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Reaction of β-Nitroenones with Thiophenol Synthesis of 5-Hydroxy-4-(Phenylthio)-2-Isoxazoline 2-Oxides

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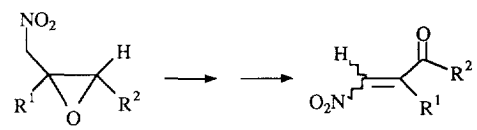
Abstract: A new synthesis of 2-isoxazoline 2-oxides starting from unsaturated nitro compounds is described. A facile and convenient preparation of β-alkyl substituted β-nitroenones and their conversion to β-nitrosulfides are recorded. Treatment of these compounds with potassium tert-butoxide at -78°C followed by immediate quenching with acetic acid provides access to 5-hydroxy-4-(phenylthio)-2-isoxazoline 2-oxides via intramolecular addition of the nitronate anion to the carbonyl group.

Introduction

Aliphatic nitro compounds are versatile synthetic intermediates that offer access to a variety of nitro or nitro-free compounds.[1] In spite of their synthetic potential and contrary to nitroalkenes which have frequently been used as Michael acceptors,[2] β-nitroenones have found little use in organic synthesis.[3,4]

Recently we reported the facile and high yield preparation of acyclic β-nitroenones **2** bearing an hydrogen atom on position β and of 2-(1-nitroalkylidene) cycloalkanones based on the regioselective opening of nitroepoxides **1** with silica gel or aluminium isopropoxide (Scheme 1).[5,6]

Scheme 1

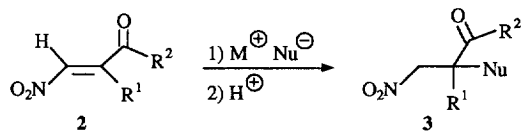


1 **2**

R^1, R^2 = alkyl

We have also reported preliminary results of some compounds **2** with sodium carbanions of bis-activated methylene compounds and with sodium or potassium alkoxides leading to highly functionalized derivatives **3** (Scheme 2).[7]

Scheme 2



$Nu^{\ominus}$ = $^{\ominus}CR^4Z^1Z^2$ or $RO^{\ominus}$
with R^4 = H, OAc or alkyl and Z^1,Z^2 = E.W.G.
$M^{\oplus}$ = $Na^{\oplus}$ or $K^{\oplus}$

We showed that adducts **3** obtained from unsaturated alkoxides were efficient intermediates for the synthesis of 6,6-disubstituted furo [3,4-c] isoxazoles and 7,7-disubstituted pyrano [3,4-c] isoxazoles.[7b]

In the present paper, we wish to report first the synthesis of acyclic β-nitroenones substituted in position β by an alkyl group, then the reactivity of these new compounds and those previously described towards thiophenol.

Synthesis of aliphatic β-alkyl substituted β-nitroenones

Compounds **4** (in poor yields) and **5** (Table I) were prepared as previously described by Tamura et al.[8] But, contrary to 1-nitro-2,3-epoxyalkanes derivatives previously studied,[5] compounds **5** were stable on silica gel and gave only complex mixtures of products when they were treated with aluminium isopropoxide in refluxing toluene.

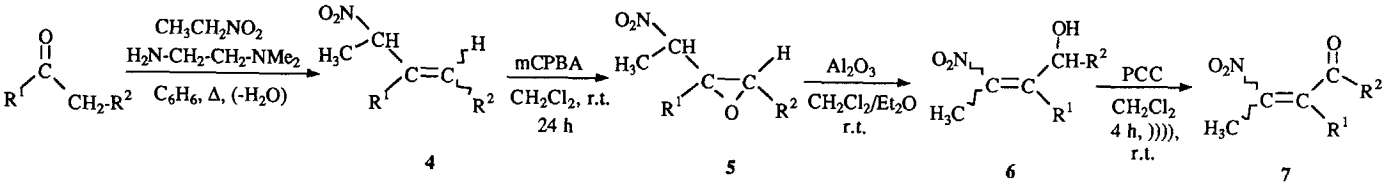
Their selective transformation into γ-hydroxy-α-nitroalkenes **6** was performed with neutral alumina (activity I according to Brokmann).

Oxidation of compounds **6** with pyridinium chlorochromate in dichloromethane under sonochemical conditions led to mixtures of the (*Z*) and (*E*) isomers of the desired β-alkyl substituted β-nitroenones **7** which could be easily separated by column chromatography. Overall isolated yields are shown in Table I.

However, compounds **8**, readily prepared from nitromethane and aliphatic ketones,[8] reacted with methyl vinyl ketone in the presence of a catalytic amount of potassium tert-butoxide in ethanol[9,10] to give Michael adducts **9** in good yields. Only the (*Z*) isomer of the allylic nitro compounds **9** could be easily separated by silica gel chromatography from the non-reacted starting material. Epoxidation of the carbon-carbon double bond with mCPBA in dichloromethane, opening of the nitroepoxides **10** with neutral alumina followed by the oxidation of the γ-hydroxy-α-nitroalkenes **11** gave the β-alkyl substituted β-nitroenones **12**. Only the (*Z*) isomer of compounds **12** could be separated from the non-oxidized alcohol (Table II).

Stereochemistry of the carbon-carbon double bond of compounds **6**, **7**, **11** and **12** was established according to our preliminary results obtained on 2-(1-nitroalkylidene) cycloalkenones[6] by IR : $\nu\ (NO_2)Z^{asym}$ = 1532-1530 cm^{-1} > $\nu\ (NO_2)E^{asym}$ = 1528-1526 cm^{-1} ; $\nu\ (NO_2)Z^{sym}$ = 1358-1357 cm^{-1} > $\nu\ (NO_2)E^{sym}$ =

Table I. Synthesis of β-nitroenones 7.

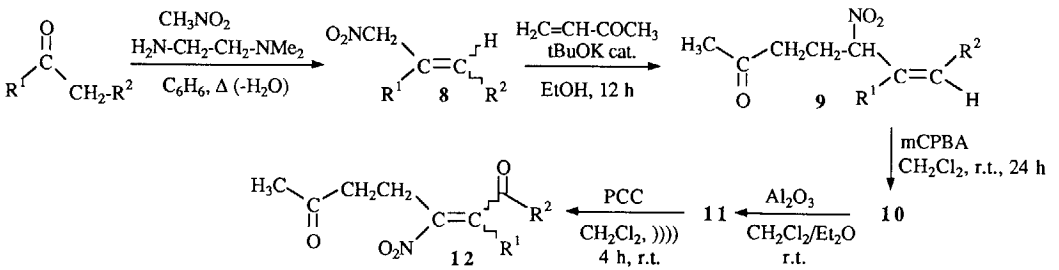


4 5 6 7

Entry	R1	R2	4			5		6			7	
			Eb (°C/mmHg)	Z/E(a)	Yield %	Eb (°C/mmHg)	Yield %	Reaction time (h)	Z/E(a)	Yield %	Z/E(a)	Yield %
a	CH3	CH3	65/38	78/22	37(b)	80/38	87(b)	2	78/22	93(c)	86/14	69(c)
b	CH3	CH3CH2	83/14	89/11	23(b)	50/7	97(b)	2	70/30	80(c)	62/38	73(c)
c	CH3CH2	CH3	90/14	88/12	30(b)	45/2	91(b)	3	65/35	76(c)	59/41	95(c)
d	CH3CH2CH2	CH3CH2	-	100/0	38(c)	65/3	94(b)	4	74/26	70(c)	70/30	95(c)

(a) Determined by ^{1}H NMR on the crude reaction products.
(b) Yields of distilled products.
(c) Yields of chromatographed products.

