



One-Pot Synthesis of 5,6-Dihydro-4*H*-1,2-Oxazines by Cyclization of Ketoximes with Derivatives of Allylbenzene

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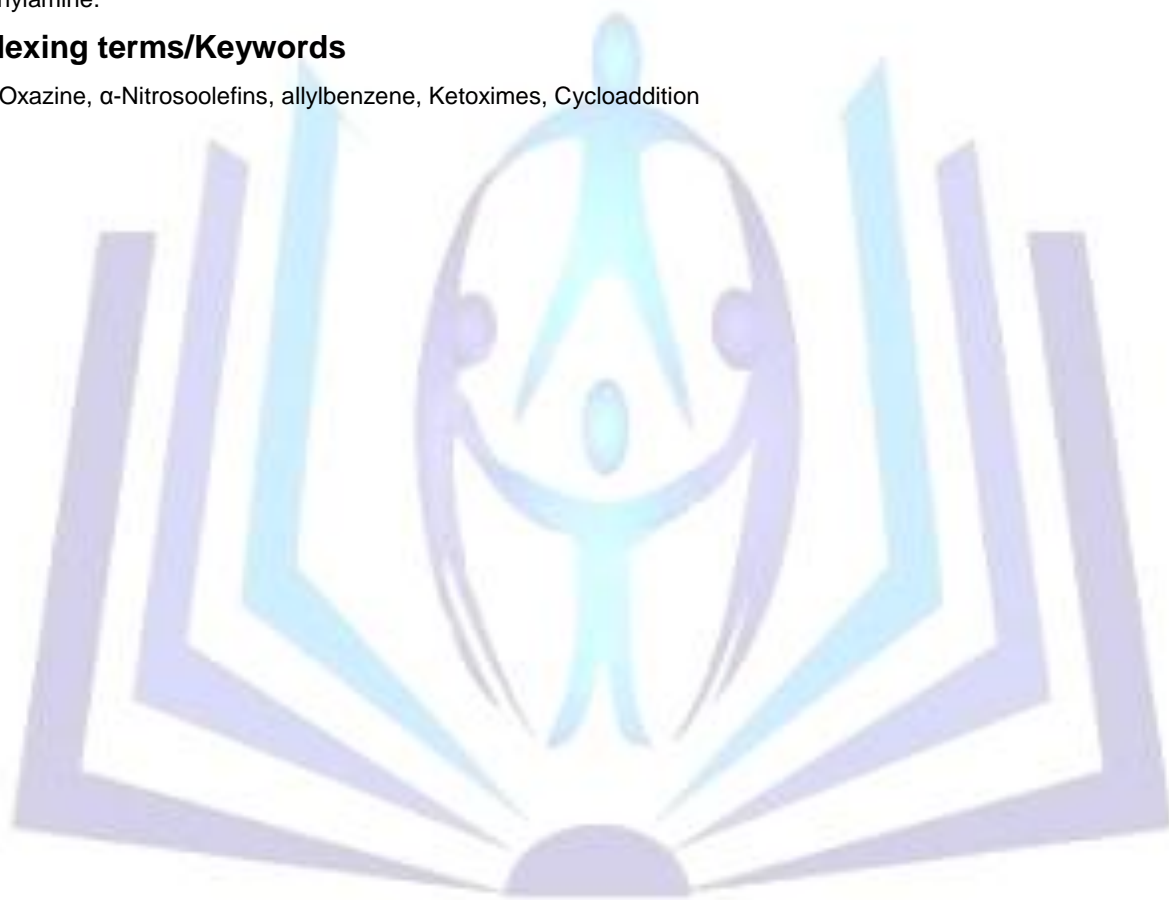
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ABSTRACT

A new series of 5,6-dihydro-4*H*-1,2-oxazines were synthesized via hetero Diels-Alder reaction of α -nitrosolefins with derivatives of allylbenzene. α -Nitrosoolefins were generated from ketoximes by the action of chloramine-T and triethylamine.

Indexing terms/Keywords

1,2-Oxazine, α -Nitrosoolefins, allylbenzene, Ketoximes, Cycloaddition



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INTRODUCTION

[4+2] cycloaddition of α -nitrosoolefins with olefinic compounds yields 5,6-dihydro-4*H*-1,2-oxazines which are useful intermediates for the synthesis of bifunctional compounds. The nitrosoolefins which are used in the reaction are transient species [1-5]. 5,6-Dihydro-4*H*-1,2-oxazines which are of biological importance, viz. used as intermediates during the synthesis of glycosidase inhibitor analogues [6-8] and of functionalized pyrroles [9]. Tetrahydro-4*H*-1,2-oxazines are the important structural constituents of many fungicides, herbicides [10] and microbicides [11]. Oxazines are used as key building blocks in the synthesis of natural products [12]. For instance, oxazine are used as synthones to synthesize pyrroles [13,14], pyrrolidine [15], pyridines [16] and γ -lactones [17]. α -Nitrosoolefins are usually generated *in situ* from α -haloketoximes, by reaction with a heterogeneous base such as sodium carbonate in an organic solvent (dichloromethane, diethyl ether or methyl *t*-butyl ether) at room temperature [18-20]. 1,2-Oxazines are also available from alkenyl ketoximes by reacting them with *N*-bromosuccinimide [21], trifluoroacetic acid [22] and UV mediated cyclizations of alkenyl-substituted oximes [23]. 1,2-Oxazines have also been prepared by base-mediated cyclizations of γ -chloroximes [24] and γ -sulfonyloximes [25]. Other synthetic approaches to 1,2-oxazines rely on Lewis-acid catalyzed reactions of allenoximes [26], acid-catalyzed cyclization of cyclopropyloximes [27] and on cyclizations of γ -nitroketones [28]. Langer *et al* reported the synthesis of 1,2-oxazines by cyclization of oxime dianions with epibromohydrin [29]. Recently Goanker and Rai prepared 5,6-dihydro-4*H*-1,2-oxazines by generating α -nitrosoolefins from ketoximes and further reacting them with olefinic compounds [30]. With this background, herein we report the cycloaddition reaction of different α -nitrosoolefins with various derivatives of allylbenzene.

