Nitroisoxazoles by Manganese(IV) Oxide Oxidation of Nitro-4,5-dihydroisoxazoles

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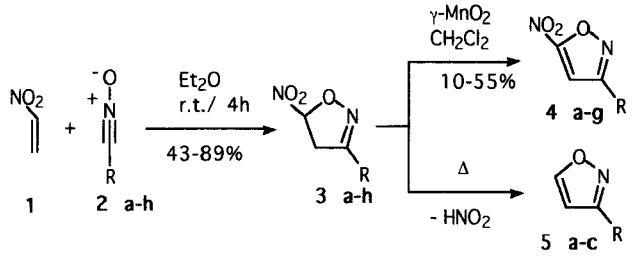
Aryl and alkyl substituted 3- and 5-nitroisoxazole derivatives were prepared from the appropriate 3- and 5-nitro-4,5-dihydroisoxazoles using manganese(IV) oxide as oxidizing agent. Some of the 3-nitro-4-substituted isoxazoles were prepared directly by reaction of 2-substituted 3-bromo-1-halopropanes with sodium nitrite.

Among the derivatives of isoxazoles, nitro compounds form a class of well known interest in organic and medicinal chemistry.[1] Boyer's monograph on nitroazoles deals specifically with the synthesis, reactivity and biological properties of 4-nitroisoxazoles as well as with the few reports concerning 3- and 5-nitroisoxazole derivatives.[2]

As our group is interested in the synthesis[3] and the antibacterial activity[4] of nitroisoxazoles we addressed our work toward: (1) a new synthesis of the 5-nitro-3-substituted isoxazoles; (2) a simple and general synthesis of the unknown 3-nitro-4-substituted isoxazoles.

Regarding the first point, 5-nitro-3-phenylisoxazole **(4a)** is the only known compound in its class; it has been obtained by the 1,3-cycloaddition of benzonitrile oxide to 1-chloro-2-nitroethylene, a synthetic equivalent of the unknown nitroacetylene, but no attempt to extend this original reaction to a general synthetic method has been reported.[5]

We however turned to an alternative, classic procedure, depicted in Scheme 1, where the 1,3-dipolar cycloaddition of nitrile oxides **2a–h** to nitroethylene **(1)**, followed by the oxidation of the 5-nitro-4,5-dihydroisoxazole cycloadducts **3a–h**, gave the 5-nitroisoxazoles **4a–g**.



2–5	R	2–5	R
a	Ph	**e**	Me
b	4-$NO_2C_6H_4$	**f**	*t*-Bu
c	4-$MeOC_6H_4$	**g**	CO_2Et
d	Pyridin-3-yl	**h**	H

Scheme 1

The first step is well known, and the 5-nitro-4,5-dihydroisoxazoles **3a–c** have already been described;[6] the regioselectivity of these cycloadditions is well known, and leads only to the 5-nitro regioisomer.[7]

The oxidation of such compounds has not been described; however, easy thermal elimination of nitrous acid has been described[8,9] and the thermal conversion of compounds **3a–c** to **5a–c** has been reported.[6]

The oxidation of 4,5-dihydroisoxazoles has generally been performed by means of mild reagents such as manganese(IV) oxide,[10] DDQ,[11] or nitrogen dioxide.[12] The latter was employed in the aromatization of some 3,5-diaryl-4-nitroisoxazoles but proved unsuccessful with the 5-nitro analogues.[12]

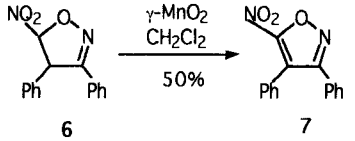
With the use of activated manganese(IV) oxide we were able to aromatize the 5-nitro compounds **3a–g**, thus obtaining the 5-nitroisoxazoles **4a–g** with yields of practical interest in some cases.

The following conditions were strictly required for the oxidation of the compounds **3**. Manganese(IV) oxide had to be activated the the γ-form according to Fatiadi's "method B" (absence of solvent, 130 °C, 18 h).[13] Different procedures, including azeotropic distillation, gave a reagent the use of which resulted in unfractionable mixtures of oxidation compounds.

