A Convenient Practical Synthesis of Alkyl and Aryl Oxime Esters

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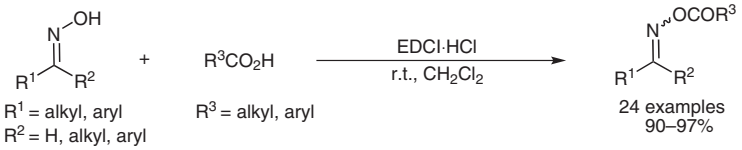
Received: 03.02.2014; Accepted after revision: 30.05.2014

PSP No 275

Abstract: A facile access to the synthesis of alkyl and aryl oxime esters of ketoximes and aldoximes in high yields (90–97%) is reported. The reactions were performed using *N*-[3-(methylamino)propyl]-*N*′-ethylcarbodiimide hydrochloride (EDCI) reagent in the presence of 4-(dimethylamino)pyridine (DMAP) as a catalyst at room temperature. The isolation and purification of products is very simple and in cases where product is solid, column chromatography is avoided.

Key words: oxime esters, aldoximes, ketoximes, EDCI, esterification, dehydration



Scheme 1 Synthesis of oxime esters

Oxime esters are a small, but important, class of biologically useful compounds the for synthesis of fragrances,[1] crop protection,[2] and therapeutic studies.[3] They are useful building blocks in peptide synthesis.[4] Oxime esters are selective covalent inhibitors of serine hydrolase retinoblastoma-binding protein 9 (RBBP9) and cleave DNA under photolytic conditions.[5,6] They also possess fungicidal,[7] herbicidal,[8] insecticidal,[9] and antitumor activity.[10] Oxime esters of dihydrocoumaric acid have been synthesized and they are reported to have antibacterial activity.[11] Aromatic benzophenone oxime esters and dibenzosuberone oxime esters are pharmacologically important.[12] Vanillin-derived piperidin-4-one oxime esters have been tested for antioxidant and antimicrobial potential.[13] The oxime esters derived from nafimidone have been tested as potential anticonvulsant compounds.[14] Various methods have been used for the preparation of oxime esters, but there is scope for improvement in the development of new methods in terms of simplification of the experimental protocol and improvement of yields. A convenient preparative protocol with simple purification and general applicability to the oxime esters is required (Scheme 1).

The classic preparation of oxime esters involves either the condensation of acid chlorides with oximes under basic conditions or the use of acid anhydrides in presence of strong acids.[1,6a,b,11,13,14] Though the yields of oxime esters are good, this route cannot be used for acid and base sensitive functionalities. Also, the methodology requires an additional step, the preparation of the acid chloride from a carboxylic acid, and the acid chloride must be used immediately for oxime preparation. Since acid chlorides are susceptible to hydrolysis, anhydrous reaction conditions have to be maintained to afford good yields of oxime esters. Also, the purification of products is cumbersome and invariably requires column chromatography. A few alternate syntheses of oxime esters are also reported, such as the preparation of benzoyl esters of alkyl- and aryl-substituted oximes using benzoyl peroxide, but the method is applicable mainly to benzoyl esters of oximes.[15] Oxime esters can be prepared using α,β-unsaturated aldehydes and oximes using a N-heterocyclic carbene as a redox esterification catalyst.[16]

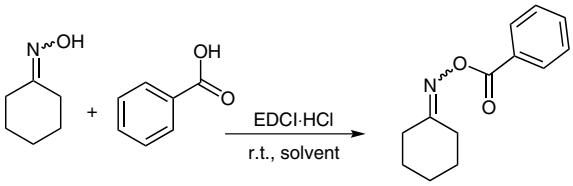
Owing to the importance of oxime esters, we have developed a simple and very efficient synthetic protocol that affords the product in high yields. The synthesis involves the treatment of alkyl- or aryl-substituted oximes with aliphatic or aromatic acids in the presence of *N*-[3-(methylamino)propyl]-*N*′-ethylcarbodiimide hydrochloride (EDCI) reagent (Scheme 1). The products are obtained in high yields in most solvents. The reactions were complete in a reasonable time at room temperature. The products were easily isolated and purification involves no chromatographic separation. The solid products were isolated in pure form by simple concentration of the solvent and treatment with few drops of petroleum ether and agitation in a bath-type sonicator. The liquid products were purified

SYNTHESIS 2014, 46, 1847–1852
Advanced online publication: 24.06.2014
DOI: 10.1055/s-0034-1378350; Art ID: ss-2014-z0086-psp

by passing through small pad of silica gel. Since EDCI is easily available, inexpensive, and soluble in water, the present protocol is very useful for the synthesis of various oxime esters.

