Aqueous-Mediated Ring Opening of Epoxides with Oximes: A Rapid Entry into β-Hydroxy Oxime *O*-Ethers as Potential β-Adrenergic Blocking Agents

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Received 8 February 2008; revised 7 April 2008

Abstract: Novel β-hydroxy oxime *O*-ethers, as potential β-adrenergic blocking agents, were synthesized from the aqueous-mediated (H_2O–DMSO, 7:3) O-alkylation of oximes with epoxides in the presence of potassium hydroxide at room temperature. The O-alkylation was regioselective and (*E*)-oxime ethers were the main products. The results of quantum mechanical studies used to rationalize the experimental outcomes are discussed.

Key words: oximes, epoxides, O-alkylations, ring opening, aqueous media

Oximes and oxime ether derivatives are important substrates in organic and medicinal chemistry.[1] Oximes and oxime ethers are widely used for the introduction of various functional groups into organic compounds,[1a,d,e] as well as for amino acid synthesis.[2] Moreover, they are a key structural motif in many drug scaffolds and bioactive compounds. Many famous drugs with various chemotherapeutic activities, such as antiviral (e.g., enviroxime)[3] and anti-inflammatory agents (e.g., pifoxime),[1b] cephalosporin antibiotics (e.g., cefixime),[4] nerve agent antidotes (e.g., pralidoxime),[1b,c] antifungal agents (e.g., oxiconazole),[5] macrolide antibiotics (e.g., roxithromycin),[6] antidepressants (e.g., fluvoxamine),[1b] and thromboxane synthase inhibitors (e.g., ridogrel),[7] contain an oxime or oxime ether moiety in their structure.

One of the most common routes to oxime ethers is the reaction of oximes with carbon electrophiles, including alkyl or aryl halides,[8,9] aryl nitrates,[10a] arenediazonium salts,[10b] alcohols under Mitsunobu conditions,[11] activated olefins,[12] trialkyl orthoformates,[13] allylic carbonates,[14a] acetates,[14a,b] phosphate esters,[14c] and Michael acceptors.[15] Oxime ethers have also been prepared from the condensation of *O*-alkylhydroxylamines with carbonyl compounds.[16] The ring opening of epoxides with oximes is an interesting and attractive strategy for obtaining β-hydroxy oxime *O*-ethers;[1a] however, there are few reports for the regioselective ring opening of epoxides using oximes.[17] In most cases, the examples are limited to the reaction of oximes with epibromohydrins to obtain oxime *O*-oxiranylmethyl ether derivatives, via nucleophilic displacement of the bromide,[18] and/or the intermolecular reaction of an oxime and epoxide as a precursor for other synthetic purposes.[19]

β-Adrenoreceptor antagonists are used clinically for the treatment of various cardiovascular diseases.[20] It is well-known that β-adrenergic blockers are very homogeneous in their chemical structures, which stem either from 2-amino-1-arylethanols **1** or 1-amino-3-(aryloxy)propan-2-ols **2** (Figure 1).[21] It has previously been shown that the insertion of a carbon–nitrogen double bond into the side chain of β-blockers does not abolish the β-adrenoreceptor activity and, in some cases, leads to potent β2-selective antagonists.[22] In this context, structure–activity relationship studies led to the design and synthesis of ketoxime *O*-[3-(alkylamino)-2-hydroxypropyl] ethers **3** as potent β2-selective antagonists (Figure 1).[18]

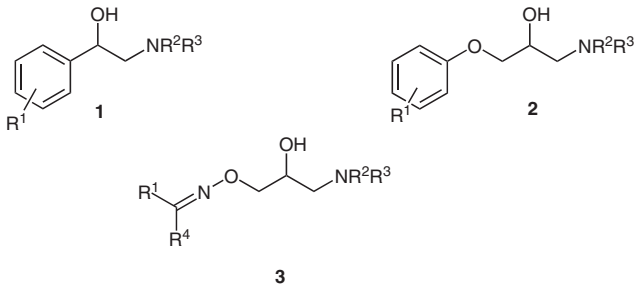


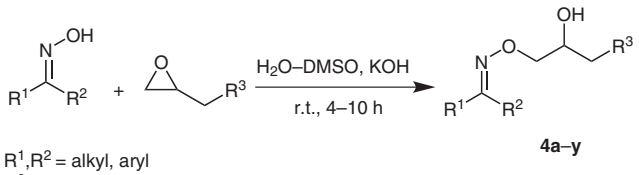
Figure 1

The use of water as a medium for promoting organic reactions has only relatively recently attracted considerable attention, despite the fact that water is the solvent in a vast majority of biochemical processes.[23] Furthermore, water is a suitable solvent for organic reactions because of its nontoxicity, cheapness, conformity with green protocols, and special characteristics, such as its high polarity and dielectric constant.[23]

Encouraged by the β-adrenergic blocking activities of compounds **3** and also as an extension of our interest in epoxide chemistry,[24] we have synthesized compounds **4** by the water–dimethyl sulfoxide (H_2O–DMSO) mediated regioselective O-alkylation of oximes with epoxides in the presence of potassium hydroxide (KOH) at room temperature (Scheme 1).

The first step to deriving this particular synthetic approach involved the optimization of the reaction conditions. Initially, we investigated the effect of using various solvents

SYNTHESIS 2008, No. 13, pp 2055–2064
Advanced online publication: 11.06.2008
DOI: 10.1055/s-2008-1067122; Art ID: Z05108SS



R^1,R^2 = alkyl, aryl
R^3 = alkyl, alkoxy, aryloxy

Scheme 1

on the model reaction of benzophenone oxime with 2-(phenoxymethyl)oxirane to afford benzophenone oxime *O*-(2-hydroxy-3-phenoxypropyl) ether. The results are depicted in Table 1.

Table 1 Effect of Various Solvents on the Ring Opening of 2-(Phenoxymethyl)oxirane with Benzophenone Oxime

Entry	Solvent	Time (h)	Yield[a,b] (%)
1	DMF	6	76
2	DMF[c]	6	64
3	DMSO	5	77
4	THF	24	NR
5	MeCN	6	70
6	H_2O	24	45
7	HMPA	10	40
8	NMP	10	66
9	toluene	24	NR
10	H_2O–DMSO[d]	4	91
11	H_2O–MeCN[e]	5	75
12	H_2O–acetone[e]	10	60

[a] Isolated yield.
[b] NR = no reaction.
[c] Anhyd DMF.
[d] In a 7:3 ratio.
[e] In a 1:1 ratio.

As the data indicate, the solution of H_2O–DMSO (7:3) (Table 1, entry 10) was the most-efficient solvent; hence, it was the solvent of choice. The use of DMSO or H_2O alone (entries 3 and 6, respectively) was not as efficient as using the H_2O–DMSO (7:3) solution. Furthermore, although the use of *N*,*N*-dimethylformamide, acetonitrile (MeCN), *N*-methyl-2-pyrrolidinone, H_2O–MeCN, and H_2O–acetone (entries 1 and 2, 5, 8, 11, and 12, respectively) also afforded good yields of the corresponding oxime ether, longer reaction times were required. Finally, when H_2O–MeCN or MeCN were used, MeCN hydrolysis was a major problem in strong basic conditions.

The choice of base is of great importance for the activation of the oximes to react with the epoxides. We studied the potency of several organic and inorganic bases within the reaction model (Table 2). The results indicated that, among the examined bases in this experiment, a slight excess of KOH (1.3 equiv, entry 2) was the most efficient base for the activation of benzophenone oxime. Sodium hydroxide (entry 1) was not as effective as KOH, even when its molar ratio was increased up to two equivalents. The other bases were not efficient at all, even with prolonged reaction times.