EXPERIMENTAL

Reagents and apparatus

All chemicals used are lab grade chemicals and were used without further purification. All reactions were monitored by TLC, which was performed on Merk Alumina foil 60 A^o TLC plates with UV indicator. The solvent system used for developing the TLC plates was CHCl₃ : petroleum ether (1:3). The ¹H NMR and ¹³C NMR spectrum were measured on Jeol, using TMS as internal standard. The IR spectra (in KBr pellets) were recorded on JASCO FT/IR-460/113257 spectrometer (Japan) in the wave number range of 4000-400 cm⁻¹. The melting points were determined on Thomas Hoover. Mass spectra obtained on a Finnigan 4021. Elemental analyses were obtained on a Vario-EL instrument.

General procedure for the synthesis of oxazine derivatives 5(a-r)

A mixture of ketoxime (5 mmol) and chloramine-T trihydrate (5.1 mmol) in ethanol (20 ml) was refluxed for 4 hours. The mixture was cooled to room temperature, triethylamine (1 ml) was added and stirred at room temperature for 1h. After this, solution of allylbenzene (5.1 mmol) in ethanol (10 ml) was added and refluxed for 12-20 hours. It was then concentrated under reduced pressure and the residue was extracted with ether (50 ml). This extract was then washed with water (15 ml), aqueous 5% NaOH (30 ml) and dried over anhydrous sodium sulfate. The solvent was evaporated and the remaining solid was recrystallized from 10% ethanol in *n*-hexane to afford the pure compound.

Synthesis of 6-benzyl-3-phenyl-5,6-dihydro-4*H*-1,2-oxazines (5a)

Obtained from **1a** (0.66 g, 5 mmol), chloramine-T.3H₂O (1.43g, 5.1mmol) and **4a** (1.43 g, 5.1 mmol) as a brown oil, Yield 65%; mp 131-132 °C; IR (KBr, cm⁻¹): 1600 (C=C), 1645 (C=N). ¹H-NMR (300 MHz, CDCl₃, δ /ppm): 1.82-2.04 (m, 2H, OCHCH₂), 2.60-2.74 (t, *J* = 7.2 Hz, 2H, CCH₂), 2.78-2.87 (m, 2H, Ph-CH₂), 3.75-3.82 (m, 1H, OCH), 7.20-7.73 (m, 10H, Ar-H), ¹³C NMR (300 MHz, CDCl₃): 17.2, 24.2, 34.9, 86.90, 118.8, 123.3, 125.3, 131.2, 135.9, 138.4, 141.8, 146.7, 165.30. Anal. Calcd. for C₁₇H₁₇NO (251.13): C, 81.24; H, 6.82; N, 5.57. Found: C, 81.44; H, 6.64; N, 5.33. LC-MS: *m/z* 252.26[M]⁺.

6-(3,4-dimethoxybenzyl)-3-phenyl-5,6-dihydro-4*H*-1,2-oxazines (5b)

Obtained from **1a** (0.66 g, 5 mmol), chloramine-T.3H₂O (1.43g, 5.1mmol) and **4b** (0.9 g, 5.1 mmol) as a yellow oil, Yield 52%; mp 110-112 °C; IR (KBr, cm⁻¹): 1600 (C=C), 1644 (C=N). ¹H-NMR (300 MHz, CDCl₃, δ /ppm): 1.83-2.02 (m, 2H, OCHCH₂), 2.65-2.76 (t, *J* = 7.2 Hz, 2H, CCH₂), 2.79-2.86 (m, 2H, Ph-CH₂), 3.72-3.81 (m, 1H, OCH), 3.86-3.92 (m, 6H, OCH₃), 6.70-6.79 (m, 3H, Ar-H), 7.24-7.72 (m, 5H, Ar-CH). ¹³C NMR (300 MHz, CDCl₃): 15.6, 25.6, 40.6, 59.9, 85.8, 109.8, 115.4, 119.7, 128.2, 130.3, 134.3, 136.4, 139.7, 146.3, 150.5, 166.3. Anal. Calcd. for C₁₉H₂₁NO₃ (311.15): C, 73.29; H, 6.80; N, 4.50. Found: C, 73.50; H, 6.54; N, 4.60. LC-MS: *m/z* 312.25 [M]⁺.

