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RESEARCH ARTICLE

Synthesis and Characterization of New Imines-Imides Functionalized Compounds Derived from Trimethoprim moiety Supplemented with Aminothiazole

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Abstract

Imides, Imines, five- and six- membered heterocyclic rings are among the compounds that have attracted a considerable attention of work due to their versatile biological activities. Therefore including these functional in the same compound perhaps enhancing the whole activity of the synthesized compounds. Trimethoprim moiety which is antibacterial drug possessing a pyrimidine ring and diamine groups, was selected as a starting material for this purpose. Mono imides (B1-B5) were prepared by treatment of the corresponding amic acids (A1-A5) (obtained by the reaction of equimolar amount of selected anhydrides and trimethoprim), with a suitable dehydrating agents. The remaining amino group was converted to the aminothiazole via the ring closure of the corresponding acetyl chloride amides (C1-C5) with thiourea in refluxing DMF. The target new imines (D1-D5) were synthesized by reaction of certain aldehydes and ketones with the new thiazoleamines. The structures of all the synthesized compounds were elucidated by considering the data of the FTIR, ^{1}H-NMR, and other physical properties.

Keywords: *Trimethoprim, Imines, Imides, Cyclic anhydrides.*

Introduction

Heterocyclic compounds fields have a very large applications e.g. in agriculture, medicine, photodiodes and other fields [1]. These compounds have also industrialized applications like accelerators [2], copolymers [3], corrosion inhibitors [4] and dyes [5]. Pyrimidines are six member heterocyclic compounds containing nitrogen atoms in positions 1and 3 and consider the configures many of antibiotic and vitamins [6]. The pyrimidines and its derivatives have biological activity through using their as anti-Inflammatory [7] and anti-HIV [8] and anti-tubercular [9] in addition to that its use as analgesic and antipyretic [10].

Cyclic imides and their N-derivatives are an important class of organic compounds; contain bis-amide linkages with a general structure of [-CO-N(R)-CO-]. Their hydrophobicity and neutral structures enable them to easily cross biological membranes [11-16]. These molecules were reported to exhibit valuable biological effects including antifungal [17-19], anti-inflammatory [20]. Thiazole is a heterocyclic compound having both nitrogen and sulfur atoms as part of the aromatic five-membered ring [21].

Thiazoles are a significant for their large number of pharmaceutical and biological properties [22]. and thiazole derivatives are known have an array of biological activities like an anticonvulsant, antimicrobial, anti-inflammatory, anticancer, anti-diabetic, anti-Alzheimer's, antihypertensive, antioxidant, anti-HIV [23]. Imines or Schiff's bases are the compounds that are prepared by thermal condensation between aromatic or aliphatic, primary amines with carbonyl compounds. Schiff bases are also known as azomethine compounds [24]. Imines are also known to possess different biological activities like anticancer [25], antibacterial [26, 27] etc.

Experimental

- All the chemicals were purchased from BDH, Merck, Fluka and sigma Aldrich companies and were used without further purification.
- Melting points were recorded on electro thermal melting point apparatus in University of Anbar College of science without correction.

- FTIR spectra were recorded on Shimadzu FT-IR 8400 Fourier Transform Infrared Spectrophotometer in University of Bagdad College of science.
- ^{1}H-NMR was measured on a Bruker-300 MHz spectrophotometer using DMSO-D6 Solvent and TMS as an internal standard (chemical shifts expressed in δ ppm).

Preparation Methods

General Procedure for Preparation of amic Acid Derivatives (A1-A5)

Literature procedure was used with some modifications [28, 29]. To a solution of (0.01 mol, 0.98-1.93 gm) of cyclic anhydrides in 20 ml of acetone, (0.01 mol, 3 gm) of trimethoprim in 200 ml of acetone was added drop wise with stirring and cooling in ice path. Stirring was continued for three hours at room temperature, the resulted precipitate was filtered off, washed, dried and recrystallized from glacial acetic acid. The physical properties of compounds (A1-A5) are shown in Table (1).

General Procedure for Cyclic Imides Preparation (B1-B5)

A mixture of (0.01 mol, 3.88-4.83 gm) of amic acids in 20 ml, acetic anhydride and (0.01mol, 0.82 gm) of anhydrous sodium acetate was refluxed for three hours with stirring [28, 29]. The resulted homogenous solution was cooled to room temperature and pouring into cooled water. The precipitated solids of cyclic imides (B1-B5) were filtered, washed with cooled water and recrystallized from glacial acetic acid. Physical properties of these compounds are shown in Table (2).

General Procedure for Synthesis of chloroacetyl Substituted Amides (C1-C5)

Literature procedure was used with some modifications [30]. In a 100 ml round bottom flask the prepared imides (0.01mol, 3.70-4.65 gm) were dissolved in 10 ml of DMF then cooled to 0-5 ^{o}C and 2-3 drops of TEA were added. Chloroacetyl chloride (0.01mol, 1.13 gm) in 10 ml of DMF was slowly added to the mixture with vigorous stirring for 3 hours at room temperature. After that the mixture was poured into cooled distilled water (25ml). The product was dried and recrystallized from glacial acetic acid. The physical properties of compounds (C1-C5) are shown in Table (3).

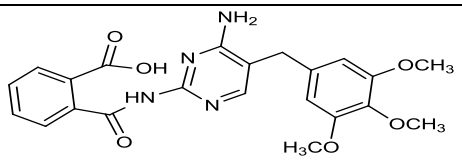
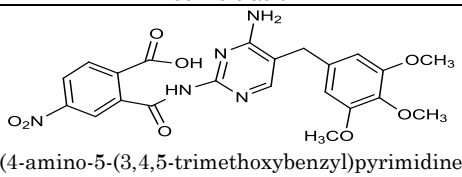
General Procedure for the Preparation of Amino thiazole Compounds (D1-D5)

Literature procedure was used with some modifications [31]. In 100 ml round bottom flask (0.01mol, 4.46-5.41gm) of chloroacetyl substituted amides and (0.01mol, 0.76 gm) of thiourea were dissolved in 10 ml DMF. The mixture was heated under reflux for 3 hour. Upon which the completion of the reaction, the mixture was poured into 25 ml water and washed with 5% $NaHCO_3$ and thoroughly with distilled water. The product was dried and recrystallized from glacial acetic acid. The physical properties of compounds (D1-D5) are shown in Table (4).