The ratio of activated manganese(IV) oxide to substrate of 10:1 w/w was determined by counterbalancing the requirements of the oxidation against the product recovery: at ratios $>>10$ we observed complete oxidation in a few minutes, but the recovery was poor; at ratios <10 we noted slow and incomplete oxidations.

The loss of nitrous acid became quantitatively relevant when the oxidation time was increased. The best results were achieved using halogenated solvents (chloroform, dichloromethane).

The reactions required anhydrous conditions in order to avoid the hydrolytic opening of the 4,5-dihydroisoxazoles ring catalyzed by manganese(IV) oxide.[14] Although the above conditions were respected, the oxidation of **3h** gave a complex, unfractionable mixture. On the other hand, when the method was applied to 5-nitro-3,4-diphenyl-4,5-dihydroisoxazole **(6)**, the corresponding 5-nitroisoxazole **7** was obtained in 50% yield (Scheme 2); this reaction failed when nitrogen dioxide was used as a dehydrogenating agent.[12]



Scheme 2

In conclusion, the method reported here for the synthesis of aryl and alkyl substituted 5-nitroisoxazoles is simple and general, although in some of the examples described, i.e. **4e,f**, the overall yields are far from being of practical interest.

Table 1. 3-Substituted 5-Nitro-4,5-dihydroisoxazole Derivatives **3d–h**

Products	Yield (%)	mp (°C) (solvent)	Molecular Formula[a] or Lit. mp (°C)	IR ν (cm^{-1})	^{1}H NMR ($CDCl_3$) δ, J (Hz)
3d	79	101 (EtOH)	$C_8H_7N_3O_3$ (193.2)	1600, 1590, 1560[b]	4.04 (d, 2H, J = 5.4), 6.32 (t, 1H, J = 5.4), 7.39–7.46 (m, 1H), 8.07–8.13 (m, 1H), 8.75 (dd, 1H, J = 4.8, 1.6), 8.85 (dd, 1H, J = 2.2, 0.7)[c]
3e	50	oil	$C_4H_6N_2O_3$ (130.1)	1555, 1360[d]	2.1 (s, 3H), 3.6 (d, 2H, J = 5), 6.1 (t, 1H, J = 5)
3f	67	36 (EtOH)	$C_7H_{12}N_2O_3$ (172.2)	1555, 1360[d]	1.25 (s, 9H), 3.6 (d, 2H, J = 5), 6.1 (t, 1H, J = 5)
3g	43	oil	$C_6H_8N_2O_5$ (188.1)	1730, 1610, 1570[d]	1.4 (t, 3H, J = 6), 3.85 (d, 2H, J = 5), 4.4 (q, 2H, J = 6), 6.3 (t, 1H, J = 5)
3h	89	oil	$C_3H_4N_2O_3$ (116.1)	3040, 1610, 1560[d]	3.7 (dd, 2H, J = 5, 2), 6.15 (t, 1H, J = 5), 7.5 (t, 1H, J = 2)

[a] Satisfactory elemental analyses (C, H, N ±0.4% from the theoretical value) were obtained.
[b] Nujol.
[c] Recorded at 200 MHz.
[d] Film.

