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Antimony(III) chloride-catalysed Biginelli reaction: a versatile method for the synthesis of dihydropyrimidinones through a different reaction mechanism

Ivica Cepanec,* Mladen Litvić, Mirela Filipan-Litvić and Ivana Grüngold

BELUPO Pharmaceuticals Inc., Research Department, Radnička c. 224, 10000 Zagreb, Croatia

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Abstract—Antimony(III) chloride (20 mol %) in refluxing acetonitrile efficiently catalyses the synthesis of dihydropyrimidinones (50–90% yields) by the Biginelli reaction of aromatic aldehydes, acetoacetate esters and urea. This reaction proceeds through 3-ureido-crotonates followed by cyclisation with an aromatic aldehyde to the dihydropyrimidinone.

1. Introduction

The Biginelli reaction is the most effective route to dihydropyrimidinones.[1] These products exhibit biological activity, e.g., as calcium channel blockers.[2] Classically, the Biginelli reaction is conducted in boiling ethanol in the presence of catalytic amounts of hydrochloric acid.[3] This simple procedure has been successful in a number of Biginelli reactions involving substrates lacking sterically demanding groups. During the last few years, numerous catalytic methods have been developed in order to improve the yield and scope of the Biginelli reaction. Most of them are based on protic or Lewis acid-catalysed reactions.[4–20] The most effective methods involve reagent(s) which are stoichiometric dehydrating agents and protic or Lewis acids at the same time: ethyl polyphosphate,[21] TMSCl,[22] TMSCl/NaI,[23] $FeCl_3$/$Si(OEt)_4$,[24] etc. These methods give good results in the cases of sterically encumbered aldehydes and/or acetoacetate esters. In order to achieve further improvements in the synthesis of sterically hindered dihydropyrimidinones we have studied a few potentially active reagents. Among them, antimony(III) chloride ($SbCl_3$) has shown a profound catalytic activity. It has been employed in organic synthesis as a Lewis acid in Friedel–Crafts acylations,[25] reductions with $NaBH_4$,[26,27] cleavage of trityl ethers,[28] and in the synthesis of some heterocycles.[29]

2. Results and discussion

We wish to report that antimony(III) chloride ($SbCl_3$) catalyses the Biginelli reaction of aromatic aldehydes (**I**), acetoacetate esters (**II**) and urea yielding the dihydropyrimidinones (**III**). Initially the catalytic effect of $SbCl_3$ was studied on the model reaction of urea, benzaldehyde (**1a**) and sterically demanding methyl isobutyrylacetate (**2a**) to give 6-isopropyl-5-methoxycarbonyl-4-phenyl-3,4-dihydropyrimidin-2(1*H*)-one (**3a**) (Scheme 1). The reactions were conducted in refluxing toluene, absolute ethanol and acetonitrile as solvents. The latter solvent proved to be the most effective. In order to study the efficiency of this new method, several published methods were tested on the same model reaction. The results from this study are presented in Table 1.

With respect to other published Biginelli reaction catalysts, $SbCl_3$ was shown to be significantly more effective than $FeCl_3$, $NiCl_2$, $BiCl_3$, $BiONO_3$, $Cu(OTf)_2$ and CuCl/HOAc in the presence of stoichiometric $BF_3 \cdot Et_2O$ (entry 1 vs entries 9–14). At the same time $SbCl_3$ was shown to be of similar activity as zinc triflate and ytterbium triflate. Generally these are the most active Biginelli reaction catalysts. Moreover $SbCl_3$ is far less expensive than these triflate salts. Concerning the molar ratio of $SbCl_3$, we concluded that 20 mol % gives acceptable results, whereas a stoichiometric amount (100 mol %) might provide better results with more sterically hindered substrates.

Antimony(III) chloride (20 mol %) in refluxing acetonitrile was further examined in the model Biginelli reactions of different aromatic aldehydes (**1a–i**), acetoacetate esters (**2a–e**) and urea affording the corresponding dihydropyrimidinones (**3a–p**) in good-to-high yields (Table 2). As the reactions proceeded, white-to-slightly yellow precipitates appear due to the formation of the expected dihydropyrimidinones and antimony oxychloride (SbOCl). The work-up of the reaction mixture includes the evaporation of the reaction solvent (MeCN), trituration of the crude product

* Corresponding author. Fax: +385 1 2408 074; e-mail: ivica.cepanec@belupo.hr

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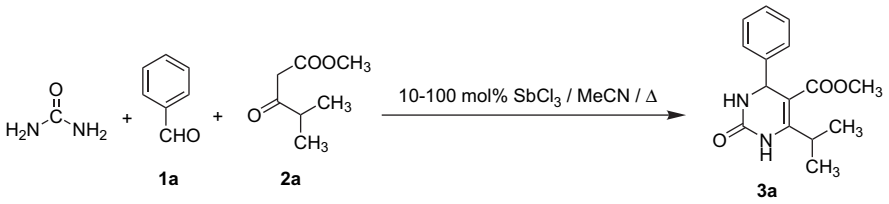


Scheme 1.