An optimization experiment was carried out to select the solvent for the preparation of oxime esters using EDCI as the reagent. All reactions were carried out at ambient temperature under a nitrogen atmosphere. The esters were obtained in all solvents in excellent yields. Cyclohexanone oxime (**1a**) was esterified with benzoic acid (**2a**) in polar aprotic, protic, and chlorinated solvents (Table 1). The reactions were faster, and the yield of the product **3aa** was higher (>92%) in chlorinated solvents compared to other common solvents (80–88%). The reaction in dichloromethane was found to be the best choice for oxime ester preparation.

Table 1 Oxime Ester Preparation in Different Solvents



1a **2a** **3aa**

Entry	Solvent	Time (h)	Yield[a] (%)
1	MeCN	15	82
2	THF	20	85
3	EtOH	18	88
4	MeOH	12	80
5	CH_2Cl_2	8	96
6	$CHCl_3$	9	92

[a] Isolated yield.

To optimize the reaction conditions for the stoichiometric ratio of oxime to acid, a reaction was carried out with equimolar quantities of cyclohexanone oxime (**1a**) and benzoic acid (**2a**) in the presence of one equivalent of EDCI. The reaction was very slow and only 50% conversion could be realized in 24 hours. The reaction using an equimolar ratio of acid to oxime with two equivalents of EDCI was complete in 12 hours, but the reaction using 2.5 equivalents of EDCI was faster (8 h).

Under the optimized conditions, cyclohexanone oxime (**1a**) was treated with different alkyl- and aryl-substituted aromatic acids **2a**–**e** (Table 2). The reaction with butanoic acid (**2b**) was fast, whereas the reactions with 4-aminobenzoic acid (**2c**) and *p*-toluic acid (**2d**) took longer. In all cases the conversion was complete and the products were recovered in over 94% isolated yield. In the case of 4-aminobenzoic acid (**2d**), a substrate containing both amino and carboxylic groups, the oxime ester was selectively formed without any self-condensation product from the acid and amine groups. Hence, the present protocol is also selective and affords the oxime ester over the amide product, which otherwise is the major expected product by self condensation of acid and amine groups.

We studied the reaction of carvone oxime (**1b**) with acids **2a**–**e**. The products **3ba**–**be** were obtained in over 92% isolated yield. Butanoic acid reacted faster than the unsubstituted and substituted aromatic acids. The acetophenone oxime (**1c**) was found to react faster with the acids in affording the corresponding oxime esters in high yield. Similarly, benzophenone oxime (**1d**) and benzaldehyde oxime (**1e**) gave oxime esters in high yields in the optimum time. Substituent tolerance of the reaction was checked for 3-methylcyclohexanone and 4-chlorobenzaldehyde oxime with benzoic acid. The product yield in both cases was >95% (see the Supporting Information; ^1H and ^{13}C NMR spectra provided).

In conclusion, we have developed a convenient protocol for preparation of oxime esters of alkyl- and aryl-substituted carboxylic acids. Both aldoximes and ketoximes gave the title compounds in excellent yields. The protocol is operationally simple and commercially available inexpensive EDCI reagent was used for esterification. The reactions are fast and afford products in high yield. It is important to note the selectivity of esterification for oximes with acids over intermolecular acid–amine coupling under the present experimental conditions. The purification of products involves no chromatography in the case of solid products. Hence, the present protocol is facile and very convenient for oxime esters preparations.

Laboratory grade solvents were generally used. Petroleum ether (PE) refers to the fraction with bp 60–80 °C. Pre-coated aluminum silica 60 F_{254} plates from Merck were used for TLC analyses. Column chromatography was performed using silica gel 200–400 mesh using PE–EtOAc mixtures (PE = petroleum ether). NMR spectra were recorded on a 500 MHz NMR spectrometer (Bruker Avance, Reinstetten, Germany) using $CDCl_3$ solvent with reference to signals at δ = 7.26 ($CHCl_3$, ^1H) and δ = 77.16 ($CDCl_3$, ^{13}C). Mass spectral analysis were carried out using HRMS (Waters Q-Tof Ultima, Manchester, UK) in ESI positive mode. The IR spectra (KBr pellets) were recorded on a FT Raman-Nicolet 5700 instrument.

