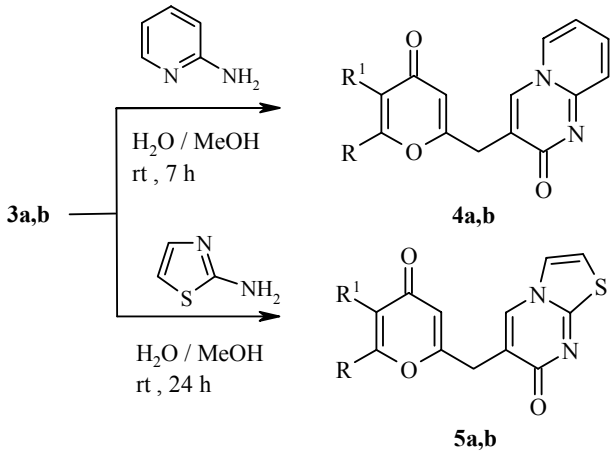
2a,b **3a,b**

3 a R = H, R^1 = OCH_2Ph; **b** R = Ph, R^1 = H; **3a,b** EWG = CO_2Me

We then treated acetates **3a,b** with 2-aminopyridine in MeOH–H_2O (1:1, v/v) at room temperature, and products **4a,b** were obtained by a simple work up in good yields. The mechanism of these reactions as described before [12] includes Michael attack of ring nitrogen onto the acrylate moiety and subsequent attack of amino group to ester. Since the reaction of Baylis–Hillman acetates as 1,3-dielectrophilic units with amidines and as 1,3-dinucleophiles for the synthesis of substituted pyrimidine derivatives, has also been reported [22], and 2-aminopyridine has an amidine-like moiety in its structure, we thought that other amidine type heterocycles such as 2-aminothiazole and 2-aminopyrimidine may similarly react with acetates of Baylis–Hillman adducts to produce other fused pyrimidone compounds. The treatment of acetates **3a,b** with 2-aminothiazole under the same conditions gave the 7H-thiazolo[3,2-*a*]pyrimidin-7-ones **5a,b**, which were characterized by spectroscopic methods.

Simultaneously with our studies, Weike et al. reported the reaction of Baylis–Hillman acetates with 2-aminothiazole under solvent-free conditions for the synthesis of 5H-thiazolo[3,2-*a*]pyrimidin-5-ones [23]. According to the literature [24], 2-aminothiazole is tautomerized to the imine form in solutions at room temperature and this can cause the reaction pathway involving a conjugative attack of ring nitrogen of 2-aminothiazole to be predominant. The reaction of 2-aminothiazoline with methyl α-bromoacrylate in methanol, as a similar system, proceeds by this regioselectivity and produces tetrahydroimidazothiazole derivative [25].

We also examined the reaction of acetates **3a,b** with 2-aminopyrimidine under these conditions, but we have obtained only the nonreacted starting materials even for a longer reaction time.



In conclusion, we have reported convenient conditions for Baylis–Hillman reaction of 2-formyl-4-pyrones with alkyl acrylates and acrylonitrile. The acetates of Baylis–Hillman adducts of methyl acrylate, under cyclization with 2-aminopyridine and 2-aminothiazole in aqueous media at room temperature, have been converted to pyridopyrimidone and thiazolopyrimidone derivatives of 4-pyrones.

EXPERIMENTAL

Melting points were determined on an Electrothermal MEL-TEMP apparatus (model 1202D) and are uncorrected. FT-IR spectra (KBr) were obtained on a Bruker Tensor 27 spectrometer. ^{1}H and ^{13}C NMR spectra were recorded on a Bruker Spectrospin Avance 400 spectrometer operating at 400 and 100 MHz, respectively (compound **2f** – on a Bruker Spectrospin Avance 500 spectrometer) relative to TMS used as internal standards. NMR spectra were recorded in $CDCl_3$ (compounds **2a**–**f**, **3a**,**b**), $CDCl_3$–CD_3OD, 2:1 (v/v) (**4a,b**), and $CDCl_3$–CD_3OD, 1:1 (v/v) (**5a,b**). Mass spectra were measured by a Shimadzu (70 eV) spectrometer, and elemental analyses were measured by a Vario EL III apparatus (Elementar Co.). Preparative layer chromatography (PLC) was done using silica gel (Merk Kieselgel 60 $PF_{254+366}$).

