Preparation of 1-Substituted-5-[(2-oxo-2-phenyl)ethyl]imidazoles

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New high yield preparation methods were developed for the pharmaceutically interesting compounds, 1-benzyl-, 1-methyl-, and 1*H*-5-[(2-oxo-2-phenyl)ethyl]imidazoles **1a-c**, respectively. The title compounds were synthesized by four different methods using various starting materials. Two of the methods involved transformation reactions of the key intermediates, 1-substituted-5-[(2-nitro-2-phenyl)ethenyl]imidazoles **2a-c** and 1-substituted-5-[(2-nitro-2-phenyl)ethyl]imidazoles **3a-c**, while the other two utilized the oxidation of 1-substituted-5-[(2-hydroxy-2-phenyl)ethyl]imidazoles **4a-c**, with chromic oxide, and the umpolung reaction of benzaldehyde followed by a condensation reaction of the *umpolung* intermediate with imidazolecarboxaldehydes **6a-c**.

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Synthetic methods devoted to the preparation of new azoles are of great interest in the medicinal chemistry field because of potential biological activity of those compounds. Examples of new drugs from synthesis of azoles are, cimetidine (H_2-antihistamine) [1], clonidine (antihypertensive) [2], metronidazole (antiprotozoal) [3], clotrimazole and other antifungals [4] as well, detomidine and its methyl derivatives (valuable drugs in veterinary medicine) [5-6]. Despite considerable pharmaceutical importance of imidazole derivatives and the widespread interest in their chemistry, often even simple imidazoles are not readily accessible. Most reactions include several steps, are laborious, purification is tedious and yields are often low. There is a need for additional versatile syntheses of imidazoles with specific regiochemistry and the ability to incorporate a wide variety of substituents.

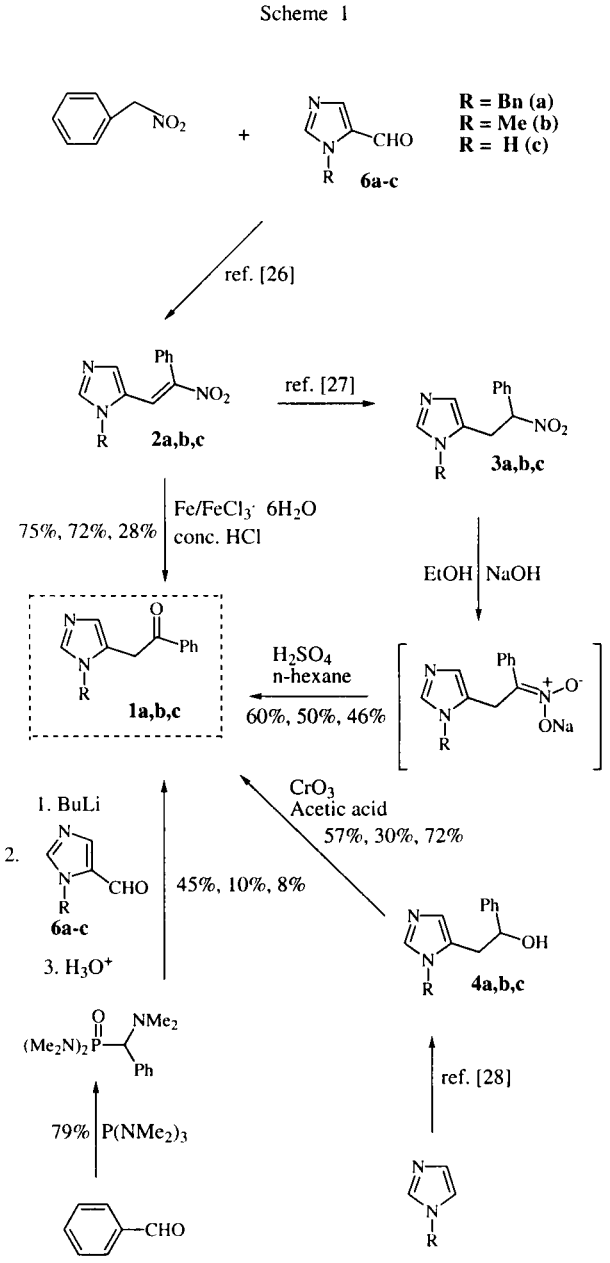
Our main goal was to develop simple efficient high yield synthetic routes to a series of new 5-[2-aryl-2-(functional group)ethyl]imidazoles (Scheme 1), for use as model compounds of new lipophilic histamine analogues [7-9], such as histamine H_3-receptor agonists [10]. On the other hand, they may also serve as homologues of some α_2-adrenoceptors active agents [11-15]. Valuable key intermediates for the synthesis of the target molecules **1a-c** are (1*R*)-5-[(2-nitro-2-phenyl)ethenyl]-imidazoles **2a-c** (R = Bn, Me, H, respectively) and the corresponding nitroethylimidazoles **3a-c**, because of the ability of the conjugated nitroalkenes to be transformed into numerous new groups of the heterocyclic and carbocyclic compounds. Also, the nitro group is transformable to a large number of functionalities [16-25]. Both types of compounds were prepared in our laboratory. The nitroethenes **2a-c** were prepared in good to moderate yields from imidazolecarboxaldehydes **6a-c** and phenylnitromethane, as we reported earlier [26], and the nitroethanes **3a-c** were obtained conveniently by reduction of **2a-c** with $NaBH_4$ in tetrahydrofuran methanol [27]. The hydroxyethylimidazole derivatives **4a-c** were prepared using the metal exchange reaction of the parent imidazole [28] in good yields. Known reactions, which have not been reported in connection with imidazoles, were applied and the results of each method was compared. The structures of the compounds were verified with ir, ^1H and ^{13}C nmr, X-ray crystallography, and high resolution mass spectrometry. Surprisingly enough, these seemingly simple compounds **1a-c** and interesting side products **5a-c** provide a new class of β-oxoethylimidazoles not documented well earlier in the literature.

