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Selective approaches to synthesize a new series of fused 4-amino pyrimidine derivatives by using of 4- amino nicotino nitrile as an effective precursor

Mustafa. H. Sami
University of Mosul, College of Science, Department of Chemistry
Email: Mustafa.houmam1994@gmail.com

Shaymaa. K. Younis
University of Mosul, College of Science, Department of Chemistry
Email: shaymaakhazaal@uomosul.edu.iq

***Abstract*---**Pyrimidines and it's derivatives are one of the most fascinating type of six membered heterocyclic compounds which received a great deals of attention due to it`s diverse importance and activity in many different field such as biological, medicinal, pharmaceutical and also in industrial and agricultural field. In this presentation, fused 4-amino pyrimidine derivatives were achieved using green chemistry technique represented by solid phase one–pot multicomponent reaction, microwave irradiation and grinding and also by traditional methods. Firstly, equimolar of aromatic(heterolytic) amines, piperonal and malononitriles were grinding for few minutes then accelerated by microwave irradiation (MWI) at (270 watt) for 3 minutes to afford fused 4-amino nicotino nitrile (1a-e) which then underwent cycloaddition reaction with formamide, urea and thiourea via traditional methods using acidic or basic conditions to afford a new series of fused 4-amino pyrimidines represented by compounds (2a-e), (3a-e) and (4a-e) respectively. All prepared compounds were illustrated by the available physical and spectral methods.

***Keywords*---**Fused pyrimidine, Green chemistry, One-pot multicomponent reaction, 4-amino nicotino nitrile, Microwave irradiation.

1 Introduction

Fused heterocyclic compounds containing pyrimidine moiety consist of high activity in many different field especially in medical field as anti cancer (Boger et

al., 1989; Fathalla et al., 2009; Prachayasittikul et al., 2017), anti hypertensive (Darwish, Abdelrahman, & Salaheldin, 2011; Farghaly et al., 2019), anti HIV(Farouk Elsadek, Mohamed Ahmed, & Fawzi Farahat, 2021; Kumar, Deep, & Narasimhan, 2019), anti inflammatory (Amer, El-Eraky, & Mahgoub, 2018; Thakur, 2011), antibacterial (Mahfoudh, Abderrahim, Leclerc, & Campagne, 2017; Raghavendra, Bhojya Naik, & Sherigara, 2006), antimicrobial (Mallikarjunaswamy, Mallesha, Bhadregowda, & Pinto, 2017),and antifungal activity(Maddila, Gorle, Seshadri, Lavanya, & Jonnalagadda, 2016; Naik & Chikhalia, 2007). Thus considering the importance of fused pyrimidine, this research focuses on the synthesis a unique poly fused heterocyclic system starting from solid phase one-pot multi component reaction among piperonal, aromatic(heterolytic) amines and malononitrile which grinding for few minutes then accelerated via microwave irradiation (MWI) in power (270 watt) for few minutes (3 min.) to achieve 6-piperonyl-4-amino fused nicotine nitriles (1a-e). These compounds then used as active precursor to prepare a new series of fused 4-amino pyrimidine via cycloaddition reaction in acidic or basic conditions with formic acid, urea and thiourea and also represented by the compounds (2a-e),(3a-e) and (4a-e) respectively. In fact, solid phase one-pot multicomponent reaction was used in the first step of preparation due to it's supreme properties as rapid, environmentally safe, inexpensive and yield enhancement (Bariwal, Trivedi, & Eycken, 2010).

2 Materials and Methods

Synthesis of 4-amino nicotinonitrile (1_{a-e})(Shi, Tu, Fang, & Li, 2005):
A mixture of equimolar (0.003mol) of piperonal, malononitrile and aromatic amine where well grinding for few minutes followed by irradiated via microwave oven at power (270 watt/3min.). The reaction mixture allowed to cool, the formed sticky mass was solidified by washing thoroughly with cold water with stirring. Followed by filtration, dried then recrystallization with appropriate solvent to produce (1a-e) in good yields, Table (1).

