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Synthesis and Identification of Some New 2,3-Disubstituted 1,3-Oxazepine-4,7-dione Derivatives Containing Azo Group and 1,3,4-Thiadiazole Moiety

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Azoaldehyde derivatives (**1a-f**) were prepared through coupling reactions between diazonium salts of six primary aromatic amines and alkaline solution of 2-hydroxy benzaldehyde. Compounds (**1a-f**) were then introduced in acid-catalyzed condensation reactions with 2-amino-5-mercapto-1,3,4-thiadiazole to obtain six new azoimines (**2a-f**). (2+5) Cycloaddition of (**2a-f**) with each maleic and phthalic anhydrides respectivily gave nine new oxazepines (**3a-f**) and (**4b, 4d, 4e**). The synthesized compounds might have some biological activity.

Keywords: 1,3,4-Thiadiazole, Azoimines, (2+5) Cycloaddition, 1,3-Oxazepine.

INTRODUCTION

Oxazepine refers to any seven-membered ring containing an oxygen and nitrogen atom. The 1,3-oxazepine is a branch of many types of the heterocyclic oxazepine[1-3]. The core structure of 1,3-oxazepine-4,7-dione consists of unsaturated seven-membered ring along with two carbonyl groups. A large number of oxazepine derivatives are known to have wide spectrum of biological activity. For example, 2-chloro-11-piperazine-1-y)-dibenzo*[b,f]*[1,4]oxazepine (amoxapine) **A** is used as active drug for despression[4] and schizophrenia[5] (Fig. 1). 7-Hydroxy amoxapine **B** used as an effective drug on CNS system[6]. 1,4-Oxazepine derivatives **C** show ability to reduce the sensitivity of the receptors in cell membrane[7]. 1,4-Oxazepine derivative **D** has been investigated as inhibitors for telomerase enzyme which has effective role in cancer cell proliferation[8]. Oxazepine derivative **E** showed measurable antifungal activity[9].

Azo compounds are highly important, well known and widely used substances in the textile, paper, coloring agents for foods and cosmetics industries. Other applications include emerging technologies like liquid crystals, organic photoconductors and non-linear optics[10,11]. Azo compounds are known to be involved in a number of biological reactions such as inhibition of DNA, RNA and protein synthesis[12], azo compounds were reported to show a variety of biological activities including antibacterial[13], antifungal[14], antiviral[15] and anti-inflammatory[16] activities.

It was shown that substituted 1,3,4-thiadiazoles exhibit antimicrobial[17], anticancer[18], while other compounds act on the CNS as anticonvulsants[19], effect on Tyrosinase enzyme[20]. A family of selective 1,3,4-thiadiazoles are phosphodiesterase inhibitors[21] and selective orally active cyclooxygenase inhibitors[22]. 1,3,4-Thiadiazoles are thus a group of heterocycles whose derivatives are important in industry, medicine and agriculture[23,24]. Thus, in this article, we reported here the synthesis of 1,3-oxazepine derivatives containing biologically active azo group and 1,3,4-thiadiazole moiety, which probably have some biological activity.

EXPERIMENTAL

The chemicals used in this work were obtained from Fluka, Sigma Aldrich, GCC, Merck and S.D. Fine and were used without further purification. Silica TLC plates were used with an aluminum backing (0.2 mm, 60 F_{254}). The reactions were monitored by TLC and visualized by development of the TLC plates with an alkaline potassium permanganate dip or with iodine vapour. Melting points were determined on an Electro thermal Stuart SMP 30 capillary melting point apparatus. Infrared spectra were recorded on SHIMADZU FTIR-8400S infrared spectrophotometer as potassium bromide discs. ^{1}H NMR spectra were collected on NMR spectrometer, Bruker 2009 spectrometer at 400 MHz in DMSO-d_6 as solvent and TMS as an internal standard at Kashan University, Iran. Elemental analysis (CHNS) was carried out with Micro analytical unit, Euro vector S.P.A. E.A 3000-CHNS Elemental analyzer at Kufa University. Azoaldehyde derivatives **1a-f** was prepared following the method described by Acton[25].

Synthesis of azoimine derivatives (2a-f): Azoaldehyde derivatives **1a-f** (0.003 mol) was dissolved in 15 mL of absolute

