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Synthesis of Derivatives of 6*H*-1,2-Oxazine by Cyclization of Ketoximes With Derivatives of Terminal Acetylene Compounds

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Abstract

A new series of 6*H*-1,2-oxazines were synthesized by the reaction of ketones with hydroxylamine hydrochloride in the presence of sodium acetate to give ketoximes **1(a-e)**. Chloramine-T was used as an effective reagent for the generation of α-nitrosolefins from ketoximes **1(a-e)** which subsequently underwent hetero Diels-Alder reaction with terminal acetylenes **4(a-d)**, to give 6*H*-1,2-Oxazine derivatives **5(a-t)**.

Keywords: 6*H*-1,2-Oxazine, α-nitrosolefins, terminal acetylene, ketoximes, cycloaddition

1. Introduction

A broad range of synthetic applications demonstrates that 1,2-oxazine derivatives constitute a versatile class of N,O heterocycles (Gilchrist, 1983; Tsoungas, 2002; Zimmer et al., 2009; Lyapkalo & Ioffe, 1998; Tishkov et al., 2002; Young & Kerr, 2003; Helms et al., 2005; Cardona & Goti, 2005; Sibi et al., 2005; Kumarn et al., 2006; Lu & Zakarian, 2008; Brasholz et al., 2009; Sukhorukov et al., 2009). Considerable attention has been paid to 6*H*-1,2-oxazines bearing a C-4, C-5-double bond (Homann et al., 1998; Zimmer et al., 2002; Zimmer & Reissig, 1988; Zimmer & Reissig, 1991; Zimmer & Reissig, 1992) which are useful intermediates in the synthesis of γ-lactams (Zimmer et al., 1992), γ-aminoacids, aminoalcohols (Zimmer et al., 1992), aziridines (Zimmer et al., 1993), pyrrolizidines (Zimmer et al., 2008), pyrrolidine derivatives (Zimmer et al., 2002; Buchholz & Reissig, 2003; Reissig et al., 2007), 2-acetylpyridines (Thomas et al., 1987) and 2-(aminoalkyl) benzoic acids (Gilchrist & Wood, 1996).

α-Nitrosolefins are usually generated *in situ* from an α-haloketoxime, by reaction with a heterogenous base such as sodium carbonate in an organic solvent (dichloromethane, diethyl ether, or methyl *t*-butyl ether) at room temperature (David et al., 1983; Shigeo et al., 1991; Mori & Wu, 1991). Sung et al. (2001) prepared 1-aryl-2,2-dihaloethanone oximes from 1-aryl-2,2-dihaloethanone and hydroxylamine hydrochloride and then treated with sodium carbonate in dried ether. Manjula et al. (2009) used chloramine-T for the generation α-nitrosolefins from ketoximes bearing α-Hydrogen.

6*H*-1,2-Oxazines were prepared from 1-bromo-2-ethoxyethene and α-bromo-(*p*-methoxy) acetophenonoxime via 4+2 cycloaddition followed by HBr elimination (Buchholz & Reibig, 2003). An unusual synthesis of 6*H*-1,2-oxazines was accomplished by the reaction of nitrile oxides with vinylcarbene (Mark et al., 1993), which apparently involves 3-centre plus 3-centre cycloaddition of the dipole to the intermediate vinylcarbene. In this work we react various acetophenone oximes with chloramine-T and triethyl amine to afford α-nitrosolefins which are subsequently reacted with terminal acetylenes to yield derivatives of 6*H*-1,2-oxazine.

2. Experimental Section

2.1 General

Analytical thin layer chromatography (TLC) was performed on 0.25 mm silica gel 60-F plates and visualized by ultraviolet irradiation and $KMnO_4$. Melting points were determined on Thomas Hoover melting point apparatus and are uncorrected. ^{1}H NMR spectra were recorded on a Bruker AM (300 MHz) spectrometer using $CDCl_3$ as solvent and tetramethylsilane as internal standard. ^{13}C NMR spectra were measured on Jeol 400 (300 MHz) instrument. Mass spectra obtained on a Finnigan 4021. Elemental analyses were carried out using Flash EA 1112 Series, CHN Analyzer (Thermo). IR spectra in KBr pellets were recorded on JASCO FT/IR-4100 FTIR spectrophotometer.

2.2 General Procedure for the Synthesis of Oxazine Derivatives 5(a-t)

A mixture of ketoxime (5 mmol) and chloramine-T trihydrate (5.1 mmol) in ethanol (20 ml) were refluxed for 4 hrs. The mixture was cooled to room temperature; triethylamine (1 ml) was added and stirred at room temperature for 1h. After this, solution of terminal acetylene (5.1 mmol) in ethanol (5 ml) was added and stirred at reflux for 15-20 hours. It was then concentrated under reduced pressure and the residue is 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.