Table II. Synthesis of β-nitroenones **12**.



Entry	R1	R2	8	9	10	11			12	
			Yield[a] %	Yield[b] %	Yield[b] %	Reaction time (h)	Z/E[c]	Yield[b] %	Z/E[c]	Yield[b] %
a	CH_3	CH_3	60	83	85	1	78/22	75	75/25	73
b	CH_3	CH_3CH_2	70	61	92	1	77/23	73	78/22	70
c	CH_3	$CH_3(CH_2)_4$	60	64	91	1	68/32	69	63/37	59
d	CH_3CH_2	CH_3	80	70	95	2	70/30	74	69/31	62

(a) Yields of distilled products.

(b) Yields of chromatographed products.

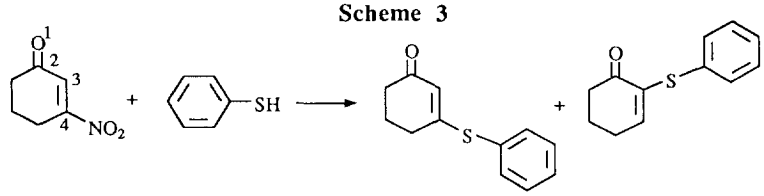
(c) Determined by ^1H NMR on the crude reaction products.

1340 cm-1 and by UV : (*E*)-β-nitroenones showed stronger absorptions than the corresponding (Z) compounds in the wave length region of 260-275 nm (NO_2 group).

Addition of thiophenol to β-nitroenones. Synthesis of 2-isoxazoline 2-oxides.

The Michael addition of thiols to nitroalkenes has been frequently used in organic synthesis.[2b, 11] The reactivity of 3-nitrocyclohex-2-en-1-one towards thiophenol has already been studied by Vankar et al. (Scheme 3).[4] Depending on the reaction conditions, the addition occurs on positions 3 and/or 4 with loss of the nitro group.

Scheme 3



We carried out the reaction of thiophenol with the (*E*) isomer of **2** and with the (Z) isomers of β-alkyl substituted compounds **7** and **12**.

In the absence of base, addition of thiophenol to β-nitroenones **2**, **7** and **12** was slow. With compound **2** ($R^1 = R^2 = CH_3$) for instance, the yield was 57 % after 48 hours reaction time at room temperature. In the presence of catalytic amounts of base such as triethylamine or morpholine, in acetonitrile, the addition proceeded much faster (1 hour).

In all cases, β-nitrosulfides **13**, resulting from the regioselective addition of thiophenol on the position 3 of the β-nitroenones, were isolated in good yields (Table III). These results appeared interesting considering that β-nitrosulfides are often biologically active compounds[12] and useful intermediates in organic synthesis.[13]

When R^3 was an alkyl group, the product **13** was a mixture of two diastereomers. The ratios are indicated in Table III. The (*l*)-stereochemistry of the main diastereomer of compounds **13** has been ascertained by X-ray crystallography by examining the case of 3-methyl-4-nitro-3-(phenylthio)pentan-2-one **13b**, selected as a representative of this class of compounds (figure 1).

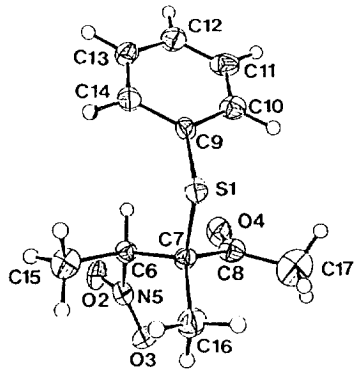
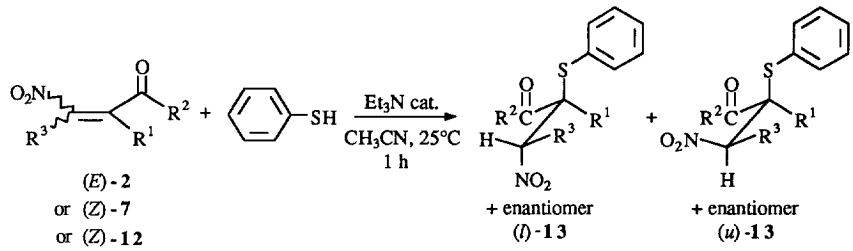


Figure 1. An ORTEP stereoview of the molecule **13b**

Table III. Preparation of β-nitrosulfides **13**



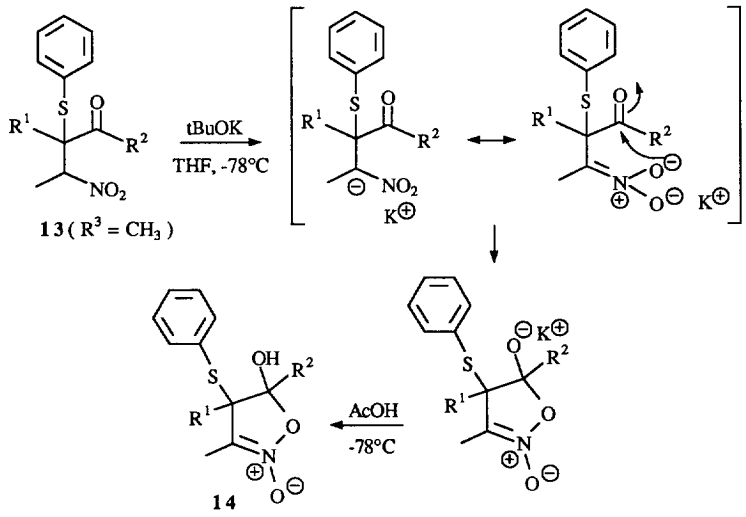
Entry	R1	R2	R3	Diastereomeric ratio[a] *l/u*	Yield[b] %
a	CH_3	CH_3	H	-	61
b	CH_3	CH_3	CH_3	78/22	79
c	CH_3	CH_2CH_3	H	-	93
d	CH_3	CH_2CH_3	CH_3	79/21	85
e	CH_3	CH_2CH_3	$CH_2CH_2COCH_3$	72/28	97
f	CH_3	$(CH_2)_4CH_3$	H	-	61
g	CH_2CH_3	CH_3	H	-	85
h	CH_2CH_3	CH_3	CH_3	53/47	55
i	CH_2CH_3	CH_3	$CH_2CH_2COCH_3$	86/14	64
j	$(CH_2)_2CH_3$	CH_2CH_3	H	-	63
k	$(CH_2)_2CH_3$	CH_2CH_3	CH_3	57/33	57

(a) Determined by ^1H NMR on the crude reaction products.
(b) Isolated yields.

Kamimura et al. have reported[11] improved stereochemical control of the formation of β-nitrosulfides. Addition of lithium thiolates to nitroalkenes in tetrahydrofuran at 0°C or deprotonation of a diastereomeric mixture of β-nitrosulfides with potassium tert-butoxide followed by stereoselective reprotonation of the nitronate intermediate with acetic acid at -78°C, allowed for the preparation of (*u*)-β-nitrosulfides.

However, lithium thiophenolate gave only complex mixtures of products when it reacted with our β-nitroenones. When a mixture of diastereomers **13b, 13d, 13h** and **13k** were respectively reacting in the presence of potassium tert-butoxide in tetrahydrofuran at -78°C and followed immediately by reprotonation, 4,5 dialkyl-5-hydroxy-3-methyl-4-(phenylthio)-2-isoxazoline 2-oxides **14**, resulting from the nucleophilic attack of nitronate oxygen on the carbonyl function, were solely obtained in good yields (Scheme 4).

