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Lipase-catalyzed separation of the enantiomers of 1-arylideneamino-3-aryloxypropan-2-ol-*N*-oxides. Preparation of optically active nitrones

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Abstract—Several racemic 1-arylideneamino-3-aryloxypropan-2-ol-*N*-oxides have been prepared and separated into enantiomers by a lipase-catalyzed transesterification with vinyl acetate as the acyl donor.

1. Introduction

As well known scavengers of free radicals, nitrones exhibit an antioxidant activity[1] in biological systems and therefore may be considered as prospective drugs for the treatment of oxidative stress in brain.[2] On the other hand, owing to their 1,3-dipolar structure, nitrones are valuable synthons in addition and cycloaddition reactions.[3] Chiral nitrones, in most cases those derived from tartaric acid or carbohydrates, were used in the preparation of a few types of optically active heterocycles,[4] some of which displayed biological activity. The methods used for the preparation of optically active nitrones were basically the same as those used for preparing racemates or achiral compounds. In general, they depend on the N-oxidation of optically active secondary amines[5] or on the reaction of monosubstituted hydroxyamines with aldehydes, one or both reagents being chirality carriers.

Since enzymes can recognize chirality, there is a question as to whether an enzyme-catalyzed reaction can be used for the kinetic separation of nitrone racemates by way of the lipase-catalyzed esterification of α- or β-hydroxynitrones. It is generally known[6] that acylating agents convert nitrones into unstable O-acylated nitrones in both acidic and basic media. These can further rearrange to the corresponding amides,[7] diacylamines,[8] α-acyloxyimines,[9] or *N*-acyloxyoxazolidines,[10] the final product depending on the substrate and the acylating agent. For this reason, a standard synthetic acylation of the hydroxy or amino function in nitrones seems rather impracticable. On the other hand, nitrones with a secondary alcohol function have not been employed to date as substrates in hydrolase-catalyzed reactions. In the present research, we focused our attention on investigating selective enzyme-catalyzed acetylation of the hydroxy group in nitrones. *N*-Oxides of 1-arylideneamino-3-aryloxypropan-2-ols, readily accessible[11] from the appropriate monosubstituted hydroxyamines and aldehydes, have been selected as model compounds in this investigation.

2. Results and discussion

1-Arylideneamino-3-aryloxypropan-2-ol-*N*-oxides **2** were prepared[11] from the appropriate 3-aryloxy-1-hydroxyaminopropan-2-ols **1** and aromatic aldehydes according to Scheme 1.

Our attempts to acetylate the hydroxy group with acetyl chloride or acetic anhydride were unsuccessful. Complex product mixtures were formed in either case. On the contrary, acetylation of **2a** with vinyl acetate and Novozym SP 435 (*Candida antarctica* lipase) as the catalyst proceeded with high selectivity for the secondary hydroxy group with no change to the nitrone moiety. This prompted us to investigate the applicability of the reaction in the kinetic separation of β-hydroxynitrone enantiomers.

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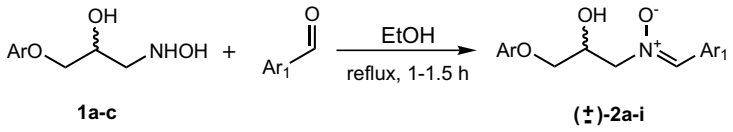
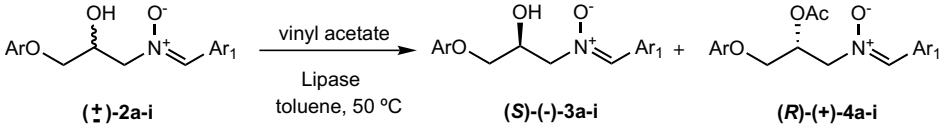


1a-c (±)-2a-i

Scheme 1. Synthesis of (±)-**2a**–**i**.



(±)-2a-i (S)-(-)-3a-i (R)-(+)-4a-i

Scheme 2. Acetylation reaction of (±)-**2a**–**i**.

The conditions for lipase-catalyzed acetylation of racemic β-hydroxynitrones (±)-**2a**–**i** were optimized by conventional methods[12] (Scheme 2). At first, reaction enantioselectivity was determined and analyzed in order to determine to what extent it was affected by changing the lipase type, solvent, and the aromatic substituent attached to the azomethine carbon atom.

The nitrones investigated (±)-**2a**–**i** are almost insoluble in the volatile apolar organic solvents used in the lipase-catalyzed esterifications. This prompted us to use toluene at elevated temperature as the reaction medium. Thus, 1-benzylideneamino-3-phenoxy-propan-2-ol-*N*-oxide **2a** was allowed to react at 45–50 °C in a toluene solution with 10 equivalents of vinyl acetate in the presence of the tested lipase. The relatively high reaction temperature determined the choice of the enzyme; only the immobilized *C. antarctica* lipase preparations were thermostable enough to be tested. In the control experiments carried out in the absence of the enzyme or at a lower temperature, no transesterification was observed. Thin layer chromatography was applied for monitoring the reactions, which were stopped when the conversion reached approximately 50%. The enzyme was removed by filtration and the resulting solution of the enantiomerically enriched alcohol **3a** and acetate **4a** was used for the determination of the conversion degree (c%) and the enantiomeric excess (ee%). The results presented in Table 1 indicate only a moderate enantioselectivity of the tested lipase preparations, although Novozym SP 435 and Chirazym L-2, c-f, c-2, lyo may be considered as promising catalysts. A further optimization of the substrate structure is to be continued.

Since the results produced in Table 1 indicated the superiority of Novozym SP 435, this enzyme preparation was chosen for further investigation of the substrate structure effects on the reaction enantioselectivity. Thus, racemic mixtures of 1-arylideneamino-3-aryloxypropan-2-ol-*N*-oxi-

Table 1. Results of the lipase-catalyzed kinetic resolution of (±)-**2a** by transesterification[a]

Entry	Enzyme	Time (h)	c[b] (%)	ee_{sub}[c] (%)	ee_{prod}[c] (%)	E[b]
1	Novozyme SP 435	96	47	69	77	16
2	Chirazyme L-2, c-f, lyo	120	12	10	74	7
3	Chirazyme L-2, c-f, c-2, lyo	96	42	57	79	15

[a] Conditions: 1 mmol of (±)-**3a**, 10 mmol of vinyl acetate, 300 mg of appropriate enzyme, and 50 ml of toluene at 45–50 °C.
[b] Conversion c% and E-values were calculated from the enantiomeric excess of substrate **3a** (ees) and product **4a** (eep) using the known formula: $E = \mathrm{Ln}[(1 - ees)(eep/(ees + eep))]/\mathrm{Ln}[(1 + ees)(eep/(ees + eep))]$, conversion $c = ees/(ees + eep)$.
[c] Determined by HPLC analysis using (S,S)-Whelk-0,1 column.