2-methoxy-4-(3-phenyl-5,6-dihydro-4*H*-1,2-oxazin-6-yl) methyl} phenol (5c)

Obtained from **1a** (0.66 g, 5 mmol), chloramine-T.3H₂O (1.43 g, 5.1mmol) and **4c** (0.85 g, 5.1 mmol) as a white solid, Yield 62%; mp 87-88 °C; IR (KBr, cm⁻¹): 1600 (C=C), 1646 (C=N), 3350 (HO). ¹H-NMR (300 MHz, CDCl₃, δ /ppm): 1.85-2.03 (m, 2H, OCHCH₂), 2.64-2.75 (t, *J* = 7.2 Hz, 2H, CCH₂), 2.79-2.84 (m, 2H, PhCH₂), 3.74-3.81 (m, 1H, OCH), 3.86 (s, 3H, OCH₃), 5.65 (s, 1H, OH), 6.50-6.62 (m, 3H, Ar-H), 7.50 (t, *J* = 6Hz, 2H, Ar-H), 7.70-7.80 (m, 3H, Ar-H). ¹³C NMR (300 MHz, CDCl₃): 16.7, 23.2, 42.2, 60.5, 85.9, 110.1, 118.5, 121.9, 125.5, 128.8, 132.2, 133.4, 135.5, 145.8, 148.5, 166.7. Anal. Calcd. for C₁₈H₁₉NO₃ (297.14): C, 72.71; H, 6.44; N, 4.71. Found: C, 72.50; H, 6.70; N, 4.60. LC-MS: *m/z* 298.26 [M]⁺.

6-benzyl-3-*p*-tolyl-5,6-dihydro-4*H*-1,2-oxazine (5d)

Obtained from **1b** (0.74 g, 5 mmol), chloramine-T.3H₂O (1.43 g, 5.1 mmol) and **4a** (0.6 g, 5.1 mmol) as a white solid, Yield 68%; mp 124-126 °C; IR (KBr, cm⁻¹): 1600 (C=C), 1644 (C=N), 2995 (CH-aliph.). ¹H-NMR (300 MHz, CDCl₃, δ /ppm): 1.86-



2.05 (m, 2H, OCHCH₂), 2.39 (s, 3H, CH₃), 2.64-2.76 (t, *J* = 7.2 Hz, 2H, CCH₂), 2.79-2.88 (m, 2H, PhCH₂), 3.76-3.84 (m, 1H, OCH), 7.10 (dd, *J* = 6 Hz, *J* = 2 Hz, 2H, Ar-H), 7.20 (t, *J* = 6Hz, 2H, Ar-H), 7.35 (m, 3H, Ar-H), 7.58 (dd, *J* = 6 Hz, *J* = 2Hz, 2H, Ar-H). ¹³C NMR (300 MHz, CDCl₃): 15.5, 23.9, 25.7, 41.4, 87.6, 122.9, 126.9, 129.7, 131.3, 133.4, 135.2, 139.9, 170. Anal. Calcd. for C₁₈H₁₉NO (265.35): C, 81.47; H, 7.22; N, 5.28. Found: C, 81.66; H, 6.99; N, 6.66. LC-MS: *m/z* 266.44 [M]⁺.

6-(3,4-dimethoxybenzyl)-3-p-tolyl-5,6-dihydro-4H-oxazine (5e)

Obtained from **1b** (0.74 g, 5 mmol), chloramine-T.3H₂O (1.43 g, 5.1 mmol) and **4b** (0.9 g, 5.1 mmol) as a colorless solid, Yield 62%; mp 110-112 °C; IR (KBr, cm⁻¹): 1598 (C=C), 1647 (C=N), 2994 (CH-aliph.). ¹H-NMR (300 MHz, CDCl₃, δ/ppm): 1.84-2.03 (m, 2H, OCHCH₂), 2.40 (s, 3H, CH₃), 2.66-2.76 (t, *J* = 7.2Hz, 2H, CCH₂), 2.79-2.88 (m, 2H, PhCH₂), 3.77-3.82 (m, 1H, OCH), 3.87-3.93 (m, 6H, OCH₃), 6.55-6.66 (m, 3H, Ar-H), 7.20 (dd, *J* = 6 Hz, *J* = 2Hz, 2H, Ar-H), 7.65 (dd, *J* = 6 Hz, *J* = 2 Hz, 2H, Ar-H). ¹³C NMR (300 MHz, CDCl₃): 15.6, 23.9, 24.8, 40.8, 59.7, 88.1, 115.6, 117.8, 126.7, 129.7, 132.4, 136.4, 137.8, 146.6, 148.9, 155.8, 166.5. Anal. Calcd. for C₂₀H₂₃NO₃ (325.17): C, 73.82; H, 7.12; N, 4.30. Found: C, 73.99; H, 6.89; N, 4.50. LC-MS: *m/z* 326.29 [M]⁺.