Table 2 Effect of Various Bases on the Ring Opening of 2-(Phenoxymethyl)oxirane with Benzophenone Oxime

Entry	Base	Time (h)	Yield[a] (%)
1	NaOH	6	70
2	KOH	4	91
3	K_2CO_3	24	NR[b]
4	Et_3N	12	35
5	DBU	18	22
6	DBN	18	20
7	DMAP	18	10
8	DABCO	12	34

[a] Isolated yield.
[b] No reaction.

To evaluate the generality and versatility of this method and with the aim of attaining some novel analogues of compound **3**, the optimized conditions were applied to various structurally diverse terminal and cyclic epoxides and symmetric and dissymmetric oximes (*E*- and *Z*-isomers). The results of these reactions are given in Table 3. Most of the oximes used in this research were commercially available or could be easily prepared using the procedure reported in the literature.[25] The dissymmetric oximes, in most cases, were used as mixtures of their *E*- and *Z*-isomers. The ring opening of epoxides with oximes under basic conditions usually takes place in an S_N2 fashion. Consequently, the reaction of cyclohexene oxide with acetophenone oxime, benzophenone oxime, and 1-(4-chlorophenyl)ethanone oxime afforded the corresponding β-hydroxy oxime *O*-cyclohexyl ethers **4g**, **4h**, and **4q** (entries 7, 8, and 17, respectively) as the *trans*-isomers (determined by NMR analysis). The ring opening of the terminal epoxides with oximes was mostly achieved regioselectively by preferential attack at the less-hindered carbon atom of the epoxide. However, an exception to this was the reaction of styrene oxide with oximes that afforded two regioisomers in a ratio of approximately 1:3. Thus, compounds **4d**, **4n**, and **4u** (entries 4, 14, and 21, respectively) were obtained as the main products from the attack at the less-hindered side; whereas, their regioisomers **4e**, **4o**, and **4v** (entries 5, 15, and 22, respectively) were produced from attacking the side that was more hindered. The regioisomers were separated by short column chromatography techniques and their structures were characterized by ^1H and ^{13}C NMR spectroscopic analysis.

Table 3 β-Hydroxy Oxime *O*-Ethers Synthesized by the Ring Opening of Epoxides with Oximes

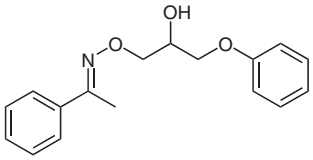
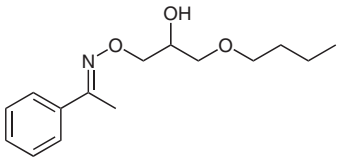
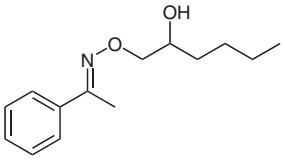
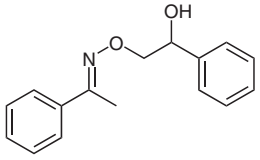
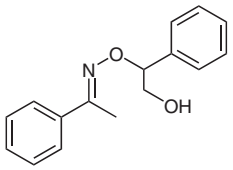
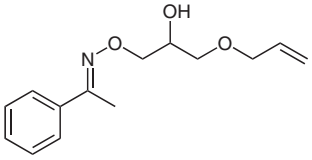
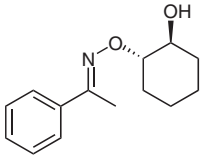
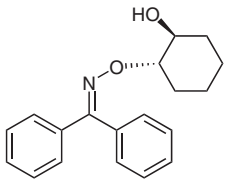
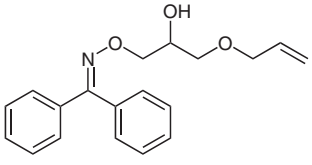
Entry	Product[a]	Product number	Time (h)	Yield[b] (%)
1		**4a**	10	85
2		**4b**	7	82
3		**4c**	5	80
4		**4d**	6	73
5		**4e**	[c]	23
6		**4f**	4	87
7		**4g**	10	89
8		**4h**	6	90
9		**4i**	5	83

Table 3 β-Hydroxy Oxime *O*-Ethers Synthesized by the Ring Opening of Epoxides with Oximes (continued)

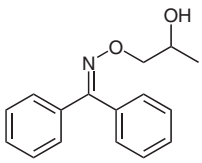
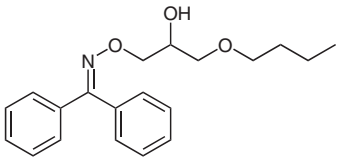
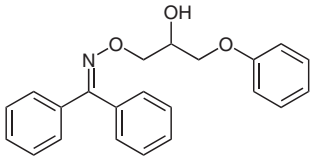
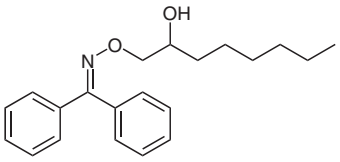
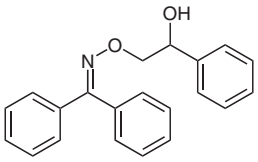
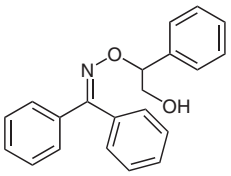
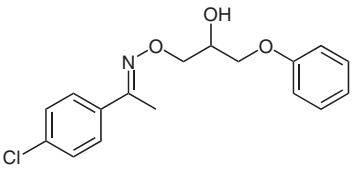
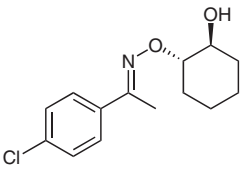
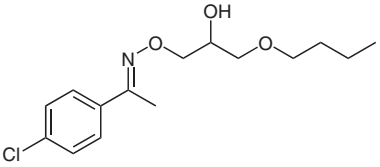
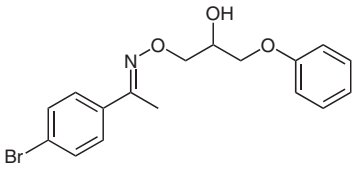
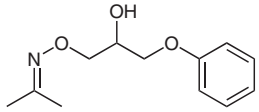
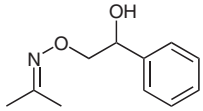
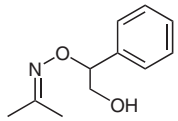
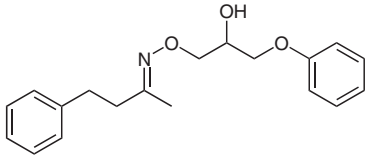
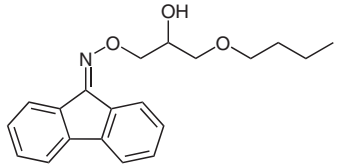
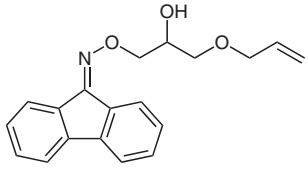
Entry	Product[a]	Product number	Time (h)	Yield[b] (%)
10		**4j**	6	80
11		**4k**	5	89
12		**4l**	4	91
13		**4m**	6	87
14		**4n**	6	75
15		**4o**	[d]	19
16		**4p**	6	88
17		**4q**	10	87
18		**4r**	4	90