Aldehyde **1a** was obtained from commercially available kojic acid by benzylation of phenolic OH [26] and then oxidation of the hydroxymethyl group with MnO_2. Aldehyde **1b** was synthesized from the corresponding ethoxycarbonyl derivative according to the reported procedure [27]. The ethoxycarbonyl derivative itself was prepared through cyclization of the related 1,3,5-triketone derivative under acidic conditions, which is an important method for the synthesis of a variety of 4-pyrone structures [28–31].

5-Benzyloxy-2-formyl-4H-pyran-4-one (1a). To a mixture of commercial kojic acid (1.7 g, 12 mmol) and NaOH (0.514 g, 12.8 mmol) in MeOH (17 ml) and H_2O (1.7 ml), benzyl bromide (1.65 ml, 13.8 mmol) was added and the mixture was heated at 56°C for 4 h. After cooling, water (50 ml) was added with stirring. The precipitated product was filtered off, washed several times with H_2O, and dried first on air and then in an oven at 55°C for 12 h to give 2.08 g (75% yield) of 5-benzyloxy-2-hydroxymethyl-4H-pyran-4-one (benzyl ether of kojic acid) as a white solid (mp 128-130°C). A solution of benzyl ether of kojic acid (1.16 g, 5 mmol) in dry CH_2Cl_2 (60 ml) was mixed with fresh prepared MnO_2 (3.8 g, 43.7 mmol), and the suspension was stirred at room temperature for 48 h. After filtering and removal of CH_2Cl_2 by a rotary evaporator 0.57 g (yield 50%) of compound **1a** (mp 118–120°C) was obtained as a white solid. FT-IR spectrum, ν, cm^{-1}: 3087, 2923, 2860 (aldehyde CH), 1713 (aldehyde C=O), 1647 (pyrone C=O), 1615, 1211, 1139. ^{1}H NMR, δ, ppm: 5.16 (2H, s, OCH_2Ph); 7.02 (1H, s, H-3 pyrone); 7.36–7.43 (5H, m, C_6H_5); 7.69 (1H, s, H-6 pyrone); 9.67 (1H, s, CHO).

Synthesis of Baylis–Hillman Adducts 2a-d (General Method). To a solution of aldehydes **1a** or **1b** (2 mmol) and DABCO (0.224 g, 2 mmol) in dioxane–H_2O, 1:1 (v/v) (10 ml), alkyl acrylate (8 mmol) was added and the solution was stirred at room temperature for 45 min. After adding water (100 ml), the mixture was extracted with ethyl acetate (4×30 ml). The combined ethyl acetate extract was washed with 100 ml H_2O, dried over Na_2SO_4, and concentrated to dryness. The residue was purified by preparative layer chromatography (silica gel, acetone–chloroform–*n*-hexane, 1:1:2) to give products **2a-d**.

