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A fast and highly efficient protocol for Michael addition of *N*-heterocycles to α,β-unsaturated compound using basic ionic liquid [bmIm]OH as catalyst and green solvent

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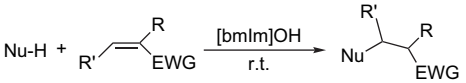
Abstract—A fast and green protocol for the Michael addition of *N*-heterocycles to α,β-unsaturated compounds at room temperature was developed using a basic ionic liquid, 1-methyl-3-butylimidazolium hydroxide, [bmIm]OH, as a catalyst and a reaction medium. The reactions were performed at room temperature with good yields in short reaction times (0.5–3 h). This strategy is quite general and it works with a broad range of *N*-heterocycles, including five-membered *N*-heterocycles, pyrimidines and purines. The recovered ionic liquid could be reused for several cycles with consistent activity.

1. Introduction

In recent years, there has been a growing interest in the synthesis of biologically interesting compounds in the field of organic chemistry. *N*-Substituted imidazoles, triazoles, pyrazoles, pyrimidines, purines and their derivatives obtained through Michael addition are usually pharmacologically active and may be applied as potential therapeutic alternatives.[1] Generally these reactions require strong bases or Lewis acids to activate nucleophiles or Michael acceptors. These would lead to environmentally hazardous residues and undesirable side-products.[2] To avoid typical disadvantages resulting from the presence of such a catalyst, a large number of alternative strategies have been developed in the past few years using basic clays,[3] KF/Al_2O_3,[4] guanidine,[5] microwave irradiation[6] and enzyme.[7] Unfortunately, many of these procedures require long reaction times (several days), rigorous reaction conditions or highly dangerous chemicals. Moreover, the use of solvents such as DMSO or DMF is inevitable for some *N*-heterocycles such as pyrimidines and purines. Generally the catalyst could not be recycled. Thus, development of a fast and facile protocol that could be performed at ambient temperature for the Michael addition of *N*-heterocycles to α,β-unsaturated compounds becomes particularly fascinating and remains a great challenge.

Room temperature ionic liquids (RTLs) containing imidazolium cations can act as a powerful medium in some organic reactions to accelerate the reaction.[8] RTLs include acidic, neutral and basic ionic liquids. The acidic[9] and neutral ionic liquids[10] have been well recognized and successfully applied in many organic reactions. However, the related report about the basic ionic liquids was rare. Supported choline hydroxide was used as a catalyst for aldol condensation reactions between several ketones and aldehydes.[11] A basic ionic liquid [bmIm]OH has been successfully applied to catalyze the Michael addition of active methylene compounds to conjugated ketones, carboxylic esters and nitriles.[12] We also found that [bmIm]OH could be used as an efficient catalyst for the Markovnikov addition of *N*-heterocycles and vinyl esters.[13] As a part of our study on environmentally friendly organic synthesis with ionic liquid,[13,14] we have accomplished, for the first time, the use of [bmIm]OH as a novel and a recyclable reaction medium, as well as an efficient catalyst for the Michael addition of *N*-heterocycles and α,β-unsaturated compounds to generate the corresponding 1,4-aducts in high yields at room temperature (Scheme 1). Some control experiments were also carried out to understand the catalytic property of [bmIm]OH.



EWG=CN, CO_2CH_3, $COCH_3$

Scheme 1. Michael addition of *N*-heterocycles to α,β-carbonyl compound promoted by [bmIm]OH.