Table 1. Antimony(III) chloride-catalysed reaction of urea, benzaldehyde (**1a**) and methyl isobutyrylacetate (**2a**) (Scheme 1). Comparative study with published methods

Entry	Method (literature reference)	Reaction solvent	Temp (°C)	Time[a] (h)	Yield of **3a**[b] (%)
1	10 mol % $SbCl_3$	MeCN	82	20	62
2	10 mol % $SbCl_3$	abs EtOH	79	20	61
3	10 mol % $SbCl_3$	Toluene	110	20	54
4	20 mol % $SbCl_3$	MeCN	82	18	77
5	30 mol % $SbCl_3$	MeCN	82	18	78
6	50 mol % $SbCl_3$	MeCN	82	20	78
7	100 mol % $SbCl_3$	MeCN	82	18	90
8	10 mol % $Zn(OTf)_2$[30]	MeCN	82	20	64
9	10 mol % $FeCl_3 \cdot 6H_2O$[4]	96% EtOH	78	20	57
10	10 mol % CuCl/HOAc/ 100 mol % $BF_3 \cdot Et_2O$[31]	THF	67	20	52
11	10 mol % $NiCl_2 \cdot 6H_2O$[4]	96% EtOH	78	20	27
12	10 mol % $BiCl_3$[11]	MeCN	82	20	43
13	10 mol % $BiONO_3$[32]	MeCN	82	20	29
14	10 mol % $Cu(OTf)_2$[33]	MeCN	82	20	53
15	10 mol % $Yb(OTf)_3$[13]	MeCN	82	20	69

[a] Determined by TLC.
[b] Yields of pure products isolated by chromatography.

(dihydropyrimidinone+SbOCl) with aqueous hydrochloric acid, followed by separation of crude dihydropyrimidinone by filtration. The latter treatment allows the dissolution of SbOCl according to the equation:

$$SbOCl + 2HCl \rightarrow SbCl_3 + H_2O$$

The crude dihydropyrimidinones were purified by recrystallisation or by chromatography.

Although this method does not give excellent yields, it provides a simple, effective and inexpensive access to highly substituted dihydropyrimidinones with significant steric hindrances.

Afterwards, we studied the reaction mechanism of the $SbCl_3$-catalysed Biginelli reaction. The generally accepted Biginelli reaction mechanism includes the acid-catalysed formation of a C=N bond from the parent aldehyde **1a** and urea, followed by addition of the acetoacetate ester **2b** to the arylidene-urea **4a** and cyclodehydration (via **5b** and **6b**) yielding dihydropyrimidinone **3b** (Scheme 2).[34–36]

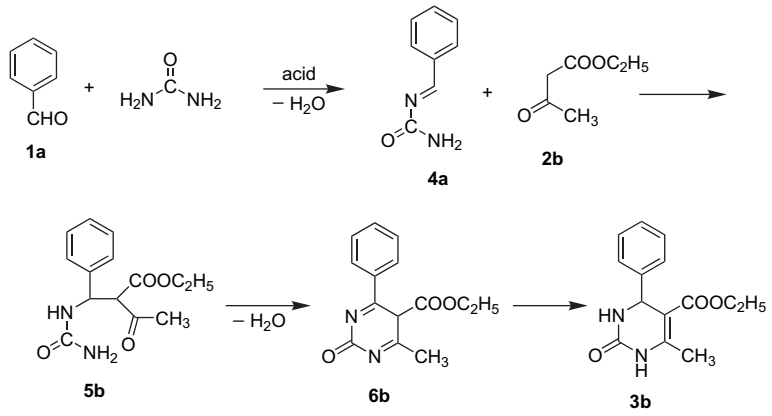
In order to clarify the role of $SbCl_3$ in the Biginelli reaction, we have tested the following reactions at an equimolar ratio of the following reactants:

(a) benzaldehyde (**1a**) and urea,
(b) benzaldehyde (**1a**) and ethyl acetoacetate (**2b**) and
(c) ethyl acetoacetate (**2b**) and urea.

Table 2. $SbCl_3$-catalysed Biginelli reaction of aromatic aldehydes **1a–i**, acetoacetate esters **2a–e** and urea

