ORIGINAL PAPER

# The pseudo-Michael reaction of 1-aryl-4,5-dihydro-1*H*-imidazol-2-amines with ethyl ethoxymethylenecyanoacetate

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**Abstract** The pseudo-Michael reaction of 1-aryl-4,5-dihydro-1*H*-imidazol-2-amines with ethyl 2-cyano-3-methoxyprop-2-enoate (ethyl ethoxymethylenecyanoacetate) is investigated. At −10 °C reaction takes place on the exocyclic nitrogen atom, giving exclusively ethyl esters of 2-cyano-3-[(1-phenyl-4,5-dihydro-1*H*-imidazol-2-yl)amino]-prop-2-enoic acid. The formation of isomeric enamines which may be a theoretical product of the reaction on N3 ring nitrogen atom is not observed. The N6 enamines, heated in boiling acetic acid, yield cyclic 1-aryl-5-oxo-2,3-dihydroimidazo[1,2-*a*]pyrimidine-6-carbonitriles. Heating of the enamines to the temperature of 120–140 °C without a solvent makes it possible to obtain a mixture of 1-aryl-5-oxo-2,3-dihydroimidazo[1,2-*a*]pyrimidine-6-carbonitriles and ethyl 1-aryl-5-imino-2,3-dihydroimidazo[1,2-*a*]pyrimidine-6-carboxylates. The reaction of the respective hydrobromides of 1-aryl-4,5-dihydro-1*H*-imidazol-2-amines with ethyl ethoxymethylenecyanoacetate in the presence of triethylamine gives selectively 1-aryl-5-oxo-1,2,3,5-dihydroimidazo[1,2-*a*]pyrimidine-6-carbonitriles.

**Keywords** Annelation · Michael addition · X-ray structure determination
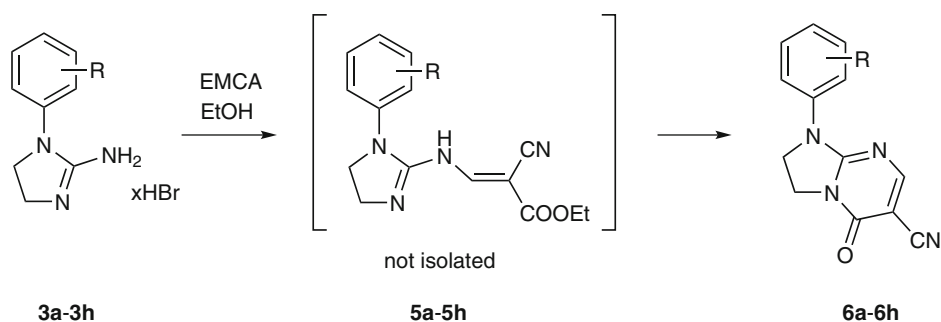
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## Introduction

Ethyl 2-cyano-3-methoxyprop-2-enoate (ethyl ethoxymethylenecyanoacetate, EMCA, **1**) (Scheme 1) is a widely used reagent for heterocyclic annelation [1]. In particular, EMCA is applied as the Michael acceptor in Michael addition [1]. Reaction of EMCA with 4,5-dihydro-1*H*-imidazol-2-amines leads to 2,3-dihydroimidazo[1,2-*a*]pyrimidines [1–4] and represents one of the synthetic methods of this heterocyclic system by reaction of imidazol-2-amine derivatives with electrophilic compounds (the main alternative involves the imidazole ring closure by condensation of pyrimidin-2-amines with an appropriate compound) [5]. The imidazo[1,2-*a*]pyrimidine system is present in many biologically active compounds which have been reported to exhibit anti-inflammatory and analgesic [6–9], antibacterial [10–14], antiviral [15], antifungal [16, 17], insectidal, acaricidal, and nematocidal [18], central nervous system (CNS) [19–23], hormonal [24], mutagenic [25], anticancer [26, 27], and cardiovascular [28] activity.

We have previously reported the pseudo-Michael reaction of 4,5-dihydro-1*H*-imidazol-2-amines with diethyl (methoxymethylidene)propanedioate (diethyl ethoxymethylenemalonate, DEEM, **2**) (Scheme 1) [29]. The isolation of chain enamines was not possible for the adducts with DEEM [29] which is in agreement with corresponding literature data (for review see [1]). In the case of EMCA it is relatively easy to isolate the adducts which are the direct

**Scheme 1**



products of Michael reaction [1]. Such adducts may possess the EMCA part connected with nitrogen (enamines) [30–32], carbon [33], and sulfur [34] atoms and may be further cyclized via ester [1, 35, 36] or cyano [1, 37, 38] group.

In this paper we present the pseudo-Michael reaction of 4,5-dihydro-1*H*-imidazol-2-amines with EMCA and structural studies of the respective products.

## Results and discussion

The hydrobromides **3a–3f** of 4,5-dihydro-1*H*-imidazol-2-amines **4a–4f** were obtained from the respective *N*-aryl-1,2-diaminoethanes and cyanogen bromide, as previously reported [29, 39, 40]. The hydrobromides **3a–3f** were then transformed into free bases **4a–4f** by action of sodium hydroxide and extraction with methylene chloride. The 4,5-dihydro-1*H*-imidazol-2-amines **4a–4f** were subjected to the pseudo-Michael reaction with EMCA in propan-2-ol solution at −10 °C (Scheme 2). In these conditions the only isolated products were chain enamines (**5a**, **5c–5h**), formed as a result of the reaction on the N6 exocyclic nitrogen atom. The attempt to obtain derivative **5b** with 2-chloro substituent failed, probably due to the steric hindrance. The reaction on the N6 nitrogen atom was in

contrast to our earlier results on the pseudo-Michael reaction of 4,5-dihydro-1*H*-imidazol-2-amines with DEEM [29]. In the case of DEEM, at −10 °C reaction took place on the N3 ring nitrogen atom, but the isolation of the respective chain enamines was not possible due to the fast cyclization process, even at low temperature. Instead, ethyl 1-aryl-7-oxo-2,3-dihydroimidazo[1,2-*a*]pyrimidine-6-carboxylates were obtained exclusively. As was found previously, the pseudo-Michael reaction of 4,5-dihydro-1*H*-imidazol-2-amines with DEEM was temperature-dependent; therefore, we tried first to perform the corresponding reaction with EMCA at room temperature and then at higher temperatures (up to the boiling point of propan-2-ol). Theoretically, formation of the mixture of isomeric N3 and N6 enamines is possible in the case of both Michael reagents, but in the case of EMCA we observed the formation of N3 enamines neither at −10 °C nor at higher temperatures. The N6 enamines **5a**, **5c–5h** formed exclusively underwent cyclization to 1-aryl-5-oxo-2,3-dihydroimidazo[1,2-*a*]pyrimidine-6-carbonitriles **6a**, **6c–6h** when the pseudo-Michael reaction was performed at ambient or higher temperature (the derivative **6b** could not be obtained by this method as the preparation of enamine **5b** was not successful). On the contrary, in the case of DEEM, at room temperature the reaction yielded mixtures with varying ratio of isomeric 1-aryl-5-oxo-2,3-dihydro-imidazo[1,2-*a*]pyrimidine-6-carboxylates and 1-aryl-7-oxo-2,3-dihydroimidazo[1,2-*a*]pyrimidine-6-carboxylates. Alternatively, to obtain compounds **6a** and **6c–6h**, the enamines **5a** and **5c–5h** should be heated in boiling acetic acid (Scheme 2). In such conditions the cyclization takes place via the ester group of **5a** and **5c–5h**, giving **6a** and **6c–6h** exclusively. Myiamoto [41], when performing the similar cyclization reaction under acidic conditions (MeOH

**Scheme 2**



R: **a**, H; **b**, 2-Cl; **c**, 3-Cl; **d**, 4-Cl; **e**, 2-CH₃; **f**, 4-CH₃; **g**, 2-OCH₃; **h**, 4-OCH₃

**Scheme 3**



not isolated

**3a-3h**                          **5a-5h**                          **6a-6h**

saturated with HCl), observed the cyclization via cyano group only, leading to appropriate imines. Analogs of **6a–6h** were obtained by Myiamoto [41] in basic conditions (Et$_3$N/MeOH).

In the next stage we heated enamines **5a** and **5c–5h** to 120–140 °C without a solvent. In such conditions the mixtures of the cyclization products both via ester group (**6a** and **6c–6h**) and via cyano group, 1-aryl-5-imino-2,3-dihydroimidazo[1,2-*a*]pyrimidine-6-carboxylates (**7a** and **7c–7h**) were obtained (Scheme 2). The mixtures were separated with preparative thin-layer chromatography. After preparative TLC separation, compounds **7a** and **7c–7h** were extracted from silica gel with methanol. During extraction process some transesterification occurred which resulted in mixtures of ethyl and methyl esters. The percentage of methyl ester in the mixture depended on the substituent in the phenyl group and varied from 10 to 45 % by NMR. The obtained mixtures of ethyl and methyl esters were practically impossible to separate, and thus, they were analysed as received.

Finally, the reactions of respective 4,5-dihydro-1*H*-imidazol-2-amine hydrobromides **3a–3h** with EMCA in the presence of base (Et$_3$N) led to reaction on N6 nitrogen atom (which is in agreement with our previous results obtained for DEEM [29]) and cyclization via the ester group, resulting in compounds **6a–6h** (Scheme 3). This method made it possible to obtain the derivative **6b** with 2-chloro substituent.

The course of all reactions was confirmed by elementary analysis and spectral data ($^1$H and $^{13}$C NMR, MS). All the compounds were characterized with the aid of NMR spectroscopy. Assignments of $^1$H and $^{13}$C chemical shifts and $^1$H–$^1$H coupling constants were achieved by a combination of several 2D NMR techniques. Since there are not that many protons in heterocyclic rings, the most important experiment for assignments was HMBC spectrum. By HMBC, one can see a long range correlation between H-2 and aromatic substituent at N-1. This proves the assignment of H-2 and H-3 protons. The protons and the carbons at the aromatic substituent are easily assigned by DQF-

COSY and HSQC spectra. The most difficult part is the assignment of quaternary carbons at positions 5, 6, and 8a. H-7 showed HMBC correlations to all of those. However, C-8a can be identified by a long range correlation from both H-2 and H-3. A correlation between H-3 and C-5 was not observed, so the assignments of C-5 and C-6 were done based on the very different chemical shift values. Therefore, as an example, the structures of **5f** and **7f** were modeled by DFT method B3LYP/6-31G(d,p) and the NMR chemical shifts were calculated by the same method [42]. The good agreement (the results are not shown here) with experimental values proved the correct assignments. The multiplicities of proton signals H-2 and H-3 are noteworthy. Those methylene protons at positions 2 (H-2a and H-2b) and 3 (H-3a and H-3b) have nearly the same chemical shifts, respectively. However, the vicinal coupling constants between H-2 and H-3 differ. Actually there are four coupling constants: $J_{2a,3a}$, $J_{2a,3b}$, $J_{2b,3a}$, and $J_{2b,3b}$ and the signals can be analysed, for example by simulation and iteration software PERCH [43].[1] It was found that they are all between 7 and 12 Hz. This makes the signals look roughly like triplets, but the unequal coupling constants as well as the second order effects make the signals rather complicated. Therefore, these are stated as multiplets (m) at the experimental section.