2.2.1 (3-Phenyl-6H-1,2-Oxazine-6-yl)-Methanol (5a)

Obtained from **1a** (0.74 g, 5 mmol), chloramine-T.$3H_2O$ (1.43 g, 5.1 mmol) and **4a** (0.28 g, 5.1 mmol) as a colorless solid, yield (0.6g, 64.5%), m.p. 89-90 ^oC, ^1H NMR ($CDCl_3$, 300 MHz): δ 2.13 (br, 1H, OH), 3.75-3.93 (m, 2H, CH_2), 4.20 (m, 1H, C6), 6.33 (dd, *J* = 4.6 Hz, *J* = 10.1 Hz, 1H, C5), 6.69 (d, *J* = 10.2 Hz, 1H, C4), 7.40 (t, *J* = 6 Hz, 2H, CH), 7.66-7.69 (m, 3H, CH).^{13}C NMR (300 MHz, $CDCl_3$); 64.7, 90.1, 110.9, 126.5, 127.8 130.1, 132.3, 137.6, 156.2. IR (KBr pellets cm^{-1}) ν 1280, 1450, 1600, 1615, 2970, 3105, 3340. Anal. CHN: calcd C 69.83, H 5.86, N 7.40, found C 69.64, H 5.94, N 7.33. LC-MS: calcd for $C_{11}H_{11}NO_2$ [M^+]: 189.08, found 189.90.

2.2.2 (3-p-Tolyl-6H-1,2-Oxazine-6-yl)-Methanol (5b)

Obtained from **1b** (0.74 g, 5 mmol), chloramine-T.$3H_2O$ (1.43 g, 5.1 mmol) and **4a** (0.28 g, 5.1 mmol) as a brown solid, yield (0.6 g, 60%), m.p. 131-132 ^oC, ^1H NMR ($CDCl_3$, 300 MHz): δ 2.15 (br, 1H, OH), 2.36 (s, 3H, CH_3), 3.77-3.95 (m, 2H, CH_2), 4.22 (m, 1H, C6), 6.28 (dd, *J* = 4.6 Hz, *J* = 10.1 Hz, 1H, C5), 6.70 (d, *J* = 10.2, 1H, C4), 7.19 (dd, *J* = 7 Hz, *J* = 2 Hz, 2H, CH), 7.60 (dd, *J* = 6 Hz, *J* = 2 Hz, 2H, CH).^{13}C NMR (300 MHz, $CDCl_3$); 23.3, 64.3, 90.2, 110.6, 125.2, 127.7, 133.2, 140.8, 156.3. IR (KBr pellets cm^{-1}) ν1280, 1445, 1600, 1612, 2980, 3110, 3350. Anal. CHN: calcd C 70.92, H 6.45, N 6.89, found C 70.99, H 6.35, N 6.99. LC-MS: calcd for $C_{12}H_{13}NO_2$ [M^+]: 203.09, found 204.10.

2.2.3 (3-(4-Chlorophenyl)-6H-1,3-Oxazin-6-yl)-Methanol (5c)

Obtained from **1c** (0.84 g, 5 mmol), chloramine-T.$3H_2O$ (1.43 g, 5.1 mmol) and **4a** (0.28 g, 5.1 mmol) as a brown oil, yield (0.6 g, 54%), ^1H NMR ($CDCl_3$, 300 MHz): δ 2.16 (br, 1H, OH), 3.76-3.90 (m, 2H, CH_2), 4.23 (m, 1H, OCH), 6.25 (dd, *J* = 4.6 Hz, *J* = 10.1 Hz, 1H, C5), 6.32 (d, *J* = 10.1 Hz, 1H, C4), 7.44 (d, *J* = 8.7 Hz, 2H, CH), 7.68 (d, *J* = 8.7 Hz, 2H, CH).^{13}C NMR (300 MHz, $CDCl_3$); 65.6, 90.3, 110.6, 125.5, 127.9, 129.8, 133.3, 139.8, 156.3. IR (neat, cm^{-1}) ν1285, 1440, 1600, 1610, 2960, 3100, 3360. Anal. CHN: calcd C 59.07, H 4.51, N 6.26, found C 59.17, H.4.41, N6.36. LC-MS: calcd for $C_{11}H_{10}ClNO_2$ [M^+]: 223.04, found 225.05.

2.2.4 (3-(4-Methoxyphenyl)-6H-yl)-Methanol (5d)

Obtained from **1d** (0.82 g, 5 mmol), chloramine-T.$3H_2O$ (1.43 g, 5.1 mmol) and **4a** (0.28 g, 5.1 mmol) as a brown oil, yield (0.7 g, 64.8%), ^1H NMR ($CDCl_3$, 300 MHz): δ 2.14 (br, 1H, OH), 3.77-3.95 (m, 5H, CH_2, OCH_3), 4.24 (m, 1H, C6), 6.28 (dd, *J* = 4.6 Hz, *J* = 10.1 Hz, 1H, C5), 6.68 (d, *J* = 10.2 Hz, 1H, C4), 7.19 (dd, *J* = 7 Hz, *J* = 2 Hz, 2H, CH), 7.60 (dd, *J* = 6 Hz, *J* = 2 Hz, 2H, CH).^{13}C NMR (300 MHz, $CDCl_3$); 58.8, 65.2, 90.6, 110.9, 118.8, 126.1, 127.7, 134.4, 156.3, 166.7. IR (neat, cm^{-1}) ν1247, 11290, 1442, 1618, 2950, 3000, 3030, 3070, 3360. Anal. CHN: calcd C 65.74, H 5.98, N 6.39, found C 65.80, H 5.88, N6.50. LC-MS: calcd for $C_{12}H_{13}NO_3$ [M^+]:219.09, found .219.93.