Entry[a]	ArCHO, Ar=	R^1, R^2	Product	Time[b] (h)	Yield of **3**[c] (%)
1	C_6H_5 (**1a**)	CH_3, $CH(CH_3)_2$ (**2a**)	**3a**	20	77
2	C_6H_5 (**1a**)	C_2H_5, CH_3 (**2b**)	**3b**	22	75
3	C_6H_5 (**1a**)	$CH(CH_3)_2$, CH_3 (**2c**)	**3c**	23	55 (71)[d]
4	C_6H_5 (**1a**)	$CH_2CH(CH_3)_2$, CH_3 (**2d**)	**3d**	24	88
5	C_6H_5 (**1a**)	$CH_2C_6H_5$, CH_3 (**2e**)	**3e**	18	77
6	4-ClC_6H_4 (**1b**)	C_2H_5, CH_3 (**2b**)	**3f**	22	89
7	2-ClC_6H_4 (**1c**)	C_2H_5, CH_3 (**2b**)	**3g**	21	87
8	4-$CH_3OC_6H_4$ (**1d**)	CH_3, $CH(CH_3)_2$ (**2a**)	**3h**	24	64
9	2-$CH_3OC_6H_4$ (**1e**)	CH_3, $CH(CH_3)_2$ (**2a**)	**3i**	22	72
10	2,4-$(CH_3)_2C_6H_3$ (**1f**)	CH_3, $CH(CH_3)_2$ (**2a**)	**3j**	24	54 (63)[d]
11	2,6-$Cl_2C_6H_3$ (**1g**)	$CH(CH_3)_2$, CH_3 (**2c**)	**3k**	22	59
12	1-$C_{10}H_8$ (**1h**)	CH_3, $CH(CH_3)_2$ (**2a**)	**3l**	24	59
13	1-$C_{10}H_8$ (**1h**)	$CH_2CH(CH_3)_2$, CH_3 (**2d**)	**3m**	24	81
14	9-$C_{14}H_9$ (**1i**)	CH_3, $CH(CH_3)_2$ (**2a**)	**3n**	20	70
15	9-$C_{14}H_9$ (**1i**)	$CH_2C_6H_5$, CH_3 (**2e**)	**3o**	22	79
16	2-$CH_3OC_6H_4$ (**1e**)	$CH_2C_6H_5$, CH_3 (**2e**)	**3p**	24	51 (78)[d]

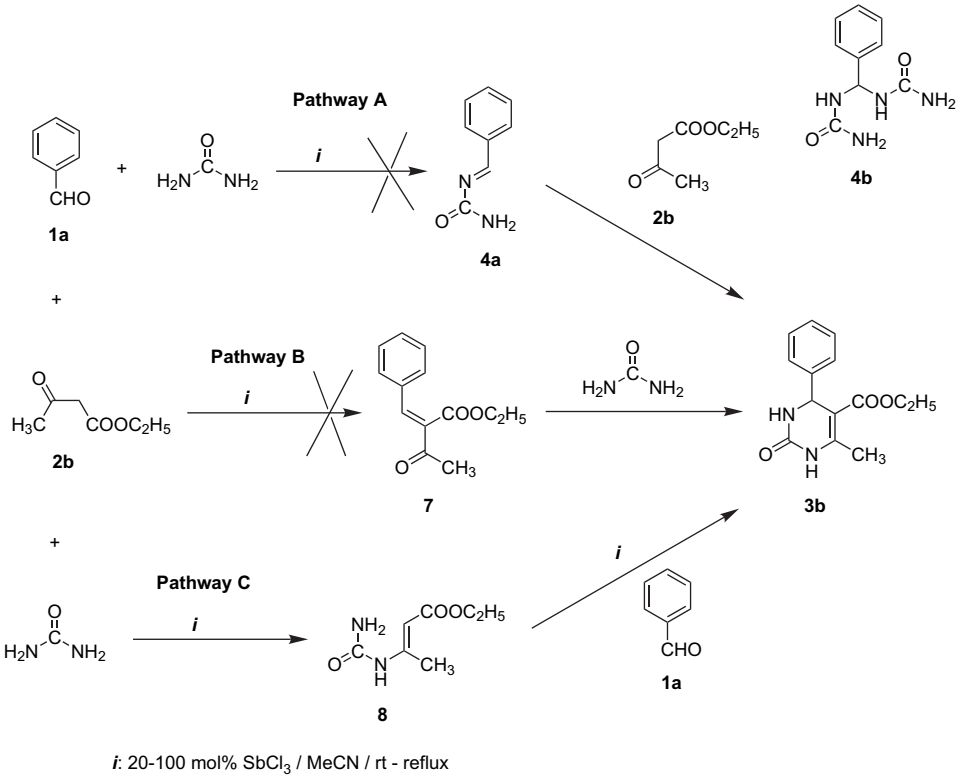
[a] All reactions were performed at a molar ratio aldehyde/acetoacetate ester/urea=1:1:1.5 with 20 mol % $SbCl_3$ in refluxing MeCN unless otherwise noted.
[b] Determined by TLC.
[c] Yields of pure products isolated by chromatography.
[d] The reactions were conducted with 100 mol % $SbCl_3$.



Scheme 2.

The reactions were performed in acetonitrile as the solvent, in the presence of 20–100 mol % $SbCl_3$ at room temperature (rt) to reflux. We were very surprised that benzaldehyde (**1a**) and urea, under these reaction conditions, did not undergo the expected reaction to yield *N*-benzylidene-urea (**4a**), or the corresponding *N*,*N*′-benzylidenebisurea (**4b**) (pathway A). Moreover benzaldehyde (**1a**) did not react with ethyl acetoacetate (**2b**) to give the Knoevenagel product **7** (pathway B). Finally ethyl acetoacetate (**2b**) was subjected to the reaction with urea yielding the corresponding *N*-(1-ethoxycarbonyl-propen-2-yl)urea (**8**) as the sole product (pathway C). The latter smoothly reacted with benzaldehyde (**1a**), even at room temperature, to give the dihydropyrimidinone **3b** in almost quantitative yield (Scheme 3). Although the intermediate **8** was isolated by preparative chromatography in a 9% yield only, we assumed that this was due to the decomposition on a silica gel column.