Results and Discussion.

Nitroethenes **2a-c** were converted in good yields to the oxo analogues **1a-c** by applying the literature procedure of Myers and coworkers [29], which uses ferric chloride, a large excess of iron chips, and concentrated hydrochloric acid. The unsaturated nitro compounds transform under the action of iron in hydrochloric acid into keto-oximes and further into ketones [20]. The interesting side products, 1-substituted-5-[(1,2-dioxo-2-phenyl)ethyl]imidazoles **5a-c**, were obtained and 1-methyl-5-[(1,2-dioxo-2-phenyl)ethyl]imidazole **5b** was isolated. Unlike the oxoethyl compounds **1a-c**, the dioxo compound crystallized easily and the vicinal diketone structure was confirmed with X-ray crystallography (Figure 1, Tables 1-4).

The transformation of nitroalkanes into carbonyl compounds can be brought about by a variety of methods. In

Scheme 1



nearly all cases the overall oxidation is due to the tautomeric capability of nitroalkane [30]. Thus tautomerization of nitroalkane **7**, in which the carbon linked to nitrogen is at the oxidation level of an alcohol, leads to the *aci*-nitro compound **8**. In this case the carbon is at the oxidation level of a carbonyl group, and cleavage of the carbon-nitrogen bond, by either hydrolytic means (with or without prior reduction to an imine) or by oxidative reaction, leads to the formation of the carbonyl compound **9** (Scheme 2). Alternatively, the formation of the salt of a nitroalkane on treatment of the latter with base leads to the formation of the resonance-stabilized nitronate anion, **10**. The major resonance contributor is

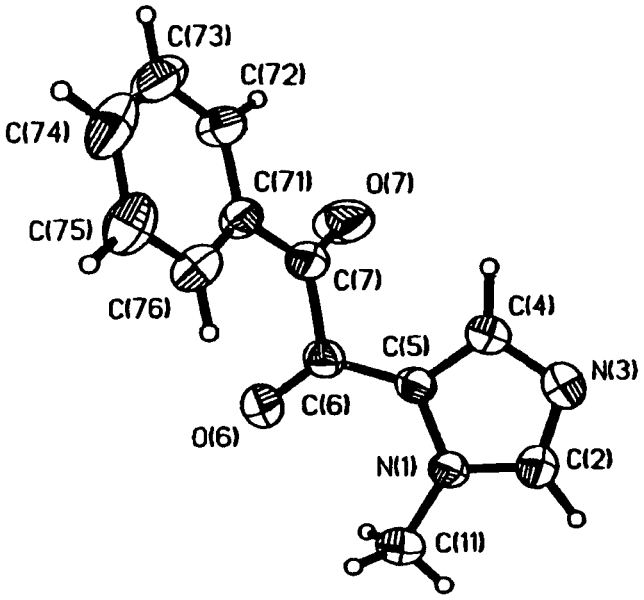


Figure 1. Molecular structure of **5b**: Selected bond lengths (Å) and bond angles (°): N1-C2 1.342 (2), N1-C5 1.384 (2), N3-C2 1.322 (2), N3-C4 1.354 (2), C5-C4 1.365 (2), C5-C6 1.438 (2), C6-O6 1.222 (2), C6-C7 1.530 (2), C7-O7 1.212 (2), C7-C71 1.475 (2); N1-C2-C5 106.3 (2), N1-C2-N3 112.6 (2), C2-N3-C4 104.8 (2), N3-C4-C5 111.1 (2), C4-C5-N1 105.2 (2), C5-N1-C2 106.3 (2).