Keywords: Ionic liquid; Michael addition; *N*-Heterocycle; α,β-Unsaturated compounds.
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2. Results and discussion

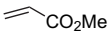
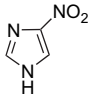
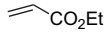
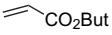
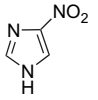
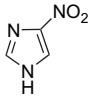
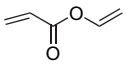
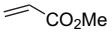
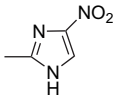
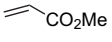
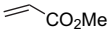
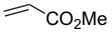
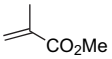
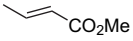
The ionic liquid [bmIm]OH was synthesized according to the procedure reported in the literature.[12] Reactions were typically carried out by addition of methyl acrylate (1.5 mmol) to the ionic liquid (1 mL) containing 4-nitroimidazole (1.0 mol). Generally, after 1–2 h, the reaction solution turned pellucid, indicating the end of the reaction. The adduct was extracted with ethyl acetate and purified by flash chromatography. The structure of this compound was confirmed by IR, ^{1}H NMR, ^{13}C NMR and ESI-MS. The residual ionic liquid was washed with ethyl ether, dried under vacuum at 90 °C for 2 h to eliminate any water trapped from moisture and reused for subsequent reactions. The recovered ionic liquid could be used for four runs with 91%, 96%, 90% and 92% yields. After five runs, about 50% fresh ionic liquid was added to maintain consistent activity due to the loss of ionic liquid.

A variety of structurally diverse imidazoles and α,β-unsaturated carbonyl compounds underwent Michael additions smoothly without any other catalyst to generate the corresponding imidazole derivatives in moderate to good yields. The results are summarized in Table 1. Generally, the reactivity decreased with increasing chain length of acceptor, the longer chain the acrylates had, the lower reactivity was observed (entries 1–3, Table 1). Apart from acrylate ester, acrylonitrile and methyl vinyl acetone can also be the substrates of this reaction to afford the desired products in good yields and in short reaction times (entries 4, 5 and 7, Table 1). Vinyl acrylate showed higher reactivity than methyl acrylate (entry 6, Table 1). We have found that [bmIm]OH could also catalyze the Markovnikov addition of *N*-heterocycles and vinyl ester.[13] In the reaction of 4-nitroimidazole with vinyl acrylate, it is worthwhile to note that no Markovnikov adduct was detected by TLC and HPLC under the current conditions. The Michael addition was much more favoured than Markovnikov addition. Because vinyl acrylate was excess in the reaction, only Michael adduct was obtained.

In order to extend the scope of this methodology, α,β-substituted Michael acceptors like methyl methacrylate and methyl crotonate were tested under the same conditions (entries 12 and 13, Table 1). Both of the acceptors showed rather lower reactivity because of the strong steric hindrance. Accordingly, higher temperature (50 °C) and longer reaction times were required. Similar results were observed using imidazole as the nucleophile (entries 7 and 8, Table 1). The four substituted imidazoles examined underwent Michael addition with methyl acrylate favourably and all substituted imidazoles could be obtained in good yields in short reaction times (entries 1, 7, 9–11, Table 1). The reactivity was in accordance with the nucleophilicity of imidazole derivatives. Sterically hindered imidazole underwent Michael addition much more slowly (entry 10, Table 1).

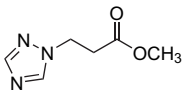
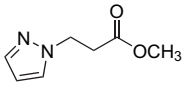
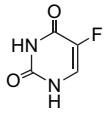
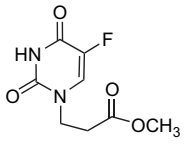
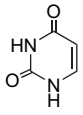
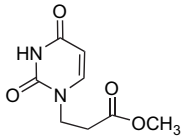
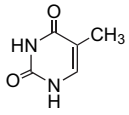
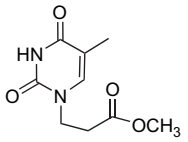
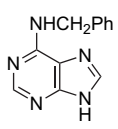
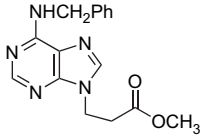
Having obtained favourable results with imidazoles, we then examined the addition of other *N*-heterocycles to methyl acrylate. Other five-membered *N*-heterocycles such as pyrazole and triazole also exhibited high reactivity (entries 1 and 2, Table 2). Among them, triazole reacted faster due to its strong nucleophilicity. More complicated *N*-heterocycles, such as pyrimidines and purines, also can be used as nucleophiles to obtain the corresponding Michael adducts in high yields. Among the substituted pyrimidines, fluorouracil reacted faster than uracil and thymine. It is worthwhile to mention that at room temperature (25 °C) only *N*-1 adducts were prepared (also monitored by TLC and HPLC). When the reaction was carried out at 25 °C under the catalysis of sodium