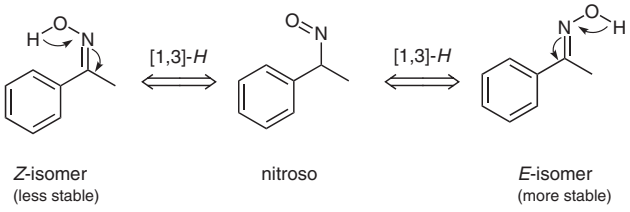
Table 3 β-Hydroxy Oxime *O*-Ethers Synthesized by the Ring Opening of Epoxides with Oximes (continued)

Entry	Product[a]	Product number	Time (h)	Yield[b] (%)
19		**4s**	6	86
20		**4t**	4	91
21		**4u**	4	70
22		**4v**	[e]	26
23		**4w**	6	87
24		**4x**	4	78
25		**4y**	4	80

[a] All products were characterized by ^{1}H and ^{13}C NMR and IR spectroscopy, MS, and CHN analysis.
[b] Isolated yield.
[c] Product formed in the same reaction that gave **4d**.
[d] Product formed in the same reaction that gave **4n**.
[e] Product formed in the same reaction that gave **4u**.

Oximes are known to be ambident nucleophiles.[26] The alkylation of an oxime can be achieved at the oxygen to afford an *O*-alkyl ether or at the nitrogen to generate nitrones.[27] Like other ambident systems, the site of alkylation in the oxime anion is affected by a number of factors, such as the base and solvent types, the nature of the alkylating agents and the cation, the geometry of the substrate, any functional groups present on the oxime, and the degree of dissociation of the oxime salts.[27,28] However, using our presented method, mainly *O*-alkyl ethers were obtained and nitrones were not detected, even in trace amounts.

Dissymmetric ketoximes usually exist as a mixture of the *E*- (or *anti*) and *Z*- (or *syn*) isomers, and tautomeric interconversions of the (*E*)- and (*Z*)-oximes occur readily (via 1,3-*H* shift) (Scheme 2).[29] The propensity of these interconversions is toward the formation of the more-stable *E*-isomer, as was found in the case of acetophenone oxime and its derivatives: quantum mechanical calculation methods, including ab initio 6-31G or semiempirical Austin Model 1 (AM1) and Parameterized Model 3 (PM3),[30] indicated that (*E*)-acetophenone oxime is slightly more stable than its *Z*-isomer. However, the results of the O-alkylation of acetophenone oxime with 2-(phenoxymethyl)oxirane to give product **4a** (Table 3, entry 1) indicated that the *E*-isomer was produced exclusively (85%). To rationalize this observation, the quantum mechanical calculation methods described above were used and the results indicated that there is a considerable energy difference between (*E*)- and (*Z*)-oxime ethers **4a** in comparison with (*E*)- and (*Z*)-acetophenone oxime. The bulkiness of the *O*-alkyl group is largely responsible for encouraging the product to form as the more-stable (*E*)-oxime ether. This diastereoselectivity could also be rationalized as a function of steric hindrance caused by the phenyl group in the *Z*-isomers rather than the methyl group in the *E*-isomers. The same situation was also observed for compounds **4d** and **4e**. Notwithstanding, it could be expected to obtain four oxime ether isomers from the reaction of (*E*)- and (*Z*)-acetophenone oxime with styrene oxide; however, only the formation of **4d** and **4e** was detected. Furthermore, aside from the stereoelectronic factor controlling the regioselective ring opening of styrene oxide, the limited synthesis of **4e** in comparison with **4d** could also be attributed to the steric repulsion between the phenyl group in the 2-phenylethanol moiety of **4e** and the methyl group.



Scheme 2 Interconversions of the *E*- and *Z*-isomers of acetophenone oxime via nitroso–oxime tautomerization (1,3-*H* shift)

The tautomeric interconversions of (*E*)- and (*Z*)-oximes are known to be accelerated in acidic or basic media.[28,31] On this basis, when (*E*)-acetophenone oxime (>98% purity, indicated by HPLC)[32] was O-alkylated with 2-(phenoxymethyl)oxirane, a trace amount of the synthesized (*Z*)-oxime ether was observed. The geometry of compound **4a**, for both the *E*- and *Z*-isomeric forms, was optimized using ab initio 6-31G calculations (Figures 2 and 3, respectively). In the structure shown in Figure 2, the carbon–carbon bond frameworks are nearly coplanar, and this condition allows for ideal conjugation between the phenyl moiety in the oxime and the carbon–nitrogen double bond. However, because of the steric repulsion be-

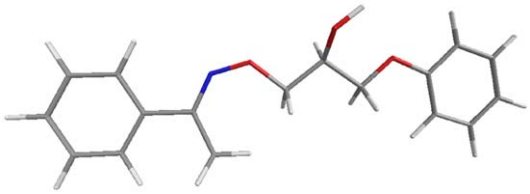


Figure 2 Optimized geometry for the *E*-isomer of acetophenone oxime *O*-(2-hydroxy-3-phenoxypropyl) ether (**4a**)

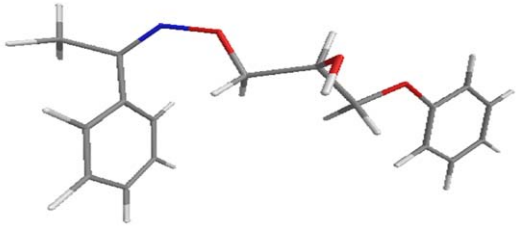


Figure 3 Optimized geometry for the *Z*-isomer of acetophenone oxime *O*-(2-hydroxy-3-phenoxypropyl) ether (**4a**)

tween the phenyl moiety in the oxime and the *O*-alkyl group, the phenyl group deviates from coplanarity in the structure in Figure 3.

The synthesized compounds **4a**–**y** have similar features to compounds **1**–**3**. On comparison of the structure of **1** with **4d**, **4n**, and **4u**, and also that of **2** with products such as **4a**, **4p**, **4s**, and **4w**, the oxime ether products delineate compounds **1** and **2** with the amino group being replaced with an oxime moiety. Most of the synthesized compounds take the form of **3** in which the amino group is replaced with various aryloxy, alkoxy, and alkyl groups. The β-blocking activities of the title compounds are under biological investigation and will be reported in due course.

In conclusion, a convenient and highly efficient synthetic methodology has been described for the preparation of novel β-hydroxy oxime *O*-ethers via the O-alkylation of oxime anions with epoxides in H_2O–DMSO (7:3) at room temperature. The regio- and diastereoselectivity of the reaction, its conformity with green protocols, simplicity, mild reaction conditions, and high yields of products indicate the characteristics of this method. Finally, to rationalize the experimental outcomes, quantum mechanical studies have been used to support the considerable preference for (*E*)-oxime ether formation.

All chemicals were obtained from Merck, Fluka, and Acros chemical companies. Some of the oximes used in this research were prepared using the described method.[25] Solvents were purified and dried according to the reported methods[33] and stored over 3-Å molecular sieves. The progress of the reaction was followed by TLC using silica gel SILG/UV 254 plates. Silica gel 60 (0.063–0.200 mm, 70–230 mesh ASTM) was used for column chromatography. Melting points (mp) were recorded on a Büchi 510 apparatus in open capillary tubes and are uncorrected. Infrared spectra were run on a Shimadzu FTIR-8300 spectrophotometer. The ^{1}H (300 MHz) and ^{13}C NMR (75 MHz) spectra were run on a Brüker DPX-300 FT-NMR spectrometer using TMS as an internal standard. High resolution mass spectra (HRMS) were performed on a VG 70S Magnetic Sector Mass Spectrometer using FAB ionization technique. Microanalyses were performed on a Perkin–Elmer 240-B microanalyzer.

