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Ammonium Acetate Promoted Rapid and Efficient Synthesis of γ-Benzopyranones and 3, 4-Dihydropyrimidin-2(1*H*)-ones/thiones Under Solvent-free Conditions: A Parallel Scrutiny of Microwave Irradiation versus Conventional Heating

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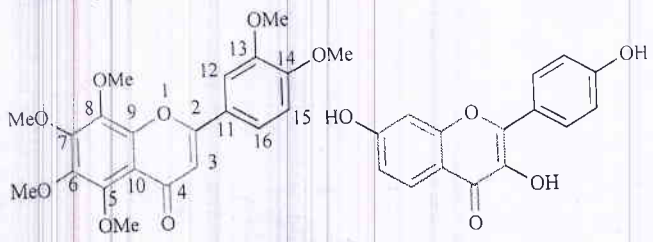
Abstract: A simple and highly efficient approach for the synthesis of γ-Benzopyranones and 3, 4-Dihydropyrimidin-2(1*H*)-ones/thiones using ammonium acetate as a promoter under thermal as well as microwave irradiation using solvent-free conditions has been demonstrated.

Keywords: γ-Benzopyranones, 3, 4-dihydropyrimidin-2(1*H*)-ones/thiones, ammonium acetate, solvent-free synthesis, promoter.

INTRODUCTION

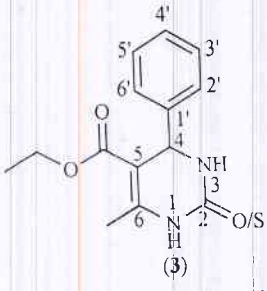
The γ-Benzopyranone structural motif is frequently found in many natural products such as nobiletin (**1**) and Kaempferol (**2**). Due to their fascinating structural features, they exhibit array of biological activities, especially, anti-inflammatory, antimicrobial, antitumoric, and cytotoxic (Fig. **1**) [1]. Out of the several reported approaches for the synthesis of a γ-benzopyranone skeleton one of the most commonly used methods is acid-catalyzed cyclization of 1, 3-dione derivatives prepared from 2-hydroxyacetophenones [2].



Nobiletin (**1**) Kaempferol (**2**)

Fig. (1). γ-Benzopyranone structural containing natural products.

Similarly, 3, 4-dihydropyrimidin-2(1*H*)-one derivatives (DHPMs) (**3**) are important core in marine natural products (Fig. **2**) [3]. A suitably functionalized DHPMs have various biological activities such as anticancer [4], antihypertensive [5], antibacterial [6], antiviral [7] as well as calcium channel modulating [8] activities etc. and a large number of DHPM-based scaffolds have already been developed into drugs or lead compounds. Several approaches have been used for the synthesis of 3, 4-dihydropyrimidin-2(1*H*)-one derivatives [9].



(**3**)

Fig. (2). 3, 4-Dihydropyrimidin-2(1*H*)-one derivatives (DHPMs) core.

Even though the reported methods for the synthesis of both γ-benzopyranones and 3, 4-dihydropyrimidin-2(1*H*)-ones/thiones are practical tools and provide the synthetic requirements, most of them suffer from considerable restrictions such as use of harsh reaction conditions, prolonged reaction time, low yields, toxic and expensive catalysts/reagents and solvents. In view of these restrictions, there is still a need for exploration of effortless, efficient, rapid, eco-compatible, and widely applicable routes for the synthesis of γ-benzopyranones and 3, 4-dihydropyrimidin-2(1*H*)-ones/thiones owing to their immense synthetic and medicinal relevance. Also, due to the severe and burgeoning environmental regulations, organic chemists are called for the development of environmentally benevolent synthetic methodologies. Organic reactions under solvent-free conditions using microwave irradiation and conventional heating techniques [10] have become the centre of attraction for researchers over the years.