Table 1. Michael addition of imidazoles to vinyl esters promoted by [bmIm]OH[a]

Entry	Imidazole	α,β-Carbonyl compound	Time (h)	Yield[b] (%)
1			1	(**3a**) 95
2			1.5	(**3b**) 96
3			3	(**3c**) 92
4			1	(**3d**) 90
5			0.5	(**3e**) 92
6			0.5	(**3f**) 96
7			1	(**3g**) 92
8			1	(**3h**) 88
9			3	(**3i**) 94
10			2	(**3j**) 80
11			1	(**3k**) 85
12[c]			6	(**3l**) 60
13[c]			6	(**3m**) 65

[a] Reactions were carried out on 1.0 mmol scale of substrate with 1.5 equiv of vinyl ester in 1 mL ionic liquid at 25 °C.
[b] Isolated yields.
[c] Reaction was performed at 50 °C.

Table 2. Michael addition of other *N*-heterocycles with methyl acrylate promoted by [bmIm]OH[a]

Entry	Substrate	Product	Time (h)	Yield[b] (%)
1			1	(**5a**) 95
2			1	(**5b**) 85
3			1	(**5c**) 94
4			2	(**5e**) 94
5			2	(**5f**) 89
6			2	(**5g**) 90

[a] Reactions were carried out on 1.0 mmol scale of substrate with 1.5 equiv of methyl acrylate in 1 mL ionic liquid at 25 °C.
[b] Isolated yields.

hydroxide in DMF, however, *N*-1 and *N*-3 bis-alkylated adduct was generated as the main product. This result revealed that ionic liquid [bmIm]OH exhibited higher regioselectivity relative to some solid bases such as sodium hydroxide.

Some control experiments were also carried out to demonstrate the catalysis of [bmIm]OH. When the reaction was carried out in some common organic solvents such as THF and DMSO in the absence of [bmIm]OH, it was observed that the addition reaction of 4-nitroimidazole to methyl acrylate produced the corresponding product in less than 5% yield in 48 h. On the other hand, the ionic liquid remained intact (^{1}H NMR) and was used for subsequent runs without any difficulty. These results revealed that ionic liquid [bmIm]OH played a significant role as a catalyst as well as a reaction medium during the reaction process. It has been reported that acidic C2-H of ionic liquids could interact with the carbonyl group and influence the reaction results.[15] We designed ionic liquid 1-butyl-2,3-dimethylimidazolium hydroxide ([bdmIm]OH) in order to understand the role of acidic C2-H in the Michael addition reaction. When [bdmIm]OH was used to catalyze the Michael addition of 4-nitroimidazole with methyl acrylate, 93% isolated yield was obtained in 60 min. This result was comparable with that in [bmIm]OH, indicating that acidic C2-H of [bmIm]OH did not play a significant role in the catalysis. Thus, we speculated that the catalysis of basic ionic liquid [bmIm]OH may be attributed to the following reasons. First, *N*-heterocycles exhibited higher nucleophilicity in ionic liquids compared to the nucleophilicity in organic solvents.[16] Second, hydroxide anion of the ionic liquid [bmIm]OH could assist in the formation of nucleophilic anions, which increased the nucleophilicity of *N*-heterocycles further.