Table 2. Results of the Novozym 435 lipase-catalyzed transesterification of (±)-**2a**–**i** in a toluene solution at 45–50 °C[a]

Entry		Ar[1]	Ar	Time (h)	c[b] (%)	ee_{sub}[c] (%)	ee_{prod}[c] (%)	E[b]
1	**2a**	C_6H_5–	C_6H_5–	96	47	69	77	16
2	**2b**	4-NO_2–C_6H_4–	C_6H_5–	69	56.5	95	73	23
3	**2c**	4-CH_3O–C_6H_4–	C_6H_5–	68.5	24	30	93	38
4	**2d**	3,4-Di-CH_3O–C_6H_3–	C_6H_5–	68	47	80	88	38
5	**2e**	4-CH_3–C_6H_4–	C_6H_5–	72	45	65	80	18
6	**2f**	2,4,6-Tri-CH_3–C_6H_2–	C_6H_5–	138	~10	nd[d]	nd[d]	—
7	**2g**	4-Cl–C_6H_4–	C_6H_5–	68	47	74	84	26
8	**2h**	C_6H_5–	4-CH_3–C_6H_4–	97	47	64	73	12
9	**2i**	C_6H_5–	4-Cl–C_6H_4–	96	42	60	84	20

[a–c] See Table 1.
[d] nd—not determined.

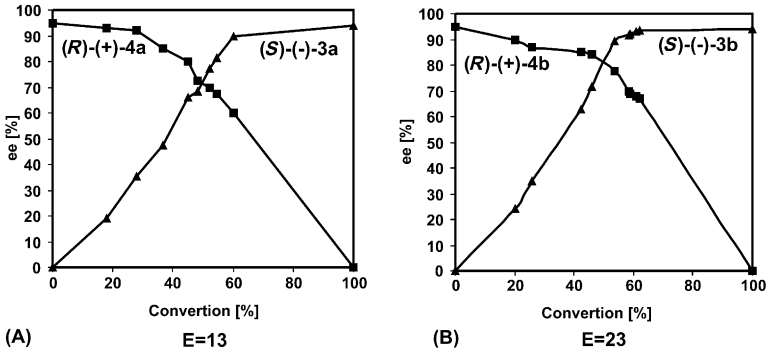


Figure 1. Dependence of the enantiomeric purities ee (%) of **3a** and **4a** (graph A) and **3b** and **4b** (graph B) on the conversion degree of (±)-**2a** and (±)-**2b** during the Novozym SP 435-catalyzed acetylation with vinyl acetate in a toluene solution at 45–50 °C.

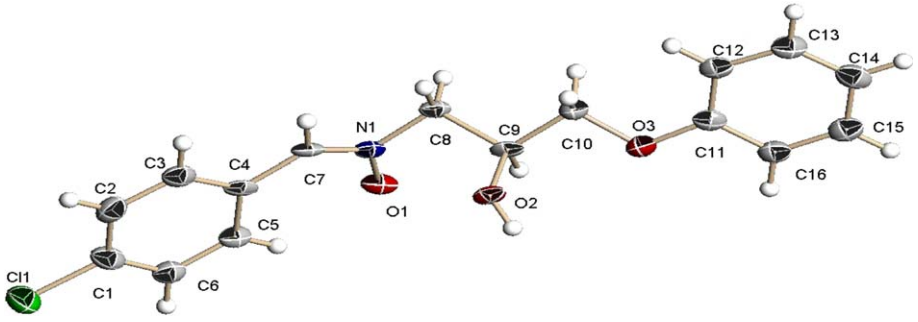


Figure 2. An ORTEP plot of (*S*)-(−)-1-(4-chlorobenzylideneamino)-3-phenoxy-propan-2-ol-*N*-oxide (−)-**3g** with thermal ellipsoids drawn at 50% probability level.

des were subjected to the lipase-catalyzed transesterification with vinyl acetate in a toluene solution. As can be seen in Table 2, the stereochemical results of the reactions were improved when mono- or disubstitution of the aromatic ring in Ar^1 increased its bulkiness. The kinetic resolution of **2a–i** prepared from mono- and di-substituted benzaldehydes proceeded with moderate-to-good enantioselectivities ($E = 12–38$). When the volume of Ar^1 was increased further by the introduction of a third substituent (±)-**2f**, the substrate was poorly recognized by the enzyme and the reaction rate was drastically slowed.

The enantiomeric excess of the products of the kinetic separation reactions of the faster and slower reacting enantiomers of **2a** and **2b** plotted against the conversion degree (Fig. 1, plots A and B, respectively) indicate moderate enantioselectivity of both reactions.

It was also a matter of interest as to whether the substitution of the Ar aromatic ring had any influence on the stereochemical course of the reaction. Thus, nitrones (±)-**2h** and (±)-**2i** were prepared from the appropriately chloro- and methyl-substituted **1** and benzaldehyde. In the kinetic enantiomer separation reaction under the above outlined conditions, they gave results similar to those obtained with the unsubstituted analog (±)-**2a**.

The result of the X-ray crystallographic investigation of 1-(4-chlorobenzylideneamino)-3-phenoxy-propan-2-ol-*N*-oxide **3g** combined with the specific rotation data for all **3** and **4** infers that the slower reacting enantiomer of **3** has an (*S*)-(−)-configuration (Fig. 2), and the faster one, yielding acetates **4**, a (*R*)-(+)-configuration.

3. Conclusion

The investigation revealed that the lipase-catalyzed acylation of a hydroxy group in the presence of a nitrone moiety in the same molecule proceeds chemoselectively to yield the corresponding *O*-acyloxy nitrones. Enantioselectivities of the reactions were satisfactory.

4. Experimental

4.1. General

^1H (400 MHz) and ^{13}C NMR (100 MHz) spectra were recorded on a Varian Mercury 400 MHz spectrometer in $CDCl_3$ or DMSO-d_6 solution, and chemical shifts (δ) are reported in parts per million. IR spectra were taken on a Carl Zeiss Specord M80 instrument. HPLC–MS were recorded on HPLC Waters 2695 Micromass ZQ4000 apparatus (Ace C18 (3 × 75 mm) column) using methanol/water (0.01 M formic acid) gradient. Mass spectra were recorded on Mariner apparatus (Applied Biosystems) using electron-spray ionization. Enantiomeric excesses of nitrones (*S*)-(−)-**3a–i** and esters (*R*)-(+)-**4a–i** were determinated on a Thermo-Separation Products P-100 instrument and

(*S*,*S*)-Whelk-0,1 column (in *n*-hexane/ethanol 9:1; 0.8 ml/min for alcohols and esters) using racemic compounds as references. Optical rotations were measured in $CHCl_3$ with PolAAr 32 polarimeter. Elemental analyses were performed on CHNS/O Perkin Elmer type 2400 instrument. The reactions were monitored by TLC on Silica gel 60 F_{254} plates and by column chromatography on Silica gel 60 (230–400 mesh). The arylglycidyl ethers were prepared by the Williamson reaction from the appropriate phenols and epichlorohydrin in an aqueous NaOH solution. Novozym SP 435 was kindly granted by Novo-Nordisk. Chirazymes were supplied by Roche Molecular Biochemicals (Germany).

