An Efficient One-Pot Synthesis of Oxime Ethers from Alcohols Using Triphenylphosphine/Carbon Tetrachloride

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Abstract: A convenient and efficient one-pot O-alkylation of oximes from alcohols using triphenylphosphine in carbon tetrachloride is described. In this method, treatment of alcohols with a mixture of triphenylphosphine, carbon tetrachloride, oxime, and DBU in the presence of catalytic amounts of tetrabutylammonium iodide in refluxing acetonitrile regioselectively furnishes the corresponding *O*-alkyl ethers in good yields. This methodology is highly efficient O-alkylation of oximes with various structurally diverse alcohols. Semiempirical quantum-mechanic calculations (AM1) for unsymmetrical oxime ethers, indicated a lower heat of formation for *Z*-isomers.

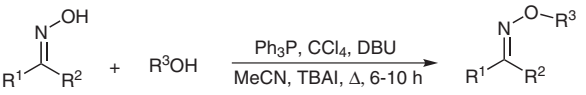
Key words: oxime, alcohol, O-alkylation, triphenylphosphine, carbon tetrachloride, DBU

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 types of chemotherapeutic activity, 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] epoxides,[1a,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] In view of the wide diversity and availability of alcohols and their lower toxicity and ease of handling with respect to alkyl halides, the one-pot reaction of oximes with alcohols seems to be a suitable and attractive strategy. Indeed, there are a few reports that have exemplified the one-pot O-alkylation of oximes with alcohols which mostly are based on Mitsunobu conditions.[17] However, the use of diethyl azodicarboxylate restricts the applicability of this method, since it is an explosive, expensive, toxic, thermally unstable, shock-sensitive, and photosensitive reagent.

The use of the well-known combination of tertiary phosphines with tetrahalomethanes has found increasing application in preparative chemistry for halogenations, dehydrations, and P–N linking reactions.[18] Among these combinations, triphenylphosphine in carbon tetrachloride is a famous reagent that can convert an alcohol into the corresponding alkyl halide[19] under mild conditions. Moreover, the triphenylphosphine in carbon tetrachloride system has various important applications including: conversion of alcohols into nitriles[20] and esters,[21] chlorination and chlorodehydration of 1,2-diols,[22] cyclodehydration of chiral diols,[23] dehydration of aldoximes[24a] and amides,[24b] conversion of carboxylic acids into amides[25a] and acid chlorides,[25b] and synthesis of benzoxazoles,[26a] 1,3,4-oxadiazoles,[26b] β-lactams,[26c] and *N*-acylindolines.[26d]

Encouraged by the significance role of oxime ethers in medicinal chemistry and also in continuation of our interests in use of triphenylphosphine and carbon tetrachloride for organic transformations,[27] herein, we described the preparation of compounds **1a**–**p** via O-alkylation of oximes with alcohols using triphenylphosphine and carbon tetrachloride in the presence of 1,8-diazabicyclo[5.4.0]undec-7-ene and catalytic amounts of tetrabutylammonium iodide in anhydrous acetonitrile (Scheme 1).



Scheme 1 Preparation of oxime *O*-alkyl ethers from alcohols using triphenylphosphine and carbon tetrachloride

The first step of this synthetic approach was to find the optimized reaction conditions. The optimization began by studying the effect of various solvents on the model reaction of 9*H*-fluoren-9-one oxime, allyl alcohol, and DBU in the presence of a mixture of triphenylphosphine in carbon tetrachloride and a catalytic amount of tetrabutylammonium iodide (Table 1).

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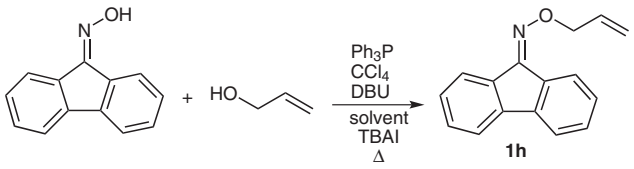
As the data in Table 1 indicates, anhydrous acetonitrile (entry 4) was the most appropriate solvent and was used for all further reactions. In view of the fact that the generated reactive intermediates in the reaction mixture are very susceptible to moisture, the use of a well-dried solvent is essential and highly recommended. The explicit interference of moisture was easily observed by comparing the obtained results in hydrous and anhydrous acetonitrile (entries 3 and 4). Using dimethyl sulfoxide and *N*,*N*-dimethylformamide afforded a moderate yield of the corresponding 9*H*-fluoren-9-one *O*-allyloxime (**1h**) (entries 6 and 7). Other solvents were inefficient even if the reaction time was prolonged (72 h).

