Synthesis of some novel Heterocyclic Chalcone Derivatives

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Abstract:

The derivatives of Chalcones were synthesized by reaction of 2,3-Dichlorobenzaldehyde with 2-Hydroxy acetophenone in the base medium, then the product react with thiourea, urea and hydrazine to preper the derivatives of thiazine, oxazine and isoxazole respectively. The structures of the synthesized compounds have been characterized by (IR, ^{1}HNMR, ^{13}CNMR and elemental analysis).

Keywords: Chalcone, Urea, Claisen-Schmidt condensation, Oxazine and Isoxazole.

Chemistry Classifiication QD241-441

Introduction:

Chalcones (α,β-unsaturated ketones) are prepared by condensing of acetophenone or its derivatives with aromatic aldehydes in basic medium, The structure of chalcone consists from two aromatic rings joined by ketoethylenic group (– CO – CH=CH-) **[1]**. Many methods are available for formation of carbon- carbon bonds in the synthesis of chalcones The simplest method include Claisen-Schmidt condensation of equal molar quantities of acetophenone with aromatic aldehyde under an basic condition. Chalcones are also very useful intermediates for the synthesis of many important heterocyclic compounds. They are have five- **[2,3]**, six- **[2,4]** and seven-rigs **[5]**.

Material and Methods:

All the chemical and solvents used in the preparation of compounds were purchased from Sigma-Aldrich and Merch. All the reported melting points were determined using an electrically heated block with calibrated thermometer; samples were taken in open capillaries and were uncorrected. The IR Spectra were taken from Alpha Bruker IR spectrophotometer. ^{1}HNMR and ^{13}CNMR spectra were recorded on Bruker NMR (400 MHz) in DMSO.

General procedure for synthesis of chalcone (1):

2,3-Dichlorobenzaldehyde (0.1 mol) and 2-Hydroxyacetophenone (0.1 mol) were dissolved in (300 mL) of ethanoic Sodium hydroxide (10%) and the mixture was mixed for (24 hrs) at RT then it was poured in (400 mL) of cold water with constant stirring and acidified with 10% HCl. The mixture left for (24 hrs) in Refrigerator. The solid product obtained was filtered, washed and recrystallized from ethanol.

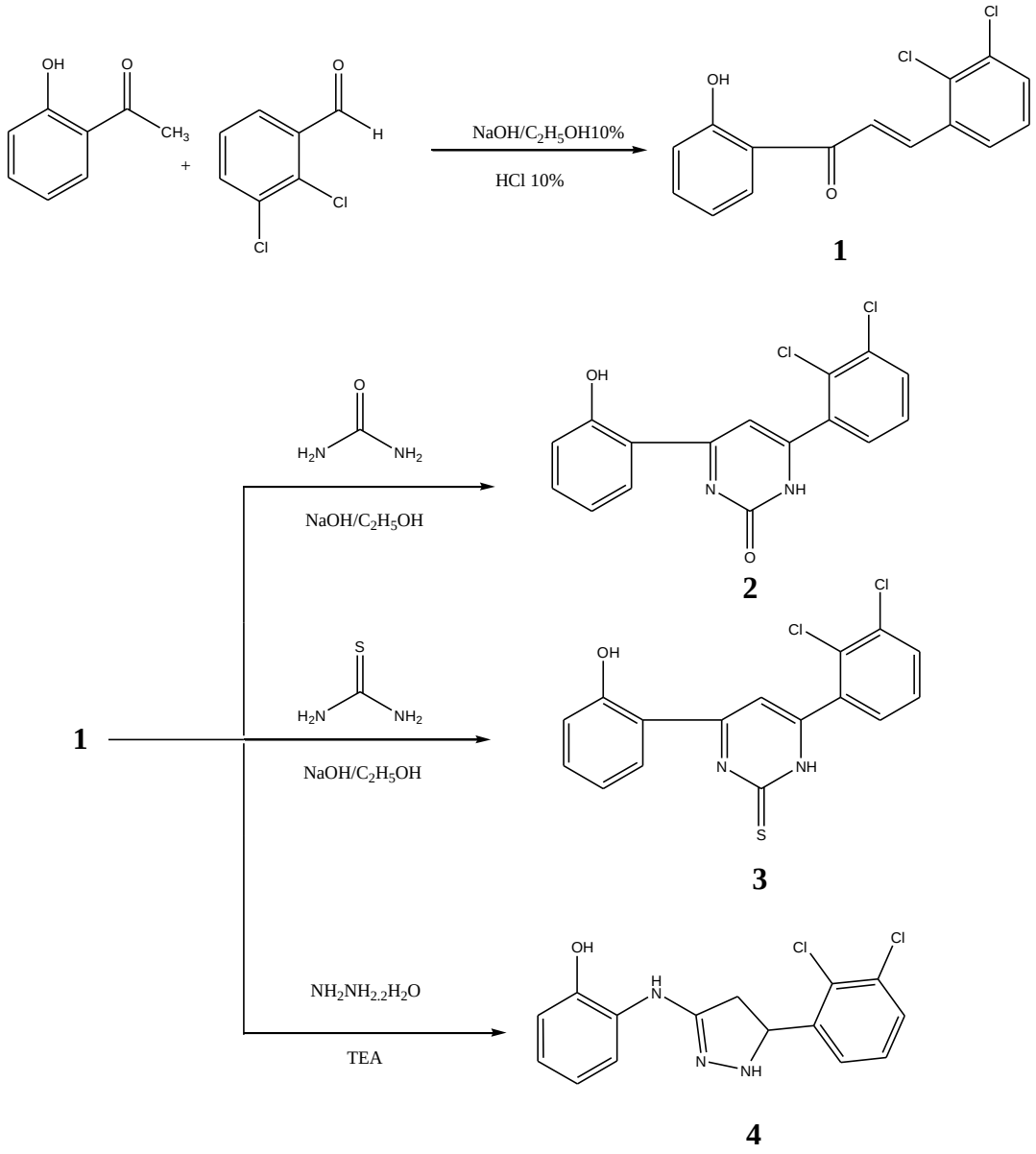
Preparation of thiazine/ oxazine derivatives:

A mixture of Chalcone (1) (0.2 mol), thiourea/ urea (0.2 mol) were dissolved in (100 ml) of ethanolic sodium hydroxide, the mixture was left for (4 hrs) with stirring at RT. Then the mixture was poured into (400 ml) of cold water with continuous stirring for an hour and then kept in refrigerator for (24 hrs). The precipitate obtained was filtered, washed and recrystallized. The completion of the reaction was monitored by TLC.

Preparation the derivative of isoxazole:

A mixture of Chalcone (1) (0.2 mol) and hydrazine hydrate (0.2 mol) were heated in

tri ethyl amine (50 ml) when the mixture began boiling (5 min) the heat was stopped. The mixture was left to cool and poured into cold water. The solid product was filtered, washed and recrystallized by ethanol.



Scheme 1. Synthetic procedure for preparation of title compounds.

3-(2,3-dichlorophenyl)-1-(2-hydroxyphenyl)prop-2-en-1-one (1):
Yellow solid, M.p: 210 C^{o}, Yield: 90%, IR (ν cm^{-1}): 3350 (O-H), 3071 (=C-H), 2874, 2746 (C-H $_{aromatic}$), 1733 (C=O), 1683 (C=N), 1557 (C=C), ^{1}H NMR (DMSO): δ 2.64 (s, H, OH), 6.95-7.92 (m, 7H, H $_{aromatic}$), 8.05-8.08 (d, 2H, =C-H), ^{13}C-NMR (CDCl3): δ 193.4 (C=O), 161.9 (C-OH), 139.08 (=C-ph), 136.9, 135.1, 133.02, 132.06, 131.8, 130.01, 129.01, 128.08, 127.2, 121.08, 119.6, 118.2 (phenyl group).

Anal. Calc. For $C_{15}H_{10}C_{l2}O_2$ C,61.46; H: 3.44. Found. C, 71.52; H, 5.24.

6-(2,3-dichlorophenyl)-4-(2-hydroxyphenyl)pyrimidin-2(1H)-one (2):

Orang solid, M.p: 230 C^o, Yield: 75%, IR (ν cm^{-1}): 3310 (O-H), 2991 (=C-H), 2936, 2835 (C-$H_{aromatic}$), 1636 (C=O), 1558 (C=C). ^{1}HNMR (CDCl3): 2.5 (s, H, C=C-H), 5.76 (s, H, OH), 6.99-7.84 (m, 7H, C-$H_{aromatic}$), 8.04 (N-H). ^{13}C-NMR (DMSO): 193.36 (N=C), 191.31 (C-N), 139.08, 136.9, 135.17, 133.08, 132.05, 131.4, 130.02, 129.19, 128.9, 127.2, 126.9, 122.6, 121.5, 119.6, 118.5 (phenyl group). 76.66 (=C-H). Anal. Calc. For $C_{16}H_{10}Cl_2N_2O_2$ C, 57.68; H, 3.03; N, 8.41. Found. C, 61.47; H, 4.21; 9.78.