2.2.5 (3-(4-Nitrophenyl)-6H-1,2-Oxazin-6-yl)-Methanol (5e)

Obtained from **1e** (0.9 g, 5 mmol), chloramine-T.$3H_2O$ (1.43 g, 5.1 mmol) and **4a** (0.28 g, 5.1 mmol) as a colorless solid, yield (0.7 g, 60%), m.p. 131-132 ^oC, ^1H NMR ($CDCl_3$, 300 MHz): δ 2.16 (br, 1H, OH), 3.70-3.90 (m, 2H, CH_2), 4.21 (m, 1H, C6), 6.26 (dd, *J* = 4.6, *J* = 10.1 Hz, 1H, C5), 6.71 (d, *J* = 10.2 Hz, 1H, C4), 8.30 (d, *J* = 8.9 Hz, 2H, CH), 8.34 (d, *J* = 8.9 Hz, 2H, CH).^{13}C NMR (300 MHz, $CDCl_3$); 65.3, 90.7, 110.5, 125.2, 127.9, 134.5, 136.7, 154.3, 156.3. IR (KBr pellets cm^{-1}) ν1125, 1435, 1520, 1615, 2980, 3030, 3100, 3365. Anal. CHN: calcd C 56.41, H 4.30, N 11.96, found C 56.56, H 4.20, N 11.90. LC-MS: calcd for $C_{11}H_{10}N_2O_4$ [M^+]: 234.06, found 235.25.

2.2.6 6-Phenyl-3-p-Tolyl-6H-1,2-Oxazine (5f)

Obtained from **1a** (0.67 g, 5 mmol), chloramine-T.$3H_2O$ (1.43 g, 5.1 mmol) and **4b** (0.52 g, 5.1 mmol) as pale brown oil, yield (0.6 g, 51.7%), ^1H NMR ($CDCl_3$, 300 MHz): δ 5.32 (m, 1H, C6), 6.27 (dd, *J* = 4.6 Hz, *J* = 10.1 Hz, 1H, C5), 6.72 (d, *J* = 10.2 Hz, 1H, C4), 7.12 (dd, J = 6 Hz, *J* = 2 Hz, 2H, CH), 7.20-7.22 (m, 5H, CH), 7.40 (t, *J* = 6 Hz, 2H, CH), 7.70-7.74 (m, 3H, CH).^{13}C NMR (300 MHz, $CDCl_3$); 90.4, 110.8, 127.9, 128.2, 129.1, 131.1, 133.2, 135.1, 136.8, 138.1, 156.4. IR (neat, cm^{-1}) ν1600, 1610, 2980, 3108. Anal. CHN: calcd C 81.68, H

5.57, N 5.95, found C 81.77, H 5.44, N 6.05. LC-MS: calcd for $C_{17}H_{15}NO$ [M^+]: 249.12, found 249.95.

2.2.7 3,6-Diphenyl-6H-1,2-Oxazine (5g)

Obtained from **1b** (0.74 g, 5 mmol), chloramine-T.3H_2O (1.43 g, 5.1 mmol) and **4b** (0.52 g, 5.1 mmol) as colorless solid, yield (0.7 g, 56.9%), m.p. 212-214 ^oC, ^1H NMR ($CDCl_3$, 300 MHz): δ 2.38 (s, 3H, CH_3), 5.33 (m, 1H, C6), 6.70 (d, *J* = 10.2 Hz, 1H, C4), 6.30 (dd, *J* = 4.6 Hz, *J* = 10.1, 1H, C5), 7.30 (t, *J* = 6.1Hz, 2H, CH), 7.65-7.68 (m, 3H, CH), 8.33 (d, *J* = 8.9 Hz, 2H, CH), 8.37 (d, *J* = 8.9 Hz, 2H, CH),^{13}C NMR (300 MHz, $CDCl_3$); 24.4, 90.5, 110.9, 125.4, 127.9, 129.3, 131.2, 133.2, 135.5, 141.2, 156.4. IR (neat, cm^{-1}) ν1370, 1590, 1620, 2980, 3080. Anal. CHN: calcd C 81.90, H 6.06, N 5.62, found C 81.80, H 6.24, N 4.51. LC-MS: calcd for $C_{16}H_{13}NO$ [M^+]: 235.10, found 235.95.