Table 1 Effect of Various Solvents on the Conversion of 9*H*-Fluoren-9-one Oxime into 9*H*-Fluoren-9-one *O*-Allyloxime (**1h**)



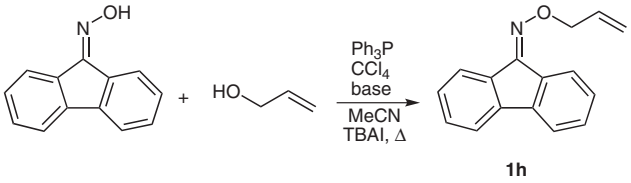
Entry	Solvent[a]	Time (h)	Yield[b] (%)
1	CCl_4	12	20
2	THF	18	15
3	MeCN	72	–[c]
4	MeCN	6	75
5	HMPA	12	25
6	DMSO	10	32
7	DMF	10	35
8	toluene	72	–[c]
9	acetone	72	–[c]

[a] All solvents were anhydrous, with the exception of MeCN (entry 3).
[b] Isolated yield.
[c] No reaction after 72 h at reflux.

The choice of the base for the activation of the O–H bond in the oxime for reaction with alkoxyphosphonium salt intermediates is of great significance. In this case, we evaluated the effect of various organic and inorganic bases on the model reaction (Table 2). In the absence of base, no reaction took place even after prolonged reaction times (72 h). DBU (entry 3) proved to be the most efficient base for conversion of 9*H*-fluoren-9-one oxime into 9*H*-fluoren-9-one *O*-allyloxime (**1h**) (entry 3). Some bases, such as DBN, Cs_2CO_3, and K_2CO_3 (Table 2, entries 2, 7, and 8), afforded lower yields of **1h**, while other bases were far less efficient.

We also investigated the role of various phase-transfer catalysts on the model reaction. In this case, tetrabutylammonium halides (TBAX, X = F, Cl, Br, I) were employed. In the absence of the phase-transfer catalyst, the reaction occurred but only in low yields (<50%). However, using

Table 2 Effect of Various Bases on the Conversion of 9*H*-Fluoren-9-one Oxime into 9*H*-Fluoren-9-one *O*-Allyloxime (**1h**) in Anhydrous Acetonitrile



Entry	Base	Time (h)	Yield[a] (%)
1	none	72	–[b]
2	DBN	12	35
3	DBU	6	75
4	DABCO	24	trace
5	DMAP	24	trace
6	MgO	72	–
7	Cs_2CO_3	8	42
8	K_2CO_3	12	38
9	Et_3N	12	25

[a] Isolated yield.
[b] No reaction after 72 h at reflux.

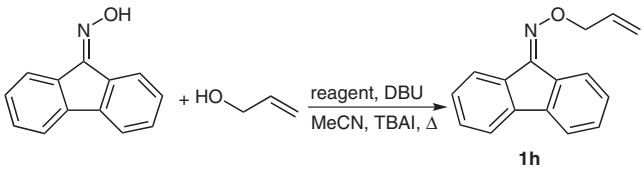
tetrabutylammonium iodide provided **1h** in higher yields and with a shorter reaction time. Other phase-transfer catalysts were not as effective as tetrabutylammonium iodide.

In other experiments, we investigated the influence of several reagents as sources for positive-halogen in combination with triphenylphosphine instead of carbon tetrachloride. As shown by the results in Table 3, the triphenylphosphine and carbon tetrachloride system was found to be the most suitable and efficient reagent for the conversion of allyl alcohol into **1h**. Using *N*-chlorosuccinimide, *N*-bromosuccinimide, isocyanuric chloride, and bromine (entries 2–5) did not afford satisfactory results. 2,3-Dichloro-5,6-dicyano-1,4-benzoquinone and triiodomethane (entries 6 and 7) were inefficient even after 72 hours at reflux.

The optimized stoichiometric ratio of Ph_3P/CCl_4/ROH/oxime/DBU for the conversion of allyl alcohol into **1h** was found to be 1.5:2:1.5:1:1.

