Synthesis and Selected Transformations of 1*H*-Imidazole 3-Oxides Derived from Amino Acid Esters

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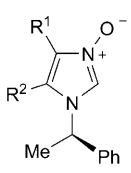
A series of new optically active 1*H*-imidazole 3-oxides **5** with a substituted acetate group at N(1) as the chiral unit were prepared by the reaction of α-(hydroxyimino) ketones, α-amino acid methyl esters, and formaldehyde. In an analogous reaction, ethyl 2-(hydroxyimino)-3-oxobutyrate and 1,3,5-trialkylhexahydro-1,3,5-triazines gave 3-oxido-1*H*-imidazole-4-carboxylates **14**, which easily rearranged into the 2-oxo derivatives **15**. Selected examples of *N*-oxides **5** could be transformed into the corresponding 2,3-dihydro-1*H*-imidazole-2-thione derivatives **10** *via* a 'sulfur-transfer reaction', and the reduction of the histidine derivative **5i** with *Raney*-Ni yielded the optically active 2,3-bis(imidazolyl)propanoate **12**. Furthermore, reaction of the (1*H*-imidazol-1-yl)acetates with primary amines yielded the corresponding acetamides.

1. Introduction. – In a series of recent articles, a versatile method for the synthesis of 2-unsubstituted 1*H*-imidazole 3-oxides based on a three-component reaction of an α-(hydroxyimino) ketone, formaldehyde, and a primary amine was described [1–3]. In general, aliphatic primary amines are required, and diamines can also be applied leading to bis[imidazole 3-oxides]. Starting with enantiomerically pure amines, *e.g.*, 1-phenylethylamine or *trans*-cyclohexane-1,2-diamine, optically active 1*H*-imidazole 3-oxides **1** and **2**, respectively, were obtained without racemization [4][5].



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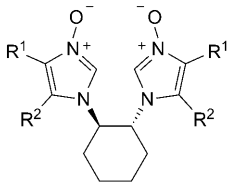

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[1]) Part of the Ph.D. thesis of *M. J.*, University of Łódź, 2008.

1*H*-Imidazole 3-oxides without a substituent at C(2) undergo reactions similar to nitrones according to the mechanism of 1,3-dipolar cycloadditions. The initially formed [2 + 3] cycloadducts spontaneously undergo conversion to 1*H*-imidazole derivatives functionalized at C(2) [1][2][6–8]. These reactions show that 1*H*-imidazole 3-oxides are versatile starting materials for the preparation of diverse imidazole derivatives, which, in some instances, exhibit attractive biological activities [9][10].

With the aim of preparing further optically active 1*H*-imidazole 3-oxides, we turned our attention to α-amino acid derivatives as the amino component containing the stereogenic center. A few years ago, *Lettau et al.* reported the synthesis of some optically active 1*H*-imidazole 3-oxides by treatment of diacetylmonooxime with aldehydes and α-amino acids [11] (see also [12]). Whereas the reactions with formaldehyde yielded optically active products, the experiments with acetaldehyde, benzaldehyde, and isobutyraldehyde, respectively, led to completely racemized products. The products obtained from formaldehyde and enantiomeric amino acids showed the opposite optical rotation (± 30%), but the enantiomeric purity has not been determined. The authors claimed that, in contrast to other representatives [13] (see also [14]), these products do not isomerize to give the corresponding 1*H*-imidazol-2-ones. The unusual stability was explained by 'the association between the *N*-oxide and the COOH group'. Furthermore, the products are insoluble in most organic solvents, and, therefore, they could not be transformed into other imidazole derivatives[2]).

Prompted by this observation, we elaborated a protocol for the preparation of amino acid-derived 1*H*-imidazole 3-oxides by using α-amino acid esters as the amino component. We expected that these products will display more advantageous properties, which allow further transformations of both the imidazole ring and the carboxylic group. Such transformations are of interest with respect to further application of imidazole derivatives, *e.g.*, in organocatalysis.

2. Results and Discussion. – To optimize the reaction conditions, first experiments were carried out with glycine methyl ester (**4a**), formaldehyde, and butane-2,3-dione monooxime (**3a**) in boiling EtOH (*Method A*). After 3 h, the reaction was complete, and the *N*-oxide **5a** was obtained as viscous oil (*Scheme 1* and *Table 1*). The structure of the product was confirmed by the presence of the characteristic absorptions of H–C(2) of the imidazole ring at 8.09 ppm (*s*) and of the CH_2 group of the glycine moiety at 4.64 ppm (*s*) in the ^{1}H-NMR spectrum ($CDCl_3$). The IR spectrum (film) shows a strong absorption band for the ester group at 1741 cm^{-1}.

For comparison, the same reaction was carried out in glacial AcOH at room temperature overnight, followed by treatment with HCl gas (*Method B*). Subsequent workup led to **5a** in better yield and higher purity (*Table 1*). The analogous reaction with **4a** and α-(hydroxyimino) ketones **3b**–**3d** yielded the expected products **5b**–**5d**, respectively, and, in all cases, *Method B* turned out to be more advantageous.

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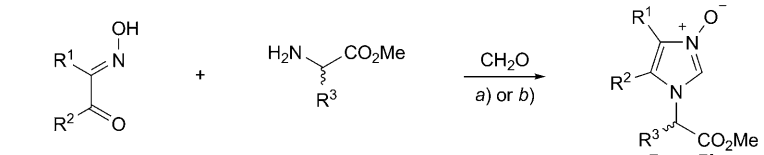
[2]) Attempts to convert the glycine derivative obtained with diacetylmonooxime and formaldehyde [12] into the corresponding 1*H*-imidazole-2-thione or into the methyl ester by treatment with CH_2N_2 or $MeOH/H_2SO_4$ were unsuccessful [15].

Scheme 1



3a $R^1 = R^2 = Me$
3b $R^1 = Ph$, $R^2 = Me$
3c $R^1 = Me$, $R^2 = Ph$
3d $R^1 = R^2 = Ph$

4a $R^3 = H$
(*S*)-4b $R^3 = Me$ (*S*)
(*R*)-4b $R^3 = Me$ (*R*)
4c $R^3 = Me_2CH$ (*S*)
4d $R^3 = Me_2CHCH_2$ (*S*)
4e $R^3 = Ph$ (*R*)
4f $R^3 = 4\text{-ImCH}_2$ (*S*)
4g $R^3 = 4\text{-HOC}_6H_4CH_2$ (*S*)

5a – 5j

a) EtOH, reflux, 3 h (*Method A*). *b*) AcOH, 16 h, HCl (g), $NaHCO_3$ (*Method B*).

Table 1. *Preparation of 2-(3-Oxido-1*H*-imidazol-1-yl)acetates* **5**

5	R^1	R^2	R^3	$[\alpha]_D^{20}$ ($c = 0.2$, CH_2Cl_2)	Yield [%]	
					Method A	*Method B*
a	Me	Me	H		65	88
b	Ph	Me	H		71	90
c	Me	Ph	H		49	58
d	Ph	Ph	H		55	71
e (*S*)	Me	Me	Me (*S*)	+47.1	50	67
e (*R*)	Me	Me	Me (*R*)	−48.5		72
f	Me	Me	Me_2CH (*S*)	+31.3		90
g	Me	Me	Me_2CHCH_2 (*S*)	+10.6		44
h	Me	Me	Ph (*rac*)	0	43[a]), 22[a])[b])	81[a])
i	Me	Me	(4-Im)CH_2 (*S*)	−26.0		70
j	Me	Me	4-$HOC_6H_4CH_2$ (*S*)	−99.5	63	81[a])

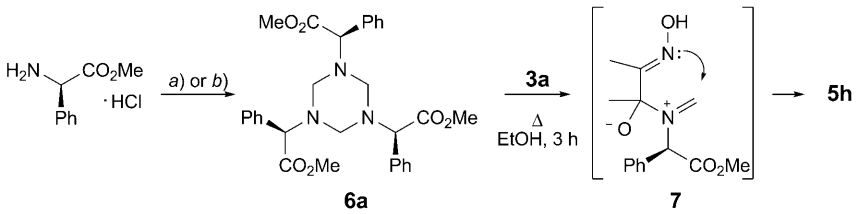
[a]) Racemate. [b]) Modified *Method A:* MeOH, paraformaldehyde, reflux 6 h.

Based on the results obtained with **4a**, reactions of **3a** with the methyl esters of (*S*)-alanine ((*S*)-**4b**), (*R*)-alanine ((*R*)-**4b**), (*S*)-valine (**4c**), (*S*)-leucine (**4d**), (*R*)-phenylglycine (**4e**), (*S*)-histidine (**4f**), and (*S*)-tyrosine (**4g**) were performed according to *Method B*. The spectroscopic data of the products, which were obtained in good yields, were in agreement with the expected structures of 1*H*-imidazole 3-oxides of type **5** (*Table 1*). However, in the case of **5h** and **5j** (phenylglycine and tyrosine derivatives, resp.) using *Method B*, the products showed no optical activity. Repetition of the reactions according to *Method A* gave **5h** again as racemate; however, in the case of **5j**, the product was optically active (*Table 1*).

To obtain more information about the racemization in the case of **5h**, the optically active hexahydro-1,3,5-triazine **6a** [16] was prepared from (*R*)-phenylglycine methyl ester and HCHO (*Scheme 2*). The optical activity of the crystalline **6a** did not change in

boiling EtOH after 2 h. However, using the optically active **6a** in the reaction with **3a** (*Method A*) resulted again in the formation of racemic **5h**. Therefore, we propose that the crucial intermediate **7** in the formation of **5h** undergoes fast racemization. The appearance of such an intermediate also allows racemization under acidic conditions in the case of tyrosine **5j**. Surprisingly, the formation of the histidine derivative **5i** occurs without racemization by using *Method B*.

Scheme 2



a) 1N NaOH, 37% CH_2O, H_2O/benzene. *b*) $(CH_2O)_n$, MeOH, $NaHCO_3$, r.t., 14 h.

The enantiomeric purity of all optically active *N*-oxides **5** was determined by ^{1}H-NMR spectroscopy using 1 equiv. of (+)-(*R*)-(*tert*-butyl)(phenyl)phosphonothioic acid as a chiral solvating agent [4][5][17]. The results obtained with **5e** are shown in *Fig. 1*. Whereas in the case of *rac*-**5e**, the ^{1}H-NMR spectrum of the 1:1 mixture showed clearly separated *singlet*s for the diagnostic H–C(2) (9.13 and 8.98 ppm), the corresponding spectra of the optically active products (*S*)-**5e** and (*R*)-**5e** revealed in each case only one signal. In addition, the other signals of the spectra confirmed the presence of a single stereoisomer. To check the accuracy of the spectroscopic determination, a mixture of 98% of (*S*)-**5e** and 2% of (*R*)-**5e** was analyzed, and, in this case, the signal of the minor isomer could be detected clearly. Thus, the ee value of the isolated products was higher than 96%.