2.2.8 3-(4-Chlorophenyl)-6-Phenyl-6H-1,2-Oxazine (5h)

Obtained from **1c** (0.84 g, 5 mmol), chloramine-T.3H_2O (1.43 g, 5.1 mmol) and **4b** (0.52 g, 5.1 mmol) as a colorless solid, yield (0.7 g, 52.6%), m.p. 131-132^oC, ^1H NMR ($CDCl_3$, 300 MHz): δ 5.35 (m, 1H, C6), 6.71 (d, *J* = 10.2 Hz, 1H, C4), 6.31 (dd, *J* = 4.6 Hz, *J* = 10.1 Hz, 1H, C5), 7.30 (t, *J* = 6 Hz, 2H, CH), 7.42 (d, *J* = 8.7 Hz, 2H), 7.63 (d, *J* = 8.7 Hz, 2H, CH), 7.75-7.78 (m, 3H, CH).^{13}C NMR (300 MHz, $CDCl_3$); 90.4, 110.7, 126.6, 127.9 128.9, 129.9, 133.2, 135.5, 138.9, 146.4, 156.3. IR (KBr pellets cm^{-1}) ν1580, 1615, 2965, 3100. Anal. CHN: calcd C 71.25, H 4.48, N 5.19, found C 71.40, H 4.34, N 5.40. LC-MS: calcd for $C_{16}H_{12}ClNO$ [M^+]: 269.06, found 271.05.

2.2.9 3-(4-Methoxyphenyl)-6-Phenyl-6H-1,2-Oxazine (5i)

Obtained from **1d** (0.82 g, 5 mmol), chloramine-T.3H_2O (1.43 g, 5.1 mmol) and **4b** (0.52 g, 5.1 mmol) as a brown oil, yield (0.8 g, 61%),^1H NMR ($CDCl_3$, 300 MHz): δ 3.77 (s, 3H, OCH_3), 5.30 (m, 1H, OCH), 6.72 (d, *J* = 10.2 Hz, 1H, C4), 6.28 (dd, *J* = 4.6 Hz, *J* = 10.1 Hz, 1H, C5), 6.90 (dd, *J* = 7 Hz, *J* = 2 Hz, 2H, CH), 7.33 (t, *J* = 6 Hz, 2H, CH), 7.55-7.65 (m, 3H, CH), 7.70 (dd, *J* = 7 Hz, *J* = 2 Hz, 2H, CH), ^{13}C NMR (300 MHz, $CDCl_3$); 58.7, 90.7, 110.5, 112.8, 122.5, 127.6, 129.9, 130.3, 133.2, 134.9, 140.1, 156.3, 166.1. IR (neat, cm^{-1}) ν1240, 1600, 1612, 2830, 2945, 3000, 3065. Anal. CHN: calcd C 76.96, H 5.70, N 5.28, found C 76.90, H 5.84, N 5.40. LC-MS: calcd for $C_{17}H_{15}NO_2$ [M^+]: 265.11, found 265.95.

2.2.10 3-(4-Nitrophenyl-6-Phenyl-6H-1,2-Oxazine (5j)

Obtained from **1e** (0.9 g, 5 mmol), chloramine-T.3H_2O (1.43 g, 5.1 mmol) and **4b** (0.52 g, 5.1 mmol) as a pale yellow oil, yield (0.8 g, 57.1%), ^1H NMR ($CDCl_3$, 300 MHz): δ 5.35 (m, 1H, C6), 6.72 (d, *J* = 10.2 Hz, 1H, C4), 6.30 (dd, *J* = 4.6 Hz, *J* = 10.1 Hz, 1H, C5), 7.40 (t, *J* = 6 Hz, 2H, CH), 7.61-7.64 (m, 3H, CH), 7.90 (d, 2H, *J* = 8.8 Hz), 8.29 (d, 2H, *J* = 8.8 Hz).^{13}C NMR (300 MHz, $CDCl_3$); 90.7, 110.7, 125.5, 127.8, 128.9, 130.6, 132.3, 135.5, 138.7, 146.6, 152.6, 156.4. IR (neat, cm^{-1}) ν1345, 1520, 1580, 1610, 3075, 3110. Anal. CHN: calcd C 68.56, H 4.32, N 9.99, found C 68.67, H 4.24, N 9.80. LC-MS: calcd for $C_{16}H_{12}N_2O_3$ [M^+]: 280.08, found 280.93.

2.2.11 Ethyl-3-Phenyl-6H-1,2-Oxazine-6-Carboxylate (5k)

Obtained from **1a** (0.67 g, 5 mmol), chloramine-T.3H_2O (1.43 g, 5.1mmol) and **4c** (0.5g, 5.1 mmol) as a colorless solid, yield (0.6 g, 52.6%), m.p. 131-132 ^oC,^1H NMR ($CDCl_3$, 300 MHz): δ 1.38 (t, *J* = 7.2 Hz, 3H, -CO_2-CH_2-CH_3), 4.30 (q, *J* = 7.2 Hz, 2H, OCH_2), 5.10 (d, *J* = 4.5 Hz, 1H, C6), 6.26 (dd, *J* = 4.6 Hz, *J* = 10.1, 1H, C5), 6.69 (d, *J* = 10.2 Hz, 1H, C4), 7.33 (t, *J* = 6 Hz, 2H, CH), 7.64-7.67 (m, 3H, CH).^{13}C NMR (300 MHz, $CDCl_3$); 16.6, 65.5, 93.7, 110.6, 125.6, 127.9, 129.9, 131.3, 135.5, 156.5, 175.4. IR (KBr pellets cm^{-1}) ν 1375, 1440, 1600, 1615, 1745, 2975, 3100. Anal. CHN: calcd C 67.52, H 5.67, N 6.06, found C 67.59, H 5.54, N 6.20. LC-MS: calcd for $C_{13}H_{13}NO_3$ [M^+]: 231.09, found 232.05.