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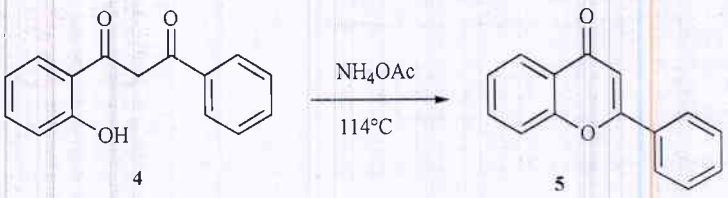
Table 1. Effect of amount of catalyst on the synthesis of γ-Benzopyranones.[a]



4 — 1-(2-hydroxyphenyl)-3-phenylpropane-1,3-dione

5 — 2-phenyl-4H-chromen-4-one

Entry	Catalyst (equiv)	Conventional Heating		Microwave Heating	
		Time (min)	(%) Yield	Time (min)	(%) Yield
1	**0.1**	60	19	30	21
2	**0.2**	50	23	25	24
3	**0.4**	41	25	20	27
4	**0.6**	33	32	15	34
5	**0.8**	24	38	10	40
6	**1.0**	10	90	5	92

[a]Reagent: 1-(2-hydroxyphenyl)-3-phenylpropane-1,3-dione (0.5 g.).

Ammonium acetate is a convenient, easily available and cheap reagent, which has been used as a catalyst in few organic transformations [11]. However, the role of ammonium acetate is limited to a substantial extent due to the use of an organic solvents and low yield. As an extension of our interest in solvent-free organic reactions [2e, 12], herein we report a solvent-free methodology for the ammonium acetate assisted synthesis of γ-benzopyranones and 3, 4-dihydropyrimidin-2(1*H*)-ones/thiones synthesis by microwave irradiation and conventional heating with improved efficiencies, cost effectiveness and excellent yields.

RESULTS AND DISCUSSION

We started our study on the basis of our progressive endeavors in exploring solvent-free protocols for the synthesis of heterocyclic frameworks [2e], we wish to uncover a more practical and contrive synthesis of γ-benzopyranones and 3,4-dihydropyrimidin-2(1*H*)-ones/thiones. In our preliminary experiments, we investigated the optimal conditions regarding the effect of amount of ammonium acetate in the synthesis of γ-benzopyranones and 3,4-dihydropyrimidin-2(1*H*)-ones/thiones.

Optimization of Reaction Condition for Synthesis of γ-Benzopyranones

To study the catalytic activity, cyclodehydration of 1-(2-hydroxyphenyl)-3-aryl-1,3-propanedione **4** (0.5 g, 2.08 mmol) was selected as a model reaction. For this, we first examined the synthesis of 2-phenyl-4H-chromen-4-one (**5**) in the presence of 0.1 equivalents (0.016 g, 0.21 mmol) of ammonium acetate. While performing conventional heating, After 60 min. of reaction time, the desired product **6** was formed in a low amount (Table **1**, entry 1). Using 0.2 (0.032 g, 0.41 mmol) and 0.4 (0.064 g, 0.83 mmol) equivalent of catalyst afforded the desired product with moderate yields (Table **1**, entries 2 and 3), while using 0.6 (0.96 g, 1.25 mmol) and 0.8 (0.12 g, 1.66 mmol) equivalent of catalyst there was slight but not significant increase in the yield of the product (Table **1**, entry 4 and 5). Finally we observed that 1.0 (0.16 g, 2.08 mmol) equivalent of ammonium acetate was the most appropriate amount of catalyst for achieving the desired conversion (Table **1**, entry 6). By applying the same strategy under microwave irradiation, we observed that the time taken for completion of reaction has now reduced to half of the time taken by convention heating (Table **1**).

Next, to explore the diversity of this methodology, various 1-(2-hydroxyphenyl)-3-aryl-1,3-propanediones (**6**) were tested under the above reaction condition. Results showed that the cyclodehydration of various 1-(2-hydroxyphenyl)-3-aryl-1,3-propanediones proceeded smoothly to completion within a short reaction time to give the corresponding γ-benzopyranones in good to excellent yields under both heating conditions (Table **2**, entry 1-18).

