Unexpected Course of the Reaction of 2-Unsubstituted 1*H*-Imidazole 3-Oxides with Ethyl Acrylate

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The attempted ethenylation at C(2) of 2-unsubstituted 1*H*-imidazole *N*-oxides with ethyl acrylate (= prop-2-enoate) in the presence of $Pd(OAc)_2$ does not occur. In contrast to the other aromatic *N*-oxides, the [2 + 3] cycloaddition of imidazole *N*-oxides predominates, and 3-hydroxyacrylates, isomeric with the cycloadducts, are key products for the subsequent reaction. The final products were identified as dehydrated 2 + 1 adducts of 1*H*-imidazole *N*-oxide and ethyl acrylate. The role of the catalyst is limited to the dehydration of the intermediate 3-hydroxypropanoates to give 1*H*-imidazol-2-yl-substituted acrylates.

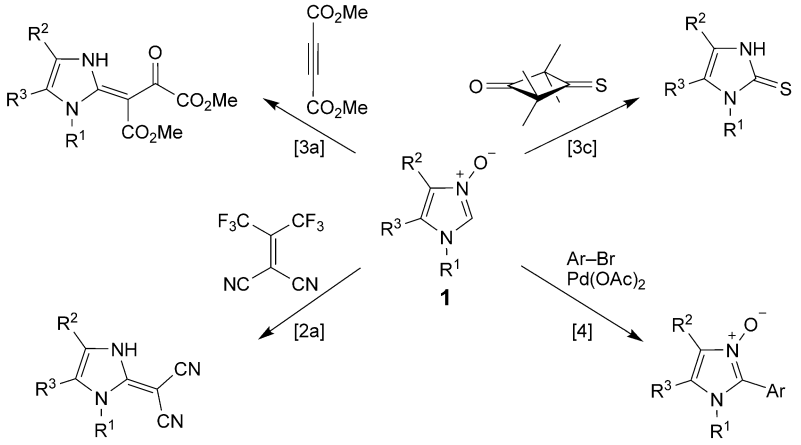
1. Introduction. – In recent years, several reports on the synthesis and applications of 2-unsubstituted imidazole 3-oxides **1** were published. In contrast to six-membered aromatic heterocyclic *N*-oxides, they cannot be prepared by direct oxidation of the parent system, but the condensation of α-hydroxyimino ketones with methylidene amines offers a convenient access to this group of reactive 1*H*-imidazole derivatives [1][2]. One of the most characteristic features of their structure is the 'nitrone-like' pattern, which enables diverse 1,3-dipolar cycloadditions with electron-deficient acetylenes and ethenes, as well as isocyanates and thiocarbonyl compounds [2][3]. The initially formed [2 + 3] cycloadducts have never been isolated, and secondary processes occur leading to the products depicted in *Scheme 1*.

On the other hand, **1** can easily be arylated at C(2) in the presence of $Pd(OAc)_2$ with preservation of the *N*-oxide function [4]. The conversion of *N*-oxides **1** to the corresponding imidazoles occurs smoothly upon treatment with *Raney*-Ni at room temperature [5].

The metal-catalyzed formation of new C,C bonds in aromatic and heteroaromatic rings is a challenging task in modern organic synthesis, and the state of the art in the field of imidazole derivatives has recently been reviewed [6]. A frequently studied reaction is the ethenylation with acrylates leading to 3-arylprop-2-enoates. Despite the potential importance of ethenylations of aromatic *N*-oxides, there are, to the best of our knowledge, only two reports on Pd-catalyzed reactions of this type (*Scheme 2*). In one case, pyridine 1-oxides **2** were converted regioselectively into 3-(pyridin-2-yl)prop-2-enoates **3** with a preserved *N*-oxide group in high yields [7]. The second reaction

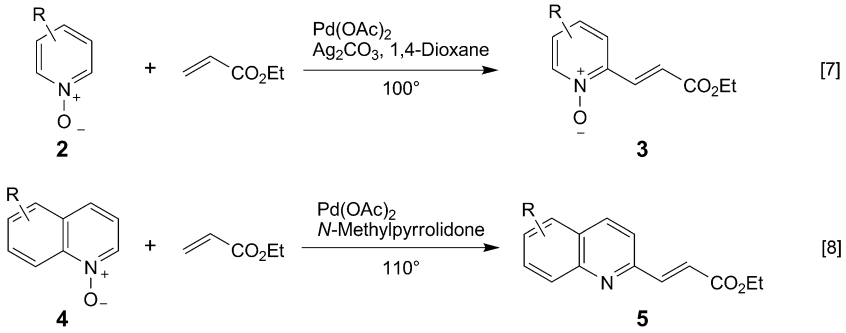
[1]) Master thesis of *A. W.*, University of Łódź, 2011.