2-[(5-Benzyloxy-4-oxo-4H-pyran-2-yl)hydroxymethyl]acrylic Acid Methyl Ester (2a). A white solid, 75% yield; mp 106°C. FT-IR spectrum, ν, cm^{-1}: 3302 (OH), 3093, 2952, 1717 (ester C=O), 1636 (pyrone C=O), 1604, 1440, 1197, 1144. ^{1}H NMR spectrum, δ, ppm: 3.74 (3H, s, CH_3); 5.00 (2H, s, OCH_2Ph); 5.28 (1H, s, CH–O); 6.00 (1H, s, H-3 pyrone); 6.43 (1H, s, $=CH_2$); 6.53 (1H, s, $=CH_2$); 7.30-7.37 (5H, m, C_6H_5); 7.49 (1H, s, H-6 pyrone). ^{13}C NMR spectrum, δ, ppm: 51.2 (CH_3); 69.2 (CH_2O); 70.8 (CH–O); 111.8, 126.7, 127.3, 127.6, 127.9, 134.5, 136.5, 140.2, 146.0, 164.8, 165.5, 173.8. Mass spectrum, *m/z* (I_{rel}, %): 316 $[M]^+$ (25), 210 $[M\text{-}PhCHO]^+$ (62), 181 $[M\text{-}PhCHO\text{–}OCH_3]$ (20), 91 $[PhCH_2]^+$ (100). Found, %: C 64.30; H 5.30. $C_{17}H_{16}O_6$. Calculated, %: C 64.55; H 5.06.

2-[Hydroxy(4-oxo-6-phenyl-4H-pyran-2-yl)methyl]acrylic Acid Methyl Ester (2b). A white solid, 74% yield; mp 96-98°C. FT-IR spectrum, ν, cm^{-1}: 3166 (OH), 3070, 2958, 1734 (ester C=O), 1644 (pyrone C=O), 1584, 1410, 1256, 1059. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 3.78 (3H, s, CH_3); 5.44 (1H, s, CH–O); 6.15 (1H, s, H pyrone); 6.53-6.54 (2H, m, $=CH_2$); 6.69 (1H, d, *J* = 2.2, H pyrone); 7.42-7.51 (3H, m, C_6H_5); 7.66-7.68 (2H, m, C_6H_5). ^{13}C NMR spectrum, δ, ppm: 51.3 (CH_3), 69.3 (CH–O), 110.0, 111.8, 124.8, 127.9, 128.0, 129.8, 130.5, 136.8, 162.6, 164.9, 166.3, 179.4. Mass spectrum, *m/z* (I_{rel}, %): 286 $[M]^+$ (48), 226 $[M\text{-}HCOOMe]^+$ (17), 173 $\{M\text{-}[CH_2{=}C(CO_2Me)CHO]\text{–}1\}^+$ (75), 69 (100). Found, %: C 66.77; H 4.99. $C_{16}H_{14}O_5$. Calculated, %: C 67.13; H 4.89.

2-[(5-Benzyloxy-4-oxo-4H-pyran-2-yl)hydroxymethyl]acrylic Acid Ethyl Ester (2c). A white solid, 85% yield; mp 57°C. FT-IR spectrum, ν, cm^{-1}: 3342 (OH), 3093, 2983, 1715 (ester C=O), 1643 (pyrone C=O), 1611, 1214, 1148, 1062. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.26 (3H, t, *J* = 7.1, $OCH_2C\underline{H}_3$); 3.85 (1H, br. s, OH); 4.20 (2H, q, *J* = 7.1, OCH_2Me); 5.03 (2H, s, OCH_2Ph); 5.27 (1H, s, CH–O); 5.97 (1H, s, H-3 pyrone); 6.43 (1H, s, $=CH_2$); 6.57 (1H, s, $=CH_2$); 7.29–7.36 (5H, m, Ph); 7.51 (1H, s, H-6 pyrone). ^{13}C NMR spectrum, δ, ppm: 13.0 (ester CH_3), 60.4 (ester CH_2), 69.3 (CH_2O), 70.8 (CH–O), 111.7, 126.7, 127.4, 127.6, 127.7, 134.5, 136.7, 140.3, 146.0, 164.3, 165.8, 173.8. Mass spectrum, *m/z* (I_{rel}, %): 330 $[M]^+$ (25), 224 $[M\text{–}PhCHO]^+$ (38), 201 $[M\text{-}1\text{–}HOC\text{–}C(CO_2Et){=}CH_2]^+$ (35), 130 $[HOCH_2C(CO_2Et){=}CH_2]^+$ (30), 91 (100). Found, %: C 65.19; H 5.66. $C_{18}H_{18}O_6$. Calculated, %: C 65.45; H 5.45.