Scheme 4



These compounds were stable and some of them were purified by chromatography on silica gel. Analysis of the ^1H NMR spectra of 2-isoxazoline 2-oxides **14** revealed the presence of diastereomeric non separable mixtures in each case. The diastereomeric ratios and selected spectroscopic data of these compounds are collected in Table IV.

Table IV. Preparation and selected spectroscopic data of 2-isoxazoline 2-oxides **14**

14	R^1	R^2	Diastereomeric ratio[a]	IR (cm^{-1}) ν (C=N)	RMN ^{13}C (ppm) δ C (1)	Yield[d] (%)
a	CH_3	CH_3	93/7	1638	117.08[b]	54
b	CH_2CH_3	CH_3	70/30	1638	122.07[c]	67
c	CH_3	CH_2CH_3	66/34	1645	121.13[c]	75
d	$(CH_2)_2CH_3$	CH_2CH_3	92/8	1638	118.17[b]	60

(a) Determined by ^1H NMR on the crude reaction products.
(b) Recorded in $CDCl_3$.
(c) Recorded in DMSO d_6.
(d) Isolated yields.

When β-nitrosulfides **13e** and **13i** were treated in the same conditions, IR and NMR spectra of the crude reaction products indicated the presence of 2-isoxazoline 2-oxides. However, attempts to purify these compounds failed.

Only secondary nitronates were able to react intramolecularly with the carbonyl function. When R^3 is an hydrogen atom, the deprotonation-reprotonation procedure leaves the starting material unchanged.

2-isoxazoline 2-oxides have been prepared from nitroacetic esters,[14] from nitroalkenes,[15] bromonitroalkenes[16] or nitrocyclopropanes[17] and may be converted[18] into the corresponding 2-isoxazolines which are important starting materials for the stereodefined construction of a variety of β-hydroxyketones or γ-aminoalcohols.[19]

The present method for the synthesis of 2-isoxazoline 2-oxides is in our knowledge the sole resulting from the nucleophilic attack of a nitronate oxygen on a carbonyl group.

In this laboratory, further aspects of the reactivity of β-nitroenones are under continued investigation.

Experimental.

General remarks. Melting points were determined with a Büchi Tottoli apparatus and are reported uncorrected. Reaction courses were monitored by thin-layer chromatography on silica gel coated plates F_{254} Merck. ^1H NMR spectra were recorded on Bruker AW 80 (80 MHz) and Bruker AM 400 (400 MHz) instruments in $CDCl_3$ unless otherwise noted. Chemical shifts are expressed in parts per million downfield from tetramethylsilane. ^{13}C NMR spectra were recorded on a Bruker AC 250 (62.9 MHz) in $CDCl_3$ solutions unless otherwise noted. Infrared spectra were obtained using a Perkin-Elmer VP 1750 FTIR spectrophotometer. Elemental analyses were performed by the CIBA Micro-Analysis Laboratory, Bâle, Switzerland. All organic solvents were appropriately dried and purified prior to use.

Allylic nitrocompounds **4** and **8** were prepared as described by Tamura et al.[8] Nitroepoxides **5** and **10** were obtained by oxidation of the corresponding allylic nitro compounds **4** and **9** with 1.0 eq. of mCPBA in dichloromethane.

Preparation of γ-hydroxy-α-nitroalkenes 6 and 11 by opening of nitroepoxides 5 and 10 with alumina. General procedure.

Neutral alumina (0.6 g, activity I according to Brockmann) was added at room temperature to the nitroepoxides **5** (or **10**) (3 mmol) in solution in 5 ml of a mixture of Et_2O/CH_2Cl_2 (1/1). Stirring was continued for the times indicated in Tables I and II.

The reaction mixture was then filtered and alumina was washed several times with ether and dichloromethane. After evaporation, the crude product was purified by column chromatography on silica gel.

(*Z*)- and (*E*)-3-methyl-4-nitropent-3-en-2-ol 6a.

Yield 93 %. *Z*/*E* = 78/22. ^1H NMR : (*Z*) (δ) : 4.70 (q, J = 6.7 Hz, 1 H) ; 2.19 (q, J = 1.5 Hz, 3 H) ; 1.88 (q, J = 1.2 Hz, 3 H) ; 1.32 (d, J = 6.7 Hz, 3 H) ; (*E*) (δ) : 4.76 (q, J = 6.7 Hz, 1 H) ; 2.17 (q, J = 0.9 Hz, 3 H) ; 1.85 (q, J = 0.9 Hz, 3 H) ; 1.33 (d, J = 6.7 Hz, 3 H). IR (neat) : 3411, 1521 and 1347 cm^{-1}. Anal. Calcd for $C_6H_{11}NO_3$: C, 49.65, H, 7.64, N, 9.65, O, 33.07. Found : C, 49.2, H, 7.89, N, 9.2.

(*Z*)- and (*E*)-4-methyl-4-nitrohex-4-en-2-ol 6b.

Yield 80 %. *Z*/*E* = 70/30. ^1H NMR : (*Z*) (δ) : 4.41 (t, J = 7.0 Hz, 1 H) ; 2.19 (q, J = 1.5 Hz, 3 H) ; 1.84 (q, J = 1.5 Hz, 3 H) ; 1.78-1.50 (m, 2 H) ; 0.94 (t, J = 7.5 Hz, 3 H) ; (*E*) (δ) : 4.44 (d, J = 5.5 Hz, 1 H) ; 4.42 (d, J = 5.5 Hz, 1 H) ; 2.17 (q, J = 0.9 Hz, 3 H) ; 1.81 (q, J = 0.9 Hz, 3 H) ; 1.78-1.50 (m, 2 H) ; 0.93 (t, J = 7.5 Hz, 3 H). IR (neat) : 3440, 1524 and 1354 cm^{-1}. Anal. Calcd for $C_7H_{13}NO_3$: C, 52.82, H, 8.23, N, 8.80, O, 30.15. Found : C, 52.9, H, 8.4, N, 8.3.

(*Z*)- and (*E*)-3-ethyl-4-nitropent-3-en-2-ol 6c.

Yield 76 %. *Z*/*E* = 65/35. ^1H NMR : (*Z*) (δ) : 4.68 (q, J = 6.7 Hz, 1 H) ; 2.26 (brq, J = 7.3 Hz, 2 H) ; 2.21 (s, 3 H) ; 1.36 (d, J = 6.7 Hz, 3 H) ; 1.15 (t, J = 7.3 Hz, 3 H) ; (*E*) (δ) : 4.75 (q, J = 6.7 Hz, 1 H) ; 2.25 (brq, J = 7.3 Hz, 2 H) ; 2.19 (s, 3 H) ; 1.36 (d, J = 6.7 Hz, 3 H) ; 1.14 (t, J = 7.3 Hz, 3 H). IR (neat) : 3425, 1521 and 1354 cm^{-1}. Anal. Calcd for $C_7H_{13}NO_3$: C, 52.82, H, 8.23, N, 8.80, O, 30.15. Found : C, 52.5, H, 8.4, N, 8.7.

(*Z*)- and (*E*)-5-nitro-4-propylhex-4-en-3-ol 6d.