Table 1

Crystal Data and Structure Refinement for 1-Methyl-5-[(1, 2-dioxo-2-phenyl)ethyl]imidazole **5b**.

Empirical formula	$C_{12}H_{10}N_2O_2$
Formula weight	214.22
Temperature	293 (2) K
Wavelength	0.71073 Å
Crystal system	Orthorhombic
Space group	Pbca
Unit cell dimensions	a = 12.078 (2) Å
	b = 7.567 (2) Å
	c = 23.577(5)Å
Volume	2154.8 (8) $Å^3$
Z	8
Density (calculated)	1.321 Mg/m^3
Absorption coefficient	0.092 mm^{-1}
F(000)	896
Crystal size	0.40 x 0.40 x 0.20 mm
Theta range for data collection	2.41 to 24.99 deg.
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	1894/0/176
Goodness-of-fit on F^2	0.812
Final R indices [I>2sigma (I)]	R1 = 0.0315, wR2 = 0.0520
R indices (all data)	R1 = 0.0820, wR2 = 0.0568
Extinction coefficient	0.0076 (3)
Largest diff. peak and hole	0.103 and -0.092 e $Å^{-3}$

obviously **10c**, in which the negative charge is born by the more electronegative oxygen atoms. Carbon-nitrogen

Table 2

Atomic Coordinates (x 10^4) and Equivalent Isotropic Displacement Parameters (x 10^3) for **5b**. U (eq) is Defined as one Third of the Trace of the Orthogonalized Uij Tensor.

	x	y	z	U (eq)
O (6)	4018 (1)	-1825 (2)	3833 (1)	70 (1)
O (7)	6626 (1)	-2163 (2)	3912 (1)	93 (1)
N (1)	4119 (1)	1416 (2)	4541 (1)	45 (1)
N (3)	5578 (1)	3183 (2)	4599 (1)	68 (1)
C (2)	4548 (2)	2896 (3)	4765 (1)	57 (1)
C (4)	5825 (2)	1794 (3)	4260 (1)	57 (1)
C (5)	4946 (1)	672 (2)	4212 (1)	43 (1)
C (6)	4851 (2)	-922 (3)	3884 (1)	48 (1)
C (7)	5919 (2)	-1564 (3)	3603 (1)	56 (1)
C (11)	2996 (2)	756 (3)	4637 (1)	61 (1)
C (71)	6022 (2)	-1534 (2)	2980 (1)	50 (1)
C (72)	6967 (2)	-2235 (3)	2732 (1)	66 (1)
C (73)	7085 (2)	-2183 (3)	2151 (1)	82 (1)
C (74)	6279 (3)	-1454 (3)	1817 (1)	84 (1)
C (75)	5332 (2)	-774 (3)	2058 (1)	75 (1)
C (76)	5204 (2)	-808 (3)	2642 (1)	61 (1)

bond cleavage in the *aci*-nitro anion is due to the resonance form **10c**, which again leads to the formation of the carbonyl compound **9** (Scheme 2).

Synthetic methods for the preparation of carbonyl compounds from nitroalkanes involving only a hydrolytic step in the cleavage of **8** or the corresponding anion **10** are known as the Nef reaction.

In our work, 1-substituted-5-[(2-nitro-2-phenyl)ethyl]-imidazoles **3a-c** were transformed to the oxo compounds using the improved Nef reaction of Chikasita and coworkers [21], involving the addition of an aqueous solution of the sodium salts of the *aci*-nitro compounds **3a-c** to a two-phase solution of an acid and *n*-pentane. The original Nef reaction involves the solvolysis of alkali salts of *aci*-nitro compounds with aqueous or alcoholic acid solution, but the conversion of nitroalkane to oxo compound was found to give low yields due to an unusual instability of the carbonyl products in acid solution [31-32]. In the two-phase method [21], the product is transferred to pentane so that contact of the acid-sen-

Table 3

Bond Lengths [Å] and Angles [deg] for **5b**.