(1a) 5-amino-2-(piperonyl -5-yl)-5H-thiazolo[3,2-a]pyrimidine-6-carbonitrile :
Yellow powder, yield %(70%), m.p ^{o}C (194-197), T.L.C(R_f) (0.47) ; ^{1}H-NMR (δ ppm) : (s,3.54, CH_2-piperonal),(m,6.23-6.24,piperonal), (d-d,7.20-7.22,thiazole) , (m,7.35-7.56, aromatic) , (s,8.38 ,NH_2). FT-IR (cm^{-1}): 3372,3429 (NH_2) , 3030 (=C-H) , 2224 (CN) , 1612 (C=C) , 1568 (C=N) , 1289 asym. and 1032 sym. (C-O-C), 1111 (C-S) . U.V λ_{max} (nm):(375,340).

(1b) 4-amino-2-(piperonyl -5-yl)-4H-pyrimido[1,2-a]pyrimidine-3-carbonitrile:
Deep yellow powder, yield %(75%), m.p ^{o}C (194-196), T.L.C(R_f) (0.744) ; FT-IR (cm^{-1}): 3371,3402 (NH_2) , 3030 (=C-H) , 2224 (CN) , 1612 (C=C) , 1568 (C=N) , 1295 asym. and 1032 sym. (C-O-C). U.V λ_{max} (nm):(371,327) .

(1c) 4-amino-2-(piperonyl -5-yl)-6-nitro-1,8-naphthyridine-3-carbonitrile:
Yellow powder, yield %(65%), m.p ^{o}C (125-128), T.L.C(R_f) (0.626); ^{1}H-NMR (δ ppm) : (s,6.18, CH_2-piperonal),(m,6.49-6.51,piperonal) , (m,7.14-8.85, aromatic) , (s,9.81 ,NH_2). FT-IR (cm^{-1}): 3322,3400 (NH_2) , 3030 (=C-H) , 2194 (CN) , 1668 (C=C) , 1588 (C=N) , 1281 asym. and 1091 sym. (C-O-C), 1490 asym. and 1330 sym. (NO_2). U.V λ_{max} (nm):(302,371) .

(1d) 4-amino-2-(piperonyl -5-yl)-7,12-dioxo-7,12-dihydronaphtho[2,3-h]quinoline-3-carbonitrile:
Brown powder, yield %(80%), m.p ^{o}C (144-146), T.L.C(R_f) (0.581) ; FT-IR (cm^{-1}): 3320,3415 (NH_2) , 3037 (=C-H) , 2377 (CN) , 1676 (C=O), 1600 (C=C) , 1588 (C=N) , 1232 asym. and 1095 sym. (C-O-C). U.V λ_{max} (nm):(375,340).

(1e) 4-amino-2-(piperonyl -5-yl)-6,11-dioxo-6,11-dihydronaphtho[2,3-g]quinoline-3-carbonitrile:
Brown powder, yield %(96%), m.p ^{o}C (167-170), T.L.C(R_f) (0.36) ; ^{1}H-NMR (δ ppm): (s,6.18,CH_2-piperonal), (m,6.94-6.96,piperonal), (m,7.14-8.16, aromatic), (s,9.81, NH_2). FT-IR (cm^{-1}): 3341,3435 (NH_2) , 3064 (=C-H) , 2687 (CN) , 1672 (C=O) , 1624 (C=C) , 1587 (C=N) , 1281 asym. and 1090 sym. (C-O-C). U.V λ_{max} (nm): (444,323).

Synthesis of 2-amino pyrimidines (2_{a-e})(Mohamed, Rashad, Zaki, & Fatahala, 2005; Orlov, 2018) :

In round bottomed flask (100 ml) equipt with magnetic stirrer dissolve (0.00025 mol) of compound (1a-e) in (5ml) ethanol in acid media of glacial acetic acid (2-3 drops) as acidic catalyst followed by adding an ethanolic solution of formamide (0.00025 mol) dropwise with stirring until the mixture become homogenous followed by reflux for (4-5 hrs.) (under T.L.C control). The reaction mixture allow to cool, poured into ice-water (20ml) with shaking. The precipitate was collected by filtration then washed thoroughly with cold water, dried and recrystallized from appropriate solvent to produce compounds(2a-e) Tabel (2).