Yield 70 %. *Z*/*E* = 74/26. ^1H NMR : (*Z*) (δ) : 4.37 (d, J = 5.5 Hz, 1 H) ; 4.35 (d, J = 5.5 Hz, 1 H) ; 2.20 (s, 3 H) ; 2.19-2.07 (m, 2 H) ; 1.77-1.73 (m, 4 H) ; 0.98 (t, J = 7.3 Hz, 3 H) ; 0.93 (t, J = 7.3 Hz, 3 H) ; (*E*) (δ) : 4.41 (d, J = 4.9 Hz, 1 H) ; 4.39 (d, J = 5.1 Hz, 1 H) ; 2.23-2.07 (m, 2 H) ; 2.18 (s, 3 H) ; 1.73-1.42 (m, 4 H);

0.99 (t, J = 7.3 Hz, 3 H) ; 0.95 (t, J = 7.3 Hz, 3 H). IR (neat) : 3460, 1520 and 1351 cm^{-1}. Anal. Calcd for $C_9H_{17}NO_3$: C, 57.73, H, 9.15, N, 7.48, O, 25.63. Found : C, 57.2, H, 8.9, N, 7.6.

(*Z*)- and (*E*)-7-hydroxy-6-methyl-5-nitrooct-5-en-2-one 11a.

Yield 75 %. *Z*/*E* = 78/22. ^1H NMR : (*Z*) (δ) : 4.84 (qd, ^3J = 6.4 Hz, $^3J'$ = 3.0 Hz, 1 H) ; 2.30-2.10 (m, 4 H) ; 2.17 (s, 3 H) ; 1.80 (s, 3 H) ; 1.32 (d, J = 6.4 Hz, 3 H) ; (*E*) (δ) : 4.65 (qd, ^3J = 6.4 Hz, $^3J'$ = 3.0 Hz, 1 H) ; 2.30-2.10 (m, 4 H) ; 2.17 (s, 3 H) ; 1.87 (s, 3 H) ; 1.36 (d, J = 6.4 Hz, 3 H). IR (neat) : 3446, 1716, 1650, 1521 and 1368 cm^{-1}. Anal. Calcd for $C_9H_{15}NO_4$: C, 53.72, H, 7.51, N, 6.96, O, 31.80. Found : C, 53.7, H, 7.4, N, 7.0.

(*Z*)- and (*E*)-7-hydroxy-6-methyl-5-nitronon-5-en-2-one 11b.

Yield 73 %. *Z*/*E* = 77/23. ^1H NMR : (*Z*) (δ) : 4.54 (td, ^3J = 6.7 Hz, $^3J'$ = 3.0 Hz, 1 H) ; 2.82-2.63 (m, 4 H) ; 2.17 (s, 3 H) ; 1.77 (s, 3 H) ; 1.82-1.50 (m, 2 H) ; 0.95 (t, J = 7.3 Hz, 3 H) ; (*E*) (δ) : 4.34 (td, ^3J = 6.7 Hz, $^3J'$ = 3.0 Hz, 1 H) ; 2.82-2.63 (m, 4 H) ; 2.17 (s, 3 H) ; 1.86 (s, 3 H) ; 1.82-1.50 (m, 2 H) ; 0.92 (t, J = 7.3 Hz, 3 H). IR (neat) : 3439, 1716, 1645, 1521 and 1361 cm^{-1}. Anal. Calcd for $C_{10}H_{17}NO_4$: C, 55.80, H, 7.96, N, 6.51, O, 29.73. Found : C, 56.0, H, 7.9, N, 6.4.

(*Z*)- and (*E*)-7-hydroxy-6-methyl-5-nitrododec-5-en-2-one 11c.

Yield 69 %. *Z*/*E* = 70/30. ^1H NMR : (*Z*) (δ) : 4.61 (td, ^3J = 7.9 Hz, $^3J'$ = 2.4 Hz, 1 H) ; 3.03-2.94 (m, 1 H) ; 2.79-2.57 (m, 3 H) ; 2.16 (s, 3 H) ; 1.78 (s, 3 H) ; 1.77-1.22 (m, 11 H) ; 0.90 (t, J = 6.7 Hz, 3 H) ; (*E*) (δ) : 4.42 (td, ^3J = 7.9 Hz, $^3J'$ = 2.4 Hz, 1 H) ; 2.81-2.40 (m, 4 H) ; 2.15 (s, 3 H) ; 1.86 (s, 3 H) ; 1.77-1.22 (m, 11 H) ; 0.89 (t, J = 6.7 Hz, 3 H). IR (neat) : 3460, 1716, 1642, 1521 and 1365 cm^{-1}. Anal. Calcd for $C_{13}H_{23}NO_4$: C, 60.68, H, 9.01, N, 5.44, O, 24.87. Found : C, 60.3, H, 9.1, N, 5.2.

(*Z*)- and (*E*)-6-ethyl-7-hydroxy-5-nitrooct-5-en-2-one 11d.

Yield 74 %. *Z*/E = 68/32. ^1H NMR : (*Z*) (δ) : 4.77 (q, J = 6.7 Hz, 1 H) ; 2.95-2.60 (m, 4 H) ; 2.17 (s, 3 H) ; 2.11 (q, J = 7.6 Hz, 2 H) ; 1.36 (d, J = 6.7 Hz, 3 H) ; 1.12 (t, J = 7.6 Hz, 3 H) ; (*E*) (δ) : 4.63 (q, J = 6.7 Hz, 1 H) ; 2.95-2.60 (m, 4 H) ; 2.16 (s, 3 H) ; 2.15 (q, J = 7.6 Hz, 2 H) ; 1.35 (d, J = 6.7 Hz, 3 H); 1.16 (t, J = 7.6 Hz, 3 H). IR (neat) : 3446, 1716, 1638, 1524 and 1365 cm^{-1}. Anal. Calcd for $C_{10}H_{17}NO_4$: C, 55.8, H, 7.96, N, 6.51, O, 29.73. Found : C, 55.7, H, 7.6, N, 6.7.

Preparation of β-nitroenones 7 and 12 by oxidation of the γ-hydroxy-α-nitroalkenes 6 and 11 with PCC.

Under sonication, the alcohol **6** (or **11**) (2 mmol, 1 eq.) in dry dichloromethane (1 ml) was added at room temperature in one portion to a suspension of PCC (0.646 g, 3 mmol, 1.5 eq.) in dichloromethane. After being stirred 4 hours at the same temperature, the reaction mixture was diluted with anhydrous ether (5 ml). The organic layer was separated and the insoluble brown residue was washed with dry ether (3 x 10 ml). Combined organic layers were filtered over Florisil. After evaporation, the crude β-nitroenone **7** (or **12**) was purified by chromatography on silica gel.

(*Z*)- and (*E*)-3-methyl-4-nitropent-3-en-2-one 7a.

Yield 60 %. *Z*/*E* = 86/14. ^1H NMR : (*Z*) (δ) : 2.36 (s, 3 H) ; 2.33 (q, J = 1.5 Hz, 3 H) ; 2.04 (q, J = 1.5 Hz, 3 H) ; (*E*) (δ) : 2.35 (s, 3 H) ; 2.20 (q, J = 0.9 Hz, 3 H) ; 2.01 (q, J = 1.2 Hz, 3 H). IR (neat) : 1709, 1531 and 1357 cm^{-1}. Anal. Calcd for $C_6H_9NO_3$: C, 50.35, H, 6.34, N, 9.79, O, 33.53. Found : C, 50.0, H, 6.4, N, 9.7.

(*Z*)- and (*E*)-4-methyl-5-nitrohex-4-en-3-one 7b.