General Procedure for the Preparation of Imines Compounds (F1-F33)

A mixture of substituted amino thiazole compounds (0.01mol, 4.68-5.63 gm), aromatic aldehydes or ketones (0.01mol, 1.22-1.99 gm) and (2-3) drops of glacial acetic acid in absolute ethanol (30 ml) was refluxed for six hours [30]. After cooling the obtained precipitate was filtered off then dried and recrystallized from ethanol. Physical properties of compounds (F1-F33) are listed in Table (5).

Table 1: Physical properties of the prepared amic acids

Comp. No.	Structure and name	Color	M.P ^{o}C	Yield %	M.Wt
A1	 2-((4-amino-5-(3,4,5-trimethoxybenzyl)pyrimidine-2yl)carbamoyl) benzoic acid	White	230-231	80	438
A2	 2-((4-amino-5-(3,4,5-trimethoxybenzyl)pyrimidine-2-yl)carbamoyl)-4-nitrobenzoic acid	yellow	228-229	85	483

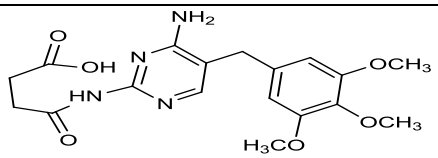
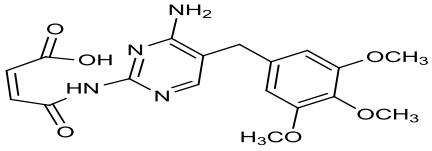
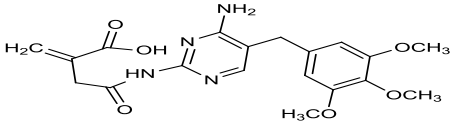
A3	 4-((4-amino-5-(3,4,5-trimethoxybenzyl)pyrimidine-2-yl)amino)-4-oxobutanoicacid	White	202-204	66	390
A4	 (z)-4-((4-amino-5-(3,4,5-trimethoxybenzyl) pyrimidine-2-yl)amino)-4-oxobut-2-enoic acid	white	157-158	75	388
A5	 4-((4-amino-5-(3,4,5-trimethoxybenzyl)pyrimidine-2-yl)amino)-2-methyl ene-4- oxobutanoic acid	Red	160-162	65	402

Table 2: Physical properties of the prepared imides

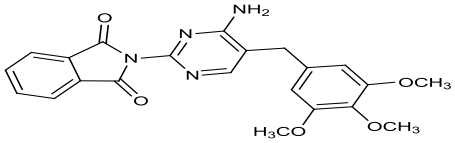
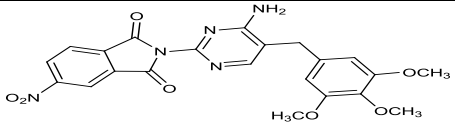
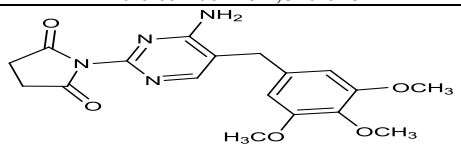
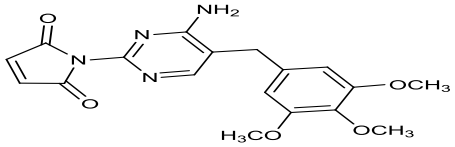
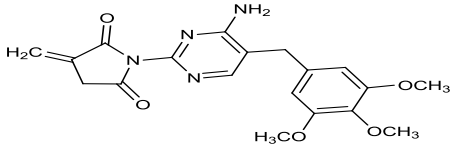
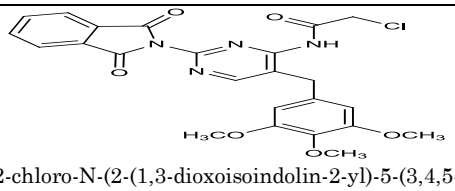
Comp. No.	Structure and name	Color	M.P °C	Yield %	M.Wt
B1	 2-(4-amino-5-(3,4,5-trimethoxyBenzyl)pyrimidin-2-yl)isoindoline-1,3-dione	white	239-241	87	420
B2	 2-(4-amino-5-(3,4,5-trimethoxyBenzyl)pyrimidin-2-yl)-5-nitroisoindoline-1,3- dione	Light yellow	223-225	90	465
B3	 1-(4-amino-5-(3,4,5-trimethoxyBenzyl)pyrimidin-2-yl)pyrrolidine-2,5-dione	white	211-213	69	372
B4	 1-(4-amino-5-(3,4,5-trimethoxyBenzyl)pyrimidin-2-yl)-1H-pyrrole-2,5-dione	White yellowish	195-196	63	370
B5	 1-(4-amino-5-(3,4,5-trimethoxyBenzyl)pyrimidin-2-yl)-3-methylene pyrrolidine- 2,5-dione	pink	191-193	60	384

Table 3: Physical properties of chloroacetyl substituted amides

Comp. No.	Structure and name	Color	M.P °C	Yield %	M.Wt
C1	 2-chloro-N-(2-(1,3-dioxoisoindolin-2-yl)-5-(3,4,5-trimethoxybenzyl) pyrimidin-4-yl) acetamide	White	285-287	78	496