Oxime Esters 3aa-ee; General Procedure

To a solution of ketoxime or aldoxime **1** (2.0 mmol) in CH_2Cl_2 (20 mL) was added the carboxylic acid **2** (2.0 mmol) followed by EDCI (5 mmol) and DMAP (0.2 mmol). The mixture was magnetically stirred at r.t. under N_2 until the reaction was complete (TLC monitoring, PE–EtOAc). The mixture was diluted with H_2O (25 mL) and the CH_2Cl_2 layer was separated, dried (anhyd Na_2SO_4), and concentrated. The crude mass obtained was treated with PE (2–3 mL); separation of a solid occurred when sonicated. The resultant solid was filtered and dried under suction to afford the oxime esters **3** in pure form in 90–97% yield. The physical and spectral data of compounds are presented below.

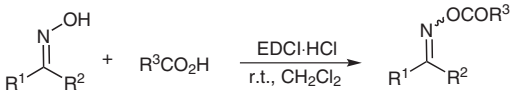
Cyclohexanone *O*-Benzoyl Oxime (3aa)[1c]

White solid; yield: 184 mg (96%); mp 64–65 °C.

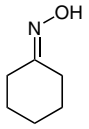
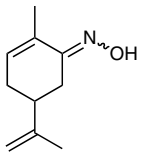
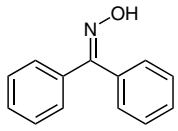
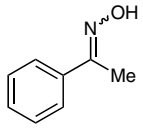
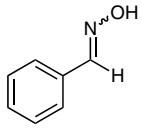
IR (KBr): 1730, 1633 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 8.06 (d, *J* = 7.27 Hz, 2 H), 7.56 (t, *J* = 7.27 Hz, 1 H), 7.44 (t, *J* = 7.94 Hz, 2 H), 2.66 (t, *J* = 6.34 Hz, 2

Table 2 Preparation of Alkyl and Aryl Oxime Esters of Alkyl and Aromatic Acids



1a–e **2a–e** **3aa–ee**

Oxime R^1R^2C=NOH	Carboxylic acid **2**	R^3	Time (h)	Product	Yield[a] (%)
	**2a**	Ph	8	**3aa**	96
	2b	Pr	6	**3ab**	95
	2c	4-$H_2NC_6H_4$	20	**3ac**	94
	2d	4-MeC_6H_4	20	**3ad**	97
	2e	4-$O_2NC_6H_4$	3	**3ae**	90
1a					
	**2a**	Ph	10	**3ba**	97
	2b	Pr	8	**3bb**	92
	2c	4-$H_2NC_6H_4$	12	**3bc**	94
	2d	4-MeC_6H_4	10	**3bd**	92
	2e	4-$O_2NC_6H_4$	3	**3be**	93
1b					
	**2a**	Ph	12	**3ca**	92
	2b	Pr	10	**3cb**	96
	2c	4-$H_2NC_6H_4$	15	**3cc**	94
	2d	4-MeC_6H_4	14	**3cd**	91
	2e	4-$O_2NC_6H_4$	4	**3ce**	95
1c					
	**2a**	Ph	6	**3da**	91
	2b	Pr	7	**3db**	95
	2c	4-$H_2NC_6H_4$	19	**3dc**	90
	2d	4-MeC_6H_4	12	**3dd**	93
	2e	4-$O_2NC_6H_4$	4	**3de**	92
1d					
	**2a**	Ph	12	**3ea**	96
	2b	Pr	10	**3eb**	90
	2c	4-$H_2NC_6H_4$	–	–[b]	–
	2d	4-MeC_6H_4	12	**3ed**	91
	2e	4-$O_2NC_6H_4$	4	**3ee**	94
1e					

[a] Yield of isolated product.
[b] No reaction.

H), 2.45 (t, J = 6.34 Hz, 2 H), 1.77 (pent, J = 6.01 Hz, 2 H), 1.72 (pent, J = 6.01 Hz, 2 H), 1.61–1.66 (m, 2 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 169.2, 163.9, 132.8, 129.1, 128.1, 31.8, 26.7, 26.4, 25.5, 25.0.