Scheme 1



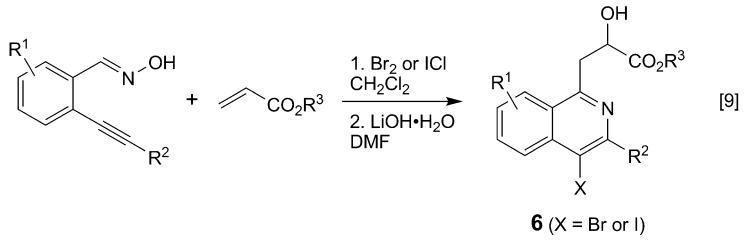
reported is the transformation of quinoline *N*-oxides **4** to the prop-2-enoates **5**. In these reactions, a spontaneous deoxygenation of the *N*-oxide occurred [8].

Scheme 2



In a recent report, the synthesis of 2-hydroxy-3-(isoquinolin-1-yl)propanoates **6**, *via* the *in situ* generated isoquinoline *N*-oxide and acrylates (= prop-2-enoates) in the presence of LiOH as a base, was described [9] (*Scheme 3*). It is worth mentioning that this reaction proceeds without transition metal catalysis.

Scheme 3

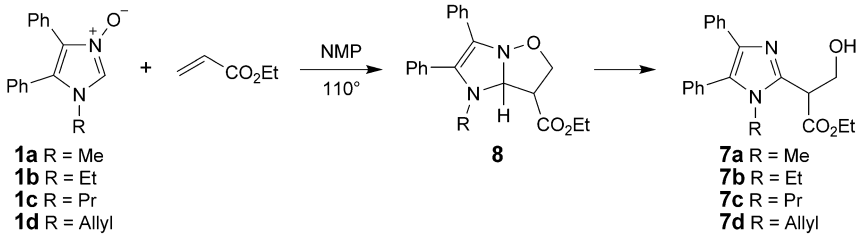


Thermal [2 + 3] cycloadditions of acrylates with aromatic *N*-oxides, which, in general, are recognized as poor 1,3-dipoles, are almost unknown. *Huisgen et al.* have shown that phenanthridine *N*-oxide and ethyl acrylate react in DMF solution at 75° to give products of type **6** [10]. The formation of the latter has been rationalized by a [2 + 3] cycloaddition, followed by a spontaneous ring opening of the intermediate isoxazolidine. In addition, the reaction of quinoline *N*-oxide with 2-methylacrylonitrile to produce an analogous product identified as 2-hydroxy-2-methyl-3-(quinolin-2-yl)propanenitrile has been reported [11].

Prompted by the results described in [7] and [8], we decided to study the reaction of ethyl acrylate with 2-unsubstituted 1*H*-imidazole 3-oxides **1** both in the presence and in the absence of a catalytic amount of $Pd(AcO)_2$.

Results and Discussion. – In a preliminary experiment, equimolar amounts of ethyl acrylate and 1-methyl-4,5-diphenyl-1*H*-imidazole 3-oxide (**1a**) were dissolved in $CHCl_3$. No reaction took place at room temperature nor when the solution was heated to reflux. Therefore, the starting **1a** and a fivefold excess of acrylate were dissolved in *N*-methylpyrrolidone (NMP; 1-methylpyrrolidin-2-one), and the solution was heated in an oil bath (110°). After *ca.* 1 h, the reaction was stopped, and chromatographic workup led to an oily product. The spectroscopic data provided the structure of the 3-hydroxypropanoate **7a** (*Scheme 4*). Analogous products **7b** – **7d** were obtained with 1-ethyl-, 1-propyl-, and 1-allyl-4,5-diphenyl-1*H*-imidazole 3-oxides, respectively, in 26 – 33% yield. Attempted reactions with the corresponding 4,5-dimethyl- or 4-methyl-5-phenyl-1*H*-imidazole 3-oxides led to complex mixtures of products.

Scheme 4



1a R = Me
1b R = Et
1c R = Pr
1d R = Allyl

8

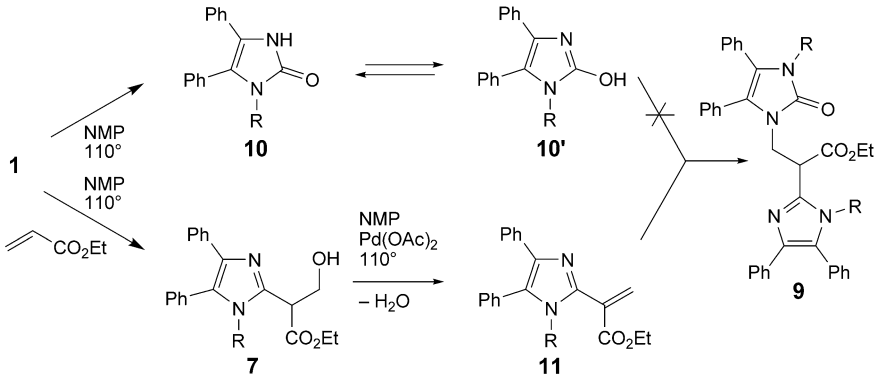
7a R = Me
7b R = Et
7c R = Pr
7d R = Allyl

The formation of the β-hydroxy esters **7** can be explained by an initial [2 + 3] cycloaddition to give **8** and subsequent opening of the isoxazolidine ring *via* cleavage of the N–O bond, and aromatization of the imidazole unit.