3. Conclusion

In summary, we have developed a procedure using a basic ionic liquid [bmIm]OH to provide an efficient and convenient protocol for Michael addition of *N*-heterocycles to α,β-carbonyl compounds without requirement of a conventional catalyst and organic solvent. The reactions have been carried out at room temperature to afford the desired products in good yields in short reaction times. This strategy is quite general and it works with a broad range of *N*-heterocycles, including five-membered *N*-heterocycles, pyrimidines and purines. The obtained *N*-heterocycle derivatives may be potentially pharmacological alternatives. The complete study of the biological activity of these new derivatives will be reported in due course.

4. Experimental

4.1. General

^{1}H and ^{13}C NMR spectra were recorded on Bruker AVANCE DMX-500 spectrometer at 500 MHz and 125 MHz in $CDCl_3$ and DMSO-d_6, respectively. Chemical shifts are reported in parts per million (δ), relative to the internal standard of tetramethylsilane (TMS). IR spectra were measured with a Nicolet Nexus FTIR 670 spectrophotometer. Mass spectrometry data were obtained on Brucker Esquire-LC for electro-spray (MS-ES) measurements (solvents: methanol; postitive mode). Melting points were determined using XT-4 apparatus and were not corrected. All chemicals were obtained from commercial suppliers and used without further purification.

4.2. Typical procedure

N-Heterocycles (1 mmol) and α,β-unsaturated carbonyl compounds (1.5 mmol) were added to a 10 mL conical flask containing 1 mL [bmIm]OH and the mixture was shaken at ambient temperature for a period of time. The reaction mixture was extracted from the ionic liquid phase with ethyl acetate (10.0 mL×3). The organic layer was dried over anhydrous sodium sulfate and evaporated under reduced pressure. The residue was purified by flash column chromatography (silica gel, petroleum ether/ethyl acetate=1/2, v/v) to obtain the corresponding Michael adduct. The ionic liquid left in the conical flask was further washed with ether, dried under vacuum at 90 °C for 2 h to eliminate any water trapped from moisture and reused for subsequent reactions. After five runs, about 50% fresh ionic liquid was added to maintain consistent activity.

4.2.1. 3-(4-Nitroimidazol-1-yl)-propionic acid methyl ester (3a). White solid, mp 109 °C; IR (KBr): 1729, 1526,

1485 cm^{-1}; ^1H NMR ($CDCl_3$, δ, ppm): 7.83 (s, 1H), 7.51 (s, 1H), 4.35 (t, 2H, J=6.1 Hz), 3.73 (s, 3H), 2.86 (t, 2H, J=6.1 Hz); ^{13}C NMR ($CDCl_3$, δ, ppm): 170.5, 148.9, 136.6, 119.7, 52.7, 43.8, 35.3; ESI-MS (m/z): 200 (M+1).

4.2.2. 3-(4-Nitroimidazol-1-yl)-propionic acid ethyl ester (3b). White solid, mp 35–37 °C; IR (KBr): 1733, 1519, 1492 cm^{-1}; ^1H NMR ($CDCl_3$, δ, ppm): 7.85 (s, 1H), 7.51 (s, 1H), 4.36 (t, 2H, J=6.1 Hz), 4.18 (q, 2H, J=7.1 Hz), 2.85 (t, 2H, J=6.1 Hz), 1.25 (t, 3H, J=7.1 Hz); ^{13}C NMR ($CDCl_3$, δ, ppm): 170.2, 148.9, 136.6, 119.7, 61.9, 43.8, 35.5, 14.3; ESI-MS (m/z): 214 (M+1).

4.2.3. 3-(4-Nitroimidazol-1-yl)-propionic acid butyl ester (3c). White solid, mp 48 °C; IR (KBr): 1727, 1521, 1488 cm^{-1}; ^1H NMR ($CDCl_3$, δ, ppm): 7.84 (s, 1H), 7.51 (s, 1H), 4.36 (t, 2H, J=6.1 Hz), 4.12 (t, 2H), 2.86 (t, 2H, J=6.1 Hz), 1.63–1.57 (m, 2H), 1.36–1.32 (m, 2H), 0.94 (t, 3H); ^{13}C NMR ($CDCl_3$, δ, ppm): 170.3, 148.9, 136.6, 119.6, 65.7, 43.8, 35.5, 30.7, 19.2, 13.8; ESI-MS (m/z): 242 (M+1).