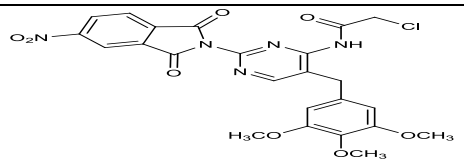
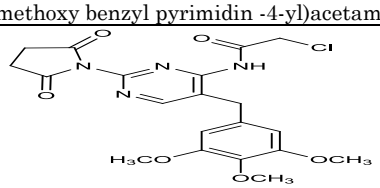
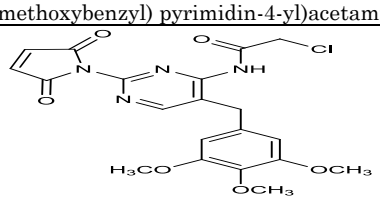
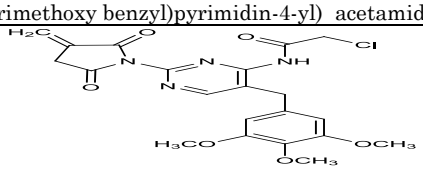
C2	 2-chloro-N-(2-(5-nitro-1,3-dioxoisoindolin-2-yl)-5-(3,4,5-trimethoxy benzyl pyrimidin -4-yl)acetamide	White	256-258	64	541
C3	 2-chloro-N-(2-(2,5-dioxopyrrolidin-1-yl)-5-(3,4,5-trimethoxybenzyl) pyrimidin-4-yl)acetamide	White	253-254	60	448
C4	 2-chloro-N-(2-(2,5-dioxo-2,5-dihydro-1H-pyrrol-1-yl)-5-(3,4,5-trimethoxy benzyl)pyrimidin-4-yl) acetamide	White	236-238	76	446
C5	 2-chloro-N-(2-(3-methylene-2,5-dioxopyrrolidin-1-yl)-5-(3,4,5-trimethoxy benzyl)pyrimidin-4-yl) acetamide	White	263-265	54	460

Table 4: Physical properties of the prepared thiazole compounds

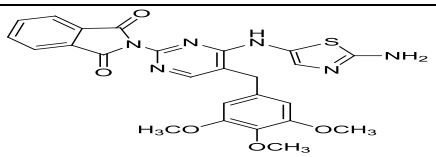
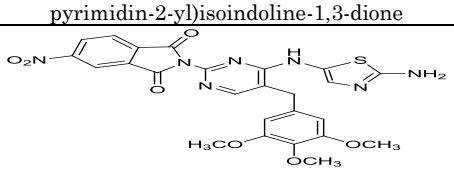
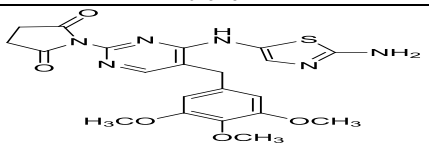
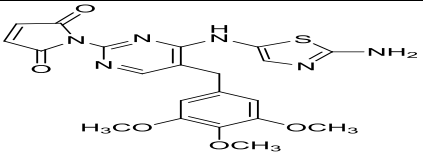
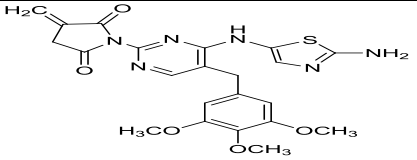
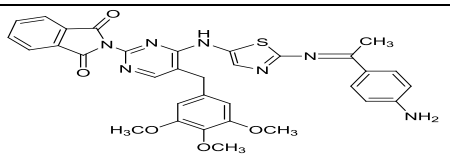
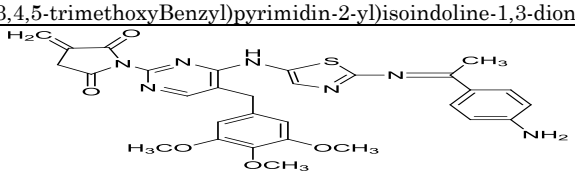