2.2.12 Ethyl-3-p-Tolyl-6H-1,2-Oxazine-6-Carboxylate (5l)

Obtained from **1b** (0.74 g, 5 mmol), chloramine-T.3H_2O (1.43 g, 5.1 mmol) and **4c** (0.5 g, 5.1 mmol) as brown solid, yield (0.7 g, 57.8%), m.p. 131-132 ^oC, ^1H NMR ($CDCl_3$, 300 MHz): δ 1.40 (t, *J* = 7.2 Hz, 3H, -CO_2-CH_2-CH_3), 2.36 (s, 3H, CH_3), 4.42 (q, *J* = 7.2 Hz, 2H, OCH_2), 5.12 (d, *J* = 4.5 Hz, 1H, C6), 6.29 (dd, *J* = 4.6, *J* = 10.1 Hz, 1H, C5), 6.68 (d, *J* = 10.2, 1H, C4), 7.20 (dd, *J* = 6 Hz, *J* = 2 Hz, 2H, CH), 7.60 (dd, *J* = 6 Hz, *J* = 2 Hz, 2H, CH).^{13}C NMR (300 MHz, $CDCl_3$); 17.7, 24.4, 65.5, 93.9, 110.7, 127.9, 128.8, 133.3, 141.9, 156.4, 175.5. IR (KBr pellets cm^{-1}) ν 1370, 1445, 1580, 1610, 1740, 2980, 3110. Anal. CHN: calcd C 68.56, H 6.16, N 5.71, found C 68.70, H 6.04, N 5.76. LC-MS: calcd for $C_{14}H_{15}NO_3$ [M^+]: 245.11, found 246.04.

2.2.13 Ethyl-3-(4-Chlorophenyl)-6H-1,2-Oxazine-6-Carboxylate (5m)

Obtained from **1c** (0.84 g, 5 mmol), chloramine-T.3H_2O (1.43 g, 5.1 mmol) and **4c** (0.5 g, 5.1 mmol) as a brown solid, yield (0.8 g, 61%), m.p. 131-132 ^oC, ^1H NMR ($CDCl_3$, 300 MHz): δ 1.39 (t, *J* = 7.2 Hz, 3H,

-CO_2-CH_2-CH_3), 4.38 (q, *J* = 7.2 Hz, 2H, OCH_2), 5.11 (d, *J* = 4.5 Hz, 1H, C6), 6.26 (dd, *J* = 4.6 Hz, *J* = 10.1 Hz, 1H, C5), 6.70 (d, *J* = 10.2 Hz, 1H, C4), 7.35 (d, *J* = 8.8 Hz, 2H, CH), 7.67 (d, *J* = 8.8 Hz, 2H, CH).^{13}C NMR (300 MHz, $CDCl_3$); 17.7, 65.5, 93.7, 110.6, 127.8, 129.9, 133.2, 135.5, 139.9, 156.3, 176.6. IR (KBr pellets cm^{-1}) ν 1375, 1440, 1590, 1615, 1745, 2975, 3120. Anal. CHN: calcd C 58.77, H 4.55, N 5.27, found C 58.55, H 4.74, N 5.13. LC-MS: calcd for $C_{13}H_{12}ClNO_3$ [M^+]: 265.05, found 267.03.

2.2.14 Ethyl-3-(4-Methoxyphenyl)-6H-1,2-Oxazine-6-Carboxylate (5n)

Obtained from **1d** (0.82 g, 5 mmol), chloramine-T.3H_2O (1.43 g, 5.1 mmol) and **4c** (0.5 g, 5.1 mmol) as a colorless solid, yield (0.7 g, 54.2%), m.p. 131-132 °C, ^{1}H NMR ($CDCl_3$, 300 MHz): δ 1.37 (t, *J* = 7.2Hz, 3H, -CO_2-CH_2-CH_3), 3.82 (s, 3H, OCH_3), 4.40 (q, *J* = 7.2 Hz, 2H, OCH_2), 5.14 (d, *J* = 4.5 Hz, 1H, C6), 6.31 (dd, *J* = 4.6 Hz, *J* = 10.1 Hz, 1H, C5), 6.71 (d, *J* = 10.2 Hz, 1H, C4), 6.80 (dd, *J* = 7 Hz, *J* = 2 Hz, 2H, CH), 7.60 (dd, *J* = 7 Hz, *J* = 2 Hz, 2H, CH).^{13}C NMR (300 MHz, $CDCl_3$); 17.7, 59.9, 63.4, 93.9, 110.9, 112.2, 124.5, 127.9, 132.2, 156.4 162.5, 176.7. IR (KBr pellets cm^{-1}) ν 1370, 1445, 1595, 1610, 1750, 2988, 3095. Anal. CHN: calcd C 64.36, H 5.79, N 5.36, found C 64.50, H 5.54, N 5.40. LC-MS: calcd for $C_{14}H_{15}NO_4$ [M^+]: 260.10, found 261.05.