Optimization of Reaction Condition for the Synthesis of 3,4-Dihydropyrimidin-2(1*H*)-ones/thiones

For the synthesis of dihydropyrimidinones (DHPMs), benzaldehyde **8** (0.5 g, 4.71 mmol), urea **9** (0.28 g, 4.71 mmol) and ethyl acetoacetate **10** (0.613 g, 4.71 mmol) were selected for a model reaction. For this, we first examined the synthesis of ethyl 1,2,3,4-tetrahydro-6-methyl-2-oxo-4-phenylpyrimidine-5-carboxylate in the presence of 0.1 (0.036 g, 0.471 mmol) equivalent of ammonium acetate. While performing conventional heating, after 60 min. of reaction time, the desired product **11** was formed in a low amount (Table **3**, entry 1). Using 0.2 (0.072 g, 0.942 mmol) and 0.4 (0.145 g, 1.88 mmol) equivalent of catalyst afforded the desired product with moderate yields (Table **3**, entries 2

6.48-6.41 (m, 2H, H-8 & H-6), 3.84 (s, 3H, OCH_3); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 174.8 (C-4), 166.7 (C-7), 165.9 (C-2), 165.3 (C-14), 163.4 (C-9), 130.1 (C-5), 128.9 (C-12 & C-16), 128.9 (C-11), 116.0 (C-10), 115.7 (C-5 & C-13), 110.0 (C-6), 108.0 (C-8), 101.3 (C-3), 55.6 (OCH_3); LCMS (ES-API) m/z: 271 $(M+H)^+$.

6-Methoxy-2-phenyl-chromen-4-one **7i** (Table **2**, entry **9**): Mp 160-161°C [2e]; IR (KBr) ν: 1641, 1618, 1488, 1361, 1255, 1030, 846, 658 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz): δ 7.91-7.88 (m, 2H, H-12 & H-16), 7.57 (d, *J* = 2.7 Hz, 1H, H-5), 7.51-7.46 (m, 4H, H-15, H-13, H-14 & H-7), 7.28 (dd, *J* = 6.7 & *J* = 3.5 Hz, 1H, H-8), 6.79 (s, 1H, H-3), 3.89 (s, 3H, OCH_3); ^{13}C NMR (CDCl3, 75 MHz): δ 178.2 (C-4), 163.0 (C-2), 156.9 (C-6), 150.8 (C-9), 131.7 (C-11), 131.4 (C-13 & C-15), 128.8 (C-14), 126.1 (C-12 & C-16), 124.4 (C-10), 123.6 (C-7), 119.4 (C-8), 106.7 (C-5), 104.7 (C-3), 55.8 (OCH_3); LCMS (ES-API) m/z: 253 $(M+H)^+$.

6-Methoxy-2-(4-methoxy-phenyl)-chromen-4-one **7j** (Table **2**, entry **10**): Mp 195-196°C [2e]; IR (KBr) ν: 1647, 1607, 1584, 1454, 1268, 1196, 1014, 817, 558 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz): δ 7.86 (d, *J* = 9.0 Hz, 2H, H-12 & H-16), 7.60 (d, *J* = 9.0 Hz, 1H, H-5), 7.58 (d, *J* = 3.0 Hz, 1H, H-7), 7.27 (m, 1H, H-8), 7.01 (d, *J* = 9.0 Hz, 2H, H-13 & H-15), 6.73 (s, 1H, H-3), 3.90 (s, 3H, OCH_3), 3.88 (s, 3H, OCH_3); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 178.2 (C-4), 163.1 (C-2), 162.3 (C-14), 156.8 (C-6), 150.9 (C-9), 127.8 (C-12 & 16), 124.4 (C-10), 124.1 (C-11), 123.5 (C-7), 119.3 (C-8), 114.4 (C-13 & C-15), 105.4 (C-5), 104.8 (C-3), 55.9 (OCH_3), 55.4 (OCH_3); LCMS (ES-API) m/z: 283 $(M+H)^+$.

