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Dedicated to Professor Luigi Panizzi on the occasion of his seventieth birthday

Oxidation of fully substituted imidazoles **1** by singlet oxygen gives in good yield fully substituted 2-hydroperoxy-2*H*-imidazoles **2**. Reduction of **2** by triphenylphosphine leads to 2-hydroxy-2*H*-imidazoles **3**. Limitations of the methods are reported.

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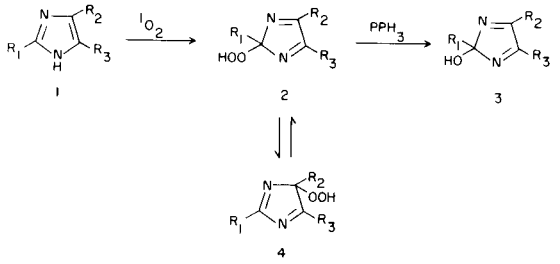
In the course of our studies on the mode of the oxidative destruction of imidazole rings by singlet oxygen, we observed that 2-methyl-4,5-diphenylimidazole (**1a**), by methylene blue-sensitized photooxygenation at -15°, gives 2-hydroperoxy-2-methyl-4,5-diphenyl-2*H*-imidazole (**2a**) as an isolable intermediate. Reduction of **2a**, *in situ*, leads to 2-hydroxy-2-methyl-4,5-diphenyl-2*H*-imidazole (**3a**) (1).

Compounds **2a** and **3a** represent the first examples of 2-hydroperoxy- and 2-hydroxy-2*H*-imidazoles. Therefore, in order to provide a useful method for the preparation of both the new classes of 2*H*-imidazole compounds and to examine the limitations of the methods, we have extended the synthetic process to other substituted imidazoles.



The dye-sensitized photooxygenations must be accomplished under strictly anhydrous conditions at -15° in that, as observed for **2a** (1), at room temperature the 2-hydroperoxy-2*H*-imidazoles **2** and the 4-hydroperoxy-4*H*-imidazoles **4** co-exist in equilibrium with the latter compounds readily undergoing irreversible hydrolysis.

As shown in Table I, the photooxidation has a wide range of applicability even though attempts to obtain 2-aryl-substituted or 2-unsubstituted 2-hydroperoxy-2*H*-imidazoles in good yield failed. Infact, by dye-sensitized photooxidation at -15°, 2,4,5-triphenylimidazole behaved essentially the same as at 18° (2-4), and 4,5-diphenylimidazole gave a very complex mixture of compounds. In all other examined cases the oxidation proceeds with good yields and the crude products **2b-g** (which can be stored at -15°) are pure expect for the presence of moderate amounts of 4-hydroperoxy-4*H*-imidazoles **4**. The composition of the reaction mixtures was deduced on the basis of their ir spectra (no C=O absorption was present) and of the integration, in the ^{1}H nmr spectra, of the α-hydrogen signals of R_1 for **2** and **4** (Table II and III). Structures **2** were assigned on the basis of active oxygen determination (Table I) and by comparison of the ir and ^{1}H nmr spectra (Table II) with those of **2a** (1).

Subsequent reduction of the hydroperoxides **2** by triphenylphosphine (5) to obtain hydroxides **3** can be conveniently carried out using directly the photooxidation solution. Hydroxides **3** were isolated by silica gel chromatography. In this way, as shown in Table IV, **3a-e** are obtained in good yield and the structures were assigned on the basis of elemental analyses and by comparison of ir and ^{1}H nmr spectra, reported in Table V, with those of **3a** (1). The hydroxides **3f** and **3g** were identified in the reaction mixture by ^{1}H nmr, however, attempts to obtain them in a pure state by chromatographic methods failed owing to their hydrolytic reactivity.

EXPERIMENTAL

Melting points are uncorrected. Ir spectra were recorded on a Perkin Elmer 399 spectrophotometer; ^{1}H nmr on a Perkin Elmer R 12 A and on a Bruker W H 270 spectrometer with TMS as an internal standard. Chloroform used in the oxidation reactions was anhydrous and ethanol free. Silica gel 0.05-0.20 mm (Merck) and light petroleum b.p. 30-50° were used for column chromatography.

General Procedure for the Preparation of the Hydroperoxides **2a-g**.

A solution of the imidazole (1 mmole) and methylene blue (8×10^{-3} mmoles) in dry chloroform (20 ml.) was irradiated with a halogen-superphot lamp (Osram 650 W). During the irradiation, dry oxygen was bubbled through the solution which was cooled at -15°. When the reaction was complete (^{1}H nmr), the solvent was removed *in vacuo* and the residue taken up with dry ether. The suspension was filtered to remove methylene blue and the solution evaporated. All the procedure was carried out at -15°. The crystalline residue (Table I) contains 5-20% of **4a-g**.