HRMS (ESI): m/z $[M + Na]^+$ calcd for $C_{13}H_{15}NO_2Na$: 240.1000; found: 240.1086.

Cyclohexanone *O*-Butanoyl Oxime (3ab)
Pale yellow liquid; yield: 154 mg (95%).

IR (neat):1760, 1642 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 2.39 (t, J = 6.46 Hz, 2 H), 2.21–2.28 (m, 4 H), 1.57–1.62 (m, 3 H), 1.50–1.56 (m, 3 H), 1.45–1.50 (m, 2 H), 0.84 (t, J = 7.48 Hz, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 170.8, 168.1, 34.4, 31.7, 26.4, 25.4, 25.0, 18.0, 13.3.

HRMS (ESI): m/z $[M + Na]^+$ calcd for $C_{10}H_{17}NO_2Na$: 206.1157; found: 206.1208.

Cyclohexanone *O*-4-Aminobenzoyl Oxime (3ac)
White solid; yield: 193 mg (94%); mp 145–146 °C.

IR (KBr): 1707, 1638 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.84 (d, J = 8.25 Hz, 2 H), 6.64 (d, J = 8.25 Hz, 2 H), 4.48 (br s, 2 H), 2.64 (t, J = 6.34 Hz, 2 H), 2.41 (t, J = 6.34 Hz, 2 H), 1.74 (q, J = 5.91 Hz, 2 H), 1.69 (q, J = 6.10 Hz, 2 H), 1.57–1.63 (m, 2 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 168.5, 164.3, 151.5, 131.2, 131.1, 117.2, 113.4, 31.8, 26.6, 26.4, 25.5, 25.1.

HRMS (ESI): m/z $[M + H]^+$ calcd for $C_{13}H_{17}N_2O_2$: 233.1290; found: 233.1317.

Cyclohexanone *O*-4-Methylbenzoyl Oxime (3ad)
White solid; yield: 198.5 mg (97%); mp 75–76 °C.

IR (KBr): 1728, 1635 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.94 (d, J = 8.17 Hz, 2 H), 7.23 (d, J = 8.08 Hz, 2 H), 2.65 (t, J = 6.25 Hz, 2 H), 2.44 (t, J = 6.54 Hz, 2

H), 2.39 (s, 3 H), 1.77 (pent, J = 5.93 Hz, 2 H), 1.72 (pent, J = 5.93 Hz, 2 H), 1.60–1.66 (m, 2 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 169.0, 164.0, 143.5, 129.2, 128.8, 31.9, 26.8, 26.4, 25.5, 25.1, 21.3.

HRMS (ESI): m/z $[M + Na]^+$ calcd for $C_{14}H_{17}NO_2Na$: 254.1156; found: 254.1139.

Cyclohexanone *O*-4-Nitrobenzoyl Oxime (3ae)
Pale yellow solid; yield: 209 mg (90%); mp 110–112 °C.

IR (KBr): 1730, 1631 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.29 (d, J = 8.85 Hz, 2 H), 8.21 (d, J = 8.85 Hz, 2 H), 2.66 (t, J = 6.49 Hz, 2 H), 2.46 (t, J = 6.19 Hz, 2 H), 1.79 (q, J = 5.81 Hz, 2 H), 1.74 (q, J = 5.81 Hz, 2 H), 1.66 (d, J = 4.30 Hz, 2 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 170.2, 162.0, 150.2, 134.6, 130.3, 123.3, 31.8, 26.9, 26.4, 25.5, 25.0.

HRMS (ESI): m/z $[M + Na]^+$ calcd for $C_{13}H_{14}N_2ONa$: 285.0852; found: 285.0813.

(*E*)-2-Methyl-5-(prop-1-en-2-yl)cyclohex-2-enone *O*-Benzoyl Oxime (3ba)
White solid; yield: 158 mg (97%); mp 92–94 °C.

IR (KBr): 1739, 1641 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.15 (d, J = 7.11 Hz, 2 H), 7.66 (t, J = 7.61 Hz, 1 H), 7.55 (t, J = 7.85 Hz, 2 H), 6.32–6.36 (m, 1 H), 4.91 (d, J = 1.11 Hz, 1 H), 4.89 (br s, 1 H), 3.35–3.39 (m, 1 H), 2.50–2.55 (m, 1 H), 2.39–2.45 (m, 2 H), 2.21–2.27 (m, 1 H), 2.10 (s, 3 H), 1.85 (s, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 164.0, 163.9, 147.1, 137.4, 133.1, 130.2, 129.5, 128.5, 110.6, 40.2, 30.4, 29.3, 27.2, 20.6, 17.7.