2-(4-Fluoro-phenyl)-6-methoxy-chromen-4-one **7k** (Table **2**, entry **11**): Mp 152-153°C; IR (KBr) ν: 1727, 1661, 1620, 1488, 1168, 1024, 910, 719 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz): δ 7.92 (d, *J* = 9Hz 2H, H-11 & H-16), 7.58 (d, *J* = 2.4 Hz, 1H, H-5), 7.48 (d, *J* = 9.3 Hz, 1H, H-7), 7.18-7.31 (m, 3H, H-13, H-14 & H8), 6.76 (s, 1H, H-3), 3.90 (s, 3H, OCH_3); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 178.1 (C-4), 166.3 (C-2), 162.1 (C-14), 157.0 (C-6), 150.9 (C-9), 128.4 (C-12 & C-16), 128.3 (C-10), 124.4 (C-11), 123.8 (C-7), 119.4 (C-8), 116.4 (C-13 & C-15), 116.1 (C-5), 104.8 (C-3), 55.9 (OCH_3); LCMS (ES-API) m/z: 271 $(M+H)^+$; HRMS (ESI) *m/z* $[M+H]^+$: calcd for $C_{16}H_{11}FO_3$: 271.0692.

6-Methoxy-2-(3-trifluoromethoxy-phenyl)-chromen-4-one **7l** (Table **2**, entry **12**): Mp 161-163 °C; IR (KBr) ν: 1637, 1577, 1490, 1263, 869, 842, 713, 693 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz): δ 7.83 (d, *J* = 8.1 Hz, 1H, H-5), 7.76 (s, 1H, H-15), 7.50 - 7.58 (m, 3H, H-7, H-8 & H-12), 7.39 (d, *J* = 8.1 Hz, 1H, H-14), 7.30 (dd, *J* = 4.2 and 2.7 Hz, 1H, H-16), 6.81 (s, 1H, H-3), 3.92 (s, 3H, OCH_3); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 177.9 (C-4), 161.2 (C-2), 157.1 (C-13), 150.9 (C-6), 149.7 (C-9), 133.9 (C-11), 130.5 (C-15), 124.5 (C-10), 124.4 (OCF_3), 123.9 (C-7), 123.6 (C-16), 122.1 (C-8), 119.5 (C-5), 118.7 (C-14), 107.5 (C-12), 104.8 (C-3), 55.9 (OCH_3); LCMS (ES-API) m/z: 337 $(M+H)^+$; HRMS (ESI) *m/z* $[M+H]^+$: calcd for $C_{17}H_{11}F_3O_4$: 337.0697, found: 337.0687.

2-(3-Trifluoromethyl-phenyl)-chromen-4-one **7m** (Table **2**, entry **13**): Mp 146-147°C [19]; IR (KBr) ν: 1664, 1610, 1582, 1571, 1439, 376, 1293, 879, 697 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz): δ 8.22 (m, 2H, H-5 & H-12), 8.09 (d, *J* = 7.8 Hz, 1H, H-7), 7.82-7.60 (m, 4H, H-14, H-15, H-16 & H-6), 7.45 (t, *J* = 7. 5 Hz, 1H, H-8), 6.87 (s, 1H, H-3); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 178.1 (C-4), 161.5 (C-2), 156.1 (C-9), 134.0 (C-7), 132.5 (C-11), 131.8 (C-5), 129.6 (C-13), 129.3 (C-16), 128.0 (C-15), 125.6 (C-14), 125.4 (C-10), 123.7 (CF_3),121.0 (C-6) 123.0 (C-8), 118.1 (C-12), 108.2 (C-3); LCMS (ES-API) m/z: 291 $(M+H)^+$.