General Procedure for the Preparation of Hydroxides **3a-e**.

To the photooxidation solution triphenylphosphine (1.2

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Table I

2-Hydroperoxy-2*H*-imidazoles (**2**)

Compound	R_1	R_2	R_3	Reaction time (a)	Yield % (b)	M.p. °C (c)	Empirical Formula	Active Oxygen % Calcd.	Found
2a (d)	CH_3	C_6H_5	C_6H_5	4	95	94	$C_{16}H_{14}N_2O_2$	6.01	5.6
2b	n-C_3H_7	C_6H_5	C_6H_5	4	95	89	$C_{18}H_{18}N_2O_2$	5.43	5.1
2c	n-C_6H_{13}	C_6H_5	C_6H_5	4	90	58	$C_{21}H_{24}N_2O_2$	4.75	4.4
2d	i-C_3H_7	C_6H_5	C_6H_5	2	90	96	$C_{18}H_{18}N_2O_2$	5.43	5.0
2e	C_6H_5-CH_2	C_6H_5	C_6H_5	2	90	125	$C_{22}H_{18}N_2O_2$	4.67	4.3
2f	CH_3	CH_3	C_6H_5	3	80	92	$C_{11}H_{12}N_2O_2$	7.83	7.5
2g	C_6H_5-CH_2	CH_3	C_6H_5	4	85	130	$C_{17}H_{16}N_2O_2$	5.71	5.4

(a) Hours required for reaction at -15°. (b) Calculated on the basis of ^{1}H nmr spectrum of the reaction mixture. (c) Not purified by recrystallization from any solvents. Melt with decomposition. (d) Reported for sake of completeness [see reference (1)].

Table II

Spectral Data of 2-Hydroperoxy-2*H*-imidazoles (**2**)

Compound	R_1	R_2	R_3	^{1}H Nmr Spectrum δ (ppm) (deuteriochloroform)	Ir Spectrum cm^{-1} (chloroform)
2a (a)	CH_3	C_6H_5	C_6H_5	1.87 (3H, s, CH_3), 7.30-7.60 (10H, m, 2 x C_6H_5), 11.85 (1H, bs, OOH) (b)	2820 (OOH· ·N) 1610, 860
2b	n-C_3H_7	C_6H_5	C_6H_5	0.91 (3H, t, CH_3), 1.35-1.51 (2H, m, C-CH_2-C), 2.15-2.30 (2H, m, O-C-CH_2), 7.26-7.59 (10H, m, 2xC_6H_5), 12.25 (1H, bs, OOH) (c)	2820, 1610, 860
2c	n-C_6H_{13}	C_6H_5	C_6H_5	0.50-1.70 (11H, m, C_5H_{11}), 2.20-2.32 (2H, m, O-C-CH_2), 7.30-7.60 (10H, m, 2 x C_6H_5), 12.30 (1H, bs, OOH) (c)	2820, 1610, 860
2d	i-C_3H_7	C_6H_5	C_6H_5	1.06 (6H, d, J = 7 Hz, 2xCH_3), 2.65 (1H, h, J = 7 Hz, CH), 7.30-7.60 (10H, m, 2 x C_6H_5), 12.27 (1H, bs, OOH) (b)	2820, 1610, 862
2e	C_6H_5-CH_2	C_6H_5	C_6H_5	3.65 (2H, s, CH_2), 7.00-7.35 (15H, m, 2 x C_6H_5) 12.25 (1H, bs, OOH) (b)	2820, 1610, 858
2f	CH_3	CH_3	C_6H_5	1.67 (3H, s, O-C-CH_3), 2.48 (3H, s, =C-CH_3), 7.35-7.65 (5H, m, C_6H_5), 12.23 (1H, bs, OOH) (b)	2820, 1630, 1605, 860
2g	C_6H_5-CH_2	CH_3	C_6H_5	2.22 (3H, s, CH_3), 3.46 (2H, s, CH_2), 7.13 (5H, s, C_6H_5), 7.35-7.65 (5H, m, C_6H_5), 12.30 (1H, bs, OOH) (b)	2820, 1630 1605, 860

(a) Reported for sake of completeness [see reference (1)]. (b) Data obtained at 60 MHz. (c) Data obtained at 270 MHz.