To achieve the ethenylation product of **1a**, a similar experiment with ethyl acrylate was carried out in the presence of 5 mol% of $Pd(OAc)_2$. After *ca.* 1 h, an analogous result was obtained as in the absence of the catalyst. When the reaction time was extended to 2.5 h, no **7a** was present in the mixture. Chromatographic workup afforded a crystalline material, which showed signals of two MeN and only one EtO group in the ^{1}H-NMR spectrum. These data suggested that the new product contains two imidazole and one propanoate moieties. The HR-MS exhibited the $[M+1]^+$ peak at *m*/*z* 583.2700, which corresponds to a structure formed from two molecules **1a** and one

molecule of ethyl acrylate after elimination of H_2O. Finally, an X-ray crystal-structure determination unambiguously disclosed the molecular structure of product **9a**, which formally corresponds to a *Michael* adduct of 1-methyl-4,5-diphenyl-1*H*-imidazol-2-one (**10a**) with 2-(1*H*-imidazol-2-yl)acrylate **11a** (*Scheme 5* and *Fig.*). Most likely, the latter compound is formed *in situ* by dehydration of **7a**. The imidazol-2-one **10a** can be

Scheme 5



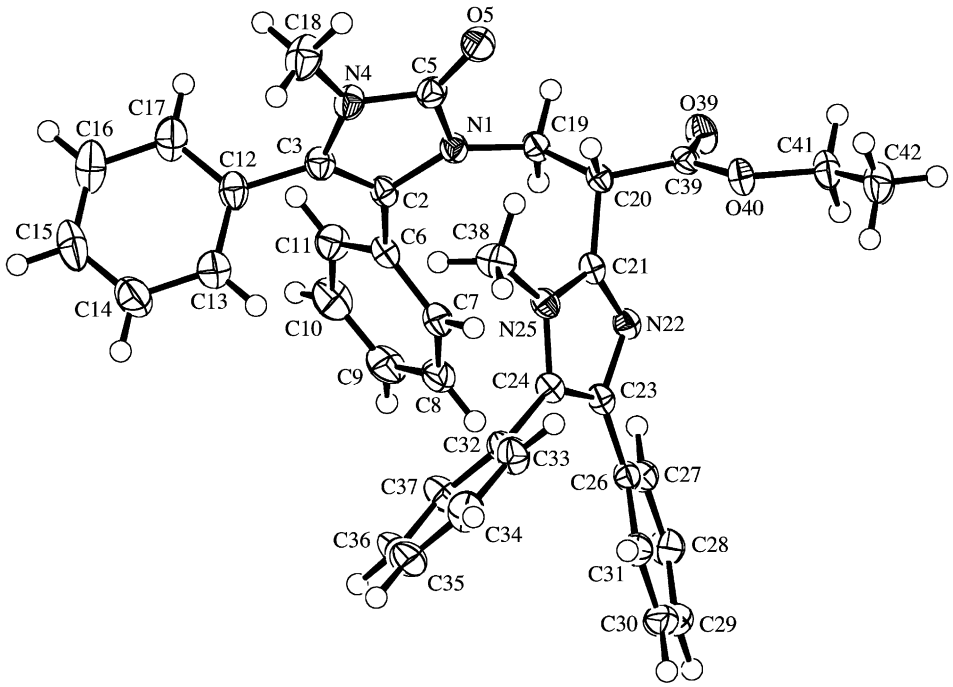


Figure. *ORTEP Plot* [13] *of the molecular structure of* **9a** (with 50% probability ellipsoids; arbitrary atom numbering)

formed *in situ via* thermal isomerization of **1a** [12]. The analogous reaction course leading to products **9** was established starting with **1b**–**1d**.

To obtain additional support for the proposed reaction mechanism, three control experiments were carried out. First, the isolated hydroxy ester **7b** was dehydrated in NMP solution at 110° in the absence, as well as in the presence, of catalytic amounts of $Pd(OAc)_2$. After 1 h, the progress of the reaction in both cases was examined by ^{1}H-NMR spectroscopy. Whereas the reaction performed in the presence of $Pd(OAc)_2$ was complete, yielding **11b** exclusively, the reaction without $Pd(OAc)_2$ gave **11b** only in traces, and more than 90% of **7b** were still present in the mixture. Second, a mixture of the isolated **11b** and imidazol-2-one **10b** (R = Et) were heated in NMP in the presence of catalytic amounts of $Pd(OAc)_2$. After 2 h, the ^{1}H-NMR spectrum of the mixture indicated the presence of unchanged substrates, and no **9b** could be detected. In the third experiment, equimolar amounts of **11b** and **1a** (R = Me) were heated in NMP solution at 110° in the absence of $Pd(OAc)_2$. After 1 h, the mixture was analyzed by ^{1}H-NMR spectroscopy. However, also in this case, no traces of the expected 'mixed product' of type **9** were found in the mixture.

These results show that the formation of products **9** does not result from the reaction of **11** either with isolated imidazol-2-ones **10** or with *N*-oxides **1**. Therefore, formulation of a convincing mechanism of a cascade reaction leading to the *Michael* adducts of type **9** is not possible at the moment.