The primary fragmentations of compounds **5a** and **5c–5h** as well as **7c–7h** are mainly initiated from the ester function (see "Experimental") or via the [M–H]$^+$ ions. As mentioned in "Experimental", compounds **7** were transesterified into mixtures of Me- and Et-esters when eluted with methanol. Therefore, they show also variable amounts of the M$^{+\cdot}$ ions of the methyl esters. On the other hand, with the exception of the [M–H]$^+$ ions, the other fragments appear almost always at the same *m/z*-values, e.g. [M–MeOH]$^{+\cdot}$ and [M–EtOH]$^{+\cdot}$ ions. The ion structures were determined by accurate mass measurements and the fragmentation routes with B/E spectra. When comparing the fragmentation patterns of compounds **5** and **7** with each

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[1] PERCH Solutions Ltd. http://perchsolutions.com

other it appears that compounds **5** may partially rearrange into compounds **7** under EI conditions (see "Experimental"). However, some differences still exist. M$^{+\cdot}$ is the base peak only for **5g** but in case of compounds **7** for **7e**, **7g**, and **7h**. The base peak for **5a**, **5e**, **5f**, and **5h** is [M–C$_2$H$_4$CO$_2$]$^{+\cdot}$ but only for **7d** and **7f**. The clearest difference is seen in the abundance of [M–ROH]$^{+\cdot}$ ion (R = Et for **5** and Me or Et for **7**) which is by far more abundant for compounds **5** being even the base peak for **5d** and **5e**. Compounds **5e** and **5g** show some ions which are indicative for the 2-Me and 2-OMe substitutions and are missing from the spectra of **5f** and **5g**. For **5e** these ions are [M–Me]$^+$ at *m/z* 283 (4 %) and [M–Me–EtOH]$^+$ at *m/z* 237 (29) and for **5g** [M–H–Me]$^{+\cdot}$, [M–Et]$^+$, and [M–OMe]$^+$ at *m/z* 298 (5), 285 (5), and 283 (36 %), respectively. Similarly 2-Me derivative **7e** gives the ion [M–Me] at *m/z* 269 (8 %) and the Et- and Me-esters the ions [M–Me–EtOH]$^+$ and [M–Me–MeOH]$^+$ at *m/z* 237 (7 %) although the latter is weaker than that for **5e**. Compound **7g** with 2-OMe substitution gives the ions [M–Me]$^{+\cdot}$ and [M–OMe]$^+$ at *m/z* 299 (14 %) and 285 (5 %), 283 (33 %) and 269 (47 %) for Et- and Me-esters, respectively. It should be mentioned that *m/z* 269 corresponds also [M–OEt]$^+$ for the Et-ester (**7g**).

Compounds **6a**–**6h** understandably behave differently. M$^{+\cdot}$ is always the base peak except the 2-Cl derivative **6b** where [M–Cl]$^+$ ion is the base peak due to the ortho effect. Another ion which originates via the ortho effect is [M–Cl–C$_2$H$_2$]$^+$ at *m/z* 211 (10 %). Similarly 2-Me derivative **6e** shows one ion which is indicative for the ortho methyl, namely [M–Me]$^+$ at *m/z* 237 (24 %), which is absent from the mass spectrum of 4-Me derivative **6f**. The presence of ortho-OMe substitution in **6g** is reflected by the ions [M–OMe]$^+$ at *m/z* 237 (92 %) and [M–CH$_2$O]$^{+\cdot}$ at *m/z* 238 (20 %) which are missing from the spectrum of **6h** except for a small amount of ion 237 (9 %). On the other hand, the 4-OMe derivative **6h** shows the ions [M–Me]$^+$ at *m/z* 253 (32 %) and [M–Me–CO]$^+$ at m/z 225 (7 %) which are missing from the spectrum of **6g**.

We also succeeded in the preparation of crystals suitable for X-ray structure determination for **6c** and **6d** [44]. The X-ray analyses of compounds **6c** and **6d** were performed in order to confirm the synthetic pathway and the position of the oxo group (5-oxo/7-oxo; Scheme 2). The crystal structure of **6c** is shown in Fig. 1. It was found that the investigated compounds contain an oxo group at position 5. The geometric parameters (bond lengths, angles, torsion angles, and planarity of the rings) are very similar to those observed in a previously reported structure of 1-(4-chlorophenyl)-5-oxo-1,2,3,5-tetrahydroimidazo[1,2-*a*]pyrimidine-6-carbonitrile (**6d**) [44]. The molecule as a whole adopts a nearly planar conformation with the torsion angle C2–N1–C21–C26 of 1.2(4)°. This conformation is stabilized by an intramolecular C26–H26···N6 interaction leading to the formation of a
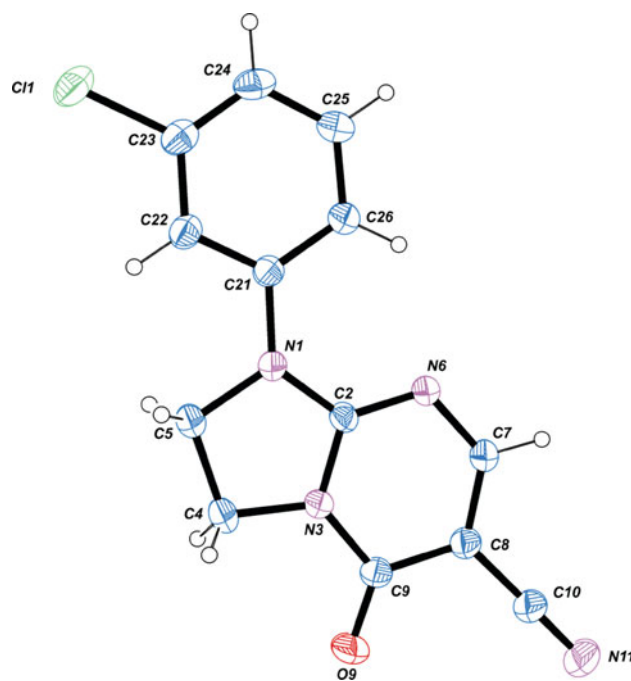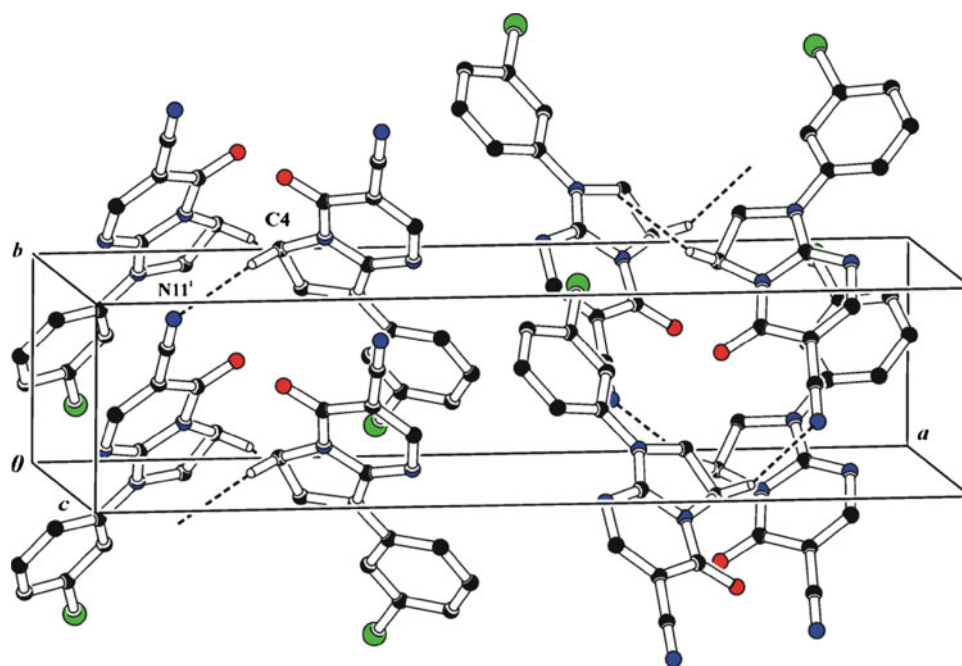


**Fig. 1** A view of the X-ray molecular structure of **6c** with the atomic labeling scheme

six-member ring described by the S(6) graph-set symbol [2, 45]; C26–H26 = 0.93, H26···N6 = 2.25, C26···N6 = 2.894(4) Å, and C26–H26···N6 = 126°. In the crystal structure, the molecules related by *c* glade plane and *b* translation are linked to form C(7) chains along [011] direction by C4-H4B…N11$^{(i)}$ intermolecular hydrogen bonds (C4–H4B = 0.97, H4B···N11 = 2.56, C4···N11 = 3.281(5) Å, C4–H4B···N11 = 132° and (*i*) = ½−*x*, −1 + *y*, −½ + *z*) (Fig. 2). Moreover, the π-electron systems of the pairs of pyrimidine ring at (*x*, *y*, *z*) and phenyl ring at (*x*, 1 + *y*, *z*) and phenyl ring at (*x*, *y*, *z*) and pyrimidine ring at (*x*, −1 + *y*, *z*) overlap each other, with centroid-to-centroid separation of 3.5695(18) Å. The π···π distances between overlapping planes are alternately 3.4648(11) and 3.4564(13) Å and the angle between them is 3.21(14)°.

Theoretical calculations at DFT/B3LYP/6-311 ++ G(d,p) ab initio level [42] show that that 5-oxo isomeric form of **6c** and **6d** (the initial geometries were built from their crystallographic data) obtained after energy minimization and geometry optimization in the gaseous phase is more energetically stable than 7-oxo form, with a difference in the energy between the 7-oxo and 5-oxo forms of 45.6 and 46.0 kJ mol$^{-1}$ for **6c** and **6d**, respectively. In solution (water ($\varepsilon$ = 78.35) and chloroform ($\varepsilon$ = 4.71), CPCM model [46]) the energy difference between form 7-oxo and 5-oxo is 18.8 kJ mol$^{-1}$ (aqueous solution) and 27.2 kJ mol$^{-1}$ (chloroform solution) for **6c** and 19.3 kJ mol$^{-1}$ (aqueous solution) and 27.6 kJ mol$^{-1}$ (chloroform solution) for **6d**. Thus, the population of the

7-oxo form in vacuum and polar (water) and non-polar (chloroform) solutions estimated using a non-degenerate Boltzmann distribution is below the threshold of the detectability of conventional analytical methods.

## Experimental

All reagents and solvents were purchased and used without additional purification. In particular, EMCA was purchased from Merck. Reactions were routinely monitored by thin-layer chromatography (TLC) in silica gel (60 $F_{254}$ Merck plates, DS horizontal chamber, Chromdes, Lublin, Poland) in toluene-ethyl acetate–methanol (1:3:0.5) eluent system and the products were visualized with ultraviolet light of 254 nm wavelength.

NMR spectra were acquired using Bruker Avance 500 spectrometer (equipped with BBO 5 mm Z-grad probe) operating at 500.13 MHz for $^1$H and 125.77 MHz for $^{13}$C. Spectra were recorded at 25 °C using DMSO-$d_6$ as solvent with a non-spinning sample in 5 mm NMR tubes. Spectra were processed by a PC with Windows XP operating system and TopSpin software. Proton and carbon spectra were referenced to tetramethylsilane (TMS: 0.00 ppm). In addition to normal $^1$H and $^{13}$C NMR spectra, also a variety of gradient selected 2D measurements were used to receive an unequivocal assignment of all compounds. DQF-COSY spectra were acquired with cosygpmfqf pulse program (pulse programs refer to original ones installed by Bruker) and NOESY spectra were acquired with noesygpph pulse program with mixing time of 300 ms. $^1$H-$^{13}$C HSQC

spectra were acquired with hsqcetgpsisp.2 pulse program (using shaped pulses) with 145 Hz one-bond coupling constant. $^1$H-$^{13}$C HMBC spectra were acquired with hmbcgplpndqf pulse program with 10 Hz long-range coupling constant. Computational methods were used to confirm the assignment of some quaternary carbons. The geometry optimizations and NMR chemical shift calculations were done by density functional B3LYP equipped with basis set 6-31G(d,p). Calculations were done by Gaussian 03 W software [42]. Numbering of atoms for **5a–5g** in NMR assignments corresponds to the numbering of the final products **6a–6g** and **7a–7g** and is shown in Scheme 2.