These findings clearly indicate that the $SbCl_3$-catalysed Biginelli reaction proceeds through pathway C. Obviously in anhydrous conditions (MeCN) in the presence of relatively strong Lewis acid ($SbCl_3$), the formation of ureidocrotonates, e.g. **8**, becomes a dominant bimolecular reaction. These intermediates smoothly react with aldehydes yielding the dihydropyrimidinones. This is completely opposite to the protic acid-catalysed Biginelli reaction as postulated by Folkers and Johnson,[34] and recently re-examined by Kappe.[36] This might be also the case in numerous mechanistically related (suitable Lewis acid-catalyst+aprotic conditions) synthetic methods for performing the Biginelli



Scheme 3.

reaction, which have been published in recent years. Most of them have assumed the plausible mechanism according to Folkers, Johnson and Kappe without any real proof.

This reaction mechanism also explains the fact that the method is tolerant to various sterically demanding substituents in either the aldehyde or acetoacetate reaction counterpart. In contrast, this is not the case in the methods based on the *N*-benzylidene-ureas as first intermediates. There the rate determining step is the formation of C=N bond between the parent aldehyde and urea which is actually troublesome in the cases of aldehydes with significant steric hindrances.

3. Conclusion

Antimony(III) chloride acts as efficient catalyst of the Biginelli reaction of urea, aromatic aldehydes and acetoacetate esters yielding dihydropyrimidinones in good-to-high yields. Although the $SbCl_3$ is not an ideal catalyst, it allows the preparation of otherwise hardly accessible, sterically hindered dihydropyrimidinones in good yield. The proposed reaction mechanism of the $SbCl_3$-catalysed Biginelli reaction includes the reaction of urea with acetoacetate ester yielding ureidocrotonate as the first step. The latter intermediate reacts with aromatic aldehyde to produce the cyclic transient intermediate which, by elimination of water, gives the dihydropyrimidinone. We believe that this method offers a simple, inexpensive and versatile approach to the synthesis of sterically demanding Biginelli compounds.

4. Experimental

4.1. General

IR spectra were recorded on a Perkin–Elmer Spectrum One spectrometer. ^1H and ^{13}C NMR spectra were recorded on an AV Bruker (600 MHz) spectrometer, and shifts (δ) are given in parts per million downfield from TMS as an internal standard. TLC analyses were performed on Merck's (Darmstadt, Germany) DC-alufolien with Kieselgel $60F_{254}$. Preparative chromatography was carried out on silica gel, ϕ 0.063–0.2 mm (Merck, Germany). Melting points (mp) were determined on a Büchi B-540 instrument. The term room temperature means 20–25 °C.

4.2. Synthesis of 5-methoxycarbonyl-6-isopropyl-4-phenyl-3,4-dihydropyrimidin-2(1*H*)-one (3a) with different amounts of $SbCl_3$

To a solution of benzaldehyde (**1a**, 1.06 g, 0.01 mol) and methyl isobutyrylacetate (**2a**, 1.44 g, 0.01 mol) in anhydrous acetonitrile (8 mL), urea (0.90 g, 0.015 mol, 1.5 equiv) and antimony(III) chloride (0.23 g, 10 mol %; 0.46 g, 20 mol %; 0.68 g, 30 mol %; 1.14 g, 50 mol %; 2.28 g, 100 mol %) were added. The reaction mixture was heated with stirring to the reflux temperature (83 °C), and stirred at this temperature for the time indicated in Table 1. Then the reaction mixture was evaporated to dryness. The residue was cooled to room temperature, and triturated with diluted hydrochloric acid (2 mL of 37% HCl+8 mL of distilled water) at room temperature for 1 h. The crude product **3a** (R_f 0.29) was separated by filtration, dried in high vacuum and purified by chromatography on silica gel column (200 g) with dichloromethane/2-propanol (9.8:0.2) as an eluent.

The model reactions employing alternative Lewis acids were performed according to the procedures described in the literature: $Zn(OTf)_2$,[30] $FeCl_3\cdot 6H_2O$,[4] $CuCl/HOAc/BF_3\cdot Et_2O$,[31] $NiCl_2\cdot 6H_2O$,[4] $BiCl_3$,[11] $BiONO_3$,[32] $Cu(OTf)_2$,[33] $Yb(OTf)_2$.[13]

4.2.1. 5-Methoxycarbonyl-6-isopropyl-4-phenyl-3,4-dihydropyrimidin-2(1*H*)-one (3a). Colourless needles; mp 229.5–232.1 °C; yields are given in Table 1; found: C, 65.5; H, 6.7; N, 10.1. $C_{15}H_{18}N_2O_3$ requires C, 65.68; H, 6.61; N, 10.21; R_f (CH_2Cl_2/2-PrOH, 9.8:0.2) 0.29; ν_{max} (KBr) 3414, 2918, 1715, 1663, 1493, 1449, 1271, 1167, 1027 cm^{-1}; δ_H (600 MHz, $CDCl_3$) 8.92 (1H, s, N*H*), 7.79 (1H, s, N*H*), 7.35–7.22 (5H, m, arom.), 5.15 (1H, d, J=3.3 Hz, benzylic), 4.19–4.10 (1H, m, C*H*(CH_3)$_2$), 3.52 (3H, s, COOC*H*$_3$), 1.17–1.12 (6H, m, CH(C*H*$_3$)$_2$); δ_C (600 MHz, $CDCl_3$) 165.9 (*C*OOMe), 156.8, 152.8, 144.6, 128.6, 127.4, 126.2, 98.0, 53.7, 51.0, 27.1, 19.2, 19.0.