2.2.15 Ethyl-3-(4-Nitrophenyl)-6H-1,2-Oxazine-6-Carboxylalate (5o)

Obtained from **1e** (0.9 g, 5 mmol), chloramine-T.3H_2O (1.43 g, 5.1 mmol) and **4c** (0.5 g, 5.1 mmol) as a pale yellow solid, yield (0.8 g, 58.3%), m.p. 131-132 °C, ^{1}H NMR ($CDCl_3$, 300 MHz): δ 1.40 (t, *J* = 7.2 Hz, 3H, -CO_2-CH_2-CH_3), 4.39 (q, *J* = 7.2 Hz, 2H, OCH_2), 5.15 (d, *J* = 4.5 Hz, 1H, C6), 6.29 (dd, *J* = 4.6, *J* = 10.1 Hz, 1H, C5), 6.73 (d, *J* = 10.2 Hz, 1H, C4), 8.30 (d, *J* = 8.9 Hz, 2H, CH), 8.34 (d, *J* = 8.9 Hz, 2H, CH).^{13}C NMR (300 MHz, $CDCl_3$); 17.7, 65.6, 93.3, 110.6, 127.9, 129.8, 130.9, 142.2, 153.4, 156.5, 176.8. IR (KBr pellets cm^{-1}) ν 1370, 1440, 1525, 1595, 1615, 2990, 3070, 3110. Anal. CHN: calcd C 56.52, H 4.38, N 10.14, found C 56.40, H 4.54, N 10.04. LC-MS: calcd for $C_{13}H_{12}N_2O_5$ [M^+]: 276.07, found 277.05.

2.2.16 3-Phenyl-6-Propyl-6H-1,2-Oxazine (5p)

Obtained from **1a** (0.67 g, 5 mmol), chloramine-T.3H_2O (1.43 g, 5.1 mmol) and **4d** (0.35 g, 5.1 mmol) as a brown solid, yield (0.6 g, 58.2%), m.p. 131-132 °C, ^{1}H NMR ($CDCl_3$, 300 MHz): δ 0.93 (s, 3H, CH_3), 1.37-1.42 (m, 4H, CH_2-CH_2), 4.20 (m, 1H, C6), 6.28 (dd, *J* = 4.6 Hz, *J* = 10.1 Hz, 1H, C5), 6.68 (d, *J* = 10.2 Hz, 1H, C4), 7.39 (t, *J* = 6 Hz, 2H, CH), 7.60-7.63 (m, 3H, CH).^{13}C NMR (300 MHz, $CDCl_3$); 16.2, 20.1, 30.3, 85.2, 110.9, 125.5, 127.9, 129.9, 132.8, 137.7, 156.3. IR (KBr pellets cm^{-1}) ν 1455, 1600, 1615, 2975, 3110. Anal. CHN: calcd C 77.58, H 7.51, N 6.96, found C 77.70, H 7.40, N 6.99. LC-MS: calcd for $C_{13}H_{15}NO$ [M^+]: 201.12, found 202.02.

2.2.17 6-Propyl-3-p-Tolyl-6H-1,2-Oxazine (5q)

Obtained from **1b** (0.74 g, 5 mmol), chloramine-T.3H_2O (1.43 g, 5.1 mmol) and **4d** (0.35 g, 5.1 mmol) as a brown solid, yield (0.6 g, 54.5%), m.p. 131-132 °C, ^{1}H NMR ($CDCl_3$, 300 MHz): δ 0.94 (t, 3H, CH_3), 1.39-1.44 (m, 4H, CH_2-CH_2), 2.35 (s, 3H, CH_3), 4.18 (m, 1H, C6), 6.28 (dd, *J* = 4.6 Hz, *J* = 10.1, 1H, C5), 6.70 (d, *J* = 10.2 Hz, 1H, CH2), 7.20 (dd, *J* = 7 Hz, *J* = 2 Hz, 2H, CH), 7.65 (dd, *J* = 7 Hz, *J* = 2 Hz, 2H, CH).^{13}C NMR (300 MHz, $CDCl_3$); 16.2, 20.4, 23.5, 30.1, 85.9, 110.7, 127.9, 130.3, 133.1, 143.2, 156.4. IR (KBr pellets cm^{-1}) ν 1375, 1450, 1600, 1610, 2985, 3105. Anal. CHN: calcd C 78.10, H 7.96, N 6.51, found C 78.30, H 7.84, N 6.64. LC-MS: calcd for $C_{14}H_{17}NO$ [M^+]: 215.13, found 216.05.

