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Research Article

# Synthesis of Some Oxazine Compounds Derived from TDI and Schiff Bases

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## Abstract

It is known from ongoing research on heterocyclic compounds that these compounds are used as drug and drug carriers, According to FDI reports that these compounds forms 90% drug for cancer and 75% drugs for different diseases. It was also known from our studies on oxazine compounds that this type of heterocyclic compounds had versatile application in medicine. In this study, new 3,1-Benzoxazine compounds (S7-12) were prepared by cyclization reaction of some 2-(benzylidene-amino) benzoic acids (S1-6) with Toluene diisocyanate (TDI) under reflex conditions in chloroform. The structure of the synthesized compounds were confirmed by IR, 1HNMR spectral studies.

**Keywords:** Oxazine Compounds; Insects; Fungi; 1HNMR

## Introduction

It is well established that Oxazine compounds are quite useful and effective in pharmaceutical and other medical areas, These compounds prove to have anti-bacterial [1,2], anti-plasmodia [3], anti-cancer [4], anti-depressant [5], ant-toxicity [6], and anti-neoplastic effects [7]. The oxazine compounds are considered to be a significant type of heterocyclic compounds toward drug and drug discovery programs. The first time that the oxazine compounds were synthesized was in the year of 1944 by Holly and Cope using the traditional Mannich condensation of phenol, formaldehyde and amines [8]. Other researchers are currently interested in the synthesis using other methods such as solvent-free synthesis [9-11], hetero Diels-alder reaction [12], Some researchers have used induced condensation reaction for the synthetic reaction of this type of compounds [13,14] and cyclization reaction with chalcones [2]. Many vital and significant factors, such as reactant structures, solvent-effect [15], reaction temperature [16], and reaction duration time [17] play a decisive role in the synthesis process and have an impact on the properties of these types of compounds. Moreover, all the previous studies of this type of compounds are very valuable in the chemistry of natural products owing to the formation of acetal-glycoside in a plant [18], which acts as a plant's own factor of resistance against insects, pests, fungi and microbic diseases [19]. In accordance with the above-mentioned importance of this type of compounds, we have chosen, for this research, cyclization reaction as a method of preparation new oxazine derivatives from Schiff bases and isocyanates for the synthesis of series of these new oxazine compounds in our drug discovery program.

## Experimental

All melting points were uncorrected using thermal SMP30 UK melting point apparatus. IR spectra were recorded using Alpha

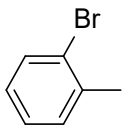
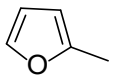
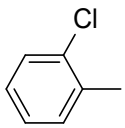
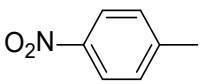
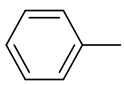
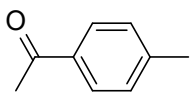
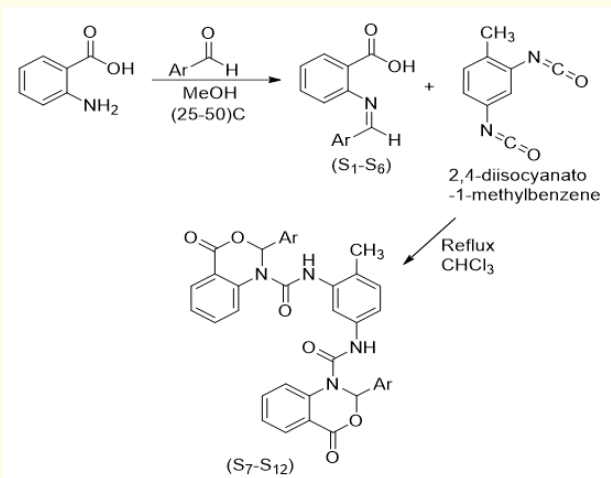
| Comp. No. | Ar. | Molecular Formula | M.Wt gm/mol | M.P. (C) | Yield % | Colour |
|---|---|---|---|---|---|---|
| $S_1$ |  | $C_{14}H_{10}BrNO_2$ | 304 | 95-97 | 75 | Brown |
| $S_2$ |  | $C_{12}H_9NO_2$ | 215 | 142-144 | 93 | purple |
| $S_3$ |  | $C_{14}H_{10}ClNO_2$ | 259 | 75-77 | 96 | Brown |
| $S_4$ |  | $C_{14}H_{10}N_2O_4$ | 270 | 131-132 | 96 | Brown |
| $S_5$ |  | $C_{14}H_{11}NO_2$ | 225 | 67-68 | 97 | purple |
| $S_6$ |  | $C_{15}H_{13}NO_3$ | 255 | 141-143 | 70 | brown |

**Table 1:** Physical properties of compounds ($s_{1-6}$).

(ATR) instrument. $^1$HNMR spectra were recorded using Varian Agilent 499.53MHZ instrument, DMSO as internal solvent. All chemical were supplied by sigma –Aldrich, BHD and Fluka companies.