The electron ionization (EI) mass spectra were recorded on a VG Analytical (Manchester, UK) ZABSpec instrument, equipped with Opus data system. Samples were introduced using a direct insertion probe at ambient temperature. Accurate mass measurements were performed at a resolving power of 8,000–10,000 (10 % valley definition) using peak matching technique and perfluorokerosene (PFK) as a reference compound. The elementary analyses were performed on a Perkin-Elmer analyzer. Melting points were determined with a Boetius apparatus.

X-ray data of **6c** were collected on a Kuma KM4 four-circle diffractometer at room temperature; crystal sizes $0.60 \times 0.30 \times 0.20$ mm, CuK$\alpha$ ($\lambda = 1.54178$ Å) radiation, $\omega$–$2\theta$ scans. The XABS2 absorption correction was applied [47]; $T_{min} = 0.2071$, $T_{max} = 0.7898$. The structure was solved by direct methods using SHELXS97 [48] and refined by full-matrix least-squares with SHELXL97 [48]. The H atoms were positioned geometrically and treated as

riding on their parent C atoms with C–H distances of 0.93 Å (aromatic) and 0.97 Å (CH$_2$). All H atoms were refined with isotropic displacement parameters taken as 1.5 times those of the respective parent atoms. The flack parameter of −0.02(2) confirmed that the correct absolute structure was refined [49]. All calculations were performed using WINGX version 1.64.05 package [50]. CCDC 912327 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge at http://www.ccdc.cam.ac.uk/conts/retrieving.html (or from the Cambridge Crystallographic Data Centre (CCDC), 12 Union Road, Cambridge CB2 1EZ, UK; fax: +44(0) 1223 336 033; email: deposit@ccdc.cam.ac.uk).

### General procedure to obtain compounds 5a–5h

1-Aryl-4,5-dihydro-1*H*-imidazol-2-amine (**4a–4h**, 0.01 mol) was dissolved in 40 cm$^3$ of propan-2-ol and cooled down to the temperature of −10 °C. A solution of 1.69 g of EMCA (**1**, 0.01 mol) in 40 cm$^3$ of propan-2-ol was added dropwise at constant stirring. The reaction mixture was stirred at −10 °C for 2 h. The precipitation obtained was filtered off and washed a few times with *n*-hexane, toluene, and a mixture of toluene-ethyl acetate (10:1).

### Ethyl 2-cyano-3-[(1-phenyl-4,5-dihydro-1H-imidazol-2-yl)amino]prop-2-enoate (5a, C$_{15}$H$_{16}$N$_4$O$_2$)

According to general method with 1.61 g of **4a**. The method afforded 1.42 g (60 %) of **5a**. M.p.: 133–134 °C; $R_f$ = 0.48 (toluene/ethyl acetate/methanol 1:3:0.5); $^1$H NMR (500 MHz, DMSO-$d_6$): $\delta$ = 8.82 (br s, 1H, H-8), 8.56 (s, 1H, H-7), 7.69 (d, 2H, $J$ = 7.7 Hz, H-2′, H-6′), 7.36 (t, 2H, $J$ = 7.7 Hz, H-3′, H-5′), 7.14 (t, 1H, $J$ = 7.7 Hz, H-4′), 4.14 (m, 2H, H-2), 4.14 (q, 2H, $J$ = 7.1 Hz, OCH$_2$CH$_3$), 3.69 (m, 2H, H-3), 1.22 (t, 3H, $J$ = 7.1 Hz, OCH$_2$CH$_3$) ppm; $^{13}$C NMR (125 MHz, DMSO-$d_6$): $\delta$ = 165.37 (C=O), 164.55 (C-7), 161.23 (C-8a), 138.82 (C-1′), 128.38 (C-3′, C-5′), 123.96 (C-4′), 120.86 (C-2′, C-6′), 117.30 (C-5), 82.30 (C-6), 59.56 (OCH$_2$CH$_3$), 47.83 (C-2), 40.31 (C-3), 14.33 (OCH$_2$CH$_3$) ppm; MS (EI): M$^{+\cdot}$ C$_{15}$H$_{16}$N$_4$O$_2^{+\cdot}$ calc. 284.1273, found 284.1272; *m/z* (%): M$^{+\cdot}$ 284 (65), [M–H]$^+$ 283 (7), [M–OEt]$^+$ 239 (22), [M–EtOH]$^{+\cdot}$ 238 (26), [M–H–EtOH]$^+$ 237 (36), [M–C$_2$H$_4$OOC]$^{+\cdot}$ 212 (100), [M–EtOOC]$^+$ 211 (6), 119 (6), 118 (8), 106 (30), 105 (12), 104 (13), 91 (12), 77 (42).

### Ethyl 3-[[1-(3-chlorophenyl)-4,5-dihydro-1H-imidazol-2-yl]amino]-2-cyanoprop-2-enoate (5c, C$_{15}$H$_{15}$ClN$_4$O$_2$)

According to general method with 1.95 g of **4c**. The method afforded 1.52 g (56 %) of **5c**. M.p.: 128–129 °C; $R_f$ = 0.50 (toluene/ethyl acetate/methanol 1:3:0.5); $^1$H NMR (500 MHz, DMSO-$d_6$): $\delta$ = 8.96 (br s, 1H, H-8), 8.56 (s, 1H, H-7), 8.01 (t, 1H, $J$ = 1.9 Hz, H-2′), 7.60 (dd, 1H, $J$ = 1.9 Hz, 8.2 Hz, H-6′), 7.38 (t, 1H, $J$ = 8.2 Hz, H-5′),7.18 (dd, 1H, $J$ = 1.9 Hz, 8.2 Hz, H-4′), 4.15 (m, 2H, H-2), 4.15 (q, 2H, $J$ = 7.0 Hz, OCH$_2$CH$_3$), 3.68 (m, 2H, H-3), 1.23 (t, 3H, $J$ = 7.0 Hz, OCH$_2$CH$_3$) ppm; $^{13}$C NMR (125 MHz, DMSO-$d_6$): $\delta$ = 165.16 (C=O), 164.23 (C-7), 160.87 (C-8a), 140.31 (C-1′), 132.98 (C-3′), 129.90 (C-5′), 123.36 (C-4′), 120.30 (C-2′), 118.60 (C-6′), 117.00 (C-5), 83.43 (C-6), 59.70 (OCH$_2$CH$_3$), 47.49 (C-2), 39.40 (C-3), 14.31 (OCH$_2$CH$_3$) ppm; MS (EI): M$^{+\cdot}$ C$_{15}$H$_{15}$ClN$_4$O$_2^{+\cdot}$ calc. for $^{35}$Cl 318.0884, found 318.0882; *m/z* (%): M$^{+\cdot}$ $^{37}$Cl: 320 (19), [M–H]$^+$ + isotopic 319 (12), [M–OEt]$^+$ 275 (6), [M·EtOH]$^{+\cdot}$ + isotopic 274 (7), [M–H–EtOH]$^+$ 273 (23), [M–C$_2$H$_4$OOC]$^{+\cdot}$ 248 (32), [M–H–C$_2$H$_4$OOC]$^{+\cdot}$ + isotopic 247 (21), $^{35}$Cl: 318 (55), [M–H]$^+$ 317 (6), [M–OEt]$^+$ 273 (23), [M–EtOH]$^{+\cdot}$ 272 (12), [M–H–EtOH]$^+$ 271 (21), [M–C$_2$H$_4$OOC]$^{+\cdot}$ 246 (100), [M–EtOOC]$^+$ 245 (19), 152 (5), 142 (8), 140 (28), 138 (10), 111 (22), 105 (7), 77 (8), 75 (14).

### Ethyl 3-[[1-(4-chlorophenyl)-4,5-dihydro-1H-imidazol-2-yl]amino]-2-cyanoprop-2-enoate (5d, C$_{15}$H$_{15}$ClN$_4$O$_2$)

According to general method with 1.95 g of **4d**. The method afforded 1.54 g (57 %) of **5d**. M.p.: 134–136 °C; $R_f$ = 0.48 (toluene/ethyl acetate/methanol 1:3:0.5); $^1$H NMR (500 MHz, DMSO-$d_6$): $\delta$ = 8.92 (br s, 1H, H-8), 8.56 (s, 1H, H-7), 7.73 (d, 2H, $J$ = 8.6 Hz, H-2′, H-6′), 7.40 (d, 2H, $J$ = 8.6 Hz, H-3′, H-5′), 4.14 (m, 2H, H-2), 4.14 (q, 2H, $J$ = 7.0 Hz, OCH$_2$CH$_3$), 3.68 (m, 2H, H-3), 1.22 (t, 3H, $J$ = 7.0 Hz, OCH$_2$CH$_3$) ppm; $^{13}$C NMR (125 MHz, DMSO-$d_6$): $\delta$ = 165.26 (C=O), 164.42 (C-7), 160.94 (C-8a), 137.82 (C-1′), 128.16 (C-3′, C-5′), 127.77 (C-4′), 122.33 (C-2′, C-6′), 117.22 (C-5′), 82.85 (C-6), 59.64 (OCH$_2$CH$_3$), 47.69 (C-2), 40.32 (C-3), 14.32 (OCH$_2$CH$_3$) ppm; MS (EI): M$^{+\cdot}$ C$_{15}$H$_{15}$ClN$_4$O$_2^{+\cdot}$ calc. for $^{35}$Cl 318.0884, found 318.0885; *m/z* (%): M$^{+\cdot}$ $^{37}$Cl: 320 (8), [M–H–EtOH]$^{+\cdot}$ 274 (34), [M–C$_2$H$_4$OOC]$^{+\cdot}$ 248 (14), [M–H–C$_2$H$_4$OOC]$^+$ + isotopic 247 (9), [M–C$_2$H$_4$OOC]$^{+\cdot}$ 246 (41), [M–H–C$_2$H$_4$OOC]$^+$ 245 (11), $^{35}$Cl: 318 (26), $^{35}$Cl: [M–OEt]$^+$ 273 (41), [M–EtOH]$^{+\cdot}$ 272 (100), [M–H–EtOH]$^+$ 271 (59), [M–C$_2$H$_4$OOC]$^{+\cdot}$ 246 (41), [M–EtOOC]$^+$ 245 (11), 152 (6), 140 (18), 138 (17), 125 (11), 111 (31), 105 (22), 77 (9), 75 (24).