To evaluate the generality and versatility of this method, the optimized conditions were employed with various structurally diverse primary, secondary, tertiary, allylic, and benzylic alcohols as well as symmetric and unsymmetrical oximes. The data in Table 4 indicates that the method is suitable and efficient for various alcohols including: primary and secondary alcohols, while tertiary alcohols did not give satisfactory results. For example, O-alkylation of benzophenone oxime with *tert*-butyl alcohol did not afford the corresponding product **1e**. The generality of the method was confirmed with respect to allylic **1b**,

Table 3 Effect of Various Reagents on Conversion of 9*H*-Fluoren-9-one Oxime into 9*H*-Fluoren-9-one *O*-Allyloxime (**1h**)



Entry	Reagent	Time (h)	Yield[a] (%)
1	Ph_3P, CCl_4	6	75
2	Ph_3P, NCS	12	25
3	Ph_3P, NBS	12	34
4	Ph_3P, isocyanuric chloride	24	21
5	Ph_3P, Br_2	24	14
6	Ph_3P, DDQ	72	10
7	Ph_3P, CHI_3	72	12

[a] Isolated yield.

1h, and **1m**, benzylic **1l** and **1p**, aliphatic **1d**, **1g**, **1j**, and **1k**, and other alcohols containing N-heterocycles **1i** and **1n**. Moreover, this method is applicable for all symmetrical and unsymmetrical oximes including aliphatic and aromatic residues. Most of the oximes used in this research were commercially available or could be easily prepared using the procedure reported in the literature.[28] The unsymmetrical oximes were used as mixtures of their *E*- and *Z*-isomers.

The selectivity of this method was demonstrated via a competitive reaction of a mixture consisting of 2-phenylethanol, *i*-PrOH, Ph_3P, CCl_4, benzophenone oxime and DBU in the molar ratio of (1.5:1.5:1.5:2:1:1) under the optimized conditions. The results in Table 5 demonstrate the selectivity between primary and secondary alcohols. There was high selectivity for the O-alkylation of oximes using the primary alcohol rather than the secondary analogue (entry 1). The same result was observed when a mixture of butanol and isopropyl alcohol was investigated in the O-alkylation of 9*H*-fluoren-9-one oxime (entry 2).

Oximes are known to be ambident nucleophiles.[29] The alkylation of an oxime can be achieved at the oxygen to afford an *O*-alkyl ether or at the nitrogen to generate a nitrone.[30] Like other ambident systems, the site of alkylation in the oxime anion is affected by a number of factors, such as the base and the solvent types, the nature of the alkylating agents and the cation, the geometry of the substrate, functional groups present on the oxime, and the degree of dissociation of the oxime salts.[30,31] However, using the present method, *O*-alkyl ethers were mainly obtained and nitrones were not detected, even in trace amounts.

Table 4 One-Pot O-Alkylation of Oximes via Alcohols Using Ph_3P, CCl_4, DBU and TBAI in Refluxing Acetonitrile

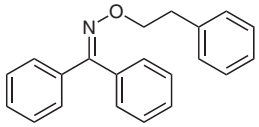
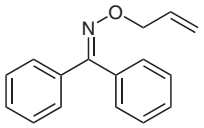
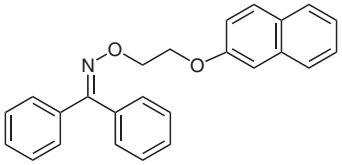
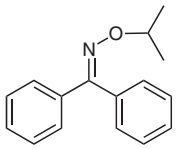
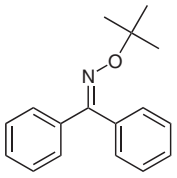
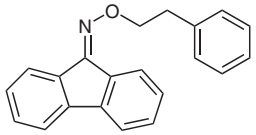
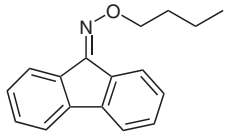
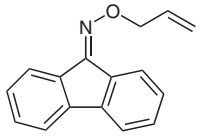
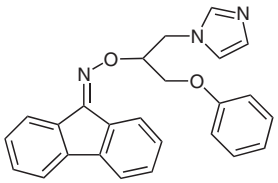
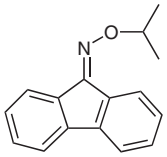
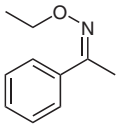
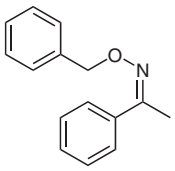
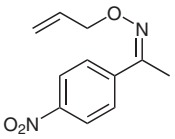
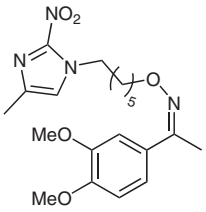
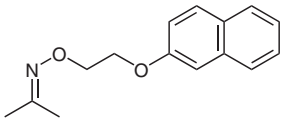
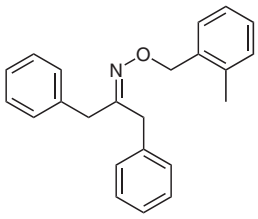
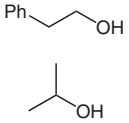
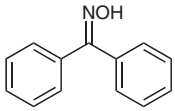
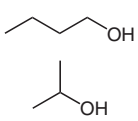
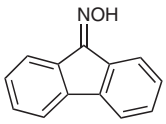
Entry	Compd	Structure[a]	Time (h)	Yield[b] (%)
1	**1a**		6	72
2	**1b**		6	74
3	**1c**		7	68
4	**1d**[17]		9	52
5	**1e**		72	–[c]
6	**1f**		7	71
7	**1g**		6	70
8	**1h**		6	75
9	**1i**		10	48
10	**1j**		8	56