2-methoxy-4-[(3-p-tolyl-5,6-dihydro-4H-1,2-oxazin-6-yl)-methyl]-phenol (5f)

Obtained from **1b** (0.74 g, 5 mmol), chloramine-T.3H₂O (1.43 g, 5.1 mmol) and **4c** (0.85 g, 5.1 mmol) as a pale yellow solid, Yield 58%; mp 63-64 °C; IR (KBr, cm⁻¹): 1600 (C=C), 1644 (C=N), 2994 (CH-aliph.), 3450 (HO). ¹H-NMR (300 MHz, CDCl₃, δ/ppm): 1.84-2.04 (m, 2H, OCHCH₂), 2.38 (s, 3H, CH₃), 2.63-2.73 (t, *J* = 7.2Hz, 2H, CCH₂), 2.77-2.85 (m, 2H, PhCH₂), 3.77-3.83 (m, 1H, OCH), 3.88 (s, 3H, OCH₃), 5.42 (s, 1H, OH), 6.55-6.78 (m, 3H, Ar-H), 7.15 (dd, *J* = 6 Hz, *J* = 2Hz, 2H, Ar-H), 7.70 (dd, *J* = 6 Hz, *J* = 2Hz, 2H, Ar-H). ¹³C NMR (300 MHz, CDCl₃): 18.6, 24.9, 26.9, 40.4, 55.7, 86.9, 110.9, 117.6, 120.8, 125.6, 129.1, 131.6, 137.7, 142.1, 147.5, 149.6, 164.3. Anal. Calcd. for C₁₉H₂₁NO₃ (315.15): C, 73.29; H, 6.80; N, 4.50. Found: C, 73.20; H, 6.90; N, 4.80. LC-MS: *m/z* 316.28 [M]⁺.

6-benzyl-3-(4-chlorophenyl)-5,6-dihydro-4H-1,2-oxazine (5g)

Obtained from **1c** (0.85 g, 5 mmol), chloramine-T.3H₂O (1.43 g, 5.1 mmol) and **4a** (0.6 g, 5.1 mmol) as a colorless solid, Yield 60%; mp 74-76 °C; IR (KBr, cm⁻¹): 1598 (C=C), 1646 (C=N), 2994 (CH-aliph.). ¹H-NMR (300 MHz, CDCl₃, δ/ppm): 1.87-2.03 (m, 2H, OCHCH₂), 2.64-2.74 (t, *J* = 7.2, 2H, CCH₂), 2.77-2.87 (m, 2H, PhCH₂), 3.74-3.82 (m, 1H, OCH), 7.20 (t, *J* = 6Hz, 2H, Ar-H), 7.35 (m, 3H, Ar-H), 7.50 (d, *J* = 6Hz, 2H, Ar-H), 7.65 (d, *J* = 6Hz, 2H, Ar-H). ¹³C NMR (300 MHz, CDCl₃): 16.7, 23.2, 40.3, 86.6, 122.4, 128.1, 130.1, 133.2, 136.5, 140.9, 165.8. Anal. Calcd. for C₁₇H₁₆ClNO (285.09): C, 71.45; H, 5.64; N, 4.90. Found: C, 71.50; H, 5.34; N, 5.08. LC-MS: *m/z* 285 [M]⁺, 287.18 [M⁺+2],

3-(4-chlorophenyl)-6-(3,4-dimethoxybenzyl)-5,6-dihydro-4H-1,2-oxazine (5h)

Obtained from **1c** (0.85 g, 5 mmol), chloramine-T.3H₂O (1.43 g, 5.1 mmol) and **4b** (0.9 g, 5.1 mmol) as a pale yellow solid, Yield 69%; mp 67-68 °C; IR (KBr, cm⁻¹): 1600 (C=C), 1647 (C=N), 2990 (CH-aliph.). ¹H-NMR (300 MHz, CDCl₃, δ/ppm): 1.84-2.01 (m, 2H, OCHCH₂), 2.65-2.74 (t, *J* = 7.2Hz, 2H, CCH₂), 2.78-2.87 (m, 2H, PhCH₂), 3.73-3.83 (m, 1H, OCH), 3.91-3.96 (m, 6H, OCH₃), 6.55-6.66 (m, 3H, Ar-H), 7.40 (d, *J* = 6Hz, 2H, Ar-H), 7.60 (d, *J* = 6Hz, 2H, Ar-H). ¹³C NMR (300 MHz, CDCl₃): 15.9, 25.5, 41.3, 57.3, 85.4, 109.9, 117.9, 120.8, 128.4, 130.2, 133.2, 135.7, 139.9, 148.4, 150.5, 165.1. Anal. Calcd. for C₁₉H₂₀ClNO₃ (345.11): C, 65.99; H, 5.83; N, 4.05. Found: C, 65.66; H, 6.10; N, 4.26. LC-MS: *m/z* 345 [M]⁺, 347.12 [M⁺+2],

4-[(3-(4-chlorophenyl)-5,6-dihydro-4H-1,2-oxazin-6-yl)-methyl]-2-methoxyphenol (5i)

Obtained from **1c** (0.85 g, 5 mmol), chloramine-T.3H₂O (1.43 g, 5.1 mmol) and **4c** (0.85 g, 5.1 mmol) as a colorless solid, Yield 54%; mp 82-83 °C; IR (KBr, cm⁻¹): 1600 (C=C), 1645 (C=N), 2990 (CH-aliph.), 3456 (HO). ¹H-NMR (300 MHz, CDCl₃, δ/ppm): 1.87-2.02 (m, 2H, OCHCH₂), 2.66-2.74 (t, *J* = 7.2Hz, 2H, CCH₂), 2.78-2.87 (m, 2H, PhCH₂), 3.75-3.84 (m, 1H, OCH), 3.90 (s, 3H, CH₃), 5.51 (s, 1H, OH), 6.60-6.70 (m, 3H, Ar-H), 7.45 (d, *J* = 6Hz, 2H, Ar-H), 7.62 (d, *J* = 6Hz, 2H, Ar-H). ¹³C NMR (300 MHz, CDCl₃): 15.7, 23.9, 41.4, 58.6, 85.8, 112.2, 117.8, 120.9, 124.8, 128.5, 130.1, 133.9, 136.5, 147.7, 149.3, 166.9. Anal. Calcd. for C₁₈H₁₈ClNO₃ (331.10): C, 65.16; H, 5.47; N, 4.22. Found: C, 65.40; H, 5.30; N, 4.50. LC-MS: *m/z* 331 [M]⁺, 333.12 [M⁺+2].