### General procedure for the synthesis of 2-carboxy arylidine aniline ($s_{1-6}$) [20]

A mixture of (1 mmol) of an anthranilic acid and (1.2 mmol) of an aryl aldeyde in methanol was stirred for about 1 h. at room temperature. The solvent was removed under reduced pressure to give crude product which was washed with n-hexane and recrystallized from ethanol to afford the Schiff bases ($S_{1-6}$) as pure compounds. Physical properties were listed in table 1.




**Scheme 1:** The synthetic pathway for the synthesis of compounds (S1-12).

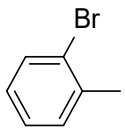
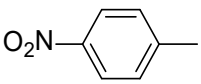
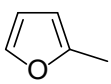
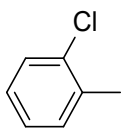
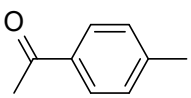
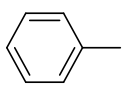
| Comp. No. | Ar. | Molecular Formula | M.Wt gm/mol | M.P. (°C) | Yield % | Color |
|---|---|---|---|---|---|---|
| $S_7$ |  | $C_{37}H_{26}Br_2N_4O_6$ | 782.5 | 219 dec. | 65 | white |
| $S_8$ |  | $C_{37}H_{26}N_6O_{10}$ | 714.6 | 258-260 | 97 | yellow |
| $S_9$ |  | $C_{33}H_{24}N_4O_6$ | 604 | 101-102 | 93 | orange |
| $S_{10}$ |  | $C_{37}H_{26}Cl_2N_4O_6$ | 693.5 | 97-98 | 71 | brown |
| $S_{11}$ |  | $C_{39}H_{32}N_4O_8$ | 648 | 154-155 | 95 | white |
| $S_{12}$ |  | $C_{37}H_{28}N_4O_6$ | 624.6 | 197-99 | 75 | orange |

**Table 2:** Physical properties of compounds ($s_{7-12}$).

### General procedure for the preparation Bis[(2-Aryl-6H-1,2-dihydro-6-oxo[2,1-e](1,3) benzoxazine-1,1'-yl)]-2,4-diamido-toluene [21]

To a solution of (1.5 mmol) of Schiff bases ($S_{1-6}$) and (2.5 mmol, 2.0 gm) of toluene diisocyanate in 1 ml of Chloroform the reaction mixture was refluxed for (3.0h). After the removal of the solvent under reduced pressure, the precipitate was washed with 2 ml of *n*-hexane (three times) and filtered to remove any traces of toluene Diisocyanate. The final product was washed with 10% $NaHCO_3$ and water then dried. The physical properties of the synthesized compounds were illustrated in table 2.

## Results and Discussion

### 2-carboxy arylidine aniline ($s_{1-6}$)

These compounds were synthesized using similar procedure [20] and were characterized by IR as shown in table 3. The following main absorption bands ($\upsilon_{max}cm^{-1}$) at (1585-1654) for C=N, (1402-1626) for C=C,C=C Aromatic, (1619-1718) for C=O while O-H appeared at (3328-3424) other stretching absorptions can be seen in the following Table. The NMR spectral data were indicated in table 4.

### Bis[(2-Aryl-6H-1,2-dihydro-6-oxo[2,1-e](1,3) benzoxazine-1,1'-yl)-2,4-diamidotoluene

These compounds were synthesized by cyclization of Schiff bases with toluene diiso cyanate using similar procedure[21] and were characterized by IR and showed the following main absorption bands ($\upsilon_{max}cm^{-1}$) at (1216-1260) for C-N, (1023-115) for C-O-C, (1446-1661) for C=C, C=C. (1661-1770) for C=O While N-H at (3248-3327) other band were shown in table 5.

The NMR spectra were discussed in details as shown in the following table 6.