Table 4 One-Pot O-Alkylation of Oximes via Alcohols Using Ph_3P, CCl_4, DBU and TBAI in Refluxing Acetonitrile (continued)

Entry	Compd	Structure[a]	Time (h)	Yield[b] (%)
11	**1k**[8g,h]		6	73
12	**1l**[8g,h]		7	78
13	**1m**		6	78
14	**1n**		7	73
15	**1o**		8	69
16	**1p**		6	76

[a] All products were characterized by IR, ^1H and ^{13}C NMR, MS, and CHN analysis.
[b] Isolated yield.
[c] No reaction after 72 h at reflux.

Table 5 Competitive O-Alkylation of Oximes with Primary/Secondary Alcohols Using Ph_3P and CCl_4

Entry	Alcohol mixture	Oxime	Compd	Time (h)	Yield[a] (%)
1			**1a** **1d**	6	70 4
2			**1g** **1j**	6	68 3

[a] Isolated yield.

All compounds were fully characterized, and their structures were confirmed by IR, ^1H and ^{13}C NMR, MS, and elemental analysis. Compounds **1k–n** were expected to be produced as two geometrical isomers (*E*- or *Z*-isomers); however, *Z*-isomers were obtained predominantly as shown by ^1H and ^{13}C NMR analysis; the minor *E*-isomer was also detected in trace amounts (<5%). To rationalize this fact, *AM1* semiempirical quantum mechanic calculation was applied using *MOPAC* in *CS Chem 3D Ultra 8* (Cambridge Soft, 2004) or *Hyperchem* (Hypercube Inc., Version 7). The results are summarized in Table 6, in which ΔE refers to the discrepancy of energy between the *Z*- and *E*-isomers [$\Delta E = E_Z - E_E$ (kcal/mol)]. As can be seen, all ΔE values calculated for oxime ethers **1k–n** have a negative value. There is conformity to the experimental observations and calculated data (Table 6) which endorse the higher stability of *Z*-isomers in comparison with *E*-isomers, and, hence, the predominant formation of *Z*-products.

Table 6 Calculated Heat of Formation of Synthesized Unsymmetrical Oxime Ethers **1k–n** Using *AM1*

Compound	E_E[a]	E_Z[b]	ΔE[c]
1k	24.99990	23.13776	–1.86214
1l	60.62718	57.73976	–2.88742
1m	53.26502	51.05852	–2.2065
1n	–11.84439	–12.53704	–0.69265

[a] Heat of formation of the *E*-isomer (kcal/mol).
[b] Heat of formation of the *Z*-isomer (kcal/mol).
[c] $\Delta E = E_Z - E_E$ (kcal/mol).

In summary, a convenient and efficient synthetic methodology for the preparation of some novel oxime ethers via the O-alkylation of oximes using alcohols in the presence of triphenylphosphine, carbon tetrachloride, 1,8-diazabicyclo[5.4.0]undec-7-ene, and tetrabutylammonium iodide (cat.) in refluxing acetonitrile has been established. In this method various primary, secondary allylic, and benzylic alcohols underwent reaction with oximes to afford the corresponding *O*-alkyl ethers in good yields.

All chemicals, except oximes, were purchased from either Fluka or Merck. The oximes were prepared by established methods. Solvents were purified and dried by standard procedures, and stored over 3Å molecular sieves. Reactions were followed by TLC using SILG/UV 254 silica gel plates. Column chromatography was performed on silica gel 60 (0.063–0.200 mm, 70–230 mesh; ASTM). Melting points were obtained using a Büchi-510 apparatus in open capillaries and are uncorrected. IR spectra were obtained using a Shimadzu FT-IR-8300 spectrophotometer. ^1H and ^{13}C NMR spectra were obtained using a Bruker Avance-DPX-250 spectrometer operating at 250/62.5 MHz, respectively. GC/MS were performed on a Shimadzu GC/MS-QP 1000-EX apparatus. Elemental analyses were performed on a Perkin-Elmer 240-B microanalyzer. Full analytical data are provided for novel products and references are given for known compounds (see Table 4).