4-(2-hydroxybenzyl)-6-(2,3-dichlorophenyl)pyrimidine-2(1H)-thione (3):

Brawn solid, M.p: 287 C^o, Yield: 70 %, IR (ν cm^{-1}): 3432 (O-H), 3018, (=C-H), 2935, 2929 (C-$H_{aromatic}$), 1648 (C=N), 1399 (C=S_{as}), 753 (C=S $_s$). ^{1}H NMR (DMSO): 2.25 (s, H, N-H), 4.83 (s, H, =C-H), 5.25 (s, H, O-H), 7.42-8.1 (m, 7H, $CH_{aromatic}$). ^{13}C-NMR (DMSO): 182 (C=S), 178 (=C-NH), 146 (C=N), 142.5, 142, 136.5, 133.5, 133, 130.5, 126.5, 126, 121, 120, 110 (phenyl group), 104 (=C-H).

Anal. Calc. For $C_{16}H_{10}Cl_2N_2OS$ C, 55.04; H, 2.90; N, 8.01; S, 9.16 Found. C, 60.14; H, 3.09; N,7.85; S, 10.63.

2-(5-(2,3-dichlorophenyl)-4,5-dihydro-1H-pyrazol-3-ylamino)phenol (4):

Yellow-brawn solid, M.p:310 C^o, Yield: 75 %, IR (ν cm^{-1}): 3423 (OH), 3018, 2935 (C-$H_{aromatic}$), 2929 (CH_2), 1584 (C=N), ^{1}H NMR (DMSO): 1.05 (d, 2H, CH_2), 3.35-3.4 (m, H, CH), 5.21 (s, H, OH), 7.45-8.14 (m, 7H, $H_{aromatic}$), 18.5 (CH), 44 (CH_2), 169.6 (C=N), 159, 152, 152.5, 146, 145, 134, 132.5, 131, 129, 126, 125, 123, 120.5, 114.5 (phenyl group). Anal. Calc. For $C_{15}H_{13}Cl_2N_3O$ C, 55.92; H, 4.07; N, 13.04 Found. C, 58.47; H, 5.47; N, 15.14.

Results and Discussion:

Spectroscopic characterization:

3-(2,3-dichlorophenyl)-1-(2 hydroxyphenyl)prop-2-en-1-one was prepared as per Claisen-Schmidt condensation reaction which was converted to 6-(2,3-dichlorophenyl)-4-(2-hydroxyphenyl)pyrimidin-2(1H)-one,4-(2-hydroxybenzyl)-6-(2,3-dichlorophenyl) pyrimidine-2(1H)-thione and 2-(5-(2,3-dichlorophenyl)-4,5-dihydro-1H-pyrazol-3-ylamino) phenol by using urea, thiourea and hydrazine hydrate respectively. The IR spectra of compounds show absorption bands at (3310, 3350, 3423, 3432), (1648, 1584) and (1733, 1636) due to OH, C=N and C=O groups respectively. The ^{1}H NMR spectra of compounds show a singlet at 2.64-5.21 attributed to OH protons.