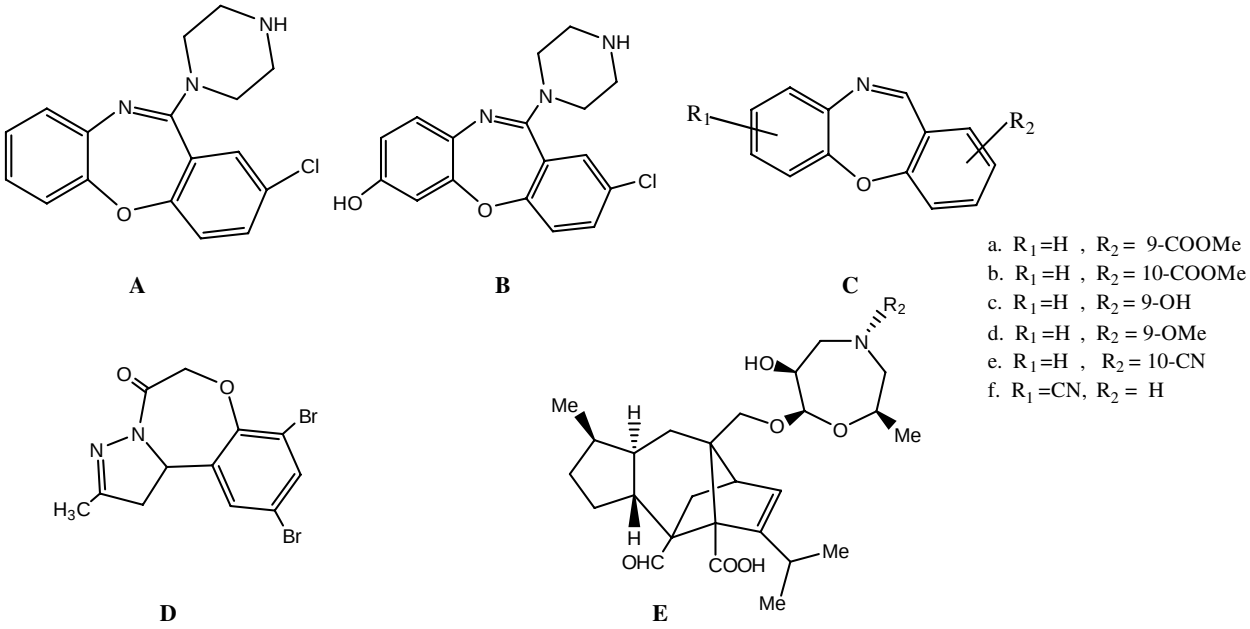


Fig. 1. Structure of some bioactive oxazepine derivatives

ethanol containing two drops of glacial acetic acid, then (2-amino-5-mercapto-1,3,4-thiadiazole) (0.399 g, 0.003 mol) was dissolved in 15 mL of absolute ethanol and added drop wise. The reaction mixture was refluxed with stirring on a water bath at 70 °C for 10-14 h and monitored by TLC. The mixture was then allowed to cool down to room temperature, the coloured precipitate was filtered and recrystallized from ethanol.

2-[{(5-Mercapto-1,3,4-thiadiazol-2-yl)imino}methyl]-4-(pyridin-3-yldiazenyl)phenol (2a): IR (cm^{-1}): 3281 (ν_{O-H}), 3057 ($\nu_{C-H,\ aromatic\ rings}$), 2965 ($\nu_{C-H,\ imine}$), 1595 ($\nu_{C=N}$), 1496 and 1452 ($\nu_{C=N\ and}\ \nu_{C=C,\ aromatic\ rings}$), 1415 ($\nu_{N=N}$), 1352 and 1286 ($\nu_{C-N}$), 835, 780, 754 and 696 ($\delta_{o.o.p.\ C-H,\ benzene\ rings}$).

4-[(4-Chlorophenyl)diazenyl]-2-[{(5-mercapto-1,3,4-thiadiazol-2-yl) imino}methyl]phenol (2b): IR (cm^{-1}): 3269 (ν_{O-H}), 3082 ($\nu_{C-H,\ benzene\ rings}$), 1647 ($\nu_{C=N}$), 1579 and 1498 ($\nu_{C=N\ and}\ \nu_{C=C,\ aromatic\ rings}$), 1392 and 1288($\nu_{C-N}$), 1134 ($\nu_{C-Cl}$), 921, 835 and 721 ($\delta_{o.o.p.\ C-H,\ benzene\ rings}$).

4-[(2,4-Dichlorophenyl)diazenyl]-2-[{(5-mercapto-1,3,4-thiadiazol-2-yl)imino}methyl]phenol (2c): IR (cm^{-1}): 3260 (ν_{O-H}), 3076 ($\nu_{C-H,\ benzene\ rings}$), 2874 ($\nu_{C-H,\ imine}$), 1608 ($\nu_{C=N}$), 1570, 1523 and 1475 ($\nu_{C=N\ and}\ \nu_{C=C,\ aromatic\ rings}$), 1344 and 1269 ($\nu_{C-N}$), 1101 ($\nu_{C-Cl}$), 894, 840, 804, 742, 702 and 674 ($\delta_{o.o.p.\ C-H,\ benzene\ rings}$).