HRMS (ESI): m/z $[M + Na]^+$ calcd for $C_{17}H_{19}NO_2Na$: 292.1313; found: 292.1263.

(*E*)-2-Methyl-5-(prop-1-en-2-yl)cyclohex-2-enone *O*-Butanoyl Oxime (3bb)
Pale yellow liquid; yield: 131 mg (92%).

IR (neat): 1761, 1644 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 6.20–6.27 (m, 1 H), 4.81 (d, J = 1.22 Hz, 1 H), 4.77 (br s, 1 H), 3.12–3.19 (m, 1 H), 2.45 (t, J = 7.50 Hz, 2 H), 2.28–2.38 (m, 2 H), 2.11–2.21 (m, 2 H), 1.94 (t, J = 0.91 Hz, 3 H), 1.75 (s, 3 H), 1.72 (q, J = 7.5 Hz, 2 H), 1.00 (t, J = 7.50 Hz, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 171.0, 162.4, 146.7, 136.6, 129.8, 110.1, 39.8, 34.5, 30.0, 28.7, 20.1, 18.0, 17.2, 13.3.

HRMS (ESI): m/z $[M + Na]^+$ calcd for $C_{14}H_{21}NO_2Na$: 258.1469; found: 258.1456.

(*E*)-2-Methyl-5-(prop-1-en-2-yl)cyclohex-2-enone *O*-4-Aminobenzoyl Oxime (3bc)
White solid; yield: 161.5 mg (94%); mp 192–193 °C.

IR (KBr): 1717, 1631 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.90 (d, J = 8.72 Hz, 2 H), 6.68 (d, J = 8.57 Hz, 2 H), 6.26 (d, J = 4.93 Hz, 1 H), 4.83 (d, J = 11.53 Hz, 2 H), 4.16 (br s, 2 H), 3.30 (dd, J_1 = 16.27, J_2 = 2.48 Hz, 1 H), 2.41–2.52 (m, 1 H), 2.30–2.38 (m, 2 H), 2.14–2.20 (m, 1 H), 2.03 (s, 3 H), 1.79 (s, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 163.7, 163.0, 147.0, 136.4, 131.3, 130.5, 130.1, 128.5, 118.2, 113.5, 110.1, 39.9, 30.1, 28.9, 20.3, 17.5.

HRMS (ESI): m/z $[M + H]^+$ calcd for $C_{17}H_{21}N_2O_2$: 285.1603; found: 285.1636.

(*E*)-2-Methyl-5-(prop-1-en-2-yl)cyclohex-2-enone *O*-4-Methylbenzoyl Oxime (3bd)
White solid; yield: 157.6 mg (92%); mp 73–75 °C.

IR (KBr): 1741, 1645 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.96 (d, J = 7.85 Hz, 2 H), 7.25 (d, J = 7.85 Hz, 2 H), 6.25 (d, J = 4.42 Hz, 1 H), 4.81 (d, J = 11.54 Hz, 2 H), 3.28 (dd, J_1 = 16.20 Hz, J_2 = 1.96 Hz, 1 H), 2.44 (d, J = 12.27 Hz, 1 H), 2.40 (s, 3 H), 2.32 (t, J = 14.48 Hz, 2 H), 2.11–2.17 (m, 1 H), 2.01 (s, 3 H), 1.76 (s, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 163.61, 163.48, 147.06, 146.82, 143.57, 136.89, 129.94, 129.25, 128.93, 126.31, 110.28, 39.91, 30.13, 28.94, 21.35, 20.2, 17.4.

HRMS (ESI): m/z $[M + Na]^+$ calcd for $C_{18}H_{21}NO_2Na$: 306.1469; found: 306.1495.

(*E*)-2-Methyl-5-(prop-1-en-2-yl)cyclohex-2-enone *O*-4-Nitrobenzoyl Oxime (3be)
White solid; yield: 176.7 mg (93%); mp 97–99 °C.