4.2. Preparation of 1-(hydroxyamino)-3-aryloxypropan-2-oles (1a–c)

1-(Hydroxyamino)-3-aryloxypropan-2-oles were prepared according to the earlier described method.[11] The physical and spectral properties of the **1a** are given in a paper,[11] while the properties of **1b** and **c** are listed below.

4.2.1. 1-Hydroxyamino-1-(4-methylphenoxy)propan-2-ol 1b. Yield 52%. Mp = 117–119 °C. ^{1}H MNR (DMSO-d_6) δ ppm 2.21 (s; 3H; CH_3); 2.77 (dd; 1H$_a$; CH_aH$_b$N; $J_{gem} = 12.8$ Hz; $J_1 = 6.8$ Hz); 2.85 (dd; 1H$_b$; CH$_a$$H_b$N; $J_2 = 5.2$ Hz); 3.18 (dd; 1H$_c$; OCH_cH$_d$; $J_{gem} = 10$ Hz; $J_3 = 6.4$ Hz); 3.92 (dd; 1H$_d$; OCH$_c$$H_d$; $J_4 = 4$ Hz); 3.98 (m; 1H; CH); 4.89 (d; 1H; OH; $J_5 = 4.8$ Hz); 5.67 (s; 1H; OH); 6.78–6.82 (m; 2H; aromat.); 7.05–7.07 (m; 2H; aromat.); 7.25 (s; 1H; NH). ^{13}C NMR (DMSO-d_6) δ ppm 20.07; 56.78; 66.09; 70.86; 114.28; 128.97; 129.77; 156.63. IR (Nujol mull; cm^{-1}) 3450; 3250; 1510; 1460; 1295; 1250; 1060; 1045; 1035; 810; 800. Anal. Calcd for $C_{10}H_{15}NO_3$: C, 60.90; H, 7.66; N, 7.10. Found: C, 60.81; H, 7.59; N, 7.04. HPLC MS (ES) retention time 0.8 min; *m*/*z* found: 196.96; *m*/*z* calcd for $C_{10}H_{15}NO_3$: 197.23.

4.2.2. 3-(4-Chlorophenoxy)-3-hydroxyaminopropan-2-ol 1c. Yield 35%. Mp = 95–97 °C. ^{1}H NMR (DMSO-d_6) δ ppm 2.81 (dd; 1H$_a$; $J_{gem} = 12.8$ Hz; $J =$ 6.8 Hz; CH_aH$_b$NH); 2.88 (dd; 1H$_b$; $J = 5.2$ Hz; CH$_a$$H_b$NH); 3.86 (dd; 1H$_c$; $J_{gem} = 10$ Hz; $J = 6.4$ Hz; OCH_cH$_d$); 3.96–4.03 (m; 2H; OCH$_c$$H_d$+$CH$); 5.04 (s; 1H; OH or NH); 6.92–6.96 (m; 2H; aromat.); 7.27–7.32 (m; 2H; aromat.). ^{13}C NMR (DMSO-d_6) δ ppm 56.37; 65.82; 71.17; 116.27; 124.12; 129.22; 157.62. IR (Nujol; cm^{-1}) 3440; 3350; 1745; 1510; 1490; 1455; 1245; 1040; 1030; 820. Anal. Calcd for $C_9H_{12}ClNO_3$: C, 49.67; H, 5.56; N, 6.44. Found: C, 49.58; H, 5.48; N, 6.50.

4.3. Preparation of 1-(arylideneamino)-3-aryloxypropan-2-ol-*N*-oxides (±)-3a–i

The compounds were prepared according to the earlier described[11] procedure. The physical and spectral properties of (±)-**2a**–**b** are given in the paper, and the properties of (±)-**2c**–**i** are listed below.

4.3.1. 1-(4-Methoxybenzylideneamino)-3-phenoxy-propan-2-ol-*N*-oxide (±)-2c. Yield 75%. Mp = 165–166 °C (recrystallized from ethanol). ^{1}H NMR ($CDCl_3$) δ ppm 3.85 (s; 3H; CH_3); 3.95 (dd; 1H$_a$; $J_{gem} = 9.6$ Hz; $J = 8$ Hz; –CH_aH$_b$N=); 4.13 (dd; 1H$_c$; $J_{gem} = 12.4$ Hz; $J = 6.8$ Hz; –OCH_cH$_d$–); 4.15 (dd; 1H$_b$; $J = 4.2$ Hz; –CH$_a$$H_b$N=); 4.25 (dd; 1H$_d$; $J = 2.4$ Hz; –OCH$_c$$H_d$–); 4.52 (m; 1H; C$H$); 5.47 (s; 1H; OH); 6.90–6.98 (m; 5H; aromat.); 7.27–7.31 (m; 2H; aromat.); 7.32 (s; 1H; H$_\alpha$); 8.19 (m; 2H; aromat.). ^{1}H NMR (DMSO-d_6) δ ppm 3.97–4.00 (m; 4H; 2 × CH_2); 4.44 (m; 1H; CH); 5.56 (d; 1H; $J = 5.6$ Hz; OH); 6.91–6.99 (m; 5H; aromat.); 7.26–7.30 (m; 2H; aromat.); 7.74 (s; 1H; H$_\alpha$); 8.24–8.27 (m; 2H; aromat.). ^{13}C NMR (DMSO-d_6) δ ppm 70.03; 113.70; 114.54; 120.72; 123.94; 129.51; 130.04; 134.39; 158.44; 160.20. IR (Nujol; cm^{-1}) 3140 (ν_{OH}); 1605 ($\nu_{C=N}$); 1140 (ν_{NO}). Anal. Calcd for $C_{17}H_{19}NO_4$: C, 67.67; H, 6.37; N, 4.65. Found: C, 67.60; H, 6.33; N, 4.75.