3-benzyl-4, 4a, 5,6, 7,8-hexahydro-3H-benzo[c][1,2]oxazine (5j)

Obtained from **1d** (0.56 g, 5 mmol), chloramine-T.3H₂O (1.43 g, 5.1 mmol) and **4a** (0.6 g, 5.1 mmol) as a pale yellow solid, Yield 61%; mp 89 °C; IR (KBr, cm⁻¹): 1598 (C=C), 1644 (C=N), 2998 (CH-aliph.). ¹H-NMR (300 MHz, CDCl₃, δ/ppm): 1.28-1.36 (m, 1H, CCH), 1.39-1.41 (t, *J* = 7.2Hz, 2H, CCH₂), 1.49-1.55 (m, 2H, CH₂), 1.59-1.64 (m, 2H, CH₂), 1.70-1.77 (m, 2H, CH₂), 1.86-2.09 (m, 2H, OCHCH₂), 2.80-2.87 (m, 2H, PhCH₂), 3.77-3.88 (m, 1H, OCH), 7.20 (t, *J* = 6Hz, 2H, Ar-H), 7.33 (m, 3H, Ar-H). ¹³C NMR (300 MHz, CDCl₃): 21.4, 26.6, 27.8, 32.9, 36.9, 40.9, 41.9, 84.6, 125.4, 128.9, 130.9, 140.7, 163.9. Anal. Calcd. for C₁₅H₁₉NO (229.15): C, 78.56; H, 8.35; N, 6.11. Found: C, 78.66; H, 8.20; N, 6.30. LC-MS: *m/z* 230.26 [M]⁺.

3-(3,4-dimethoxybenzyl)-4,4a,5,6,7,8-hexahydro-3H-benzo[c][1,2]oxazine (5k)

Obtained from **1d** (0.56 g, 5 mmol), chloramine-T.3H₂O (1.43 g, 5.1 mmol) and **4b** (0.9 g, 5.1 mmol) as a white solid, Yield 69%; mp 89-91 °C; IR (KBr, cm⁻¹): 1600 (C=C), 1648 (C=N), 2995 (CH-aliph.). ¹H-NMR (300 MHz, CDCl₃, δ/ppm): 1.24-1.32 (m, 1H, CCH), 1.37-1.40 (t, *J* = 7.2Hz, 2H, CCH₂), 1.47-1.56 (m, 2H, CH₂), 1.61-1.67 (m, 2H, CH₂), 1.71-1.79 (m, 2H, CH₂), 1.84-2.01 (m, 2H, OCHCH₂), 2.78-2.85 (m, 2H, PhCH₂), 3.72-3.87 (m, 1H, OCH), 3.85-3.93 (m, 6H, OCH₃), 6.50-



6.62 (m, 3H, Ar-H). ^{13}C NMR (300 MHz, CDCl_3); 21.8, 23.3, 28.8, 31.1, 38.8, 40.3, 42.9, 57.2, 83.5, 114.1, 116.5, 126.6, 133.3, 148.2, 149.9, 164.8. Anal. Calcd. for $\text{C}_{17}\text{H}_{23}\text{NO}_3$ (289.17): C, 70.56; H, 8.01; N, 4.84. Found: C, 70.66; H, 7.90; N, 4.99. LC-MS: m/z 290.29 $[\text{M}]^+$.

4-[(4,4a,5,6,7,8-hexahydro-3H-benzo[c][1,2]oxazine-3-yl)methyl]-2-methoxyphenol (5l)

Obtained from **1d** (0.56 g, 5 mmol), chloramine-T.3H₂O (1.43 g, 5.1 mmol) and **4c** (0.85 g, 5.1 mmol) as a colorless solid, Yield 66%; mp 111-112 °C; IR (KBr, cm^{-1}): 1600 (C=C), 1645 (C=N), 2995 (CH-aliph.), 3370 (HO). ^1H -NMR (300 MHz, CDCl_3 , δ/ppm): 1.23-1.33 (m, 1H, CCH), 2.72-2.89 (m, 2H, PhCH₂), 1.38-1.42 (t, $J = 7.2\text{Hz}$, 2H, CCH₂), 1.48-1.57 (m, 2H, CH₂), 1.60-1.65 (m, 2H, CH₂), 1.71-1.78 (m, 2H, CH₂), 1.82-2.03 (m, 2H, OCHCH₂), 3.74-3.85 (m, 1H, OCH), 3.89 (s, 3H, OCH₃), 5.75 (s, 1H, OH), 6.65-6.76 (m, 3H, Ar-H). ^{13}C NMR (300 MHz, CDCl_3); 22.9, 24.9, 28.9, 31.5, 36.6, 41.7, 42.3, 58.9, 83.7, 116.3, 118.8, 126.6, 131.1, 145.3, 148.8, 164.9. Anal. Calcd. for $\text{C}_{16}\text{H}_{21}\text{NO}_3$ (275.15): C, 69.79; H, 7.69; N, 5.09. Found: C, 69.66; H, 7.80; N, 4.90. LC-MS: m/z 276.27 $[\text{M}]^+$.