Table 2. 3-Substituted 5-Nitroisoxazole Derivatives **4a–g**, **7**

Products	Yield (%)	mp (°C) (solvent)	Molecular Formula[a] or Lit. mp (°C)	IR ν (cm^{-1})	^{1}H NMR ($CDCl_3$) δ, J (Hz)
4a	40	128 (EtOH)	124–125[5]	3120, 1540, 1350[b,c]	7.35 (s, 1H), 7.5–8.0 (m, 5H)[b]
4b	55	182 (EtOH)	$C_9H_5N_3O_5$ (235.2)	3140, 3080, 1610, 1590, 1550, 1350[c]	7.45 (s, 1H), 8.1–8.45 (AA'BB' system, 4H)[d]
4c	26	130 (EtOH)	$C_{10}H_8N_2O_4$ (220.2)	3120, 1610, 1535, 1350[c]	3.85 (s, 3H), 7.25 (s, 1H), 6.9–7.8 (AA'BB' system, 4H)
4d	26	112 (EtOH)	$C_8H_5N_3O_3$ (191.2)	3140, 1610, 1590, 1540, 1350[e]	7.42 (s, 1H), 7.46–7.53 (m, 1H), 8.17–8.23 (m, 1H), 8.81 (dd, 1H, J = 4.9, 1.6), 9.06 (d, 1H, J = 1.7)[d]
4e	18	oil	$C_4H_4N_2O_3$ (128.1)	3140, 1540, 1350[f]	2.4 (s, 3H), 6.8 (s, 1H)
4f	10	oil	$C_7H_{10}N_2O_3$ (170.2)	3140, 1540, 1355[f]	1.4 (s, 9H), 6.9 (s, 1H)
4g	31	oil	$C_6H_6N_2O_5$ (186.1)	1730, 1570, 1620, 1545, 1370[f]	1.45 (t, 3H, J = 7), 4.5 (q, 2H, J = 7), 7.4 (s, 1H)
7	50	143 (MeOH)	$C_{15}H_{10}N_2O_3$ (266.3)	1610, 1590, 1520, 1360[e]	7.3–8.1 (m, 10H)

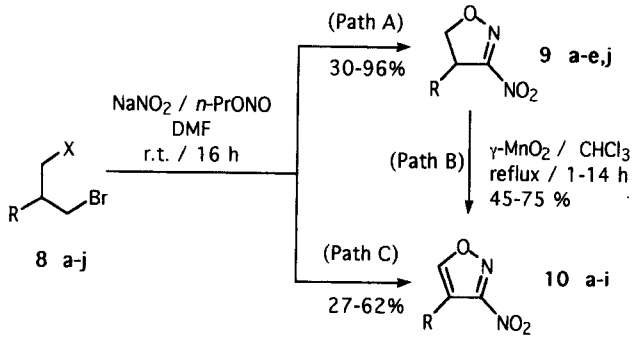
[a] Satisfactory elemental analyses (C, H, N ±0.4% from the theoretical value) were obtained.
[b] Spectroscopic data are identical to those reported in literature[5]
[c] Nujol.
[d] Recorded at 200 MHz.
[e] $CDCl_3$.
[f] Film.

In the meantime, it was demonstrated that aromatization of 4,5-dihydroisoxazoles to nitroisoxazoles is possible even when the elimination of nitrous acid appears as the most probable pathway.

With regard to the 3-nitro-4-substituted isoxazoles, the usual [3 + 2] cycloaddition could hardly be conceived for the synthesis of the desired compounds **10a–i**. Therefore, we outlined paths A and B of Scheme 3, which involve the preparation of the 3-nitro-4,5-dihydroisoxazoles **9** by a known procedure,[15] followed by the aromatization of these intermediates with a method using activated manganese(IV) oxide. The reaction conditions discussed above were not critical in this case.

The 1,3-dihalo derivatives **8a–j** were treated overnight with sodium nitrite and propyl nitrite in DMF at room temperature, thus obtaining the 3-nitro-4,5-dihydroisoxazoles **9a–e, j** in 30–96% yield (path A in Scheme 3). The mechanistic course is very likely the same that propargyl halides[3] follow in identical conditions, i.e. a process of nitration–nitrosation followed by cyclization of the resulting nitrolic acid; indeed, every mole of isoxazole we isolated was accompanied by approximately the same quantity of the 1-halo-3-hydroxypropane derivative corresponding to the starting **8a–j**.