β-Hydroxy Oxime *O*-Ethers 4; General Procedure

To a 100-mL round-bottomed flask containing a mixture of the ketoxime (0.010 mol) and KOH (0.73 g, 0.013 mol) in H_2O–DMSO (7:3, 20 mL) was added the epoxide (0.015 mol). The mixture was then stirred at r.t. until TLC monitoring indicated no further improvement in the reaction (for reaction times, see Table 3). Then, the mixture was dissolved in $CHCl_3$ (100 mL) and washed with H_2O (3 × 100 mL). The organic layer was dried (Na_2SO_4) and the solvent evaporated. The crude product was purified by column chromatography as indicated below.

Acetophenone Oxime *O*-(2-Hydroxy-3-phenoxypropyl) Ether (4a)

Column chromatography (silica gel, EtOAc–*n*-hexane, 1:9) afforded the product as a bright-yellow oil. Yield: 2.42 g (85%); R_f = 0.64 (EtOAc–*n*-hexane, 1:2).

IR (liquid film): 3298.5 (br s), 3058.4, 2931.2, 2856.7, 1651.3, 1446.9, 1115.1, 1049.5 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.15 (s, 3 H, CH_3), 3.23 (s, 1 H, OH, exchangeable with D_2O), 3.96 (dd, *J* = 4.0, 10.1 Hz, 2 H, CH_2ON), 4.30–4.35 (complex, 3 H, CHCH_2OPh), 6.82–6.85 (m, 3 H_{arom}), 7.15–7.27 (m, 5 H_{arom}), 7.50–7.53 (m, 2 H_{arom}).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 11.76, 67.60, 68.96, 73.52, 113.51, 120.17, 125.01, 127.43, 128.44, 129.84, 134.98, 154.93, 157.54.

HRMS: *m*/*z* (M^+) calcd for $C_{17}H_{19}NO_3$: 285.1365; found: 285.1362.

Anal. Calcd for $C_{17}H_{19}NO_3$: C, 71.56; H, 6.71; N 4.91. Found: C, 71.53; H, 6.70; N, 4.96.

Acetophenone Oxime *O*-(3-Butoxy-2-hydroxypropyl) Ether (4b)

Column chromatography (silica gel, EtOAc–*n*-hexane, 1:4) afforded the product as a yellow oil. Yield: 2.20 g (82%); R_f = 0.66 (EtOAc–*n*-hexane, 1:2).

IR (liquid film): 3369.8 (br s), 3052.8, 2984.5, 2865.5, 1667.3, 1428.9, 1309.5, 1028.6 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.79 (t, *J* = 7.2 Hz, 3 H, CH_2CH_3), 1.23–1.32 (m, 2 H, CH_2), 1.42–1.51 (m, 2 H, CH_2), 2.15 (s, 3 H, CH_3CN), 3.09 (s, 1 H, OH, exchangeable with D_2O), 3.36–3.44 (complex, 4 H, CH_2OCH_2), 4.04–4.08 (m, 1 H, CHOH), 4.17 (dd, *J* = 3.6, 5.3 Hz, 2 H, CH_2ON), 7.23–7.26 (m, 3 H_{arom}), 7.50–7.54 (m, 2 H_{arom}).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 12.69, 13.90, 19.26, 31.68, 70.07, 71.35, 71.75, 75.11, 126.02, 128.39, 129.22, 136.23, 155.40.

HRMS: *m*/*z* (M^+) calcd for $C_{15}H_{23}NO_3$: 265.1678; found: 265.1680.

Anal. Calcd for $C_{15}H_{23}NO_3$: C, 67.90; H, 8.74; N, 5.28. Found: C, 67.96; H, 8.78; N, 5.27.

Acetophenone Oxime *O*-(2-Hydroxyhexyl) Ether (4c)

Column chromatography (silica gel, EtOAc–*n*-hexane, 1:9) afforded the product as a bright-yellow oil. Yield: 2.12 g (80%); R_f = 0.45 (EtOAc–*n*-hexane, 1:2).

IR (liquid film): 3286.5 (br s), 3055.2, 2931.6, 2869.9, 1658.7, 1442.7, 1303.8 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.95 (t, *J* = 7.3 Hz, 3 H, CH_2CH_3), 1.38–1.58 (m, 6 H, 3 CH_2), 2.29 (s, 3 H, CH_3CN), 3.31 (s, 1 H, OH, exchangeable with D_2O), 4.16–4.28 (complex, 3 H, CHCH_2ON), 7.37–7.41 (m, 3 H_{arom}), 7.66–7.70 (m, 2 H_{arom}).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 12.37, 13.82, 22.83, 27.71, 33.03, 71.25, 78.02, 126.13, 128.69, 133.18, 136.77, 155.62.

HRMS: *m*/*z* (M^+) calcd for $C_{14}H_{21}NO_2$: 235.1572; found: 235.1569.

Anal. Calcd for $C_{14}H_{21}NO_2$: C, 71.46; H, 8.99; N, 5.95. Found: C, 71.48; H, 8.97; N, 5.98.

Acetophenone Oxime *O*-(2-Hydroxy-2-phenylethyl) Ether (4d)

Column chromatography (silica gel, EtOAc–*n*-hexane, 1:4) afforded the product as a yellow oil. Yield: 1.86 g (73%); R_f = 0.72 (EtOAc–*n*-hexane, 1:2).

IR (liquid film): 3328.9 (br s), 3057.1, 2967.5, 2839.2, 1658.6, 1476.3, 1310.2 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 2.21 (s, 3 H, C*H*$_3$), 2.92 (s, 1 H, OH, exchangeable with D_2O), 3.89 (dd, *J* = 7.9, 12.0 Hz, 2 H, C*H*$_2$ON), 5.29 (dd, *J* = 3.3, 7.8 Hz, 1 H, C*H*OH), 7.15–7.28 (m, 8 H_{arom}), 7.45–7.50 (m, 2 H_{arom}).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 13.07, 67.74, 85.81, 126.16, 126.78, 128.02, 128.47, 128.73, 129.38, 136.23, 138.55, 156.06.

HRMS: *m*/*z* (M^+) calcd for $C_{16}H_{17}NO_2$: 255.1259; found: 255.1258.

Anal. Calcd for $C_{16}H_{17}NO_2$: C, 75.27; H, 6.71; N, 5.49. Found: C, 75.29; H, 6.68; N, 5.53.

Acetophenone Oxime *O*-(2-Hydroxy-1-phenylethyl) Ether (4e)

Column chromatography (silica gel, EtOAc–*n*-hexane, 1:4) afforded the product as a yellow oil. Yield: 0.59 g (23%); R_f = 0.70 (EtOAc–*n*-hexane, 1:2).

IR (liquid film): 3326.4 (br s), 3056.3, 2968.4, 2839.2, 1658.3, 1476.7, 1310.2 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 2.24 (s, 3 H, C*H*$_3$), 2.37 (s, 1 H, OH, exchangeable with D_2O), 3.93 (complex, 2 H, C*H*$_2$OH), 4.83 (dd, *J* = 3.6, 7.1 Hz, 1 H, OC*H*Ph), 7.18–7.22 (m, 5 H_{arom}), 7.32–7.38 (m, 3 H_{arom}), 7.42–7.53 (m, 2 H_{arom}).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 13.98, 65.43, 83.18, 126.24, 126.39, 128.12, 128.52, 128.69, 129.45, 136.12, 138.59, 156.11.