### Ethyl 2-cyano-3-[[1-(2-methylphenyl)-4,5-dihydro-1H-imidazol-2-yl]amino]prop-2-enoate (5e, C$_{16}$H$_{18}$N$_4$O$_2$)

According to general method with 1.75 g of **4e**. The method afforded 1.50 g (60 %) of **5e**. M.p.: 117–118 °C; $R_f$ = 0.49 (toluene/ethyl acetate/methanol 1:3:0.5); $^1$H NMR (500 MHz, DMSO-$d_6$): $\delta$ = 8.62 (br s, 1H, H-8), 8.44 (s, 1H, H-7), 7.28 (m, 4H, H-3′, H-4′, H-5′, H-6′), 4.08 (q, 2H, $J$ = 7.1 Hz, OCH$_2$CH$_3$), 3.98 (m, 2H, H-2), 3.74 (m, 2H, H-3), 2.21 (s, 3H, 2′-CH$_3$), 1.18 (t, 3H, $J$ = 7.1 Hz, OCH$_2$CH$_3$) ppm; $^{13}$C NMR (125 MHz, DMSO-$d_6$): $\delta$ = 165.60 (C=O), 164.82 (C-7), 162.99 (C-

8a), 136.89, 135.61 (C-1′, C-2′), 130.75 (C-3′), 127.73, 126.94, 126.53 (C-4′, C-5′, C-6′), 117.22 (C-5), 80.77 (C-6), 59.38 (O$CH_2CH_3$), 49.90 (C-2), 40.50 (C-3), 17.62 (2′-CH_3), 14.32 (OCH_2$CH_3$) ppm; MS (EI): $M^{+\cdot}$ $C_{16}H_{18}N_4O_2$ calc. 298.1430, found 298.1423; m/z (%): $M^{+\cdot}$ 298 (79), $[M–H]^+$ 297 (34), $[M–OEt]^+$ 253 (31), $[M–EtOH]^{+\cdot}$ 252 (100), $[M–H–EtOH]^+$ 251 (99), $[M–Me–EtOH]^+$ 237 (29), $[M–C_2H_4OOC]^{+\cdot}$ 226 (47), $[M–EtOOC]^+$ 225 (22), 223 (8), 158 (82), 157 (18), 156 (10), 132 (11), 131 (15), 130 (16), 120 (13), 118 (31), 117 (22), 116 (13), 91 (55), 77 (21), 65 (40).

### Ethyl 2-cyano-3-[[1-(4-methylphenyl)-4,5-dihydro-1H-imidazol-2-yl]amino]prop-2-enoate (5f, $C_{16}H_{18}N_4O_2$)

According to general method with 1.75 g of 4f. The method afforded 1.62 g (64 %) of 5f. M.p.: 127–128 °C; $R_f = 0.50$ (toluene/ethyl acetate/methanol 1:3:0.5); ¹H NMR (500 MHz, DMSO-$d_6$): δ = 8.77 (br s, 1H, H-8), 8.54 (s, 1H, H-7), 7.55 (d, 2H, J = 8.1 Hz, H-2′, H-6′), 7.17 (d, 2H, J = 8.1 Hz, H-3′, H-5′), 4.13 (m, 2H, H-2), 4.13 (q, 2H, J = 7.0 Hz, O$CH_2$CH_3), 3.67 (t, 2H, J = 8.8 Hz, H-3), 2.29 (s, 3H, 4′-CH_3), 1.22 (t, 3H, J = 7.0 Hz, OCH_2$CH_3$) ppm; ¹³C NMR (125 MHz, DMSO-$d_6$): δ = 165.44 (C=O), 164.61 (C-7), 161.26 (C-8a), 136.26 (C-1′), 133.33 (C-4′), 128.83 (C-3′, C-5′), 121.05 (C-2′, C-6′), 117.35 (C-5), 82.04 (C-6), 59.53 (O$CH_2$CH_3), 47.99 (C-2), 39.46 (C-3), 20.30 (4′-CH_3), 14.34 (OCH_2$CH_3$) ppm; MS (EI): $M^{+\cdot}$ $C_{16}H_{18}N_4O_2^{+\cdot}$ calc. 298.1430, found 298.1426; m/z (%): $M^{+\cdot}$ 298 (69), $[M–H]^+$ 297 (11), $[M–OEt]^+$ 253 (23), $[M–EtOH]^{+\cdot}$ 252 (42), $[M–H–EtOH]^+$ 251 (41), $[M–C_2H_4OOC]^{+\cdot}$ 226 (100), $[M–EtOOC]^+$ 225 (25), 224 (7), 120 (35), 132 (6), 131 (6), 118 (13), 117 (7), 105 (14), 91 (42), 77 (10), 65 (20).

### Ethyl 2-cyano-3-[[1-(2-methoxyphenyl)-4,5-dihydro-1H-imidazol-2-yl]amino]prop-2-enoate (5g, $C_{16}H_{18}N_4O_3$)

According to general method with 1.91 g of 4g. The method afforded 1.79 g (67 %) of 5g. M.p.: 135–136 °C; $R_f = 0.49$ (toluene/ethyl acetate/methanol 1:3:0.5); ¹H NMR (500 MHz, DMSO-$d_6$): δ = 8.60 (br s, 1H, H-8), 8.45 (s, 1H, H-7), 7.32 (dt, 1H, J = 1.2 Hz, 7.5 Hz, H-4′), 7.28 (dd, 1H, J = 1.2 Hz, 7.8 Hz, H-6′), 6.98 (t, 1H, J = 7.4 Hz, H-5′), 7.13 (d, 1H, J = 8.2 Hz, H-3′), 4.09 (q, 2H, J = 7.0 Hz, O$CH_2$CH_3), 3.95 (dd, 2H, J = 8.5 Hz, 9.6 Hz, H-2), 3.81 (s, 3H, 2′-OCH_3), 3.71 (dd, 2H, J = 8.5 Hz, 9.6 Hz, H-3), 1.18 (t, 3H, J = 7.0 Hz, OCH_2$CH_3$) ppm; ¹³C NMR (125 MHz, DMSO-$d_6$): δ = 165.71 (C=O), 164.88 (C-7), 163.73 (C-8a), 154.61 (C-2′), 128.82 (C-4′, C-6′), 126.46 (C-1′), 120.38 (C-5′), 117.39 (C-5), 112.59 (C-3′), 80.37 (C-6), 59.34 (O$CH_2$CH_3), 55.69 (2′-OCH_3), 49.14 (C-2), 40.43 (C-3), 14.34 (OCH_2$CH_3$) ppm; MS (EI): $M^{+\cdot}$ $C_{16}H_{18}N_4O_3^{+\cdot}$ calc. 314.1379, found 314.1385; m/z (%): $M^{+\cdot}$ 314 (100), $[M–H]^+$ 313 (18), $[M–H–CH_3]^{+\cdot}$ 298 (5), $[M–Et]^+$ 285 (5), $[M–OCH_3]^+$ 283 (36), $[M–OEt]^+$ 269 (26), $[M–EtOH]^{+\cdot}$ 268 (32), $[M–H–EtOH]^+$ 267 (20), $[M–C_2H_4OOC]^{+\cdot}$ 242 (79), $[M–EtOOC]^+$ 241 (24), 237 (48), 212 (17), 211 (26), 174 (29), 136 (20), 134 (14), 121 (16), 129 (30), 119 (10), 106 (16), 105 (18), 104 (10), 93 (11), 92 (21), 91 (18), 77 (32), 65 (28).

### Ethyl 2-cyano-3-[[1-(4-methoxyphenyl)-4,5-dihydro-1H-imidazol-2-yl]amino]prop-2-enoate (5h, $C_{16}H_{18}N_4O_3$)

According to general method with 1.91 g of 4h. The method afforded 1.55 g (58 %) of 5h. M.p.: 173–174 °C; $R_f = 0.51$ (toluene/ethyl acetate/methanol 1:3:0.5); ¹H NMR (500 MHz, DMSO-$d_6$): δ = 8.66 (br s, 1H, H-8), 8.53 (s, 1H, H-7), 7.55 (d, 2H, J = 8.5 Hz, H-2′, H-6′), 6.93 (d, 2H, J = 8.5 Hz, H-3′, H-5′), 4.12 (m, 2H, H-2), 4.12 (q, 2H, J = 6.7 Hz, O$CH_2$CH_3), 3.75 (s, 3H, 4′-OCH_3), 3.67 (t, 2H, J = 8.4 Hz, H-3), 1.21 (t, 3H, J = 6.7 Hz, OCH_2$CH_3$) ppm; ¹³C NMR (125 MHz, DMSO-$d_6$): δ = 165.56 (C=O), 164.71 (C-7), 161.45 (C-8a), 156.10 (C-4′), 131.72 (C-1′), 123.03 (C-2′, C-6′), 117.38 (C-5), 113.62 (C-3′, C-5′), 81.66 (C-6), 59.49 (O$CH_2$CH_3), 55.18 (4′-OCH_3), 48.44 (C-2), 39.40 (C-3), 14.34 (OCH_2$CH_3$) ppm; MS (EI): $M^{+\cdot}$ $C_{16}H_{18}N_4O_3^{+\cdot}$ calc. 314.1379, found 314.1382; m/z (%): $M^{+\cdot}$ 314 (87), $[M–H]^+$ 313 (22), $[M–OEt]^+$ 269 (23), $[M–EtOH]^{+\cdot}$ 268 (32), $[M–H–EtOH]^+$ 267 (29), $[M–Me–HOEt]^+$ 253 (15), $[M–C_2H_4OOC]^{+\cdot}$ 242 (100), $[M–EtOOC]^+$ 241 (27), 225 (7), 136 (45), 135 (11), 134 (218), 133 (12), 121 (17), 120 (26), 106 (7), 105 (13), 93 (6), 92 (19), 91 (6), 77 (23), 65 (16).

### General procedure to obtain compounds 6a–6h

#### Method A

Enamine 5a–5h (0.01 mol) was dissolved in 10 cm³ of glacial acetic acid and refluxed under mild boiling for 4 h. The solvent was distilled off and the solid residue was crystallized from DMF.

#### Method B

1-Aryl-4,5-dihydro-1H-imidazol-2-amine hydrobromides (3a–3h, 0.01 mol) and 1.69 g of EMCA (1, 0.01 mol) were dissolved in 20 cm³ of ethanol. The solution was stirred under reflux for 4 h and then 1.02 g of triethylamine (0.01 mol) was added dropwise over a period of 15 min and the mixture was refluxed for additional 6 h. The precipitate was filtered off and washed with methanol.

### 5-Oxo-1-phenyl-2,3-dihydroimidazo[1,2-a]pyrimidine-6-carbonitrile (6a, $C_{13}H_{10}N_4O$)

According to general method A with 2.36 g of 5a. The method afforded 1.36 g (57 %) of 6a. M.p.: 210–213 °C; $R_f = 0.62$ (toluene/ethyl acetate/methanol 1:3:0.5); ¹H NMR (500 MHz, DMSO-$d_6$): δ = 8.40 (s, 1H, H-7), 7.72

(d, 2H, $J = 8.5$ Hz, H-2′, H-6′), 7.45 (dd, 2H, $J = 7.5$ Hz, 8.5 Hz, H-3′, H-5′), 7.23 (t, 1H, $J = 7.5$ Hz, H-4), 4.26 (m, 2H, H-2), 4.15 (m, 2H, H-3) ppm; $^{13}$C NMR (125 MHz, DMSO-$d_6$): $\delta = 163.57$ (C-7), 157.95 (C-5), 155.79 (C-8a), 137.65 (C-1′), 128.83 (C-3′, C-5′), 125.02 (C-4′), 120.38 (C-2′, C-6′), 115.78 (6-CN), 90.55 (C-6), 46.00 (C-2), 40.31 (C-3) ppm; MS (EI): M$^{+\cdot}$ C$_{13}$H$_{10}$N$_4$O$^{+\cdot}$ calc. 238.0842, found 238.0855; $m/z$ (%): M$^{+\cdot}$ 238 (100), [M–H]$^+$ 237 (71), [M–CN]$^+$ 212 (7), [M–HCN]$^{+\cdot}$ 211 (4), [M–H–CO]$^+$ 209 (5), 105 (10), 104 (5), 91 (7), 77 (17), 54 (9), 51 (8).