3-benzyl-3,4,4a,5,6,7-hexahydrocyclopenta[c][1,2]oxazine (5m)

Obtained from **1e** (0.5 g, 5 mmol), chloramine-T.3H₂O (1.43 g, 5.1 mmol) and **4a** (0.6 g, 5.1 mmol) as a white solid, Yield 64%; mp 132-133 °C; IR (KBr, cm^{-1}): 1598 (C=C), 1648 (C=N), 2992 (CH-aliph.). ^1H -NMR (300 MHz, CDCl_3 , δ/ppm): 1.40-1.50 (m, 2H, CH₂), 1.55-1.60 (m, 2H, CH₂), 1.66-1.72 (m, 1H, CCH), 1.85-1.94 (m, 2H, OCHCH₂), 2.75-2.79 (t, $J = 6.2\text{Hz}$, 2H, CCH₂), 2.83-2.89 (m, 2H, PhCH₂), 3.80-3.87 (m, 1H, OCH), 7.22 (t, $J = 6\text{Hz}$, 2H, Ar-H), 7.33 (m, 3H, Ar-H). ^{13}C NMR (300 MHz, CDCl_3); 21.8, 25.5, 29.9, 41.8, 42.5, 44.9, 84.9, 122.2, 126.6, 130.2, 140.4, 166.9. Anal. Calcd. for $\text{C}_{14}\text{H}_{17}\text{NO}$ (215.13): C, 78.10; H, 7.96; N, 6.51. Found: C, 78.20; H, 7.77; N, 6.88. LC-MS: m/z 216.23 $[\text{M}]^+$.

3-(3,4-dimethoxybenzyl)-3,4,4a,5,6,7-hexahydrocyclopenta[c][1,2]oxazine (5n)

Obtained from **1e** (0.5 g, 5 mmol), chloramine-T.3H₂O (1.43 g, 5.1 mmol) and **4b** (0.9 g, 5.1 mmol) as a colorless solid, Yield 65%; mp 97-98 °C; IR (KBr, cm^{-1}): 1600 (C=C), 1649 (C=N), 2990 (CH-aliph.). ^1H -NMR (300 MHz, CDCl_3 , δ/ppm): 1.42-1.55 (m, 2H, CH₂), 1.59-1.64 (m, 2H, CCH₂), 1.67-1.73 (m, 1H, CCH), 2.72-2.76 (t, $J = 6.2\text{Hz}$, 2H, CH₂), 1.82-1.91 (m, 2H, OCHCH₂), 2.79-2.85 (m, 2H, PhCH₂), 3.84-3.87 (m, 1H, OCH), 3.90-3.93 (m, 6H, OCH₃), 6.55-6.65 (m, 3H, Ar-H). ^{13}C NMR (300 MHz, CDCl_3); 22.8, 26.6, 30.3, 39.6, 41.2, 46.6, 83.9, 127.9, 129.9, 131.1, 135.7, 167.9, 169.4. Anal. Calcd. for $\text{C}_{16}\text{H}_{21}\text{NO}_3$ (275.15): C, 69.79; H, 7.69; N, 5.09. Found: C, 69.99; H, 7.50; N, 5.40. LC-MS: m/z 276.27 $[\text{M}]^+$.

4-[(3,4,4a,5,6,7-hexahydrocyclopenta[c][1,2]oxazin-3-yl)methyl]-2-methoxyphenol (5o)

Obtained from **1e** (0.5 g, 5 mmol), chloramine-T.3H₂O (1.43 g, 5.1 mmol) and **4c** (0.86 g, 5.1 mmol) as a colorless solid, Yield 61%; mp 112-113 °C; IR (KBr, cm^{-1}): 1600 (C=C), 1645 (C=N), 2995 (CH-aliph.), 3460 (HO). ^1H -NMR (300 MHz, CDCl_3 , δ/ppm): 1.67-1.76 (m, 1H, CCH), 2.72-2.77 (t, $J = 6.2\text{Hz}$, 2H, CH₂), 1.53-1.65 (m, 2H, CH₂), 1.42-1.54 (m, 2H, CH₂), 1.84-1.93 (m, 2H, OCHCH₂), 2.77-2.88 (m, 2H, PhCH₂), 3.82-3.87 (m, 1H, OCH), 3.93 (s, 3H, OCH₃), 5.45 (s, 1H, OH), 6.58-6.68 (m, 3H, Ar-H). ^{13}C NMR (300 MHz, CDCl_3); 21.7, 27.7, 30.9, 40.6, 41.2, 45.3, 58.1, 84.5, 111.2, 117.7, 120.9, 133.3, 144.5, 151.2, 168.2. Anal. Calcd. for $\text{C}_{15}\text{H}_{19}\text{NO}_3$ (261.14): C, 68.94; H, 7.33; N, 5.36. Found: C, 68.66; H, 7.60; N, 5.20. LC-MS: m/z 262.27 $[\text{M}]^+$.