The oily 1*H*-imidazole 3-oxides **5a**–**5d** easily undergo reactions with primary aliphatic amines to give the corresponding amides of type **8** (*Scheme 3* and *Table 2*). In contrast to the starting materials, the amides were obtained as crystalline substances, which are easy to handle and to purify. In the case of (*R*)-(1-phenylethyl)amine, the reactions with **5a** and **5b** led to the optically active products **8h** and **8i**, respectively. The structure of **8h** was confirmed by X-ray crystallography (*Fig. 2*).

There are four symmetry-independent molecules of **8h** and four molecules of H_2O in the asymmetric unit. The Ph ring in one of the molecules is disordered over two orientations. The space group permits the compound to be enantiomerically pure, but the absolute configuration of **8h** has not been determined. The enantiomer used in the refinement was based on the known (*R*)-configuration of the molecule. The NH group in each molecule forms an intermolecular H-bond with the oxide O-atom of a neighboring symmetry-independent molecule. These molecules, A and B, are thereby linked alternatively into extended chains which run parallel to the [1 1 0] direction and can be described by a binary graph set motif [19] of $C_2^2(8)$. Molecules C and D form similar chains which run parallel to the [1 –1 0] direction. From an analysis of O···O

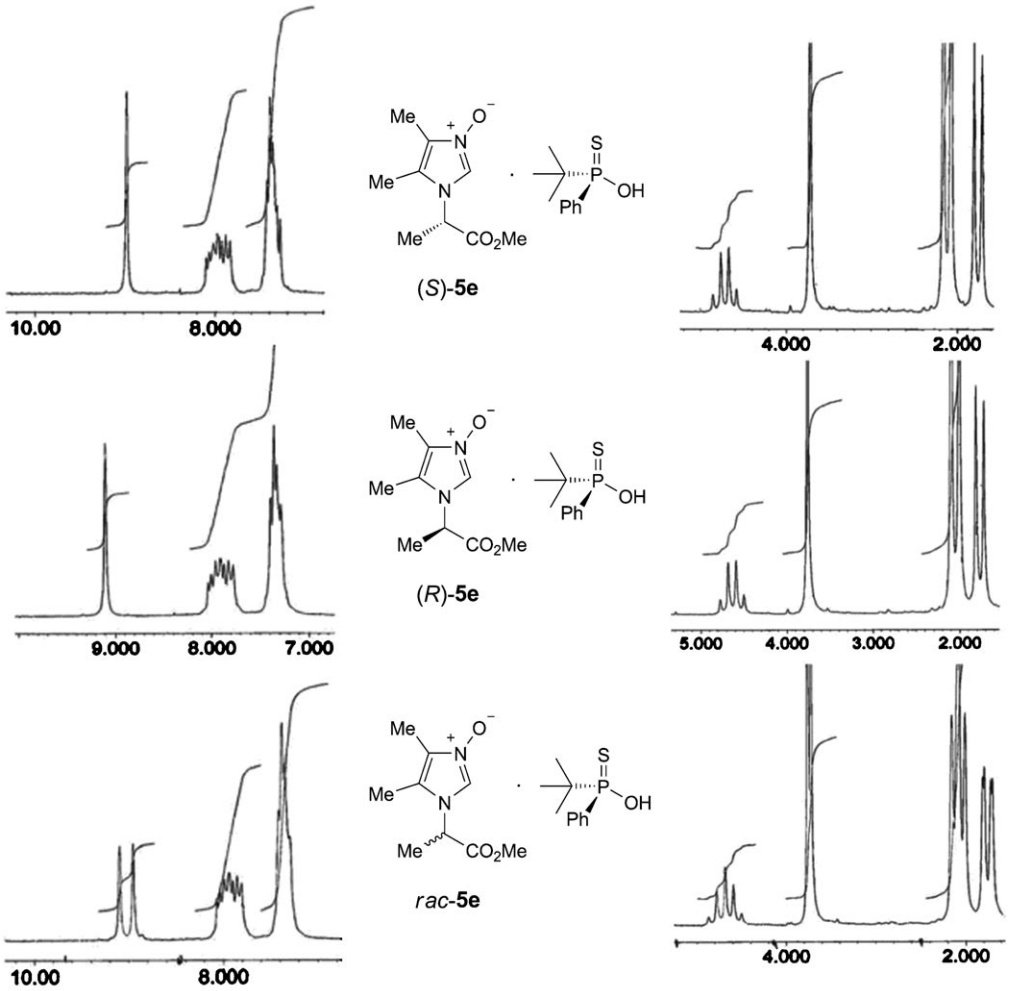


Fig. 1. *^{1}H-NMR Spectra of* (*S*)-**5e**, (*R*)-**5e**, *and rac*-**5e** *in $CDCl_3$ recorded in the presence of 1 equiv. of (+)-(*R*)-(*tert*-butyl)(phenyl)phosphonothioic acid*

distances, each H_2O molecule forms H-bonds with two O-atoms of just one molecule of **8h**.

The transformation of 2-unsubstituted 1*H*-imidazole 3-oxides into 1*H*-imidazole-2-thiones was reported earlier [1]. In the case of the glycine derivatives **5**, treatment with 2,2,4,4-tetramethylcyclobutane-1,3-dithione (**9**) in CH_2Cl_2 at room temperature gave the crystalline 1*H*-imidazole-2-thiones **10** in high yields (*Scheme 3* and *Table 3*). The analogous procedure applied to MeOH solutions of the amides of type **8** afforded the corresponding 2-thioxo-1*H*-imidazol-1-yl acetamides **11**. The characteristic absorption of the C=S group in the ^{13}C-NMR spectrum appears at *ca.* 161 ppm, in accordance with the data reported for 1*H*-imidazole-2-thiones [6]. The signals for the ester and amide

Scheme 3

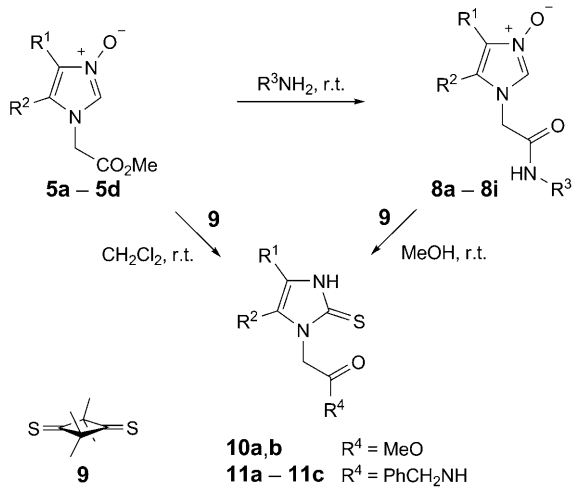


Table 2. *Preparation of 2-(3-Oxido-1*H*-imidazol-1-yl)acetamides* **8**

8	R^1	R^2	R^3	Yield [%]
a	Me	Me	$PhCH_2$	68
b	Ph	Me	$PhCH_2$	59
c	Me	Ph	$PhCH_2$	51
d	Ph	Ph	$PhCH_2$	84
e	Me	Me	Cyclopropyl	81
f	Ph	Ph	Cyclopropyl	61
g	Ph	Ph	Cyclohexyl	44
h	Me	Me	PhCHMe (*R*)	91
i	Ph	Me	PhCHMe (*R*)	77

Table 3. *Preparation of 1*H*-Imidazole-2-thiones* **10** *and* **11**

	R^1	R^2	R^4	Yield [%]
10a	Ph	Me	MeO	86
10b	Me	Ph	MeO	76
11a	Me	Me	$PhCH_2NH$	96
11b	Ph	Me	$PhCH_2NH$	57
11c	Ph	Ph	$PhCH_2NH$	60

C=O groups of **10** and **11** are located at *ca.* 168 ppm. The IR absorptions of the esters **10** and the amides **11** were observed, as expected, at *ca.* 1740 and 1650–1695 cm^{-1}, respectively.

The enhanced acidity of H–C(2) in 1*H*-imidazole 3-oxides is a characteristic property [2][20]. Therefore, the H/D exchange can be achieved in D_2O or CD_3OD. In

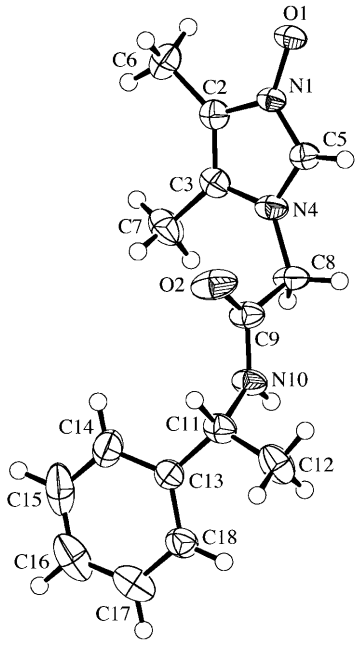


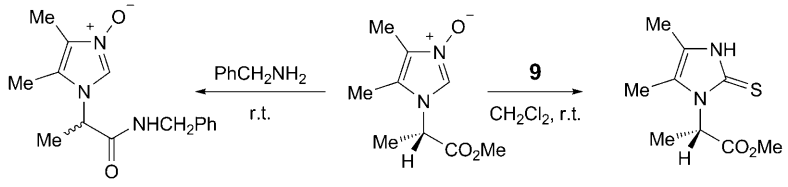
Fig. 2. *ORTEP Plot* [18] *of the molecular structure of one of the four symmetry-independent molecules of* **8h** (with 50% probability ellipsoids; arbitrary numbering of the atoms)

the case of **5c** and **8c**, heating a solution of these compounds in a mixture of D_2O and CD_3OD for 5 h led to an almost complete exchange (^{1}H-NMR).

The transformations **5** → **8** and **5** → **10** described for glycine derivatives (*Scheme 3*) were also carried out with an optically active 1*H*-imidazole 3-oxide of type **5**. Thus, treatment of (*S*)-**5e** with $PhCH_2NH_2$ led to the racemic amide **8j** with the preserved *N*-oxide function (*Scheme 4*). The S-transfer reaction with (*S*)-**5e** by using **9** in the typical manner afforded the optically active 1*H*-imidazole-2-thione **10c**. These experiments demonstrate that the optically active 1*H*-imidazole 3-oxides **5** can be converted into other optically active imidazole derivatives only in selected cases.

In a recent publication, we described the preparation of symmetrical bis-imidazole derivatives starting with α,ω-diamino-alkanes, formaldehyde, and the corresponding α-(hydroxyimino) ketones [3]. In an extension of these studies, the reaction of L-histidine

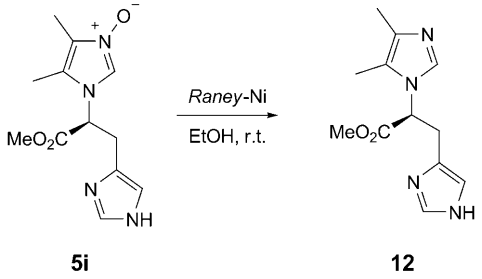
Scheme 4



8j (*S*)-**5e** **10c**

with **3a** was carried out according to *Method B*. The optically active product **5i** was isolated as a crystalline material in 70% yield (*Scheme 5*). The deoxygenation of **9** with *Raney*-Ni led to the the bis-imidazole **12**, which proved to be optically active.