4.3. General procedure for the $SbCl_3$-catalysed synthesis of dihydropyrimidinones

To a solution of an aromatic aldehyde (**1a–i**, 0.01 mol) and acetoacetate ester (**2a–e**, 0.01 mol) in anhydrous acetonitrile (10 mL), urea (0.90 g, 0.015 mol, 1.5 equiv) and antimony(III) chloride (0.46 g, 0.002 mol, 20 mol %) were added. The reaction mixture was heated with stirring to the reflux temperature (83 °C), and further stirred at this temperature for the time indicated in Table 2. Then the reaction mixture was evaporated to dryness. The residue was cooled to room temperature, and triturated with diluted hydrochloric acid (2 mL of 37% HCl+8 mL of distilled water) at room temperature for 1 h. The crude dihydropyrimidinones **3a–p** were separated by filtration. The crude products (reasonably pure for further synthetic purpose; usually >95% by ^1H NMR spectroscopy) were purified by chromatography on silica gel (100 g) column or recrystallised from 96% ethanol. Analytical results (mp, IR, ^1H and ^{13}C NMR) of products **3b**,[37] **3c**,[24] **3d**,[24] **3e**,[24] **3f**[31] and **3g**[38] were identical to those reported in the literature.

4.3.1. 6-Isopropyl-5-methoxycarbonyl-4-(4-methoxyphenyl)-3,4-dihydropyrimidin-2(1*H*)-one (3h). Colourless needles; mp 168.0–170.8 °C; yield 1.95 g (64%); found: C, 63.0; H, 6.6; N, 9.1. $C_{16}H_{20}N_2O_4$ requires C, 63.14; H, 6.62; N, 9.21; R_f (CH_2Cl_2/2-PrOH, 9.5:0.5) 0.42; ν_{max} (KBr) 3341, 3228, 3138, 2974, 2946, 1715, 1698, 1629, 1608, 1585, 1510, 1460, 1427, 1344, 1316, 1269, 1241, 1222, 1181, 1169, 1138, 1111, 1086, 1067, 1018 cm^{-1}; δ_H (600 MHz, $CDCl_3$) 8.68 (1H, s, N*H*), 7.56 (1H, s, N*H*), 7.16 (2H, d, J=8.6 Hz, arom.), 6.88 (2H, d, J=8.6 Hz, arom.), 5.12 (1H, d, J=3.2 Hz, benzylic), 4.13–4.08 (1H, m, C*H*(CH_3)$_2$), 3.73 (3H, s, OC*H*$_3$), 3.53 (3H, s, COOC*H*$_3$), 1.15 (6H, dd, J_1=7.1 Hz, J_2=7.0 Hz, CH(C*H*$_3$)$_2$); δ_C (600 MHz, $CDCl_3$) 165.6 (*C*OOCH$_3$), 158.4, 155.9, 152.4, 136.6, 127.0, 113.7, 98.3, 54.9, 53.0, 50.5, 26.9, 19.0, 18.7.

4.3.2. 6-Isopropyl-5-methoxycarbonyl-4-(2-methoxyphenyl)-3,4-dihydropyrimidin-2(1*H*)-one (3i). Colourless needles; mp 248.6–250.4 °C; yield 2.19 g (72%); found: C, 63.0; H, 6.5; N, 9.2. $C_{16}H_{20}N_2O_4$ requires C, 63.14; H, 6.62; N, 9.21; R_f (CH_2Cl_2/2-PrOH, 9.5:0.5) 0.51; ν_{max} (KBr) 3406, 3223, 3119, 2999, 2960, 2937, 2835, 1709, 1692, 1635, 1597, 1585, 1486, 1463, 1440, 1429, 1391, 1373, 1345, 1313, 1291, 1274, 1239, 1220, 1182, 1109, 1091, 1067, 1046, 1029 cm^{-1}; δ_H (600 MHz, $CDCl_3$) 8.54 (1H, s, N*H*), 7.21 (1H, t, *J*=7.1 Hz, N*H*), 7.06–6.84 (4H, m, arom.), 5.49 (1H, d, *J*=2.7 Hz, benzylic), 3.80 (3H, s, OCH_3), 3.47 (3H, s, COOCH_3), 1.17 (6H, dd, J_1=7.0 Hz, J_2=7.0 Hz, CH(CH_3)$_2$); δ_C (600 MHz, $CDCl_3$) 165.5 (*C*OOCH$_3$), 156.5, 156.3, 152.4, 131.0, 128.3, 126.4, 119.9, 111.1, 96.4, 55.1, 50.3, 49.0, 26.9, 19.1, 18.7.