Table III

Characteristic ^{1}H Nmr Spectral Data of 4-Hydroperoxy-4*H*-imidazoles (**4**)
δ (ppm - deuteriochloroform)

Compounds	R_1	R_2	R_3	CH_3-C=N	CH_2-C=N	CH-C=N	CH_3-C(=N)-O-C	
4a (a,b)	CH_3	C_6H_5	C_6H_5	2.35 (s)				
4b (c)	n-C_3H_7	C_6H_5	C_6H_5		2.46-2.60 (m)			
4c (c)	n-C_6H_{13}	C_6H_5	C_6H_5		2.42-2.69 (m)			
4d (b)	i-C_3H_7	C_6H_5	C_6H_5			2.81 (h)		
4e (b)	C_6H_5-CH_2	C_6H_5	C_6H_5		4.25 (s)			
4f (b)	CH_3	CH_3	C_6H_5	2.36 (s)			1.55 (s)	
4g (b)	C_6H_5-CH_2	CH_3	C_6H_5		4.00 (s)		1.59 (s)	

(a) Reported for sake of completeness see reference (1). (b) Data obtained at 60 MHz. (c) Data obtained at 270 MHz.

Table IV

2-Hydroxy-2*H*-imidazoles (**3**)

Compound	R_1	R_2	R_3	Yield % (a)	M.p. °C (b)	Empirical Formula	Elemental Analyses Calcd. % C	H	N	Found % C	H	N
3a (c)	CH_3	C_6H_5	C_6H_5	95	160-162	$C_{16}H_{14}N_2O$	76.78	5.64	11.19	76.66	5.56	11.26
3b	n-C_3H_7	C_6H_5	C_6H_5	75	126-128	$C_{18}H_{18}N_2O$	77.67	6.52	10.07	77.32	6.48	10.02
3c	n-C_6H_{13}	C_6H_5	C_6H_5	70	107-109	$C_{21}H_{24}N_2O$	78.71	7.55	8.74	78.65	7.67	8.50
3d	i-C_3H_7	C_6H_5	C_6H_5	70	185-187	$C_{18}H_{18}N_2O$	77.67	6.52	10.07	77.48	6.39	9.84
3e	C_6H_5-CH_2	C_6H_5	C_6H_5	75	132-134	$C_{22}H_{18}N_2O$	80.95	5.56	8.58	80.47	5.32	8.70

(a) Yield of isolated product based on imidazole **1** employed. (b) Not purified by recrystallization from any solvents. (c) Reported for sake of completeness see reference (1).

Table V

Spectral Data of 2-Hydroxy-2*H*-imidazoles (**3**)

Compound	R_1	R_2	R_3	^{1}H Nmr Spectrum δ (ppm) (deuteriochloroform) (a)	Ir Spectrum cm^{-1} (chloroform)
3a (b)	CH_3	C_6H_5	C_6H_5	1.80 (3H, s, CH_3), 6.10 (1H, bs, OH), 7.35-7.65 (10H, m, 2 x C_6H_5)	3600, 1610
3b	*n*-C_3H_7	C_6H_5	C_6H_5	0.84 (3H, t, CH_3), 1.15-1.75 (2H, m, C-CH_2-C) 1.95-2.25 (2H, m, O-C-CH_2), 5.90 (1H, bs, OH) 7.35-7.65 (10H, m, 2 x C_6H_5)	3600, 1610
3c	*n*-C_6H_{13}	C_6H_5	C_6H_5	0.50-1.70 (11H, m, C_5H_{11}), 1.85-2.35 (2H, m, O-C-CH_2), 6.00 (1H, bs, OH), 7.35-7.65 (10H, m, 2 x C_6H_5)	3600, 1610
3d	*i*-C_3H_7	C_6H_5	C_6H_5	1.02 (6H, d, J = 7 Hz, 2 x CH_3), 2.40 (1H, h, J = 7 Hz, CH), 4.80 (1H, bs, OH), 7.35-7.65 (10H, m, 2 x C_6H_5)	3600, 1610
3e	C_6H_5-CH_2	C_6H_5	C_6H_5	3.58 (2H, s, CH_2), 6.24 (1H, bs, OH), 7.10 (5H, s, C_6H_5), 7.15-7.45 (10H, m, 2 x C_6H_5),	3600, 1610
3f	CH_3	CH_3	C_6H_5	1.65 (3H, s, O-C-CH_3), 2.44 (3H, s, =C-CH_3), 6.05 (1H, bs, OH) (c)	3600, 1630 1610
3g	C_6H_5-CH_2	CH_3	C_6H_5	2.17 (3H, s, CH_3), 3.45 (2H, s, CH_2), 5.82 (1H, bs, OH) (c)	3595, 1632 1605

(a) Data obtained at 60 MHz. (b) Reported for sake of completeness see reference (1). (c) The chemical shift of the aromatic hydrogens could not be determined due to presence of triphenylphosphine oxide.

mmoles) was added at -15°. After 15 minutes the solvent was removed *in vacuo* and the residue was chromatographed on silica gel (25 g.). Elution with light petroleum/ether (3:7) gave hydroxides **3a-e** in pure form (Table IV).

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