4.3.2. 1-(3,4-Dimethoxybenzylideneamino)-3-phenoxy-propan-2-ol-*N*-oxide (±)-2d. Yield 87%. Mp = 113–114 °C (recrystallized from 2-propanol). ^{1}H NMR ($CDCl_3$) δ ppm 3.927 (s; 3H; CH_3); 3.930 (s; 3H; CH_3); 3.96 (dd; 1H$_a$; $J_{gem} = 9.6$ Hz; $J = 8$ Hz; –CH_aH$_b$N=); 4.13 (dd; 1H$_c$; $J_{gem} = 12.4$ Hz; $J = 7.2$ Hz; –OCH_cH$_d$–); 4.16 (dd; 1H$_b$; $J = 4.8$ Hz; –CH$_a$$H_b$N=); 4.26 (dd; 1H$_d$; $J = 2.8$ Hz; –OCH$_c$$H_d$–); 4.54 (m; 1H; C$H$); 5.32 (d; 1H; $J = 4.8$ Hz; OH); 6.88 (d; 1H; $J = 8.4$ Hz; aromat.); 6.90–6.93 (m; 2H; aromat.); 6.98 (m; 1H; aromat.); 7.27–7.31 (m; 2H; aromat.); 7.32 (s; 1H; Hα); 7.48 (dd; 1H; $J = 2$ Hz; $J = 8.4$ Hz; aromat.); 8.24 (d; 1H; $J = 2$ Hz; aromat.). ^{1}H NMR (DMSO-d_6) δ ppm 3.74 (s; 3H; CH_3); 3.78 (s; 3H; CH_3); 3.97–4.00 (m; 4H; 2 × CH_2); 4.45 (m; 1H; CH); 6.91–7.02 (m; 3H; aromat.); 7.26–7.31 (m; 2H; aromat.); 7.73 (s; 1H; H_α); 7.74 (m; 1H; aromat.); 8.16 (m; 1H; aromat.). ^{13}C NMR (DMSO-d_6) δ ppm 55.33; 55.47; 65.86; 68.97; 70.01; 111.09; 111.19; 114.55; 120.74; 122.35; 124.03; 129.52; 134.69; 147.90; 150.03; 158.44. IR (Nujol; cm^{-1}): 3220 (ν_{OH}); 1650 ($\nu_{C=N}$); 1110 (ν_{NO}). Anal. Calcd for $C_{18}H_{21}NO_5$: C, 65.23; H, 6.40; N, 4.23. Found: C, 65.32; H, 6.44; N, 4.31.

4.3.3. 1-(4-Methylbenzylideneamino)-3-phenoxy-propan-2-ol-*N*-oxide (±)-2e. Yield 83%. Mp = 152–153 °C (recrystallized from ethanol). ^{1}H NMR ($CDCl_3$) δ ppm 2.39 (s; 3H; CH_3); 3.96 (dd; 1H; $J_{gem} = 9.4$ Hz; $J = 7.8$ Hz; –CH_aH$_b$N=); 4.15 (dd; 1H$_b$; $J = 4.6$ Hz; –CH$_a$$H_b$N=); 4.16 (dd; 1H$_c$; $J_{gem} = 12.6$ Hz; $J = 6.6$ Hz; –OCH_cH$_d$–); 4.26 (dd; 1H$_d$; $J = 2.6$ Hz; –OCH$_c$$H_d$–); 4.53 (m; 1H; CH); 5.32 (d; 1H; $J = 4.4$ Hz; OH); 6.89–6.93 (m; 2H; aromat.); 6.97 (m; 1H; aromat.); 7.22–7.31 (m; 4H; aromat.); 7.36 (s; 1H; H$_\alpha$); 8.08–8.10 (m; 2H; aromat.). ^{13}C NMR ($CDCl_3$) δ ppm 21.71; 66.97; 68.35; 68.60; 114.48; 121.32; 126.97; 129.14; 129.29; 129.58; 136.95; 141.77; 158.19. IR (Nujol; cm^{-1}) 3180 (ν_{OH}); 1600 ($\nu_{C=N}$); 1110 (ν_{NO}). Anal. Calcd for $C_{17}H_{19}NO_3$: C, 71.55; H, 6.72; N, 4.91. Found: C, 71.49; H, 6.71; N, 4.92.

4.3.4. 1-(2,4,6-Trimethylbenzylideneamino)-3-phenoxy-propan-2-ol-*N*-oxide (±)-3f. Yield 58%. Mp = 161–162 °C (recrystallized from ethanol). ^{1}H NMR ($CDCl_3$) δ ppm 2.22 (s; 6H; 2 × CH_3); 2.25 (s; 3H; CH_3); 3.94 (dd; 1H$_a$; $J_{gem} = 9.6$ Hz; $J = 8.4$ Hz; CH_aH$_b$N); 4.10 (dd; 1H$_b$; $J = 4.8$ Hz; CH$_a$$H_b$N); 4.22 (dd; 1H$_c$; $J_{gem} = 12.2$ Hz; $J = 6.4$ Hz; OCH_cH$_d$); 4.31 (dd; 1H$_d$; $J = 2.4$ Hz; OCH$_c$$H_d$);

4.46 (m; 1H; *CH*); 5.39 (d; 1H; $J = 5.2$ Hz; *OH*); 6.86 (s; 2H; aromat.); 6.92 (m; 2H; aromat.); 6.98 (m; 1H; aromat.); 7.28–7.32 (m; 2H; aromat.); 7.63 (s; 1H; H_α). ^{1}H NMR (DMSO-d_6) δ ppm 2.18 (s; 6H; $2 \times CH_3$); 2.22 (s; 3H; CH_3); 4.01–4.12 (m; 4H; $2 \times CH_2$); 4.42 (m; 1H; *CH*); 5.57 (d; 1H; $J = 5.6$ Hz; *OH*); 6.84 (s; 2H; aromat.); 6.92–6.97 (m; 3H; aromat.); 7.27–7.31 (m; 2H; aromat.); 7.87 (s; 1H; Hα). ^{13}C NMR (DMSO-d_6) δ ppm 19.54; 20.72; 65.85; 68.01; 69.99; 114.52; 120.72; 126.81; 127.68; 129.51; 135.49; 137.20; 137.92; 158.46. IR (Nujol; cm^{-1}) 3170 (ν_{OH}); 1600 ($\nu_{C=N}$); 1110 (ν_{NO}). Anal. Calcd for $C_{19}H_{23}NO_3$: C, 72.80; H, 7.41; N, 4.47. Found: C, 72.63; H, 7.56; N, 4.47.

4.3.5. 1-(4-Chlorobenzylideneamino)-3-phenoxy-propan-2-ol-*N*-oxide (±)-2g. Yield 80%. Mp = 161–163 °C (recrystallized from ethanol). ^{1}H NMR ($CDCl_3$) δ ppm 3.97 (dd; 1H; $J_{gem} = 9.6$ Hz; $J = 7.6$ Hz; –CH_aH$_b$N=); 4.15 (dd; 1H$_b$; $J = 4.6$ Hz; –CH$_a$$H_b$N=); 4.17 (dd; 1H$_c$; $J_{gem} = 12.6$ Hz; $J = 6.8$ Hz; –OCH_cH$_d$–); 4.28 (dd; 1H$_d$; $J = 2.6$ Hz; –OCH$_c$$H_d$–); 4.56 (m; 1H; CH); 4.92 (d; 1H; $J = 4.8$ Hz; OH); 6.89–6.92 (m; 2H; aromat.); 6.98 (m; 1H; aromat.); 7.27–7.31 (m; 2H; aromat.); 7.37–7.40 (m; 2H; aromat.); 7.38 (s; 1H; H$_\alpha$); 8.13–8.16 (m; 2H; aromat.). ^{13}C NMR ($CDCl_3$) δ ppm 67.50; 68.35; 68.45; 114.45; 121.42; 128.12; 128.86; 129.61; 130.20; 135.67; 136.64; 158.12. IR (Nujol; cm^{-1}): 3190 (ν_{OH}); 1605 ($\nu_{C=N}$); 1120 (ν_{NO}). Anal. Calcd for $C_{16}H_{16}ClNO_3$: C, 62.85; H, 5.27; N, 4.58. Found: C, 62.75; H, 5.05; N, 4.59.