The 4,5-dihydroisoxazoles **9a–e** refluxed in chloroform with activated manganese dioxide gave isoxazoles **10a–e**



8–10	X	R	8–10	X	R
a	Br	Ph	**f**	Br	4-$NO_2C_6H_4$
b	Cl	Me	**g**	Br	2,4-$(NO_2)_2C_6H_3$
c	Cl	CH_2Cl	**h**	Br	COPh
d	Br	4-$MeOC_6H_4$	**i**	Br	CO_2Et
e	Br	2-$NO_2C_6H_4$	**j**	Cl	H

Scheme 3

in 45–75% yields. While these oxidations (path B in Scheme 3) proceeded as expected in general, in the case of **9j** we were unable to obtain the corresponding isoxazole, observing instead a complex mixture of degradation products of **9j**. On the other hand, when the reaction time was reduced or the temperature decreased, the reaction did not occur at all.

Surprisingly, from the reactions of dihalo derivatives **8f–i** (path C in Scheme 3) we directly isolated nitroisoxazoles **10f–i**; from **8e** we obtained both **9e** and **10e**, together with unreacted starting compound.

To explain this, we reason that isoxazoles **10e–i** arise from the oxidation of the 4,5-dihydroisoxazole intermediates, the nitrous acid containing medium acting as the oxidizing agent. Since these oxidations were observed when R is a strong electron-withdrawing group, we accept, according to Baranski's findings,[12] that the oxidation occurs by means of a radical-anion mechanism directed in our cases by the acidity of 4-H, which is in turn influenced by the electronic effect of the substituent.

Table 3. 1,3-Dibromopropanes **8e–g**

Products	Yield (%)	mp (°C)	Molecular Formula[a]	IR ν (cm^{-1})	^1H NMR ($CDCl_3$) δ, J (Hz)
8e	66	72	$C_9H_9Br_2NO_2$ (323.0)	3030, 1610, 1520, 1345[b]	3.6–4.1 (m, 5H), 7.2–8.1 (m, 4H)
8f	83	58	$C_9H_9Br_2NO_2$ (323.0)	3075, 1600, 1520, 1345[c]	3.3–3.9 (m, 5H), 7.3–8.4 (AA'BB' system, 4H)
8g	42	oil	$C_9H_8Br_2N_2O_4$ (368.0)	3000, 1600, 1530, 1345[d]	3.7–4.0 (m, 4H), 4.1–4.2 (m, 1H), 7.7–8.8 (m, 3H)[e]

[a] Satisfactory elemental analyses (C, H, N ± 0.4% from the theoretical value) were obtained.
[b] Nujol.
[c] $CDCl_3$.
[d] Film.
[e] Recorded at 200 MHz.

Table 4. 4-Substituted 3-Nitro-4,5-dihydroisoxazoles **9a–e** (Path A)

Products	Yield (%)	mp (°C) (solvent) or bp (°C)/mbar	Molecular Formula[a] or Lit. bp (°C)/mbar	IR ν (cm^{-1})	^1H NMR ($CDCl_3$) δ, J (Hz)
9a	56	59 (EtOH)	$C_9H_8N_2O_3$ (192.2)	1610, 1590, 1525, 1360[b]	4.75–5.25 (m, 3H), 7.1–7.6 (m, 5H)
9b	96	80/0.45	$C_4H_6N_2O_3$ (130.1)	1610, 1540, 1365[c]	1.4 (d, 3H, J = 7), 3.5–4.1 (m, 1H), 4.25–5.25 (m, 2H)[d]
9c	30	32 (EtOH)	$C_4H_5ClN_2O_3$ (164.6)	1610, 1525, 1365[c]	3.75–4.4 (m, 3H), 4.85–5.1 (m, 2H)[e]
9d	73	114 (EtOH)	$C_{10}H_{10}N_2O_4$ (222.2)	1600, 1530, 1365[b]	3.8 (s, 3H), 4.65–5.4 (m, 3H), 6.75–7.3 (AA'BB' system, 4H)
9e	42[f]	97 (EtOH)	$C_9H_7N_3O_5$ (237.2)	1600, 1525, 1540, 1350[c]	4.8–4.95 (dd, 1H), 5.34–5.65 (m, 2H), 7.2–8.2 (m, 4H)[e]
9j	97	86/0.8	93–94/1.4[15]	1610, 1540, 1365[c,g]	3.5 (t, 2H, J = 10), 4.9 (t, 2H, J = 10)[g]