4.3.3. 4-(2,4-Dimethylphenyl)-6-isopropyl-5-methoxycarbonyl-3,4-dihydropyrimidin-2(1*H*)-one (3j). Colourless needles; mp 225.6–227.7 °C; yield 1.63 g (54%) at 20 mol % $SbCl_3$, 1.90 g (63%) at 100 mol % $SbCl_3$; found: C, 67.4; H, 7.2; N, 9.2. $C_{17}H_{22}N_2O_3$ requires C, 67.53; H, 7.33; N, 9.27; R_f (CH_2Cl_2/2-PrOH, 9.5:0.5) 0.53; ν_{max} (KBr) 3364, 3243, 3138, 2973, 2952, 2930, 2876, 1692, 1635, 1456, 1427, 1368, 1338, 1313, 1277, 1221, 1186, 1176, 1135, 1094, 1069 cm^{-1}; δ_H (600 MHz, $CDCl_3$) 8.88 (1H, s, N*H*), 7.62 (1H, s, N*H*), 7.06 (1H, d, *J*=7.6 Hz, arom.), 6.97–6.94 (2H, m, arom.), 5.38 (1H, d, *J*=2.2 Hz, benzylic), 4.21–4.12 (1H, m, CH(CH$_3$)$_2$), 3.44 (3H, s, COOCH_3), 2.37 (3H, s, CH_3), 2.21 (3H, s, CH_3), 1.18 (6H, dd, J_1=6.9 Hz, J_2=6.9 Hz, CH(CH_3)$_2$); δ_C (600 MHz, $CDCl_3$) 165.8 (*C*OOCH$_3$), 156.3, 152.4, 140.2, 136.3, 134.6, 131.0, 127.2, 126.3, 98.2, 50.9, 50.1, 27.0, 20.6, 19.4, 19.0, 18.6.

4.3.4. 4-(2,6-Dichlorophenyl)-5-isopropoxycarbonyl-6-methyl-3,4-dihydropyrimidin-2(1*H*)-one (3k). Colourless needles; mp 224.9–227.8 °C; yield 2.02 g (59%); found: C, 52.2; H, 4.6; N, 8.1. $C_{15}H_{16}N_2O_3Cl_2$ requires C, 52.49; H, 4.70; N, 8.16; R_f (CH_2Cl_2/2-PrOH, 9.5:0.5) 0.34; ν_{max} (KBr) 3343, 3146, 2988, 1690, 1645, 1580, 1563, 1514, 1437, 1374, 1351, 1305, 1234, 1204, 1095, 1055 cm^{-1}; δ_H (600 MHz, $CDCl_3$) 9.27 (1H, s, N*H*), 7.63–7.26 (3H, m, arom.), 6.14 (1H, s, N*H*), 5.44 (1H, s, benzylic), 4.78–4.70 (1H, m, C*H*(CH$_3$)$_2$), 2.18 (3H, s, CH_3), 1.10 (3H, d, *J*=6.3 Hz, CH(CH_3)$_2$), 0.66 (3H, d, *J*=6.2 Hz, CH(CH_3)$_2$); δ_C (600 MHz, $CDCl_3$) 164.5 (*C*OO*i*-Pr), 157.0, 150.7, 137.8, 134.8, 130.1, 129.5, 94.4, 65.8, 52.3, 21.6, 20.9, 18.0.

4.3.5. 6-Isopropyl-5-methoxycarbonyl-4-(1-naphthyl)-3,4-dihydropyrimidin-2(1*H*)-one (3l). Colourless needles; mp 235.3–238.7 °C; yield 1.91 g (59%); found: C, 70.1; H, 6.1; N, 8.5. $C_{19}H_{20}N_2O_3$ requires C, 70.35; H, 6.21; N, 8.64; R_f (CH_2Cl_2/2-PrOH, 9.5:0.5) 0.46; ν_{max} (KBr) 3410, 3233, 3129, 2970, 1694, 1681, 1631, 1509, 1457, 1431, 1410, 1392, 1344, 1317, 1291, 1275, 1263, 1236, 1186, 1132, 1096 cm^{-1}; δ_H (600 MHz, $CDCl_3$) 9.01 (1H, s, N*H*), 8.32 (1H, d, *J*=8.1 Hz, N*H*), 8.00–7.73 (3H, m, arom.), 7.62–7.39 (4H, arom.), 6.07 (1H, d, *J*=3.4 Hz, benzylic), 4.30–4.21 (1H, m, C*H*(CH$_3$)$_2$), 3.36 (COOCH_3), 1.25 (6H, dd, J_1=7.0 Hz, J_2=6.9 Hz, CH(CH_3)$_2$); δ_C (600 MHz, $CDCl_3$) 165.8 (*C*OOCH$_3$), 157.2, 152.4, 139.6, 133.7, 130.1, 128.6, 128.1, 126.2, 125.8, 123.7, 123.6, 97.8, 51.0, 49.7, 27.2, 19.4, 19.1.