Oximes; General Procedure[28]

In a round-bottomed flask (100 mL) a mixture of the ketone (0.01 mol), $NH_2OH·HCl$ (1.03 g, 0.015 mol), NaOH (0.6 g, 0.015 mol), and H_2O (minimum amount for solvation of $NH_2OH·HCl$ and NaOH) was dissolved in EtOH (20 mL) and then the soln was stirred at r.t. for 24 h. The mixture was poured into ice/H_2O (20 g:10 g). An oxime precipitate immediately formed that was filtered and washed with cold H_2O and dried. Recrystallization (hot MeOH–H_2O) afforded pure oximes which were used in the next step.

One-Pot O-Alkylation of Oximes Using Alcohols; General Procedure

To a two-necked round-bottom flask (100 mL) equipped with a condenser was added a mixture of PPh_3 (0.015 mol), CCl_4 (0.02 mol), alcohol (0.015 mol), ketoxime (0.01 mol), DBU (0.01 mol), and a catalytic amount of TBAI (0.1 g) in anhyd MeCN (30 mL). The mixture was refluxed for the appropriate time until TLC monitoring indicated no further improvement in the conversion (Table 4). The solvent was evaporated under vacuum and the remaining foam was dissolved in $CHCl_3$ (100 mL) and subsequently washed with H_2O (2×100 mL). The organic layer was dried (Na_2SO_4), filtered, and evaporated. The crude product was purified by column chromatography (silica gel).

Benzophenone *O*-Phenethyloxime (1a)

Column chromatography (silica gel, EtOAc–*n*-hexane, 1:20) afforded **1a** (2.16 g, 72%) as a pale-yellow oil; R_f = 0.43 (EtOAc–*n*-hexane, 1:5).

IR (liquid film): 3057, 2967, 28.39, 1658, 1476 cm^{-1}.

^1H NMR (250 MHz, $CDCl_3$): δ = 3.00 (t, *J* = 7.0 Hz, 2 H, PhCH_2), 4.37 (t, *J* = 7.0 Hz, 2 H, CH_2ON), 7.21–7.50 (complex, 15 H, aryl).

^{13}C NMR (62.5 MHz, $CDCl_3$): δ = 36.35, 75.59, 126.70, 128.50, 128.75, 128.84, 129.15, 129.66, 129.72, 130.49, 132.74, 134.00, 137.14, 139.19, 157.07.

MS (EI): *m*/*z* (%) = 301 (35) [M^+].

Anal. Calcd for $C_{21}H_{19}NO$: C, 83.69; H, 6.35; N, 4.65. Found: C, 83.64; H, 6.37; N, 4.71.

Benzophenone *O*-Allyloxime (1b)

Column chromatography (silica gel, EtOAc–*n*-hexane, 1:20) afforded **1b** (1.75 g, 74%) as a colorless oil; R_f = 0.75 (EtOAc–*n*-hexane, 1:5).

IR (liquid film): 3056, 2937, 2854, 1658, 1449 cm^{-1}.

^1H NMR (250 MHz, $CDCl_3$): δ = 5.03–5.05 (m, 2 H, CH_2ON), 5.46–5.64 (m, 2 H, =CH_2), 6.28–6.44 (m, 1 H, =CH), 7.56–7.70 (m, 10 H, aryl).

^{13}C NMR (62.5 MHz, $CDCl_3$): δ = 75.64, 117.50, 128.22, 128.38, 128.53, 128.78, 129.02, 129.55, 133.76, 134.82, 136.87, 157.01.

MS (EI): *m*/*z* (%) = 237 (42) [M^+].

Anal. Calcd for $C_{16}H_{15}NO$: C, 80.98; H, 6.37; N, 5.90. Found: C, 80.92; H, 6.41; N, 5.97.

Benzophenone *O*-2-(Naphthalen-2-yloxy)ethyloxime (1c)

Column chromatography (silica gel, EtOAc–*n*-hexane, 1:20) afforded **1c** (2.49 g, 68%) as a white solid; mp 97.4 °C; R_f = 0.60 (EtOAc–*n*-hexane, 1:2).

IR (KBr): 3065, 2927, 2864, 1657, 1449 cm^{-1}.