HRMS: *m*/*z* (M^+) calcd for $C_{16}H_{17}NO_2$: 255.1259; found: 255.1261.

Anal. Calcd for $C_{16}H_{17}NO_2$: C, 75.27; H, 6.71; N, 5.49. Found: C, 75.28; H, 6.72; N, 5.46.

Acetophenone Oxime *O*-(3-Allyloxy-2-hydroxypropyl) Ether (4f)

Column chromatography (silica gel, EtOAc–*n*-hexane, 1:4) afforded the product as a bright-yellow oil. Yield: 2.17 g (87%); R_f = 0.54 (EtOAc–*n*-hexane, 1:2).

IR (liquid film): 3364.1 (br s), 3071.2, 2969.7, 2844.2, 1661.2, 1472.3, 1332.4, 1054.7 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 2.01 (s, 3 H, C*H*$_3$), 3.35 (dd, *J* = 5.9, 7.4 Hz, 2 H, OC*H*$_2$CHOH), 3.60 (s, 1 H, OH, exchangeable with D_2O), 3.79 (dd, *J* = 1.2, 4.3 Hz, 2 H, C*H*$_2$ON), 4.00–4.02 (m, 1 H, C*H*OH), 4.09–4.11 (m, 2 H, C*H*$_2$CH=C), 4.93 (dd, J_1, J_2 = 1.4, 10.4 Hz, 1 H, =C*H*$_A$H$_B$), 5.03 (dd, J_1, J_3 = 1.4, 17.2 Hz, 1 H, =CH$_A$*H*$_B$), 5.65–5.69 (m, 1 H, =C*H*$_{vinyl}$), 7.10–7.12 (m, 3 H_{arom}), 7.39–7.43 (m, 2 H_{arom}).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 12.59, 69.72, 71.43, 72.23, 75.10, 117.02, 126.00, 128.35, 128.83, 134.66, 136.21, 155.12.

HRMS: *m*/*z* (M^+) calcd for $C_{14}H_{19}NO_3$: 249.1365; found: 249.1360.

Anal. Calcd for $C_{14}H_{19}NO_3$: C, 67.45; H, 7.68; N, 5.62. Found: C, 67.51; H, 7.65; N, 5.63.

Acetophenone Oxime *O*-(2-Hydroxycyclohexyl) Ether (4g)

Column chromatography (silica gel, EtOAc–*n*-hexane, 3:7) afforded the product as a yellow oil. Yield: 2.08 g (89%); R_f = 0.77 (EtOAc–*n*-hexane, 1:2).

IR (liquid film): 3359.1 (br s), 3057.0, 2942.6, 2869.4, 1661.4, 1452.8, 1161.3 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 0.80–0.87 (m, 4 H, 2 C*H*$_2$), 1.18 (s, 3 H, C*H*$_3$), 1.25–1.34 (m, 4 H, 2 C*H*$_2$), 1.61 (s, 1 H, OH, exchangeable with D_2O), 4.11–4.18 (complex, 2 H, C*H*OH, C*H*ON), 7.42–7.48 (m, 3 H_{arom}), 7.60–7.65 (m, 2 H_{arom}).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.04, 22.97, 23.71, 28.90, 38.70, 59.50, 68.12, 128.43, 128.78, 130.86, 132.42, 167.74.

HRMS: *m*/*z* (M^+) calcd for $C_{14}H_{19}NO_2$: 233.1416; found: 233.1420.

Anal. Calcd for $C_{14}H_{19}NO_2$: C, 72.07; H, 8.21; N, 6.00. Found: C, 72.11; H, 8.27; N, 5.98.

Benzophenone Oxime *O*-(2-Hydroxycyclohexyl) Ether (4h)

Column chromatography (silica gel, EtOAc–*n*-hexane, 3:7) afforded the product as a white solid. Yield: 2.66 g (90%); mp 62.5 °C; R_f = 0.70 (EtOAc–*n*-hexane, 1:2).

IR (KBr): 3379.5 (br s), 3050.1, 2931.6, 2862.2, 1650.9, 1442.7, 1164.9 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 1.15–1.25 (m, 4 H, 2 C*H*$_2$), 1.56–1.59 (m, 2 H, C*H*$_2$), 1.96–1.99 (m, 2 H, C*H*$_2$), 3.54 (s, 1 H, OH, exchangeable with D_2O), 3.57–3.61 (m, 1 H, C*H*OH), 3.94–3.95 (m, 1 H, C*H*ON), 7.14–7.39 (m, 10 H_{arom}).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 23.78, 24.16, 29.63, 32.56, 73.62, 86.48, 128.21, 128.32, 128.73, 129.08, 129.35, 129.47, 133.13, 136.43, 157.23.

HRMS: *m*/*z* (M^+) calcd for $C_{19}H_{21}NO_2$: 295.1572; found: 295.1570.

Anal. Calcd for $C_{19}H_{21}NO_2$: C, 77.26; H, 7.17; N, 4.74. Found: C, 77.29; H, 7.14; N, 4.79.

Benzophenone Oxime *O*-(3-Allyloxy-2-hydroxypropyl) Ether (4i)

Column chromatography (silica gel, EtOAc–*n*-hexane, 1:4) afforded the product as a bright-yellow oil. Yield: 2.58 g (83%); R_f = 0.71 (EtOAc–*n*-hexane, 1:2).

IR (liquid film): 3386.8 (br s), 3062.7, 2925.5, 2869.9, 1650.9, 1442.7, 1326.9, 1056.1 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 3.41 (dd, *J* = 5.9, 9.8 Hz, 2 H, OC*H*$_2$CHOH), 3.64 (s, 1 H, OH, exchangeable with D_2O), 3.92–3.95 (m, 2 H, C*H*$_2$ON), 4.17 (br s, 1 H, C*H*OH), 4.26–4.28 (m, 2 H, C*H*$_2$CH=C), 5.10–5.26 (complex, 2 H, =CH$_2$), 5.77–5.87 (m, 1 H, =C*H*$_{vinyl}$), 7.21–7.51 (m, 10 H_{arom}).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 69.53, 71.43, 72.20, 75.49, 117.05, 127.99, 128.17, 128.33, 128.94, 129.31, 129.52, 133.21, 134.78, 136.27, 157.29.

HRMS: *m*/*z* (M^+) calcd for $C_{19}H_{21}NO_3$: 311.1521; found: 311.1523.

Anal. Calcd for $C_{19}H_{21}NO_3$: C, 73.29; H, 6.80; N, 4.50. Found: C, 73.34; H, 6.82; N, 4.46.

Benzophenone Oxime *O*-(2-Hydroxypropyl) Ether (4j)

Column chromatography (silica gel, EtOAc–*n*-hexane, 3:7) afforded the product as a colorless oil. Yield: 2.04 g (80%); R_f = 0.62 (EtOAc–*n*-hexane, 1:2).

IR (liquid film): 3385.6 (br s), 3055.4, 2970.2, 2877.6, 1650.9, 1488.9, 1326.9 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 1.21 (d, *J* = 6.1 Hz, 3 H, C*H*$_3$), 3.27 (s, 1 H, OH, exchangeable with D_2O), 4.06–4.14 (m, 1 H, C*H*OH), 4.16 (dd, *J* = 2.8, 8.7 Hz, 2 H, C*H*$_2$ON), 7.30–7.57 (m, 10 H_{arom}).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 19.14, 66.96, 79.48, 128.01, 128.15, 128.26, 129.27, 129.45, 129.54, 133.19, 136.23, 157.58.