3. Conclusions. – The present study showed that 2-unsubstituted 1*H*-imidazole *3*-oxides, in contrast to quinoline and pyridine *N*-oxides, do not undergo the ethenylation reaction with ethyl acrylate in the presence of $Pd(OAc)_2$. The results indicate that, under the applied conditions, the preferred reaction is the [2 + 3] cycloaddition, which occurs regioselectively, leading to 3-hydroxypropanoate, which is a product of the spontaneous ring opening of the five-membered cycloadduct. It is worth mentioning that the structures of the isolated hydroxy esters **7** do not correspond to those of the products of analogous reactions with isoquinoline and quinoline *N*-oxides, respectively [9–11]. The catalyst used in the reaction accelerates the dehydration of the hydroxy ester, formed after ring opening of the initial isoxazolidine derivative.

The authors thank PD Dr. *L. Bigler* (University of Zurich) for recording HR-MS and Mrs. *Małgorzata Celeda* (University of Łódź) for her skillful help in the preparation of starting 1*H*-imidazole *3*-oxides.

Experimental Part

1. *General.* M.p.: *MEL-TEMP. II* (*Aldrich*); uncorrected. IR Spectra: *NEXUS FT-IR* instrument; in KBr or as film; absorptions in cm^{-1}. ^{1}H- and ^{13}C-NMR spectra: *BRUKER AVANCE III* instrument (^{1}H at 600 and ^{13}C at 150 MHz) using solvent signal as reference; in $CDCl_3$; chemical shifts (δ) in ppm; coupling constants *J* in Hz. The majority of the ^{13}C signals were assigned with the aid of DEPT spectra. ESI-HR-MS: *Finnigan MAT-95* spectrometer.

2. *Starting Materials.* The used reagents and solvents such as ethyl acrylate, $Pd(OAc)_2$, *N*-methylpyrrolidone (NMP; 1-methylpyrrolidin-2-one), petroleum ether (PE), Et_2O, diisopropyl ether ($^iPr_2O$), pentane, and AcOEt are commercially available. 1*H*-Imidazole *3*-oxides **1** were prepared according to known protocols [2].

3. *Reactions of 2-Unsubstituted 1*H*-Imidazole 3-Oxides with Ethyl Acrylate.* A mixture of the corresponding oxide **1** (1 mmol), ethyl acrylate (5 mmol), $Pd(OAc)_2$ (5 mol%), and NMP (1 ml; used as

a solvent) was heated under Ar in an oil bath at 110° for 40–45 min. After evaporation of the solvent and excess ethyl acrylate by vacuum distillation (bulb-to-bulb), the residues were separated on prep. TLC plates (SiO_2; hexane or PE/AcOEt 1:1) to give products **7** as pale yellow oils. Analogous results were obtained when the reactions were carried out without the addition of catalytic amounts of $Pd(OAc)_2$.

When the reactions were carried out for 2–2.5 h, no 3-hydroxypropanoates **7** were detected in the crude mixtures. Separation by prep. TLC gave solid materials identified as products **9**, which subsequently were purified by crystallization from mixtures of PE or pentane with small amounts of Et_2O or $^iPr_2O$.

*Ethyl 3-Hydroxy-2-(1-methyl-4,5-diphenyl-1*H*-imidazol-2-yl)propanoate* (**7a**). Yield: 98 mg (28%). Pale-yellow oil. IR (film): 3355 (OH), 3062, 2981, 2959, 2934, 2248, 1733 (C=O), 1603, 1507, 1465, 1443, 1301, 1243, 1185, 1072, 1055, 1044, 910, 732, 700, 648. ^{1}H-NMR ($CDCl_3$): 1.34 (*t*, *J* = 7.1, *Me*CH_2O); 3.35 (*s*, MeN); 3.92 (*t*, *J* = 4.0, HOCH_2C*H*); 4.25–4.35 (*m*, MeCH_2O); 4.46 (*d*, *J* = 4.0, HOCH_2CH); 5.16 (br. *s*, OH); 7.14–7.52 (*m*, 10 arom. H). ^{13}C-NMR ($CDCl_3$): 14.2 (*Me*CH_2O); 31.0 (MeN); 45.9 (HOCH_2*C*H); 61.7, 63.5 (2 CH_2O); 126.4, 126.6, 128.1, 128.8, 129.1, 130.9 (10 arom. CH); 129.4, 130.8, 134.2, 136.3 (2 arom. C, C(4), C(5)); 143.9 (C(2)); 169.8 (C=O). HR-ESI-MS: 351.1730 ($[M+H]^+$, $C_{21}H_{23}N_2O_3^+$; calc. 351.1703).