3-benzyl-4,4a,5,6-tetrahydro-3H-Naphtho[1,2-c][1,2]oxazine (3p)

Obtained from **1f** (0.8 g, 5 mmol), chloramine-T.3H₂O (1.43 g, 5.1 mmol) and **4a** (0.6 g, 5.1 mmol) as a brown solid, Yield 73%; mp 140-141 °C; IR (KBr, cm^{-1}): 1600 (C=C), 1640 (C=N), 2995 (CH-aliph.). ^1H -NMR (300 MHz, CDCl_3 , δ/ppm): 1.24-1.35 (m, 1H, CCH), 1.46-1.56 (t, $J = 6.2\text{Hz}$, 2H, CH₂), 1.70-1.78 (m, 2H, CH₂), 1.85-2.02 (m, 2H, OCHCH₂), 2.77-2.88 (m, 2H, PhCH₂), 3.82-3.87 (m, 1H, OCH), 7.10 (m, 3H, Ar-H), 7.22 (t, $J = 6\text{Hz}$, 2H, Ar-H), 7.35 (m, 3H, Ar-H), 7.90 (d, $J = 6\text{Hz}$, 1H, Ar-H). ^{13}C NMR (300 MHz, CDCl_3); 27.2, 29.9, 32.1, 33.9, 40.4, 80.7, 123.9, 127.7, 128.2, 129.1, 129.9, 131.2, 131.9, 132.6, 139.1, 144.8, 155.5. Anal. Calcd. for $\text{C}_{19}\text{H}_{19}\text{NO}$ (277.15): C, 82.28; H, 6.90; N, 5.05. Found: C, 82.56; H, 6.60; N, 5.20. LC-MS: m/z 278.27 $[\text{M}]^+$.

3-(3,4-dimethoxybenzyl)-4,4a,5,6-tetrahydro-3H-Naphtho[1,2-c][1,2]oxazine (3q)

Obtained from **1f** (0.8 g, 5 mmol), chloramine-T.3H₂O (1.43 g, 5.1 mmol) and **4b** (0.9 g, 5.1 mmol) as a colorless solid, Yield 66%; mp 131-132 °C; IR (KBr, cm^{-1}): 1600 (C=C), 1648 (C=N), 2990 (CH-aliph.). ^1H -NMR (300 MHz, CDCl_3 , δ/ppm): 1.26-1.34 (m, 1H, CCH), 1.45-1.55 (t, $J = 6.2\text{Hz}$, 2H, CH₂), 1.72-1.81 (m, 2H, CH₂), 1.84-2.03 (m, 2H, OCHCH₂), 2.77-2.88 (m, 2H, PhCH₂), 3.82-3.87 (m, 1H, OCH), 3.85-3.92 (m, 6H, OCH₃), 6.50-6.60 (m, 3H, Ar-H), 7.14 (m, 2H, Ar-H), 7.95 (d, $J = 6\text{Hz}$, 1H, Ar-H). ^{13}C NMR (300 MHz, CDCl_3); 28.1, 29.9, 31.1, 33.3, 40.9, 58.9, 79.7, 111.9, 113.3, 123.8, 124.4, 125.3, 129.4, 129.9, 132.3, 138.8, 146.5, 150.4, 155.8. Anal. Calcd. for $\text{C}_{21}\text{H}_{23}\text{NO}_3$ (337.17): C, 74.75; H, 6.87; N, 4.15; Found: C, 74.66; H, 6.90; N, 4.10. LC-MS: m/z 338.28 $[\text{M}]^+$.

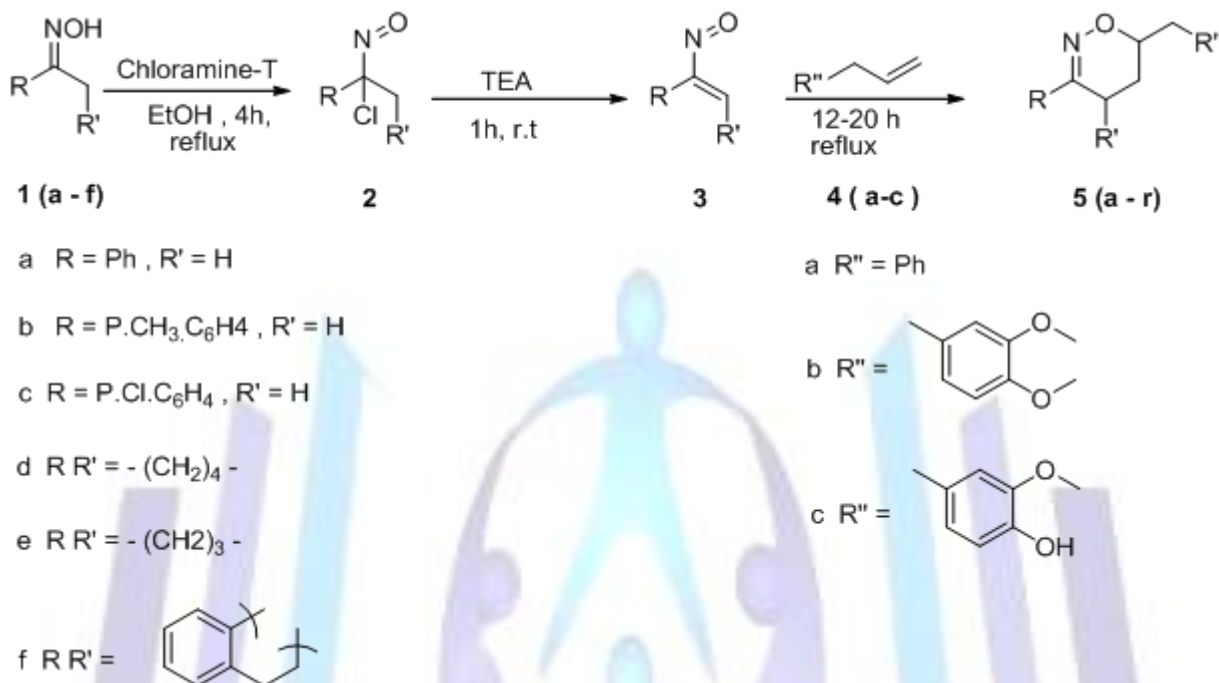
2-methoxy-4-[(4,4a,5,6-tetrahydro-3H-Naphtho[1,2-c][1,2]oxazinyl)-methyl] phenol (3r)