Yield 73 %. *Z*/*E* = 62/38. ^1H NMR : (*Z*) (δ) : 2.66 (q, J = 7.0 Hz, 2 H) ; 2.18 (s, 3 H) ; 2.05 (s, 3 H) ; 1.15 (t, J = 7.0 Hz, 3 H) ; (*E*) (δ) : 2.59 (q, J = 7.0 Hz, 2 H) ; 2.21 (s, 3 H) ; 2.02 (s, 3 H) ; 1.20 (t, J = 7.0 Hz, 3 H). IR (neat) : 1709, 1524 and 1343 cm^{-1}. Anal. Calcd for $C_7H_{11}NO_3$: C, 53.49, H, 7.05, N, 8.91, O, 30.54. Found : C, 53.4, H, 6.8, N, 8.8.

(*Z*)- and (*E*)-3-ethyl-4-nitropent-3-en-2-one 7c.

Yield 95 %. *Z*/*E* = 59/41. ^1H NMR : (*Z*) (δ) : 2.42 (q, J = 7.5 Hz, 2 H) ; 2.39 (s, 3 H) ; 2.20 (s, 3 H) ; 1.11 (t, J = 7.5 Hz, 3 H) ; (*E*) (δ) : 2.42 (q, J = 7.5 Hz, 2 H) ; 2.35 (s, 3 H) ; 2.22 (s, 3 H) ; 1.16 (t, J = 7.5 Hz, 3 H). IR (neat) : 1709, 1531 and 1357 cm^{-1}. Anal. Calcd for $C_7H_{11}NO_3$: C, 53.49, H, 7.05, N, 8.91, O, 30.54. Found : C, 53.6, H, 7.0, N, 9.2.

(Z)- and (*E*)-5-nitro-4-propylhex-4-en-3-one 7d.
Yield 95 %. *Z*/*E* = 70/30. ^{1}H NMR : (*Z*) (δ) : 2.62 (q, J = 7.3 Hz, 3 H) ; 2.35 (tq, ^{3}J = 7.9 Hz, ^{5}J = 0.9 Hz, 2 H) ; 2.20 (s, 3 H) ; 1.57-1.40 (m, 2 H) ; 1.13 (t, J = 7.3 Hz, 3 H) ; 0.92 (t, J = 7.3 Hz, 3 H) ; (*E*) (δ) : 2.53 (q, J = 7.3 Hz, 3 H) ; 2.28 (brt, J = 7.9 Hz, 2 H) ; 2.14 (s, 3 H) ; 1.57-1.40 (m, 2 H) ; 1.18 (t, J = 7.3 Hz, 3 H) ; 0.98 (t, J = 7.3 Hz, 3 H). IR (neat) : 1709, 1531 and 1340 cm^{-1}. Anal. Calcd for $C_9H_{15}NO_3$: C, 58.36, H, 8.16, N, 7.56, O, 25.91. Found : C, 58.6, H, 8.1, N, 7.3.

(Z)-6-methyl-5-nitrooct-5-en-2,7-dione 12a.
Yield 73 %. *Z*/*E* = 75/25. ^{1}H NMR : (*Z*) (δ) : 2.79 (brt, J = 7.3 Hz, 2 H) ; 2.70 (brt, J = 7.3 Hz, 2 H) ; 2.40 (s, 3 H) ; 2.14 (s, 3 H) ; 2.01 (s, 3 H). IR (neat) : 1716, 1702, 1645, 1528 and 1361 cm^{-1}. Anal. Calcd for $C_9H_{13}NO_4$: C, 54.26, H, 6.58, N, 7.03, O, 32.13. Found : C, 54.0, H, 6.7, N, 7.0.

(Z)-6-methyl-5-nitronon-5-en-2,7-dione 12b.
Yield 70 %. *Z*/*E* = 78/22. ^{1}H NMR : (*Z*) (δ) : 2.77-2.68 (m, 4 H) ; 2.70 (q, J = 7.3 Hz, 2 H) ; 2.15 (s, 3 H) ; 2.02 (s, 3 H) ; 1.16 (t, J = 7.3 Hz, 3 H). IR (neat) : 1716, 1701, 1652, 1528 and 1365 cm^{-1}. Anal. Calcd for $C_{10}H_{15}NO_4$: C, 56.33, H, 7.09, N, 6.57, O, 30.01. Found : C, 56.4, H, 7.2, N, 6.2.

(Z)-6-methyl-5-nitrododec-5-en-2,7-dione 12c.
Yield 59 %. *Z*/*E* = 63/37. ^{1}H NMR : (*Z*) (δ) : 2.73-2.70 (m, 4 H) ; 2.65 (t, J = 7.3 Hz, 2 H) ; 2.14 (s, 3 H) ; 2.01 (s, 3 H) ; 1.68-1.60 (m, 2 H) ; 1.39-1.26 (m, 4 H) ; 0.91 (t, J = 6.7 Hz, 3 H). IR (neat) : 1716, 1702, 1645, 1525 and 1361 cm^{-1}. Anal. Calcd for $C_{13}H_{21}NO_4$: C, 61.16, H, 8.29, N, 5.49, O, 25.07. Found : C, 60.8, H, 8.0, N, 5.3.

(Z)-6-ethyl-5-nitrooct-5-en-2,7-dione 12d.
Yield 62 %. *Z*/*E* = 69/31. ^{1}H NMR : (*Z*) (δ) : 2.75-2.65 (m, 4 H) ; 2.40 (s, 3 H) ; 2.37 (q, J = 7.6 Hz, 2 H) ; 2.14 (s, 3 H) ; 1.07 (t, J = 7.6 Hz, 3 H). IR (neat) : 1716, 1703, 1659, 1528 and 1361 cm^{-1}. Anal. Calcd for $C_{10}H_{15}NO_4$: C, 56.33, H, 7.09, N, 6.57, O, 30.01. Found : C, 56.5, H, 6.8, N, 6.2.

Synthesis of β-nitrosulfides 13 from β-nitroenones. General procedure.
To a mixture of β-nitroenone (3 mmol, 1.0 eq.) and thiophenol (0.396 g, 3.6 mmol, 1.2 eq.) in acetonitrile (3 ml) was added dropwise triethylamine (0.030 g, 0.3 mmol, 0.1 eq.). Stirring was continued for 1 hour. The reaction mixture was then poured into 1N hydrochloric acid (6 ml) and extracted with ethyl acetate (2 x 20 ml). The combined organic layers were washed with brine, dried over magnesium sulfate, filtered and concentrated. The crude β-nitrosulfide **13** thus obtained was purified by column chromatography on silica gel.

2-Methyl-1-nitro-2-(phenylthio)butan-3-one 13a.
Yield 61 %. mp = 47-48°C. ^{1}H NMR (δ) : 7.47-7.15 (m, 5 H) ; 4.65 (d, ^{2}J = 14.0 Hz, 1 H) ; 4.35 (d, ^{2}J = 14.0 Hz, 1 H) ; 2.32 (s, 3 H) ; 1.57 (s, 3 H). IR (KBr) : 1709, 1556 and 1368 cm^{-1}. Anal. Calcd for $C_{11}H_{13}NO_3S$: C, 55.21, H, 5.48, N, 5.85, O, 20.06, S, 13.40. Found : C, 55.5, H, 5.5, N, 5.6.