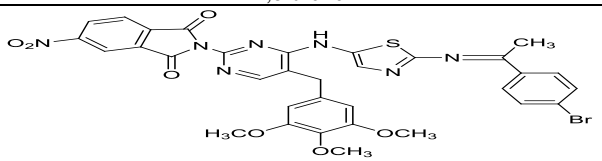
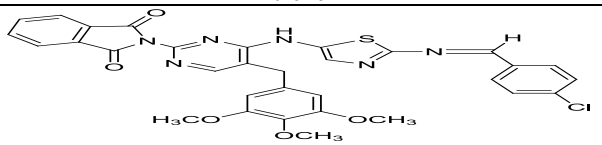
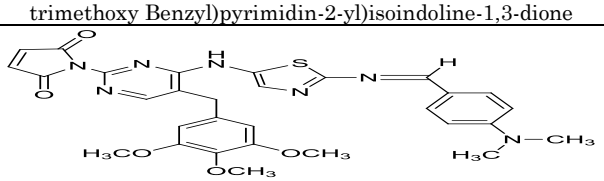
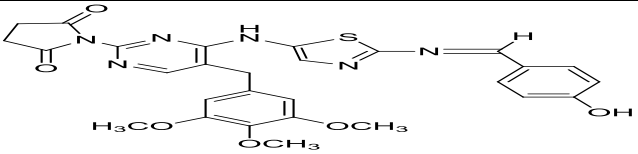
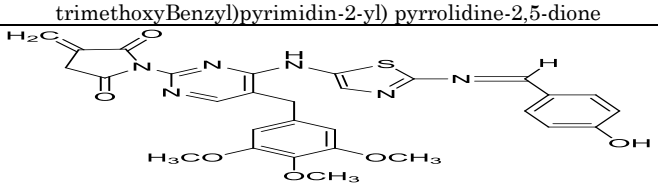
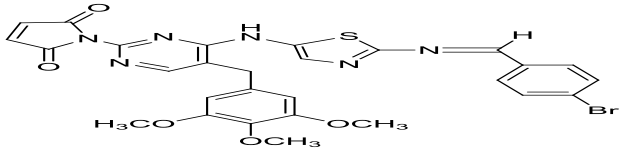
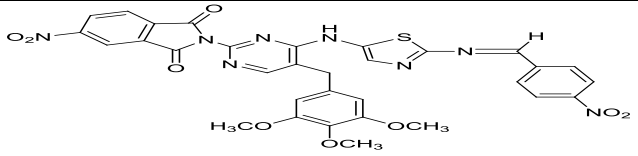
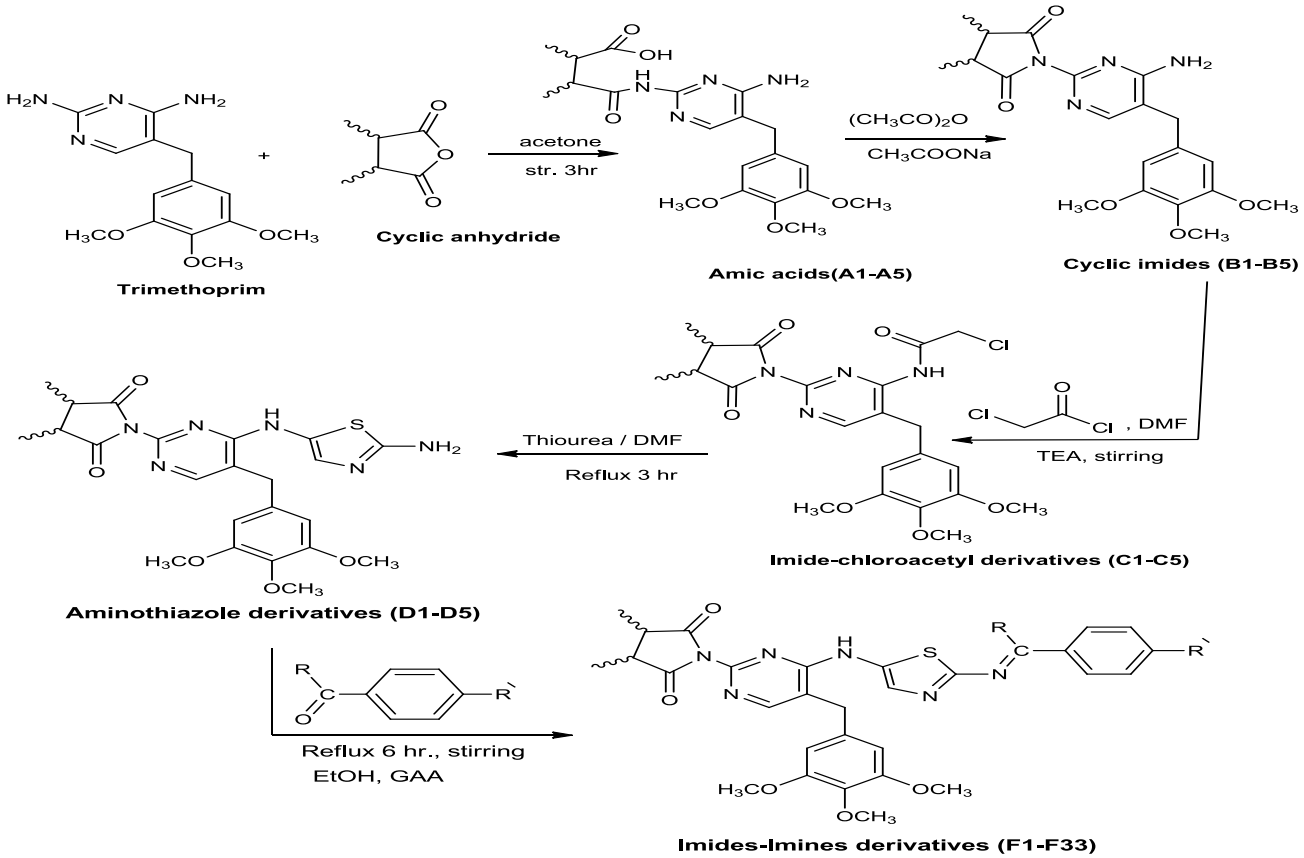
Comp. No.	Structure and name	Color	M.P °C	Yield %	M.Wt
D1	 2-(4-((2-aminothiazol-5-yl)amino)-5-(3,4,5-trimeth-oxyBenzyl) pyrimidin-2-yl)isoindoline-1,3-dione	Gray	246-248	68	518
D2	 2-(4-((2-aminothiazol-5-yl)amino)-5-(3,4,5-trimethoxyBenzyl)pyrimidin-2-yl)-5-nitroisoindoline-1,3-dione	Orange	182-183	61	563
D3	 1-(4-((2-aminothiazol-5-yl)amino)-5-(3,4,5-trimethoxyBenzyl)pyrimidin-2-yl)pyrrolidine-2,5-dione	Gray	262-264	53	470
D4	 1-(4-((2-aminothiazol-5-yl)amino)-5-(3,4,5-trimethoxyBenzyl)pyrimidin-2-yl)-1H-pyrrole-2,5-dione	Light brown	269-270	58	468
D5	 1-(4-((2-aminothiazol-5-yl)amino)-5-(3,4,5-trimethoxyBenzyl)pyrimidin-2-yl)-3-methylenepyrrolidine-2,5-dione	Light brown	267-268	45	482