### 1-(2-Chlorophenyl)-5-oxo-2,3-dihydroimidazo-[1,2-a]pyrimidine-6-carbonitrile (6b, C$_{13}$H$_9$ClN$_4$O)

According to general method B with 2.72 g of **5b**. The method afforded 1.64 g (60 %) of **6b**. M.p.: 236-240 °C; $R_f = 0.60$ (toluene/ethyl acetate/methanol 1:3:0.5); $^1$H NMR (500 MHz, DMSO-$d_6$): $\delta = 8.26$ (s, 1H, H-7), 7.65 (m, 2H, H-3′, H-6′), 7.49 (m, 2H, H-4′, H-5′), 4.28 (m, 2H, H-2), 4.14 (m, 2H, H-3) ppm; $^{13}$C NMR (125 MHz, DMSO-$d_6$): $\delta = 164.03$ (C-7), 157.99 (C-5), 157.54 (C-8a), 134.07 (C-1′), 131.47 (C-2′), 130.43 (C-5′), 130.19 (C-6′), 130.00 (C-3′), 128.40 (C-4′), 115.76 (6-CN), 90.18 (C-6), 47.63 (C-2), 41.45 (C-3) ppm; MS (EI): M$^{+\cdot}$ C$_{13}$H$_9$ClN$_4$O$^{+\cdot}$ calc. for $^{35}$Cl 272.0465, found 272.0477; $m/z$ (%): M$^{+\cdot}$ $^{37}$Cl: 274 (8), $^{35}$Cl: 272 (26), [M–Cl]$^+$ 237 (100), [M–Cl–C$_2$H$_2$]$^+$ 211 (10), 138 (3), 111 (6), 105 (4), 75 (5), 54 (7).

### 1-(3-Chlorophenyl)-5-oxo-2,3-dihydroimidazo-[1,2-a]pyrimidine-6-carbonitrile (6c, C$_{13}$H$_9$ClN$_4$O)

According to general method A with 2.72 g of **5c**. The method afforded 1.47 g (54 %) of **6c**. M.p.: 245–248 °C; $R_f = 0.65$ (toluene/ethyl acetate/methanol 1:3:0.5); $^1$H NMR (500 MHz, DMSO-$d_6$): $\delta = 8.46$ (s, 1H, H-7), 7.98 (t, 1H, $J = 2.0$ Hz, H-2′), 7.64 (dd, 1H, $J = 2.0$ Hz, 8.1 Hz, H-6′), 7.48 (t, 1H, $J = 8.1$ Hz, H-5′), 7.29 (dd, 1H, $J = 2.0$ Hz, 8.1 Hz, H-4′), 4.26 (m, 2H, H-2), 4.15 (m, 2H, H-3) ppm; $^{13}$C NMR (125 MHz, DMSO-$d_6$): $\delta = 163.42$ (C-7), 157.79 (C-5), 155.68 (C-8a), 139.15 (C-1′), 133.20 (C-3′), 130.50 (C-5′), 124.49 (C-4′), 119.72 (C-2′), 118.35 (C-6′), 115.57 (6-CN), 91.27 (C-6), 45.84 (C-2), 40.32 (C-3) ppm; MS (EI): M$^{+\cdot}$ C$_{13}$H$_9$ClN$_4$O$^{+\cdot}$ calc. for $^{35}$Cl 272.0465, found 272.0467; $m/z$ (%): M$^{+\cdot}$ $^{37}$Cl: 274 (32), $^{35}$Cl: 272 (100), [M–H]$^+$ $^{37}$Cl: 273 (35), $^{35}$Cl: 271 (60), [M–H–CO]$^+$ 243 (4), [M–HCl]$^{+\cdot}$ 246 (12), 138 (5), 125 (5), 111 (11), 105 (10), 75 (8), 54 (11).

Crystal data: C$_{13}$H$_9$ClN$_4$O, $M = 272.69$, orthorhombic, space group $Pca2_1$, $a = 22.8305(14)$ Å, $b = 5.4318(8)$ Å, $c = 9.5141(6)$ Å, $V = 1,179.9(2)$ Å$^3$, $Z = 4$, $d_{calc} = 1.535$ Mg m$^{-3}$, $F(000) = 560$, $\mu$(Cu Kα) = 2.851 mm$^{-1}$, $T = 293$ K, 1825 measured reflections ($\theta$ range 3.87–80.17°), 1,433 unique reflections ($R_{int} = 0.051$), final

$R = 0.033$, $wR = 0.099$, $S = 1.091$ for 1304 reflections with $I > 2\sigma(I)$.

### 1-(4-Chlorophenyl)-5-oxo-2,3-dihydroimidazo[1,2-a]pyrimidine-6-carbonitrile (6d, C$_{13}$H$_9$ClN$_4$O)

According to general method A with 2.72 g of **5d**. The method afforded 2.05 g (75 %) of **6d**. M.p.: 214–216 °C; $R_f = 0.62$ (toluene/ethyl acetate/methanol 1:3:0.5); $^1$H NMR (500 MHz, DMSO-$d_6$): $\delta = 8.42$ (s, 1H, H-7), 7.77 (d, 2H, $J = 9.0$ Hz, H-2′, H-6′), 7.51 (d, 2H, $J = 9.0$ Hz, H-3′, H-5′), 4.24 (m, 2H, H-2), 4.14 (m, 2H, H-3) ppm; $^{13}$C NMR (125 MHz, DMSO-$d_6$): $\delta = 163.41$ (C-7), 157.83 (C-5), 155.63 (C-8a), 136.65 (C-1′), 128.72 (C-3′, C-4′), 121.70 (C-2′, C-6′), 115.64 (6-CN), 91.00 (C-6), 45.89 (C-2), 40.30 (C-3) ppm; MS (EI): M$^{+\cdot}$ C$_{13}$H$_9$ClN$_4$O$^{+\cdot}$ calc. for $^{35}$Cl 272.0465, found 272.0463; $m/z$ (%): M$^{+\cdot}$ $^{37}$Cl: 274 (33), $^{35}$Cl: 272 (100), [M–H]$^+$ $^{37}$Cl: 273 (29), $^{35}$Cl: 271 (48), [M–H–CO]$^+$ 243 (3), C$_7$H$_5$ClN$^+$ 138 (6), C$_7$H$_6$Cl$^+$ 125 (5), C$_6$H$_4$ClN$^+$ 111 (10), C$_5$H$_3$N$_3^+$ 105 (10), C$_6$H$_3^+$ 75 (7), C$_2$H$_2$N$_2^+$ 54 (10).

### 1-(2-Methylphenyl)-5-oxo-2,3-dihydroimidazo-[1,2-a]pyrimidine-6-carbonitrile (6e, C$_{14}$H$_{12}$N$_4$O)

According to general method A with 2.51 g of **5e**. The method afforded 1.94 g (77 %) of **6e**. M.p.: 204–206 °C; $R_f = 0.57$ (toluene/ethyl acetate/methanol 1:3:0.5); $^1$H NMR (500 MHz, DMSO-$d_6$): $\delta = 8.21$ (s, 1H, H-7), 7.40 (dd, 1H, $J = 1.8$ Hz, 7.2 Hz, H-6′), 7.30–7.35 (m, 3H, H-3′, H-4′, H-5′), 4.23 (m, 2H, H-3), 4.10 (m, 2H, H-2), 2.23 (s, 3H, CH$_3$) ppm; $^{13}$C NMR (125 MHz, DMSO-$d_6$): $\delta = 164.10$ (C-7), 158.22 (C-5), 157.21 (C-8a), 135.88 (C-2′), 135.48 (C-1′), 130.89 (C-3′), 128.59 (C-4′), 127.20 (C-6′), 126.88 (C-5′), 116.04 (6-CN), 89.31 (C-6), 48.01 (C-2), 41.28 (C-3), 17.23 (2′-CH$_3$) ppm; MS (EI): M$^{+\cdot}$ C$_{14}$H$_{12}$N$_4$O$^{+\cdot}$ calc. 252.1001, found 252.1011; $m/z$ (%): M$^{+\cdot}$ 252 (100), [M–H]$^+$ 251 (88), [M–CH$_3$]$^+$ 237 (24), [M–C$_2$H$_5$]$^+$+[M–H–CO]$^+$ 223 (4), C$_{10}$H$_{10}$N$_2^+$ 158 (45), C$_9$H$_9$N$^+$ 131 (5), 130 (5), C$_8$H$_8$N$^+$ 118 (6), 117 (6), 91 (13), C$_5$H$_5^+$ 65 (9), 54 (6).

### 1-(4-Methylphenyl)-5-oxo-2,3-dihydroimidazo-[1,2-a]pyrimidine-6-carbonitrile (6f, C$_{14}$H$_{12}$N$_4$O)

According to general method A with 2.51 g of **5f**. The method afforded 1.51 g (63 %) of **6f**. M.p.: 250–254 °C; $R_f = 0.62$ (toluene/ethyl acetate/methanol 1:3:0.5); $^1$H NMR (500 MHz, DMSO-$d_6$): $\delta = 8.38$ (s, 1H, H-7), 7.59 (d, 2H, $J = 8.5$ Hz, H-2′, H-6′), 7.25 (d, 2H, $J = 8.5$ Hz, H-3′, H-5′), 4.23 (m, 2H, H-2), 4.14 (m, 2H, H-3), 2.31 (s, 3H, CH$_3$) ppm; $^{13}$C NMR (125 MHz, DMSO-$d_6$): $\delta = 163.62$ (C-7), 157.98 (C-5), 155.77 (C-8a), 135.14 (C-1′), 134.42 (C-4′), 129.24 (C-3′, C-5′), 120.48 (C-2′, C-6′), 115.85 (6-CN), 90.22 (C-6), 46.13 (C-2), 40.29 (C-3), 20.34 (4′-CH$_3$) ppm; MS (EI): M$^{+\cdot}$ C$_{14}$H$_{12}$N$_4$O$^{+\cdot}$ calc. 252.1011, found 252.1019; $m/z$ (%): M$^{+\cdot}$ 252 (100),

[M–H]$^+$ 251 (53), [M–H–CO]$^+$ 223 (4), 118 (4), 105 (9), 91 (12), 65 (4), 54 (6).