Obtained from **1f** (0.8 g, 5 mmol), chloramine-T.3H₂O (1.43 g, 5.1 mmol) and **4c** (0.85 g, 5.1 mmol) as a colorless solid, Yield 69%; mp 125-127 °C; IR (KBr, cm^{-1}): 1600 (C=C), 1648 (C=N), 2990 (CH-aliph.), 3465 (HO). ^1H -NMR (300 MHz, CDCl_3 , δ/ppm): 1.21-1.34 (m, 1H, CCH), 1.45-1.56 (t, $J = 6.2\text{Hz}$, 2H, CH₂), 1.70-1.82 (m, 2H, CH₂), 1.84-1.99 (m, 2H, OCHCH₂), 2.77-2.88 (m, 2H, PhCH₂), 3.82-3.87 (m, 1H, OCH), 3.86 (s, 3H, OCH₃), 5.55 (s, 1H, OH), 6.60-6.71 (m, 3H, Ar-H), 7.18-7.80 (m, 3H, Ar-H), 7.95 (d, $J = 6\text{Hz}$, 1H, Ar-H). ^{13}C NMR (300 MHz, CDCl_3); 27.7, 30.1, 31.2, 33.2, 41.4, 57.7, 78.9, 112.9, 116.8, 121.2, 123.3, 126.7, 128.2, 129.9, 131.1, 132.2, 140.5, 146.4, 149.9, 156. Anal. Calcd. for $\text{C}_{20}\text{H}_{21}\text{NO}_3$ (323.15): C, 74.28; H, 6.55; N, 4.36. Found: C, 74.66; H, 6.40; N, 4.50. LC-MS: m/z 324.26 $[\text{M}]^+$.



RESULTS AND DISCUSSION

The compounds **1(a-f)** were synthesized by the reaction of ketones with hydroxylamine hydrochloride in the presence of sodium acetate. Chloramine-T was used as an effective reagent for the generation of α -nitrosolefins from the corresponding ketoximes **1(a-f)** [31], which subsequently undergo hetero Diels-Alder reaction with an olefin **4(a-c)** to give 5,6-dihydro-4*H*-1,2-Oxazine derivatives **5(a-r)** (Scheme 1) [32].



SCHEME 1. Schematic representation of synthesis of 1,2-oxazine derivatives.

The regioselectivity can be interpreted in terms of interaction between the FMO of diene and dienophile. Usually, for dipolarophiles with electron-attracting groups, the dipolar-HOMO and dienophile-LUMO interaction is dominant. According to the principle of maximum overlap, the preferred isomers of each interaction can be predicted by union of two sites of the reactants having the largest coefficient value. Most dienophiles undergo reaction to give 6-substituted 1,2-oxazines with high regioselectivity[33]. The identities of compounds (**5a-r**) were established by their ¹H NMR, ¹³C NMR, IR, elemental analysis and MS. Taking **5a** as an example, the ¹H NMR spectrum of **5a** displays triplet at 2.60-2.74 and multiplets at 1.82-2.04 and 3.75-3.82 ppm due to CCH₂, OCHCH₂ and OCH in the position 4, 5 and 6 in the oxazine ring respectively. While the CH₂-Ph appears as multiplet at 2.78-2.86 ppm. Further the ten protons of two phenyl groups appeared at δ 7.20-7.73 as a multiplet. The IR spectra of 1,2-oxazine **5a** showed absorption at 1640 cm⁻¹ owing to the ring nitrogen(C=N) and 1600 cm⁻¹ due to aromatic ring. In the ¹³C NMR spectra all oxazines gave consistent signals for the newly formed ring carbons. For instance the signals in the region due to C₆ appears in the region δ 86.90 ppm while C₅, C₄ and C₃ appears in the region 17.2, 24.2 and 165.30. The mass spectrum of **5a** showed the molecular ion peak at m/z 252.26. The formation of the products was further supported by elemental analysis.

CONCLUSIONS

In conclusion a new series of 5,6-dihydro-4*H*-1,2-oxazine derivatives were synthesized from ketoximes by generation of a nitrosolefins and reacting them with derivatives of allylbenzene. We have also prepared bicyclic oxazines from cyclopentanone oxime, cyclohexanone oxime and 3,4-dihydronaphthalen-1(2*H*)-one oxime.

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