HRMS: *m*/*z* (M^+) calcd for $C_{16}H_{17}NO_2$: 255.1259; found: 255.1260.

Anal. Calcd for $C_{16}H_{17}NO_2$: C, 75.27; H, 6.71; N, 5.49. Found: C, 75.30; H, 6.76; N, 5.52.

Benzophenone Oxime *O*-(3-Butoxy-2-hydroxypropyl) Ether (4k)

Column chromatography (silica gel, EtOAc–*n*-hexane, 1:4) afforded the product as a colorless oil. Yield: 2.91 g (89%); R_f = 0.63 (EtOAc–*n*-hexane, 1:2).

IR (liquid film): 3381.6 (br s), 3055.0, 2962.2, 2869.9, 1658.7, 1442.7, 1110.9, 1056.9 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 0.75 (t, *J* = 7.2 Hz, 3 H, C*H*$_3$), 1.18–1.27 (m, 2 H, C*H*$_2$), 1.36–1.44 (m, 2 H, C*H*$_2$), 3.25 (t, *J* = 3.2 Hz, 2 H, OC*H*$_2$CH$_2$), 3.31 (s, 1 H, OH, exchangeable with D_2O), 3.32 (dd, *J* = 3.3, 4.7 Hz, 2 H, OC*H*$_2$CHOH), 4.00–4.04 (m, 1 H, C*H*OH), 4.13–4.15 (m, 2 H, C*H*$_2$ON), 7.04–7.22 (m, 8 H_{arom}), 7.34–7.38 (m, 2 H_{arom}).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.02, 19.32, 31.70, 69.60, 71.24, 71.98, 75.58, 127.96, 128.10, 128.27, 129.29, 129.45, 129.68, 133.22, 136.29, 157.26.

HRMS: *m*/*z* (M^+) calcd for $C_{20}H_{25}NO_3$: 327.1834; found: 327.1831.

Anal. Calcd for $C_{20}H_{25}NO_3$: C, 73.37; H, 7.70; N, 4.28. Found: C, 73.39; H, 7.75; N, 4.25.

Benzophenone Oxime *O*-(2-Hydroxy-3-phenoxypropyl) Ether (4l)

Column chromatography (silica gel, EtOAc–*n*-hexane, 1:9) afforded the product as a bright-yellow oil. Yield: 3.16 g (91%); R_f = 0.61 (EtOAc–*n*-hexane, 1:2).

IR (liquid film): 3379.1 (br s), 3062.7, 2921.2, 2877.6, 1668.7, 1496.7, 1242.1, 1049.2 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 3.73 (s, 1 H, OH, exchangeable with D_2O), 3.97 (br s, 2 H, C*H*$_2$ON), 4.39 (br s, 3 H, C*H*C*H*$_2$OPh), 6.86–6.99 (m, 3 H_{arom}), 7.20–7.32 (m, 10 H_{arom}), 7.51 (d, *J* = 7.5 Hz, 2 H_{arom}).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 69.27, 69.50, 75.34, 114.96, 121.28, 128.47, 128.64, 128.99, 129.26, 129.52, 129.89, 130.37, 133.36, 136.36, 158.02, 158.97.

HRMS: *m*/*z* (M^+) calcd for $C_{22}H_{21}NO_3$: 347.1521; found: 347.1524.

Anal. Calcd for $C_{22}H_{21}NO_3$: C, 76.06; H, 6.09; N, 4.03. Found: C, 76.01; H, 6.08; N, 4.05.

Benzophenone Oxime *O*-(2-Hydroxyoctyl) Ether (4m)

Column chromatography (silica gel, EtOAc–*n*-hexane, 1:9) afforded the product as a colorless oil. Yield: 2.83 g (87%); R_f = 0.83 (EtOAc–*n*-hexane, 1:2).

IR (liquid film): 3386.8 (br s), 3055.6, 2923.9, 2862.2, 1658.7, 1442.7, 1319.2, 1058.1 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 0.75 (t, *J* = 6.8 Hz, 3 H, C*H*$_3$), 1.18–1.36 (m, 10 H, 5 C*H*$_2$), 2.75 (s, 1 H, OH, exchangeable with D_2O), 3.85–3.97 (m, 1 H, C*H*OH), 4.06 (dd, *J* = 2.3, 11.1 Hz, 2 H, C*H*$_2$ON), 7.18–7.37 (m, 10 H_{arom}).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.16, 22.66, 25.43, 29.39, 31.82, 33.21, 71.17, 78.38, 127.93, 128.21, 128.33, 129.02, 129.14, 129.59, 133.07, 136.09, 157.72.

HRMS: *m*/*z* (M^+) calcd for $C_{21}H_{27}NO_2$: 325.2042; found: 325.2039.

Anal. Calcd for $C_{21}H_{27}NO_2$: C, 77.50; H, 8.36; N, 4.30. Found: C, 77.53; H, 8.41; N, 4.33.

Benzophenone Oxime *O*-(2-Hydroxy-2-phenylethyl) Ether (4n)

Column chromatography (silica gel, EtOAc–*n*-hexane, 1:4) afforded the product as a bright-yellow solid. Yield: 2.38 g (75%); mp 125.7 °C; R_f = 0.68 (EtOAc–*n*-hexane, 1:2).

IR (KBr): 3289.4 (br s), 3062.1, 2935.7, 2894.3, 1667.1, 1485.2, 1232.6 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 2.46 (s, 1 H, OH, exchangeable with D_2O), 3.64 (dd, *J* = 6.0, 19.4 Hz, 2 H, C*H*$_2$ON), 5.28 (dd, *J* = 3.7, 7.5 Hz, 1 H, C*H*OH), 7.14–7.33 (m, 15 H_{arom}).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 67.03, 86.31, 114.77, 121.45, 125.55, 126.78, 128.20, 128.30, 128.42, 129.26, 129.59, 133.24, 136.18, 138.50, 158.14.

HRMS: *m*/*z* (M^+) calcd for $C_{21}H_{19}NO_2$: 317.1416; found: 317.1415.

Anal. Calcd for $C_{21}H_{19}NO_2$: C, 79.47; H, 6.03; N, 4.41. Found: C, 79.52; H, 6.04; N, 4.37.

Benzophenone Oxime *O*-(2-Hydroxy-1-phenylethyl) Ether (4o)

Column chromatography (silica gel, EtOAc–*n*-hexane, 1:4) afforded the product as a bright-yellow oil. Yield: 0.60 g (19%); R_f = 0.66 (EtOAc–*n*-hexane, 1:2).

IR (liquid film): 3291.5 (br), 3064.5, 2938.8, 2900.4, 1665.4, 1492.6, 1232.6 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 2.41(s, 1 H, OH, exchangeable with D_2O), 3.96 (complex, 2 H, C*H*$_2$OH), 5.28 (dd, *J* = 3.5, 7.4 Hz, 1 H, OC*H*Ph), 7.16–7.38 (m, 15 H_{arom}).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 66.12, 87.75, 114.56, 121.44, 125.59, 126.83, 128.29, 128.33, 128.39, 129.24, 129.62, 133.24, 136.25, 138.54, 158.19.

HRMS: *m*/*z* (M^+) calcd for $C_{21}H_{19}NO_2$: 317.1416; found: 317.1414.