2-[Hydroxy(4-oxo-6-phenyl-4H-pyran-2-yl)methyl]acrylic Acid Ethyl Ester (2d). A white solid, 89% yield; mp 85-86°C. FT-IR spectrum, ν, cm^{-1}: 3272 (OH), 3072, 2984, 1713 (ester C=O), 1659 (pyrone C=O), 1599, 1405, 1257, 1095. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.27 (3H, t, *J* = 7.1, $OCH_2C\underline{H}_3$); 4.23 (2H, q, *J* = 7.1, $OC\underline{H}_2CH_3$); 4.91 (1H, d, *J* = 6.6, OH); 5.44 (1H, d, *J* = 5.8, CH–O); 6.16 (1H, s, H pyrone); 6.53 (2H, s, $=CH_2$); 6.67 (1H, d, *J* = 2.2, H pyrone); 7.41–7.48 (3H, m, C_6H_5); 7.66–7.68 (2H, m, C_6H_5). ^{13}C NMR spectrum, δ, ppm: 14.0 (ester CH_3), 61.4 (ester CH_2), 70.1 (CH–O), 110.9, 112.8, 125.8, 128.4, 129.0, 130.8, 131.5, 138.4, 163.7, 165.5, 167.8 (ester C=O), 180.6 (pyrone C=O). Mass spectrum, *m/z* (I_{rel}, %): 300 $[M]^+$ (30), 301 (65), 226 $[M\text{–}HCO_2Et]^+$ (18), 173 $[M{+}1\text{–}HOC\text{–}C(CO_2Et){=}CH_2]$ (75), 69 (100). Found, %: C 67.70; H 5.60. $C_{17}H_{16}O_5$. Calculated, %: C 68.00; H 5.33.

Synthesis of Baylis–Hillman Adducts 2e-f (General Method). To a solution of aldehydes **1a** or **1b** (0.75 mmol) and DABCO (0.084 g, 0.75 mmol) in THF (7 ml), acrylonitrile (3 mmol) was added and the solution was stirred at room temperature for 12 h. The mixture was concentrated by a rotary evaporator and the residue was purified by PLC chromatography (silica gel, acetone–chloroform–*n*-hexane, 1:1:2) to give products **2e–f**.

2-[(5-Benzyloxy-4-oxo-4H-pyran-2-yl)hydroxymethyl]acrylonitrile (2e). A white solid, 53% yield; mp 130°C (decomp.). FT-IR spectrum, ν, cm^{-1}: 3196 (OH), 3107, 2924, 2231 (C≡N), 1644 (pyrone C=O), 1603, 1457, 1256, 1204. ^{1}H NMR spectrum, δ, ppm: 4.98 (2H, s, OCH_2Ph); 5.02 (1H, s, CH–O); 6.13 (1H, s, $=CH_2$);

6.21 (1H, s, =CH_2); 6.63 (1H, s, H-3 pyrone); 7.32–7.37 (5H, m, C_6H_5); 7.58 (1H, s, H-6 pyrone). ^{13}C NMR spectrum, δ, ppm: 69.2 (CH_2O); 70.8 (CH–O); 111.7, 114.9, 120.8, 126.7, 127.6, 127.7, 132.1, 134.1, 140.0, 146.2, 164.3, 174.0 (pyrone C=O). Mass spectrum, *m/z* (I_{rel}, %): 283 $[M]^+$ (25), 254 (20), 201 $[M\text{-}HOCH_2C(CN)=CH_2–1]^+$ (20), 177 $[M–PhCOH]^+$ (40), 91 (100). Found, %: C 67.57; H 4.66; N 4.83. $C_{16}H_{13}NO_4$. Calculated, %: C 67.84; H 4.59; N 4.94.