IR (KBr): 1744, 1642 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.35 (d, J = 8.78 Hz, 2 H), 8.26 (d, J = 8.65 Hz, 2 H), 6.35 (dd, J_1 = 3.48, J_2 = 1.45 Hz, 1 H), 4.87 (s, 1 H), 4.83 (s, 1 H), 3.23–3.29 (m, 1 H), 2.46–2.51 (m, 1 H), 2.36–2.42 (m, 2 H), 2.17–2.24 (m, 1 H), 2.04 (s, 3 H), 1.80 (s, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 164.5, 161.8, 150.3, 146.6, 137.9, 134.6, 130.3, 129.6, 123.4, 110.5, 39.9, 30.1, 29.0, 20.2, 17.3.

HRMS (ESI): m/z $[M + Na]^+$ calcd for $C_{17}H_{18}N_2O_4Na$: 337.1164; found: 337.1107.

Benzophenone *O*-Benzoyl Oxime (3ca)[17]
White solid; yield: 140.4 mg (92%); mp 103–105 °C.

IR (KBr): 1739, 1645 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.82 (d, J = 7.35 Hz, 2 H), 7.70 (d, J = 7.35 Hz, 2 H), 7.54 (t, J = 3.26 Hz, 4 H), 7.50 (t, J = 7.35 Hz, 1 H), 7.44 (t, J = 4.62 Hz, 3 H), 7.40 (q, J = 7.62 Hz, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 165.2, 163.4, 134.3, 132.8, 130.6, 129.3, 128.8, 128.5, 128.1, 127.9.

HRMS (ESI): m/z $[M + Na]^+$ calcd for $C_{20}H_{15}NO_2Na$: 324.1000; found: 324.1046.

Benzophenone *O*-Butanoyl Oxime (3cb)
White solid; yield: 130 mg (96%); mp 55–57 °C.

IR (KBr): 1768, 1652 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.56 (d, J = 7.23 Hz, 2 H), 7.44 (d, J = 2.20 Hz, 2 H), 7.43 (d, J = 1.26 Hz, 1 H), 7.39–7.42 (m, 1 H), 7.33 (t, J = 7.89 Hz, 2 H), 7.29 (d, J = 1.99, Hz, 1 H), 7.28 (d, J = 4.11, Hz, 1 H), 2.28 (t, J = 7.40 Hz, 2 H), 1.59 (sextet, J = 7.40 Hz, 2 H), 0.88 (t, J = 7.51 Hz, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 170.7, 164.5, 130.5, 129.2, 128.7, 128.4, 128.0, 127.8, 34.5, 17.9, 13.2.

HRMS (ESI): m/z $[M + Na]^+$ calcd for $C_{17}H_{17}NO_2Na$: 290.1156; found: 290.1165.

Benzophenone *O*-4-Aminobenzoyl Oxime (3cc)
Yellow solid; yield: 150.6 mg (94%); mp 114–115 °C.

IR (KBr): 1658, 1597 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.48–7.52 (m, 9 H), 7.41 (t, J = 2.44 Hz, 1 H), 7.40 (t, J = 1.53 Hz, 1 H), 7.38 (d, J = 1.35 Hz, 2 H), 7.36 (d, J = 1.53 Hz, 2 H), 7.35 (t, J = 1.62 Hz, 1 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 157.6, 135.9, 132.4, 129.2, 129.0, 128.8, 128.1, 127.9, 127.6.

HRMS (ESI): m/z $[M + H]^+$ calcd for $C_{20}H_{17}N_2O_2$: 317.1290; found: 316.9080.

Benzophenone *O*-4-Methylbenzoyl Oxime (3cd)
White solid; yield: 145.4 mg (91%); mp 108–110 °C.

IR (KBr): 1737, 1647 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 7.65 (t, *J* = 8.46 Hz, 4 H), 7.47 (t, *J* = 2.88 Hz, 3 H), 7.42 (t, *J* = 7.11 Hz, 1 H), 7.37–7.40 (m, 2 H), 7.34 (t, *J* = 7.50 Hz, 2 H), 7.12 (d, *J* = 8.17 Hz, 2 H), 2.32 (s, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 165.0, 163.5, 143.7, 132.5, 130.6, 129.3, 128.9, 128.7, 128.5, 128.1, 127.9, 127.4, 21.3.

HRMS (ESI): *m*/*z* $[M + Na]^+$ calcd for $C_{21}H_{17}NO_2Na$: 338.1156; found: 338.1109.

Benzophenone *O*-4-Nitrobenzoyl Oxime (3ce)
Pale yellow solid; yield: 166.7 mg (95%); mp 150–152 °C.