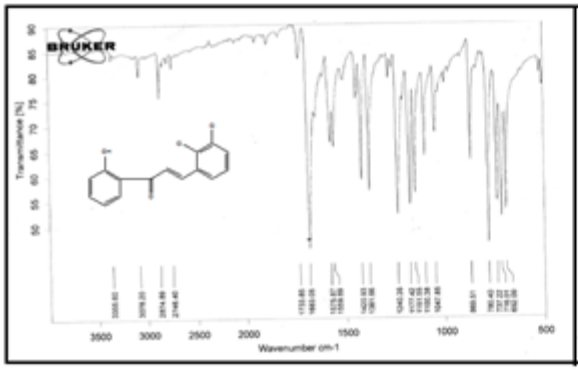


Fig 1: IR spectra of compound 1

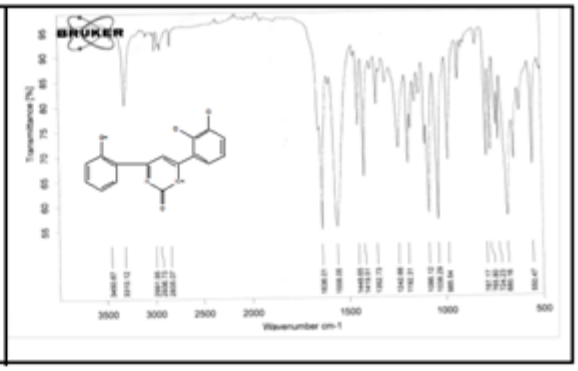


Fig 2: IR spectra of compound 2

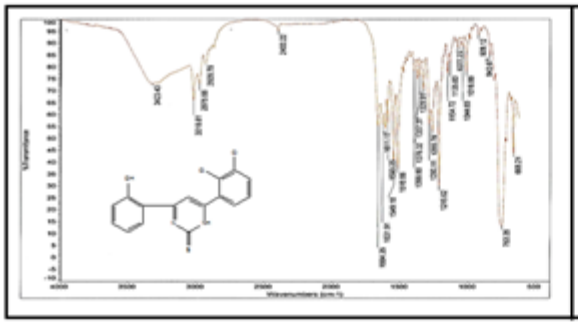


Fig 1: IR spectra of compound 3

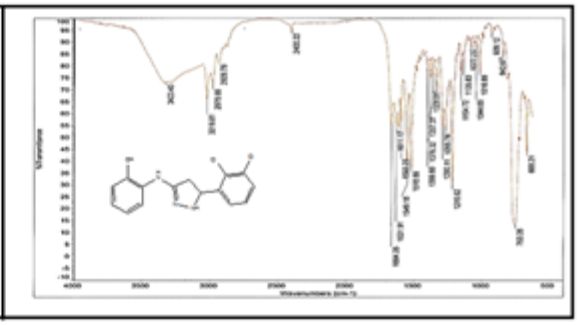


Fig 2: IR spectra of compound 4

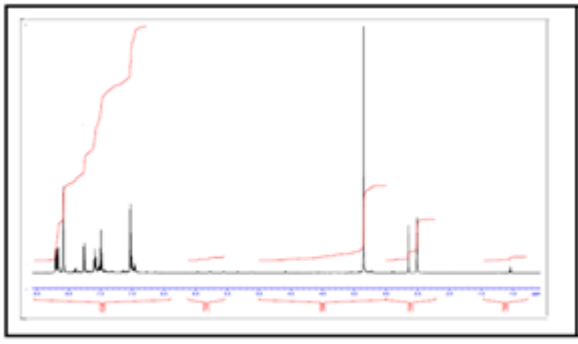


Fig 3: ^{1}HNMR spectra of compound 1

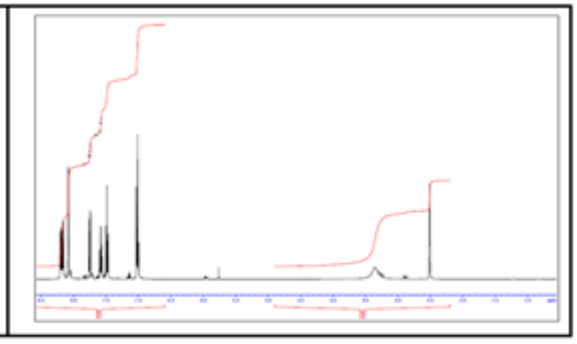


Fig 4: ^{1}HNMR spectra of compound 2

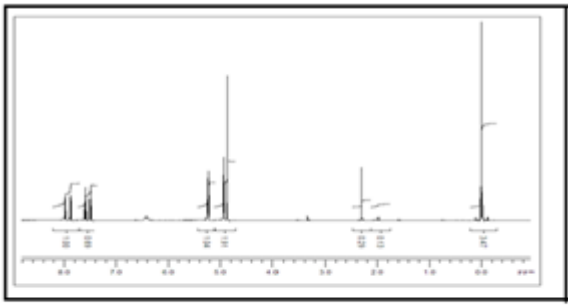


Fig 5: ^{1}HNMR spectra of compound 3

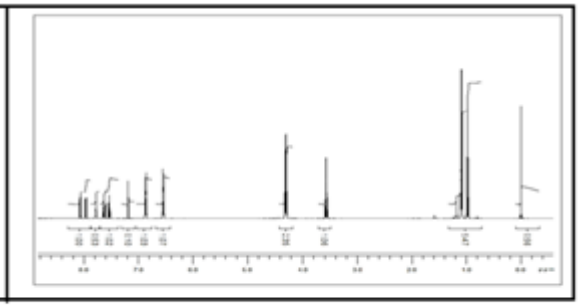


Fig 6: ^{1}HNMR spectra of compound 4

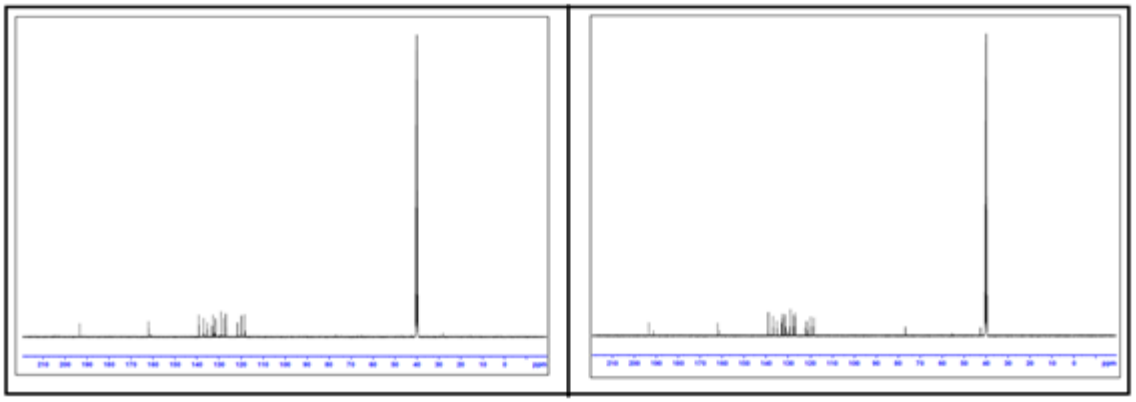


Fig 7: ^{13} CNMR spectra of compound 1

Fig 8: ^{13} CNMR spectra of compound 2

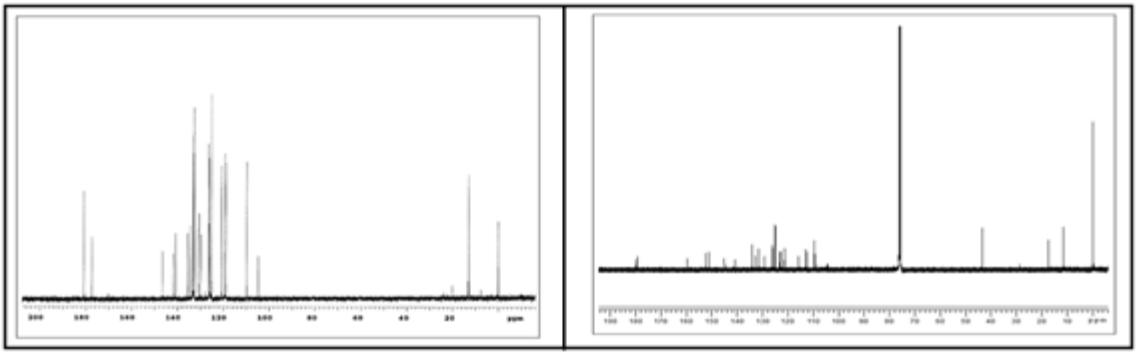


Fig 9: ^{13} CNMR spectra of compound 3

Fig 10: ^{13} CNMR spectra of compound 4

Conclusion:

In summary, we have synthesized some novel hetero chalcones having oxazine, thiazine and isoxazole moiety. All the synthesized compounds gave satisfactory spectral and analytical data.

Acknowledgement:

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تحضير بعض مشتقات الشالكون الحلقية

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الخلاصة:

تم تحضير مشتقات الشالكون من خلال تفاعل 3,2- ثنائي كلورو بنزالدهايد مع 2-هيدروكسي اسيتوفينون في وسط قاعدي. ثم بعد ذلك فوعل الناتج مع اليوريا، ثايوريا و الهايدرازين لتحضير المشتقات الحلقية للوكسازين، الثايازين و الاوكسازول على التوالي. ان التركيب الكيميائي للمشتقات المحضرة تم تحديدها باستخدام مطيافية الاشعة تحت الحمراء، الرنين النووي المغناطيسي و تحليل العناصر.

الكلمات المفتاحية: الشالكون، يوريا، تكاثف كليسن-شمدت، الاوكسازين و الايزووكسازول.