4.3.6. 5-Isobutyloxycarbonyl-6-methyl-4-(1-naphthyl)-3,4-dihydropyrimidin-2(1*H*)-one (3m). Colourless needles; mp 188.9–190.4 °C; yield 2.74 g (81%); found: C, 70.8; H, 6.5; N, 8.2. $C_{20}H_{22}N_2O_3$ requires C, 70.99; H, 6.55; N, 8.28; R_f (CH_2Cl_2/2-PrOH, 9.5:0.5) 0.36; ν_{max} (KBr) 3232, 3100, 2960, 1705, 1686, 1654, 1600, 1509, 1470, 1436, 1397, 1373, 1334, 1289, 1269, 1243, 1167, 1093, 1074 cm^{-1}; δ_H (600 MHz, $CDCl_3$) 9.31 (1H, s, N*H*), 8.32 (1H, d, *J*=8.2 Hz, N*H*), 7.99–7.80 (3H, m, arom.), 7.62–7.39 (4H, m, arom.), 6.09 (1H, d, *J*=3.1 Hz, benzylic), 3.64–3.51 (2H, m, CH_2CH(CH$_3$)$_2$), 2.41 (3H, s, CH_3), 1.50–1.37 (1H, m, CH$_2$C*H*(CH$_3$)$_2$), 0.44 (6H, dd, J_1=6.7 Hz, J_2=6.7 Hz, CH$_2$CH(CH_3)$_2$); δ_C (600 MHz, $CDCl_3$) 165.3 (*C*OO*i*-Bu), 151.7, 149.4, 140.0, 133.6, 130.1, 128.5, 127.9, 126.1, 125.70, 125.66, 123.9, 123.6, 98.7, 69.1, 49.6, 27.0, 18.52, 18.49, 17.8.

4.3.7. 4-(9-Anthryl)-6-isopropyl-5-methoxycarbonyl-3,4-dihydropyrimidin-2(1*H*)-one (3n). Colourless needles; mp 254.3–256.1 °C; yield 2.62 g (70%); found: C, 73.8; H, 5.9; N, 7.4. $C_{23}H_{22}N_2O_3$ requires C, 73.78; H, 5.92; N, 7.48; R_f (CH_2Cl_2/2-PrOH, 9.5:0.5) 0.54; ν_{max} (KBr) 3442, 3200, 3090, 2995, 2949, 1730, 1702, 1635, 1526, 1483, 1462, 1425, 1372, 1335, 1302, 1267, 1230, 1185, 1168, 1149, 1099, 1068, 1023 cm^{-1}; δ_H (600 MHz, $CDCl_3$) 8.42–8.31 (3H, m, N*H*+arom.), 7.96 (1H, d, *J*=8.8 Hz, N*H*), 7.52–7.40 (5H, m, arom.), 7.08 (1H, s, arom.), 5.40 (1H, s, benzylic), 4.03–3.91 (1H, m, C*H*(CH$_3$)$_2$), 2.98 (3H, s, COOCH_3), 1.31 (3H, d, *J*=6.9 Hz, CH(CH_3)$_2$), 1.21 (3H, d, *J*=7.0 Hz, CH(CH_3)$_2$); δ_C (600 MHz, $CDCl_3$) 165.6 (*C*OOCH$_3$), 151.5, 151.3, 132.3, 130.0, 129.3, 129.0, 126.3, 124.6, 122.8, 100.1, 51.1, 50.4, 27.7, 19.9, 18.9.

4.3.8. 4-(9-Anthryl)-5-benzyloxycarbonyl-6-isopropyl-3,4-dihydropyrimidin-2(1*H*)-one (3o). Colourless needles; mp 203.7–206.1 °C; yield 3.34 g (79%); found: C, 76.5; H, 5.1; N, 6.5. $C_{27}H_{22}N_2O_3$ requires C, 76.76; H, 5.25; N, 6.63; R_f (CH_2Cl_2/2-PrOH, 9.5:0.5) 0.39; ν_{max} (KBr) 3225, 3089, 2965, 1701, 1644, 1526, 1496, 1454, 1446, 1379, 1311, 1290, 1225, 1185, 1158, 1143, 1123, 1087, 1028 cm^{-1}; δ_H (600 MHz, $CDCl_3$) 9.47 (1H, s, N*H*), 8.57 (1H, s, N*H*), 8.47 (2H, s, arom.), 8.09 (2H, s, arom.), 7.72 (1H, s, arom.), 7.48–7.45 (4H, m, arom.), 7.10–7.06 (2H, m, arom.), 6.98–6.93 (2H, m, arom.), 6.37 (2H, d, *J*=7.5 Hz), 4.50 (2H, s, CH_2Ph), 2.27 (3H, s, CH_3); δ_C (600 MHz, $CDCl_3$) 165.1 (*C*OOBn), 150.5, 146.9, 135.9, 134.9, 131.3, 128.6, 128.0, 127.9, 127.3, 127.0, 125.8, 124.7, 124.2, 99.3, 64.3, 50.0, 17.9.