(2a) 5-(piperonyl -5-yl)-6aH-pyrimido[5,4-e]thiazolo[3,2-a]pyrimidin-4-amine:
Yellow powder, yield %(81%), m.p ^{o}C (96-99), T.L.C(R_f) (0.633) ; FT-IR (cm^{-1}): 3320, 3384
(NH_2) , 3091 (=C-H) , 1590 (C=C) , 1546 (C=N) , 1248 (C-O-C asym.) , 1103 (C-O-C sym.), 1033(C-S). U.V λ_{max} (nm):(376-366).
(2b) 5-(piperonyl -5-yl)-6aH-dipyrimido[1,2-a:5',4'-e]pyrimidin-4-amine:
Yellow powder, yield %(88%), m.p ^{o}C (186-189), T.L.C(R_f) (0.621) ; FT-IR (cm^{-1}): 3320-3368 (NH_2) , 3082 (=C-H), 1560 (C=C) , 1493 (C=N) , 1257 asym. , 1104 sym. (C-O-C). U.V λ_{max} (nm): (370,317).
(2c) 5-(piperonyl -5-yl)-9-nitropyrimido[5,4-c][1,8]naphthyridin-4-amine:
Light brown powder, yield %(84%), m.p ^{o}C (194-196), T.L.C(R_f) (0.61) ; FT-IR (cm^{-1}): 3314-3368 (NH_2) , 3015 (=C-H) , 1687 (C=C) , 1594 (C=N) , 1238 asym. and 1104 sym. (C-O-C), 1488 asym. and 1290 sym. (NO_2). U.V λ_{max} (nm): (302,271).
(2d) 1-amino-14-(piperonyl -5-yl)naphtho[2,3-h]pyrimido[5,4-c]quinoline-7,12-dione:
Reddish brown powder, yield %(81%), m.p ^{o}C (205-207), T.L.C(R_f) (0.55) ; FT-IR (cm^{-1}): 3427,3498 (NH_2) , 3066 (=C-H) , 1672(C=O),1604 (C=C), 1544 (C=N) , 1280 asym. and 1167 sym. (C-O-C),. U.V λ_{max} (nm):(378,317).
(2e)4-amino-5-(piperonyl -5-yl)naphtho[2,3-g]pyrimido[5,4-c]quinoline-8,13-dione:
Brown powder, yield %(81%), m.p ^{o}C (292-294), T.L.C(R_f) (0.57) ; ^{1}H-NMR (δ ppm): (s,3,45,NH2) (s,6.71,CH2-piperonal); (m,6.93-6.97,piperonal); (m,7.29-8.16,aromatic);. FT-IR (cm^{-1}): 3362,3439 (NH_2) , 3031 (=C-H) , 1626 (C=C) , 1587 (C=N) , 1281 (C-O-C asym.) , 1163 (C-O-C sym.), 1674(C=O). U.V λ_{max} (nm):(444,370).

Synthesis compound 4-amino pyrimidine (2-one) and (2-thion) (3_{a-e}) , (4_{a-e}) (El-Gazzar, Hegab, Swelam, & Aly, 2002; Fawzy et al., 2018) :

Equimolar (0.00025 mol) of compound (1a-e) and urea (thiourea) were dissolved in absolute ethanol (15ml) in basic media of tri ethyl amine. The reaction mixture was reflexed for (5-6 hrs.) (under T.L.C control) followed by cooling and poured into ice-water (20ml) with stirring, the formed precipitate was collected by filteration, dried and recrystallized from appropriate solvent to give compounds (3a-e) and (4a-e) respectively. Table (3),(4) respectively.

(3a)4-amino-5-(piperonyl-5-yl)-1,10a-dihydro-2H-pyrimido[5,4-e]thiazolo[3,2-a]pyrimidin-2-one:

Light brown powder, yield %(82%), m.p ^{o}C(185-186), T.L.C(R_f) (0.325); ^{1}H-NMR (δ ppm):(s,2.42,NH2); (s, 2.56, NH); (s,2.60,CH2-piperonal);(m,3.79-3.97,piperonal);(d-d,3.41-3.42,thiazole);(b,6.15,aromatic).

FT-IR (cm^{-1}): 3349,3430 (NH_2),3233 (NH) , 3014 (=C-H) , 1633 (C=O) , 1562 (C=C) , 1442(C=N), 1245 asym. and 1098 sym. (C-O-C), 1033(C-S). U.V λ_{max} (nm):(371,340).

(3b) 4-amino-5-(piperonyl-5-yl)-1,11a-dihydro-2H-[1,2-a] pyrimidopyrimidine[5',4'-e] pyrimidin-2-one:

Light Orange powder, yield %(65%), m.p ^{o}C(200-203), T.L.C(R_f) (0.404) ;FT-IR (cm^{-1}): 3344,3448 (NH_2) ,3235 (NH) , 3024 (=C-H) , 1638 (C=O) , 1553 (C=C) , 1491(C=N), 1248 asym. and 1096 sym. (C-O-C). U.V λ_{max} (nm):(341,328).