[a] Satisfactory elemental analyses (C, H, N ± 0.4% from the theoretical value) were obtained.
[b] Nujol.
[c] Film.
[d] Spectroscopic data are identical to those reported in literature.[30]
[e] Recorded also at 200 MHz.
[f] Together with 11% of **10e**.
[g] Spectroscopic data are identical to those reported in literature.[15]

Table 5. 4-Substituted 3-Nitroisoxazoles **10a–i** (Path B, C)

Products	Path	Yield (%) (h)[a]	mp (°C) (solvent)	Molecular Formula[b]	IR ν (cm^{-1})	^{1}H NMR ($CDCl_3$) δ, J (Hz)
10a	B	70 (16)	50 (EtOH)	$C_9H_6N_2O_3$ (190.2)	3120, 1610, 1545, 1345[c]	7.4 (s, 5H), 8.6 (s, 1H)
10b	B	75 (16)	oil	$C_4H_4N_2O_3$ (128.1)	3120, 1620, 1545, 1340[c]	2.3 (s, 3H), 8.4 (s, 1H)
10c	B	45 (5)	oil	$C_4H_3ClN_2O_3$ (162.5)	3120, 1550, 1345[c]	4.75 (s, 2H), 8.75 (s, 1H)
10d	B	50 (1)	55 (EtOH)	$C_{10}H_8N_2O_4$ (220.2)	3120, 1620, 1600, 1545, 1340[c]	3.85 (s, 3H), 6.85–7.5 (AA'BB' system, 4H), 8.55 (s, 1H)
10e	B	56 (5)	84	$C_9H_5N_3O_5$	3120, 1600, 1550, 1345[e]	7.3–8.4 (m, 4H), 8.6 (s, 1H)
	C	11[d]	(EtOH)	(235.2)		
10f	C	34	89 (EtOH)	$C_9H_5N_3O_5$ (235.2)	3140, 1600, 1550, 1350[e]	7.5–8.5 (AA'BB' system, 4H), 8.75 (s, 1H)
10g	C	27	113 (EtOH)	$C_9H_4N_4O_7$ (280.2)	3100, 1600, 1545, 1340[e]	7.8–9.15 (m, 3H), 9.2 (s, 1H)[f]
10h	C	62	93 (MeOH)	$C_{10}H_6N_2O_4$ (218.2)	3060, 1670, 1590, 1550, 1435, 1340[c]	7.3–8.0 (m, 5H), 8.85 (s, 1H)
10i	C	51	oil	$C_6H_6N_2O_5$ (186.1)	3120, 1735, 1600, 1560, 1350[c]	1.4 (t, 3H, J = 7), 4.4 (q, 2H, J = 7), 9.05 (s, 1H)

[a] Reaction time.
[b] Satisfactory elemental analyses (C, H, N ± 0.4% from the theoretical value) were obtained.
[c] Film.
[d] Together with 42% of **9e**.
[e] $CDCl_3$.
[f] $CDCl_3$/DMSO-d_6, 90 : 10.

We are currently exploring the utilization of the chemistry described herein to the preparation of new nitrofurane-like antibacterial agents.

Melting points were determined on a Büchi SMP-510 capillary apparatus and are uncorrected. IR spectra were obtained on a Perkin-Elmer 257 spectrometer. Mass spectra were taken on a Hitachi RMU 6L (70 eV) instrument and ^{1}H NMR spectra were recorded on Varian EM 60 or Varian EM 200 spectrometers and are reported in ppm with TMS as the internal standard.

Column chromatography was performed on silica gel 60 (200–400 mesh). Compounds **8b, 8j** were purchased from Aldrich.