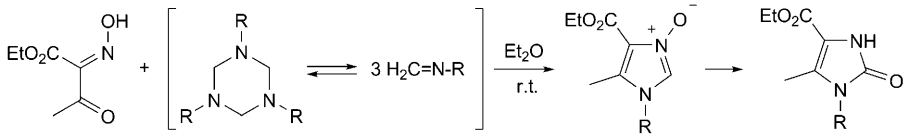
Scheme 5



5i **12**

With the aim of preparing other functionalized 1*H*-imidazole 3-oxides, the reaction of ethyl 2-(hydroxyimino)-3-oxobutanoate (**13**) with 1/3 equiv. of hexahydro-1,3,5-triazine **6** was carried out in Et_2O at room temperature. In solution, **6** is in equilibrium with the corresponding methylidenamine, which reacts with **13** according to the known mechanism [21] (*Scheme 6*). Under these conditions, the initially formed 1*H*-imidazole 3-oxides **14** easily undergo an isomerization to give the isomeric 1*H*-imidazol-2-ones **15**. In the case of **14a**, the product could be isolated in pure form, whereas, in the cases of **14b** and **14c**, *ca.* 4 : 1 mixtures of **14** and **15** were obtained. After attempted purification by crystallization from CH_2Cl_2/Et_2O, the corresponding 1*H*-imidazol-2-ones were isolated exclusively[3]).

Scheme 6



13 **6b** R = Me
6c R = Bn
6d R = cHex

14a – 14c **15a – 15c**

The *N*-oxide **14a** was transformed into the corresponding amide **16** by treatment with an excess of cyclopropylamine at room temperature (*Scheme 7*). The structure of this new amide was confirmed by the spectroscopic data. Finally, the structure was confirmed by an X-ray crystal-structure determination (*Fig. 3*).

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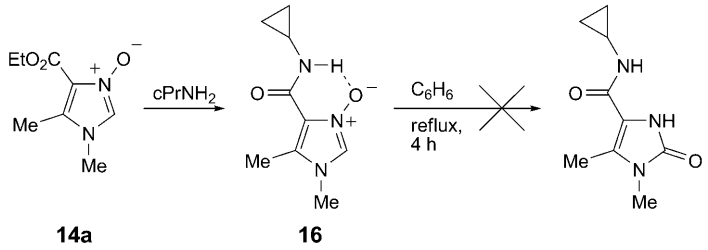
[3]) The reaction of **13** with **6** performed in MeOH at room temperature was significantly slower, and heating resulted in the formation of a complex mixture of products containing **14** and **15**, as well as transesterificated analogues.

Scheme 7



14a **16**

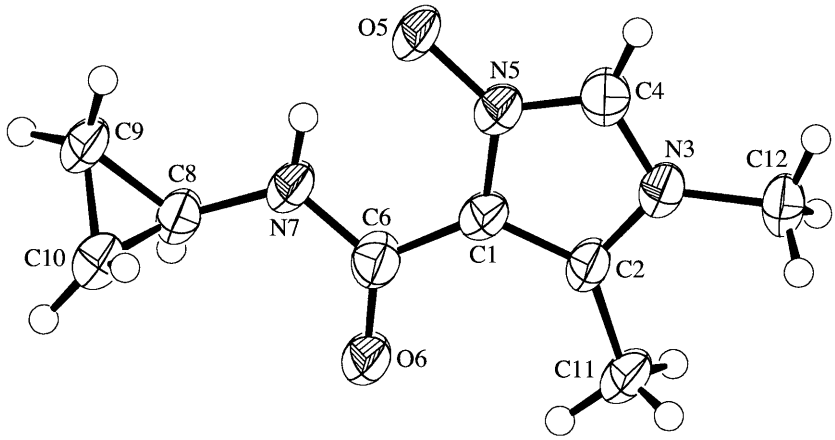


Fig. 3. *ORTEP Plot* [18] *of the molecular structure of one of the two symmetry-independent molecules of* **16** (with 50% probability ellipsoids; arbitrary numbering of the atoms)

The asymmetric unit contains two molecules of **16** plus one molecule of MeOH. In each molecule of **16**, the amide group forms an intramolecular H-bond with the oxide O-atom to give a six-membered loop, which can be described by a graph set motif [19] of S(6). The MeOH molecule forms an intermolecular H-bond with the oxide O-atom of one of the molecules of **16**; graph set motif D.

Unexpectedly, the amide **16** was thermally stable and did not isomerize to give the corresponding 1*H*-imidazol-2-one after heating in benzene for 4 h. For comparison, under the same conditions, the ester **14a** was completely converted into **15a** after 2 h. It is likely that the intramolecular H-bond stabilizes the *N*-oxide structure (see crystal structure).

3. Conclusions. – The presented study shows that α-amino acid esters can be conveniently applied as amino components in the synthesis of 1*H*-imidazole 3-oxides containing an acetate group at N(1). Diverse conversions can be performed both at the ester function and at the imidazole ring, *e.g.*, formation of amides and 1*H*-imidazole-2-thiones, respectively. 1*H*-Imidazole 3-oxides bearing the ester group at C(4) can be obtained from 2-(hydroxyimino)-3-oxobutanoate by condensation with methyliden-

amines. The presence of the ester group at C(4) enhances the ability of the *N*-oxide to undergo the rearrangement into the corresponding 1*H*-imidazol-2-one.

Starting with enantiomerically pure α-amino acid esters, the three-component reaction can be applied for the synthesis of optically active 1*H*-imidazole 3-oxides. An especially interesting case of a bis-imidazole was obtained from L-histidine. In contrast to the previously described symmetrical bis-imidazoles, this opens an access to novel unsymmetrical bis-imidazoles. New optically active imidazole and bis-imidazole derivatives are promising new ligands for asymmetric catalysis.

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Experimental Part

1. *General*. M.p.: *Melt-Temp. II* (*Aldrich*); uncorrected. Optical rotation: automatic digital polarimeter *Krüss P3002RS*. IR Spectra: *NEXUS FT-IR* spectrophotometer; in KBr; absorptions in cm^{-1}. ^1H- and ^{13}C-NMR Spectra: *Tesla BS567A* (80 and 20 MHz, resp.) or *Bruker AC 300* instrument (300 and 75.5 MHz, resp.); in $CDCl_3$ or CD_3OD; δ in ppm ($Me_4Si = 0$ ppm), coupling constants *J* in Hz. The multiplicity of the ^{13}C signals was deduced from DEPT spectra. MS: *Finnigan MAT-90* or *Finnigan SSQ-700* instruments. HR-MS: *Finnigan MAT-95*. Elemental analyses were performed in the Analytical Laboratory of the University of Zürich or in the Laboratory of the Polish Academy of Sciences (CBMiMM) in Łódź.

2. *Starting Materials*. All reagents and solvents are commercially available and used as received. α-(Hydroxyimino) ketones **3** were obtained according to known protocols: *butane-2,3-dione monooxime* (**3a**) [22a], *1-phenylpropane-1,2-dione 1-oxime* (**3b**) [22b], and *1-phenylpropane-1,2-dione 2-oxime* (**3c**) [22c] by nitrosation of the corresponding ketones by using isoamyl nitrate, and *1,2-diphenylethane-1,2-dione* monooxime (**3d**; benzil monooxime) [22d] from dibenzoyl and hydroxylamine hydrochloride. *2-(Hydroxyimino)-3-oxobutanoate* (**13**) was prepared from ethyl acetoacetate by treatment with $NaNO_2$ in glacial AcOH according to [22e]. 1,3,5-Trisubstituted hexahydro-1,3,5-triazines **6** were prepared according to known procedures: $R^2 = (Ph)(MeCO_2)CH$ [16], $R^2 = Me$ [23a], $R^2 = Bn$ [23b], $R^2 =$ cyclohexyl(cHex) [23c]. Methyl esters of glycine, (*S*)-valine, (*S*)-leucine, and (*S*)-tyrosine, **4a**, **4c**, **4d**, **4g**, resp. were obtained from the corresponding amino acids according to the general protocols and used immediately without further purification [24]. *(*R*)-Phenylglycine methyl ester* (**4e**), *(*S*)*- and *(*R*)-alanine methyl esters* ((*S*)-**4b** and (*R*)-**4b**, resp.), and *histidine methyl ester* (**4f**) are commercially available.

3. *Synthesis of Imidazole* N-*Oxides* **5**. *General Procedures. Method A*. A soln. of the corresponding α-(hydroxyimino) ketone **3** (10 mmol), amino acid methyl ester **4** (10 mmol), and HCHO (1.25 g, 15 mmol) in EtOH (30 ml) was heated under reflux for 3 h. Evaporation of the solvent under reduced pressure yielded an oil, which was washed twice with Et_2O (2×10 ml). The crude products **5** were purified by flash chromatography (FC; SiO_2; MeOH/AcOEt, 1:1), and the viscous oily substances were used in the next steps without further purification.

Method B. A soln. of **3** (10 mmol), **4** (10 mmol), and paraformaldehyde (0.83 g, 10 mmol) in glacial AcOH (10 ml) was stirred overnight at r.t. Then, gaseous HCl was bubbled through the soln. for 1 h at 0°, and Et_2O (typically *ca.* 200 ml) was added. The crude hydrochloride was separated, washed with Et_2O (3×30 ml), and dissolved in $CHCl_3$/MeOH (5:1, 30 ml). The resulting soln. was treated with excess solid $NaHCO_3$, stirred for *ca.* 30 min, and filtered. The solvent was removed *in vacuo* to give crude product **5**.

*Methyl (4,5-Dimethyl-3-oxido-1*H*-imidazol-1-yl)acetate* (**5a**). Yield: 1.20 g (65%, *Method A*), 1.62 g (88%, *Method B*). Pale yellow oil. IR (film): 3200–2800*s* (br.), 1748v*s* (C=O), 1632*m*, 1438*m*, 1400*m*, 1388*m*, 1335*m*, 1227v*s*, 1185*m*. ^1H-NMR ($CDCl_3$): 8.02 (*s*, H–C(2′)); 4.65 (*s*, CH_2); 3.79 (*s*, MeO); 2.17, 2.10 (2*s*, 2 Me). ^{13}C-NMR ($CDCl_3$): 166.9 (*s*, C=O); 126.7, 121.4 (2*s*, C(4′), C(5′)); 125.0 (*d*, C(2′)); 52.8 (*q*, MeO); 46.1 (*t*, CH_2); 8.4, 7.1 (2*q*, 2 Me). EI-HR-MS: 184.08464 (M^+, $C_8H_{12}N_2O_3^+$; calc. 184.08479).