3-Methyl-4-nitro-3-(phenylthio)pentan-2-one 13b.
Yield 79 %. Diastereomeric ratio : *l*/*u* = 78/22. Diastereomer (*l*) : mp = 85°C. ^{1}H NMR (δ) : 7.53-7.27 (m, 5 H); 4.71 (q, J = 7.2 Hz, 1 H) ; 2.45 (s, 3 H) ; 1.86 (d, J = 7.2 Hz, 3 H) ; 1.74 (s, 3 H). Diastereomer (*u*) : ^{1}H NMR (δ) : 7.53-7.27 (m, 5 H) ; 5.11 (q, J = 7.2 Hz, 1 H) ; 2.42 (s, 3 H) ; 1.69 (s, 3 H) ; 1.50 (d, J = 7.2 Hz, 3 H). IR (neat) : 1709, 1550 and 1357 cm^{-1}. Anal. Calcd for $C_{12}H_{15}NO_3S$: C, 56.90, H, 5.97, N, 5.53, O, 18.95, S, 12.66. Found : C, 56.5, H, 6.0, N, 5.2.

2-Methyl-1-nitro-2-(phenylthio)pentan-3-one 13c.
Yield 93 %. ^{1}H NMR (δ) : 7.58-7.34 (m, 5 H) ; 4.82 (d, ^{2}J = 14.0 Hz, 1 H) ; 4.50 (d, ^{2}J = 14.0 Hz, 1 H) ; 3.04 (qd, ^{2}J = 18.5 Hz, ^{3}J = 7.0 Hz, 1 H) ; 2.64 (qd, ^{2}J = 18.5 Hz, ^{3}J = 7.0 Hz, 1 H); 1.71 (s, 3 H) ; 1.16 (t, J = 7.0 Hz, 3 H). IR (neat) : 1709, 1553 and 1372 cm^{-1}. Anal. Calcd for $C_{12}H_{15}NO_3S$: C, 56.90, H, 5.97, N, 5.53, O, 18.95, S, 12.66. Found : C, 56.7, H, 5.7, N, 5.1.

3-Methyl-2-nitro-3-(phenylthio)hexan-4-one 13d.
Yield 85 %. Diastereomeric ratio : *l*/*u* = 79/21. Diastereomer (*l*) : mp = 62-63°C. ^{1}H NMR (δ) : 7.50-7.20 (m, 5 H) ; 4.76 (q, J = 7.2 Hz, 1 H) ; 3.05 (qd, ^{2}J = 18.0 Hz, ^{3}J = 7.2 Hz, 1 H) ; 2.62 (qd, ^{2}J = 18.0 Hz, ^{3}J =

7.2 Hz, 1 H) ; 1.85 (d, J = 7.2 Hz, 3 H) ; 1.75 (s, 3 H); 1.13 (t, J = 7.2 Hz, 3 H). Diastereomer (*u*) : ^{1}H NMR (δ) : 7.50-7.25 (m, 5 H) ; 5.17 (q, J = 6.7 Hz, 1 H) ; 3.11 (qd, ^{2}J = 18.0 Hz, ^{3}J = 7.2 Hz, 1 H) ; 2.58 (qd, ^{2}J = 18.0 Hz, ^{3}J = 7.2 Hz, 1 H) ; 1.68 (s, 3 H) ; 1.49 (d, J = 6.7 Hz, 3 H) ; 1.06 (t, J = 7.2 Hz, 3 H). IR (neat) : 1704, 1550 and 1385 cm^{-1}. Anal. Calcd for $C_{13}H_{17}NO_3S$: C, 58.41, H, 6.41, N, 5.24, O, 17.95, S, 11.99. Found : C, 58.3, H, 6.1, N, 5.0.

4-Methyl-5-nitro-4-(phenylthio)nonan-3,8-dione 13e.
Yield 97 %. Diastereomeric ratio : *l*/*u* = 72/28. Diastereomer (*l*) : ^{1}H NMR (δ) : 7.46-7.26 (m, 5 H) ; 4.55 (dd, ^{3}J = 11.5 Hz, ^{3}J' = 1.9 Hz, 1 H) ; 3.18-2.03 (m, 6 H) ; 2.19 (s, 3 H) ; 1.80 (s, 3 H) ; 1.10 (t, J = 7.2 Hz, 3 H). IR (neat) : 1710, 1556 and 1379 cm^{-1}. Diastereomer (*u*) : ^{1}H NMR (δ) : 7.46-7.26 (m, 5 H) ; 4.99 (dd, ^{3}J = 11.5 Hz, ^{3}J' = 1.9 Hz, 1 H) ; 3.18-2.03 (m, 6 H) ; 2.10 (s, 3 H) ; 1.71 (s, 3 H) ; 1.05 (t, J = 7.2 Hz, 3 H). IR (neat) : 1710, 1553 and 1357 cm^{-1}. Anal. Calcd for $C_{16}H_{21}NO_4S$: C, 59.42, H, 6.54, N, 4.33, O, 19.79, S, 9.91. Found : C, 59.6, H, 6.3, N, 4.2.

2-Methyl-1-nitro-2-(phenylthio)octan-3-one 13f.
Yield 61 %. ^{1}H NMR (δ) : 7.50-7.27 (m, 5 H) ; 4.81 (d, ^{2}J = 14.0 Hz, 1 H) ; 4.49 (d, ^{2}J = 14.0 Hz, 1 H) ; 2.93 (td, ^{2}J = 17.0 Hz, ^{3}J = 7.5 Hz, 1 H) ; 2.65 (td, ^{2}J = 17.0 Hz, ^{3}J = 7.5 Hz, 1 H) ; 1.79-1.25 (m, 6 H) ; 1.70 (s, 3 H) ; 0.93 (t, J = 7.0 Hz, 3 H). IR (neat) : 1708, 1554 and 1371 cm^{-1}. Anal. Calcd for $C_{15}H_{21}NO_3S$: C, 60.99, H, 7.17, N, 4.74, O, 16.25, S, 10.85. Found : C, 61.0, H, 6.8, N, 4.5.

2-Ethyl-1-nitro-2-(phenylthio)butan-3-one 13g.
Yield 85 %. ^{1}H NMR (δ) : 7.57-7.14 (m, 5 H) ; 4.65 (d, ^{2}J = 14.0 Hz, 1 H) ; 4.58 (d, ^{2}J = 14.0 Hz, 1 H) ; 2.46 (s, 3 H) ; 2.18 (qd, ^{2}J = 19.0 Hz, ^{3}J = 7.5 Hz, 1 H) ; 2.00 (qd, ^{2}J = 19.0 Hz, ^{3}J = 7.5 Hz, 1 H) ; 1.12 (t, J = 7.5 Hz, 3 H). IR (neat) : 1705, 1554 and 1374 cm^{-1}. Anal. Calcd for $C_{12}H_{15}NO_3S$: C, 56.90, H, 5.97, N, 5.53, O, 18.95, S, 12.66. Found : C, 56.4, H, 5.7, N, 5.7.

3-Ethyl-2-nitro-3-(phenylthio)pentan-4-one 13h.
Yield 55 %. Diastereomeric ratio : *l*/*u* = 53/47. Diastereomer (*l*) : ^{1}H NMR (δ) : 7.61-7.28 (m, 5 H) ; 4.84 (q, J = 7.0 Hz, 1 H) ; 2.45 (s, 3 H) ; 1.96 (q, J = 7.4 Hz, 2 H) ; 1.81 (d, J = 7.0 Hz, 3 H) ; 1.11 (t, J = 7.4 Hz, 3 H). Diastereomer (*u*) : ^{1}H NMR (δ) : 7.61-7.28 (m, 5 H) ; 5.11 (q, J = 7.0 Hz, 1 H) ; 2.50 (s, 3 H) ; 1.82 (q, J = 7.4 Hz, 2 H) ; 1.71 (d, J = 7.0 Hz, 3 H) ; 1.01 (t, J = 7.4 Hz, 3 H). IR (neat) : 1702, 1558 and 1357 cm^{-1}. Anal. Calcd for $C_{13}H_{17}NO_3S$: C, 58.41, H, 6.41, N, 5.24, O, 17.95, S, 11.99. Found : C, 58.3, H, 6.3, N, 5.2.