(3c)4-amino-5-(piperonyl -5-yl)-9-nitropyrimido[5,4-c][1,8]naphthyridin-2(1H)-one:

Browen powder, yield %(75%), m.p ^{o}C (189-192), T.L.C(R_f) (0.258); FT-IR (cm^{-1}) : 3245,3352 (NH_2), 3199 (NH), 3085(=C-H), 1589(C=O), 1547 (C=C) , 1452(C=N), 1200 asym. and 1032 sym. (C-O-C) 1442 asym. and 1273 sym. (NO_2). U.V λ_{max} (nm):(343,214).

(3d) 1-amino-14-(piperonyl -5-yl)naphtho[2,3-h]pyrimido[5,4-c]quinoline-3,7,12-(4H)-trione :

Black plate, yield %(82%), m.p ^{o}C (140-143), T.L.C(R_f) (0.73) ; FT-IR (cm^{-1}) : 3390,3434 (NH_2),3064 (NH) , 2914 (=C-H) , 1672 (C=O) , 1591 (C=C) , 1580(C=N), 1274 asym. and 1031 sym. (C-O-C). U.V λ_{max} (nm):(371,340).

(3e)4-amino-5-(piperonyl -5-yl)naphtho[2,3-g]pyrimido[5,4-c]quinoline-2,8,13(1H)-trione:

Black plate, yield %(58%), m.p ^{o}C (204-207), T.L.C(R_f) (0.5) ;. FT-IR (cm^{-1}): 3383,3437 (NH_2), 3187 (NH) , 3166(=C-H) , 1670(C=O) , 1584 (C=C) , 1573(C=N), 1244 asym. and 1029 sym. (C-O-C) 1442 asym. and 1273 sym. (NO_2). U.V λ_{max} (nm):(474,370).

(4a)4-amino-5-(piperonyl-5-yl)-1,10a-dihydro-2H-pyrimido[5,4-e]thiazolo[3,2a]pyrimidine-2-thione:

Brown powder, yield %(91%), m.p ^{o}C (186-187), T.L.C(R_f) (0.279) ; FT-IR (cm^{-1}): 3347,3446 (NH_2), 3237(NH) , 3076 (=C-H) , 1553(C=C) , 1491 (C=N) , 1347 asym. and 1245 sym. (C-O-C), 1098(C=S) , 1033(C-S). U.V λ_{max} (nm):(371,348).

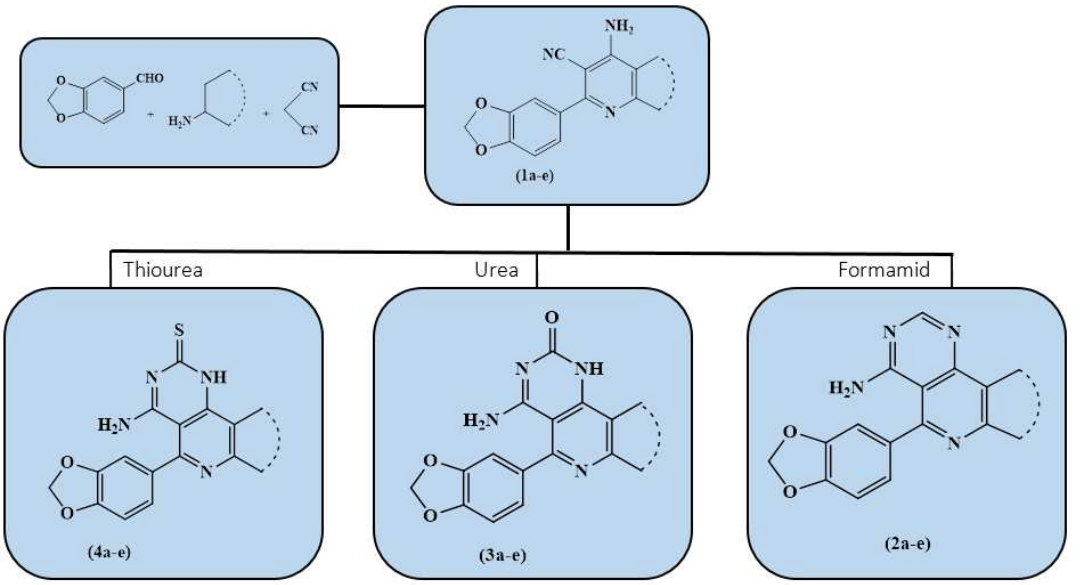
(4b)4-amino-5-(piperonyl -5-yl)-1,6a-dihydro-2H-[1,2-a] pyrimidopyrimidine[5',4'-e] pyrimidin-2-thione:

Orange powder, yield %(58%), m.p ^{o}C (207-210), T.L.C(R_f) (0.5) ; FT-IR (cm^{-1}): 3339,3440 (NH_2), 3227(NH) , 3030 (=C-H) , 1565(C=C) , 1484 (C=N) , 1369 asym. and 1245 sym. (C-O-C), 1096(C=S) . U.V λ_{max} (nm):(341,329).

(4c)4-amino-5-(piperonyl -5-yl)-9-nitropyrimido[5,4-c][1,8]naphthyridine-2(1H)-thione:
Deep green powder, yield %(74%), m.p ^{o}C (235-238), T.L.C(R_f) (0.4) ; ^{1}H-NMR (δ ppm): (s,3.26 NH_2) , (s,3.45 NH), (s,3.54, CH_2-piperonal), (m,6.49-6.51, piperonal), (m,7.56-8.86, aromatic). FT-IR (cm^{-1}): 3352,3390 (NH_2), 3314(NH) , 2971(=C-H) , 1695(C=C) , 1647 (C=N) , 1295 asym. and 1075 sym. (C-O-C), 1086(C=S), 1523(NO_2 asym.), 1380(NO_2 sym.). U.V λ_{max} (nm):(370,340).
(4d)1-amino-14-(piperonyl-5-yl)-3-thioxo-3,4-dihydronaphtho[2,3-h]pyrimido[5,4-c]quinoline-7,12-dione:
Black plate, yield %(83%), m.p ^{o}C (211-214), T.L.C(R_f) (0.28) ; FT-IR (cm^{-1}): 3413,3435 (NH_2), 3347(NH) , 3072 (=C-H) , 1635(C=C) , 1591 (C=N) , 1273 asym. and 1037 sym. (C-O-C), 1076(C=S), 1672(C=O) . U.V λ_{max} (nm):(370,340).
(4e)4-amino-5-(piperonyl-5-yl)-2-thioxo-1,2-dihydronaphtho[2,3-g]pyrimido[5,4-c]quinoline-8,13-dione:
Black plate, yield %(62%), m.p ^{o}C (76-79), T.L.C(R_f) (0.63) ; FT-IR (cm^{-1}): 2395,3421 (NH_2), 3105(NH) , 3005 (=C-H) , 1589(C=C) , 1575 (C=N) , 1327 asym. and 1020 sym. (C-O-C), 1288(C=S), 1670(C=O) . U.V λ_{max} (nm):(370,340).

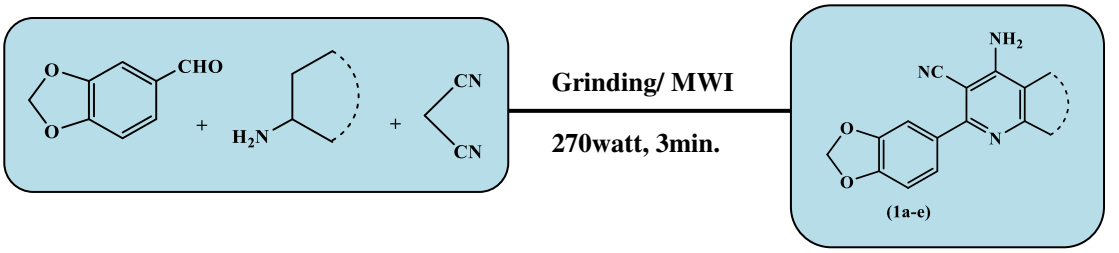
3 Results and Discussions

All compounds were prepared according to the following path way, Scheme (1):



Scheme *1.* Synthetic pathway of compounds (2_{a-e}), (3_{a-e}), (4_{a-e})

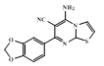
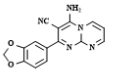
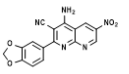
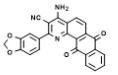
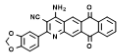
Piperonal, aromatic amine and malononitrile was underwent one-pot three component reaction in neutral media to afford fused 4-amino nicotinonitrile (1a-e), this reaction assumed proceed initially through a solvent free Knoevenagel condensation reaction between piperonal and malononitrile to afford the intermediate (I) which then undergoes Michael addition with aromatic amine to achieve the compounds (1a-e)(Borah, Dwivedi, & Chowhan, 2021) .