*Methyl (5-Methyl-3-oxido-4-phenyl-1*H*-imidazol-1-yl)acetate* (**5b**). Yield after FC (SiO_2; AcOEt/MeOH 1:1): 1.75 g (71%, *Method A*), 2.21 g (90%, *Method B*). Pale yellow oil. IR (film): 3100–2750*s* (br.), 1741v*s* (C=O), 1679*m*, 1443*m*, 1389*m*, 1347*m*, 1231*s*, 699*m*. ^{1}H-NMR ($CDCl_3$): 8.09 (*s*, H–C(2′)); 7.75–7.23 (*m*, 5 arom. H); 4.64 (*s*, CH_2); 3.78 (*s*, MeO); 2.19 (*s*, Me). ^{13}C-NMR ($CDCl_3$): 167.1 (*s*, C=O); 130.5, 126.8, 123.2 (3*s*, arom. C_q, C(4′), C(5′)); 129.9, 128.5, 128.4, 125.0 (4*d*, 5 arom. C, C(2′)); 53.1 (*q*, MeO); 46.6 (*t*, CH_2); 9.2 (*q*, Me). EI-MS: 246 (26, M^+), 230 (100), 171 (42), 130 (21), 103 (38), 77 (26). Anal. calc. for $C_{13}H_{14}N_2O_3$ (246.27): C 63.40, H 5.73, N 11.38; found: C 62.92, H 5.69, N 11.12.

*Methyl (4-Methyl-3-oxido-5-phenyl-1*H*-imidazol-1-yl)acetate* (**5c**). Yield: 1.20 g (49%, *Method A*), 1.43 g (58%, *Method B*). Colorless solid. M.p. (dec.) 158–161° (CH_2Cl_2/Et_2O). IR (KBr): 3100–2850*s* (br.), 1747v*s* (C=O), 1437*m*, 1402*m*, 1381*s*, 1335*s*, 1221v*s*, 1181*m*, 1165*m*, 1153*s*, 763*s*, 706*m*. ^{1}H-NMR ($CDCl_3$): 8.08 (*s*, H–C(2′)); 7.60–7.16 (*m*, 5 arom. H); 4.56 (*s*, CH_2); 3.73 (*s*, MeO); 2.21 (*s*, Me). ^{13}C-NMR ($CDCl_3$): 167.2 (*s*, C=O); 129.9, 129.5, 129.0, 125.9 (4*d*, 5 arom. C, C(2′)); 128.2, 126.65, 126.58 (3*s*, arom. C_q, C(4′), C(5′)); 52.6 (*q*, MeO); 46.4 (*t*, CH_2); 7.4 (*q*, Me). EI-HR-MS: 246.10033 (M^+, $C_{13}H_{14}N_2O_3^+$; calc. 246.10044).

*Methyl (3-Oxido-4,5-diphenyl-1*H*-imidazol-1-yl)acetate* (**5d**). Yield: 1.69 g (55%, *Method A*), 2.19 g (71%, *Method B*). Pale yellow oil. IR (film): 3200–2800*s* (br.), 1751v*s* (C=O), 1444*m*, 1398*m*, 1348*m*, 1225v*s*, 764*s*, 700*s*, 657*m*. ^{1}H-NMR ($CDCl_3$): 8.33 (*s*, H–C(2′)); 7.68–7.09 (*m*, 10 arom. H); 4.58 (*s*, CH_2); 3.70 (*s*, MeO). ^{13}C-NMR ($CDCl_3$): 167.2 (*s*, C=O); 130.6, 129.7, 129.5, 129.1, 128.1, 127.9, 127.1 (7*d*, 10 arom. C, C(2′)); 130.5, 127.3, 126.7, 126.6 (4*s*, 2 arom. C_q, C(4′), C(5′)); 52.8 (*q*, MeO); 46.5 (*t*, CH_2). EI-HR-MS: 308.11566 (M^+, $C_{18}H_{16}N_2O_3^+$; calc. 308.11609).

*Methyl (*S*)-2-(4,5-Dimethyl-3-oxido-1*H*-imidazol-1-yl)propanoate* ((*S*)-**5e**). Yield after CC (SiO_2; acetone, then AcOEt/MeOH 1:1): 0.99 g (50%, *Method A*), 1.33 g (67%, *Method B*). Colorless crystals. M.p. 144–146° (CH_2Cl_2/Et_2O). $[\alpha]_D^{20} = +47.1$ (*c* = 0.20, CH_2Cl_2); +30.5 (*c* = 0.2, MeOH). IR (KBr): 3100–2900*s* (br.), 1743v*s* (C=O), 1636*w*, 1434*w*, 1381*w*, 1339*m*, 1265*w*, 1208*m*, 1195*m*, 1060*w*. ^{1}H-NMR ($CDCl_3$): 7.92 (*s*, H–C(2′)); 4.75 (*q*, *J* = 6.9, 1 H); 3.77 (*s*, MeO); 2.18, 2.13 (2*s*, 2 Me); 1.73 (*d*, *J* = 6.9, Me). ^{13}C-NMR ($CDCl_3$): 169.5 (*s*, C=O); 126.6, 120.9 (2*s*, C(4′), C(5′)); 122.6 (*d*, C(2′)); 52.8 (*q*, MeO); 52.7 (*d*, CHN); 17.2, 8.4, 7.0 (3*q*, 3 Me). EI-HR-MS: 198.10081 (M^+, $C_9H_{14}N_2O_3^+$; calc. 198.10044).

*Methyl (*R*)-2-(4,5-Dimethyl-3-oxido-1*H*-imidazol-1-yl)propanoate* ((*R*)-**5e**). Yield after CC (SiO_2; acetone, then AcOEt/MeOH 1:1): 1.43 g (72%, *Method B*). Colorless crystals. M.p. 142–145° (CH_2Cl_2/Et_2O). $[\alpha]_D^{20} = -48.5$ (*c* = 0.20, CH_2Cl_2).

*Methyl (*S*)-2-(4,5-Dimethyl-3-oxido-1*H*-imidazol-1-yl)-3-methylbutanoate* (**5f**). Yield after CC (SiO_2; acetone, then AcOEt/MeOH 1:1): 2.03 g (90%, *Method B*). Colorless oil. $[\alpha]_D^{20} = +31.3$ (*c* = 0.24, CH_2Cl_2). IR (film): 3350–2850v*s* (br.), 1743v*s* (C=O), 1633*w*, 1437*m*, 1380*m*, 1332*m*, 1307*m*, 1273*m*, 1196*m*, 1178*m*, 1012*w*. ^{1}H-NMR ($CDCl_3$): 8.11 (*s*, H–C(2′)); 4.22 (*d*, *J* = 9.6, 1 H); 3.37 (*s*, MeO); 2.61–2.27 (*m*, 1 H); 2.20, 2.17 (2*s*, 2 Me); 1.03, 0.86 (2*d*, *J* = 8.0, 2 Me). ^{13}C-NMR ($CDCl_3$): 168.8 (*s*, C=O); 126.4, 122.5 (2*s*, C(4′), C(5′)); 126.2 (*d*, C(2′)); 64.9 (*d*, CHN); 53.3 (*q*, MeO); 19.3, 19.0, 9.2, 7.4 (4*q*, 4 Me). EI-HR-MS: 226.13189 (M^+, $C_{11}H_{18}N_2O_3^+$; calc. 226.13174).

*Methyl (*S*)-2-(4,5-Dimethyl-3-oxido-1*H*-imidazol-1-yl)-4-methylpentanoate* (**5g**). Yield after two CC (SiO_2; AcOEt/MeOH 1:1): 1.06 g (44%, *Method B*). Pale orange oil. $[\alpha]_D^{20} = +10.6$ (*c* = 0.20, CH_2Cl_2). IR (film): 3250–2800v*s* (br.), 1747v*s* (C=O), 1632*s* (br.), 1436*s*, 1380*s*, 1335*s*, 1275*s*, 1243*s*, 1194*s*, 1131*m*, 1042*m*, 994*m*, 732*m*. ^{1}H-NMR ($CDCl_3$): 8.09 (*s*, H–C(2′)); 4.62–4.35 (*m*, 1 H); 3.38 (*s*, MeO); 2.12 (*s*, 2 Me); 2.00–1.19 (*m*, 3 H); 1.92 (*d*, *J* = 6.4, 2 Me). ^{13}C-NMR ($CDCl_3$): 169.2 (*s*, C=O); 127.0 (*d*, C(2′)); 126.2, 122.2 (2*s*, C(4′), C(5′)); 57.2 (*d*, CHN); 53.2 (*q*, MeO); 40.0 (*t*, CH_2); 24.5 (*d*, CH); 22.4, 21.3, 9.0, 7.0 (4*q*, 4 Me). EI-HR-MS: 240.14782 (M^+, $C_{12}H_{20}N_2O_3^+$; calc. 240.14739).

*Methyl (4,5-Dimethyl-3-oxido-1*H*-imidazol-1-yl)phenylacetate* (**5h**). Yield after CC (SiO_2; acetone, then AcOEt/MeOH 1:1): 0.57 g (22%, modified *Method A*; see *Table 1*), 2.11 g (81%, *Method B*). Pale yellow oil. IR (film): 3250–2900v*s* (br.), 1747v*s* (C=O), 1632*w*, 1455*m*, 1437*m*, 1402*m*, 1380*m*, 1336*m*, 1311*m*, 1226*m*, 1200*s*, 1006*w*, 714*s*. ^{1}H-NMR ($CDCl_3$): 7.74 (*s*, H–C(2′)); 7.51–7.17 (*m*, 5 arom. H); 5.79 (*s*, 1 H); 3.83 (*s*, MeO); 2.17, 2.14 (2*s*, 2 Me). ^{13}C-NMR ($CDCl_3$ + 2 drops of CD_3OD): 170.2 (*s*, C=O); 134.3 (*s*, arom. C_q); 129.3, 128.2 (2*d*, 5 arom. C, C(2′)); 125.1, 123.7 (2*s*, C(4′), C(5′)); 65.0 (*d*, CHN); 8.6, 6.6 (2*q*, 2 Me). EI-HR-MS: 260.11596 (M^+, $C_{14}H_{16}N_2O_3^+$; calc. 260.11609).

*Methyl (*S*)-2-(4,5-Dimethyl-3-oxido-1*H*-imidazol-1-yl)-3-(1*H*-imidazol-4-yl)propanoate* (**5i**). The oily substance (2.40 g) obtained after CC (SiO_2; acetone, then AcOEt/MeOH 1:1) was heated to reflux

in acetone. After cooling, solid impurities were filtered off to give 1.85 g (70%, *Method B*) of pure **5i** as a colorless, hygroscopic solid. $[\alpha]_D^{20} = -26.0$ ($c = 0.20$, CH_2Cl_2). IR (KBr): 3350–3600v*s* (br.), 1747v*s* (C=O), 1438*m*, 1409*m*, 1383*m*, 1348*m*, 1320*m*, 1266*m*, 1203*m*, 1181*m*. ^{1}H-NMR ($CDCl_3$): 8.73 (br. *s*, NH); 8.05 (*s*, H–C(2′)); 7.39 (*d*, $J = 1.6$, 1 H); 6.56 (*s*, 1 H); 5.22 (*q*, $J = 4.8$, 1 H); 3.81 (*s*, MeO); 3.42–3.24 (*m*, 2 H); 2.07, 2.02 (2*s*, 2 Me). ^{13}C-NMR ($CDCl_3$): 169.0 (*s*, C=O); 135.8, 125.53, 125.47 (3*d*, 3 CH(imidazole)); 131.7, 122.6, 116.5 (3*s*, 3 C_q(imidazole)); 57.9 (*d*, CH); 53.1 (*q*, MeO); 29.9 (*t*, CH_2); 8.5, 6.9 (2*q*, 2 Me). EI-HR-MS: 264.12182 (M^+, $C_{12}H_{16}N_4O_3^+$; calc. 264.12224).