### 1-(2-Methoxyphenyl)-5-oxo-2,3-dihydroimidazo[1,2-a]pyrimidine-6-carbonitrile (6g, C$_{14}$H$_{12}$N$_4$O$_2$)

According to general method A with 2.67 g of **5g**. The method afforded 1.61 g (61 %) of **6g**. M.p.: 240–243 °C; $R_f$ = 0.55 (toluene/ethyl acetate/methanol 1:3:0.5); $^1$H NMR (500 MHz, DMSO-$d_6$): δ = 8.22 (s, 1H, H-7), 7.41 (d, 1H, $J$ = 7.5 Hz, H-6′), 7.40 (dt, 1H, $J$ = 1.4 Hz, 7.5 Hz, H-4′), 7.18 (d, 1H, $J$ = 7.5 Hz, H-3′), 7.03 (dt, 1H, $J$ = 1.4 Hz, 7.5 Hz, H-5′), 4.22 (m, 2H, H-3), 4.08 (m, 2H, H-2), 3.82 (s, 3H, OCH$_3$) ppm; $^{13}$C NMR (125 MHz, DMSO-$d_6$): δ = 164.12 (C-7), 158.14 (C-5), 157.67 (C-8a), 154.72 (C-2′), 129.74 (C-4′), 128.62 (C-6′), 124.78 (C-1′), 120.53 (C-5′), 116.01 (6-CN), 112.56 (C-3′), 89.43 (C-6), 55.71 (2′-OCH$_3$), 47.30 (C-2), 41.16 (C-3) ppm; MS (EI): M$^{+\cdot}$ C$_{14}$H$_{12}$N$_4$O$_2^{+\cdot}$ calc. 268.0960, found 268.0960; $m/z$ (%): M$^{+\cdot}$ 268 (100), [M–H]$^+$ 267 (22), [M–H–CH$_3$]$^+$ 252 (6), [M–H–H$_2$O]$^+$ 249 (10), [M–H–CO]$^+$ 239 (13), C$_{10}$H$_{10}$N$_2$O$^+$ 174 (10), C$_8$H$_8$NO$^+$ 134 (5), C$_6$H$_6$N$^+$+C$_6$H$_4$O$^+$ (2:5) 92 (5), C$_6$H$_5$N$^+$+ C$_7$H$_7^+$ (1:3) 91 (5), 78 (6), 77 (9), 65 (7), 54 (8), 52 (5), 51 (6).

### 1-(4-Methoxyphenyl)-5-oxo-2,3-tetrahydro-imidazo[1,2-a]pyrimidine-6-carbonitrile (6h, C$_{14}$H$_{12}$N$_4$O$_2$)

According to general method A with 2.67 g of **5h**. The method afforded 1.45 g (54 %) of **6h**. M.p.: 218–220 °C; $R_f$ = 0.57 (toluene/ethyl acetate/methanol 1:3:0.5); $^1$H NMR (500 MHz, DMSO-$d_6$): δ = 8.33 (s, 1H, H-7), 7.58 (d, 2H, $J$ = 8.9 Hz, H-2′, H-6′), 7.00 (d, 2H, $J$ = 8.9 Hz, H-3′, H-5′), 4.20 (m, 2H, H-2), 4.13 (m, 2H, H-3), 3.76 (s, 3H, OCH$_3$) ppm; $^{13}$C NMR (125 MHz, DMSO-$d_6$): δ = 163.72 (C-7), 158.04 (C-5), 156.83 (C-4′), 155.91 (C-8a), 130.44 (C-1′), 122.77 (C-2′, C-6′), 115.93 (6-CN), 114.04 (C-5′), 114.04 (C-3′), 89.85 (C-6), 55.26 (4′-OCH$_3$), 46.62 (C-2), 40.34 (C-3) ppm; MS (EI): M$^{+\cdot}$ C$_{14}$H$_{12}$N$_4$O$_2^{+\cdot}$ calc. 268.0960, found 268.0969; $m/z$ (%): M$^{+\cdot}$ 268 (100), [M–H]$^+$ 267 (14), [M–CH$_3$]$^+$ 253 (32), [M–H–CH$_3$]$^+$ 252 (6), [M–CH$_3$O]$^+$ 237 (9), [M–CH$_3$–CO]$^+$ 225 (7), 134 (9), 105 (4), 77 (5), 54 (6).

### General procedure to obtain compounds 7a and 7c–7h

Compound **5a–5h** (0.01 mol) was carefully heated in a porcelain evaporating dish to complete melting and subsequent solidification. After the chromatographic control of the completeness of melting the mixture was dissolved in 4 cm$^3$ of DMF and applied on two preparative 20 × 20 TLC plates (Merck). Each plate was developed twice with toluene-ethyl acetate–methanol (1:3:0.5) eluent system and then four times with a stronger eluent system containing higher amount of the methanol (1:3:1) until the complete

separation of two products of melting (visualization in the UV light at the wavelength of 254 nm). The band containing the adsorbed imines (mixtures of ethyl and methyl esters) was removed with the silica support and was three times extracted with boiling ethanol for 30 min and then the solvent was evaporated. Thus, compounds **7a** and **7c–7h** were obtained as mixtures of ethyl and methyl esters.

### Ethyl (methyl) 5-imino-1-phenyl-2,3-dihydro-imidazo[1,2-a]pyrimidine-6-carboxylate (7a, C$_{15}$H$_{16}$N$_4$O$_2$)

According to general method with 2.36 g of **5a**. The method afforded 0.33 g (23 %) of **7a** (a 90:10 mixture of the Et- and Me-esters based on the intensity of the CH$_2$-signals in the NMR spectrum. The abundance ratio of the M$^{+\cdot}$ ions 86:14). M.p.: 130–132 °C; $R_f$ = 0.00 (toluene/ethyl acetate/methanol 1:3:0.5); $^1$H NMR (500 MHz, DMSO-$d_6$): δ = 8.17 (s, 1H, H-7), 8.11 (br s, 1H, 5-N*H*), 7.74 (d, 2H, $J$ = 7.4 Hz, H-2′, H-6′), 7.42 (t, 2H, $J$ = 7.4 Hz, H-3′, H-5′), 7.18 (t, 1H, $J$ = 7.4 Hz, H-4′), 4.23 (m, 2H, H-2), 4.20 (q, 2H, $J$ = 7.1 Hz, OC*H*$_2$CH$_3$), 4.03 (m, 2H, H-3), 1.26 (t, 3H, $J$ = 7.1 Hz, OCH$_2$C*H*$_3$) ppm; $^{13}$C NMR (125 MHz, DMSO-$d_6$): δ = 165.23 (C=O), 157.40 (C-5), 155.27 (C-8a), 152.68 (C-7), 138.35 (C-1′), 128.68 (C-3′, C-5′), 124.16 (C-4′), 119.90 (C-2′, C-6′), 102.66 (C-6), 59.60 (OCH$_2$CH$_3$), 45.68 (C-2), 40.57 (C-3), 14.06 (OCH$_2$CH$_3$) ppm; MS (EI): calc. for C$_{15}$H$_{16}$N$_4$O$_2$ 284.1273, found 284.1269; $m/z$ (%): Et-ester: M$^{+\cdot}$ 284 (89), [M–H]$^+$ 283 (8); Me-ester: M$^{+\cdot}$ 270 (14), [M–H]$^+$ 269 (3); [M–EtO]$^+$ and [M–MeO]$^+$ 239 (22), [M–HOEt]$^+$ and [M–HOMe]$^+$ 238 (10), [M–H–HOEt]$^{+\cdot}$ and [M–H–HOMe]$^{+\cdot}$ 237 (251), [M–C$_2$H$_4$OOC]$^{+\cdot}$ and [M–H$_2$COOC]$^{+\cdot}$ 212 (100), [M–H–C$_2$H$_4$OOC]$^+$ and [M–H–H$_2$COOC]$^+$ 211 (15), 161 (12), 160 (11), 149 (7), 118 (5), 106 (34), 105 (50), 104 (7), 91 (7), 77 (23).

### Ethyl (methyl) 1-(3-chlorophenyl)-5-imino-2,3-dihydroimidazo[1,2-a]pyrimidine-6-carboxylate (7c, C$_{15}$H$_{15}$ClN$_4$O$_2$)

According to general method with 2.72 g of **5c**. The method afforded 0.49 g (31 %) of **7c** (a 56:44 mixture of the Et- and Me-esters based on the intensity of the CH$_2$-signals in the NMR spectrum. The abundance ratio of the M$^{+\cdot}$ ions was 47:56). M.p.: 153–155 °C; $R_f$ = 0.00 (toluene/ethyl acetate/methanol 1:3:0.5); NMR data for **7c**: $^1$H NMR (500 MHz, DMSO-$d_6$): δ = 8.23 (s, 1H, H-7), 8.18 (br s, 1H, 5-N*H*), 8.00 (m, 1H, H-2′), 7.64 (m, 1H, H-6′), 7.44 (t, 1H, $J$ = 8.2 Hz, H-5′), 7.23 (m, 1H, H-4′), 4.22 (m, 2H, H-2), 4.22 (q, 2H, $J$ = 7.1 Hz, OC*H*$_2$CH$_3$), 4.03 (m, 2H, H-3), 1.27 (t, 3H, $J$ = 7.1 Hz, OCH$_2$C*H*$_3$) ppm; $^{13}$C NMR (125 MHz, DMSO-$d_6$): δ = 165.11 (C=O), 157.27 (C-7), 155.15 (C-8a), 152.57 (C-5), 139.81 (C-1′), 133.10 (C-3′), 130.36 (C-5′), 123.70 (C-4′), 119.34 (C-2′), 117.90 (C-6′), 102.96 (C-6), 59.76 (OCH$_2$CH$_3$), 45.60 (C-2), 40.69

(C-3), 14.04 (OCH$_2$CH$_3$) ppm; MS (EI): M$^{+\cdot}$ C$_{15}$H$_{15}$ClN$_4$O$_2^{+\cdot}$ calc. for $^{35}$Cl (Et-ester) 318.0884, found 318.0885; calc. for $^{35}$Cl (Me-ester) 304.0727, found 304.0730; m/z (%): Et-ester: M$^{+\cdot}$ $^{37}$Cl 320 (12), $^{35}$Cl 318 (37); Me-ester: $^{37}$Cl 306 (14), $^{35}$Cl 304 (42), [M–H]$^+$ 303 (10); $^{37}$Cl: [M–OEt]$^+$ and [M–OMe]$^+$ 275 (8), $^{35}$Cl: [M–OEt]$^+$ and [M–OMe]$^+$ 273 (32), [M–HOEt]$^{+\cdot}$ and [M–HOMe]$^{+\cdot}$ 272 (14), [M–H–HOEt]$^+$ and [M–H–HOMe]$^+$ 271 (29), $^{37}$Cl: [M–C$_2$H$_4$OOC]$^{+\cdot}$ and [M–H$_2$COOC]$^{+\cdot}$ 248 (31), [M–H–C$_2$H$_4$OOC]$^{+\cdot}$ and [M–H–H$_2$COOC]$^{+\cdot}$ (+isotopic) 247 (21), $^{35}$Cl: [M–C$_2$H$_4$OOC]$^{+\cdot}$ and [M–H$_2$COOC]$^{+\cdot}$ 246 (100), [M–H–C$_2$H$_4$OOC]$^{+\cdot}$ and [M–H–H$_2$COOC]$^{+\cdot}$ 245 (18), 142 (10), 140 (34), 138 (12), 111 (27).