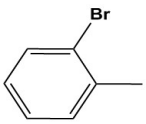
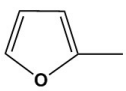
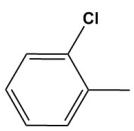
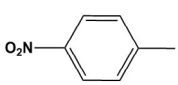
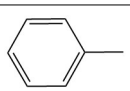
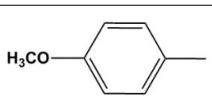
| Comp. No. | Ar. | IR ν cm$^{-1}$ | | | | |
|---|---|---|---|---|---|---|
| | | C=C Ar. | C=N | C=O | O-H | Others |
| $S_1$ |  | 1402,1495 | 1588 | 1653 | 3369 | ..... |
| $S_2$ |  | 1404,1579 | 1609 | 1651 | 3373 | ..... |
| $S_3$ |  | 1464,1513 | 1585 | 1619 | 3424 | C-Cl/657 |
| $S_4$ |  | 1496,1569 | 1623 | 1654 | 3372 | N-O sym/1311 Assy/1443 |
| $S_5$ |  | 1448,1573 | 1612 | 1663 | 3358 | ..... |
| $S_6$ |  | 1466,1626 | 1654 | 1718 | 3328 | C-O/1084 |

**Table 3**: IR spectral data for compounds ($_{S1-6}$).

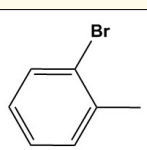
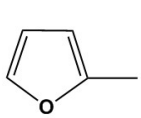
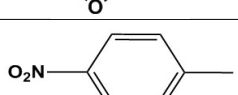
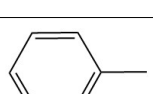
| Comp.No. | R | $^1$HNMR (PPM) DMSO-d6 |
|---|---|---|
| $S_1$ |  | 7.2-7.4 (d, 1st, 2nd, 3rd, 14th, 15th -H);7.60-7.62 (d, 16th -H)7.71-7.72 (d for 13th - H) 7.88-7.89 (d, 6th S -H) 8.62 (s, 1H) CH = N; 10.2 (S, 1H) OH |
| $S_2$ |  | 6.9-6.92 (d, 14th- -H )7.0-7.01 (d, 13th -H)7.26-.33 (m, 1st, 2nd, 3rd -H) 7.60-7.61 (s, 15th -H) 7.86-7.88 (m, 6th -H); 8.37 (S, 1H) CH=N; 9.5- 9.6 (S, 1H) OH |
| $S_3$ |  | 7.26-7.34 (d, 1st, 2nd, 3rd, 14th,16th,-H)7.86-7.89 (AB q for 13th, 17th -H)8.16-8.19 (6th -H); 8.71 (S, 1H) CH=N;9.5 (S, 1H) OH |
| $S_4$ |  | 7.26-7.38 (m, ph-H)7.39-7.7 (d, 1st 2nd 3rd -H) 7.89 (6th -H); 8.6 (S, 1H) CH=N, 10.82 (S, 1H) OH |
| $S_5$ |  | 3.78 (S, 3H) CH3; 6.95 -6.98 (14th 16th -H) 7.26-7.34 (1st, 2nd, 3rd -H) 7.71-7.74 (ABq, 13th, 17th -H) 7.78-7.789 (6th -H) 8.70 (S,1H) CH=N, S10.02 (S, 1H) OH |

**Table 4:** 1HNMR data for compounds ($s_{1-6}$).

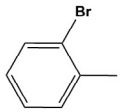
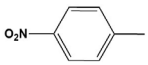
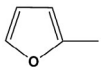
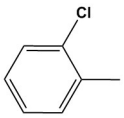
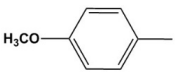
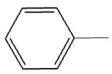
| Comp. No. | Ar. | IR ν cm$^{-1}$ | | | | | |
|---|---|---|---|---|---|---|---|
| | | N-H | C=O | C-O-C | C-N | C=C Ar. | Others |
| $S_7$ |  | 3327 | 1776 | 1023,1266 | 1260 | 1467,1573 | C-Br/635 |
| $S_8$ |  | 3282 | 1765 | 1062,1150 | 1266 | 1446,1603 | N-O sym/1380 Assy/1526 |
| $S_9$ |  | 3292 | 1767 | 1041,1154 | 1216 | 1447,1661 | ..... |
| $S_{10}$ |  | 3267 | 1704 | 1071,1101 | 1219 | 1454,1495 | C-Cl/633 |
| $S_{11}$ |  | 3294 | 1661 | 1044,1145 | 1292 | 1448,1605 | ..... |
| $S_{12}$ |  | 3248 | 1770 | 1029,1098 | 1239 | 1467,1610 | ..... |