*Methyl (*S*)-2-(4,5-Dimethyl-3-oxido-1*H*-imidazol-1-yl)-3-(4-hydroxyphenyl)propanoate* (**5j**). Yield after two CC (SiO_2; acetone, then AcOEt/MeOH 1:1): 2.17 g (63%, *Method A*), 2.35 g (81%, *Method B*). Colorless solid. M.p. 164–169° ($CHCl_3$/Et_2O). $[\alpha]_D^{20} = -99.5$ ($c = 0.20$, $CHCl_3$). IR (KBr): 3550–3300v*s*, 3200–2450v*s* (br.), 1744v*s* (C=O), 1613*m*, 1518*s*, 1448*m*, 1260*s*, 1174*m*. ^{1}H-NMR ($CDCl_3$): 8.09 (*s*, H–C(2′)); 6.72, 6.68 (2 br. *s*, 4 arom. H); 4.87–4.74 (*m*, 1 H); 3.78 (*s*, MeO); 3.53–2.98 (*m*, CH_2); 2.08, 1.79 (2*s*, 2 Me). ^{13}C-NMR ($CDCl_3$): 168.6 (*s*, C=O); 157.9, 125.8, 123.6, 122.1 (4*s*, 2 arom. C_q, C(4′), C(5′)); 129.5, 124.0, 116.2 (3*d*, 5 arom. C); 59.8 (*d*, CH); 53.1 (*q*, MeO); 38.4 (*t*, CH_2); 8.4, 6.9 (2*q*, 2 Me). EI-HR-MS: 290.12646 (M^+, $C_{15}H_{18}N_2O_4^+$; calc. 290.12666).

4. *Aminolysis of* N-*Oxides* **5**. To a sat. soln. of *N*-oxide **5** (3 mmol) in benzene (for **8b**–**8d**) or $CHCl_3$ (for **8a** and **8e**–**8g**) (*ca.* 1.0 ml), the corresponding amine (3.5 mmol, *i.e.*, 375 mg of $PhCH_2NH_2$, 200 mg of cyclopropylamine, 347 mg of cyclohexylamine, and 424 mg of (1-phenylethyl)amine, resp.) was added, and the resulting mixture was occasionally shaken. The mixture was left for 48 h at r.t. (usually, after 2 h a little precipitate was observed). The soln. was concentrated, the resulting solid was treated with Et_2O, triturated with a small portion of cold acetone, and left in the refrigerator for 30 min. The pure crystalline product was filtered and dried under reduced pressure for 2 h. The synthesis of amides **8b**, **8c**, **8e**, **8f**, and **8h**–**8i** was also performed without solvent in very good yields: to the *N*-oxide **5** (1 mmol), an excess of amine (2–2.5 mmol) was added, and the mixture left at r.t. for the required time (usually *ca.* 2–3 d) with occasional stirring. The resulting suspension was treated with Et_2O, washed with cold acetone, filtered, and purified by crystallization from the appropriate solvent.

N-*Benzyl-2-(4,5-dimethyl-3-oxido-1*H*-imidazol-1-yl)acetamide* (**8a**). Yield: 528 mg (68%), 2 d. Colorless crystals. M.p. 190–191° (CH_2Cl_2/acetone). IR (KBr): 3450–2700v*s* (br.), 1683v*s* (C=O), 1605*s*, 1453*m*, 1403*s*, 1378*m*, 1338*m*, 1275*m*, 1237*m*, 1193*m*, 1174*m*, 702*m*, 656*m*. ^{1}H-NMR (CD_3OD): 8.19 (*s*, H–C(2′)); 7.28 (*s*, 5 arom. H); 4.72, 4.38 (2*s*, 2 CH_2); 2.12, 2.10 (2*s*, 2 Me). ^{13}C-NMR (CD_3OD): 168.0 (*s*, C=O); 139.8, 128.4, 127.2 (3*s*, arom. C_q, C(4′), C(5′)); 129.8, 128.9, 128.6, 124.8 (4*d*, 5 arom. C, C(2′)); 48.8, 44.4 (2*t*, 2 CH_2); 8.3, 7.0 (2*q*, 2 Me). EI-MS: 259 (3, M^+), 241 (100, $[M - H_2O]^+$), 150 (44), 109 (28), 91 (88). Anal. calc. for $C_{14}H_{17}N_3O_2$ (259.31): C 64.85, H 6.61, N 16.20; found: C 64.69, H 6.59, N 16.07.

N-*Benzyl-2-(5-methyl-3-oxido-4-phenyl-1*H*-imidazol-1-yl)acetamide* (**8b**). Yield: 570 mg (59%), 2 d. Colorless crystals. M.p. 205–206° (MeOH/H_2O). IR (KBr): 3450–2750v*s* (br.), 1689v*s* (C=O), 1585*m*, 1497*m*, 1436*m*, 1401*m*, 1346*m*, 1263*m*, 1214*m*, 1016*m*, 764*m*, 738*m*, 698*s*, 608*m*. ^{1}H-NMR (CD_3OD): 8.03 (*s*, H–C(2′)); 7.57–7.21 (*m*, 5 arom. H); 7.28 (*s*, 5 arom. H); 4.58, 4.39 (2*s*, 2 CH_2); 2.21 (*s*, Me). ^{13}C-NMR (CD_3OD): 166.2 (*s*, C=O); 138.3, 130.5, 127.0, 124.8 (4*s*, 2 arom. C_q, C(4′), C(5′)); 130.4, 129.4, 129.2, 129.0, 128.4, 128.1, 128.0 (7*d*, 10 arom. C, C(2′)); 48.8, 44.2 (2*t*, 2 CH_2); 9.6 (*q*, Me). EI-MS: 321 (2, M^+), 303 (100, $[M - H_2O]^+$), 212 (36), 158 (13), 109 (27), 91 (54). Anal. calc. for $C_{19}H_{19}N_3O_2$ (321.38): C 71.01, H 5.96, N 13.07; found: C 71.07, H 5.80, N 13.03.

N-*Benzyl-2-(4-methyl-3-oxido-5-phenyl-1*H*-imidazol-1-yl)acetamide* (**8c**). Yield: 480 mg (51%), 2 d. Colorless crystals. M.p. 220–222° (MeOH/H_2O). IR (KBr): 3450–2600v*s* (br.), 1663v*s* (C=O), 1608*m*, 1454*m*, 1395*m*, 1369*m*, 1336*m*, 1284*m*, 1227*m*, 1165*m*, 757*m*, 702*m*, 656*m*. ^{1}H-NMR (CD_3OD): 8.10 (*s*, H–C(2′)); 7.52–7.17 (*m*, 10 arom. H); 4.51, 4.35 (2*s*, 2 CH_2); 2.16 (*s*, Me). ^{13}C-NMR (CD_3OD): 166.2 (*s*, C=O); 138.0, 135.7, 127.1, 126.5 (4*s*, 2 arom. C_q, C(4′), C(5′)); 130.5, 130.1, 129.4, 128.9, 128.1, 128.0, 127.8 (7*d*, 10 arom. C, C(2′)); 48.5, 43.8 (2*t*, 2 CH_2); 7.6 (*q*, Me). EI-MS: 321 (2, M^+), 303 (61, $[M - H_2O]^+$), 212 (28), 177 (33), 144 (20), 106 (18), 91 (100). Anal. calc. for $C_{19}H_{19}N_3O_2$ (321.38): C 71.01, H 5.96, N 13.07; found: C 69.90, H 5.87, N 12.99.

N-*Benzyl-2-(3-oxido-4,5-diphenyl-1*H*-imidazol-1-yl)acetamide* (**8d**). Yield: 970 mg (84%), 2 d. Colorless crystals. M.p. 112–116° (MeOH/H_2O). IR (KBr): 3450–2800v*s* (br.), 1675v*s* (C=O), 1603*m*, 1590*m*, 1577*m*, 1452*m*, 1404*m*, 1351*m*, 1272*m*, 1203*m*, 757*s*, 697v*s*, 657*m*. ^{1}H-NMR (CD_3OD): 8.43 (*s*, H–C(2′)); 7.60–6.98 (*m*, 15 arom. H); 4.67, 4.29 (2*s*, 2 CH_2). ^{13}C-NMR (CD_3OD): 165.8 (*s*, C=O);

138.3, 128.1, 128.0, 126.6, 126.5 (5*s*, 3 arom. C_q, C(4′), C(5′)); 130.7, 129.6, 129.5, 128.8, 128.3, 128.2, 127.9, 127.7, 127.0, 126.9 (10*d*, 15 arom. C, C(2′)); 48.0, 43.4 (2*t*, 2 CH_2). Anal. calc. for $C_{24}H_{21}N_3O_2 \cdot 1.25\ H_2O$ (405.97): C 71.01, H 5.83, N 10.35; found: C 70.82, H 5.67, N 10.11.

N-*Cyclopropyl-2-(4,5-dimethyl-3-oxido-1*H*-imidazol-1-yl)acetamide* (**8e**). Yield: 511 mg (81%), 24 h. Colorless crystals. M.p. 192–194° (acetone). IR (KBr): 3450–2750v*s* (br.), 1679v*s* (C=O), 1635*m*, 1589*s*, 1407*s*, 1357*m*, 1339*s*, 1284*s*, 1179*m*, 1151*m*, 1091*m*, 991*m*, 897*m*, 811*m*, 646*s*, 600*m*. ^{1}H-NMR (CD_3OD): 7.94 (*s*, H–C(2′)); 4.47 (*s*, CH_2); 2.77–2.63 (*m*, H–C(cPr)); 2.15, 2.14 (2*s*, 2 Me); 0.79–0.75, 0.56–0.52 (2*m*, 2 CH_2(cPr)). ^{13}C-NMR (CD_3OD): 166.9 (*s*, C=O); 126.0, 122.5 (2*s*, C(4′), C(5′)); 125.5 (*d*, C(2′)); 47.5 (*t*, CH_2); 22.2 (*d*, CH(cPr)); 7.9, 6.5 (2*q*, 2 Me); 5.5 (*t*, 2 CH_2(cPr)). EI-MS: 209 (81, M^+), 192 (56), 164 (62), 109 (100), 68 (62). Anal. calc. for $C_{10}H_{15}N_3O_2 \cdot 2\ H_2O$ (245.29): C 48.97, H 7.81, N 17.13; found: C 48.75, H 7.70, N 17.03.