*Ethyl (methyl) 1-(4-chlorophenyl)-5-imino-2,3-dihydroimidazo[1,2-a]pyrimidine-6-carboxylate (7d, C$_{15}$H$_{15}$ClN$_4$O$_2$)*

According to general method with 2.72 g of **5d**. The method afforded 0.43 g (27 %) of **7d** (a 75:25 mixture of Et and Me esters based on the intensity of the CH$_2$-signals in the NMR spectrum. The abundance ratio of the M$^{+\cdot}$ ions was 76:24). M.p.: 170–171 °C; $R_f = 0.00$ (toluene/ethyl acetate/methanol 1:3:0.5); NMR data for **7d**: $^1$H NMR (500 MHz, DMSO-$d_6$): $\delta = 8.17$ (s, 1H, H-7), 8.13 (br s, 1H, 5-N*H*), 7.79 (m, 2H, H-2′, H-6′), 7.48 (m, 2H, H-3′, H-5′), 4.21 (m, 2H, H-2), 4.21 (q, 2H, $J = 7.1$ Hz, OCH$_2$CH$_3$), 4.03 (m, 2H, H-3), 1.26 (t, 3H, $J = 7.1$ Hz, OCH$_2$C*H*$_3$) ppm; $^{13}$C NMR (125 MHz, DMSO-$d_6$): $\delta = 165.19$ (C=O), 157.13 (C-7), 155.19 (C-8a), 152.58 (C-5), 137.38 (C-1′), 128.56 (C-3′, C-5′), 127.91 (C-4′), 121.28 (C-2′, C-6′), 103.03 (C-6), 59.67 (OCH$_2$CH$_3$), 45.63 (C-2), 40.58 (C-3), 14.06 (OCH$_2$CH$_3$) ppm; MS (EI): M$^{+\cdot}$ C$_{15}$H$_{15}$ClN$_4$O$_2^{+\cdot}$ calc. for $^{35}$Cl (Et-ester) 318.0884, found 318.0885, calc. for $^{35}$Cl (Me-ester) 304.0727, found 304.0732; m/z (%): Et-ester: M$^{+\cdot}$ $^{37}$Cl 320 (17), $^{35}$Cl 318 (52), Me-ester: $^{37}$Cl 306 (5), $^{35}$Cl 304 (16), [M–H]$^+$ 303 (4), $^{37}$Cl: [M–OEt]$^+$ and [M–OMe]$^+$ 275 (7), $^{35}$Cl: [M–OEt]$^+$ and [M–OMe]$^+$ 273 (28), [M–HOEt]$^{+\cdot}$ and [M–HOMe]$^{+\cdot}$ 272 (12), [M–H–HOEt]$^+$ and [M–H–HOMe]$^+$ 271 (22), $^{37}$Cl: [M–C$_2$H$_4$OOC]$^{+\cdot}$ and [M–H$_2$COOC]$^{+\cdot}$ 248 (32), [M–H–C$_2$H$_4$OOC]$^{+\cdot}$ and [M–H–H$_2$COOC]$^{+\cdot}$ (+isotopic) 247 (21), $^{35}$Cl: [M–C$_2$H$_4$OOC]$^{+\cdot}$ and [M–H$_2$COOC]$^{+\cdot}$ 246 (100), [M–H–C$_2$H$_4$OOC]$^{+\cdot}$ and [M–H–H$_2$COOC]$^{+\cdot}$ 245 (21), 142 (7), 140 (24), 138 (7), 111 (10).

*Ethyl (methyl) 5-imino-1-(2-methylphenyl)-2,3-dihydroimidazo[1,2-a]pyrimidine-6-carboxylate (7e, C$_{16}$H$_{18}$N$_4$O$_2$)*

According to general method with 2.51 g of **5e**. The method afforded 0.31 g (21 %) of **7e** (a 70:30 mixture of the Et- and Me-esters based on the intensity of the CH$_2$-

signals in the NMR spectrum and a 72:28 mixture 86:14 mixture based on the abundance of the M$^{+\cdot}$ ions). M.p.: 155–160 °C; $R_f = 0.00$ (toluene/ethyl acetate/methanol 1:3:0.5); NMR data for **7e**: $^1$H NMR (500 MHz, DMSO-$d_6$): $\delta = 8.09$ (br s, 1H, 5-N*H*), 8.02 (s, 1H, H-7), 7.40 − 7.26 (m, 4H, H-3′, H-4′, H-5′, H-6′), 4.17 (q, 2H, $J = 7.1$ Hz, OCH$_2$CH$_3$), 4.11 (m, 2H, H-2), 4.08 (m, 2H, H-3), 2.22 (s, 3H, 2′-CH$_3$), 1.23 (t, 3H, $J = 7.1$ Hz, OCH$_2$C*H*$_3$) ppm; $^{13}$C NMR (125 MHz, DMSO-$d_6$): $\delta = 165.42$ (C=O), 158.27 (C-7), 156.68 (C-8a), 152.95 (C-5), 136.15 (C-2′), 135.96 (C-1′), 130.82 (C-3′), 128.23, 127.35, 126.80 (C-4′, C-5′, C-6′), 101.51 (C-6), 59.38 (OCH$_2$CH$_3$), 47.95 (C-2), 41.59 (C-3), 17.36 (2-CH$_3$), 14.12 (OCH$_2$CH$_3$) ppm; MS (EI): M$^{+\cdot}$ C$_{16}$H$_{18}$N$_4$O$_2^{+\cdot}$ calc. (Et-ester) 298.1430, found 298.1429, calc. (Me-ester) 284.1174, found 284.1170; m/z (%): Et-ester: M$^{+\cdot}$ 298 (100), [M–H]$^+$ 297 (44), Me-ester: M$^{+\cdot}$ 284 (39), [M–H]$^+$ 283 (25), [M–Et]$^+$ and [M–Me]$^+$ 269 (8), [M–OEt]$^+$ and [M–OMe]$^+$ 253 (25), [M–HOEt]$^{+\cdot}$ and [M–HOMe]$^{+\cdot}$ 252 (11), [M–H–HOEt]$^+$ and [M–H–HOMe]$^+$ 251 (35), [M–C$_2$H$_4$OOC]$^{+\cdot}$ and [M–H$_2$COOC]$^{+\cdot}$ 226 (70), [M–H–C$_2$H$_4$OOC]$^+$ and [M–H–H$_2$COOC]$^+$ 225 (27), 158 (61), 131 (10), 131 (12), 120 (18), 118 (32), 117 (18), 91 (48), 77 (15), 65 (28).

*Ethyl (methyl) 5-imino-1-(4-methylphenyl)-2,3-dihydroimidazo[1,2-a]pyrimidine-6-carboxylate (7f, C$_{16}$H$_{18}$N$_4$O$_2$)*

According to general method with 2.51 g of **5f**. The method afforded 0.43 g (29 %) of **7f** (a 68:32 mixture of the Et- and Me-esters based on the intensity of the CH$_2$-signals in the NMR spectrum. The abundance ratio of the M$^{+\cdot}$ ions was 73:27). M.p.: 140–142 °C; $R_f = 0.00$ (toluene/ethyl acetate/methanol 1:3:0.5); NMR data for **7f**: $^1$H NMR (500 MHz, DMSO-$d_6$): $\delta = 8.15$ (s, 1H, H-7), 8.09 (br s, 1H, 5-N*H*), 7.60 (m, 2H, H-2′, H-6′), 7.22 (m, 2H, H-3′, H-5′), 4.19 (m, 2H, H-2), 4.19 (q, 2H, $J = 7.1$ Hz, OCH$_2$CH$_3$), 2.30 (s, 3H, 4′-CH$_3$), 1.26 (t, 3H, $J = 7.1$ Hz, OCH$_2$C*H*$_3$) ppm; $^{13}$C NMR (125 MHz, DMSO-$d_6$): $\delta = 165.28$ (C=O), 157.56 (C-7), 155.31 (C-8a), 152.72 (C-5), 135.82 (C-1′), 133.51 (C-4′), 129.11 (C-3′, C-5′), 120.11 (C-2′, C-6′), 102.39 (C-6), 59.54 (OCH$_2$CH$_3$), 45.84 (C-2), 40.57 (C-3), 20.31 (4′-CH$_3$), 14.08 (OCH$_2$CH$_3$) ppm; MS (EI): M$^{+\cdot}$ C$_{16}$H$_{18}$N$_4$O$_2^{+\cdot}$ calc. (Et-ester) 298.1430, found 298.1426, calc. (Me-ester) 284.1284, found 284.1279; m/z (%): Et-ester: M$^{+\cdot}$ 298 (61), [M–H]$^+$ 297 (10), Me-ester: M$^{+\cdot}$ 284 (22), [M–H]$^+$ 283 (7), [M–OEt]$^+$ and [M–OMe]$^+$ 253 (29), [M–HOEt]$^{+\cdot}$ and [M–HOMe]$^{+\cdot}$ 252 (14), [M–H–HOEt]$^+$ and [M–H–HOMe]$^+$ 251 (29), [M–C$_2$H$_4$OOC]$^{+\cdot}$ and [M–H$_2$COOC]$^{+\cdot}$ 226 (100), [M–H–C$_2$H$_4$OOC]$^+$ and [M–H–H$_2$COOC]$^+$ 225 (26), 120 (34), 118 (14), 91 (39), 77 (10), 65 (17).

*Ethyl (methyl) 5-imino-1-(2-methoxyphenyl)-2,3-dihydroimidazo[1,2-a]pyrimidine-6-carboxylate* (**7g**, $C_{16}H_{18}N_4O_3$)

According to general method with 2.67 g of **5g**. The method afforded 0.30 g (19 %) of **7g** (a 68:32 mixture of the Et- and Me-esters based on the intensity of the $CH_2$-signals in the NMR spectrum. The abundance ratio of the $M^{+\cdot}$ ions was 67:33). M.p.: 165–168 °C; $R_f = 0.00$ (toluene/ethyl acetate/methanol 1:3:0.5); NMR data for **7g**: $^1H$ NMR (500 MHz, DMSO-$d_6$): $\delta = 8.08$ (br s, 1H, 5-N$H$), 8.02 (s, 1H, H-7), 7.38 (m, 1H, H-6′), 7.36 (m, 1H, H-4′), 7.16 (d, 1H, $J = 7.8$ Hz, H-3′), 7.01 (dt, 1H, $J = 1.2$ Hz, 7.6 Hz, H-5′), 4.17 (q, 2H, $J = 7.1$ Hz, OC$H_2$CH$_3$), 4.06 (m, 2H, H-2), 4.06 (m, 2H, H-3), 3.82 (s, 3H, 2′-OCH$_3$), 1.20 (t, 3H, $J = 7.1$ Hz, OCH$_2$C$H_3$) ppm; $^{13}C$ NMR (125 MHz, DMSO-$d_6$): $\delta = 165.39$ (C=O), 158.26 (C-7), 157.26 (C-8a), 154.90 (C-2′), 152.86 (C-5), 129.35, 128.98 (C-4′, C-6′), 125.50 (C-1′), 120.46 (C-5′), 112.48 (C-3′), 101.57 (C-6), 59.37 (O$C$H$_2$CH$_3$), 55.66 (2′-O$C$H$_3$), 47.26 (C-2), 41.50 (C-3), 14.11 (OCH$_2$$C$H$_3$) ppm; MS (EI): $M^{+\cdot}$ $C_{16}H_{18}N_4O_2^{+\cdot}$ calc. (Et-ester) 314.1379, found 314.1377, calc. (Me-ester) 300.1223, found 300.1225; *m/z* (%): Et-ester: $M^{+\cdot}$ 314 (100), $[M–H]^+$ 313 (17), Me-ester: $M^{+\cdot}$ 300 (50), $[M–H]^+$ 299 (11), $[M–OMe]^+$ 283 (29), $[M–OEt]^{+\cdot}$ and $[M–OMe]^{+\cdot}$ 269 (47), $[M–H–HOEt]^+$ and $[M–H–HOMe]^+$ 267 (17), $[M–C_2H_4OOC]^{+\cdot}$ and $[M–H_2COOC]^{+\cdot}$ 242 (71), $[M–H–C_2H_4OOC]^+$ and $[M–H–H_2COOC]^+$ 241 (11), 237 (17), 212 (14), 211 (17), 174 (34), 134 (10), 119 (11), 106 (6), 105 (5), 92 (6), 77 (8), 65 (6).