^1H NMR (250 MHz, $CDCl_3$): δ = 4.43 (t, *J* = 5.0 Hz, 2 H, CH_2ON), 4.63 (t, *J* = 5.0 Hz, 2 H, CH_2OAr), 7.23–7.58 (complex, 14 H, aryl), 7.74–7.83 (m, 3 H, aryl).

^{13}C NMR (62.5 MHz, $CDCl_3$): δ = 66.53, 72.71, 106.80, 107.01, 119.07, 123.71, 126.40, 126.84, 127.69, 127.93, 128.10, 128.30, 128.97, 129.09, 129.28, 129.46, 133.20, 134.57, 136.51, 156.88, 157.70.

MS (EI): *m*/*z* (%) = 367 (37) [M^+].

Anal. Calcd for $C_{25}H_{21}NO_2$: C, 81.72; H, 5.76; N, 3.81. Found: C, 81.67; H, 5.79; N, 3.86.

9*H*-Fluoren-9-one *O*-Phenethyloxime (1f)

Column chromatography (silica gel, EtOAc–*n*-hexane, 1:20) afforded **1f** (2.12 g, 71%) as a pale-yellow solid; mp 71.0 °C; R_f = 0.40 (EtOAc–*n*-hexane, 1:5).

IR (KBr): 3050, 2961, 2843, 1654, 1471 cm^{-1}.

^1H NMR (250 MHz, $CDCl_3$): δ = 3.36 (t, *J* = 6.9 Hz, 2 H, PhCH_2), 4.83 (t, *J* = 6.9 Hz, 2 H, CH_2ON), 7.45–7.58 (m, 9 H, aryl), 7.72–7.77 (m, 2 H, aryl), 8.05–8.08 (m, 1 H, aryl), 8.42–8.45 (m, 1 H, aryl).

^{13}C NMR (62.5 MHz, $CDCl_3$): δ = 36.15, 76.62, 120.14, 121.88, 126.63, 126.97, 128.08, 128.34, 128.75, 129.34, 129.56, 130.02, 130.80, 131.06, 135.89, 138.74, 140.46, 141.52, 152.55.

MS (EI): *m*/*z* (%) = 299 (19) [M^+].

Anal. Calcd for $C_{21}H_{17}NO$: C, 84.25; H, 5.72; N, 4.68. Found: C, 84.32; H, 5.75; N, 4.60.

9*H*-Fluoren-9-one *O*-Butyloxime (1g)

Column chromatography (silica gel, EtOAc–*n*-hexane, 1:20) afforded **1g** (1.75 g, 70%) as a pale-yellow oil; R_f = 0.42 (EtOAc–*n*-hexane, 1:5).

IR (liquid film): 3074, 2969, 2840, 1661, 1452 cm^{-1}.

^1H NMR (250 MHz, $CDCl_3$): δ = 0.86 (t, *J* = 7.3 Hz, 3 H, Me), 1.37–1.46 (m, 2 H, CH_2Me), 1.70–1.79 (m, 2 H, CH_2CH_2Me), 4.28 (t, *J* = 6.5 Hz, 2 H, CH_2ON), 7.15–7.29 (m, 4 H, aryl), 7.46–7.50 (m, 2 H, aryl), 7.65–7.67 (m, 1 H, aryl), 8.17–8.20 (m, 1 H, aryl).

^{13}C NMR (62.5 MHz, $CDCl_3$): δ = 13.99, 19.33, 31.41, 75.75, 119.71, 119.77, 119.82, 121.52, 127.79, 128.13, 129.08, 129.61, 130.70, 135.74, 140.12, 141.24, 151.83.

MS (EI): *m*/*z* (%) = 251 (45) [M^+].

Anal. Calcd for $C_{17}H_{17}NO$: C, 81.24; H, 6.82; N, 5.57. Found: C, 81.32; H, 6.89; N, 5.62.

9*H*-Fluoren-9-one *O*-Allyloxime (1h)

Column chromatography (silica gel, EtOAc–*n*-hexane, 1:20) afforded **1h** (1.76 g, 75%) as a yellow foam; R_f = 0.72 (EtOAc–*n*-hexane, 1:5).

IR (liquid film): 3053, 2937, 2856, 1654, 1449 cm^{-1}.

^1H NMR (250 MHz, $CDCl_3$): δ = 4.97–5.00 (m, 2 H, CH_2ON), 5.32–5.55 (complex, 2 H, =CH_2), 6.13–6.32 (m, 1 H, =CH), 7.31–7.45 (m, 4 H, aryl), 7.61–7.64 (m, 2 H, aryl), 7.83–7.84 (m, 1 H, aryl), 8.37–8.40 (m, 1 H, aryl).