4.3.6. 1-Benzylideneamino-3-(4-methylphenoxy)propan-2-ol-*N*-oxide (±)-2h. Yield 97%. Mp = 149.5–151.5 °C (recrystallized from ethanol). ^{1}H NMR ($CDCl_3$) δ ppm 2.28 (s; 3H; CH_3); 3.94 (dd; 1H$_a$; $J_{gem} = 9.6$ Hz; $J = 7.6$ Hz; –CH_aH$_b$N=); 4.11 (dd; 1H$_b$; $J = 4.6$ Hz; –CH$_a$$H_b$N=); 4.15 (dd; 1H$_c$; $J_{gem} = 12.8$ Hz; $J = 7.2$ Hz; –OCH_cH$_d$–); 4.26 (dd; 1H$_d$; $J = 2.8$ Hz; –OCH$_c$$H_d$–); 4.54 (m; 1H; CH); 5.14 (d; 1H; $J = 4.8$ Hz; OH); 6.79–6.82 (m; 2H; aromat.); 7.06–7.09 (m; 2H; aromat.); 7.40 (s; 1H; H$_\alpha$); 7.41–7.44 (m; 3H; aromat.); 8.17–8.20 (m; 2H; aromat.). ^{13}C NMR ($CDCl_3$) δ ppm 20.42; 67.42; 66.44; 68.61; 114.33; 128.54; 129.06; 129.66; 129.98; 130.60; 131.05; 136.87; 156.09. IR (Nujol; cm^{-1}) 3200 (ν_{OH}); 1600 ($\nu_{C=N}$); 1120 (ν_{NO}). MS (ES; MeOH) Found: 286.1 (M+1); 308.1 (M+23); Calcd: 285.341. Anal. Calcd for $C_{17}H_{19}NO_3$: C, 71.56; H 6.71; N, 4.91. Found: C, 71.45; H, 6.90; N, 4.88.

4.3.7. 1-Benzylideneamino-3-(4-chlorophenoxy)propan-2-ol-*N*-oxide (±)-2i. Yield 87%. Mp = 175–177 °C (recrystallized from ethanol). ^{1}H NMR ($CDCl_3$) δ ppm 3.96 (dd; 1H$_a$; $J_{gem} = 9.6$ Hz; $J = 7.6$ Hz; –CH_aH$_b$N=); 4.13 (dd; 1H$_b$; $J = 4.4$ Hz; –CH$_a$$H_b$N=); 4.17 (dd; 1H$_c$; $J_{gem} = 12.8$ Hz; $J = 7.6$ Hz; –OCH_cH$_d$–); 4.29 (dd; 1H$_d$; $J = 2.8$ Hz; –OCH$_c$$H_d$–); 4.53 (m; 1H; CH); 5.14 (s; 1H; OH); 6.82–6.86 (m; 2H; aromat.); 7.21–7.25 (m; 2H; aromat.); 7.39 (s; 1H; H$_\alpha$); 7.43–7.46 (m; 3H; aromat.); 8.18–8.21 (m; 2H; aromat.). ^{13}C NMR ($CDCl_3$) δ ppm 67.01; 68.57; 68.76; 115.77; 126.32; 128.63; 129.07; 129.48; 129.59; 131.21; 158.82. IR (Nujol; cm^{-1}) 3190 (ν_{OH}); 1610 ($\nu_{C=N}$); 1115 (ν_{NO}). Anal. Calcd for $C_{16}H_{16}ClNO_3$: C, 62.85; H, 5.27; N, 4.58. Found: C, 62.76; H, 5.09; N, 4.56.

4.4. Typical transesterification procedure of (±)-2a–i with Novozym SP 435

Nitrone (±)-**2a**–**i** (1 mmol) was dissolved in 50 ml of toluene and stirred for 30 min at 45–50 °C. Next, vinyl acetate (1 ml; 10 mmol) and 300 mg of Novozym SP 435 lipase were added. The conversion was monitored by TLC (95:5 v/v chloroform/methanol). After the appropriate time, the reaction was stopped by filtering off the enzyme and the solvent was evaporated under reduced pressure. The crude mixture of acetate (*R*)-(+)-**4a**–**i** and unchanged nitrones (*S*)-(−)-**3a**–**i** was separated by column chromatography on silica gel with a gradient of 0–2% methanol/chloroform. Enantiomeric excess was determined by chiral HPLC analysis using a (*S*,*S*)-WHELK-0.1 column with 9:1 v/v hexane/ethanol as the eluent (flow 0.8 ml/min, $\lambda = 246$ nm). NMR spectra of enantiomerically enriched nitrones (*S*)-(−)-**3a**–**i** were identical with those of (±)-**3a**–**i**. The optical rotations measured in $CHCl_3$ solutions for prepared enantiomerically enriched alcohols are as follows:

(*S*)-(−)-**3a**: $[\alpha]_D^{22} = -53.3$ (*c* 1.05; ee = 69%),
(*S*)-(−)-**3b**: $[\alpha]_D^{22} = -92.7$ (*c* 0.75; ee = 95%),
(*S*)-(−)-**3c**: $[\alpha]_D^{22} = -22.6$ (*c* 0.97; ee = 30%),
(*S*)-(−)-**3d**: $[\alpha]_D^{22} = -56.0$ (*c* 1.035; ee = 80%),
(*S*)-(−)-**3e**: $[\alpha]_D^{22} = -38.6$ (*c* 0.72; ee = 65%),
(*S*)-(−)-**3g**: $[\alpha]_D^{22} = -50.0$ (*c* 0.96; ee = 74%),
(*S*)-(−)-**3i**: $[\alpha]_D^{22} = -46.0$ (*c* 1.00; ee = 64%),
(*S*)-(−)-**3k**: $[\alpha]_D^{22} = -46.2$ (*c* 0.72; ee = 60%).

^{1}H and ^{13}C NMR spectra, IR data, elemental analyses, and optical rotations of obtained acetates (*R*)-(+)-**4a**–**i** are reported below.