*Ethyl (methyl) 5-imino-1-(4-methoxyphenyl)-2,3-dihydroimidazo[1,2-a]pyrimidine-6-carboxylate* (**7h**, $C_{16}H_{18}N_4O_3$)

According to general method with 2.67 g of **5h**. The method afforded 0.53 g (34 %) of **7h** (a 85:15 mixture of the Et- and Me-esters based on the intensity of the $CH_2$-signals in the NMR spectrum. The abundance ratio of the $M^{+\cdot}$ ions was 88:12). M.p.: 181–182 °C; $R_f = 0.00$ (toluene/ethyl acetate/methanol 1:3:0.5); NMR data for **7h**: $^1H$ NMR (500 MHz, DMSO-$d_6$): $\delta = 8.13$ (s, 1H, H-7), 8.08 (br s, 1H, 5-N$H$), 7.59 (dd, 2H, $J = 2.4$ Hz, 6.9 Hz, H-2′, H-6′), 6.99 (dd, 2H, $J = 2.3$ Hz, 6.9 Hz, H-3′, H-5′), 4.18 (m, 2H, H-2), 4.18 (q, 2H, $J = 7.1$ Hz, OC$H_2$CH$_3$), 4.02 (m, 2H, H-3), 3.76 (s, 3H, 4′-OCH$_3$), 1.25 (t, 3H, $J = 7.1$ Hz, OCH$_2$C$H_3$) ppm; $^{13}C$ NMR (125 MHz, DMSO-$d_6$): $\delta = 165.32$ (C=O), 157.71 (C-7), 156.28 (C-4′), 155.42 (C-8a), 152.78 (C-5), 131.21 (C-1′), 122.34 (C-2′, C-6′), 113.91 (C-3′, C-5′), 102.07 (C-6), 59.49 (O$C$H$_2$CH$_3$), 55.21 (4′-O$C$H$_3$), 46.33 (C-2), 40.62 (C-3), 14.09 ppm (OCH$_2$$C$H$_3$); MS (EI): $M^{+\cdot}$ $C_{16}H_{18}N_4O_2^{+\cdot}$ calc. (Et-ester) 314.1379, found 314.1374, calc. (Me-ester) 300.1223, found 300.1219; *m/z* (%): Et-ester: $M^{+\cdot}$ 314 (100), $[M–H]^+$ 313 (22), Me-ester: $M^{+\cdot}$ 300 (13), $[M–H]^+$ 299 (6), $[M–OEt]^{+\cdot}$ and $[M–OMe]^{+\cdot}$ 269 (21), $[M–HOEt]^+$ and $[M–HOMe]^+$ 268 (12), $[M–H–HOEt]^+$ and $[M–H–HOMe]^+$ 267 (32), $[M–C_2H_4OOC]^{+\cdot}$ and $[M–H_2COOC]^{+\cdot}$ 242 (87), $[M–H–C_2H_4OOC]^+$ and $[M–H–H_2COOC]^+$ 241 (21), 136 (30), 134 (10), 121 (10), 77 (5).

## References

1. Kaczor A, Matosiuk D (2005) Curr Org Chem 9:1237
2. Williams LA (1962) J Chem Soc 2222. http://www.rsc.org/Publishing/Journals/JS/Article.asp?
3. Miyamoto Y (2002) J Heterocycl Chem 39:157
4. Badawey ES, Kappe T (1995) J Heterocycl Chem 32:1003
5. Siskovic DR (1996) In: Karitzky AR, Rees CW, Scriven EVF (eds) Comprehensive heterocyclic chemistry II. Pergamon Press, London
6. Freeman C, Turner J, Ward A (1978) Aust J Chem 31:179
7. Abignente E, Sacchi A, Laneri S, Rossi F, D'Amico M, Berrino L, Calderaro V, Parrillo C (1994) Eur J Med Chem 29:279
8. Sacchi A, Laneri S, Arena F, Luraschi E, Attigente E, D'Amico M, Berrino L, Rossi F (1997) Eur J Med Chem 32:677
9. Vidal A, Ferrándiz ML, Ubeda A, Acero-Alarcón A, Sepulveda-Arques J, Alcaraz MJ (2001) Inflamm Res 50:317
10. Rival Y, Grassy G, Michel G (1992) Chem Pharm Bull 40:1170
11. Al-Tel TH, Al-Qawasmeh RA (2010) Eur J Med Chem 45:5848
12. Steenackers HP, Ermolat'ev DS, Savaliya B, De Weerdt A, De Coster D, Shah A, Van der Eycken EV, De Vos DE, Vanderleyden J, De Keersmaecker SC (2011) J Med Chem 54:472
13. Steenackers HP, Ermolat'ev DS, Savaliya B, De Weerdt AD, De Coster DD, Shah A, Van der Eycken EV, De Vos DE, Vanderleyden J, De Keersmaecker SC (2011) Bioorg Med Chem 19:3462
14. Moraski GC, Markley LD, Chang M, Cho S, Franzblau SG, Hwang CH, Boshoff H, Miller MJ (2012) Bioorg Med Chem 20:2214
15. Gueiffier A, Lhassani M, Elhakmaoui A, Snoeck R, Andrei G, Chavignon O, Teulade JC, Kerbal A, Essassi EM, Debouzy JC, Witvrouw M, Blache Y, Balzarini J, De Clercq E, Chapat JP (1996) J Med Chem 39:2856
16. Rival Y, Grassy G, Taudou A, Ecalle R (1991) Eur J Med Chem 26:13
17. Rival Y, Taudou A, Ecalle R (1993) Farmaco 48:857
18. Dehuri SN, Pradhan PC, Nayak A (1983) J Indian Chem Soc 60:475
19. Matosiuk D, Tkaczyński T, Stefańczyk J (1996) Acta Pol Pharm 53:209
20. Tully WR, Gardner CR, Gillespie RJ, Westwood R (1991) J Med Chem 34:2060
21. Jensen MS, Hoerrner RS, Li W, Nelson DP, Javadi GJ, Dormer PG, Cai D, Larsen RD (2005) J Org Chem 70:6034

22. Blackaby WP, Atack JR, Bromidge F, Castro JL, Goodacre SC, Hallett DJ, Lewis RT, Marshall GR, Pike A, Smith AJ, Street LJ, Tattersall DF, Wafford KA (2006) Bioorg Med Chem Lett 16:1175

23. Goodacre SC, Street LJ, Hallett DJ, Crawforth JM, Kelly S, Owens AP, Blackaby WP, Lewis RT, Stanley J, Smith AJ, Ferris P, Sohal B, Cook SM, Pike A, Brown N, Wafford KA, Marshall G, Castro JL, Atack JR (2006) J Med Chem 49:35

24. Sasaki S, Imaeda T, Hayase Y, Shimizu Y, Kasai S, Cho N, Harada M, Suzuki N, Furuya S, Fujino M (2002) Bioorg Med Chem Lett 12:2073

25. Turner JV, Ward AD, Freeman CG (1978) Mutat Res 57:135

26. Guo C, Linton A, Kephart S, Ornelas M, Pairish M, Gonzalez J, Greasley S, Nagata A, Burke BJ, Edwards M, Hosea N, Kang P, Hu W, Engebretsen J, Briere D, Shi M, Gukasyan H, Richardson P, Dack K, Underwood T, Johnson P, Morell A, Felstead R, Kuruma H, Matsimoto H, Zoubeidi A, Gleave M, Los G, Fanjul AN (2011) J Med Chem 54:7693

27. Linton A, Kang P, Ornelas M, Kephart S, Hu Q, Pairish M, Jiang Y, Guo C (2011) J Med Chem 54:7705

28. Okabe T, Bhooshan B, Novinson T, Hillyard IW, Garner GE, Robins RK (1983) J Heterocycl Chem 20:735

29. Matosiuk D, Pihlaja K, Ovcharenko VV, Dybała I, Kozioł AE, Gdaniec M, Szumiło H, Karczmarzyk Z (2003) J Heterocycl Chem 40:93

30. Naceur S, Zantaur H (1999) J Soc Chem Tunis 4:393

31. Bagrov FV, Naskin OE, Skobolev SP (1999) Russ J Org Chem 35:756

32. Zhang SL, Zhai X, Zhang SJ, Yu HH, Gong P (2010) Chin Chem Lett 21:939

33. Kakehi A, Ito S, Matsubara K (1995) Bull Chem Soc Jpn 68:2409

34. Itoh T, Honmo M, Oguro H (1976) Chem Pharm Bull 24:1390

35. El-Emary TI (2007) J Chin Chem Soc 54:507

36. Chang SP, Hungerford WM, McDonald WS, Maguire RJ, Malony KQ, Subramanyam C (2010) Tetrahedron Lett 51:952

37. El-Kashef H, Farghaly A-R, Al-Hazmi A, Terme T, Vanelle P (2010) Molecules 15:2651

38. Ramesh B, Bhalgat CM (2011) Eur J Med Chem 46:1882

39. Matosiuk D, Karczmarzyk Z, Krycki A, Fruziński A (2005) Anal Sci 21:x19

40. Dobrowolski M, Cyrański MK, Pisklak M, Wawer I, Matosiuk D (2007) Pol J Chem 81:1037

41. Miyamoto Y (2002) J Het Chem 39:157

42. Frisch MJ, Trucks GW, Schlegel HB, Scuseria GE, Robb MA, Cheeseman JR, Montgomery Jr JA, Vreven T, Kudin KN, Burant JC, Millam JM, Iyengar SS, Tomasi J, Barone V, Mennucci B, Cossi M, Scalmani G, Rega N, Petersson GA, Nakatsuji H, Hada M, Ehara M, Toyota K, Fukuda R, Hasegawa J, Ishida M, Nakajima T, Honda Y, Kitao O, Nakai H, Klene M, Li X, Knox JE, Hratchian HP, Cross JB, Bakken V, Adamo C, Jaramillo J, Gomperts R, Stratmann RE, Yazyev O, Austin AJ, Cammi R, Pomelli C, Ochterski JW, Ayala PY, Morokuma K, Voth GA, Salvador P, Dannenberg JJ, Zakrzewski VG, Dapprich S, Daniels AD, Strain MC, Farkas O, Malick DK, Rabuck AD, Raghavachari K, Foresman JB, Ortiz JV, Cui Q, Baboul AG, Clifford S, Cioslowski J, Stefanov BB, Liu G, Liashenko A, Piskorz P, Komaromi I, Martin RL, Fox DJ, Keith T, Al-Laham MA, Peng CY, Nanayakkara A, Challacombe M, Gill PMW, Johnson B, Chen W, Wong MW, Gonzalez C, Pople JA (2004) Gaussian 03, Revision C.02. Gaussian, Inc., Wallingford CT

43. Laatikainen R, Niemitz M, Weber U, Sundelin J, Hassinen T, Vepsäläinen J (1996) J Magn Reson Ser A 120:1

44. Wysocki W, Matosiuk D, Karczmarzyk Z, Pihlaja K, Kaczor A, Kijkowska-Murak U, Urbańczyk-Lipkowska Z (2008) Anal Sci 24:x119

45. Bernstein J, Davis RE, Shimoni L, Chang N-L (1995) Angew Chem Int Ed 34:1555

46. Cossi M, Rega N, Scalmani G, Barone V (2003) J Comp Chem 24:669

47. Parkin S, Moezzi B, Hope H (1995) J Appl Crystallogr 28:53

48. Sheldrick GM (2007) Acta Crystallogr A 64:112

49. Flack HD (1983) Acta Crystallogr A 39:876

50. Farrugia LJ (1999) J Appl Crystallogr 32:837