2-[{(5-Mercapto-1,3,4-thiadiazol-2-yl)imino}methyl]-4-((4-nitrophenyl)diazenyl)phenol(2d): IR (cm^{-1}): 3248 (ν_{O-H}), 3068 ($\nu_{C-H,\ benzene\ rings}$), 2851 ($\nu_{C-H,\ imine}$), 1631 ($\nu_{C=N}$), 1496 br ($\nu_{C=N,}\ \nu_{C=C,\ aromatic\ rings\ and}\ \nu_{as.}\ NO_2$, $_{vib.\ coupling}$),1348 br ($\nu_{C-N and}$ $\nu s.\ NO_{2,vib.\ coupling}$), 866 ($\delta_{o.o.p.\ C-H,\ benzene\ rings}$).

2-[{(5-Mercapto-1,3,4-thiadiazol-2-yl)imino}methyl]-4-[(4-methoxyphenyl)diazenyl]phenol (2e): IR (cm^{-1}): 3261 (ν_{O-H}), 3068 ($\nu_{C-H,\ benzene\ rings}$), 2958($\nu as.C-H,\ CH_3$), 2862($\nu s.C-H,\ CH_3$), 1593 ($\nu_{C=N}$), 1498 ($\nu_{C=N\ and}\ \nu_{C=C,\ aromatic\ rings,\ vib.\ coupling}$), 1253 ($\nu_{C-N}$), 1043 ($\nu_{S.\ C-O-C,\ ether}$) 844, 761, 688($\delta_{o.o.p.\ C-H,\ benzene\ rings}$).

4-[(2,4-Dimethylphenyl)diazenyl]-2-[{(5-mercapto-1,3,4-thiadiazol-2-yl) imino}methyl]phenol (2f): IR (cm^{-1}): 3427 and 3271 (ν_{O-H}), 3088 ($\nu_{C-H,\ benzene\ rings}$), 2956 ($\nu as.C-H,\ CH_3$), 2782 ($\nu s.C-H,\ CH_3$), 2720 ($\nu_{C-H,\ imine}$), 2688 ($\nu_{S-H}$), 1639 ($\nu_{C=N}$), 1610 and 1506 ($\nu_{C=N\ and}\ \nu_{C=C,\ aromatic\ rings}$), 1396 ($\delta s.C-H,\ CH_3$), 1317 ($\nu_{C-N}$), 872, 812 and 682 ($\delta_{o.o.p.\ C-H,\ benzene\ rings}$).

Synthesis of 1,3-oxazepine-4,7-dione derivatives (3a-f): A mixture of azoimine derivatives **2a-f** (0.002 mol) and maleic anhydride (0.196 g, 0.002 mol) in dry benzene (20 mL) was refluxed on a water bath at70 ºC for 20-24 h and monitored by TLC. The mixture was then allowed to cool down to room temperature, dried upon filter paper then in oven and recrystallized from ethanol.

2-[2-Hydroxy-5-(pyridin-3-yldiazenyl)phenyl]-3-(5-mercapto-1,3,4-thiadiazol-2-yl)-2,3-dihydro-1,3-oxazepine-4,7-dione (3a): IR (cm^{-1}): 3459 (ν_{O-H}), 3059 ($\nu_{C-H,\ benzene\ rings}$), 2920 ($\nu_{C-H,\ CH=CH,\ oxazepine}$), 2607 ($\nu_{S-H}$), 1708 ($\nu_{C=O,\ O=C-O,oxazepine}$), 1637 ($\nu_{C=O,\ O=C-N,oxazepine}$), 1593, 1570 and 1462 ($\nu_{C=N\ and}\ \nu_{C=C,\ aromatic\ rings}$), 1433 ($\nu_{N=N}$), 1265 ($\nu_{C-N}$), 864, 834 and 780 ($\delta_{o.o.p.\ C-H,\ benzene\ rings}$).

^{1}H NMR (400 MHz, DMSO-d_6): δ = 2.509 (DMSO solvent), 2.770 (s, 1H, 1 × S-H), 6.266 (s, 1H, 1 × olefinic = C-H proton bonded with O–C=O inside oxazepine ring), 6.635 (s, 1H, 1 × olefinic =C-H proton bonded with O=C–N inside oxazepine ring), 6.962-8.411 (Ar-H and C-H proton of oxazepine ring), 8.833-8.848 (d, 1H, 1 × O-H phenolic proton). 6.962-7.000 (1H, 1 × H_a), 7.022-7.058 (1H, 1 × H_b), 7.234-7.256 (d, 1H, 1 × H_c), 7.476 (s, 1H, 1 × H_d, oxazepine), 7.786-7.801 (d, 1H, 1 × H_e), 8.157-8.186 (d, 1H, 1 × H_f), 8.234-8.273 (1H, 1 × H_g), 8.411(s, 1H, 1 × H_h). Elemental analysis (%) calc. for $C_{18}H_{12}N_6O_4S_2$; C 49.08, H 2.75, N 19.08, S 14.56; Found: C 49.47, H 2.36, N 19.16, S 14.10.