4.4.1. (*R*)-(+)-1-Benzylideneamino-3-phenoxy-propan-2-ol-*N*-oxide acetate 4a. ^{1}H NMR ($CDCl_3$) δ ppm 2.06 (s; 3H; CH_3); 4.23 (dd; 1H$_a$; $J_{gem} = 10.8$ Hz; $J = 4$ Hz; CH_aH$_b$N); 4.29 (dd; 1H$_c$; $J_{gem} = 12.8$ Hz; $J = 4.4$ Hz; OCH_cH$_d$); 4.36 (dd; 1H$_b$; $J = 3.6$ Hz; CH$_a$$H_b$N); 4.37 (dd; 1H$_d$; $J = 7.6$ Hz; OCH$_c$$H_d$); 5.80 (m; 1H; *CH*); 6.91–6.94 (m; 2H; aromat.); 6.96–7.00 (m; 1H; aromat.); 7.27–7.32 (m; 2H; aromat.); 7.42 (s; 1H; H_α); 7.42–7.44 (m; 3H; aromat.); 8.20–8.23 (m; 2H; aromat.). ^{13}C NMR ($CDCl_3$) δ ppm 20.83; 66.58; 66.85; 69.33; 114.48; 121.41; 128.48; 128.60; 129.52; 130.06; 130.67; 136.01; 158.12; 170.00. IR (Nujol, cm^{-1}) 3220 (ν_{OH}); 1600 ($\nu_{C=N}$); 1100 (ν_{NO}). Anal. Calcd for $C_{18}H_{19}NO_4$: C, 69.00; H, 6.11; N, 4.47. Found: C, 69.18; H, 6.30; N, 4.50. $[\alpha]_D^{22} = +27.4$ (*c* 1.56, $CHCl_3$), ee = 77%.

4.4.2. (*R*)-(+)-1-(4-Nitrobenzylideneamino)-3-phenoxy-propan-2-ol-*N*-oxide acetate 4b. Mp = 74–75 °C. ^{1}H NMR ($CDCl_3$) δ ppm 2.06 (s; 3H; CH_3); 4.21 (dd; 1H$_a$; $J_{gem} = 10.6$ Hz; $J = 3.8$ Hz; CH_aH$_b$N); 4.32 (dd; 1H$_b$; $J = 3.8$ Hz; CH$_a$$H_b$N); 4.36 (dd; 1H$_c$; $J_{gem} = 12.8$ Hz; $J = 4.4$ Hz; OCH_cH$_d$); 4.44 (dd; 1H$_d$; $J = 7.6$ Hz; OCH$_c$$H_d$); 5.79 (m; 1H; *CH*); 6.89–6.92 (m; 2H; aromat.); 6.96–7.01 (m; 1H; aromat.); 7.26–7.31 (m; 2H; aromat.); 7.58 (s; 1H; H_α); 8.22–8.25 (m; 2H; aromat.); 8.34–8.37

(m; 2H; aromat.). ^{13}C NMR ($CDCl_3$) δ ppm 20.78; 66.69; 67.28; 69.17; 114.43; 121.57; 123.74; 128.82; 129.58; 133.87; 135.59; 147.85; 158.00; 169.90. IR (Nujol; cm^{-1}) 1740; 1595; 1510; 1375; 1340; 1225; 1160; 860. Anal. Calcd for $C_{18}H_{18}N_2O_6$: C, 60.33; H, 5.06: N, 7.82. Found: C, 60.36; H, 5.28: N, 7.77. $[\alpha]_D^{22} = +30.8$ (c 0.85, $CHCl_3$), ee = 73%.

4.4.3. (*R*)-(+)-1-(4-Methoxybenzylideneamino)-3-phenoxypropan-2-ol-*N*-oxide acetate 4c. ^{1}H NMR ($CDCl_3$) δ ppm 2.05 (s; 3H; CH_3CO); 3.84 (s; 3H; OCH_3); 4.22 (dd; 1H$_a$; $J_{gem} = 10.4$ Hz; $J = 4$ Hz; CH_aH$_b$N); 4.27 (dd; 1H$_c$; $J_{gem} = 12.8$ Hz; $J = 4.4$ Hz; OCH_cH$_d$); 4.32 (dd; 1H$_d$; $J = 7.6$ Hz; OCH$_c$$H_d$); 4.35 (dd; 1H$_b$; $J = 3.6$ Hz; CH$_a$$H_b$N); 5.79 (m; 1H; CH); 6.90–6.94 (m; 4H; aromat.); 6.98 (m; 1H; aromat.); 7.26–7.35 (m; 2H; aromat.); 7.35 (s; 1H; H_α); 8.19–8.122 (m; 2H; aromat.). ^{13}C NMR ($CDCl_3$) δ 20.89; 55.34; 66.11; 66.91; 69.39; 113.89; 114.52; 121.42; 123.02; 129.56; 130.73; 135.91; 158.18; 161.33; 170.12. IR (Nujol; cm^{-1}) 1735; 1595; 1505; 1460; 1250; 1225; 1170; 1025; 840; 750. Anal. Calcd for $C_{19}H_{21}NO_5$: C, 66.46; H, 6.16; N, 4.08. Found: C, 66.17; H, 6.32; N, 3.85. $[\alpha]_D^{22} = +16.7$ (c 1.20, $CHCl_3$), ee = 93%.

4.4.4. (*R*)-(+)-1-(3,4-Dimethoxybenzylideneamino)-3-phenoxy-propan-2-ol-*N*-oxide acetate 4d. ^{1}H NMR ($CDCl_3$) δ ppm 2.04 (s; 3H; CH_3CO); 3.89 (s; 3H; OCH_3); 3.90 (s; 3H; OCH_3); 4.21 (dd; 1H$_a$; $J_{gem} = 11$ Hz; $J = 4$ Hz; CH_aH$_b$N); 4.24 (dd; 1H$_c$; $J_{gem} = 13.2$ Hz; $J = 4.8$ Hz; OCH_cH$_d$); 4.32 (dd; 1H$_d$; $J = 7.2$ Hz; OCH$_c$$H_d$); 4.33 (dd; 1H$_b$; $J = 3.6$ Hz; CH$_a$$H_b$N); 5.77 (m; 1H; CH); 6.85–6.91 (m; 3H; aromat.); 6.93–6.97 (m; 1H; aromat.); 7.24–7.29 (m; 2H; aromat.); 7.34 (s; 1H; H_α); 7.46 (dd; 1H; aromat.; $J_{gem} = 4.8$ Hz; $J =$ Hz); 8.27 (d; 1H; aromat.; $J = 2$ Hz). ^{13}C NMR ($CDCl_3$) δ ppm 20.82; 55.80; 66.08; 66.76; 69.27; 110.50; 110.85; 114.44; 121.37; 123.22; 129.49; 136.17; 148.37; 150.91; 158.09; 170.04. IR (Nujol; cm^{-1}) 1740; 1595; 1510; 1500; 1270; 1230; 1165; 1020; 755; 730. Anal. Calcd for $C_{20}H_{23}NO_6$: C, 64.33; H, 6.21: N, 3.75. Found: C, 64.40; H, 6.39; N, 3.69. $[\alpha]_D^{22} = +22.1$ (c 0.73, $CHCl_3$), ee = 88%.