2.2.18 3-(4-Chlorophenyl)-6-Propyl-6H-1,2-Oxazine (5r)

Obtained from **1c** (0.84 g, 5 mmol), chloramine-T.3H_2O (1.43 g, 5.1 mmol) and **4d** (0.35 g, 5.1 mmol) as a colorless solid, yield (0.65 g, 53.7%), m.p. 131-132 °C, ^{1}H NMR ($CDCl_3$, 300 MHz): δ 0.92 (t, 3H, CH_3), 1.38-1.43 (m, 4H, CH_2-CH_2), 4.21 (m, 1H, C6), 6.24 (dd, *J* = 4.6 Hz, *J* = 10.1 Hz, 1H, C5), 6.72 (d, *J* = 10.2 Hz, 1H, C4), 7.42 (d, *J* = 8.7 Hz, 2H, CH), 7.46 (d, *J* = 8.7 Hz, 2H, CH). ^{13}C NMR (300 MHz, $CDCl_3$); 16.2, 20.4, 30.3, 85.4, 110.9, 127.8, 129.8, 131.2, 133.7, 137.7, 156.5. IR (KBr pellets cm^{-1}) ν 1440, 1600, 1615, 2965, 3112. Anal. CHN: calcd C 66.24, H 5.99, N 5.94, found C 66.40, H 5.94, N 5.84. LC-MS: calcd for $C_{13}H_{14}ClNO$ [M^+]: 235.08, found 237.02.

2.2.19 3-(4-Methoxyphenyl)-6-Propyl-6H-1,2-Oxazine (5s)

Obtained from **1d** (0.82 g, 5 mmol), chloramine-T.3H_2O (1.43 g, 5.1 mmol) and **4d** (0.35 g, 5.1 mmol) as a colorless solid, yield (0.7 g, 59.3%), m.p. 131-132 °C, ^{1}H NMR ($CDCl_3$, 300 MHz): δ 0.89 (t, 3H, CH_3), 1.38-1.44 (m, 4H, CH_2-CH_2), 3.82 (s, 3H, OCH_3), 4.20 (m, 1H, C6), 6.31 (dd, *J* = 4.6 Hz, *J* = 10.1 Hz, 1H, C5), 6.72 (d, *J* = 10.2 Hz, 1H, C4), 7.10 (dd, *J* = 8.7 Hz, *J* = 2 Hz, 2H, CH), 7.65 (dd, *J* = 6 Hz, *J* = 2 Hz, 2H, CH).^{13}C NMR (300 MHz, $CDCl_3$); 16.1, 20.7, 30.2, 58.6, 85.1, 110.5, 114.4, 127.9, 130.1, 133.1, 156.3, 160.7. IR (KBr pellets cm^{-1}) ν 1240, 1445, 1600, 2955, 3040, 3075. Anal. CHN: calcd C 72.70, H 7.41, N 6.06, found C 72.60,

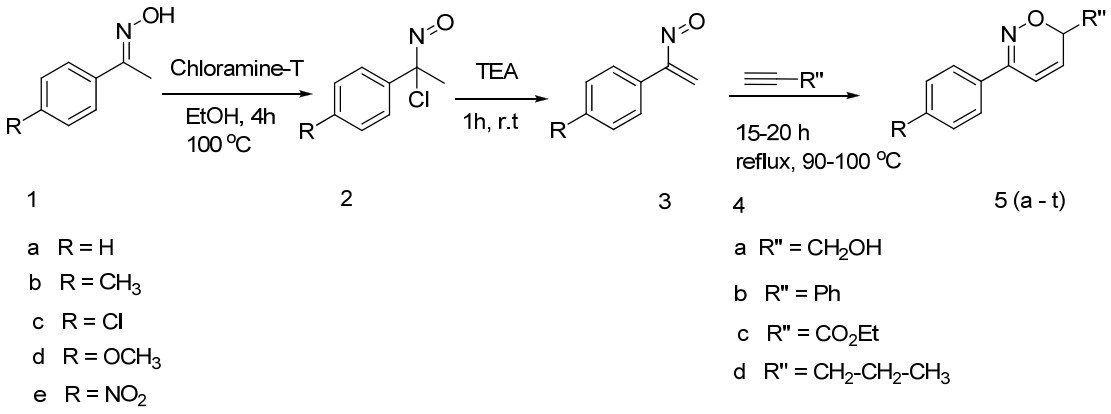
H 7.54, N 6.14. LC-MS: calcd for $C_{14}H_{17}NO_2$ [M^+]: 231.13, found 232.05.

2.2.20 3-(4-Nitrophenyl)-6-Propyl-6H-1,2-Oxazine (5t)

Obtained from **1e** (0.9 g, 5 mmol), chloramine-T.3H_2O (1.43 g, 5.1 mmol) and **4d** (0.35 g, 5.1 mmol) as a pale yellow solid, yield (0.7 g, 55.5%), m.p. 131-132 °C, ^{1}H NMR ($CDCl_3$, 300 MHz): δ 0.90 (t, 3H, CH_3), 1.40-1.46 (m, 4H, CH_2-CH_2), 4.22 (m, 1H, C6), 6.32 (dd, J = 4.6, J = 10.1, 1H, C5), 6.70 (d, J = 10.2, 1H, C4), 7.80 (d, J = 8.8 Hz, 2H, CH), 8.15 (d, J = 8.8 Hz, 2H, CH). ^{13}C NMR (300 MHz, $CDCl_3$); 16.2, 20.4, 30.3, 85.2, 110.8, 122.3, 127.9, 129.8, 138.8, 153.3, 156.4. IR (KBr pellets cm^{-1}) ν 1435, 1520, 1600, 1615, 2985, 3035, 3075. Anal. CHN: calcd C 63.40, H 5.73, N 11.38, found C 63.50, H 5.54, N11.44. LC-MS: calcd for $C_{13}H_{14}N_2O_3$ [M^+]: 246.10, found 247.85.