2-[Hydroxy(4-oxo-6-phenyl-4H-pyran-2-yl)methyl]acrylonitrile (2f). A white solid, 47% yield; mp 128°C (decomp.). FT-IR spectrum, ν, cm^{-1}: 3342 (OH), 3107, 2925, 2310 (C≡N), 1655 (pyrone C=O), 1596, 1411, 1219. ^{1}H NMR spectrum (500 MHz), δ, ppm (*J*, Hz): 5.27 (1H, s, CH–O); 6.28 (1H, s, H pyrone); 6.39 (1H, d, *J* = 0.7, H pyrone); 6.69 (1H, d, *J* = 1.5, =CH_2); 6.78 (1H, d, *J* = 1.7, =CH_2); 7.49–7.56 (3H, m, C_6H_5); 7.78-7.80 (2H, m, C_6H_5). ^{13}C NMR spectrum (125 MHz), δ, ppm: 70.8 (CH–O), 112.7, 114.9, 121.1, 125.9, 127.3, 127.7, 131.9, 134.1, 140.0, 146.4, 164.7, 174.0 (pyrone C=O). Mass spectrum, *m/z* (I_{rel}, %): 253 $[M]^+$ (25), 69 (100). Found, %: C 70.77; H 4.56; N 5.83. $C_{15}H_{11}NO_3$. Calculated, %: C 71.14; H 4.34; N 5.53.

Synthesis of Baylis-Hillman Acetates 3a,b (General Method). To a solution of alcohols **2a-b** (1 mmol) in dry CH_2Cl_2 (3 ml), acetyl chloride (0.3 ml, 4.2 mmol) and pyridine (0.06 ml) were added and the solution was stirred at room temperature for 4 h. The mixture was concentrated by a rotary evaporator and the residue was purified by PLC chromatography (silica gel, acetone–*n*-hexane, 1:3).

2-[Acetoxy(5-benzyloxy-4-oxo-4H-pyran-2-yl)methyl]acrylic Acid Methyl Ester (3a). A colorless liquid, 67% yield. FT-IR spectrum, ν, cm^{-1}: 3089, 2953, 1756 (ester C=O), 1725 (ester C=O), 1665 (pyrone C=O), 1436, 1372, 1208. ^{1}H NMR spectrum, δ, ppm: 2.14 (3H, s, CH_3CO); 3.76 (3H, s, CO_2CH_3); 5.04 (2H, s, OCH_2Ph); 5.96 (1H, s, CH–O); 6.42 (1H, s, =CH_2); 6.46 (1H, s, =CH_2); 6.53 (1H, s, H-3 pyrone); 7.29–7.39 (5H, m, C_6H_5); 7.54 (1H, s, H-6 pyrone). ^{13}C NMR spectrum, δ, ppm: 19.5 ($\underline{C}H_3CO$), 51.2 (OCH_3), 67.8 (CHOAc), 70.7 (OCH_2Ph), 113.0, 126.5, 127.3, 127.5, 128.0, 134.1, 134.4, 140.1, 146.2, 161.3, 163.3, 167.6 (ester C=O), 173.1 (pyrone C=O). Found, %: C 63.82; H 4.96. $C_{19}H_{18}O_7$. Calculated, %: C 63.68; H 5.02.