4.2.4. 3-(4-Nitroimidazol-1-yl)-propionitrile (3d). White solid, mp 105–106 °C; IR (KBr): 2252, 1526, 1492 cm^{-1}; ^1H NMR (DMSO-d_6, δ, ppm): 8.47 (s, 1H), 7.93 (s, 1H), 4.38 (t, 2H, J=6.3 Hz), 3.17 (t, 2H, J=6.3 Hz); ^{13}C NMR (DMSO-d_6, δ, ppm): 147.6, 138.1, 121.9, 118.6, 43.5, 19.4; ESI-MS (m/z): 167 (M+1).

4.2.5. 4-(4-Nitroimidazol-1-yl)-butanone (3e). Yellow solid, mp 65–67 °C; IR (KBr): 1741, 1523, 1490 cm^{-1}; ^1H NMR ($CDCl_3$, δ, ppm): 7.82 (d, 1H, J=1.46 Hz), 7.49 (d, 1H, J=1.42 Hz), 4.32 (t, 2H, J=5.92 Hz), 3.02 (t, 2H, J=5.92 Hz), 2.21 (s, 3H,); ^{13}C NMR ($CDCl_3$, δ, ppm): 204.3, 148.1, 136.8, 120.1, 43.8, 42.4, 30.2; ESI-MS (m/z): 184 (M+1).

4.2.6. 3-(4-Nitroimidazol-1-yl)-propionic acid vinyl ester (3f). White solid, mp 94–96 °C; IR (KBr): 1743, 1649, 1526, 1486 cm^{-1}; ^1H NMR ($CDCl_3$, δ, ppm): 7.88 (s, 1H), 7.54 (s, 1H), 7.26–7.22 (m, 1H), 4.95–4.91, 4.67 (m, 2H), 4.41 (t, 2H, J=6.1 Hz), 2.98 (t, 2H, J=6.1 Hz); ^{13}C NMR ($CDCl_3$, δ, ppm): 167.6, 148.9, 140.8, 136.7, 119.8, 99.4, 43.4, 35.1; ESI-MS (m/z): 212 (M+1).

4.2.7. 3-Imidazol-1-yl-propionic acid methyl ester (3g). Yellow oil; IR (neat): 1732, 1509 cm^{-1}; ^1H NMR ($CDCl_3$, δ, ppm): 7.54 (s, 1H), 7.05 (s, 1H), 6.93 (s, 1H), 4.27 (t, 2H, J=6.6 Hz), 3.70 (s, 3H), 2.78 (t, 2H, J=6.6 Hz); ^{13}C NMR ($CDCl_3$, δ, ppm): 170.3, 136.6, 128.5, 118.2, 51.1, 41.5, 34.9; ESI-MS (m/z): 155 (M+1).

4.2.8. 3-Imidazol-1-yl-propionitrile (3h). Yellow oil; IR (neat): 2253, 1509 cm^{-1}; ^1H NMR ($CDCl_3$, δ, ppm): 7.56 (s, 1H), 7.07 (s, 1H), 7.03 (s, 1H), 4.24 (t, 2H, J=6.5 Hz), 2.82 (t, 2H, J=6.5 Hz); ^{13}C NMR ($CDCl_3$, δ, ppm): 137.1, 130.5, 118.8, 116.7, 42.7, 20.8; ESI-MS (m/z): 122 (M+1).