3-Ethyl-4-nitro-3-(phenylthio)octan-2,7-dione 13i.
Yield 64 %. Diastereomeric ratio : *l*/*u* = 86/14. Diastereomer (*l*) : ^{1}H NMR (δ) : 7.52-7.33 (m, 5 H) ; 4.72 (dd, ^{3}J = 11.5 Hz, ^{3}J' = 2.1 Hz, 1 H) ; 2.97-2.25 (m, 4 H) ; 2.44 (s, 3 H) ; 2.14 (s, 3 H) ; 1.94 (qd, ^{2}J = 14.4 Hz, ^{3}J = 7.2 Hz, 1 H) ; 1.66 (qd, ^{2}J = 14.4 Hz, ^{3}J = 7.2 Hz, 1 H) ; 1.11 (t, J = 7.2 Hz, 3 H). Diastereomer (*u*) : ^{1}H NMR (δ) : 7.52-7.33 (m, 5 H) ; 4.87 (dd, ^{3}J = 10.9 Hz, ^{3}J' = 2.1 Hz, 1 H) ; 2.66-2.10 (m, 4 H) ; 2.46 (s, 3 H) ; 2.14 (s, 3 H) ; 2.04 (qd, ^{2}J = 14.5 Hz, ^{3}J = 7.2 Hz, 1 H) ; 1.82 (qd, ^{2}J = 14.5 Hz, ^{3}J = 7.2 Hz, 1 H) ; 1.09 (t, J = 7.2 Hz, 3 H). IR (neat) : 1716, 1553 and 1357 cm^{-1}. Anal. Calcd for $C_{16}H_{21}NO_4S$: C, 59.42, H, 6.54, N, 4.33, O, 19.79, S, 9.91. Found : C, 59.3, H, 6.6, N, 4.2.

1-Nitro-2-(phenylthio)-2-propylpentan-3-one 13j.
Yield 63 %. ^{1}H NMR (δ) : 7.44-7.51 (m, 5 H) ; 4.67 (d, ^{2}J = 14.0 Hz, 1 H) ; 4.62 (d, ^{2}J = 14.0 Hz, 1 H) ; 3.13 (qd, ^{2}J = 18.0 Hz, ^{3}J = 7.3 Hz, 1 H) ; 2.61 (qd, ^{2}J = 18.0 Hz, ^{3}J = 7.3 Hz, 1 H) ; 2.08 (ddd, ^{2}J = 16.5 Hz, ^{3}J = 12.5 Hz, ^{3}J' = 4.4 Hz, 1 H) ; 1.87 (ddd, ^{2}J = 16.5 Hz, ^{3}J = 12.5 Hz, ^{3}J' = 4.4 Hz, 1 H) ; 1.75-1.65 (m, 1 H) ; 1.38-1.25 (m, 1 H) ; 1.14 (t, J = 7.3 Hz, 3 H) ; 1.00 (t, J = 7.3 Hz, 3 H). IR (neat) : 1705, 1554 and 1371 cm^{-1}. Anal. Calcd for $C_{14}H_{19}NO_3S$: C, 59.76, H, 6.81, N, 4.98, O, 17.06, S, 11.39. Found : C, 59.5, H, 6.9, N, 4.7.

5-Nitro-4-(phenylthio)-4-propylhexan-3-one 13k.
Yield 57 %. Diastereomeric ratio : *l*/*u* = 65/35. Diastereomer (*l*) : ^{1}H NMR (δ) : 7.57-7.35 (m, 5 H) ; 4.83 (q, J = 7.0 Hz, 1 H) ; 3.02 (qd, ^{2}J = 18.1 Hz, ^{3}J = 7.1 Hz, 1 H) ; 2.58 (qd, ^{2}J = 18.1 Hz, ^{3}J = 7.1 Hz, 1 H) ; 1.80 (q, J = 7.0 Hz, 1 H) ; 1.75-1.32 (m, 4 H) ; 1.15 (t, J = 7.1 Hz, 3 H) ; 0.93 (t, J = 7.0 Hz, 3 H).

Diastereomer (*u*) : ^{1}H NMR (δ) :7 .57-7.35 (m, 5 H) ; 5.18(q, J = 7.0 Hz, 1 H) ; 3.12 (qd, ^{2}J = 18.2 Hz, ^{3}J = 7.2 Hz, 1 H) ; 2.70 (qd, ^{2}J = 18.2 Hz, ^{3}J = 7.2Hz, 1 H) ; 1.75-1.32 (m, 4 H) ; 1.68 (d, J = 7.0 Hz, 1H) ; 1.13 (t, J = 7.2 Hz, 3 H) ; 0.85 (t, J = 7.0 Hz, 3 H). IR (neat) : 1709, 1550 and 1361 cm^{-1}. Anal. Calcd for $C_{15}H_{21}NO_3S$: C, 60.99, H, 7.17, N, 4.74, O, 16.25, S, 10.85. Found : C, 61.1, H, 7.1, N, 4.5.

X-ray crystal structure determination for 13b.

Formula : $C_{12}H_{15}NO_3S$; M = 253.32 ; crystal size : 0.45 · 0.35 · 0.10 mm ; orthorhombic ; space group : $P2_12_12_1$; a = 6.873 (1) Å, b = 12.929 (1) Å, c = 14.988 (1) Å ; V = 1331.8 (5) Å^3 ; Z = 4 ; ρ_{calcd} : 1.263 g.cm^{-3} ; diffractometer : Enraf-Nonius CAD4 ; CuKα radiation (graphite monochromator) ; wave length : 1.5418 Å ; scan mode Θ/2 Θ ; 2 Θ range : 6 < 2 Θ < 150 ; reflections used : 2267 [I>2σ(I)] ; direct method : SHELXS 86 ; refinement method : full matrix ; R = 0.058, R_w = 0.063 ;weight W = 1/σ^2(F).

Selected bond lengths and angles are given in Tables V and VI. Full atomic coordinates, for this work are available on request from the Director of the Cambridge Crystallographic Data Centre.

Table V. Selected bond angles (Å) for compound **13b.**

S(1)	C(7)	1.834(5)	S(1)	C(9)	1.768(6)
O(2)	N(5)	1.250(7)	O(3)	N(5)	1.189(7)
O(4)	C(8)	1.185(9)	N(5)	C(6)	1.535(7)
C(6)	C(7)	1.530(8)	C(6)	C(15)	1.531(8)
C(7)	C(8)	1.528(8)	C(7)	C(16)	1.536(8)
C(8)	C(17)	1.53(1)	C(9)	C(10)	1.390(8)
C(9)	C(14)	1.411(8)	C(10)	C(11)	1.38(1)
C(11)	C(12)	1.39(1)	C(12)	C(13)	1.36(1)
C(13)	C(14)	1.403(9)			

Table VI. Selected bond angles (°) for compound **13b.**

C(9)	S(1)	C(7)	105.1(3)	O(3)	N(5)	O(2)	123.3(6)
C(6)	N(5)	O(2)	114.2(6)	C(6)	N(5)	O(3)	122.5(6)
C(7)	C(6)	N(5)	114.4(5)	C(15)	C(6)	N(5)	104.9(5)
C(15)	C(6)	C(7)	116.0(5)	C(6)	C(7)	S(1)	108.3(4)
C(8)	C(7)	S(1)	106.8(4)	C(8)	C(7)	C(6)	108.6(6)
C(16)	C(7)	S(1)	104.5(4)	C(16)	C(7)	C(6)	114.2(4)
C(16)	C(7)	C(8)	114.0(6)	C(7)	C(8)	O(4)	121.2(7)
C(17)	C(8)	O(4)	121.8(7)	C(17)	C(8)	C(7)	116.8(8)
C(10)	C(9)	S(1)	120.6(5)	C(14)	C(9)	S(1)	119.5(5)
C(14)	C(9)	C(10)	119.4(6)	C(11)	C(10)	C(9)	120.5(7)
C(12)	C(11)	C(10)	120.0(7)	C(13)	C(12)	C(11)	120.6(7)
C(14)	C(13)	C(12)	120.6(7)	C(13)	C(14)	C(9)	118.8(6)

Synthesis of 5-hydroxy-4-(phenylthio)-2-isoxazoline 2-oxides 14. General procedure.