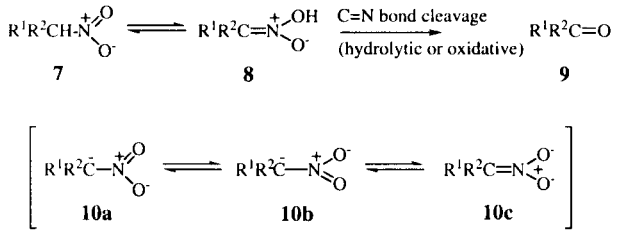
O(6) - C(6)	1.222 (2)	O(7) - C(7)	1.212 (2)
N(1) - C(2)	1.342 (2)	N(1) - C(5)	1.384 (2)
N(1) - C(11)	1.463 (2)	N(3) - C(2)	1.322 (2)
N(3) - C(4)	1.354 (2)	C(2) - H(2)	0.99 (2)
C(4) - C(5)	1.365 (2)	C(4) - H(4)	1.02 (2)
C(5) - C(6)	1.438 (2)	C(6) - C(7)	1.530 (2)
C(7) - C(71)	1.475 (2)	C(11) - H(11)	0.99 (2)
C(11) - H(12)	0.96 (2)	C(11) - H(13)	0.95 (2)
C(71) - C(76)	1.382 (2)	C(71) - C(72)	1.388 (2)
C(72) - C(73)	1.377 (3)	C(72) - H(72)	1.02 (2)
C(73) - C(74)	1.369 (3)	C(73) - H(73)	0.92 (2)
C (74) - C(75)	1.377 (3)	C(74) - H(74)	0.97 (2)
C(75) - C(76)	1.387 (3)	C(75) - H(75)	0.97 (2)
C(76) - H(76)	0.95 (2)	C(2) - N(1) - C(5)	106.3 (2)
C(2) - N(1) - C(11)	125.6 (2)	C(5) - N(1) - C(11)	128.0 (2)
C(2) - N(3) - C(4)	104.8 (2)	N(3) - C(2) - N(1)	112.6 (2)
N(3) - C(2) - H(2)	126.3 (11)	N(1) - C(2) - H(2)	121.0 (11)
N(3) - C(4) - C(5)	111.1 (2)	N(3) - C(4) - H(4)	122.0 (10)
C(5) - C(4) - H(4)	126.8 (10)	C(4) - C(5) - N(1)	105.2 (2)
C(4) - C(5) - C(6)	128.9 (2)	N(1) - C(5) - C(6)	125.8 (2)
O(6) - C(6) - C(5)	126.0 (2)	O(6) - C(6) - C(7)	118.3 (2)
C(5) - C(6) - C(7)	115.6 (2)	O(7) - C(7) - C(71)	123.1 (2)
O(7) - C(7) - C(6)	116.9 (2)	C(71) - C(7) - C(6)	119.9 (2)
N(1) - C(11) - H(11)	108.9 (11)	N(1) - C(11) - H(12)	111.5 (11)
H(11) - C(11) - H(12)	105 (2)	N(1) - C(11) - H(13)	107.8 (12)
H(11) - C(11) - H(13)	119 (2)	H(12) - C(11) - H(13)	104 (2)
C(76) - C(71) - C(72)	119.9 (2)	C(76) - C(71) - C(7)	121.2 (2)
C(72) - C(71) - C(7)	118.9 (2)	C(73) - C(72) - C(71)	119.5 (2)
C(73) - C(72) - H(72)	126.1 (10)	C(71) - C(72) - H(72)	114.4 (10)
C(74) - C(73) - C(72)	120.8 (2)	C(74) - C(73) - H(73)	118.0 (12)
C(72) - C(73) - H(73)	121.2 (12)	C(73) - C(74) - C(75)	120.2 (2)
C(73) - C(74) - H(74)	120.4 (11)	C(75) - C(74) - H(74)	119.4 (11)
C(74) - C(75) - C(76)	119.8 (2)	C(74) - C(75) - H(75)	121.8 (11)
C(76) - C(75) - H(75)	118.0 (11)	C(71) - C(76) - C(75)	119.9 (2)
C(71) - C(76) - H(76)	119.7 (11)	C(75) - C(76) - H(76)	120.4 (11)

Table 4

Anisotropic Displacement Parameters ($Å^2 \times 10^3$) for **5b**.
The Anisotropic Displacement Factor Exponent Takes the Form:
$-2\pi^2 [h^2 a^{*2} U_{11} + \ldots + 2 h k a^* b^* U_{12}]$

	U11	U22	U33	U23	U13	U12
O (6)	56 (1)	82 (1)	71 (1)	-22 (1)	2 (1)	-13 (1)
O (7)	64 (1)	14 4(2)	71 (1)	-9 (1)	-10 (1)	42 (1)
N (1)	38 (1)	54 (1)	43 (1)	-3 (1)	-1 (1)	0 (1)
N (3)	55 (1)	66 (1)	81 (1)	-14 (1)	0 (1)	-12 (1)
C (2)	55 (1)	60 (2)	57 (1)	-12 (1)	-4 (1)	3 (1)
C (4)	42 (1)	67 (1)	62 (1)	-7 (1)	2 (1)	-2 (1)
C (5)	37 (1)	54 (1)	39 (1)	1 (1)	0 (1)	0 (1)
C (6)	43 (1)	60 (1)	41 (1)	-2 (1)	-2 (1)	-1 (1)
C (7)	44 (1)	67 (2)	56 (1)	-10 (1)	-5 (1)	8 (1)
C (11)	44 (1)	73 (2)	68 (2)	-3 (2)	10 (1)	-1 (1)
C (71)	51 (1)	47 (1)	52 (1)	-8 (1)	7 (1)	2 (1)
C (72)	57 (1)	71 (2)	70 (2)	-14 (1)	17 (1)	1 (1)
C (73)	86 (2)	77 (2)	82 (2)	-22 (2)	42 (2)	-11 (2)
C (74)	134 (3)	63 (2)	55 (2)	-12 (2)	27 (2)	-23 (2)
C (75)	105 (2)	62 (2)	58 (2)	0 (1)	1 (1)	6 (2)
C (76)	73 (2)	55 (1)	56 (2)	-5 (1)	10 (1)	9 (1)