^{13}C NMR (62.5 MHz, $CDCl_3$): δ = 76.71, 118.04, 119.86, 119.91, 121.19, 127.89, 128.22, 129.37, 129.85, 130.64, 130.93, 134.02, 135.65, 140.27, 141.38, 152.41.

MS (EI): *m*/*z* (%) = 235 (54) [M^+].

Anal. Calcd for $C_{16}H_{13}NO$: C, 81.68; H, 5.57; N, 5.95. Found: C, 81.74; H, 5.53; N, 5.90.

9*H*-Fluoren-9-one *O*-1-(1*H*-Imidazol-1-yl)-3-phenoxypropan-2-yloxime (1i)

Column chromatography (silica gel, EtOAc–*n*-hexane, 4:1) afforded **1i** (1.89 g, 48%) as a yellow oil; R_f = 0.23 (EtOAc–*n*-hexane, 8:1).

IR (liquid film): 3055, 2942, 2865, 1663, 1458 cm^{-1}.

^{1}H NMR (250 MHz, $CDCl_3$): δ = 4.00–4.07 (m, 1 H, CHON), 4.19–4.36 (m, 2 H, NCH_2), 4.50–4.55 (m, 2 H, PhOCH_2), 6.90–6.99 (complex, 5 H, $H4_{imid}$, $H5_{imid}$, aryl), 7.22–7.26 (m, 4 H, aryl), 7.39–7.43 (m, 4 H, aryl), 7.61–7.66 (complex, 3 H, $H2_{imid}$, aryl).

^{13}C NMR (62.5 MHz, $CDCl_3$): δ = 46.62, 56.51, 65.48, 114.55, 114.60, 120.03, 121.51, 121.77, 121.84, 127.99, 128.39, 128.58, 129.36, 129.56, 129.61, 129.69, 131.52, 131.90, 131.95, 134.96, 141.53, 153.77, 158.06.

MS (EI): *m*/*z* (%) = 395 (21) [M$^+$].

Anal. Calcd for $C_{25}H_{21}N_3O_2$: C, 75.93; H, 5.35; N, 10.63. Found: C, 75.97; H, 5.30; N, 10.68.

9*H*-Fluoren-9-one *O*-Isopropyloxime (1j)
Column chromatography (silica gel, EtOAc–*n*-hexane, 1:20) afforded **1j** (1.32 g, 56%) as a pale-yellow oil; R_f = 0.36 (EtOAc–*n*-hexane, 1:5).

IR (liquid film): 3064, 2970, 2857, 1658, 1469 cm^{-1}.

^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.30 (d, *J* = 6.2 Hz, 6 H, 2 Me), 4.44–4.59 (m, 1 H, CHON), 7.11–7.18 (m, 4 H, aryl), 7.40–7.44 (m, 2 H, aryl), 7.64–7.65 (m, 1 H, aryl), 8.16–8.17 (m, 1 H, aryl).

^{13}C NMR (62.5 MHz, $CDCl_3$): δ = 21.93, 77.60, 119.79, 119.85, 121.52, 127.80, 128.11, 129.15, 129.55, 130.65, 130.72, 135.95, 140.10, 141.25, 151.52.

MS (EI): *m*/*z* (%) = 237 (58) [M$^+$].

Anal. Calcd for $C_{16}H_{15}NO$: C, 80.98; H, 6.37; N, 5.90. Found: C, 81.02; H, 6.31; N, 5.98.

1-(4-Nitrophenyl)ethanone *O*-Allyloxime (1m)
Column chromatography (silica gel, EtOAc–*n*-hexane, 1:20) afforded **1m** (1.71 g, 78%) as a yellow solid; mp 50.3 °C; R_f = 0.74 (EtOAc–*n*-hexane, 1:5).

IR (KBr):3058, 2936, 2857, 1659, 1445 cm^{-1}.

^{1}H NMR (250 MHz, $CDCl_3$): δ = 2.26 (s, 3 H, Me), 4.72 (d, *J* = 5.7 Hz, 2 H, CH_2ON), 5.22–5.37 (complex, 2 H, $=CH_2$), 5.97–6.12 (m, 1 H, =CH), 7.78 (d, *J* = 8.9 Hz, 2 H, aryl), 8.16 (d, *J* = 8.9 Hz, 2 H, aryl).

^{13}C NMR (62.5 MHz, $CDCl_3$): δ = 12.42, 75.59, 117.78, 123.53, 126.68, 133.97, 142.57, 147.91, 152.68.