2-[5-{(4-Chlorophenyl)diazenyl}-2-hydroxyphenyl]-3-(5-mercapto-1,3,4-thiadiazol-2-yl)-2,3-dihydro-1,3-oxazepine-4,7-dione (3b): IR (cm^{-1}): 3215 (ν_{O-H}), 2872 ($\nu_{C-H,\ oxazepine}$), 1718 ($\nu_{C=O,\ O=C-O,oxazepine}$), 1668 ($\nu_{C=O,\ O=C-N,oxazepine}$), 1622 ($\nu_{C=C,\ oxazepine}$), 1573 and 1477 ($\nu_{C=N\ and}\ \nu_{C=C,\ aromatic\ rings}$), 1407 ($\nu_{N=N}$), 1381 and 1284 ($\nu_{C-N}$), 1089 ($\nu_{C-Cl}$), 904, 833, 771 and 734 ($\delta_{o.o.p.\ C-H,\ benzene\ rings}$).

^{1}H NMR (400 MHz, DMSO-d_6): δ = 2.505-2.513 (DMSO solvent),6.281 (s, 1H, 1 × olefinic =C-H proton bonded with O–C=O inside oxazepine ring), 6.65 (s, 1H, 1 × olefinic =C-H proton bonded with O=C–N inside oxazepine ring), 7.196-8.191 (Ar-H and C-H proton of oxazepine ring), 11.590 (s, 1H, 1 × O-H phenolic proton).7.196-7.218 (d, 1H, 1 × H_a), 7.635-7.657 (d, 2H, 2 × H_b), 7.870- 7.892 (d, 1H, 1 × H_c), 8.088 (s, 1H, 1 × H_d), 8.184-8.191 (d, 2H, 2 × H_e). Elemental analysis (%) calc. for $C_{19}H_{12}N_5O_4S_2Cl$, C 48.15, H 2.55, N 14.78, S 13.53; Found: C 48.70, H 2.72, N 14.21, S 13.97.

2-[5-{(2,4-Dichlorophenyl)diazenyl}-2-hydroxyphenyl]-3-(5-mercapto-1,3,4-thiadiazol-2-yl)-2,3-dihydro-1,3-oxazepine-4,7-dione (3c): IR (cm^{-1}): 3259 (ν_{O-H}), 3091 ($\nu_{C-H,\ benzene\ rings}$), 2928 ($\nu_{C-H,\ CH=CH,\ oxazepine}$), 2863 ($\nu_{C-H,\ oxazepine}$), 1664 ($\nu_{C=O,\ O=C-O\ and\ O=C-N,vib.\ Coupling,\ oxazepine}$), 1620 ($\nu_{C=C,\ oxazepine}$), 1586 and 1492 ($\nu_{C=N\ and}$ $\nu_{C=C,\ aromatic\ rings}$), 1375, 1323 and 1286 ($\nu_{C-N}$), 1101 ($\nu_{C-Cl}$), 900, 875, 829, 769, 753 and 700 ($\delta_{o.o.p.\ C-H,\ benzene\ rings}$).

^{1}H NMR (400 MHz, DMSO-d_6): δ =2.505-2.513 (DMSO solvent), 6.280 (s, 1H, 1 × olefinic =C-H proton bonded with O–C=O inside oxazepine ring), 6.635 (s, 1H, 1 × olefinic =C-H proton bonded with O=C–N inside oxazepine ring), 7.221-8.124 (Ar-H and C-H proton of oxazepine ring), 8.214 (s, 1H, 1 × O-H phenolic proton). 7.221-7.243 (d, 1H, 1 × H_a), 7.551-7.556 (d, 1H, 1 × H_b), 7.573- 7.578 (d, 1H, 1 × H_c, oxazepine), 7.681-7.702 (d, 1H, 1 × H_d), 7.894-7.899 (d, 1H, 1 × H_e), 8.095-8.102 (d, 1H, 1 × H_f), 8.117-8.124 (d, 1H, 1 × H_g). Elemental analysis (%) calc. for $C_{19}H_{11}N_5O_4S_2Cl_2$, C 44.89, H 2.18, N 13.78, S 12.61; Found: C 44.76, H 2.41, N 13.70, S 13.10.

2-[2-Hydroxy-5-{(4-nitrophenyl)diazenyl}phenyl]-3-(5-mercapto-1,3,4-thiadiazol-2-yl)-2,3-dihydro-1,3-oxazepine-4,7-dione (3d): IR (cm^{-1}): 3163 and 3103 (ν_{O-H}), 3076 ($\nu_{C-H,\ benzene\ rings}$), 2868 ($\nu_{C-H,\ oxazepine}$), 1722 ($\nu_{C=O,\ O=C-O,\ oxazepine}$), 1666 ($\nu_{C=O,\ O=C-N,oxazepine}$), 1612 ($\nu_{C=C,\ oxazepine}$), 1579 and 1479 ($\nu_{C=N\ and}$ $\nu_{C=C,\ aromatic\ rings}$), 1527 ($\nu as.NO_2$), 1344 ($\nu s.NO_2$), 1375, 1319 and 1284 ($\nu_{C-N}$), 906, 854, 750, 719 and 688 ($\delta_{o.o.p.\ C-H,\ benzene\ rings}$).