2-[Acetoxy(4-oxo-6-phenyl-4H-pyran-2-yl)methyl]acrylic Acid Methyl Ester (3b). A white solid, 70% yield; mp 93°C. FT-IR spectrum, ν, cm^{-1}: 3066, 2952, 1752 (ester C=O), 1725 (ester C=O), 1660 (pyrone C=O), 1445, 1394, 1219. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 2.19 (3H, s, CH_3CO); 3.79 (3H, s, CO_2CH_3); 6.08 (1H, s, CH–O); 6.41 (1H, d, *J* = 2.0, H pyrone); 6.59 (2H, s, =CH_2); 6.74 (1H, d, *J* = 2.1, H pyrone); 7.45-7.53 (3H, m, C_6H_5); 7.69-7.71 (2H, m, C_6H_5). ^{13}C NMR spectrum, δ, ppm: 19.7 ($\underline{C}H_3CO$), 51.4 (OCH_3), 68.0 (CHOAc), 110.3, 110.4, 113.1, 124.8, 128.0, 128.1, 129.8, 130.6, 134.5, 162.1, 162.6, 167.8 (ester C=O), 178.6 (pyrone C=O). Found, %: C 65.49; H 4.63. $C_{18}H_{16}O_6$. Calculated, %: C 65.85; H 4.88.

Synthesis of fused pyrimidones 4, 5 (General Method). To a solution of acetates **3a,b** (0.5 mmol) in MeOH–H_2O, 1:1 (v/v), (12 ml) a solution of 2-aminopyridine or 2-aminothiazole (0.5 mmol) in MeOH–H_2O, 1:1 (v/v), (6 ml) was added and the mixture was stirred at room temperature for 7 h (for 2-aminopyridine) and for 24 h (for 2-aminothiazole). The resullting precipitate was collected by filtration. The precipitate obtained from the reaction of compounds **3a,b** with 2-aminopyridine was washed with acetone and dried *in vacuo* to give products **4a,b** as white solids. The crude products obtained from the reaction of compounds **3a,b** with 2-aminothiazole were purified by PLC chromatography (silica gel, dichloromethane–methanol, 10:1) to give products **5a,b** as white solids.

3-[(5-Benzyloxy-4-oxo-4H-pyran-2-yl)methyl]-2H-pyrido[2,1-*a*]pyrimidin-2-one (4a). A white solid, 76% yield; mp 220-222°C (decomp.). FT-IR spectrum, ν, cm^{-1}: 3080, 2940, 1637 (C=O), 1596, 1485, 1218. ^{1}H NMR spectrum, δ, ppm: 3.70 (2H, s, CH_2 pyrimidone); 4.83 (2H, s, OCH_2Ph); 6.32 (1H, s, H-3 pyrone); 6.88 (1H, t, *J* = 6.8, Py); 7.15-7.26 (6H, m, Ph (5H), Py (1H)); 7.62 (1H, t, *J* = 7.5, Py); 7.67 (1H, s, H-6 pyrone); 8.08 (1H, d, *J* = 6.6, Py); 8.21 (1H, s, H pyrimidone). ^{13}C NMR spectrum, δ, ppm: 31.0 (CH_2), 70.2 (OCH_2), 113.1, 113.4, 121.8, 122.3, 126.8, 127.2, 127.6, 132.7, 133.7, 136.0, 136.6, 139.4, 145.9, 150.1, 163.8, 166.5, 173.7. Mass spectrum, *m/z* (I_{rel}, %): 360 $[M]^+$ (17), 269 (24), 213 (25), 184 (80), 91 (100). Found, %: C 69.82; H 4.76; N 7.83. $C_{21}H_{16}N_2O_4$. Calculated, %: C 70.00; H 4.44; N 7.78.