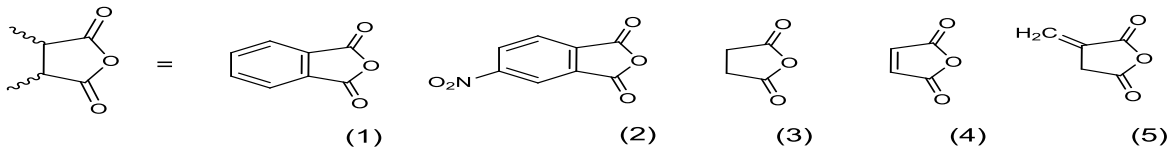
Table 5: Physical properties of the prepared imines compounds

Comp No.	Structure and name	Color	M.P ◦C	Yield %	M. Wt
F1	 2-(4-((2-(((1(4aminophenyl)ethylidene)amino)thiazol-5-yl)amino)-5-(3,4,5-trimethoxyBenzyl)pyrimidin-2-yl)isoindoline-1,3-dione	Pale green	101-102	83	635
F5	 1-(4-((2-(((1(4aminophenyl)ethylidene)amino)thiazol-5-yl)amino)-5-(3,4,5-trimethoxyBenzyl)pyrimidin-2-yl)-3-methylenepyrrolidine-2,5-dione	brown	185-187	80	599
F7	 2-(4-((2-(1-(4-bromophenyl)ethylidene)amino)thiazol -5-yl)amino)-5-(3,4,5-trimethoxyBenzyl)pyrimidin-2-yl)-5-nitroisoindoline-1,3-dione	Pale yellow	132-134	85	744
F11	 2-(4-((2-((4-chlorobenzylidene)amino)thiazol-5-yl)amino)-5-(3,4,5-trimethoxy Benzyl)pyrimidin-2-yl)isoindoline-1,3-dione	Light gray	164-166	78	640
F19	 1-(4-((2-((4-(dimethylamino)benzylidene)amino)thiazol-5-yl)amino)-5-(3,4,5-trimethoxyBenzyl) pyrimidin-2-yl)-1H-pyrrole-2,5-dione	Brown	196-198	67	599
F23	 1-(4-((2-((4-hydroxybenzylidene)amino)thiazol-5-yl)amino)-5-(3,4,5-trimethoxyBenzyl)pyrimidin-2-yl) pyrrolidine-2,5-dione	Light brown	111-113	60	574
F25	 1-(4-((2-((4-hydroxybenzylidene)amino)thiazol-5-yl)amino)-5-(3,4,5-trimethoxyBenzyl)pyrimidin-2-yl)-3-methylenepyrrolidine-2,5-dione	Gray	188-190	58	586
F29	 1-(4-((2-((4-bromobenzylidene)amino)thiazol-5-yl)amino)-5-(3,4,5-trimethoxyBenzyl)pyrimidin-2-yl)-1H-pyrrole-2,5-dione	Light brown	240-242	70	635
F31	 5-nitro-2-(4-((2-((4-nitrobenzylidene)amino)thiazol-5-yl)amino)-5-(3,4,5-trimethoxyBenzyl)pyrimidin-2-yl) isoindoline-1,3-dione	Light red	179-181	74	696

Result and Discussion

The starting material for the synthetic imines-imides for trimethoprim is trimethoprim which reacted with different cyclic anhydride then with chloroacetyl chloride in DMF and after that thiourea was added under reflux then the produce compounds reacted with different aromatic aldehydes or ketones. The mechanism is shown in the schemes below.





R = H, CH3- ; R` = NH_2, -Br, -Cl, $-N(CH_3)_2$, -OH, NO_2

Scheme 1: Total synthesis sequence for all compounds

The structure of the prepared compounds was elucidated by melting points, FTIR and ^{1}H-NMR spectroscopy. The FTIR absorption-spectra of compounds (A1-A5) showed absorption bands at the region (3359-3469) cm^{-1} due to non-reacted NH_2 of trimethoprim with the appearance of new absorption stretching bands due to O-H group of carboxylic moiety at (3321-3340) cm^{-1}. The C=O (carboxylic acid) at (1654-1710)cm^{-1},whereas the N-H (amide) at (3178-3282) cm^{-1}, the amide carbonyl C=O (amid) at (1591-1664) cm^{-1} and C=N (endocyclic) for pyrimidine ring at (1541-1595) cm^{-1}, the C-N stretching at (1234 -1240)cm^{-1}, C-O at (1120-1128) cm^{-1} [32, 33]. All these regions are shown in Table (6).

Table 6: FTIR spectral data of compounds (A1-A5) in (cm^{-1})

No.	υNH_2 1°amine	υN-H 2°amine	υC-H arom.	υC-H aliph.	υC=O carbox.	υC=O amide	υC-N	υO-H carbox.
A1	3419 3359	3180	3139 3001	2939	1666	1591	1240	3338
A2	3460 3394	3209	3141 3060	2935	1662	1623	1234	3334
A3	3469 3413	3282	3163	2995	1658	1637	1236	3321
A4	3442 3404	3178	3078	2939	1710	1664	1238	3340
A5	3448 3398	3224	3062	2941	1654	1591	1240	3332

The FT-IR spectra of compounds (B1-B5) showed disappearance of (O-H) and (N-H) absorption bands at (3321-3340) cm^{-1}, (3178-3282) cm^{-1} respectively and appearance of new bands at the region (1664-1591) cm^{-1} for asym. and sym. (C=O) imide. The bands of (C=C) aromatic at (1506-1508) cm^{-1} and (C-N) imide appeared at (1236-1242) cm^{-1}. All the other absorptions are listed in table (7). ^{1}H-NMR spectrum of compound B3 showed a signal at δ 7.51 ppm of (s,2H,NH_2), a signal at δ 7.63 ppm of (s,1H,N=CH), a signal at δ 3.61 ppm for the (s,2H,-CH_2-) group, a signal at δ 3.75 ppm for the (s,9H,CH_3-O-), a signal at δ 3.63 ppm for the (s,4H,-CH_2CH_2-) group and signal at δ 6.64ppm of (s,2H,Ar-H).

Table 7: FTIR spectral data of the imides compounds (B1-B5) in (cm^{-1})

No.	υNH_2 1°amine	υC-H arom.	υC-H aliph.	υC=O	υC=N	υC=C	υC-N	υC-O
B1	3419 3350	3190 3002	2939	1664 1591	1541	1506	1242	1128
B2	3448 3427	3193	2906	1662 1596	1548	1508	1236	1124
B3	3448 3427	3161	2995	1660 1593	1537	1506	1238	1124
B4	3469 3400	3139	2933	1664 1637	1593	1506	1236	1126
B5	3502 3406	3176	2939	1662 1591	1529	1508	1240	1130

FTIR spectrum of compounds (C1-C5) showed the disappearance of the absorption band at (3350-3469) cm^{-1} of NH_2 group and the appearance of new region in (3203-3332)) cm^{-1} due to (N-H) group, (1706-1782) cm^{-1} for the (C=O) amide and the absorption band at (715-763)) cm^{-1} due to the (C-Cl) group and the other absorptions are shown in table (8). ^{1}H-NMR spectrum of compound C4showed a signal at δ 6.21 ppm for the (s,1H,N-H) group, a signal at δ 2.35 ppm of (s,2H,-CH_2-Ar), a signal at δ 3.73 ppm of (s,9H,CH_3-O-), a singlet signal at δ= 3.54 ppm for the (s,2H,-CH_2Cl), a signal at δ 6.42 ppm of (s,1H,-CH=N-), a signal at δ 7.49 ppm of (s,2H,-CH=CH-) and signal at δ 6.57 ppm of (s,2H,Ar-H). ^{1}H-NMR spectrum of compound C3 showed a signal at δ 7.50 ppm for the (s,1H,N-H) group, a signal at δ 7.61 ppm of (s,1H,-CH=N-), a signal at δ 3.35 ppm for the (s,2H,-CH_2-) group, a signal at δ 3.75 ppm of (s,9H,CH_3-O-), a signal at δ 3.61 ppm for the (s,2H,-CH_2Cl), a signal at δ 3.63 ppm for the (s,4H,-CH_2CH_2-) group and a signal at δ 6.64 ppm of (s,2H,Ar-H).