Anal. Calcd for $C_{21}H_{19}NO_2$: C, 79.47; H, 6.03; N, 4.41. Found: C, 79.50; H, 6.05; N, 4.41.

1-(4-Chlorophenyl)ethanone Oxime *O*-(2-Hydroxy-3-phenoxypropyl) Ether (4p)

Column chromatography (silica gel, EtOAc–*n*-hexane, 3:7) afforded the product as a white foam. Yield: 2.81 g (88%); R_f = 0.65 (EtOAc–*n*-hexane, 1:2).

IR (liquid film): 3286.5 (br s), 3052.4, 2994.4, 2878.4, 1664.2, 1458.7, 1325.3, 1054.2 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 2.51 (s, 3 H, C*H*$_3$), 4.43–4.45 (complex, 3 H, OH, C*H*$_2$ON), 4.83 (br s, 3 H, C*H*C*H*$_2$OPh), 7.28–7.31 (m, 3 H_{arom}), 7.58–7.65 (m, 4 H_{arom}), 7.82–7.85 (m, 2 H_{arom}).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 12.91, 69.57, 69.86, 75.52, 115.18, 121.61, 127.88, 129.07, 129.63, 135.03, 135.60, 154.87, 159.21.

HRMS: *m*/*z* (M^+) calcd for $C_{17}H_{18}ClNO_3$: 319.0975; found: 319.0970.

Anal. Calcd for $C_{17}H_{18}ClNO_3$: C, 63.85; H, 5.67; Cl, 11.09; N, 4.38. Found: C, 63.91; H, 5.66; Cl, 11.12; N, 4.34.

1-(4-Chlorophenyl)ethanone Oxime *O*-(2-Hydroxycyclohexyl) Ether (4q)

Column chromatography (silica gel, EtOAc–*n*-hexane, 3:7) afforded the product as a bright-yellow oil. Yield: 2.32 g (87%); R_f = 0.56 (EtOAc–*n*-hexane, 1:2).

IR (liquid film): 3387.2 (br s), 3052.2, 2965.5, 2878.4, 1652.9, 1445.1, 1168.2 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 1.17–1.33 (m, 4 H, 2 C*H*$_2$), 1.61–1.67 (m, 2 H, C*H*$_2$), 1.96–2.00 (m, 2 H, C*H*$_2$), 2.14 (s, 3 H, C*H*$_3$), 3.59–3.68 (complex, 2 H, C*HOH*), 3.92–3.93 (m, 1 H, C*H*ON), 7.21–7.31 (m, 2 H_{arom}), 7.51–7.53 (m, 2 H_{arom}).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 12.56, 23.73, 24.18, 29.66, 32.56, 74.29, 86.07, 125.99, 127.24, 128.61, 135.22, 154.13.

HRMS: *m*/*z* (M^+) calcd for $C_{14}H_{18}ClNO_2$: 267.1026; found: 267.1023.

Anal. Calcd for $C_{14}H_{18}ClNO_2$: C, 62.80; H, 6.78; Cl, 13.24; N, 5.23. Found: C, 62.76; H, 6.75; Cl, 13.29; N, 5.27.

1-(4-Chlorophenyl)ethanone Oxime *O*-(3-Butoxy-2-hydroxypropyl) Ether (4r)

Column chromatography (silica gel, EtOAc–*n*-hexane, 1:4) afforded the product as a bright-yellow oil. Yield: 2.70 g (90%); R_f = 0.63 (EtOAc–*n*-hexane, 1:2).

IR (liquid film): 3364.8 (br s), 3057.3, 2957.6, 2871.4, 1642.4, 1453.1, 1161.7, 1041.9 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 0.74 (t, *J* = 7.3 Hz, 3 H, CH_2CH_3), 1.18–1.27 (m, 2 H, CH_2), 1.37–1.45 (m, 2 H, CH_2), 2.05 (s, 3 H, CH_3CN), 3.30 (t, *J* = 6.6 Hz, 2 H, OCH_2CH_2), 3.34 (s, 1 H, OH, exchangeable with D_2O), 3.38 (dd, *J* = 6.0, 9.1 Hz, 2 H, OCH_2CHOH), 4.00–4.04 (m, 1 H, CHOH), 4.12–4.14 (m, 2 H, CH_2ON), 7.14–7.19 (m, 2 H_{arom}), 7.38–7.42 (m, 2 H_{arom}).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 12.28, 13.83, 19.18, 31.57, 69.58, 71.25, 71.87, 75.26, 127.17, 128.41, 134.60, 134.98, 153.75.

HRMS: *m*/*z* (M^+) calcd for $C_{15}H_{22}ClNO_3$: 299.1288; found: 299.1291.

Anal. Calcd for $C_{15}H_{22}ClNO_3$: C, 60.09; H, 7.40; Cl, 11.83; N, 4.67. Found: C, 60.12; H, 7.46; Cl, 11.78; N, 4.69.

1-(4-Bromophenyl)ethanone Oxime *O*-(2-Hydroxy-3-phenoxypropyl) Ether (4s)

Column chromatography (silica gel, EtOAc–*n*-hexane, 1:4) afforded the product as a white solid. Yield: 3.13 g (86%); mp 55.9 °C; R_f = 0.58 (EtOAc–*n*-hexane, 1:2).

IR (KBr): 3378.5 (br s), 3058.3, 2944.2, 2886.3, 1657.6, 1495.6, 1245.7, 1047.9 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 2.12 (s, 3 H, CH_3), 3.65 (s, 1 H, OH, exchangeable with D_2O), 4.00 (br s, 2 H, CH_2ON), 4.35 (br s, 3 H, $CHCH_2OPh$), 6.84–6.92 (m, 3 H_{arom}), 7.17–7.23 (m, 2 H_{arom}), 7.34–7.37 (m, 4 H_{arom}).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 12.64, 68.95, 69.60, 74.95, 114.69, 121.61, 123.72, 127.69, 129.63, 131.99, 134.99, 154.76, 158.66.

HRMS: *m*/*z* (M^+) calcd for $C_{17}H_{18}BrNO_3$: 363.0470; found: 363.0472.

Anal. Calcd for $C_{17}H_{18}BrNO_3$: C, 56.06; H, 4.98; N, 3.85. Found: C, 56.02; H, 5.01; N, 3.89.

Propan-2-one Oxime *O*-(2-Hydroxy-3-phenoxypropyl) Ether (4t)

Column chromatography (silica gel, EtOAc–*n*-hexane, 1:4) afforded the product as a bright-yellow oil. Yield: 2.03 g (91%); R_f = 0.65 (EtOAc–*n*-hexane, 1:2).

IR (liquid film): 3300.5 (br s), 3054.5, 2933.5, 2855.1, 1650.3, 1443.4, 1115.5, 1052.5 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 1.95 (s, 6 H, 2 CH_3), 3.30 (s, 1 H, OH, exchangeable with D_2O), 3.87 (dd, *J* = 3.8, 10.1 Hz, 2 H, CH_2ON), 4.32–4.37 (complex, 3 H, $CHCH_2OPh$), 7.23–7.35 (m, 5 H_{arom}).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 15.67, 21.88, 67.23, 68.36, 74.07, 114.02, 120.17, 128.44, 154.45, 157.55.

HRMS: *m*/*z* (M^+) calcd for $C_{12}H_{17}NO_3$: 223.1208; found: 223.1211.

Anal. Calcd for $C_{12}H_{17}NO_3$: C, 64.55; H, 7.67; N, 6.27. Found: C, 64.50; H, 7.70; N, 6.30.