2-(4-Bromo-2-fluoro-phenyl)-6-methyl-chromen-4-one **7n** (Table **2**, entry **14**): Mp 153°C; IR (KBr) ν: 1753, 1679, 1571, 1480, 1257, 1192, 1071, 760, 613 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz): δ 8.02 (t, *J* = 8.1 Hz, 1H, H-5), 7.88 (d, *J* = 7.8 Hz, 1H, H-7), 7.58 (m, 1H, H-16), 7.25-7.45 (m, 3H, H-15, H-13 & H-8), 7.23 (s, 1H, H-3), 2.55 (s, 3H, CH_3); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 197.3 (C-4), 163.7 (C-2), 160.1 (C-12) 148.7 (C-9), 133.6 (C-7), 133.6 (C-6), 130.5 (C-5), 130.5 (C-16), 128.9 (C-15), 127.7 (C-14), 126.4 (C-10), 123.8 (C-11), 121.7 (C-13), 120.7 (C-8), 106.9 (C-3), 29.2 (CH_3); LCMS (ES-API) m/z: 334 $(M+H)^+$; HRMS (ESI) *m/z* $[M+H]^+$: calcd for $C_{16}H_{10}BrFO_2$: 332.9848.

6-Fluoro-2-phenyl-chromen-4-one **7o** (Table **2**, entry **15**): Mp 128-129°C [17]; IR (KBr) ν: 1660, 1624, 1570, 1359, 1176, 835, 767 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz): δ 7.93- 7.85 (m, 3H, H-5, H-12 & H-14), 7.61-7.50 (m, 4H, H-13, H-15, H-14 & H-7), 7.46-7.39 (m, 1H, H-8), 6.82 (s, 1H, H-3); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 177.5 (C-4), 163.1 (C-2), 161.1 (C-6) 152.3 (C-9), 131.7 (C-11), 131.3 (C-14), 129.0 (C-13 & C-15), 126.2 (C-12 & C-16), 122.0 (C-10), 121.7 (C-7), 120.2 (C-8), 110.7 (C-5), 106.7 (C-3); LCMS (ES-API) m/z: 241 $(M+H)^+$.

6-Chloro-2-phenyl-chromen-4-one **7p** (Table **2**, entry **16**): Mp 183-184°C [2e]; IR (KBr) ν: 1651, 1601, 1567, 1457, 1438, 1307, 1132, 908, 682 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz): δ 8.17 (d, *J* = 2.3 Hz, 1H, H-5), 7.90-7.88 (m, 2H, H-12 & H-16), 7.65-7.61 (m, 1H, H-7), 7.56-7.50 (m, 4H, H-13, H-14, H-15 & H-8), 6.82 (s, 1H, H-3); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 177.1 (C-4), 163.7 (C-2), 154.4 (C-9), 133.0 (C-7), 131.8 (C-5), 131.2 (C-11), 131.1 (C-6), 129.1 (C-13 & C-15), 126.3 (C-14), 125.1 (C-12 & C-16), 124.7 (C-10), 119.7 (C-8), 107.3 (C-3); LCMS (ES-API) m/z: 257 $(M+H)^+$.

2-Cyclohexyl-chromen-4-one **7q** (Table **2**, entry **17**): Mp 127-129°C [2e]; IR (KBr) ν: 1736, 1676, 1606, 1580, 1469, 1024, 844, 758, 617 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz): δ 8.18 (m, 1H, H-7), 7.64 (m, 1H, H-5), 7.39 (m, 2H, H-6 & H-8), 6.17 (s, 1H, H-3), 2.52 (m, 1H, CH), 2.11-1.20 (m, 10H, CH_2); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 178.6 (C-4), 173.4 (C-2), 156.4 (C-9), 133.3 (C-7), 125.5 (C-5), 124.7 (C-10), 123.7 (C-6), 117.7 (C-8), 107.8 (C-3), 42.7 (C-11), 30.3 (C-14), 25.7 (C-12 & C-16), 25.6 (C-13 & C-15); LCMS (ES-API) m/z: 229 $(M+H)^+$.