The nitrile oxides **2a–h** were prepared in situ by dehydrohalogenation of the corresponding hydroximic acid chloride.[16]

Compounds **1**,[17] **3a–c**,[6] **6**,[18] **8a**,[19] **8c**,[20] **8d**,[21] **8h**,[22] **8i**,[23], **9j**,[15] *N*-hydroxy-3-pyridinecarboximidoyl chloride,[24] *N*-hydroxyethanimidoyl chloride,[25] *N*-hydroxy-2,2-dimethylpropanimidoyl chloride,[25] chloro(hydroxyimino)acetic acid ethyl ester,[26] *N*-hydroxyformimidoyl iodide,[27] propylnitrite,[28] 1,3-dihydroxy-2-(2-nitrophenyl)propane,[29] 1,3-dihydroxy-2-(4-nitrophenyl)propane,[29] and 2-(2,4-dinitrophenyl)-1,3-dihydroxypropane[29] were prepared by literature methods. From the last three compounds, applying Schubert's method,[19] we synthesized compounds **8e–g**, respectively.

3-Substituted 4,5-Dihydro-5-nitroisoxazoles 3a–h, 6; General Procedure:
A solution of nitroethylene[17] (25 mmol) in Et_2O (25 mL) was mixed with a solution of the appropriate hydroximic acid chloride (10 mmol) in Et_2O (50 mL). To the solution thus obtained, after cooling to 0°C, Et_3N (10 mmol) in a minimal amount of Et_2O (≈ 5 mL) was added dropwise. The mixture was stirred at r.t. for 4 h, during which an amorphous mass was formed; the organic phase was separated from the solid, which was extracted with Et_2O (2 × 50 mL) and then with CH_2Cl_2 (2 × 50 mL); all organic phases thus obtained were washed with water (15 mL), collected, dried (Na_2SO_4) and finally evaporated in vacuo. The crude products were purified by crystallization **(3d)** or by column chromatography on silica gel (eluent CH_2Cl_2 for **3e** and **3h**; cyclohexane/EtOAc, 8 : 2 for **3f, g**) (Table 1).

3-Substituted 5-Nitroisoxazoles 4a–g, 7; General Procedure:
A solution of **3a–h** or **6** (0.20 g) in dry CH_2Cl_2 (2 mL) was rapidly added to a suspension of MnO_2 (2 g), previously activated (absence of solvent, 130°C, 18 h),[13] in the same solvents (38 mL). The suspension was stirred for 10 min at r.t., then refluxed for 1 h and finally filtered on Celite, washing the layer of MnO_2 with hot solvent (2 × 40 mL). The filtrate was evaporated in vacuo giving crude products which were purified by crystallization **(4a–d)** or by column chromatography on silica gel (**4e–g** and **7**; eluent cyclohexane/EtOAc, 8 : 2) (Table 2).

Mass spectra were performed for selected compounds **(4a, 7)**. The fragmentation patterns are consistent with the given structures.
4a; MS: *m/z* (%) = 190 (M^+, 70), 144 ($M^+ - NO_2$, 74), 77 (Ph, 100).
7; MS: *m/z* (%) = 266 (M^+, 43), 119 (PhCNO, 25), 105 (100), 77 (Ph, 85).

1,3-Dibromopropanes 8e–g; General Procedure:
PBr_3 (10 mmol) was added slowly to an ice-cooled, stirred mixture of the suitable 1,3-dihydroxypropane (10 mmol) and a catalytic amount of pyridine (0.01 mL). The mixture was kept at r.t. overnight, then heated at 90–100°C for 1 h. Brine (10 g) was added, then extractions with Et_2O were made (3 × 10 mL). The ethereal solution was washed with sat. aq $NaHCO_3$ (10 mL), then with water (10 mL), and finally dried (Na_2SO_4) and evaporated in vacuo Compounds **8e–g** (see Table 3) were obtained from the residue by column chromatography on silica gel (cyclohexane/EtOAc, 9 : 1).