*Ethyl 2-(1-Ethyl-4,5-diphenyl-1*H*-imidazol-2-yl)-3-hydroxypropanoate* (**7b**). Yield: 120 mg (33%). Pale-yellow oil. IR (film): 3355 (OH), 3057, 2982, 2937, 2875, 2305, 1736 (C=O), 1603, 1507, 1473, 1446, 1327, 1266, 1181, 1072, 1045, 1029, 955, 738, 774, 700. ^{1}H-NMR ($CDCl_3$): 1.14 (*t*, *J* = 7.2, *Me*CH_2N); 1.34 (*t*, *J* = 7.0, *Me*CH_2O); 3.77–3.84 (*m*, MeCH_2N); 3.92 (*t*, *J* = 4.0, HOCH_2C*H*); 4.21–4.34 (*m*, MeCH_2O); 4.42 (*d*, *J* = 4.0, HOCH_2CH); 5.22 (br. *s*, OH); 7.14–7.52 (*m*, 10 arom. H). ^{13}C-NMR ($CDCl_3$): 14.2 (*Me*CH_2O); 15.9 (*Me*CH_2N); 38.7 (Me*C*H_2N); 45.8 (HOCH_2*C*H); 61.7, 62.9 (2 CH_2); 126.3, 126.5, 128.0, 128.9, 129.1, 131.1 (10 arom. CH); 128.6, 131.2, 134.2, 136.6 (2 arom. C, C(4), C(5)); 143.2 (C(2)); 170.1 (C=O). HR-ESI-MS: 365.1870 ($[M+H]^+$, $C_{22}H_{25}N_2O_3^+$; calc. 365.1860).

*Ethyl 2-(4,5-Diphenyl-1-propyl-1*H*-imidazol-2-yl)-3-hydroxypropanoate* (**7c**). Yield: 110 mg (29%). Pale-yellow oil. IR (film): 3351 (OH), 3060, 2970, 2935, 2876, 1736 (C=O), 1603, 1507, 1470, 1445, 1369, 1239, 1179, 1073, 1046, 1028, 968, 775, 699. ^{1}H-NMR ($CDCl_3$): 0.78 (*t*, *J* = 7.4, *Me*CH_2CH_2N); 1.34 (*t*, *J* = 7.1, *Me*CH_2O); 1.47–1.54 (*m*, MeCH_2CH_2N); 3.68–3.71 (*m*, CH_2N); 3.93 (*t*, *J* = 4.2, HOCH_2C*H*); 4.27–4.32 (*m*, MeCH_2); 4.43 (*d*, *J* = 4.2, HOCH_2CH); 5.18 (br. *s*, OH); 7.13–7.51 (*m*, 10 arom. CH). ^{13}C-NMR ($CDCl_3$): 11.0 (*Me*CH_2CH_2N); 14.2 (*Me*CH_2); 23.8 (Me*C*H_2CH_2N); 45.5 (CH_2N); 45.9 (HOCH_2*C*H); 61.5, 62.9 (2 CH_2); 126.3, 126.5, 128.0, 128.8, 129.1, 131.1 (10 arom. CH); 128.0, 131.2, 134.2, 136.5 (2 arom. C, C(4), C(5)); 143.5 (C(2)); 170.1 (C=O). HR-ESI-MS: 379.2013 ($[M+H]^+$, $C_{23}H_{27}N_2O_3^+$; calc. 379.2016).

*Ethyl 2-(4,5-diphenyl-1-(prop-2-en-1-yl)-1*H*-imidazol-2-yl)-3-hydroxypropanoate* (**7d**). Yield: 100 mg (27%). Pale-yellow oil. IR (film): 3366 (OH), 3058, 2982, 2936, 2868, 1736 (C=O), 1603, 1508, 1462, 1444, 1370, 1328, 1266, 1181, 1100, 1044, 1030, 924, 775, 738, 701. ^{1}H-NMR ($CDCl_3$): 1.34 (*t*, *J* = 7.1, *Me*CH_2O); 3.86 (*t*, *J* = 4.1, HOCH_2C*H*); 4.24–4.31 (*m*, MeCH_2O); 4.34–4.37 (*m*, HOCH_2CH); 4.38–4.42 (*m*, CH_2N); 4.92 (*dd*, *J* = 17.0, 0.7, CH_2=CH); 5.20 (*dd*, *J* = 10.0, 0.7, CH_2=CH); 5.77–5.85 (*m*, CH_2=C*H*); 7.14–7.50 (*m*, 10 arom. CH). ^{13}C-NMR ($CDCl_3$): 14.2 (*Me*CH_2); 45.7 (HOCH_2C*H*); 45.9 (CH_2N); 61.7, 62.8 (2 CH_2); 117.1 (CH=*C*H_2); 126.4, 126.6, 128.1, 128.9, 129.0, 131.0, 132.9 (10 arom. CH, *C*H=CH_2); 128.0, 131.2, 134.2, 136.5 (2 arom. C, C(4), C(5)); 143.5 (C(2)); 170.0 (C=O). HR-ESI-MS: 377.1860 ($[M+H]^+$, $C_{23}H_{25}N_2O_3^+$; calc. 377.1864).