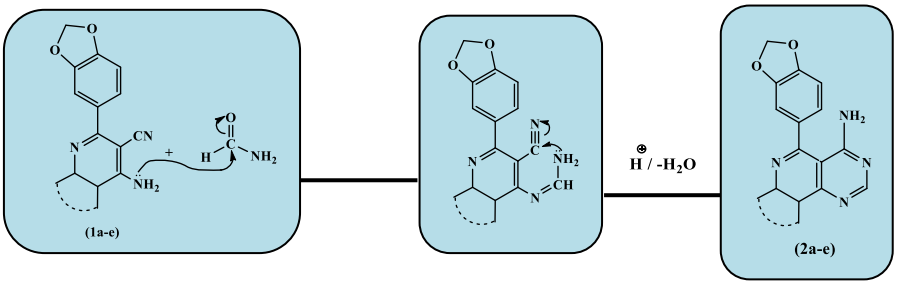
Scheme *2*. synthetic equation of compounds ($_{1a\text{-}e}$)

The structure of compounds (1a-e) were illustrated by spectral data so, they show two types of absorption in u.v spectroscopy at λ max (nm), (475) and (271) refer to n → π* and π→π* respectively. Whereas in FT-IR these compounds gave a significant absorption peak for amino group at (3341-3435) cm^{-1} while the cyano group appears as a weak peak at (2687) cm^{-1} additionally to the other spectral data listed in the experimental part. The ^{1}H-NMR for compounds (1a, 1c and 1e) shown clear a singlet peak at (δ ppm) (8.38, 9.82 and 9.81) refer to the amino group in addition to the other absorption peaks listed in experimental section, which came in agreement with the suggested structure.

Table 1
Spectrum properties of compounds ($_{1a\text{-}e}$)

Comp. No.	Structure of amine	Structure of enamine	FT- IR (cm^{-1})								U.V/MeOH λ max (nm)
			NH	=C-H	C≡N	C=C	C=N	C-O-C asym.	C-O-C sym.	Others	
1_a			3372,3429	3030	2224	1612	1568	1289	1032	C-S 1111	375,340
1_b			3371,3402	3030	2224	1612	1568	1290	1032	–	371,327
1_c			3322,3400	3030	2194	1668	1589	1281	1091	NO_2 asym. 1490 sym. 1330	302,271
1_d			3320,3415	3037	2377	1600	1588	1232	1095	C=O 1676	475,340
1_e			3341,3435	3064	2687	1624	1587	1281	1090	C=O 1672	444,323

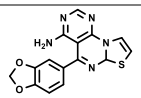
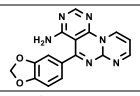
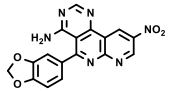
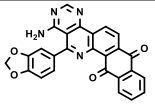
After proving the structural formula, compounds (1a-e) then used as active precursor to prepare the fused pyrimidines. actually, compounds (1a-e) were reacted with formamide to afford Fused-2-amino pyrimidine (2a-e) through cycloaddition reaction in presence of catalytic amount of acetic acid as acid catalyst as shown in the following mechanism, (Scheme 3) (Ghorab et al., 2006):

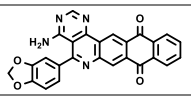


Scheme 3. Synthetic mechanism of compounds (2_{a-e})