Scheme 2



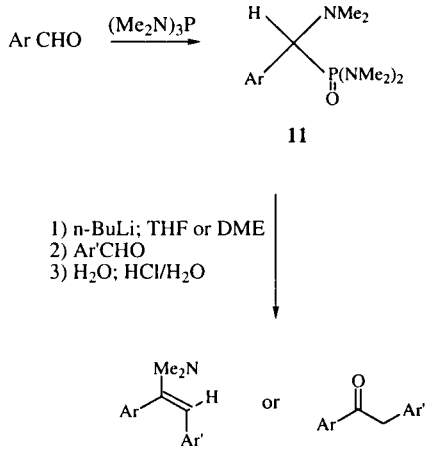
sitive product with the acid is avoided and yields are moderate or good. In the present work, pentane was replaced by hexane to assist the isolation process. This did not significantly affect the yields or the rate of the reaction.

A great number of oxidizing agents effect the conversion of an alcohol to a carbonyl compound. The susceptibility of aldehydes to further oxidation narrows the choice of reagents for the oxidation of primary alcohols, in good yield; if the alcohol group is a part of a complex molecule that is sensitive to acidic or basic reagents, then the choice of effective oxidant is narrowed still further. The majority of oxidation methods for the preparation of carbonyl compounds from corresponding alcohols utilize metal compounds as oxidizing agents, and the largest group of these are derived from chromium.

Our choice for oxidation of 1-substituted-5-[(2-hydroxy-2-phenyl)ethyl]imidazoles **4a-c** was chromium trioxide in glacial acetic acid [33-35], which gave rise the target products **1a-c** in moderate to good yields. Chromium trioxide is not appreciably soluble in acetic acid, therefore it was dissolved into 80% aqueous acetic acid, which enhanced the solubility.

An alternative approach to the transformation of nitroalkenes **2** and nitroalkanes **3** or the oxidation of hydroxyalkanes **4** for the preparation of oxoethanes **1** is to utilize an *umpolung* reagent. The reaction between the arylaldehydes and hexamethylphosphorous triamide leads to the *umpolung* intermediates [aryl(dimethylamino)methyl]phosphonic bis(dimethylamides) **11**. The intermediate is easily deprotonated by *n*-butyllithium in 1,2-dimethoxyethane or tetrahydrofuran and condenses with arylaldehydes to afford enamines or deoxybenzoins in fair to good yields (Scheme 3) [36].

Scheme 3



In the present work, the reaction between benzaldehyde and hexamethylphosphorous triamide was catalyzed with dimethylamine hydrochloride, and the *umpolung* intermediate **11** that was produced was deprotonated and allowed to react with imidazolecarboxaldehydes **6a-c** in tetrahydrofuran (Scheme 1). According to the literature [36], use of a catalyst has no effect on the yield of the intermediate. However, in this work the use of a catalyst increased the yield of diamide **11** from 51% to 79%. The pH had to be carefully maintained to get maximum final product. Despite several attempts, the yields of final product were moderate or low, but the products were pure, which is an important benefit in imidazole preparation. This reaction showed clearly that the introduction of the imidazole moiety in a later step gave purer compounds than did the formation of the imidazole at the outset.

In conclusion, the reduction of nitroethenes **2a-c**, using ferric chloride and the large excess of iron chips with concentrated hydrochloric acid, gave the best yields for **1a** and **b** (R = Bn or Me). The interesting side products, 1-substituted-5-[(1,2-dioxo-2-phenyl)ethyl]imidazoles **5a-c** were crystallized easily, especially when R = Me. The improved Nef reaction gave moderate yields for **1a-c**, the products were pure after evaporation at its best, but often a mixture of the product, the unreacted starting

material or side products was also found. The reaction of benzaldehyde with hexamethylphosphorous triamide and further with imidazolecarboxaldehydes **6a-c** gave the following advantages: the synthesis required less steps than in the other methods, and when the intermediate was purified by column chromatography, the final product was obtained in pure form.