*Ethyl 3-(2,3-Dihydro-3-methyl-2-oxo-4,5-diphenyl-1*H*-imidazol-1-yl)-2-(1-methyl-4,5-diphenyl-1*H*-imidazol-2-yl)propanoate* (**9a**). Yield: 60 mg (21%). Pale-yellow crystals. M.p. 193–195° (PE/^{i}Pr_2O). IR (KBr): 3057, 2978, 2954, 1736 (C=O), 1684 (C=O), 1602, 1505, 1452, 1395, 1368, 1297, 1208, 1156, 1072, 1025, 918, 852, 777, 700, 615, 505. ^{1}H-NMR ($CDCl_3$): 1.23 (*t*, *J* = 7.1, *Me*CH_2O); 3.22 (*s*, MeN); 3.35 (*s*, MeN); 4.09–4.14 (*m*, 1 H of MeCH_2O); 4.17–4.23 (*m*, 1 H of MeCH_2O); 4.42 (*dd*, *J* = 14.0, 8.2, 1 H of CH_2N); 4.58 (*dd*, *J* = 14.0, 7.0, 1 H of CH_2N); 4.90 (*t*, *J* = 7.5, CH_2C*H*); 7.07–7.22 (*m*, 20 arom. CH). ^{13}C-NMR ($CDCl_3$): 14.1 (*Me*CH_2); 28.8, 31.1 (2 MeN); 42.1 (CH_2*C*H); 42.6 (CH_2N); 61.4 (Me*C*H_2); 126.0, 126.8, 127.9, 128.0, 128.4, 128.5, 129.0, 130.1, 130.6, 130.9 (20 arom. CH); 121.5, 121.6, 128.6, 129.0, 129.5, 131.3, 134.7, 137.0, 142.5 (4 arom. C, 2 C(4), 2 C(5), C(2)); 153.9, 169.6 (2 C=O). HR-ESI-MS: 583.2700 ($[M+H]^+$, $C_{37}H_{35}N_4O_3^+$; calc. 583.2703).

Crystals of **9a** suitable for the X-ray crystal-structure determination were grown from CH_2Cl_2/$^iPr_2O$.

*Ethyl 3-(2,3-Dihydro-3-ethyl-2-oxo-4,5-diphenyl-1*H*-imidazol-1-yl)-2-(1-ethyl-4,5-diphenyl-1*H*-imidazol-2-yl)propanoate* (**9b**). Yield: 70 mg (23%). Pale-yellow crystals. M.p. 165–168° (PE/Et_2O). IR (KBr): 3063, 2979, 2934, 1744 (C=O), 1674 (C=O), 1602, 1506, 1446, 1407, 1352, 1302, 1229, 1201, 1061, 1027, 958, 862, 772, 700, 609, 542. ^{1}H-NMR ($CDCl_3$): 1.06–1.14 (*m*, 2 *Me*CH_2N); 1.23 (*t*, *J* = 7.1, *Me*CH_2O); 3.66–3.72 (*m*, 1 H of MeC*H*$_2$N); 3.72–3.77 (*m*, 1 H of MeC*H*$_2$N); 3.79–3.85 (*m*, 1 H of MeC*H*$_2$N); 3.89–3.95 (*m*, 1 H of MeC*H*$_2$N); 4.06–4.12 (*m*, 1 H of MeC*H*$_2$O); 4.19–4.24 (*m*, 1 H of MeC*H*$_2$O); 4.40 (*dd*, *J* = 14.0, 7.0, 1 H of CH_2N); 4.63 (*dd*, *J* = 14.0, 8.0, 1 H of CH_2N); 4.94 (*t*, *J* = 7.4, CH_2C*H*); 7.08–7.49 (*m*, 20 arom. CH). ^{13}C-NMR ($CDCl_3$): 14.0, 14.7 (2 *Me*CH_2N); 16.2 (*Me*CH_2); 36.6, 38.6 (2 Me*C*H_2N); 41.5 (CH_2*C*H); 43.3 (CH_2N); 61.3 (Me*C*H_2); 125.9, 126.7, 127.8, 127.9, 127.9, 128.3, 128.4, 128.5, 129.0, 130.3, 130.5, 130.9 (20 arom. CH); 120.9, 121.8, 128.4, 128.5, 129.3, 131.7, 134.7, 137.3, 142.0 (4 arom. C, 2 C(4), 2 C(5), C(2)); 153.4, 169.6 (2 C=O). HR-ESI-MS: 611.3020 ($[M+H]^+$, $C_{39}H_{39}N_4O_3^+$; calc. 611.3016).