7-Methoxy-2-Cyclohexyl-chromen-4-one (Table **2**, entry **18**): Mp 152-154°C (18); IR (KBr) ν: 1641, 1606, 1572, 1502, 1442, 1384, 1238, 1026, 923, 831 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz): δ 8.06 (d, *J* = 8.7 Hz, 1H, H-5), 6.95-6.83 (m, 2H, H-6 & H-8), 6.09 (s, 1H, H-3), 3.88 (s, 3H, OCH_3), 2.47 (m, 1H, CH), 1.86-1.45 (m, 10H, CH_2); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 177.9(C-4), 172.7 (C-2), 163.7 (C-7), 158.0 (C-9), 126.7 (C-5), 117.5 (C-10), 113.9 (C-6), 107.5 (C-3), 99.9 (C-8), 55.6 (OCH_3), 42.5 (C-11), 30.3 (C-

3H, $CH_2\underline{CH_3}$); ^{13}C NMR (DMSO-d_6, 75 MHz): δ 165.7 (EtO<u>C</u>=O), 152.2 (C-2), 148.3 (C-6), 148.0 (C-3′), 147.9 (C-4′), 137.3 (C-1′), 117.8 (C-6′), 111.6 (C-2′), 110.4 (C-5′), 99.3 (C-5), 59.1 ($\underline{CH_2}$-CH_3), 55.3 (C-4), 17.6 (CH_3), 14.1 (CH_2-$\underline{CH_3}$); LCMS (ES-API) m/z: 321 $(M+H)^+$.

***6-Methyl-4-phenyl-2-thioxo-1,2,3,4-tetrahydro-pyrimidine-5-carboxylic acid ethyl ester* 14j** (Table **4**, entry **10**): Mp 205-207°C [11]; IR (KBr) ν: 3328, 3177, 2366, 1735, 1703, 1667, 1578, 1196, 723 cm^{-1}; ^{1}H NMR (DMSO-d_6, 300 MHz): δ 10.54 (bs, 1H, NH), 9.86 (bs, 1H, NH), 7.58-7.43 (m, 5H, H-2′, H-3′, H-4′, H-5′& H-6′), 5.37 (s, 1H, H-4), 4.21 (q, J = 7.1 Hz, 2H, $\underline{CH_2}CH_3$), 2.50 (s, 3H, CH_3), 1.30 (t, J = 7.1 Hz, 3H, $CH_2\underline{CH_3}$); ^{13}C NMR (DMSO-d_6, 75 MHz): δ 179.3 (C-2), 170.2 (EtO<u>C</u>=O), 167.1 (C-6), 150.1 (C-1′), 148.5 (C-3′& C-5′), 131.5 (C-2′& C-6′), 133.4 (C-4′), 105.8 (C-5), 64.6 ($\underline{CH_2}$-CH_3), 59.2 (C-4), 22.3 (CH_3), 19.1 (CH_2-$\underline{CH_3}$); LCMS (ES-API) m/z: 277.2 $(M+H)^+$.

6-Methyl-2-thioxo-4-p-tolyl-1,2,3,4-tetrahydro-pyrimidine-5-carboxylicacid ethyl ester 14k (Table **4**, entry **11**): Mp 188-190°C [36]; IR (KBr) ν: 3325, 3108, 2981, 1731, 1673, 1577, 1196, 761 cm^{-1}; ^{1}H NMR (DMSO-d_6, 300 MHz): δ 10.30 (s, 1H, NH), 9.61 (s, 1H, NH), 7.16- 7.08 (m, 4H, H-2′, H-3′, H-5′& H-6′), 5.12 (s, 1H, H-4), 4.02 (q, J = 7.2, 2H, $\underline{CH_2}CH_3$), 2.28 (s, 3H, Ar-CH_3), 2.25 (s, 3H, CH_3), 1.10 (t, J = 7.2, 3H, $CH_2\underline{CH_3}$); ^{13}C NMR (DMSO-d_6, 75 MHz): δ 174.5 (C-2), 165.6 (EtO<u>C</u>=O), 145.3 (C-6), 141.0 (C-1′), 137.4 (C-4′), 129.5 (C-3′& C-5′), 126.7 (C-2′& C-6′), 101.2 (C-5), 60.0 ($\underline{CH_2}$-CH_3), 54.1 (C-4), 21.1 (Ar-CH_3), 17.6 (CH_3), 14.5 (CH_2-$\underline{CH_3}$); LCMS (ES-API) m/z: 291.2 $(M+H)^+$.