N-*Cyclopropyl-2-(3-oxido-4,5-diphenyl-1*H*-imidazol-1-yl)acetamide* (**8f**). Yield: 610 mg (61%), 24 h. Colorless crystals. M.p. 176–179° (acetone). IR (KBr): 3450–2950v*s* (br.), 1678v*s* (br., C=O), 1557*m*, 1445*m*, 1393*m*, 1357*m*, 1277*m*, 1201*m*, 762*m*, 698*s*, 655*m*. ^{1}H-NMR (CD_3OD): 8.21 (*s*, H–C(2′)); 7.48–7.07 (*m*, 10 arom. H); 4.45 (*s*, CH_2); 2.69–2.59 (*m*, H–C(cPr)); 0.78–0.71, 0.54–0.44 (2*m*, 2 CH_2(cPr)). ^{13}C-NMR (CD_3OD): 166 (*s*, C=O); 134.1, 130.2, 126.1, 125.7 (4*s*, 2 arom. C_q, C(4′), C(5′)); 130.5, 129.6, 129.5, 128.8, 128.4, 127.9, 126.5 (7*d*, 10 arom. C, C(2′)); 48.7 (*t*, CH_2); 22.2 (*d*, CH(cPr)); 5.6 (*t*, 2 CH_2(cPr)). EI-MS: 333 (36, M^+), 315 (100, $[M - H_2O]^+$), 286 (75), 249 (58), 178 (34), 104 (45). Anal. calc. for $C_{20}H_{19}N_3O_2 \cdot H_2O$ (351.41): C 68.36, H 6.02, N 11.96; found: C 68.42, H 5.89, N 11.94.

N-*Cyclohexyl-2-(3-oxido-4,5-diphenyl-1*H*-imidazol-1-yl)acetamide* (**8g**). Yield: 495 mg (44%), 2 d. Colorless crystals. M.p. 192–193° (acetone). IR (KBr): 3500–2600v*s* (br.), 1679*s*, 1635v*s* (C=O), 1507*m*, 1487*m*, 1447*m*, 1382*s*, 1352*m*, 1304*m*, 1204*m*, 1185*m*, 769*m*, 740*m*, 698*s*, 666*m*. ^{1}H-NMR (CD_3OD): 8.36 (*s*, H–C(2′)); 7.45–7.26 (*m*, 10 arom. H); 4.42 (*s*, CH_2); 2.95–2.77 (*m*, H–C(cHex)); 2.02–0.95 (*m*, 5 CH_2(cHex)). ^{13}C-NMR (CD_3OD): 170.9 (*s*, C=O); 130.4, 129.6, 129.0, 128.8, 128.3, 128.0, 125.7 (7*d*, 10 arom. C, C(2′)); 128.9, 128.4, 126.2, 125.8 (4*s*, 2 arom. C_q, C(4′), C(5′)); 50.2 (*d*, CH(cHex)); 49.7 (*t*, CH_2); 30.6, 24.4, 24.0 (3*t*, 5 CH_2(cHex)). EI-HR-MS: 376.2021 (M^+, $C_{23}H_{25}N_3O_2^+$; calc. 376.2025).

*2-(4,5-Dimethyl-3-oxido-1*H*-imidazol-1-yl)-*N*-[(*R*)-1-phenylethyl]acetamide* (**8h**). Yield: 745 mg (91%), 3 d. Colorless crystals. M.p. (dec.) 205–209° (MeOH/H_2O). $[\alpha]_D^{20} = +137$ ($c = 0.20$, MeOH). IR (KBr): 3300–2700v*s* (br.), 1671v*s* (C=O), 1601*m*, 1565*m*, 1581*m*, 1450*m*, 1408*m*, 1381*m*, 1340*m*, 1281*m*, 1182*w*, 758*w*, 701*m*. ^{1}H-NMR ($CDCl_3$): 7.79 (*s*, H–C(2′)); 7.27 (br. *s*, 5 arom. H); 5.04 (*q*, $J = 6.9$, 1 H); 4.49 (*s*, 2 H); 2.13, 2.08 (2*s*, 2 Me); 1.49 (*d*, $J = 6.9$, Me). ^{13}C-NMR ($CDCl_3$ + 2 drops of CD_3OD): 164.8 (*s*, C=O); 142.9 (*s*, arom. C_q); 128.7, 127.5, 126.2, 125.6 (4*d*, 5 arom. C, C(2′)); 126.5, 122.8 (2*s*, C(4′), C(5′)); 48.1 (*d*, Ph*C*H); 49.2 (*t*, CH_2); 21.4, 8.4, 7.0 (3*q*, 3 Me). EI-HR-MS: 273.14751 (M^+, $C_{15}H_{19}N_3O_2^+$; calc. 273.14773).

Suitable crystals for a crystal-structure determination were obtained from acetone by slow evaporation of the solvent.

*2-(5-Methyl-3-oxido-4-phenyl-1*H*-imidazol-1-yl)-*N*-[(*R*)-1-phenylethyl]acetamide* (**8i**). Yield: 775 mg (77%). Colorless crystals. M.p. (dec.) 226–231° (MeOH/H_2O). $[\alpha]_D^{20} = +139.6$ ($c = 0.25$, MeOH). IR (KBr): 3250–2650v*s* (br.), 1686v*s* (C=O), 1581*m*, 1402*m*, 1271*m*, 1219*m*, 774*m*, 758*m*, 702*s*. ^{1}H-NMR (CD_3OD): 8.07 (*s*, H–C(2′)); 7.66–7.17 (*m*, 5 arom. H); 7.29 (*s*, 5 arom. H); 5.07 (*q*, $J = 7.2$, 1 H); 4.62 (*s*, CH_2); 2.20 (*s*, Me); 1.52 (*d*, $J = 7.2$, Me). ^{13}C-NMR (CD_3OD): 164.6 (*s*, C=O); 143.0, 129.9, 127.1, 124.6 (4*s*, 2 arom. C_q, C(4′), C(5′)); 129.8, 128.9, 128.8, 128.7, 127.4, 126.1, 126.0 (7*d*, 10 arom. C, C(2′)); 48.2 (*t*, CH_2); 30.8 (*d*, CH); 21.6, 9.0 (2*q*, 2 Me). EI-HR-MS: 335.1629 (M^+, $C_{20}H_{21}N_3O_2^+$; calc. 335.1634).

N-*Benzyl-2-(4,5-dimethyl-3-oxido-1*H*-imidazol-1-yl)propanamide* (**8j**). Yield: 696 mg (85%). Colorless solid. M.p. 127–132°. IR (KBr): 3300–2700v*s* (br.), 1671v*s* (C=O), 1615*m*, 1454*m*, 1411*m*, 1389*m*, 1335*s*, 1225*m*, 1195*m*, 703*m*. ^{1}H-NMR (CD_3OD): 8.09 (*s*, H–C(2′)); 7.30 (*s*, 5 arom. H); 4.76 (*q*, $J = 6.9$, 1 H); 4.38 (*s*, CH_2); 2.14, 2.11 (2*s*, 2 Me); 1.72 (*d*, $J = 6.9$, Me). ^{13}C-NMR (CD_3OD): 171.0 (*s*, C=O); 139.5 (*s*, arom. C_q); 129.7, 128.8, 128.5, 126.0 (4*d*, 5 arom. C, C(2′)); 127.1, 123.8 (2*s*, C(4′), C(5′)); 56.2 (*d*, CHN); 44.5 (*t*, CH_2); 18.4, 8.6, 7.0 (3*q*, 3 Me). EI-HR-MS: 273.14763 (M^+, $C_{15}H_{19}N_3O_2^+$; calc. 273.14773).

5. *Synthesis of 1*H-*Imidazole-2-thiones* **10** (ester derivatives). To a magnetically stirred soln. of the corresponding 1*H*-imidazole *N*-oxide (**5b**, **5c**, and **5e**; 1.0 mmol) in CH_2Cl_2 (1.0 ml), a soln. of 2,2,4,4-tetramethylcyclobutane-1,3-dithione (**9**; 0.6 mmol) in CH_2Cl_2 (1.0 ml) was added dropwise at 0°. The addition was complete after *ca.* 10 min, and stirring was continued for 1 h while a little precipitate was formed. Then, the solvent was removed under reduced pressure, the resulting solid was washed with hexane (to remove remaining **9** and the by-product 2,2,4,4-tetramethylcyclobutane-1,3-dione), and filtered (in the case of **10c**, the by-products were sublimed off at 50°/60 mm Hg). The crude product **10** was recrystallized from the appropriate solvent to give anal. pure samples.

*Methyl (2,3-Dihydro-5-methyl-4-phenyl-2-thioxo-1*H-*imidazol-1-yl)acetate* (**10a**). Yield: 226 mg (86%). Colorless solid. M.p. 205–207° (EtOH). IR (KBr): 3450–2750v*s* (br.), 1739v*s* (C=O), 1497*s*, 1438*m*, 1410*s*, 1364*m*, 1224*s* (br.), 1182*m*, 768*m*, 700*m*. ^{1}H-NMR ($CDCl_3$): 11.22 (br. *s*, NH); 7.48–7.26 (*m*, 5 arom. H); 4.99 (*s*, CH_2); 3.80 (*s*, MeO); 2.25 (*s*, Me). ^{13}C-NMR ($CDCl_3$): 167.8, 161.5 (2*s*, C=O, C=S); 129.0, 128.2, 127.2 (3*d*, 5 arom. C); 128.3, 123.5, 122.3 (3*s*, arom. C_q, C(4′), C(5′)); 52.8 (*q*, MeO); 45.6 (*t*, CH_2); 10.1 (*q*, Me). EI-MS: 262 (100, M^+), 230 (7, $[M-S]^+$), 204 (37), 203 (30), 144 (9), 115 (13), 103 (9). Anal. calc. for $C_{13}H_{14}N_2O_2S$ (262.33): C 59.52, H 5.38, N 10.68; found: C 59.32, H 5.20, N 10.49.

*Methyl (2,3-Dihydro-4-methyl-5-phenyl-2-thioxo-1*H-*imidazol-1-yl)acetate* (**10b**). Yield: 199 mg (76%). Colorless solid. M.p. 132–134° (MeOH). IR (KBr): 3200–2750v*s* (br.), 1742v*s* (C=O), 1601*w*, 1508*s*, 1441*m*, 1417*s*, 1375*s*, 1290*w*, 1227v*s* (br.), 1005*w*, 955*w*, 765*m*, 742*m*, 702*s*. ^{1}H-NMR ($CDCl_3$): 12.15 (br. *s*, NH); 7.64–7.15 (*m*, 5 arom. H); 4.69 (*s*, CH_2); 3.72 (*s*, MeO); 2.17 (*s*, Me). ^{13}C-NMR ($CDCl_3$): 168.5, 161.1 (2*s*, C=O, C=S); 130.5, 129.5, 129.4 (3*d*, 5 arom. C); 128.4, 127.7, 122.5 (3*s*, arom. C_q, C(4′), C(5′)); 52.6 (*q*, MeO); 46.4 (*t*, CH_2); 9.4 (*q*, Me). EI-MS: 262 (100, M^+), 230 (20, $[M-S]^+$), 203 (38), 144 (9), 115 (18). Anal. calc. for $C_{13}H_{14}N_2O_2S$ (262.33): C 59.52, H 5.38, N 10.68; found: C 59.49, H 5.30, N 10.74.