*Ethyl 3-(2,3-Dihydro-2-oxo-4,5-diphenyl-3-propyl-1*H*-imidazol-1-yl)-2-(4,5-diphenyl-1-propyl-1*H*-imidazol-2-yl)propanoate* (**9c**). Yield: 50 mg (16%). Pale-yellow crystals. M.p. 136–138° (PE/Et_2O). IR (KBr): 3057, 2965, 2934, 2875, 1740 (C=O), 1683 (C=O), 1603, 1505, 1448, 1403, 1367, 1296, 1227, 1196, 1155, 1073, 1027, 918, 868, 775, 699, 645, 616, 509. ^{1}H-NMR ($CDCl_3$): 0.65, 0.67 (2*t*, *J* = 7.4, 2 *Me*$CH_2$$CH_2$N); 1.23 (*t*, *J* = 7.1, *Me*CH_2O); 3.58–3.84 (*m*, 2 MeC*H*$_2$C*H*$_2$); 4.07–4.13 (*m*, 1 H of MeC*H*$_2$O); 4.17–4.23 (*m*, 1 H of MeC*H*$_2$O); 4.43 (*dd*, *J* = 14.0, 8.0, 1 H of CH_2N); 4.65 (*dd*, *J* = 14.0, 6.7, 1 H of CH_2N); 4.90 (*t*, *J* = 7.4, CH_2C*H*); 7.07–7.49 (*m*, 20 arom. CH). ^{13}C-NMR ($CDCl_3$): 11.0 (2 *Me*$CH_2$$CH_2$N); 14.0 (*Me*$CH_2$); 22.5, 24.0 (2 MeC*H*$_2$$CH_2$N); 41.6 ($CH_2$C*H*); 43.2, 43.3 (2 Me$CH_2$C*H*$_2$N); 45.3 ($CH_2$N); 61.3 (MeC*H*$_2$); 125.9, 126.8, 127.7, 127.8, 127.9, 128.3, 128.4, 128.5, 128.9, 130.3, 130.6, 131.0 (20 arom. CH); 121.2, 121.8, 128.7, 129.4, 131.8, 134.7, 137.2, 142.4 (4 arom. C, 2 C(4), 2 C(5), C(2)); 153.6, 169.6 (2 C=O). HR-ESI-MS: 639.3333 ($[M+H]^+$, $C_{41}H_{43}N_4O_3^+$; calc. 639.3329).

*Ethyl 3-[2,3-Dihydro-2-oxo-4,5-diphenyl-3-(prop-2-en-1-yl)-1*H*-imidazol-1-yl]-2-[4,5-diphenyl-1-(prop-2-en-1-yl)-1*H*-imidazol-2-yl]propanoate* (**9d**): Yield: 65 mg (21%). Pale-yellow crystals. M.p. 132–134° (pentane/Et_2O). IR (KBr): 3439, 3061, 3025, 2980, 2923, 1734 (C=O), 1694 (C=O), 1602, 1505, 1445, 1396, 1351, 1256, 1228, 1194, 1161, 1098, 1071, 1028, 944, 923, 866, 777, 702, 667, 650, 615, 543, 502. ^{1}H-NMR ($CDCl_3$): 1.20 (*t*, *J* = 7.1, *Me*CH_2O); 4.05–4.10 (*m*, 1 H of MeC*H*$_2$O); 4.15–4.20 (*m*, 1 H of MeC*H*$_2$O); 4.20–4.30 (*m*, NC*H*$_2$CH=CH); 4.35–4.48 (*m*, NC*H*$_2$CH=CH); 4.43 (*dd*, *J* = 14.0, 7.5, 1 H of CH_2N); 4.62 (*dd*, *J* = 14.0, 7.0, 1 H of CH_2N); 4.81–4.85 (*m*, CH_2=CH); 4.97 (*dd*, *J* = 10.0, 0.7, 1 H of C*H*$_2$=CH); 5.06 (*dd*, *J* = 10.0, 0.7, 1 H of C*H*$_2$=CH); 5.09 (*t*, *J* = 7.0, CH_2*CH*); 5.73–5.83 (*m*, 2 CH_2=C*H*); 7.08–7.45 (*m*, 20 arom. CH). ^{13}C-NMR ($CDCl_3$): 14.0 (*Me*CH_2); 41.8 (CH_2*C*H); 43.1, 43.9, 45.8 (3 CH_2N); 61.3 (CH_2O); 116.6, 116.8 (2 *C*H_2=CH); 126.0, 126.8, 127.9, 128.01, 128.02, 128.3, 128.4, 128.7, 128.8, 130.4, 130.6, 131.1, 133.3, 133.4 (2 CH_2=*C*H, 20 arom. CH); 121.3, 121.8, 128.1, 128.5, 129.0, 129.04, 129.1, 131.3 (4 arom. C, 2 C(4), 2 C(5), C(2)); 153.4, 169.5 (2 C=O). HR-ESI-MS: 635.3011 ($[M+H]^+$, $C_{41}H_{39}N_4O_3^+$; calc. 635.3016).