Altogether, the benzyl-substituted oxoethanes were usually obtained in best yields and they were easier to handle than the methyl derivatives or unsubstituted oxoethanes. The preparation of methyl-substituted oxoethanes **1b** from nitroethenes **2b** and **3b** did not, however, differ substantially from that of the benzyl-substituted compound in either yield or ease of handling, and the oxidation of hydroxyethanes **4a-c** gave exceptionally high yields for 1*H*-5-[(2-oxo-2-phenyl)ethyl]-imidazole **1c**.

EXPERIMENTAL

Melting points were determined with a Büchi 510 melting point apparatus and are uncorrected. The ^{1}H nmr and ^{13}C nmr spectra were recorded on a Bruker AM 250 MHz spectrometer using tetramethylsilane as internal standard for proton spectra. The ir spectra were measured with a Nicolet 20 SXC FTIR spectrometer. Low resolution mass spectra were measured with a Jeol JMS D300 mass spectrometer equipped with Windows-based software: The Schrader System. Elemental compositions of molecular ions were determined with Bruker BioApex 47e Fourier transform ion cyclotron resonance mass spectrometer using broadband mode. Elemental analysis were made with Carlo Erba 1106 CHN + O Analyzer.

The Preparation of the Compounds.

Preparation of (1*R*)-5-[(2-oxo-2-phenyl)ethyl]imidazoles **1a-c** from the Nitroethenes **2a-c**.

A mixture of (1*R*)-5-[(2-nitro-2-phenyl)ethenyl]imidazole **2a, b**, or **c**, (0.02 mole) iron chips (0.15 mole, 8.4 g), ferric chloride hexahydrate (0.4 g), and water (148 ml) was heated to 100°. Concentrated hydrochloric acid (40 ml) was added dropwise and the reaction mixture was refluxed for three to five hours. After cooling to room temperature the mixture was extracted with chloroform, the organic layer was washed with 10% aqueous sodium bicarbonate and water, dried over magnesium sulfate, and the solvent was removed under reduced pressure. After column chromatography (silica gel; methanol:chloroform) 4.2 g (75%) of **1a**, 2.4 g (72%) of **1b**, and 1.0 g (28%) of **1c** was obtained. In addition, especially in the case of **1b**, 1-methyl-5-[(1,2-dioxo-2-phenyl)ethyl]imidazole **5b** was crystallized easily. The structure was confirmed with X-ray crystallography.

Crystallographic data were collected on a Nicolet R3m diffractometer, and the structure was solved and refined with full matrix least-squares analysis using SHEL86 [G. M. Sheldrick, *Acta Crystallogr.*, **A 46**, 467 (1990)] and SHELXL93 (G. M. Sheldrick, "SHELXL93, Program for the Refinement of Crystal Structures", University of Göttingen, Germany, 1993).

Crystallographic summary: $C_{12}H_{10}N_2O_2$, M_r = 214.22, Orthorhombic, Pbca, a = 12.078 (2), b = 7.567 (2), c = 23.577 (5) Å, V = 2154.8 (6) Å^3, Z = 8, D_c = 1.321 g/cm^3, MoK_α, radiation, λ = 0.71073 Å, μ = 0.09 mm^{-1}, F(ooo) = 896, T = 293 K, conventional R(F) = 0.0315 for 894 unique reflections I) 2σ(I) and wR(F^2) = 0.0568 for all 1894 unique data.

From the Nitroethyl Compounds **3a-c**.

To a solution of sodium hydroxide (20.0 mmoles, 0.8 g) in absolute ethanol (10 ml) was added a solution of 1-substituted-5-[(2-nitro-2-phenyl)ethyl]imidazole **3a, b**, or **c** (5.0 mmoles) in 10 ml of absolute ethanol dropwise at room temperature under nitrogen. After stirring for 5 minutes the solvent was removed under reduced pressure at room temperature. Water (20 ml) was added to the residue and the solution was added dropwise to a mixture of sulfuric acid (2.5 ml of concentrated sulfuric acid in 24 ml of water) and hexane (20 ml) at room temperature. Stirring was continued until the starting material disappeared. The mixture was neutralized with saturated sodium bicarbonate and methylene chloride was added. The organic layer was separated and the aqueous layer was extracted with methylene chloride. The organic layers were combined and washed with water and dried over sodium sulfate. Filtration through silica gel gave 60% yield of clean compound **1a**, 50% of **1b**, and 46% of **1c**.

From Hydroxyethylimidazoles **4a-c**.

(1*R*)-5-[(2-hydroxy-2-phenyl)ethyl]imidazoles **4a, b** or **c** (R = Bn, Me, H) were prepared in good yields in our laboratory.