Under a nitrogen atmosphere, potassium tert-butoxide (0.224 g, 2.0 mmol, 1.0 eq.) in anhydrous tetrahydrofuran (5 ml) was cooled to -78°C. The β-nitrosulfide **13** (2.0 mmol, 1.0 eq.) in THF (2 ml) was then added in one portion. The mixture was stirred during 10 seconds and acidified at -78°C with acetic acid (2.5 ml). The temperature of the reaction was then allowed to warm up gradually to 25°C during 1 hour. The mixture was poured into water (30 ml) and extracted with dichloromethane (2 x 40 ml). The combined organic layers were then successively washed with a 5% $NaHCO_3$ solution (20 ml), water (20 ml), brine (20 ml), dried over magnesium sulfate and concentrated under reduced pressure. 5-Hydroxy-4-(phenylthio)-2-isoxazoline 2-oxides **14a** and **14d** were purified by washing the white solids obtained after evaporation with ether. Compounds **14b** and **14c** were chromatographed on silica gel.

5-hydroxy-3,4,5-trimethyl-4-(phenylthio)-2-isoxazoline 2-oxide 14a.

Yield 54 %. Diastereomeric ratio : diastereomer 1/diastereomer 2 = 93/7. Diastereomer 1 : ^{1}H NMR (DMSO D_6) (δ) : 7.50-7.27 (m, 5 H) ; 1.77 (s, 3H) ; 1.69 (s, 3 H) ; 1.41 (s, 3 H). ^{13}C NMR (DMSO D_6) (δ) : 135.85, 130.06, 129.29, 128.76, 117.08, 104.79, 66.83, 19.80, 17.49, 9.5. Diastereomer 2 : ^{1}H NMR (DMSO D_6) (δ) : 7.50-7.27 (m, 5 H) ; 1.86 (s, 3H) ; 1.65 (s, 3 H) ; 1.45 (s, 3 H). ^{13}C NMR (DMSO D_6) (δ) : 135.85, 130.06, 129.29, 128.76, 118.63, 105.22, 65.00, 20.05, 15.45, 9.73. IR (KBr) : 3184 and 1638 cm^{-1}. Anal. Calcd for $C_{12}H_{15}NO_3S$: C, 56.90, H, 5.97, N, 5.53, O, 18.95, S, 12.66. Found : C, 56.7, H, 6.0, N, 5.5, S, 12.6.

4-Ethyl-5-hydroxy-3,5-dimethyl-4-(phenylthio)-2-isoxazoline 2-oxide 14b.
Yield 67 %. Diastereomeric ratio : diastereomer 1/diastereomer 2 = 70/30. Diastereomer 1 : ^{1}H NMR (δ) : 7.62-7.27 (m, 5 H) ; 4.97 (OH) ; 2.19 (qd, ^{2}J = 15.5 Hz, ^{3}J = 7.5 Hz, 3 H) ; 1.87 (s, 3 H) ; 1.68 (s, 3 H) ; 1.20 (t, J = 7.5 Hz, 3 H). ^{13}C NMR (δ) : 136.35, 129.71, 129.11, 128.98, 122.07, 105.89, 70.13, 25.78, 22.31, 10.18, 8.50. Diastereomer 2 : ^{1}H NMR (δ) : 7.62-7.27 (m, 5 H) ; 5.55 (OH) ; 2.00 (qd, ^{2}J = 15.5 Hz, ^{3}J = 7.5 Hz, 2 H) ; 1.82 (s, 3 H) ; 1.58 (s, 3 H) ; 1.10 (t, J = 7.5 Hz, 3 H). ^{13}C NMR (δ) : 136.99, 130.35, 129.38, 128.98, 122.07, 105.86, 70.13, 27.18, 20.91, 10.70, 8.50. IR (KBr) : 3210 and 1638 cm^{-1}. Anal. Calcd for $C_{13}H_{17}NO_3S$: C, 58.41, H, 6.41, N, 5.24, O, 17.95, S, 11.99. Found : C, 58.1, H, 6.5, N, 5.3.

5-Ethyl-5-hydroxy-3,4-dimethyl-4-(phenylthio)-2-isoxazoline 2-oxide 14c.
Yield 75 %. Diastereomeric ratio : diastereomer 1/diastereomer 2 = 64/36. Diastereomer 1 : ^{1}H NMR (δ) : 7.61-7.17 (m, 5 H) ; 4.58 (q, J = 7.0 Hz, 1 H) ; 1.84 (s, 3 H) ; 1.56 (s, 3 H) ; 1.20 (t, J = 7.0 Hz, 3 H). ^{13}C NMR (δ) : 136.00, 130.25, 129.73, 128.98, 121.13, 106.90, 66.80, 27.04, 18.36, 9.75, 7.50. Diastereomer 2 : ^{1}H NMR (δ) : 7.61-7.17 (m, 5 H) ; 2.26 (q, J = 7.0 Hz, 2 H) ; 1.91 (s, 3 H) ; 1.44 (s, 3 H) ; 1.14 (t, J = 7.0 Hz, 3 H). ^{13}C NMR (δ) : 136.72, 129.91, 129.17, 128.98, 121.13, 106.13, 66.80, 27.49, 18.60, 9.98, 7.36. IR (KBr) : 3198 and 1645 cm^{-1}. Anal. Calcd for $C_{13}H_{17}NO_3S$: C, 58.41, H, 6.41, N, 5.24, O, 17.95, S, 11.99. Found : C, 58.5, H, 6.5, N, 5.2.

5-Ethyl-5-hydroxy-3-methyl-4-(phenylthio)-4-propyl-2-isoxazoline 2-oxide 14d.
Yield 60 %. Diastereomeric ratio : diastereomer 1/diastereomer 2 = 92/8. Diastereomer 1 : ^{1}H NMR (DMSO D_6) (δ) : 7.46-7.25 (m, 5 H) ; 3.39 (brs, OH) ; 2.46-1.35 (m, 6 H) ; 1.62 (s, 3 H) ; 1.01 (t, J = 7.0 Hz, 3H); 0.91 (t, J = 7.0 Hz, 3H);. ^{13}C NMR (DMSO D_6) (δ) : 136.80, 130.56, 130.32, 129.90, 118.17, 106.52, 71.76, 35.77, 29.13, 18.12, 15.36, 10.92, 8.54. IR (KBr) : 3255 and 1638 cm^{-1}. Anal. Calcd for $C_{15}H_{21}NO_3S$: C, 60.99, H, 7.17, N, 4.74, O, 16.25, S, 10.85. Found : C, 60.1, H, 7.3, N, 4.4.

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