**Table 5:** IR spectral data for compounds ($S_{7-12}$).

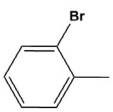
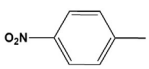
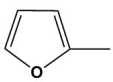
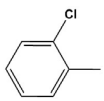
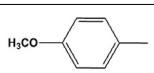
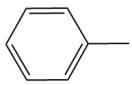
| Comp. No. | R | $^1$HNMR (PPM) DMSO-d6 |
|---|---|---|
| $S_7$ |  | 2.47 (S, 3H) CH3; 7.27-8.13 (m, 18H, 5Ar-H and CH), 7.8 (S, 2H) 2NH |
| $S_8$ |  | 2.34 (S, 3H) CH3; 7.14-8.18 (m, 19H, 5Ar-H and CH) |
| $S_9$ |  | 2.22 (S, 3H) CH3; 6.4 -7.98 (m, 17H) 3Ar -H, 2furfuryl ring and CH); 7.74 (S, 2H) NH |
| $S_{10}$ |  | 2.46 (S, 3H) CH3; 7.14 -7.74 (m, 19H, 5Ar-H and CH); 7.99 (S, 2H) 2NH |
| $S_{11}$ |  | 2.446 (S, 3H) CH3; 3.77 (S, 3H) OCH3; 6.89-7.74 (m, 19H, 5Ar-H and CH); 7.98 (S, 2H) 2NH |
| $S_{12}$ |  | 2.54 (S, 3H) CH3; 7.14 -7.75 (M, 21H, 5Ar-H and CH) 7.99 (S, 2H) 2NH |