IR (KBr): 1753, 1651 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 8.22 (d, *J* = 8.97 Hz, 2 H), 7.95 (d, *J* = 8.80 Hz, 2 H), 7.69 (d, *J* = 7.28 Hz, 2 H), 7.53–7.57 (m, 3 H), 7.50 (d, *J* = 7.45 Hz, 1 H), 7.42 (t, *J* = 7.54 Hz, 4 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 166.3, 161.5, 150.2, 134.0, 133.7, 132.2, 131.0, 130.3, 129.6, 128.8, 128.2, 128.1, 127.9, 123.3.

HRMS (ESI): *m*/*z* $[M + Na]^+$ calcd for $C_{20}H_{14}N_2O_4Na$: 369.0851; found: 369.0836.

(*E*)-Acetophenone *O*-Benzoyl Oxime (3da)[17]
White solid; yield: 161 mg (91%); mp 85–87 °C.

IR (KBr): 1743, 1647 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 8.08 (d, *J* = 7.66 Hz, 2 H), 7.77 (d, *J* = 6.89 Hz, 2 H), 7.55 (t, *J* = 7.50 Hz, 1 H), 7.43 (t, *J* = 7.66 Hz, 2 H), 7.34–7.40 (m, 3 H), 2.44 (s, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 163.4, 163.3, 154.8, 134.4, 133.0, 130.4, 130.3, 130.2, 129.3, 129.2, 128.7, 128.3, 128.2, 126.8, 14.1.

HRMS (ESI): *m*/*z* $[M + Na]^+$ calcd for $C_{15}H_{13}NO_2Na$: 262.0843; found: 262.0872.

(*E*)-Acetophenone *O*-Butanoyl Oxime (3db)
White solid; yield: 144 mg (95%); mp 89–91 °C.

IR (KBr): 1762, 1614 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 7.73 (d, *J* = 6.84 Hz, 2 H), 7.36–7.43 (m, 3 H), 2.48 (t, *J* = 7.32 Hz, 2 H), 2.36 (s, 3 H), 1.76 (sextet, *J* = 7.32 Hz, 2 H), 1.01 (t, *J* = 7.32 Hz, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 170.8, 162.2, 134.6, 130.2, 128.2, 126.6, 34.6, 18.0, 14.0, 13.4.

HRMS (ESI): *m*/*z* $[M + H]^+$ calcd for $C_{12}H_{16}NO_2$: 206.1181; found: 206.1161.

(*E*)-Acetophenone *O*-4-Aminobenzoyl Oxime (3dc)
White solid; yield: 169 mg (90%); mp 166–167 °C.

IR (KBr): 1708, 1600 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 7.93 (d, *J* = 8.23 Hz, 2 H), 7.81 (d, *J* = 6.76 Hz, 2 H), 7.40–7.46 (m, 3 H), 6.68 (d, *J* = 8.23 Hz, 2 H), 4.28 (br s, 2 H), 2.50 (s, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 163.7, 162.5, 151.2, 134.8, 131.4, 130.1, 128.2, 126.7, 117.6, 113.5, 14.2.

HRMS (ESI): *m*/*z* $[M + Na]^+$ calcd for $C_{15}H_{14}N_2O_2Na$: 277.0952; found: 277.0952.

(*E*)-Acetophenone *O*-4-Methylbenzoyl Oxime (3dd)
White solid; yield: 174 mg (93%); mp 115–117 °C.

IR (KBr): 1732, 1606 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 7.96 (d, *J* = 7.86 Hz, 2 H), 7.75 (d, *J* = 7.73 Hz, 2 H), 7.33–7.39 (m, 3 H), 7.20 (d, *J* = 7.99 Hz, 2 H), 2.41 (s, 3 H), 2.34 (s, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 163.4, 163.0, 143.8, 134.5, 130.2, 129.2, 129.1, 128.8, 128.5, 128.1, 128.8, 126.7, 125.9, 21.2, 14.1.

HRMS (ESI): *m*/*z* $[M + H]^+$ calcd for $C_{16}H_{16}NO_2$: 254.1181; found: 254.1150.

(*E*)-Acetophenone *O*-4-Nitrobenzoyl Oxime (3de)
White solid; yield: 193.3 mg (92%); mp 167–169 °C.