Propan-2-one Oxime *O*-(2-Hydroxy-2-phenylethyl) Ether (4u)

Column chromatography (silica gel, EtOAc–*n*-hexane, 1:9) afforded the product as a yellow oil. Yield: 1.35 g (70%); R_f = 0.45 (EtOAc–*n*-hexane, 1:2).

IR (liquid film): 3368.4 (br s), 3058.5, 2977.5, 2856.3, 1574.2, 1328.4 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 1.80 (s, 6 H, 2 CH_3), 3.65 (s, 1 H, OH, exchangeable with D_2O), 3.92 (dd, *J* = 8.2, 12.0 Hz, 2 H, CH_2ON), 4.92 (dd, *J* = 2.1, 8.2 Hz, 1 H, CHOH), 7.18–7.33 (m, 5 H_{arom}).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 15.64, 21.93, 74.11, 78.19, 126.26, 127.66, 128.45, 140.43, 156.29.

HRMS: *m*/*z* (M^+) calcd for $C_{11}H_{15}NO_2$: 193.1103; found: 193.1105.

Anal. Calcd for $C_{11}H_{15}NO_2$: C, 68.37; H, 7.82; N, 7.25. Found: C, 68.39; H, 7.86; N, 7.23.

Propan-2-one Oxime *O*-(2-Hydroxy-1-phenylethyl) Ether (4v)

Column chromatography (silica gel, EtOAc–*n*-hexane, 1:9) afforded the product as a bright-yellow oil. Yield: 0.50 g (26%); R_f = 0.43 (EtOAc–*n*-hexane, 1:2).

IR (liquid film): 3371.4 (br s), 3059.4, 2978.4, 2857.4, 1577.2, 1330.2 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 1.82 (s, 6 H, 2 CH_3), 3.54 (s, 1 H, OH, exchangeable with D_2O), 3.92 (complex, 2 H, CH_2OH), 4.97 (dd, *J* = 3.6, 7.7 Hz, 1 H, OCHPh), 7.21–7.30 (m, 5 H_{arom}).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 15.66, 22.00, 73.81, 78.22, 126.23, 127.72, 128.41, 140.48, 156.32.

HRMS: *m*/*z* (M^+) calcd for $C_{11}H_{15}NO_2$: 193.1103; found: 193.1104.

Anal. Calcd for $C_{11}H_{15}NO_2$: C, 68.37; H, 7.82; N, 7.25. Found: C, 68.40; H, 7.81; N, 7.27.

4-Phenylbutan-2-one Oxime *O*-(2-Hydroxy-3-phenoxypropyl) Ether (4w)

Column chromatography (silica gel, EtOAc–*n*-hexane, 1:4) afforded the product as a bright-yellow oil. Yield: 2.73 g (87%); R_f = 0.58 (EtOAc–*n*-hexane, 1:2).

IR (liquid film): 3397.4 (br s), 3061.2, 2952.1, 2874.8, 1667.3, 1495.6, 1245.2, 1047.9 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 1.96 (s, 3 H, CH_3), 2.02 (s, 1 H, OH, exchangeable with D_2O), 2.53 (t, *J* = 7.1 Hz, 2 H, CH_2CN), 2.88 (t, *J* = 7.1 Hz, 2 H, CH_2Ph), 4.11–4.13 (m, 2 H, CH_2ON), 4.22–4.24 (m, 1 H, CHOH), 4.34–4.37 (m, 2 H, CH_2OPh), 7.05–7.11 (m, 3 H_{arom}), 7.27–7.42 (m, 7 H_{arom}).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.59, 32.65, 37.75, 69.13, 69.83, 74.18, 114.83, 121.14, 126.36, 128.29, 128.53, 129.71, 141.09, 158.12, 158.94.

HRMS: *m*/*z* (M^+) calcd for $C_{19}H_{23}NO_3$: 313.1678; found: 313.1675.

Anal. Calcd for $C_{19}H_{23}NO_3$: C, 72.82; H, 7.40; N, 4.47. Found: C, 72.88; H, 7.36; N, 4.45.

Fluoren-9-one Oxime *O*-(3-Butoxy-2-hydroxypropyl) Ether (4x)

Column chromatography (silica gel, EtOAc–*n*-hexane, 3:7) afforded the product as a yellow oil. Yield: 2.54 g (78%); R_f = 0.55 (EtOAc–*n*-hexane, 1:2).

IR (liquid film): 3374.6 (br s), 3053.5, 2975.7, 2884.2, 1651.4, 1449.6, 1113.4, 1058.2 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 0.63 (t, *J* = 5.2 Hz, 3 H, CH_3), 1.05–1.11 (m, 2 H, CH_2), 1.27–1.29 (m, 2 H, CH_2), 3.14–3.16 (m, 2 H, CH_2), 3.32–3.34 (m, 2 H, OCH_2CHOH), 3.64 (s, 1 H, OH, exchangeable with D_2O), 4.08 (br s, 1 H, CHOH), 4.28–4.31 (m, 2 H, CH_2ON), 6.91–7.15 (m, 6 H_{arom}), 7.47–7.49 (m, 1 H_{arom}), 8.03–8.05 (m, 1 H_{arom}).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.13, 19.19, 31.60, 69.44, 71.21, 71.89, 76.81, 116.83, 119.66, 121.48, 127.66, 128.01, 129.22, 129.76, 130.29, 130.84, 135.21, 140.07, 141.17, 152.44.

HRMS: *m*/*z* (M^+) calcd for $C_{20}H_{23}NO_3$: 325.1682; found: 325.1682.

Anal. Calcd for $C_{20}H_{23}NO_3$: C, 73.82; H, 7.12; N, 4.30. Found: C, 73.79; H, 7.14; N, 4.36.

Fluoren-9-one Oxime *O*-(3-Allyloxy-2-hydroxypropyl) Ether (4y)

Column chromatography (silica gel, EtOAc–*n*-hexane, 3:7) afforded the product as a yellow oil. Yield: 2.47 g (80%); R_f = 0.45 (EtOAc–*n*-hexane, 1:2).

IR (liquid film): 3374.3 (br s), 3051.7, 2954.1, 2875.9, 1654.7, 1447.2, 1321.3, 1059.2 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.52–3.53 (m, 2 H, OCH_2CHOH), 3.86 (s, 1 H, OH, exchangeable with D_2O), 3.91–3.93 (m, 2 H, CH_2ON), 4.26–4.28 (m, 1 H, C*H*OH), 4.44–4.46 (m, 2 H, CH_2CH=C), 5.10–5.22 (complex, 2 H, =CH_2), 5.75–5.91 (m, 1 H, =CH_{vinyl}), 7.13–7.35 (m, 6 H_{arom}), 7.63–7.66 (m, 1 H_{arom}), 8.17–8.20 (m, 1 H_{arom}).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 69.50, 71.36, 72.23, 76.73, 117.08, 119.76, 121.56, 127.76, 128.10, 129.29, 129.87, 130.31, 130.95, 134.60, 135.21, 140.12, 141.22, 152.57, 160.84.

HRMS: *m*/*z* (M^+) calcd for $C_{19}H_{19}NO_3$: 309.1365; found: 309.1369.

Anal. Calcd for $C_{19}H_{19}NO_3$: C, 73.77; H, 6.19; N, 4.53. Found: C, 73.79; H, 6.23; N, 4.59.

Acknowledgment

We wish to thank the Shiraz University of Technology Research Council for partial support of this work. We are also grateful to Professor G. H. Hakimelahi for helpful discussions.

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