To a solution of (1*R*)-5-[(2-hydroxy-2-phenyl)ethyl]imidazoles **4a, b**, or **c** (6.4 mmoles, 1.9 g) in glacial acetic acid (1.8 ml) was added dropwise under vigorous stirring chromic oxide (5.0 mmoles, 0.5 g) in acetic acid (80%, 1.8 ml), while the temperature of the reaction mixture was kept under 50°. The mixture was allowed to stand at room temperature for 24 hours and then it was extracted first with 10 ml, then two times with 5 ml of toluene, the combined organic layers were washed with aqueous sodium bicarbonate and water and dried over sodium sulfate. After evaporation of the solvent 57% of **1a**, 30% of **1b** and 72% of **1c** was obtained.

Preparation of Oxoethylimidazoles Starting from Benzaldehyde.

Benzaldehyde was distilled before it was used. Hexamethylphosphorous triamide (97%) was used as received from Aldrich. Tetrahydrofuran was distilled from sodium-benzophenone ketal. Dimethylamine hydrochloride was dried in vacuum. The reactions were carried out under nitrogen.

Preparation of *N,N'*-dimethyl-*P*-[phenyl(dimethylamino)-methyl]phosphonic diamide **11**.

To a stirred solution of benzaldehyde (42.0 mmoles, 4.2 ml) and dimethylamine hydrochloride (4.4 mmoles, 0.36 g) in 30 ml of tetrahydrofuran was added dropwise hexamethylphos-

phorous triamide (42.3 mmoles, 7.7 ml) at room temperature. After stirring for 50 hours the solvent was removed under reduced pressure. A pale yellow precipitate was purified by column chromatography (silica gel; ether:methanol; 95:5) and 9.0 g (79%) of the white clean product was obtained, mp 109-112°. Without the use of the catalyst, dimethylamine hydrochloride, the yield was 51%. The spectral data of the compound **11** were: ^{1}H nmr: δ_H (250 MHz, deuteriochloroform): 2.23 (s, 6H, CHN(CH_3)$_2$, 2.28 (d, 6H, PN(CH_3)$_2$), 2.75 (d, 6H, PN(CH_3)$_2$), 3.83 (d, 1H, CH), 7.32-7.50 (d, 5H, Ph); ^{13}C nmr: δ_C (250 MHz, deuteriochloroform): 36.14, 36.61 (q, PN(CH_3)$_2$), 42.90 (q, CN(CH_3)$_2$), 65.09 (d, CH), 127.76-131.57 (d, aromatic C, Ph).

Anal. Calcd. for $C_{13}H_{24}N_3OP$: C, 57.99; H, 8.92; N, 15.61. Found: C, 58.17; H, 9.09; N, 15.61.

Preparation of (1*R*)-5-[(2-oxo-2-phenyl)ethylimidazoles **1a-c**.

N,N'-Dimethyl-*P*-[phenyl(dimethylamino)methyl]phosphonic diamide (1.67 mmoles, 0.45 g) and dry tetrahydrofuran (15 ml) was cooled to 0° in ice bath and a solution of *n*-butyllithium (1.94 mmoles, 1.24 ml, 1.6 M in hexane) was added dropwise under vigorous stirring. Stirring of the yellow solution was continued for 30 minutes at 0° and imidazolecarboxaldehyde **6a**, **b**, or **c** (1.61 mmoles) in tetrahydrofuran (2.5 ml) was added dropwise. The mixture was allowed to warm to room temperature and it was stirred for one hour and then quenched with aqueous hydrochloric acid (5%, 8 ml). The mixture was extracted with ether (10 ml), which was rejected, followed by extraction with chloroform (three times with 10 ml), the combined chloroform phases were washed with water and dried over sodium sulfate. After evaporation of the solvent, clean products were obtained; 0.2 g (45%) of **1a**, mp 148-152°, 0.03 g (10%) of **1b** and 0.02 g (8%) of **1c**.

Compound **1a**, 1-benzyl-5-[(2-oxo-2-phenyl)ethyl]imidazole, was obtained as pale brown powder; ir (chloroform): ν 3010, 2980, 1950, 1850, 1670 (CO), 1580, 1500, 1480, 1450, 1350, 1250, 1130, 1100, 980, 890, 670, 645 cm^{-1}; ^{1}H nmr: δ_H (250 MHz; deuteriochloroform): 4.27 (s, 2H, CH_2CO), 5.34 (s, 2H, CH_2Ph), 7.19-7.66 (m, 10H Ph-H), 7.89 (s, 1H, imid. C(4)H), 7.92 (s, 1H, imid. C(2)H); ^{13}C nmr: δ_C (250 MHz, deuteriochloroform): 34.20 (t, CH_2CO), 53.93 (t, CH_2Ph), 121.88 (d, C(4)), 127.57-129.33 (m, Ph), 133.19 (s, Ar-C), 135.32 (s, C(5)), 136.30 (d, C(2)), 193.83 (s, CO); ms: m/z (relative intensity) 276 (4) M$^{+\cdot}$, 186 (16), 135 (14), 134 (100), 105 (42), 91 (82), 77 (33), 65 (17), 51 (17), 45 (18), 44 (37), 42 (21), 36 (15).