^{1}H NMR (400 MHz, DMSO-d_6): δ = 2.505-2.513 (DMSO solvent),3.388 (H_2O in DMSO), 7.198-7.220 (d, 2H, 2 × olefinic =C-H protons inside oxazepine ring), 8.002-8.399 (Ar-H and C-H proton of oxazepine ring), 11.765 (s, 1H, 1 × O-H phenolic proton).8.002-8.024 (d, 1H, 1 × H_a), 8.102-8.131 (t, 2H, 1 × H_b+1 × H_c, oxazepine ring), 8.209-8.215 (d, 3H, 3 × H_d), 8.376-8.399 (d, 2H, 2 × H_e). Elemental analysis (%) calc. for $C_{19}H_{12}N_6O_6S_2$, C 47.10, H 2.50, N 17.35, S 13.24; Found: C 46.94, H 2.78, N 17.46, S 13.09.

2-[2-Hydroxy-5-{(4-methoxyphenyl)diazenyl}phenyl]-3-(5-mercapto-1,3,4-thiadiazol-2-yl)-2,3-dihydro-1,3-oxazepine-4,7-dione (3e): IR (cm^{-1}): 3265 (ν_{O-H}), 3070 ($\nu_{C-H,\ benzene\ rings}$), 2968 ($\nu_{as.}$C-H, CH_3), 2870 ($\nu_{s.}$C-H, CH_3), 2584 ($\nu_{S-H,\ thioenol\ form}$), 1701 ($\nu_{C=O,\ O=C-O\ and\ O=C-N,vib.\ Coupling,oxazepine}$), 1600 and 1502 ($\nu_{C=N\ and}$ $\nu_{C=C,\ aromatic\ rings}$), 1352, 1273 ($\nu_{C-N}$), 1247 ($\nu_{as.\ C-O-C,\ ether}$), 1030($\nu s._{\ C-O-C,\ ether}$), 896, 837, 788, 750 and 690($\delta_{o.o.p.\ C-H,\ benzene\ rings}$).

^{1}H NMR (400 MHz, DMSO-d_6): δ = 2.509 (DMSO solvent), 3.867 (s, 3H, 1 × H_3C-O), 6.204 (s, 1H, 1 × olefinic =C-H proton bonded with O–C=O inside oxazepine ring), 6.637 (s, 1H, 1 × olefinic =C-H proton bonded with O=C–N inside oxazepine ring), 7.117-8.054 (Ar-H and C-H proton of oxazepine ring), 8.384 (s, 1H, 1 × O-H phenolic proton).7.117 (d, 1H, 1 × H_a), 7.198 (d, 2H, 2 × H_b), 7.369 (s, 1H, 1 × H_c, oxazepine ring), 7.772 (s, 1H, 1 × H_d), 7.873 (d, 1H, 1 × H_e), 8.026-8.032 and 8.048-8.054 (dd, 2H, 2 × H_f). Elemental analysis (%) calc. for $C_{20}H_{15}N_5O_5S_2$, C 51.16, H 3.22, N 14.92, S 13.66; Found: C 51.44, H 3.34, N 14.79, S 13.04.

2-[5-{(2,4-Dimethylphenyl)diazenyl}-2-hydroxyphenyl]-3-(5-mercapto-1,3,4-thiadiazol-2-yl)-2,3-dihydro-1,3-oxazepine-4,7-dione (3f): IR (cm^{-1}): 3410(ν_{O-H}), 3060($\nu_{C-H,\ benzene\ rings}$), 2980 and 2929 ($\nu as.$C-H, CH_3), 2868 ($\nu s.$ C-H, CH_3), 2551 (ν_{S-H}), 1720 ($\nu_{C=O,\ O=C-O\ and\ O=C-N,vib.\ Coupling,oxazepine}$), 1626 ($\nu_{C=C,\ oxazepine}$), 1539 and 1506 ($\nu_{C=N\ and}$ $\nu_{C=C,\ aromatic\ rings}$), 1454 ($\delta as.$C-H, CH_3), 1381 ($\delta s.$C-H, CH_3), 1257 and 1236 (ν_{C-N}), 860, 819, 773, 742 and 694 ($\delta_{\ o.o.p.\ C-H,\ benzene\ rings}$).