*Methyl (*S*)-2-(2,3-Dihydro-4,5-dimethyl-2-thioxo-1*H-*imidazol-1-yl)propanoate* (**10c**). Yield: 180 mg (84%). Colorless solid. M.p. 146–147° (CH_2Cl_2/Et_2O). $[\alpha]_D^{20} = +38.2$ ($c = 0.20$, CH_2Cl_2). IR (KBr): 3250–2800v*s* (br.), 1740v*s* (C=O), 1660*m*, 1497*s*, 1436*s*, 1408*s*, 1331*m*, 1314*s*, 1240*s*, 1110*s*, 1069*m*, 959*m*. ^{1}H-NMR ($CDCl_3$): 11.50 (br. *s*, NH); 5.90 (*q*, $J = 7.3$, 1 H); 3.76 (*s*, MeO); 2.08, 2.02 (2*s*, 2 Me); 1.65 (*d*, $J = 7.3$, 3 H). ^{13}C-NMR ($CDCl_3$): 170.8, 158.9 (2*s*, C=O, C=S); 120.9, 120.8 (2*s*, C(4′), C(5′)); 53.1 (*q*, MeO); 52.6 (*d*, CH); 15.8, 9.3, 8.8 (3*q*, 3 Me). EI-HR-MS: 217.07758 (M^+, $C_9H_{14}N_2O_2S^+$; calc. 214.07760).

6. *Synthesis of 1*H-*Imidazol-2-thiones* **11** (amide derivatives). To a magnetically stirred MeOH soln. of the corresponding *N*-oxide **8** (1.0 mmol), a soln. of **9** (0.6 mmol) in $CHCl_3$ (*ca.* 1.0 ml) was added dropwise. After 1 h, the solvents were removed, and the resulting solid was washed with Et_2O and recrystallized.

N-*Benzyl-2-(2,3-dihydro-4,5-dimethyl-2-thioxo-1*H-*imidazol-1-yl)acetamide* (**11a**). Yield: 264 mg (96%). Colorless solid. M.p. 229–232° (MeOH). IR (KBr): 3450–2750v*s* (br.), 1662v*s* (C=O), 1570*m*, 1497*m*, 1480*m*, 1453*m*, 1429*m*, 1411*m*, 1249*w*, 1221*w*, 1188*w*, 737*w*, 698*m*. ^{1}H-NMR (CD_3OD): 7.36 (br. *s*, 5 arom. H); 4.81, 4.43 (2*s*, 2 CH_2); 2.09, 2.07 (2*s*, 2 Me). ^{13}C-NMR (CD_3OD): 169.7, 162.0 (2*s*, C=O, C=S); 141.1, 124.3, 121.3 (3*s*, arom. C_q, C(4′), C(5′)); 130.5, 129.5, 129.1 (3*d*, 5 arom. C); 48.6, 44.7 (2*t*, 2 CH_2); 10.2, 10.1 (2*q*, 2 Me). EI-HR-MS: 275.1092 (M^+, $C_{14}H_{17}N_3OS^+$; calc. 275.1092). Anal. calc. for $C_{14}H_{17}N_3OS$ (275.38): C 61.06, H 6.22, N 15.26; found: C 60.67, H 6.13, N 15.16.

N-*Benzyl-2-(2,3-dihydro-5-methyl-4-phenyl-2-thioxo-1*H-*imidazol-1-yl)acetamide* (**11b**). Yield: 192 mg (57%). Colorless solid. M.p. 248–250° (MeOH). IR (KBr): 3450–2750v*s* (br.), 1652v*s* (C=O), 1602*w*, 1541*m*, 1496*s*, 1454*m*, 1410*m*, 1260*w*, 1216*w*, 1182*w*, 766*m*, 740*m*, 698*s*. ^{1}H-NMR (CD_3OD): 7.60, 7.47 (2 br. *s*, 10 arom. H); 5.02, 4.50 (2*s*, 2 CH_2); 2.39 (*s*, Me). ^{13}C-NMR (CD_3OD): 168.7, 159.6 (2*s*, C=O, C=S); 138.7, 130.9, 128.5, 125.2 (4*s*, 2 arom. C_q, C(4′), C(5′)); 130.8, 130.6, 130.2, 129.3, 129.1, 128.7 (6*d*, 10 arom. C); 49.3, 44.2 (2*t*, 2 CH_2); 11.6 (*q*, Me). EI-MS: 337 (76, M^+), 304 (100, $[M-SH]^+$), 230 (12), 204 (25), 191 (32), 190 (25), 91 (18, $C_7H_7^+$). Anal. calc. for $C_{19}H_{19}N_3OS$ (337.45): C 67.63, H 5.67, N 12.45; found: C 67.52, H 5.72, N 12.17.

N-*Benzyl-2-(2,3-dihydro-4,5-diphenyl-2-thioxo-1*H-*imidazol-1-yl)acetamide* (**11c**). Yield: 240 mg (60%). Colorless solid. M.p. 260–261° (MeOH). IR (KBr): 3450–2750v*s* (br.), 1694v*s* (C=O), 1529*m*, 1509*m*, 1493*s*, 1446*w*, 1422*m*, 1395*m*, 1242*m*, 1227*m*, 1203*m*, 770*m*, 756*m*, 700*s*. ^{1}H-NMR

(CD_3OD): 7.71–7.33 (*m*, 5 arom. H); 7.46 (br. *s*, 10 arom. H); 4.75, 4.44 (2*s*, 2 CH_2). ^{13}C-NMR (CD_3OD): 166.0, 162.1 (2*s*, C=O, C=S); 138.7, 128.4, 127.9, 126.9, 123.9 (5*s*, 3 arom. C_q, C(4′), C(5′)); 130.6, 129.2, 128.8, 128.2, 128.0, 127.3, 126.8, 126.5, 126.0 (9*d*, 15 arom. C); 46.4, 41.7 (2*t*, 2 CH_2). EI-HR-MS: 399.1396 (M^+, $C_{24}H_{21}N_3OS^+$; calc. 399.1405). Anal. calc. for $C_{24}H_{21}N_3OS$ (399.52): C 72.15, H 5.30, N 10.52; found: C 71.90, H 5.29, N 10.66.

7. *Synthesis of Methyl (*S*)-2-(4,5-Dimethyl-1*H*-imidazol-1-yl)-3-(1*H*-imidazol-4-yl)propanoate* (**12**): To a soln. of **5i** (1.0 mmol) in EtOH (2 ml), a suspension of freshly prepared *Raney*-Ni in EtOH was added in small portions, and the progress of the reaction was followed by TLC (MeOH/AcOEt 1:3). After the starting *N*-oxide was completely reduced, the mixture was filtered through a silica-gel plug (*ca.* 2 cm, EtOH), and the filtrate was concentrated and dried under reduced pressure. The highly pure product obtained was analyzed without further purification. Yield: 159 mg (64%). Colorless solid. M.p. 51–53°. $[\alpha]_D^{20} = -13.9$ ($c = 0.20$, CH_2Cl_2). IR (KBr): 3250–2500v*s* (br.), 1747v*s* (C=O), 1496*m*, 1440*m*, 1271*m*, 1235*m*, 1205*s*, 1163*m*, 733*m*, 627*m*. ^{1}H-NMR ($CDCl_3$): 7.48, 7.45, 6.53 (3*s*, 3 arom. H); 5.02 (*dd*, $J = 9.6$, 5.6, 1 H); 3.73 (*s*, MeO); 3.65–3.04 (*m*, 2 H); 2.07, 1.99 (2*s*, 2 Me). ^{13}C-NMR ($CDCl_3$): 171.5 (*s*, C=O); 136.6, 135.6, 124.3 (3*d*, 3 CH(imidazole)); 134.5, 133.3, 117.5 (3*s*, 3 C_q(imidazole)); 62.4 (*d*, CH); 53.4 (*q*, MeO); 31.3 (*t*, CH_2); 12.4, 8.5 (2*q*, 2 Me). EI-HR-MS: 248.12733 (M^+, $C_{12}H_{16}N_4O_2^+$; calc. 248.12725).

8. *Synthesis of Ethyl 1,5-Dimethyl-3-oxido-1*H*-imidazole-4-carboxylate* (**14a**). To the soln. of **13** (1.0 g, 6.3 mmol) in Et_2O (15 ml) cooled in an ice-bath, a soln. of hexahydro-1,3,5-triazine **6a** (0.35 g, 8.0 mmol) in Et_2O (10 ml) was added dropwise at 0°. After 30 min, the ice-bath was removed, and the mixture was stirred magnetically overnight. The colorless precipitate was filtered and recrystallized. Yield: 0.80 g (69%). Colorless needles. M.p. 76–78° (CH_2Cl_2/Et_2O). IR (KBr): 3150–2900v*s* (br.), 1735–1690v*s* (br., C=O), 1374*m*, 1313*m*, 1279*m*, 1237*m*, 1165*m*, 1070*m*, 1039*m*. ^{1}H-NMR ($CDCl_3$): 8.45 (*s*, H–C(2)); 4.37 (*q*, $J = 7.1$, CH_2O); 3.66 (*s*, MeN); 2.46 (*s*, Me); 1.38 (*t*, $J = 7.1$, *Me*CH_2O). ^{13}C-NMR ($CDCl_3$): 158.7 (*s*, C=O); 132.4, 120.9 (C(4), C(5)); 128.0 (*d*, C(2)); 60.6 (*t*, CH_2O); 32.4, 14.0, 9.8 (3*q*, 3 Me). EI-HR-MS: 184.0839 (M^+, $C_8H_{12}N_2O_3^+$; calc. 184.0848).

9. *Synthesis of Ethyl 2,3-Dihydro-1,5-dimethyl-2-oxo-1*H*-imidazole-4-carboxylate* (**15a**). A soln. of **14a** (0.15 g, 0.9 mmol) in benzene (3 ml) was heated at 80° for 2 h. Then, the solvent was removed under reduced pressure, and the resulting solid was recrystallized. Yield: 0.13 g (87%). Colorless crystals. M.p. 193–196° (CH_2Cl_2/Et_2O). IR (KBr): 3200–2900v*s* (br.), 1690v*s* (br., C=O), 1455*m*, 1368*m*, 1319*s*, 1213*m*, 1186*m*, 1163*m*, 1076*m*. ^{1}H-NMR ($CDCl_3$): 9.35 (br. *s*, NH); 4.29 (*q*, $J = 6.7$, CH_2O); 3.22 (*s*, MeN); 2.39 (*s*, Me); 1.35 (*t*, $J = 6.7$, *Me*CH_2O). ^{13}C-NMR ($CDCl_3$): 160.3, 153.0 (2*s*, 2 C=O); 130.7, 109.2 (C(4), C(5)); 60.4 (*t*, CH_2O); 27.1, 14.2, 10.0 (3*q*, 3 Me). EI-HR-MS: 184.08444 (M^+, $C_8H_{12}N_2O_3^+$; calc. 184.08479).