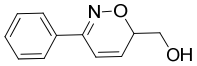
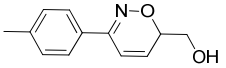
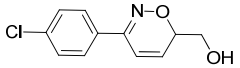
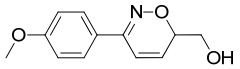
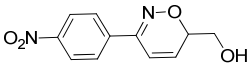
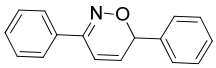
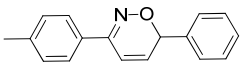
3. Results and Discussion

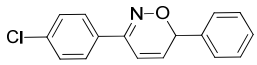
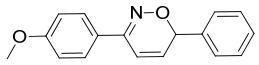
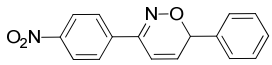
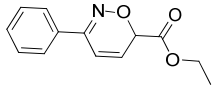
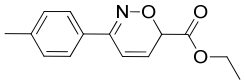
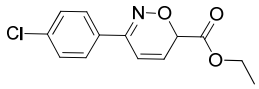
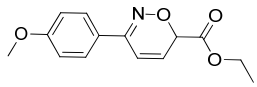
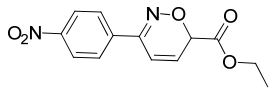
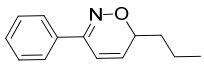
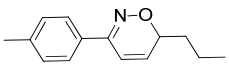
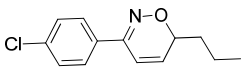
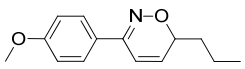
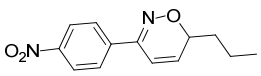
The compounds **1(a-e)** were synthesized by the reaction of ketones with hydroxylamine hydrochloride in the presence of sodium acetate (Brian et al., 2006). Chloramine-T was used as an effective reagent for the generation of α-nitrosoolefins from the corresponding ketoximes **1(a-e)** (Gaonkar & Rai, 2005; Manjula et al., 2009), which subsequently underwent hetero Diels-Alder reaction with terminal acetylenes **4(a-d)**, to give 6*H*-1,2-Oxazine derivatives **5(a-t)** in good yield (Table1).



Scheme 1. One-pot synthesis of 6*H*-1,2-oxazine derivatives

Table 1. Structural formulae, time of reaction to convert compounds 3 to 5 and % yields of the synthesized compounds **5 (a-t)**

Compound	6H-1,2-Oxazine	Time(3→5)hrs	Yield %
5a		15	64
5b		15	60
5c		17	54
5d		16	64
5e		18	60
5f		15	51
5g		16	56

5h		16	52
5i		15	61
5j		16	57
5k		16	52
5l		16	57
5m		17	61
5n		16	54
5o		15	68
5p		16	58
5q		16	54
5r		16	53
5s		19	59
5t		18	55

The identities of compounds **(5a–t)** were established by their ^{1}H NMR, ^{13}C NMR, IR, elemental analysis and MS. Taking **(5a)** as an example, the ^{1}H NMR spectrum of (**5a)** displays broad band at 2.13 due to OH. The CH_2 displays multiplets at 3.75-3.93, while the oxazine ring protons appear as a doublet at 6.69, doublet of doublet at 6.33 and multiplets at 4.20 ppm for the respective protons in the position 4, 5 and 6. The five protons of phenyl groups appeared as triplets at δ 7.40 with coupling constant 6Hz and multiplets at 7.66-7.69 ppm. The IR spectra of 6H-1,2-oxazine derivative **(5a)** showed absorption at 1615 cm^{-1} owing to the ring nitrogen (C=N) and 1600 cm^{-1} due to aromatic ring. The OH group appears as an absorption band at 3340 cm^{-1}. In the ^{13}C NMR spectra all oxazines gave consistent signals for the newly formed ring carbons. For instance the signals in the region due to C_6 appear in the region δ 82.4-89.9 ppm while C_5, C_4 and C_3 appears in the region 90.1, 110.9 and 156.2. The mass spectrum of **(5a)** showed the molecular ion peak at m/z 189.08. The formation of the products was further supported by elemental analyses. 1,2-Oxazine can be used as a synthone in the synthesis of γ-hydroxy ketones, 1,4-diketones etcetera (Sunil & Rai, 2012).

4. Conclusions

In conclusion a new series of 6*H*-1,2-oxazine derivatives were synthesized from ketoximes and terminal alkynes.

Chloramine-T was used to accomplish this reaction. Yields were moderate to good. Instead of the formation of 4*H*-1,2-Oxazine we observed that this reaction yielded 6*H*-1,2-Oxazine.This was attributed to the formation of a conjugated diene like system.

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