Table 8: FTIR spectral data of compounds (C1-C5) in (cm^{-1})

No.	υN-H 2°amine	υC-H arom.	υC-H aliph.	υC=O imide	υC=N	υC=C	υC=O amide	υC-Cl
C1	3203	3060	2941	1749 1737	1602	1504	1774	715
C2	3323	3168 3068	2941	1660 1647	1589	1506	1720	763
C3	3332	3161	2933	1674 1645	1589	1502	1774	763
C4	3325	3174	2958	1645 1622	1589	1527	1782	761
C5	3321	3172	2950	1645 1622	1589	1529	1706	761

FTIR of compounds (D1-D5) showed the disappearance of the absorption band of (υC=O) amide at (1706-1782) cm^{-1} , absorption band of (υC-Cl) group at (715-763) cm^{-1} and the appearance of new band at (3467-3406) cm^{-1} of (NH_2) group and new absorption at (1531-1544) cm^{-1} of (υN=C) group and the other regains are listed in table (9). ^{1}H-NMR spectrum of compound D2 showed signal at δ 5.75 ppm for the (s,1H,N-H) group, a signal at δ 3.53 ppm for the(s,2H,-CH_2-) group, a signal at δ 3.72 ppm of (s,9H,CH_3-O-), a signal at δ 6.13 ppm for the (s,1H,C-H of thiazole ring), a signal at δ 7.52 ppm for the (s,2H,-NH_2), a signal at δ 7.95 ppm for the (s,1H,-N=CH of pyrimidine),), a signal at δ 6.55 ppm for the (s,2H,Ar-H) and signals at δ (8.06-8.62) ppm of (m,3H,Ar-H).

Table 9: FTIR spectral data of compounds (D1-D5) in (cm^{-1})

No.	υN-H 2°amine	υC-H arom.	υC-H aliph.	υC=O imid	υC=N heter.	υN=C thiazol	υC=C	υNH_2
D1	3338	3186 3064	2939	1662 1627	1593	1544	1506	3448 3427
D2	3234	3151 3128	2993	1739 1637	1600	1537	1504	3467 3425
D3	3326	3164 3097	2902	1743 1662	1596	1533	1508	3448 3419
D4	3325	3164	2931	1676 1643	1589	1531	1502	3440 3406
D5	3286	3170	2968	1674 1645	1589	1531	1502	3445 3419

FT-IR spectra of compounds (F1-F33) showed disappearance of the two characteristic absorption bands at (3467-3406) cm^{-1} due to (NH_2) group in substituted aminothiazole compounds and appearance of new clear absorption band at (1512-1564) cm^{-1} due to (N=C) imine. These two points are excellent proofs for the success of imines formation [34].

Besides FT-IR spectra of compounds (F1-F33) showed clear absorption bands at (1778-1591) cm^{-1} due to asym. And sym. (C=O) imide. Other absorptions appeared at (1596-1564) cm^{-1} and (1452-1512) cm^{-1} due to (C=N) pyrimidine and (C=C) aromatic respectively. All these regains and the others are listed in table (10). ^{1}H-NMR spectrum of compound F1 showed signal at δ 3.64 ppm for (s,3H,CH3-), a signal at δ 3.35 ppm for the (s,1H,N-H), a signal at δ 7.43 ppm for the (s,2H,NH_2), a signal at δ 3.59 ppm for the (s,2H,-CH_2-), a signal at δ 3.75 ppm of (s,1H,CH_3-O-), a signal at δ 7.30 ppm for the (s,1H,C-H of thiazole ring), a signal at δ 6.61 ppm for the (s,2H,Ar-H) and signals at δ (7.50-8.11) ppm of (m,8H,Ar-H).

^{1}H-NMR spectrum of compound F23 showed signal at δ 3.73 ppm of (s,4H,CH_2CH_2), a signal at δ 3.56 ppm of (s,1H,N-H), a signal at δ 6.77 ppm for the (s,1H,-CH=N- of imine), a signal at δ 3.63 ppm for the (s,2H,-CH_2-), a signal at δ 2.38 ppm of (s,9H,CH_3-O-) proton, a signal at δ 6.39 ppm due to the (s,1H,C-H of thiazole ring), a signal at δ 6.03 ppm for the (s,1H,O-H), a signal at δ 7.83 ppm for the (s,2H,Ar-H) and signals at δ (6.56-7.68) ppm of (m,4H,Ar-H).

Table 10: FTIR spectral data of compounds (F1-F33) in (cm^{-1})

No.	υN-H 2°amin	υC-H arom.	υC-H aliph.	υC=O	υC=N	υC=C	υN=C imine	others
F1	3226	3064	2906	1724 1650	1591	1510	1564	3398 NH_2 3332
F3	3226	3184	2941	1645 1591	1564	1508	1533	3400 NH_2 3332
F5	3228	3066	2939	1645 1591	1564	1508	1531	3398 NH_2 3332
F6	3332	3174	2933	1674 1645	1589	1502	1529	972 C-Br
F7	3330	3182	2937	1674 1641	1591	1504	1533	970 C-Br
F11	3338	3186	2939	1726 1662	1593	1506	1538	968 C-Cl
F12	3330	3182	2939	1724 1664	1591	1502	1533	908 C-Cl
F17	3326	3164	2902	1743 1662	1596	1508	1533	1371 -$N(CH_3)_2$
F19	3328	3168	2925	1676 1662	1595	1508	1531	1371 -$N(CH_3)_2$
F22	3226	3110	2941	1718 1660	1598	1510	1546	3400 O-H
F23	3330	3184	2937	1720 1660	1591	1504	1533	3406 O-H
F26	3326	3166	2966	1778 1670	1596	1452	1512	833 C-Br
F27	3323	3182	2941	1718 1660	1596	1508	1544	837 C-Br
F29	3325	3170	2933	1676 1641	1589	1504	1531	842 C-Br
F31	3328	3190	2937	1722 1660	1595	1506	1529	854 NO_2