MS (EI): *m*/*z* (%) = 220 (68) [M$^+$].

Anal. Calcd for $C_{11}H_{12}N_2O_3$: C, 59.99; H, 5.49; N, 12.72. Found: C, 59.91; H, 5.54; N, 12.79.

1-(3,4-Dimethoxyphenyl)ethanone *O*-6-(2-Methyl-4-nitro-1*H*-imidazol-1-yl)hexyloxime (1n)
Column chromatography (silica gel, EtOAc–*n*-hexane, 4:1) afforded **1n** (2.95 g, 73%) as a pale-yellow solid; mp 94.1 °C; R_f = 0.35 (EtOAc–*n*-hexane, 8:1).

IR (KBr): 3052, 2980, 2874, 1660, 1438 cm^{-1}.

^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.35–1.48 (m, 4 H, 2 CH_2), 1.64–1.81 (m, 4 H, 2 CH_2), 2.16 (s, 3 H, MeCNO), 2.39 (s, 3 H, 2-CH_3 imid), 3.85–3.92 (complex, 8 H, 2 OMe, CH_2ON), 4.11 (t, *J* = 6.4 Hz, 2 H, NCH_2), 6.79 (d, *J* = 8.4 Hz, 1 H, aryl), 7.09 (d, *J* = 8.4 Hz, 1 H, aryl), 7.24 (s, 1 H, aryl), 7.65 (s, 1 H, $H5_{imid}$).

^{13}C NMR (62.5 MHz, $CDCl_3$): δ = 12.53, 13.06, 25.60, 26.25, 28.93, 30.22, 30.60, 47.12, 55.87, 73.59, 108.59, 110.57, 119.05, 119.49, 129.44, 129.78, 144.57, 148.77, 149.98, 153.94.

MS (EI): *m*/*z* (%) = 404 (15) [M$^+$].

Anal. Calcd for $C_{20}H_{28}N_4O_5$: C, 59.39; H, 6.98; N, 13.85. Found: C, 59.46; H, 6.94; N, 13.89.

Propan-2-one *O*-2-(Naphthalen-2-yloxy)ethyloxime (1o)
Column chromatography (silica gel, EtOAc–*n*-hexane, 1:20) afforded **1o** (1.67 g, 69%) as a white foam; R_f = 0.50 (EtOAc–*n*-hexane, 1:5).

IR (liquid film): 3055, 2986, 2862, 1665, 1451 cm^{-1}.

^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.75 (s, 6 H, 2 Me), 4.16 (t, *J* = 5.0 Hz, 2 H, CH_2ON), 4.29 (t, *J* = 5.0 Hz, 2 H, CH_2OAr), 7.01–7.31 (m, 4 H, aryl), 7.57–7.64 (m, 3 H, aryl).

^{13}C NMR (62.5 MHz, $CDCl_3$): δ = 21.89, 29.19, 66.58, 71.67, 106.59, 106.87, 119.10, 123.55, 126.37, 126.75, 127.67, 129.04, 129.38, 155.64, 156.96.

MS (EI): *m*/*z* (%) = 243 (41) [M$^+$].

Anal. Calcd for $C_{15}H_{17}NO_2$: C, 74.05; H, 7.04; N, 5.76. Found: C, 74.12; H, 7.08; N, 5.70.

1,3-Diphenylpropan-2-one *O*-(2-Methylbenzyl)oxime (1p)
Column chromatography (silica gel, EtOAc–*n*-hexane, 1:20) afforded **1p** (2.50 g, 76%) as a pale-yellow foam; R_f = 0.75 (EtOAc–*n*-hexane, 1:5).

IR (liquid film): 3070, 2958, 2852, 1659, 1457 cm^{-1}.

^{1}H NMR (250 MHz, $CDCl_3$): δ = 2.78 (s, 3 H, Me), 3.87 (s, 2 H, PhCH_2), 4.07 (s, 2 H, PhCH_2), 5.71 (s, 2 H, CH_2ON), 7.51–7.66 (m, 14 H, aryl).

^{13}C NMR (62.5 MHz, $CDCl_3$): δ = 19.49, 33.60, 40.07, 74.58, 126.31, 126.90, 127.19, 128.46, 129.02, 129.22, 129.41, 129.63, 129.72, 130.66, 136.49, 136.99, 137.22, 137.42, 158.55.

MS (EI): *m*/*z* (%) = 329 (36) [M$^+$].

Anal. Calcd for $C_{23}H_{23}NO$: C, 83.85; H, 7.04; N, 4.25. Found: C, 83.93; H, 7.09; N, 4.20.

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