3-[(4-Oxo-6-phenyl-4H-pyran-2-yl)methyl]-2H-pyrido[2,1-*a*]pyrimidin-2-one (4b). A white solid, 74% yield; mp 234–236°C (decomp.). FT-IR spectrum, ν, cm^{-1}: 3067, 2996, 1654 (C=O), 1589, 1470, 1399, 1149. ^{1}H NMR spectrum, δ, ppm: 4.01 (2H, s, CH_2 pyrimidone); 6.36 (1H, s, H pyrone); 6.77 (1H, d, *J* = 0.9, H pyrone); 7.06 (1H, t, *J* = 6.8, Py); 7.35 (1H, d, *J* = 9.0, Py); 7.47–7.56 (3H, m, C_6H_5); 7.75 (1H, t, *J* = 8.1, Py); 7.82 (2H, d, *J* = 7.4, C_6H_5); 8.17 (1H, d, *J* = 6.6, Py); 8.50 (1H, s, H pyrimidone). ^{13}C NMR spectrum, δ, ppm: 31.1 (CH_2), 108.9, 112.9, 113.4, 122.1, 122.2, 124.8, 127.9, 129.4, 130.6, 132.5, 136.2, 137.4, 150.7, 163.9, 165.3, 167.2, 180.2. Mass spectrum, *m/z* (I_{rel}, %): 330 $[M]^+$ (18), 210 (50), 184 (48), 105 (80), 77 (100). Found, %: C 72.60; H 4.40; N 8.20. $C_{20}H_{14}N_2O_3$. Calculated, %: C 72.72; H 4.24; N 8.48.

6-[(5-Benzyloxy-4-oxo-4H-pyran-2-yl)methyl]-7H-thiazolo[3,2-*a*]pyrimidin-7-one (5a). A white solid, 59% yield; mp 222–224°C (decomp.). FT-IR spectrum, ν, cm^{-1}: 3082, 2932, 1642 (C=O), 1607, 1485, 1220. ^{1}H NMR spectrum, δ, ppm: 3.74 (2H, s, CH_2 pyrimidone); 4.98 (2H, s, OCH_2Ph); 6.35 (1H, s, H-3 pyrone); 7.16 (1H, d, *J* = 4.7, H thiazole); 7.29–7.36 (5H, m, C_6H_5); 7.59 (1H, d, *J* = 4.5, H thiazole); 7.76 (1H, s, H-6 pyrone); 8.34 (1H, s, H pyrimidone). ^{13}C NMR spectrum, δ, ppm: 30.2 (CH_2); 69.7 (OCH_2); 110.6, 112.1, 117.1, 123.4, 126.1, 126.7, 126.8, 133.8, 134.8, 139.8, 145.3, 163.6, 163.9, 165.9, 173.7. Mass spectrum, *m/z* (I_{rel}, %): 366 $[M]^+$ (18), 276 (25), 219 (45), 190 (100), 166 (100). Found, %: C 62.02; H 3.55; N 7.70. $C_{19}H_{14}N_2O_4S$. Calculated, %: C 62.29; H 3.82; N 7.65.

6-[(4-Oxo-6-phenyl-4H-pyran-2-yl)methyl]-7H-thiazolo[3,2-*a*]pyrimidin-7-one (5b). A white solid, 55% yield; mp 235–236°C (decomp.). FT-IR spectrum, ν, cm^{-1}: 3081, 2926, 1650 (C=O), 1607, 1483, 1261. ^{1}H NMR spectrum, δ, ppm: 3.86 (2H, s, CH_2 pyrimidone); 6.27 (1H, d, *J* = 2.1, H pyrone); 6.72 (1H, d, *J* = 2.1, H pyrone); 7.08 (1H, d, *J* = 4.8, H thiazole); 7.42–7.51 (3H, m, C_6H_5); 7.53 (1H, d, *J* = 4.8, H thiazole); 7.74-7.77 (2H, m, C_6H_5); 8.34 (1H, s, H pyrimidone). ^{13}C NMR spectrum, δ, ppm: 31.1 (CH_2), 109.2, 110.5, 113.0, 118.2, 123.7, 125.0, 125.1, 128.2, 129.6, 130.8, 134.6, 164.0, 164.2, 165.4, 180.3. Mass spectrum, *m/z* (I_{rel}, %): 336 $[M]^+$ (30), 237 (18), 210 (70), 190 (100), 77 (65). Found, %: C 64.50; H 3.21; N 8.37. $C_{18}H_{12}N_2O_3S$. Calculated, %: C 64.28; H 3.57; N 8.33.

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