4.2.9. 3-(2-Methyl-4-nitroimidazol-1-yl)-propionic acid methyl ester (3i). Yellow liquid; IR (neat): 1729, 1508 cm^{-1}; ^1H NMR ($CDCl_3$, δ, ppm): 7.76 (s, 1H), 4.25 (t, 2H, J=6.4 Hz), 3.72 (s, 3H), 2.82 (t, 2H, J=6.4 Hz), 2.48 (s, 3H); ^{13}C NMR ($CDCl_3$, δ, ppm): 173.2, 148.9, 147.8, 123.1, 54.7, 45.0, 36.9, 15.5; ESI-MS (m/z): 214 (M+1).

4.2.10. 3-(2-Methyl-imidazol-1-yl)-propionic acid methyl ester (3j). Yellow oil; IR (neat): 1733, 1508 cm^{-1}; ^1H NMR ($CDCl_3$, δ, ppm): 6.90 (s, 1H), 6.84 (s, 1H), 4.16 (t, 2H, J=6.8 Hz), 3.69 (s, 3H), 2.74 (t, 2H, J=6.8 Hz), 2.41 (s, 3H); ^{13}C NMR ($CDCl_3$, δ, ppm): 170.6, 144.1, 126.8, 118.6, 51.6, 41.0, 34.8, 12.4; ESI-MS (m/z): 183 (M+1).

4.2.11. 3-(4-Methyl-imidazol-1-yl)-propionic acid methyl ester (3k). Yellow oil; IR (neat): 1732, 1508 cm^{-1}; ^1H NMR ($CDCl_3$, δ, ppm): 7.44 (s, 0.4H), 7.38 (s, 0.6H), 6.75 (s, 0.4H), 6.62 (s, 0.6H), 4.18–4.15 (m, 2H), 3.69 (s, 3H), 2.76–2.74 (m, 2H), 2.21 (d, 3H); ^{13}C NMR ($CDCl_3$, δ, ppm): 171.2, 171.0, 138.6, 136.9, 136.4, 126.9, 115.4, 52.1, 42.3, 40.0, 35.8, 35.3, 13.6, 9.1; ESI-MS (m/z): 183 (M+1).

4.2.12. 2-Methyl-3-(4-nitroimidazol-1-yl)-propionic acid methyl ester (3l). White solid, mp 64–65 °C; IR (KBr): 1726, 1527, 1485 cm^{-1}; ^1H NMR ($CDCl_3$, δ, ppm): 7.8 (s, 1H), 7.46 (s, 1H), 4.34–4.30, 4.16–4.12 (m, 2H), 3.71 (s, 3H), 2.97–2.94 (m, 1H), 1.28 (d, 3H); ^{13}C NMR ($CDCl_3$, δ, ppm): 173.7, 148.4, 136.8, 119.9, 52.7, 50.4, 41.2, 15.2; ESI-MS (m/z): 214 (M+1).

4.2.13. 3-(4-Nitroimidazol-1-yl)-butyric acid methyl ester (3m). White solid, mp 113–114 °C; IR (KBr): 1734, 1543, 1489 cm^{-1}; ^1H NMR ($CDCl_3$, δ, ppm): 7.85 (s, 1H), 7.55 (s, 1H), 4.81–4.77 (m, 1H), 3.68 (s, 3H), 2.84 (d, 2H), 1.64 (d, 3H); ^{13}C NMR ($CDCl_3$, δ, ppm): 170.0, 148.7, 135.4, 117.5, 52.5, 51.8, 42.0, 21.5; ESI-MS (m/z): 214 (M+1).

4.2.14. 3-[1,2,4]Triazol-1-yl-propionic acid methyl ester (5a). Yellow oil; IR (neat): 1735, 1507, 1440 cm^{-1}; ^1H NMR ($CDCl_3$, δ, ppm): 8.17 (s, 1H), 7.93 (s, 1H), 4.49 (t, 2H, J=6.3 Hz), 3.69 (s, 3H), 2.93 (t, 2H, J=6.3 Hz); ^{13}C NMR ($CDCl_3$, δ, ppm): 171.0, 152.2, 143.8, 52.2, 44.9, 34.0; ESI-MS (m/z): 156 (M+1).