**Table 6**: $^1$HNMR data for compounds ($s_{7-12}$).

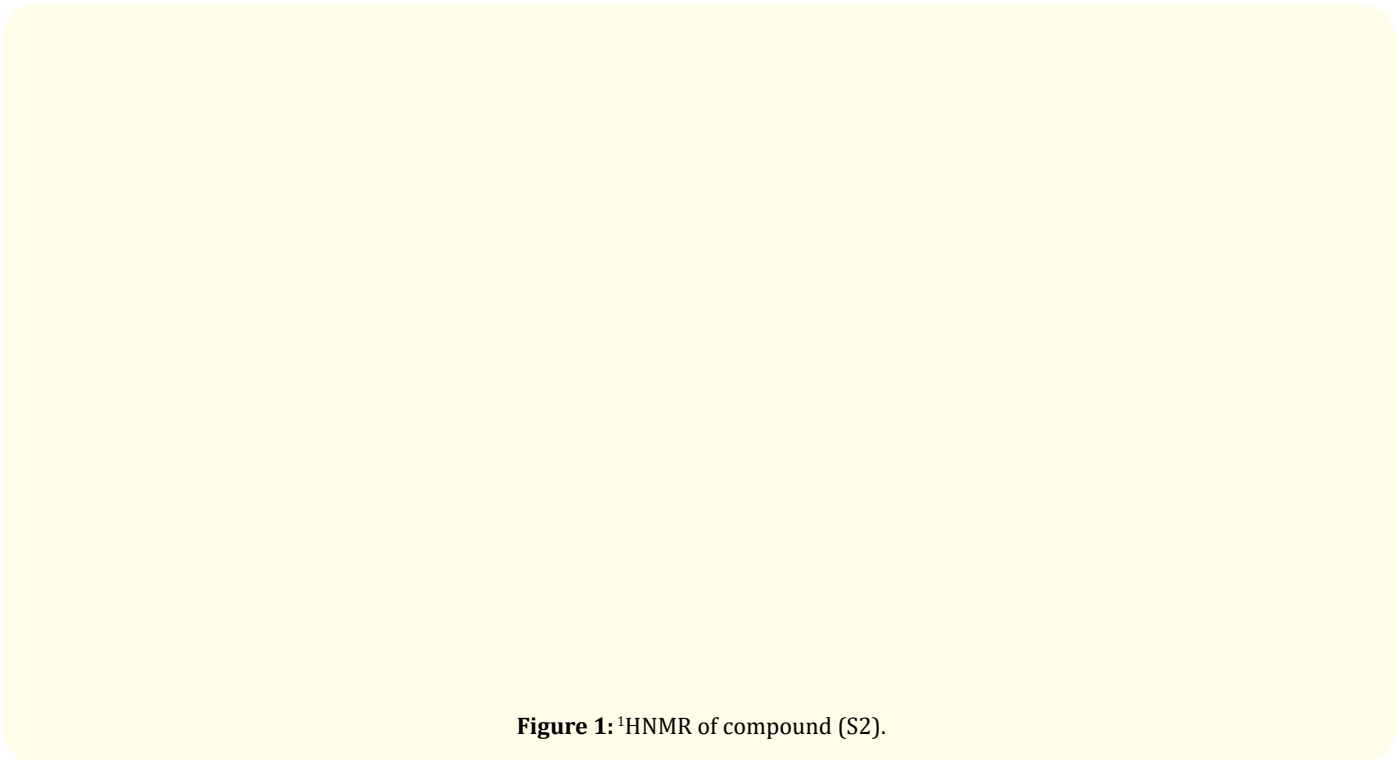


**Figure 1:** $^{1}$HNMR of compound (S2).

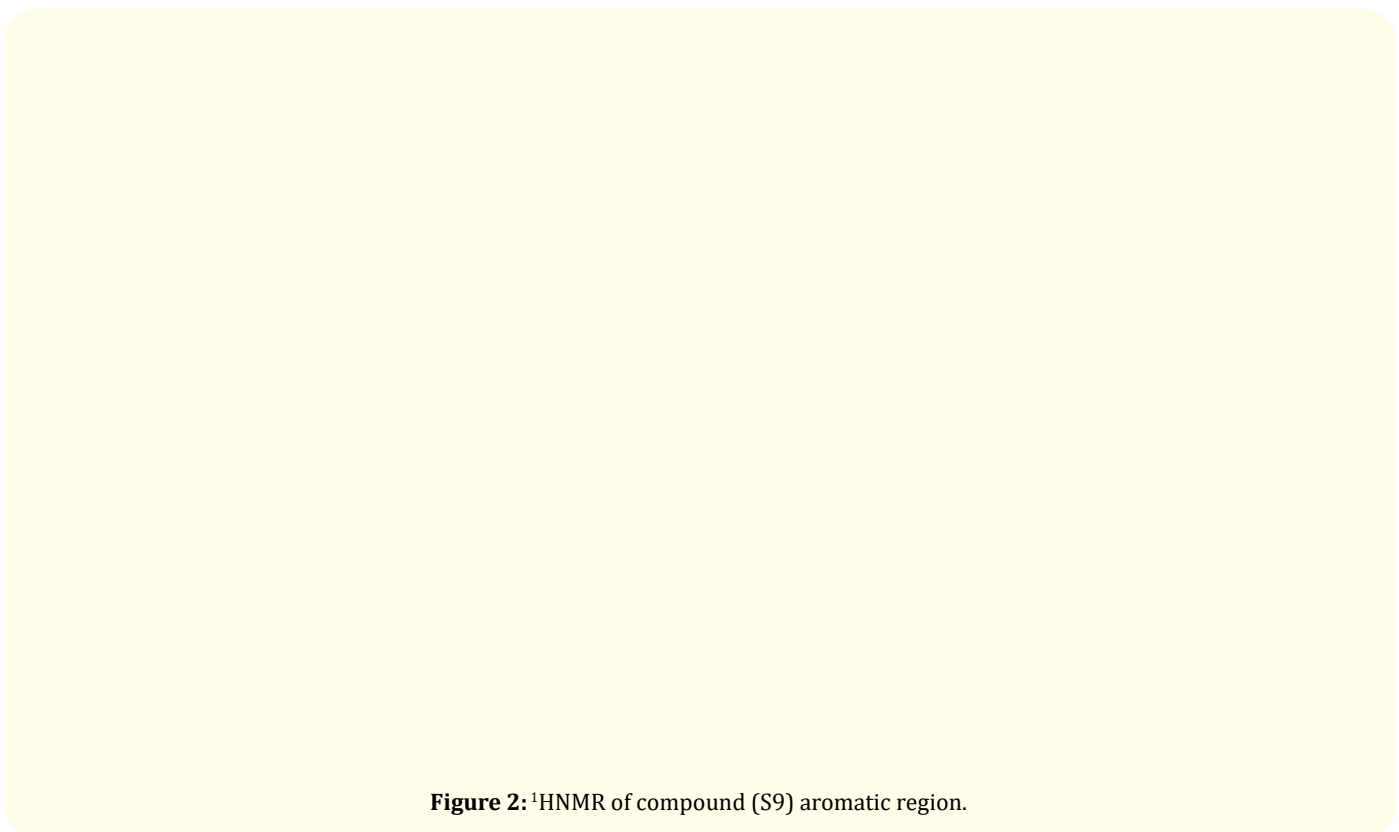


**Figure 2:** $^{1}$HNMR of compound (S9) aromatic region.

**Figure 3:** $^{1}$HNMR of compound ($S_9$).

## Conclusion

We conclude from the above study that Oxazine compounds were successively synthesized from the reaction of the corresponding schiff based of antharanalic acid schiff base with TDI according to the given spectral data. These compound will be studied for their biological activity based on our drug discovery program in our upcoming paper.

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