^{1}H NMR (400 MHz, DMSO-d_6): δ =2.387 (s, 6H, 2 × CH_3), 2.509 (DMSO solvent),2.509 (DMSO solvent), 6.250-6.367 (s,1H, 1 × olefinic =C-H proton bonded with O–C=O inside oxazepine ring), 6.638 (s,1H, 1 × olefinic =C-H proton bonded with O=C–N inside oxazepine ring), 7.249-7.643 (Ar-H and C-H proton of oxazepine ring), 8.154 (s, 1H, 1 × O-H phenolic proton).7.249-7.251 (d, 1H, 1 × H_a), 7.275-7.290 (d, 1H, 1 × H_b), 7.320 (s, 1H, 1 × H_c), 7.344 (s, 1H, 1 × H_d, oxazepine ring), 7.430 (s, 2H, 2 × H_e), 7.631-7.643 (d, 1H, 1 × H_f). Elemental analysis (%) calc. for $C_{21}H_{17}N_5O_4S_2$, C 53.95, H 3.66, N 14.98, S 13.72; Found: C 53.79, H 3.81, N 14.70, S 13.61.

Synthesis of 1,3-oxazepine-4,7-dione derivatives (4b, 4d, 4e): A mixture of azoimine derivatives **(2b, 2d, 2e)** (0.002 mol) and phthalic anhydride (0.296 g, 0.002 mol) in dry benzene (20 mL) was refluxed on a water bath at 70 ºC for 20-24 h and monitored by TLC. The mixture wasthen allowed to cool down to room temperature, dried upon filter paper then in oven and recrystallized from ethanol.

2-[5-{(4-Chlorophenyl)diazenyl}-2-hydroxyphenyl]-3-(5-mercapto-1,3,4-thiadiazol-2-yl)-2,3-dihydrobenzo-[e][1,3]oxazepine-4,7-dione (4b): IR (cm^{-1}): 3269 (ν_{O-H}), 3080 ($\nu_{C-H,\ benzene\ rings}$), 1734 ($\nu_{C=O,\ O=C-O,\ oxazepine}$), 1674 and 1639 ($\nu_{C=O,\ O=C-N,oxazepine}$), 1573 and 1504 ($\nu_{C=N\ and}$ $\nu_{C=C,\ aromatic\ rings}$), 1388 and 1292 ($\nu_{C-N}$), 1134 ($\nu_{C-Cl}$), 896, 839,808, 764, 720 and 683 ($\delta_{\ o.o.p.\ C-H,\ benzene\ rings}$).

^{1}H NMR (400 MHz, DMSO-d_6): δ = 2.509-2.513 (DMSO solvent), 3.355 (H_2O in DMSO), 3.573 (s, 1H, 1 × S-H proton), 7.372 (s, 1H, 1 × O-H phenolic proton). 7.522-7.973 (Ar-H and C-H proton of oxazepine ring). 7.522-7.530 (dd, 3H, 1 × H_a and 2 × H_b), 7.656-7.750 (dd, 2H, 1 × H_c and 1 × H_d), 7.772 (s, 3H, 3 × H_e), 7.814 (s, 2H, 2 × H_f), 7.954-7.973 (d, 1H, 1 × H_g). Elemental analysis (%) calc. for $C_{23}H_{14}N_5O_4S_2Cl$, C 52.72, H 2.69, N 13.36, S 12.24; Found: C 52.58, H 2.69, N 13.93, S 12.19.

2-[2-Hydroxy-5-{(4-nitrophenyl)diazenyl}phenyl]-3-(5-mercapto-1,3,4-thiadiazol-2-yl)-2,3-dihydrobenzo-[e][1,3]oxazepine-4,7-dione (4d): IR (cm^{-1}): 3265 and 3200 (ν_{O-H}), 3074 ($\nu_{C-H,\ benzene\ rings}$), 2881 ($\nu_{C-H,\ oxazepine}$), 1734 ($\nu_{C=O,\ O=C-O,\ oxazepine}$), 1666 ($\nu_{C=O,\ O=C-N,oxazepine}$), 1599 and 1574 ($\nu_{C=N\ and}$ $\nu_{C=C,\ aromatic\ rings}$), 1525 ($\nu as.NO_2$), 1344 ($\nu s.NO_2$), 1288 ($\nu_{C-N}$), 898, 852, 808, 758 and 711 ($\delta_{\ o.o.p.\ C-H,\ benzene\ rings}$).

^{1}H NMR (400 MHz, DMSO-d_6): δ = 2.50-2.51 (DMSO solvent), 3.57 (H_2O in DMSO), 7.18-8.43 (Ar-H and C-H

proton of oxazepine ring). 7.18-7.21 (d, 1H, 1 × H_a), 7.51-7.53 (dd, 2H, 1 × H_b and 1 × H_c), 7.94 (t, 2H, 2 × H_d), 8.03-8.06 (d, 3H, 3 × H_e), 8.13-8.16 (d, 1H, 1 × H_f), 8.014 (s, 1H, 1 × O-H phenolic proton), 8.41-8.43 (d, 2H, 2 × H_g). Elemental analysis (%) calc. for $C_{23}H_{14}N_6O_6S_2$, C 51.68, H 2.64, N 15.72, S 12.00; Found: C 51.56, H 2.54, N 15.36, S 12.63.