10. *Synthesis of Ethyl 1,5-Disubstituted 2,3-Dihydro-3-oxo-1*H*-imidazole-4-carboxylates* **15b** and **15c**. To the soln. of **13** (1.6 g, 10 mmol) in Et_2O (25 ml), a cooled mixture of the corresponding hexahydro-1,3,5-triazine (15 mmol; 1.8 g of **6b** or 1.7 g of **6c**) in Et_2O (10 ml) was added dropwise at 0°. After 30 min, the ice-bath was removed, and the mixture stirred magnetically for the required time (TLC monitoring). The resulting oil was separated and washed with Et_2O (3 × 15 ml). The crude mixture contained the corresponding *N*-oxide **14** and **15** in a ratio of *ca.* 4:1 (^{1}H-NMR). Crystallization from the appropriate solvent gave pure 1*H*-imidazol-2-ones **15**. ^{1}H-NMR ($CDCl_3$) of **14b** and **14c** (from the mixtures): Data of **14b**: 7.99 (*s*, H–C(2)); 7.46–7.06 (*m*, 5 arom. H); 5.08 (*s*, CH_2); 4.33 (*q*, $J = 7.1$, CH_2O); 2.26 (*s*, Me); 1.32 (*t*, $J = 7.1$, *Me*CH_2O). Data of **14c**: 7.92 (*s*, H–C(2)); 4.42 (*q*, $J = 7.2$, CH_2O); 4.07–3.62 (*m*, 1 H, cHex); 2.49 (*s*, Me); 2.22–1.20 (3*m*, cHex); 1.40 (*t*, $J = 7.1$, *Me*CH_2O).

*Ethyl 1-Benzyl-2,3-dihydro-5-methyl-2-oxo-1*H*-imidazole-4-carboxylate* (**15b**). 48 h. Yield: 1.95 g (75%). Colorless crystals. M.p. 194–198° (CH_2Cl_2/Et_2O). IR (KBr): 3250–2900v*s* (br.), 1690v*s* (br., C=O), 1626*w*, 1455*m*, 1409*m*, 1363*m*, 1325*m*, 1180*m*, 1088*m*, 1075*m*, 745*m*, 733*m*. ^{1}H-NMR ($CDCl_3$): 9.70 (br. *s*, NH); 7.37–7.21 (*m*, 5 arom. H); 4.91 (*s*, CH_2); 4.28 (*q*, $J = 7.1$, CH_2O); 2.29 (*s*, Me); 1.32 (*t*, $J = 7.1$, *Me*CH_2O). ^{13}C-NMR ($CDCl_3$): 160.0, 152.9 (2*s*, 2 C=O); 136.3, 130.6, 109.6 (3*s*, arom. C_q, C(4), C(5)); 128.8, 127.7, 127.0 (3*d*, 5 arom. C); 60.5, 44.4 (2*t*, 2 CH_2); 14.2, 10.2 (2*q*, 2 Me). EI-HR-MS: 260.1166 (M^+, $C_{14}H_{16}N_2O_3^+$; calc. 260.1161).

*Ethyl 1-Cyclohexyl-2,3-dihydro-5-methyl-2-oxo-1*H*-imidazole-4-carboxylate* (**15c**). 72 h. Yield: 1.73 g (69%). Colorless crystals. M.p. 195–198° (CH_2Cl_2/Et_2O). IR (KBr): 2950–2850*s* (br.), 1686v*s*

(br., C=O), 1627*m*, 1452*m*, 1370*w*, 1314*m*, 1188*m*, 1077*m*. ^{1}H-NMR ($CDCl_3$): 9.45 (br. *s*, NH); 4.28 (*q*, $J = 7.1$, CH_2O); 3.88–3.80 (*m*, 1 H, cHex); 2.52 (*s*, Me); 2.27–2.17, 1.89–1.68, 1.39–1.20 (3*m*, 10 H, cHex); 1.36 (*t*, $J = 7.1$, *Me*CH_2O). ^{13}C-NMR ($CDCl_3$): 160.1, 152.5 (2*s*, 2 C=O); 130.7, 109.3 (C(4), C(5)); 60.4 (*t*, CH_2O); 54.3 (*d*, CH(cHex)); 30.3, 26.1, 25.1 (3*t*, 5 CH_2(cHex)); 14.3, 10.5 (2*q*, 2 Me). EI-MS: 252 (20, M^+), 170 (100, $[M - \text{cHex} + 1]^+$), 142 (30), 125 (19), 124 (51). Anal. calc. for $C_{13}H_{20}N_2O_3$ (252.32): C 61.88, H 7.99, N 11.10; found: C 61.92, H 8.00, N 11.29.

11. *Synthesis of* N-*Cyclopropyl-1,5-dimethyl-3-oxido-1*H-*imidazole-4-carboxamide* (**16**). A mixture of **14a** (1.52 g, 8.3 mmol) and cyclopropylamine (1.3 g, 23 mmol) was stirred at r.t. for 3 d. The crude mixture was diluted with Et_2O (50 ml) and filtered to give a colorless solid containing mainly the target molecule **16** contaminated with small amounts of **15a**. Pure amide **16** was obtained after CC (SiO_2; MeOH/AcOEt 8:1). Yield: 744 mg (46%). Colorless solid. M.p. 204–206° (MeOH). IR (KBr): 3150–2900*s* (br.), 1656v*s*, 1604*s*, 1557*m*, 1448*m*, 1411*m*, 1290*m*, 1037*m*, 616*m*, 599*m*. ^{1}H-NMR ($CDCl_3$): 10.58 (br. *s*, NH); 7.76 (*s*, H–C(2)); 3.58 (*s*, Me); 3.08–2.66 (*m*, 1 H, cPr); 2.61 (*s*, Me); 0.88–0.56 (*m*, 4 H, cPr). ^{13}C-NMR ($CDCl_3$): 162.9 (*s*, C=O); 133.8, 122.7 (C(4), C(5)); 128.8 (*d*, C(2)); 33.5 (*d*, CH(cPr); 23.0, 10.6 (2*q*, 2 Me); 7.7 (*t*, 2 CH_2(cPr). EI-HR-MS: 195.10063 (M^+, $C_9H_{14}N_3O_2^+$; calc. 195.10078).

Suitable crystals for a crystal-structure determination were obtained from MeOH by slow evaporation of the solvent.

12. *X-Ray Crystal-Structure Determination of* **8h** *and* **16** (*Table*, and *Figs. 2* and *3*)[4]). All measurements were performed on a *Nonius KappaCCD* diffractometer [25] using graphite-monochromated MoK_α radiation (λ 0.71073 Å) and an *Oxford Cryosystems Cryostream* 700 cooler. The data collection and refinement parameters are given in *Table 4*, and views of the molecules are shown in *Figs. 2* and *3*. Data reduction was performed with HKL Denzo and Scalepack [26]. The intensities were corrected for *Lorentz* and polarization effects but not for absorption. Equivalent reflections were merged. The structures were solved by direct methods using SHELXS97 [27], which revealed the positions of all non-H-atoms. The asymmetric unit of **8h** contains four symmetry-independent molecules of **8h** and four molecules of H_2O. The atomic coordinates of the molecules were tested carefully for a relationship from a higher symmetry space group using the program PLATON [28], but none could be found. The Ph ring in one of the molecules is disordered over two orientations. Two sets of overlapping positions were defined for the atoms of this Ph group, and the site occupation factor of the major conformation of the ring was refined to 0.57(3). Similarity restraints were applied to the chemically equivalent bond lengths and angles involving all disordered C-atoms, while neighboring atoms within and between each conformation of the disordered Ph rings were restrained to have similar atomic displacement parameters. The asymmetric unit of **16** contains two molecules of **16** plus one molecule of MeOH. The non-H-atoms of **8h** and **16** were refined anisotropically. In the case of **8h**, the amide H-atoms were placed in the positions indicated by a difference electron-density map, and their positions were allowed to refine with individual isotropic displacement parameters. The H-atoms of the H_2O molecules could not be located reliably and were omitted from the model. All remaining H-atoms and all H-atoms of **16** were placed in geometrically calculated positions and refined using a riding model where each H-atom was assigned a fixed isotropic displacement parameter with a value equal to $1.2U_{eq}$ of its parent C-atom (1.5 U_{eq} for the Me groups). The refinement of each structure was carried out on F^2 using full-matrix least-squares procedures, which minimized the function $\Sigma w(F_o^2 - F_c^2)^2$. A correction for secondary extinction was applied for **8h**. In the cases of **8h** and **16**, two and one reflection, resp., whose intensities were considered to be extreme outliers, were omitted from the final refinement. The available crystals of **16** were of poor quality, and the crystal structure is correspondingly of diminished quality. Nonetheless, the composition and connectivity of the molecule has been established unequivocally. Neutral atom scattering factors for non-H-atoms were taken from [29a], and the scattering factors for H-atoms were taken from [30]. Anomalous dispersion effects were included in F_c [31]; the values for f' and f'' were those of [29b]. The values of the mass-attenuation coefficients are those of [29c]. All calculations were performed using the SHELXL97 [32] program.

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[4]) CCDC-688309–688310 contain the supplementary crystallographic data for this article. These data can be obtained free of charge from the *Cambridge Crystallographic Data Centre*, *via* www.ccdc.cam.ac.uk/data_request/cif.

Table 4. *Crystallographic Data for Compounds* **8h** *and* **16**

	8h	**16**
Crystallized from	acetone	MeOH
Empirical formula	$C_{15}H_{19}N_3O_2 \cdot H_2O$	$C_9H_{13}N_3O_2 \cdot 0.5$ MeOH
Formula weight	291.35	211.24
Crystal color, habit	colorless, prism	colorless, prism
Crystal dimensions [mm]	$0.17 \times 0.20 \times 0.35$	$0.17 \times 0.22 \times 0.25$
Temp. [K]	160(1)	160(1)
Crystal system	triclinic	triclinic
Space group	$P1$	$P\bar{1}$
Z	4	4
Reflections for cell determination	8938	3483
2θ range for cell determination [°]	4–60	4–50
Unit cell parameters a [Å]	9.0797(3)	7.6510(7)
b [Å]	13.1025(5)	9.945(1)
c [Å]	14.0338(3)	14.746(2)
α [°]	74.340(2)	83.311(6)
β [°]	81.753(2)	85.927(7)
γ [°]	87.957(2)	69.088(7)
V [Å^3]	1590.95(9)	1040.5(2)
D_x [g cm^{-3}]	1.216	1.348
$\mu(\mathrm{Mo}K_\alpha)$ [mm^{-1}]	0.0859	0.0994
Scan type	ϕ and ω	ω
$2\theta_{(\max)}$ [°]	60	50
Total reflections measured	43631	14870
Symmetry independent reflections	9195	3572
Reflections with $I > 2\sigma(I)$	6829	2221
Reflections used in refinement	9193	3571
Parameters refined; restraints	841; 178	277; 0
Final $R(F)$ [$I > 2\delta(I)$ reflections]	0.0622	0.1184
$wR(F^2)$ (all data)	0.1749	0.3549
Weighting parameters [a; b][a])	0.1084; 0.0792	0.1860; 0.4617
Goodness-of-fit	1.034	1.105
Secondary extinction coefficient	0.022(6)	–
Final $\Delta_{\max}/\sigma$	0.003	0.001
$\Delta\rho$ (max; min) [e Å^{-3}]	0.54; −0.26	0.77; −0.47

$w^{-1} = \sigma^2 (F_o^2) + (aP)^2 + bP$ where $P = (F_o^2) + 2F_c^2)/3$.

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