4-Substituted 3-Nitro-4,5-dihydroisoxazoles 9a–e and 4-Substituted 3-Nitroisoxazoles 10e–i; General Procedure (Paths A, C):
To a solution of the suitable 2-substituted 1-halo-3-bromopropane **8a–i** (5 mmol) in dry DMF (25 mL), freshly distilled propyl nitrite (2.5 mmol) was added. The mixture was stirred and treated with $NaNO_2$ (10 mmol), added at r.t. in small portions over 8–10 h, then further stirred at r.t. for 16 h. The reaction mixture was poured into cold water (250 mL), and extracted with CH_2Cl_2 (4 × 50 mL); the layers were separated, and the organic phase was washed with water (2 × 20 mL), dried (Na_2SO_4), and evaporated in vacuo. The crude products were purified by crystallization **(9d)**, or by column chromatography on silica gel (eluent cyclohexane/EtOAc, 8 : 2) **(9a, c, e; 10e–i)**, or by distillation **(9b)** (see Table 4). In the case of **8e**, unreacted starting product (0.88 g, 2.7 mmol) was recovered.

^{1}H NMR spectra were assigned for selected compounds **(9c, e)** using 2-D and NOE experiments. The ^{1}H NMR parameters were calculated using Bruker software (Panic) and matched with experimental spectra.

9c; ^{1}H NMR: δ = 3.79 (dd, 1 H, J = 11.7, 2.9, H-5), 4.02 (dd, 1 H, J = 11.7, 5.6, H-5'), 4.27 (qd, 1 H, J = 2.9, 5.6, 7.15, 11.6, H-4), 4.95 (dd, 1 H, J = 7.15, 9.54, CHCl), 5.05 (dd, 1 H, J = 11.6, 9.54, CH'Cl).

9e; ^{1}H NMR: δ = 4.87 (dd, 1 H, J = 5.7, 8.9, H-5), 5.45 (dd, 1 H, J = 8.9, 11.8, H-5'), 5.58 (dd, 1 H, J = 5.7, 11.8, H-4), 7.23–8.16 (m, 4 H, H_{arom}).

Mass spectra were performed for selected compounds **(9a,c,e)**. The fragmentation patterns are consistent with the given structures.

9a; MS: m/z (%) = 192 (M^+, 23), 116 (100), 89 (30).

9c; MS: m/z (%) = 164 (M^+, 70), 129 ($M^+ - Cl$, 100), 115 ($M^+ - CH_2Cl$, 3).

9e; MS: m/z (%) = 191 ($M^+ - NO_2$, 33), 144 ($M^+ - 2NO_2$, 39), 134 (68), 104 (100).

Aromatization of the 4-Substituted 3-Nitro-4,5-dihydroisoxazoles (9a–e) to the Corresponding 3-Nitroisoxazoles 10a–e; General Procedure (Path B):

A solution of **9a–e** (0.20 g) in dry $CHCl_3$ (4 mL) was rapidly added to a suspension in the same solvent (76 mL) of MnO_2 (4.0 g), previously activated (absence of solvent, 130 °C, 18 h).[13] The suspension was stirred for 10 min at r. t., and then refluxed until the starting material had reacted (TLC analysis); times are reported in Table 5. The suspension was filtered on Celite, washing the layer of MnO_2 with hot solvent (2 × 80 mL). The filtrate was evaporated in vacuo giving practically pure (TLC) crude products which were purified by crystallization **(10a)** or by column chromatography on silica gel (eluent cyclohexane/EtOAc, 8:2) **(10b–e)**.

Mass spectra were performed for selected molecules **(10a, e)**. The fragmentation patterns are consistent with the given structures.

10a; MS: m/z (%) = 190 (M^+, 31), 160 ($M^+ - NO$, 2), 144 ($M^+ - NO_2$, 35), 132 (17), 116 (100), 104 (15), 89 (85).

10e; MS: m/z (%) = 235 (M^+, 9), 189 ($M^+ - NO_2$, 2), 159 (60), 134 (67), 131(39), 104 (95), 76 (100).

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† Died suddenly in July, 1992

(1) For recent reviews:
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