4.4.5. (*R*)-(+)-1-(4-Methylbenzylideneamino)-3-phenoxypropan-2-ol-*N*-oxide acetate 4e. Mp = 95–96 °C. ^{1}H NMR ($CDCl_3$) δ ppm 2.05 (s; 3H; CH_3CO); 2.39 (s; 3H; CH_3); 4.23 (dd; 1H$_a$; $J_{gem} = 10.8$ Hz; $J = 4$ Hz; CH_aH$_b$N); 4.27 (dd; 1H$_c$; $J_{gem} = 12.8$ Hz; $J = 4.4$ Hz; OCH_cH$_d$); 4.35 (dd; 1H$_d$; $J = 7.2$ Hz; OCH$_c$$H_d$); 4.37 (dd; 1H$_b$; $J = 3.6$ Hz; CH$_a$$H_b$N); 5.79 (m; 1H; CH); 6.91–6.93 (m; 2H; aromat.); 6.98 (m; 1H; aromat.); 7.22–7.31 (m; 5H; aromat.); 7.39 (s; 1H; H_α); 8.10–8.13 (m; 2H; aromat.). ^{13}C NMR ($CDCl_3$) δ ppm 20.77; 21.56; 66.30; 66.81; 69.28; 114.43; 121.32; 127.38; 128.60; 129.12; 129.42; 36.02; 141.16; 158.10; 169.95. IR (Nujol; cm^{-1}) 1735; 1465; 1380; 1255; 1235; 1155; 760. Anal. Calcd for $C_{19}H_{21}NO_4$: C, 69.71; H, 6.46; N, 4.28. Found: C, 69.98; H, 6.62; N, 4.25. $[\alpha]_D^{22} = +31.6$ (c 1.90, $CHCl_3$), ee = 80%.

4.4.6. (*R*)-(+)-1-(4-Chlorobenzylideneamino)-3-phenoxypropan-2-ol-*N*-oxide acetate 4g. Mp = 116–118 °C. ^{1}H NMR ($CDCl_3$) δ ppm 2.05 (s; 3H; CH_3CO); 4.22 (dd; 1H$_a$; $J_{gem} = 10.8$ Hz; $J = 4.2$ Hz; CH_aH$_b$N); 4.28 (dd; 1H$_c$; $J_{gem} = 12.8$ Hz; $J = 4$ Hz; OCH_cH$_d$); 4.35 (dd; 1H$_d$; $J = 7.2$ Hz; OCH$_c$$H_d$); 4.37 (dd; 1H$_b$; $J = 3.6$ Hz; CH$_a$$H_b$N); 5.78 (m; 1H; CH); 6.90–6.93 (m; 2H; aromat.); 6.99 (m; 1H; aromat.); 7.26–7.31 (m; 2H; aromat.); 7.37–7.41 (m; 3H; H_α+aromat.); 8.16–8.18 (m; 2H; aromat.). ^{13}C NMR ($CDCl_3$) δ ppm 20.85; 66.67; 66.81; 69.28; 114.48; 121.50; 128.54; 128.78; 129.58; 129.75; 134.85; 136.13; 158.10; 169.99. IR (Nujol; cm^{-1}) 1735; 1465; 1250; 1230; 1155; 1090; 760. Anal. Calcd for $C_{18}H_{18}ClNO_4$: C, 62.16; H, 5.22; N, 4.58. Found: C, 62.10; H, 5.31; N, 4.63. $[\alpha]_D^{22} = +35.2$ (c 1.25, $CHCl_3$), ee = 84%.

4.4.7. (*R*)-(+)-1-Benzylideneamino-3-(4-methylphenoxy)-propan-2-ol-*N*-oxide acetate 4h. ^{1}H NMR ($CDCl_3$) δ ppm 2.05 (s; 3H; $COCH_3$); 2.84 (s; 3H; CH_3); 4.19 (dd; 1H$_a$; $J_{gem} = 11$ Hz; $J = 4$ Hz; CH_aH$_b$N); 4.28 (dd; 1H$_c$; $J_{gem} = 12.8$ Hz; $J = 4.4$ Hz; OCH_cH$_d$); 4.32 (dd; 1H$_b$; $J = 3.6$ Hz; CH$_a$$H_b$N); 4.36 (dd; 1H$_d$; $J = 7.6$ Hz; OCH$_c$$H_d$); 5.79 (m; 1H; CH); 6.80–6.83 (m; 2H; aromat.); 7.07–7.09 (m; 2H; aromat.); 7.41–7.43 (m; 4H; H$_\alpha$+aromat.); 8.20–8.23 (m; 2H; aromat.). ^{13}C NMR ($CDCl_3$) δ ppm 20.38; 20.83; 66.60; 67.03; 69.37; 114.35; 128.46; 128.58; 129.93; 130.08; 130.64; 130.67; 135.97; 156.06; 169.99. IR (Nujol; cm^{-1}) 1725 ($\nu_{C=O}$); 1580 ($\nu_{C=N}$); 1090 ($\nu_{N=O}$). Anal. Calcd for $C_{19}H_{21}NO_4$: C, 69.71; H, 6.46; N, 4.28. Found: C, 69.50; H, 6.64: N, 4.29. $[\alpha]_D^{22} = +34.6$ (c 0.92, $CHCl_3$), ee = 73%.

4.4.8. (*R*)-(+)-1-Benzylideneamino-3-(4-chlorophenoxy)-propan-2-ol-*N*-oxide acetate 4i. ^{1}H NMR ($CDCl_3$) δ ppm 2.05 (s; 3H; $COCH_3$); 4.22 (dd; 1H$_a$; $J_{gem} = 10.8$ Hz; $J = 4.4$ Hz; CH_aH$_b$N); 4.28 (dd; 1H$_c$; $J_{gem} = 12.8$ Hz; $J = 5.2$ Hz; OCH_cH$_d$); 4.33 (dd; 1H$_b$; $J = 3.6$ Hz; CH$_a$$H_b$N); 4.34 (dd; 1H$_d$; $J = 7.2$ Hz; OCH$_c$$H_d$); 5.76 (m; 1H; CH); 6.83–6.87 (m; 2H; aromat.); 7.21–7.25 (m; 2H; aromat.); 7.41–7.45 (m; 4H; H$_\alpha$+aromat.); 8.20–8.22 (m; 2H; aromat.). ^{13}C NMR ($CDCl_3$) δ ppm 20.87; 66.47; 67.33; 69.26; 115.83; 126.38; 128.56; 128.68; 129.44; 129.98; 130.86; 136.26; 156.77; 170.06. IR (Nujol; cm^{-1}) 1750 ($\nu_{C=O}$). 1590 ($\nu_{C=N}$). 1090 ($\nu_{N=O}$). Anal. Calcd for $C_{18}H_{18}ClNO_4$: C, 62.16; H, 5.22; N, 4.58. Found: C, 62.05; H, 5.34; N, 4.60. $[\alpha]_D^{22} = +28.2$ (c 1.17, $CHCl_3$), ee = 84%.