4.2.15. 3-Pyrazol-1-yl-propionic acid methyl ester (5b). Yellow oil; IR (neat), 1739, 1514, 1439 cm^{-1}; ^1H NMR ($CDCl_3$, δ, ppm): 7.50 (d, 1H), 7.43 (d, 1H), 6.21 (t, 1H), 4.43 (t, 2H, J=6.6 Hz), 3.67 (s, 3H), 2.90 (t, 2H, J=6.6 Hz); ^{13}C NMR ($CDCl_3$, δ, ppm): 171.6, 139.8, 129.8, 105.5, 52.0, 47.4, 34.9; ESI-MS (m/z): 155 (M+1).

4.2.16. 3-(5-Fluorouracil-1-yl)-propionic acid methyl ester (5c). Yellow solid, mp 145–146 °C; IR (KBr): 1729, 1692, 1663 cm^{-1}; ^1H NMR ($CDCl_3$, δ, ppm): 7.52 (s, 1H), 3.97 (t, 2H, J=5.8 Hz), 3.72 (s, 3H, O–CH_3), 2.79 (t, 2H, J=5.8 Hz); ^{13}C NMR ($CDCl_3$, δ, ppm): 172.0, 157.5, 157.3, 149.6, 141.2, 139.2, 130.5, 130.3, 52.5, 45.8, 32.9; ESI-MS (m/z): 217 (M+1).

4.2.17. 3-Uracil-1-yl-propionic acid methyl ester (5d). White solid, mp 127–128 °C; IR (KBr): 1733, 1696, 1662 cm^{-1}; ^1H NMR ($CDCl_3$, δ, ppm): 2.80 (t, 3H, J=5.9 Hz), 3.71 (s, 3H), 4.00 (t, 2H, J=5.9 Hz), 5.68 (d, 1H, J=7.9 Hz), 7.40 (d, 1H, J=7.9 Hz), 9.03 (s, 1H); ^{13}C NMR ($CDCl_3$, δ, ppm): 172.1, 164.0, 151.0, 146.0, 102.0, 52.4, 45.5, 33.0; ESI-MS (m/z): 199 (M+1).

4.2.18. 3-Thymin-1-yl-propionic acid methyl ester (5e). White solid, mp 120–121 °C; IR (KBr): 1735, 1698, 1655 cm^{-1}; ^1H NMR ($CDCl_3$, δ, ppm): 8.87 (s, 1H), 7.20 (s, 1H), 3.96 (t, 2H, J=6.0 Hz), 3.71 (s, 3H), 2.78 (t, 2H, J=6.0 Hz), 1.91 (s, 3H); ^{13}C NMR ($CDCl_3$, δ, ppm): 172.1, 164.6, 151.1, 141.8, 110.6, 52.3, 45.3, 33.1, 12.5; ESI-MS (m/z): 213 (M+1).

4.2.19. 3-(6-Benzylamino-purin-1-yl)-propionic acid methyl ester (5f). Yellow solid, mp 124–125 °C; IR (KBr): 3366, 3097, 1724, 1613 cm^{-1}; ^1H NMR ($CDCl_3$, δ, ppm): 8.52 (s, 1H), 7.87 (s, 1H), 7.41–7.27 (m, 5H), 6.45 (t, 1H), 4.85 (d, 2H), 4.59 (t, 2H, J=6.0 Hz), 3.63 (s, 3H), 2.92 (t, 2H, J=6.0 Hz); ^{13}C NMR ($CDCl_3$, δ, ppm): 171.6, 155.0, 153.4, 140.7, 138.8, 128.9, 128.0, 127.7, 121.0, 52.3, 42.0, 39.6, 34.2; ESI-MS (m/z): 312 (M+1).

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Supplementary data

Supplementary data associated with this article can be found in the online version, at doi:10.1016/j.tet.2006.11.013.

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