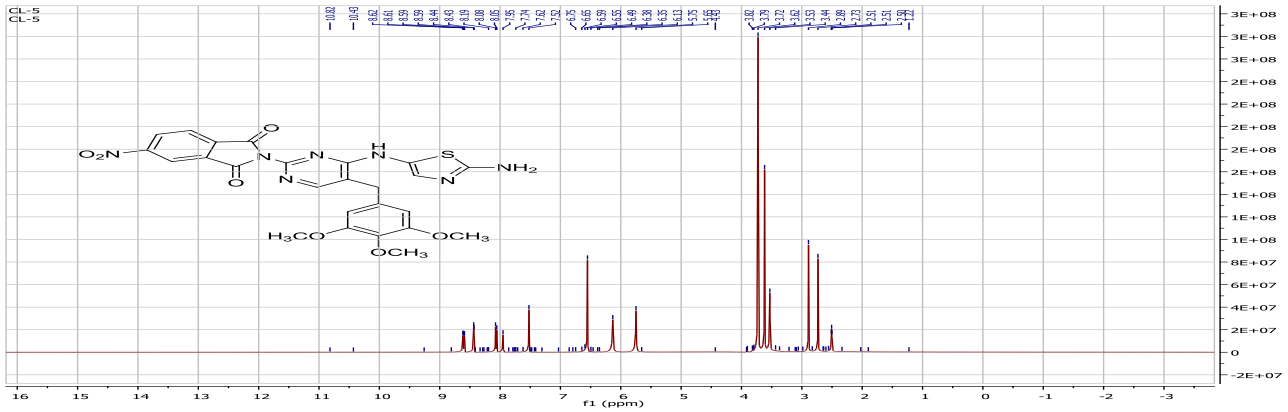


Figure 1: ^{1}H-NMR spectrum of compound D2

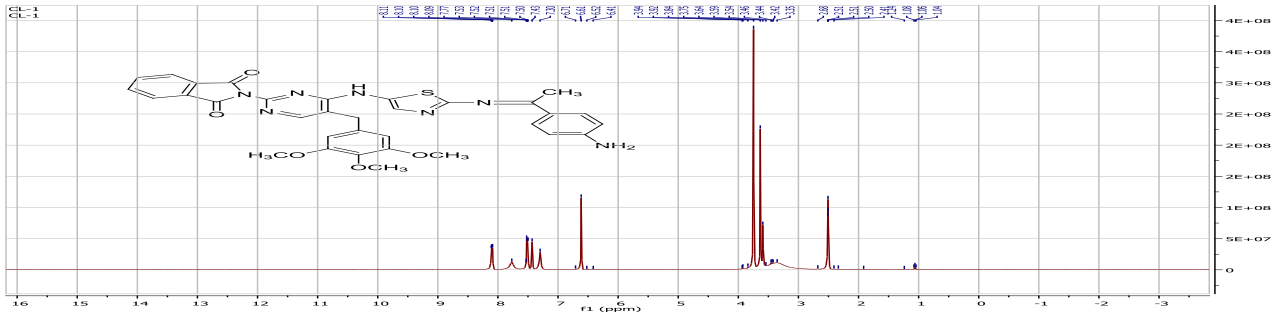


Figure 2: ^{1}H-NMR spectrum of compound F1

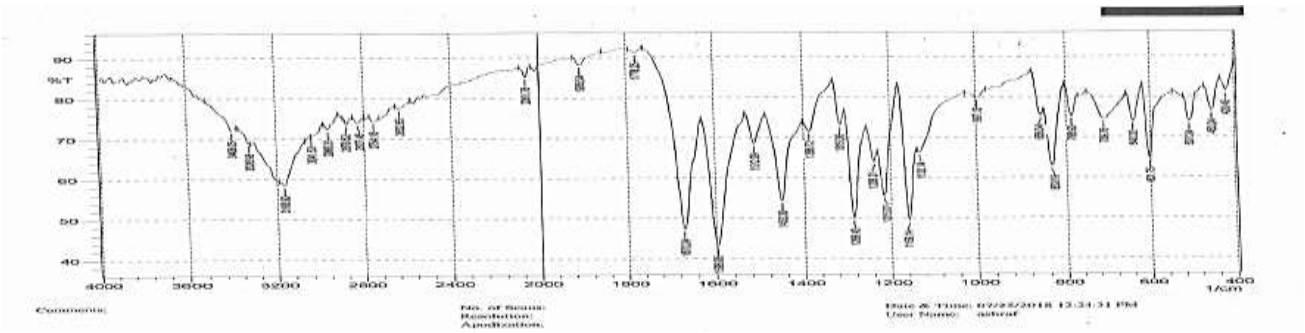


Figure 3: FT- IR spectrum for compound F26

References

1. Khurana J (2006) Organic compounds, chemistry of heterocyclic compounds, 3rd ed., Willy-Inter sciences, India.
2. Unsinn A, Stefan HW, Knochel P (2013) Accelerated zincations for an Efficient and Mild Functionalization of Aromatics and Heterocycles, Advanced synthesis and catalysis, 355 (5): 989-995.
3. Paulo J, Coelh A, Ceu M, Sousa M, Cidalia R, Castro A, Mauricio C, Fonseca M, Manuela M, Raposo P (2013) Fast thermal cis and trans isomerization of heterocyclic azo dyes in PMMA polymers, Optical. Martial., 35: 1167-1172.
4. Nables A, Negm A, Tawfik S (2013) Impact of synthesized and natural compounds in corrosion Inhibition of carbon Steel and Aluminum in Acidic Media, Recent Patents on Corrosion Sci., 3:1-11.
5. Shihab N, Intedhar NM (2013) Synthesis of some novel Heterocyclic azo dyes for acridine derivatives and evaluation of Their antibacterial activities, J. Chema. & Pharma. Res., 5(5):345-354.
6. Brown HC, Braude EA, Nachod FC (1955) Determination of Organic structures by physical Methods", Academic Press, New York.
7. Sondhi SM, Dinodia M, Rani R, Shukla R, Raghubir R (2009) Synthesis, anti-inflammatory and analgesic activity evaluation of some pyrimidine derivatives, Indian Journal of Chemistry, 49B: 273-281.
8. Putz MV, Dudaş NA, Isvoran A (2015) Double variational binding-(SMILES) conformational analysis by docking mechanisms for anti-HIV pyrimidine ligands. International journal of molecular sciences, 16(8): 19553-19601.