***4-(4-Fluoro-phenyl)-6-methyl-2-thioxo-1,2,3,4-tetrahydro-pyrimidine-5-carboxylic acid ethyl ester* 14l** (Table **4**, entry **12**): Mp 182-184°C [37]; IR (KBr) ν: 3326, 3175, 2991, 1729, 1707, 1681, 1577, 1228, 742 cm^{-1}; ^{1}H NMR (DMSO-d_6, 300 MHz): δ 10.56 (s, 1H, NH), 9.85 (s, 1H, NH), 7.41 (d, J = 5.2 Hz, 2H, H-2′& H-6′), 7.39 (d, J = 5.2 Hz, 2H, H-3′& H-5′), 5.18 (s, 1H, H-4), 4.19 (q, J = 7.1 Hz, 2H, $\underline{CH_2}CH_3$), 2.50 (s, 3H, CH_3), 1.27 (t, J = 7.1 Hz, 3H, $CH_2\underline{CH_3}$); ^{13}C NMR (DMSO-d_6, 75 MHz): δ 174.17 (C-2), 165.13 (EtO<u>C</u>=O), 159.5 (C-6), 139.7 (C-4′), 128.5 (C-1′), 128.3 (C-2′& C-6′), 115.4 (C-3′& C-5′), 100.5 (C-5), 59.6 ($\underline{CH_2}$-CH_3), 53.4 (C-4), 17.1 (CH_3), 13.9 (CH_2-$\underline{CH_3}$); LCMS (ES-API) m/z: 295 $(M+H)^+$.

***4-(4-Chloro-phenyl)-6-methyl-2-thioxo-1,2,3,4-tetrahydro-pyrimidine-5-carboxylic acid ethyl ester* 14m** (Table **4**, entry **13**): Mp 187-189°C [11]; IR (KBr) ν: 3323, 3176, 3105, 2985, 1708, 1669, 1576, 1457, 1281, 747 cm^{-1}; ^{1}H NMR (DMSO-d_6, 300 MHz): δ 10.59 (s, 1H, NH), 9.80 (s, 1H, NH), 7.62 (d, J = 8.0 Hz, 2H,H-3′& H-5′), 7.43 (d, J = 8.0 Hz, 2H, H-2′& H-6′), 5.37 (s, 1H, H-4), 4.21 (q, J = 7.1 Hz, 2H, $\underline{CH_2}CH_3$), 2.50 (s, 3H, CH_3), 1.30 (t, J = 7.1 Hz, 3H, $CH_2\underline{CH_3}$); ^{13}C NMR (DMSO-d_6, 75 MHz): δ 174.2 (C-2), 164.9 (EtO<u>C</u>=O), 145.3 (C-6), 142.3 (C-1′), 132.2 (C-4′), 128.5 (C-3′& C-5′), 128.2 (C-2′& C-6′), 100.3 (C-5), 59.6 ($\underline{CH_2}$-CH_3), 53.4 (C-4), 17.1 (CH_3), 13.9 (CH_2-$\underline{CH_3}$); LCMS (ES-API) m/z: 311$(M+H)^+$.

CONFLICT OF INTEREST

The authors confirm that this article content has no conflict of interest.

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