Anal. Calcd. for $C_{18}H_{16}N_2O$: C, 78.16; H, 5.80; N, 10.14; M$^{+\cdot}$ 276.1262. Found: C, 78.44; H, 5.61; N, 9.72; M$^{+\cdot}$ 276.1254.

Compound **1b**, 1-methyl-5-[(2-oxo-2-phenyl)ethyl]imidazole, was obtained as a brown oil; ir (chloroform): ν 3020, 2930, 2860, 1950, 1900, 1680 (CO), 1660, 1600, 1580, 1450, 1370, 1210, 1140, 910, 850, 780, 710 cm^{-1}; ^{1}H nmr: δ_H (250 MHz; deuteriochloroform): 3.82 (s, 2H, CH_2CO), 3.95 (s, 3H, CH_3), 7.09-7.68 (m, 5H, Ph-H), 7.93 (s, 1H, C(4)H), 7.97 (s, 1H, C(2)H); ^{13}C nmr: δ_C (250 MHz, deuteriochloroform): 29.57 (q, CH_3), 42.57 (t, CH_2CO), 122.18 (d, C(4)), 127.18-131.27 (m, Ph), 135.23 (s, C(5)), 140.28 (d, C(2)), 193.80 (s, CO); ms: m/z (relative intensity) 186 (31), 122 (23), 105 (100), 77 (54), 51 (19), 28 (12).

Anal. Calcd. for $C_{12}H_{12}N_2O$: C, 72.00; H, 6.00; N, 14.00; M$^{+\cdot}$ 200.0944. Found: C, 71.95; H, 5.61; N, 14.08; M$^{+\cdot}$ 200.0943.

Compound **1c** 1*H*-5(4)-[(2-oxo-2-phenyl)ethyl]imidazole was also obtained as a brown oil; ir (chloroform): ν 3010, 2950, 2860, 1725 (CO), 1670, 1600, 1580, 1490, 1465, 1380, 1280, 1180, 1075, 775, 730 cm^{-1}; ^{1}H nmr: δ_H(250 MHz, deuteriochloroform): 4.21 (s, 2H, CH_2CO), 7.26-7.53 (m, 5H, Ph-H), 7.91 (s, 1H, C(5/4)H), 7.99 (s, 1H, C(2)H); ^{13}C nmr: δ_C (250 MHz, deuteriochloroform): 29.47 (t, CH_2CO), 128.25-132.30 (m, Ph), 132.49 (d, C(5/4)), 134.85 (s, C, Ar-C), 191.08 (s, CO); ms: m/z (relative intensity) 186 (3) M$^{+\cdot}$, 149 (20), 134 (25), 121 (39), 105 (100), 91 (19), 77 (68), 71 (14), 57 (16), 55 (11), 51 (25), 50 (11), 43 (17), 41 (13).

Anal. Calcd. for $C_{11}H_{10}N_2O$: M$^{+\cdot}$ 186.0788. Found: M$^{+\cdot}$ 186.0780. Satisfactory elemental analysis results for **1c** were not obtained probably, because the compound took moisture from the environment.

The dioxo compound, 1-methyl-5-[(1,2-dioxo-2-phenyl)-ethyl]imidazole **5b** was obtained as yellow crystals; ir (chloroform): ν 1680, 1650 (CO) cm^{-1}; ^{1}H nmr: δ_H (250 MHz, deuteriochloroform): 4.07 (s, 3H, CH_3), 7.48-7.98 (m, Ph-H), 7.99 (s, C(4)H), 8.02 (s, C(2)H); ^{13}C nmr: δ_C (250 MHz, deuteriochloroform): 34.75 (q, CH_3), 127.53-134.78 (m, Ar-C), 143.55 (d, imid. C(4)), 144.92 (d, imid. C(2)), 183.42 (s, CO); ms: m/z (relative intensity): 214 (4) M$^{+\cdot}$, 186 (31), 122 (23), 109 (40), 105 (100), 77 (54), 51 (19), 28 (12).

Anal. Calcd. for $C_{12}H_{10}N_2O_3$: C, 67.82; H, 4.67; N, 13.08; M$^{+\cdot}$ 214.0737. Found: C, 66.55; H, 4.84; N, 12.86; M$^{+\cdot}$ 214.0729.

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