9. Cai D, Zhang ZH, Chen Y, Yan XJ, Zou LJ, Wang YX, Liu XQ (2015) Synthesis, Antibacterial and Antitubercular Activities of Some 5H-Thiazolo [3, 2-a] pyrimidin-5-ones and Sulfonic Acid Derivatives. Molecules, 20(9): 16419-16434.
10. El-Ansary AKED, Taher AT, El-Rahmany AAEH, El Awdan S (2014) Synthesis, anti-inflammatory, analgesic and antipyretic activities of novel pyrano [2, 3-c] pyrazoles and related fused ring derivatives. Journal of American Science, 10: 10.
11. Marulasiddaiah R, Kalkhambkar RG, Kulkarni MV (2012) Synthesis and Biological Evaluation of Cyclic Imides with Coumarins and Azacoumarins, Open J. Med. Chem., 2: 89-97.
12. Patil MM, Rajput SS (2014) Succinimides: synthesis, reaction, and biological activity, Int. J. Pharm. Sci., 6(11):8-14.
13. Dhivare RS, Rajput SS (2015) Synthesis and antimicrobial activity of five membered cyclic imide derivatives of mono, di and tri substituted aromatic amines and napthylamin, World J. Pharm. Sci., 4(6):1650-1658.
14. Al-Majidi SMH, Ahmad MR, Kareem Khan A (2013) Synthesis and characterization of novel 1,8-Naphthalimide derivatives containing 1,3-oxazoles,1,3-thiazoles, 1,2,4-triazoles as antimicrobial agents, J. Al-Nahrain Uni., 16 (4):55-66.
15. Al-Azzawi AA, Hassan AS (2011) Synthesis and preliminary evaluation of Antimicrobial activity of new sulfonamido and acetamido cyclic imides linked to benzothiazole moiety, K. J. Pharm. Sci., 2: 59-80.
16. Tozato Prado SR, Cechinel-Filho V, Campos-Buzzi F, Correa R, Correia Suter CSM, Martinelli de Oliveira MB (2004) Biological evaluation of some selected cyclic imides:Mitochondrial effects and in vitro cytotoxicity, Z Naturforsch. 59c:663D672. [Pub Med]
17. Gayoso CW, Lima EO, Souza EL, Filho VC, Trajano VN, Pereira FO, Lima IO (2006) Antimicrobial effectiveness of maleimides on fungal strains isolated from onychomycosis, Brazilian Archives of Bio & Tech., 49(4):661-664.
18. Sortino M, Filho VC, Corre R, Zacchino S (2008) N-Phenyl and N-phenylalkyl maleimides acting against Candida spp.: Time-to-kill, stability, interaction with maleamic acids, Bioorg. Med. Chem., 16: 560-568. [Pub Med]
19. Dhivare RS, Rajput SS (2016) Microwave assisted solvent free synthesis and antifungal evaluation of 3, 5-bis-(4-hydroxy-3-methoxybenzylidene) n-phenyl piperidine-2, 6-dione derived from N-phenyl glutarimides, Int. J. Chem. Tech. Res., 9(3):325-331.
20. Campos-Buzzid F, Corread R, Souzaa MM, Yunes RA, Nunes RJ, Cechinel-Filho V (2002) Studies on new cyclic imides obtained from aminophenazone with analgesic properties, Arzneim. -Forsch. /Drug Res., 52(6): 455-461. [Pub Med]
21. Kashyap SJ, Garg VK, Sharma PK, Kumar N, Dudhe R, Gupta JK (2011) Thiazoles: having diverse biological activities, Med. Chem. Res., 21: 2123-2132.
22. Siddiqui N, Arshad MF, Ahsan W, Alam MS (2009) Thiazoles : A Valuable Insight into the Recent Advances and Biological Activities, IJPSDR, 1: 136-143.
23. Siddiqui N, Kumar S, Ahsan W, Azad B (2011) Diverse biological activities of Thiazoles : A Retrospect, Int. J. Drug Dev. & Res., 3: 55-67.
24. Brodowska K, Lodyga-Chruscinska E (2014) Schiff bases-interesting range of applications in various fields of science CHEMIK, 2 (68):129-134.
25. Sompriya C, Sauvik B (2015) Schiff bases as a source of potent molecules with anti-cancer potential, Asian Journal of Biochemistry and Pharmacy Research, 4(5): 86-97.
26. Yusra HA, Jawad KS, Ahmad NA (2015) Synthesis, characterization and antibacterial activity of new Schiff's bases with 1, 2, 4-triazole moiety, Journal of Science, 5(5): 293-299.
27. Anita R, Manoj K, Rajshree K, Hardeep ST (2015) Schiff bases as an antimicrobial agent: a review, Journal of Biochemistry Science, 2(1): 62-91.
28. Al-Azzawi AM, Mehdi SA (2010) Synthesis, characterization and biological activity study of N-substituted sulfonamido maleimides substituted with different heterocycles, Baghdad Science Journal, 7(1): 641-653.

29. Al-Azzawi AM, Hassan AS (2014) Synthesis and antimicrobial activity of new succinimides bearing different heterocycles, International Journal of Research in Pharmacy and Chemistry, 4(4): 755-762.
30. Vogel AI (1974) A text book in practical organic chemistry, 3rd Ed long man group limited, London, 389.
31. Sujit, K, Anuradha K, Harika M, Sarada P, Jenny S (2015) Synthesis, Characterization and Antimicrobial Activity of Some Oxazole and Thiazole Derivatives, J. Serb. Chem. Soc., 2(3): 60-66.
32. RM Silverstein, GC Bassler, DJ Kiemle (2005) Spectroscopic Identification of Organic Compounds, Seventh Edition, John Wiley and Sons. New York.
33. Sharma YR (2009) Elementary Organic Spectroscopy, 4th Edition, Ramnagar, New Delhi Ind., 122: 233.
34. RT Conley (1972) Infrared spectroscopy, 2nd Edition, Boston.