4.3.9. 5-Benzyloxycarbonyl-4-(2-methoxyphenyl)-6-methyl-3,4-dihydropyrimidin-2(1*H*)-one (3p). Colourless needles; mp 199.3–200.8 °C; yield 1.80 g (51%) at 20 mol % $SbCl_3$, 2.75 g (78%) at 100 mol % $SbCl_3$; found: C, 68.2; H, 5.6; N, 7.9. $C_{20}H_{20}N_2O_4$ requires C, 68.17; H, 5.72; N, 7.95; R_f (CH_2Cl_2/MeOH, 9.5:0.5) 0.40; ν_{max} (KBr) 3239, 3115, 3026, 2954, 2937, 2837, 1721, 1712, 1682, 1639, 1598, 1587, 1487, 1464, 1437, 1380, 1335, 1316, 1283, 1242, 1218, 1186, 1167, 1144, 1100, 1073, 1028, 1051 cm^{-1}; δ_H (600 MHz, $CDCl_3$) 9.23 (1H, s, N*H*), 7.34 (1H, s, N*H*), 7.27–7.24 (4H, m, arom.), 7.07–6.85 (5H, m, arom.), 5.58 (1H, d, *J*=2.8 Hz, benzylic), 5.02–4.93 (2H, m, CH_2Ph), 3.72 (3H, s, OCH_3), 2.32 (3H, s, CH_3); δ_C (600 MHz, $CDCl_3$) 165.0 (*C*OOBn), 156.4,

152.1, 149.9, 136.6, 131.5, 128.7, 128.2, 127.5, 127.1, 127.0, 120.2, 111.1, 97.1, 64.5, 55.3, 48.6, 17.8.

4.4. Antimony(III) chloride-catalysed synthesis of ureidocrotonate 8

To a solution of ethyl acetoacetate (**2b**, 2.60 g, 0.02 mol) in anhydrous acetonitrile (20 mL), urea (1.20 g, 0.02 mol) and antimony(III) chloride (0.92 g, 0.004 mol, 20 mol %) were added at once. The reaction mixture was stirred at room temperature for 24 h. Then the reaction mixture was evaporated to dryness. Thus obtained crude residue (R_f 0.57) was subjected to column chromatography on silica gel (200 g) with dichloromethane/methanol (9:1) as an eluent.

4.4.1. Ethyl 3-ureido-crotonate (8). Colourless needles; mp 157.6–159.3 °C, lit.[39] mp 158–160 °C; yield 0.32 g (9%); found: C, 48.6; H, 7.1; N, 16.1. $C_7H_{12}N_2O_3$ requires C, 48.83; H, 7.02; N, 16.27; ν_{max} (KBr) 3420, 3321, 3245, 2980, 2931, 2904, 2870, 2852, 1723, 1691, 1661, 1642, 1607, 1499, 1476, 1443, 1378, 1363, 1317, 1273, 1264, 1189, 1118, 1064, 1041, 1024 cm^{-1}; δ_H (600 MHz, $CDCl_3$) 10.67 (1H, s, N*H*), 5.03 (2H, s, NH_2), 4.83 (1H, s, C*H*), 4.12 (2H, q, *J*=7.1 Hz, CH_2CH$_3$), 2.36 (3H, s, CH_3), 1.25 (3H, t, *J*=7.1 Hz, CH$_2$CH_3); δ_C (600 MHz, $CDCl_3$) 169.7 (*C*OOEt), 156.6 (H_2N*C*ONH), 154.2 (Me*C*(NHCONH$_2$)=CH), 93.7 (*C*H), 59.5 (COO*C*H$_2$CH$_3$), 21.5 (*C*H$_3$), 14.2 (COOCH$_2$*C*H$_3$).

4.5. Antimony(III) chloride-catalysed synthesis of 5-ethoxycarbonyl-6-methyl-4-phenyl-3,4-dihydropyrimidin-2(1*H*)-one (3b)

To a solution of ethyl 3-ureido-crotonate (**8**, 172 mg, 1 mmol) in anhydrous acetonitrile (1.7 mL), benzaldehyde (**1a**, 106 mg, 1 mmol) and antimony(III) chloride (46 mg, 0.2 mmol, 20 mol %) were added at once. The reaction mixture was stirred at room temperature for 24 h. Then the reaction mixture was evaporated to dryness. The residue was triturated with 10% aqueous hydrochloric acid (2 mL) at room temperature for 1 h. The crude product was separated by filtration, washed with distilled water (2×1 mL) dried in high vacuum, and subjected to a column chromatography (R_f 0.52) on a silica gel column (30 g) with dichloromethane/2-propanol (9:1) as an eluent yielding 246 mg (95%) of pure 5-ethoxycarbonyl-6-methyl-4-phenyl-3,4-dihydropyrimidin-2(1*H*)-one (**3b**) as colourless needles; mp 201.1–202.9 °C, lit.[37] mp 201–203 °C. The spectroscopic data (^{1}H and ^{13}C NMR) of thus obtained compound **3b** correspond to those from the literature.[37]

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