2-[2-Hydroxy-5-{(4-methoxyphenyl)diazenyl}phenyl]-3-(5-mercapto-1,3,4-thiadiazol-2-yl)-2,3-dihydrobenzo-[e][1,3]oxazepine-4,7-dione(4e): IR (cm^{-1}): 3255 (ν_{O-H}), 3097 ($\nu_{C-H,\ benzene\ rings}$), 2966 (νas.C-H, CH_3), 2899 (νs.C-H, CH_3), 1735 ($\nu_{C=O,\ O=C-O,oxazepine}$), 1689 ($\nu_{C=O,\ O=C-N,\ oxazepine}$), 1600 and 1504 ($\nu_{C=N\ and}$ $\nu_{C=C,\ aromatic\ rings}$), 1462 (δ as.C-H, CH_3), 1350 (δ s. C-H, CH_3), 1305 and 1253 (ν_{C-N}), 1028 (νs. $_{C-O-C,\ ether}$), 893, 839, 790, 738, 711 and 682 (δ $_{o.o.p.\ C-H,\ benzene\ rings}$).

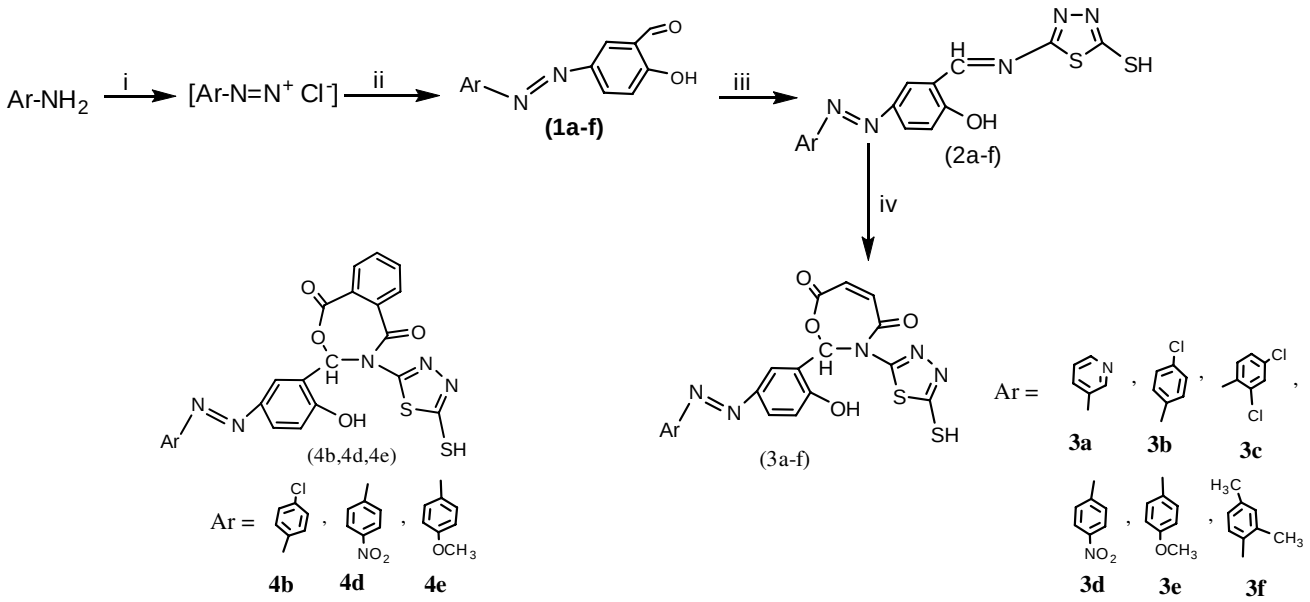
^{1}H NMR (400 MHz, DMSO-d_6): δ = 2.509 (DMSO solvent), 3.332 (H_2O in DMSO), 3.573 (s,1H, 1 × S-H), 3.870 (s, 3H, 1 × CH_3-O), 7.143-8.395 (Ar-H and C-H proton of oxazepine ring) 13.333-13.341 (s, 1H, 1 × O-H phenolic proton).7.143 (1H, 1 × H_a), 7.639-7.727 (m, 2H, 2 × H_b) 7.805 (s, 1H, 1 × H_c, oxazepine), 7.863-7899 (dd, 2H, 2 × H_d), 7.943-7.978 (m, 3H, 3 × H_e), 8.044-8.058 (d, 2H, 2 × H_f), 8.395 (s, 1H, 1 × H_g). Elemental analysis (%) calc. for $C_{24}H_{17}N_5O_5S_2$, C 55.48, H 3.30, N 13.48, S 12.34; Found: C 55.06, H 3.34, N 13.45, S 12.02.