4.5. Assignment of the absolute configuration of 1-(4-chlorobenzylideneamino)-3-phenoxy-propan-2-ol-*N*-oxide (−)-3g

Crystal data regarding the structure of (−)-1-(4-chlorobenzylideneamino)-3-phenoxy-propan-2-ol-*N*-oxide are given in Table 3, together with the refinement details. All measurements of the crystal were performed on a Kuma KM4CCD κ-axis diffractometer with graphite-monochromated Mo Kα radiation. The crystal was positioned at 62.25 mm from the KM4CCD camera. As many as 1204 frames were measured at 1° intervals with a counting time of 30 s. The data were corrected for Lorentz and polarization effects. The numeric absorption correction was applied. Data collection, cell refinement, and data reduction were carried out with the Kuma Diffraction programs: CrysAlis CCD and CrysAlis RED.[12] The structure was solved by direct methods[13] and refined using SHELXL.[14] The refine-

Table 3. Crystal data and structure refinement details

Empirical formula	$C_{16}H_{16}ClNO_3$
Formula weight	305.75
T/K	100(2)
λ/Å	0.71073
Crystal system	Monoclinic
Space group	$P2_1$
a/Å	5.980(2)
b/Å	7.583(2)
c/Å	16.153(4)
β/°	95.64(2)
V/Å^3	729.0(3)
Z	2
D_c/Mg m^{-3}	1.393
μ/mm^{-1}	0.271
F(000)	320
Crystal size/mm	$0.2 \times 0.2 \times 0.1$
Diffractometer	Kuma KM4CCD
θ Range for data collection/°	3.21–24.99
Index ranges	$-7 \leqslant h \leqslant 7$, $-9 \leqslant k \leqslant 9$, $-19 \leqslant l \leqslant 19$
Reflections collected	11,132
Independent reflections	2540 [R(int) = 0.1697]
Max. and min. transmission	0.98436 and 0.89911
Data/parameters	2540/192
Goodness-of-fit (F^2)	1.029
Final R_1/wR_2 indices ($I > 2\sigma_I$)	$R1 = 0.0749$, $wR2 = 0.1859$
Absolute structure parameter	0.05(15)
Extinction coefficient	0.000(7)
Largest diff. peak/hole/e Å^{-3}	0.625 and −0.410

ment was based on F^2 for all reflections except those with very negative F^2. Weighted R factors wR and all goodness-of-fit S values are based on F^2. Conventional R factors are based on F with F set to zero for negative F^2. The $F_o^2 > 2s(F_o^2)$ criterion was used only for calculating R factors and is not relevant to the choice of reflections for the refinement. The R factors based on F^2 are about twice as large as those based on F. All hydrogen atoms were located from a differential map and refined isotropically. Scattering factors were taken from Tables 6.1.1.4 and 4.2.4.2 in Ref. 15. The largest residual maximum on the electron density map (0.625 e Å^{-3}) is 1.079 Å distant from the chlorine atom. Crystallographic data (excluding structural factors) for the structure reported in this paper have been deposited with the Cambridge Crystallographic Data Centre and allocated the deposition number CCDC 602967. Copies of the data can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB2 1EW, UK (fax: Int code +(1223)336-033; e-mail: deposit@ccdc.cam.ac.uk).

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References

1. Janzen, E. G.; West, M. S.; Poyer, J. L. *J. Am. Chem. Soc.* **1969**, *90*, 5909; Janzen, E. G. *Acc. Chem. Res.* **1971**, *4*, 31.
2. Green, R. A.; Ashwood, T.; Odergren, T.; Jackson, D. M. *Pharmacol. Ther.* **2003**, *100*, 195.
3. Totssell, K. B. G. *Nitrile Oxides, Nitrones and Nitronates in Organic Synthesis. Novel Strategies in Synthesis*; VCH, 1988.
4. Closa, M.; Wightman, R. H. *Synth. Commun.* **1998**, *28*, 3443; Herczegh, P.; Kovacs, I.; Szilagyi, L.; Varga, T.; Dinya, Z.; Sztaricskai, F. *Tetrahedron Lett.* **1993**, *34*, 1211.
5. McCaig, A. E.; Meldrum, K. P.; Wightman, R. H. *Tetrahedron* **1998**, *54*, 9429; McCaig, A. E.; Wightman, R. H. *Tetrahedron Lett.* **1993**, *34*, 3939.
6. Bonnett, R.; Rown, R. F. C.; Clark, V. M.; Sutherland, I. O.; Todd, A. *J. Chem. Soc.* **1959**, 2094; Barton, D. H. R.; Gutteridge, N. J. A.; Hesse, R. H.; Pechet, M. M. *J. Org. Chem.* **1969**, *34*, 1473; Gutteridge, N. J. A.; Dales, J. R. M. *J. Chem. Soc. (C)* **1971**, 122.
7. Tamagaki, S.; Oae, S. *Bull. Chem. Soc. Jpn.* **1971**, *44*, 2851.
8. Heine, H. W.; Zibuck, R.; VandenHeuvel, W. J. A. *J. Am. Chem. Soc.* **1982**, *104*, 3691.
9. Cummis, C. H.; Coates, R. M. *J. Org. Chem.* **1983**, *48*, 4070.
10. Kliegel, W. *Chem. Ber.* **1969**, *102*, 1776; Kliegel, W.; Becker, H. *Chem. Ber.* **1977**, *110*, 2090.
11. Dąbkowska, K.; Dąbrowska, P.; Drabik, J.; Kopczyk, D.; Strosznajder, J. B.; Plenkiewicz, J.; Wielechowska, M. *Synth. Commun.* **2005**, *35*, 1440.
12. Oxford Diffraction *CrysAlis CCD and CrysAlis RED*; Oxford Diffraction Poland: Wrocław, Poland, 2001.
13. Sheldrick, G. M. *Acta Crystallogr., Sect. A* **1990**, *46*, 467–473.
14. Sheldrick, G. M. SHELXL93 *Program for the Refinement of Crystal Structures*; University of Göttingen: Germany, 1993.
15. *International Tables for Crystallography*; Wilson, A. J. C., Ed.; Kluwer: Dordrecht, 1992: Vol. C.