IR (KBr): 1744, 1604 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 8.31 (q, *J* = 8.75 Hz, 4 H), 7.81 (d, *J* = 7.26 Hz, 2 H), 7.42–7.49 (m, 3 H), 2.54 (s, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 164.2, 161.6, 150.3, 134.3, 134.0, 130.6, 130.4, 128.3, 126.8, 123.44, 14.4.

HRMS (ESI): *m*/*z* $[M + Na]^+$ calcd for $C_{15}H_{12}N_2O_4Na$: 307.0694; found: 307.0673.

(*E*)-Benzaldehyde *O*-Benzoyl Oxime (3ea)[17]
White solid; yield: 178.3 mg (96%); mp 105–107 °C.

IR (KBr): 1743, 1652 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 8.54 (s, 1 H), 8.13 (d, *J* = 7.29 Hz, 2 H), 7.80 (d, *J* = 7.10 Hz, 2 H), 7.59 (t, *J* = 7.29 Hz, 1 H), 7.47 (t, *J* = 7.66 Hz, 3 H), 7.42 (t, *J* = 7.66 Hz, 2 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 163.6, 156.5, 133.1, 131.4, 129.8, 129.39, 128.6, 128.2, 128.1.

HRMS (ESI): *m*/*z* $[M + Na]^+$ calcd for $C_{14}H_{11}NO_2Na$: 248.0687; found: 248.0627.

(*E*)-Benzaldehyde *O*-Butanoyl Oxime (3eb)
Liquid; yield: 142 mg (90%).

IR (neat): 1760, 1645 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 8.29 (d, *J* = 5.10 Hz, 1 H), 7.67 (d, *J* = 6.93 Hz, 2 H), 7.32–7.41 (m, 3 H), 2.38 (q, *J* = 6.93 Hz, 2 H), 1.65–1.74 (m, 2 H), 0.96 (t, *J* = 7.29 Hz, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 170.6, 155.5, 131.2, 129.8, 128.5, 127.9, 34.2, 29.3, 17.9, 13.2.

HRMS (ESI): *m*/*z* $[M + Na]^+$ calcd for $C_{11}H_{13}NO_2Na$: 214.0843; found: 214.0828.

(*E*)-Benzaldehyde *O*-4-Methylbenzoyl Oxime (3ed)
White solid; yield: 179.6 mg (91%); mp 125–127 °C.

IR (KBr): 1730, 1608 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 8.54 (s, 1 H), 8.03 (d, *J* = 7.90 Hz, 2 H), 7.81 (d, *J* = 7.90 Hz, 2 H), 7.49 (t, *J* = 6.67 Hz, 1 H), 7.44 (t, *J* = 7.55 Hz, 2 H), 7.28 (d, *J* = 8.07 Hz, 2 H), 2.42 (s, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 163.7, 156.2, 143.9, 131.3, 131.1, 130.8, 129.9, 129.4, 129.1, 128.9, 128.5, 128.1, 125.5, 21.4.

HRMS (ESI): *m*/*z* $[M + Na]^+$ calcd for $C_{15}H_{13}NO_2Na$: 262.0843; found: 262.0806.

(*E*)-Benzaldehyde *O*-4-Nitrobenzoyl Oxime (3ee)
Pale yellow solid; yield: 209.5 mg (94%); mp 159–161 °C.

IR (KBr): 1740, 1606 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 8.60 (s, 1 H), 8.34 (q, *J* = 8.86 Hz, 4 H), 7.83 (d, *J* = 7.15 Hz, 2 H), 7.54 (t, *J* = 7.26 Hz, 1 H), 7.49 (t, *J* = 7.26 Hz, 2 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 161.7, 157.3, 150.4, 133.8, 131.8, 130.5, 129.3, 128.7, 128.3, 123.4.

HRMS (ESI): *m*/*z* $[M + Na]^+$ calcd for $C_{14}H_{10}N_2O_4Na$: 293.0538; found: 293.0550.

Acknowledgment

Author S.C.S.K. thanks University Grants Commission, New Delhi, India, for the award of a Senior Research Fellowship. We thank Mr. Mukund Padmere Laxman, CFTRI, Mysore, for HRMS analysis and Mr. J. R. Manjunatha, CFTRI, Mysore for NMR spectral analysis.

Supporting Information for this article is available online at http://www.thieme-connect.com/products/ejournals/journal/10.1055/s-00000084.

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