RESULTS AND DISCUSSION

We started this work by coupling reactions between the diazonium salts of the primary aromatic amines (3-amino-pyridine, 4-chloroaniline, 2,4-dichloroaniline, 4-nitroaniline, 4-methoxyaniline and 2,4- dimethylaniline) and phenoxide salt of 2-hydroxybenzaldehyde at 0-5 °C which afforded azoaldehyde derivatives **1a-f.**

Compounds **1a-f** were reacted with 2-amino-5-mercapto-1,3,4-thiadiazole in acidic medium to give azoimines **2a-f** as the platforms for our work (**Scheme-I** and **II**).

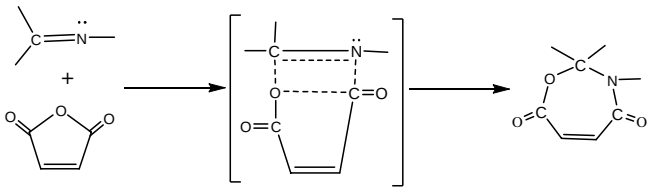
The (2+5) cycloadditions of **2a-f** with maleic and phthalic anhydrides respectively in dry benzene at 70 °C for 20-24 h gave the oxazepines **3a-f** and (**4b, 4d, 4e**) in good yields (Table-1).



Scheme-I: Synthesis of 1,3-oxazepines, Reagents and conditions (i) $NaNO_2$, HCl, 0-5 °C; (ii) NaOH 10 %, 5 °C; (iii) AMT, Abs. EtOH, 70 °C, 10-14 h; (iv) maleic or phthalic anhydrides, dry benzene, 70 °C, 20-24 h

TABLE-1
PHYSICAL PROPERTIES OF THE SYNTHESIZED COMPOUNDS

Product	Physical state	R_f (eluent)	m.p. (°C)	Time (h)	Weight (g) / Yield (%)
2a	Light orange solid	0.70 (*n*-hexane/ethanol, 1:2)	253-255	10	0.8422 / 82
2b	Light green solid	0.70 (*n*-hexane/Et_2O, 1:1)	208-210	12	0.8569 / 76
2c	Orange solid	0.54 (*n*-hexane/Et_2O, 1:1)	230-233	11	0.9108 / 74
2d	Light orange solid	0.34 (*n*-hexane/Et_2O, 1:1)	240-242	10	0.9853 / 85
2e	Brown solid	0.48 (*n*-hexane/Et_2O, 1:2)	210-212	13	0.7577 / 68
2f	Dark brown solid	0.83 (*n*-hexane/Et_2O, 1:3)	222-224	14	0.6539 / 59
3a	Dark brown solid	0.48 (*n*-hexane/ethanol, 1:1)	209-211	23	0.6606 / 75
3b	Greenish yellow solid	0.70 (*n*-hexane/Et_2O, 1:1)	201-203	22	0.7298 / 77
3c	Brown solid	0.66 (*n*-hexane/Et_2O, 1:3)	141-143	21	0.8032 / 79
3d	Orange solid	0.21 (*n*-hexane/Et_2O, 1:3)	198-200	24	0.7751 / 80
3e	Orange solid	0.70 (*n*-hexane/Et_2O, 1:2)	205-207	20	0.6385 / 68
3f	Dark brown solid	0.65 (*n*-hexane/EtOAc, 2:1)	156-158	21	0.6732 / 72
4b	Light brown solid	0.58 (*n*-hexane/EtOAc, 1:3)	211-213	23	0.8278 / 79
4d	Light brown solid	0.78 (*n*-hexane/Et_2O, 1:3)	170-172	24	0.9087 / 85
4e	Greenish yellow solid	0.75 (*n*-hexane/Et_2O, 1:2)	130-132	20	0.7689 / 74



T.S

Scheme-II: Proposed mechanism for the formation of oxazepine ring

The structures of all target compounds synthesized were deduced from IR, ^{1}H NMR and (CHNS) analysis.

Conclusion

All cycloaddition reactions for the synthesis of oxazepine derivatives required relatively long time for completion. The reason may be due to the relative stability of the synthesized azoimine derivatives due to the extending conjugation with azo group which leads to decrease the characteristic of π-bond in (C=N) group. Some of cycloadditions did not take place, the reason may be steric which decreases the coplanarity of transition state for addition. In general, the rates of cycloaddition reactions are relatively increased in presence of electron-donating groups substituted in benzene ring and relatively decreased in presence of electron with-drawing groups substituted in the same ring. The reason may be attributed to increase stability of transition state for the cycloaddition.

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