4. *Dehydration of 3-Hydroxypropanoate* **7b**. *Experiment A* (in the presence of $Pd(OAc)_2$). A soln. of **7b** (1 mmol) in NMP (1 ml) was heated in an oil bath at 110° for 1 h in the presence of a cat. amount (*ca.* 15 mg) of $Pd(OAc)_2$. Then, the solvent was evaporated by vacuum distillation, and the crude mixture was separated by prep. TLC (SiO_2; PE/AcOEt 3 :2) to give *ethyl 2-(1-ethyl-4,5-diphenylimidazol-2-yl)prop-2-enoate* (**11b**) as a semi-solid material. This quite unstable compound was used for further experiments with no additional purification. Yield after chromatographic workup: 240 mg (68%). IR (KBr): 3058, 2963, 2932, 2872, 1734, 1602, 1506, 1261, 1096, 1024, 803, 773, 696. ^{1}H-NMR ($CDCl_3$): 1.06 (*t*, *J* = 7.2, *Me*CH_2N); 1.36 (*t*, *J* = 7.1, *Me*CH_2O); 3.80 (*q*, *J* = 7.2, MeC*H*$_2$N); 4.34 (*q*, *J* = 7.1, MeC*H*$_2$O); 6.36, 6.79 (*2d*, *J* = 1.4, =CH_2); 7.14–7.49 (*m*, 10 arom. CH). ^{13}C-NMR ($CDCl_3$): 14.2, 19.9 (2 *Me*CH_2); 39.6 (CH_2N); 61.5 (CH_2O); 126.2, 126.8, 128.0, 128.7 129.0, 131.0 (10 arom. CH); 133.9 (C=*C*H_2); 129.4, 131.3, 132.9, 134.5, 137.7, 142.9 (2 arom. C, C(2), C(4), C(5), *C*=CH_2); 165.3 (C=O). ESI-MS (MeCN): 369 (20, $[M+Na]^+$), 347 (100, $[M+1]^+$). HR-EI-MS (70 eV): 346.1681 (M^+, $C_{22}H_{22}N_2O_2^+$; calc. 346.1687).

Experiment B (in the absence of $Pd(OAc)_2$). A soln. of **7b** (1 mmol) in NMP (1 ml) was heated in an oil bath at 110° for 1 h. Then, the solvent was evaporated by vacuum distillation, and the crude, oily mixture was analyzed by ^{1}H-NMR spectroscopy. In this case, **7b** was still the main component of the crude mixture.

5. *X-Ray Crystal-Structure Determination of* **9a** (*Table* and *Fig.*)[2]). All measurements were conducted on an *Agilent Technologies SuperNova* area-detector diffractometer [14], with MoK_α radiation ($\lambda = 0.71073$ Å) from a micro-focus X-ray source, and an *Oxford Instruments Cryojet XL* cooler. Data reduction was performed with CrysAlisPro [14]. The intensities were corrected for *Lorentz* and polarization effects, and an empirical absorption correction using spherical harmonics [14] was applied. The space group was uniquely determined by the systematic absences. Equivalent reflections were merged. The data collection and refinement parameters are compiled in the *Table*. A view of the molecule is shown in the *Figure*. The structure was solved by direct methods using SHELXS97 [15], which revealed the positions of all non-H-atoms. The non-H-atoms were refined anisotropically. All of the H-atoms were placed in geometrically calculated positions and refined by using a riding model where

Table. *Crystallographic Data for Compound* **9a**

Crystallized from		$CH_2Cl_2/^iPrO_2$
Empirical formula		$C_{37}H_{34}N_4O_3$
Formula weight [g mol^{-1}]		582.70
Crystal color, habit		colorless, prism
Crystal dimensions [mm]		0.08 × 0.20 × 0.40
Temp. [K]		160(1)
Crystal system		monoclinic
Space group		$P2_1/c$
Z		4
Reflections for cell determination		9701
2θ Range for cell determination [°]		4 – 59
Unit cell parameters	a [Å]	15.5476(6)
	b [Å]	10.0461(3)
	c [Å]	19.8750(7)
	β [°]	95.067(3)
	V [Å^3]	3092.20(19)
D_x [g cm^{-3}]		1.252
μ(MoK_α) [mm^{-1}]		0.0805
Scan type		ω
$2\theta_{(max)}$ [°]		59.1
Transmission factors (min; max)		0.731; 1.000
Total reflections measured		28418
Symmetry independent reflections		7690
Reflections with $I > 2\sigma(I)$		5820
Reflections used in refinement		7690
Parameters refined		401
Final	$R(F)$ [$I > 2\sigma(I)$ reflections]	0.0447
	$wR(F^2)$ (all data)	0.1160
Weights		$w = [\sigma^2(F_o^2) + (0.0484P)^2 + 0.9470P]^{-1}$ where $P = (F_o^2 + 2F_c^2)/3$
Goodness of fit		1.030
Secondary extinction coefficient		0.0026(5)
Final Δ_{max}/σ		0.001
$\Delta\rho$ (max; min) [e Å^{-3}]		0.30; −0.20

[2]) CCDC-859644 contains the supplementary crystallographic data for this contribution. These data can be obtained free of charge from the *Cambridge Crystallographic Data Centre*, *via* www.ccdc.cam.ac.uk/data_request/cif.

each H-atom was assigned a fixed isotropic displacement parameter with a value equal to 1.2 U_{eq} of its parent C-atom (1.5 U_{eq} for the Me groups). The refinement of the structure was carried out on F^2 by 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. Neutral-atom scattering factors for non-H-atoms were taken from [16a], and the scattering factors for H-atoms were taken from [17]. Anomalous dispersion effects were included in F_c [18]; the values for f' and f'' were those of [16b]. The values of the mass attenuation coefficients are those of [16c]. The SHELXL97 program [15] was used for all calculations.

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