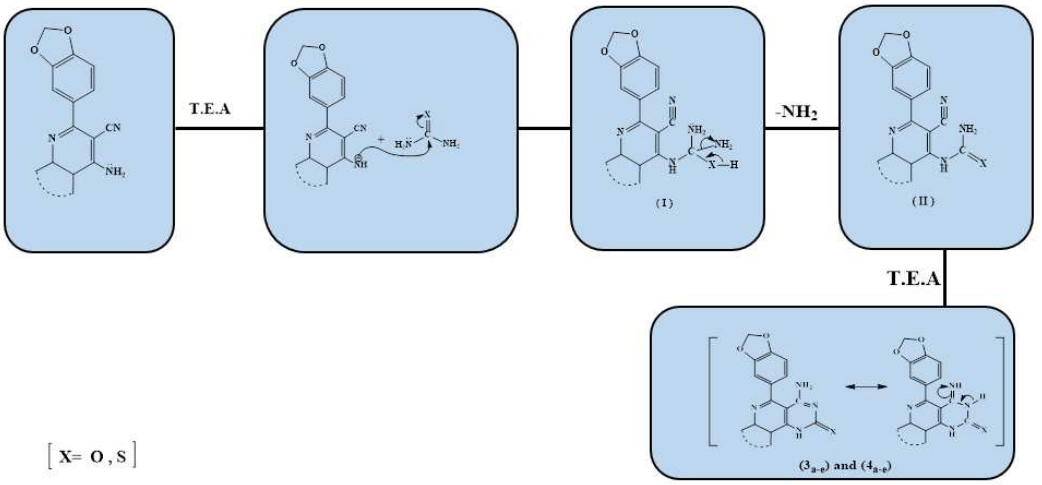
The cyclization reaction occurred through elimination of water molecular followed by intra cyclization reaction by the action of the amino group on the cyano functional group to achieve the compounds (2a-e). By using the spectroscopic methods, the structures were proved on the bases of it`s spectral data. So, in FT-IR these compounds revealed the absence of cyano functional group, while the absorption band for amino group still appear, Table (2). The ^{1}H-NMR spectroscopy for compound (2_c and 2_e) and because of the decreasing of electronegativity of molecule by losing of cyno functional group , they shown low significant peaks at δ (3.26 and 3.45 ppm) as a singlet peak refer to the NH_2 functional group as well as to the other absorption peaks listed in the experimental section which came in agreement with the suggested structure.

Table 2
Spectrum properties of compounds (2_{a-e})

Comp. No.	Structure of pyrimidine	FT- IR (cm^{-1})						Others	U.V/MeOH λ max (nm)
		NH_2	=C-H	C=C	C=N	C-O-C asym.	C-O-C sym.		
2_a		3320,3384	3091	1590	1546	1248	1103	C-S 1033	376,366
2_b		3320,3368	3082	1560	1493	1257	1104	—	370,317
2_c		3314,3368	3015	1687	1594	1238	1104	NO_2 asym. 1488 sym. 1290	346,209
2_d		3427,3489	3066	1604	1544	1280	1167	C=O 1672	378,317

2e		3362,3439	3031	1626	1587	1281	1163	C=O 1674	444,370

On the other hand, fused 4-amino pyrimidine 2-one (thion) (3a-e) and (4a-e) respectively were obtained through the reaction of compounds (1a-e) with urea and thiourea with catalytic amount of tri ethyl amine (TEA) as basic catalyst, (Scheme 4) (Aslam et al., 2018):



Scheme 4. Synthetic mechanism for compounds (3_{a-e}) , (4_{a-e})

Tri ethyl amine were used to achieve the negative charge on amino pyridine which attack the thion group to afford the intermediate (I) followed by losing of ammonia molecule to give the intermediate (II) which in turn underwent the intracyclization reaction by the action of amino group to give the fused 4-amino pyrimidines-2-one (thion) (3a-e) and (4a-e) respectively. The ^{1}H-NMR spectrum for compounds (3a and 4c) as examples showed a singlet peak at (δppm): (2.6 and 3.45) belong to the primary amine (NH_2) and at (2.42 and 3.26) refer to the secondary amine (NH) of pyrimidine ring. Whereas in FT-IR spectroscopy these compounds display absorption bands refer to the NH_2, NH, (C=O) and (C=S) functional groups, in addition to the other absorption bands listed in Table (3) and (4).

Table 3
Spectrum properties of compounds (3_{a-e})

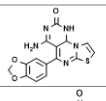
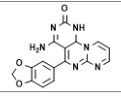
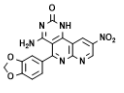
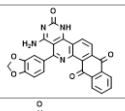
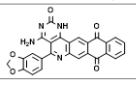
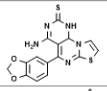
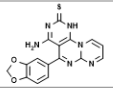
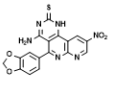
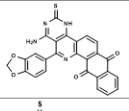
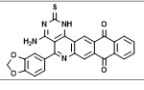
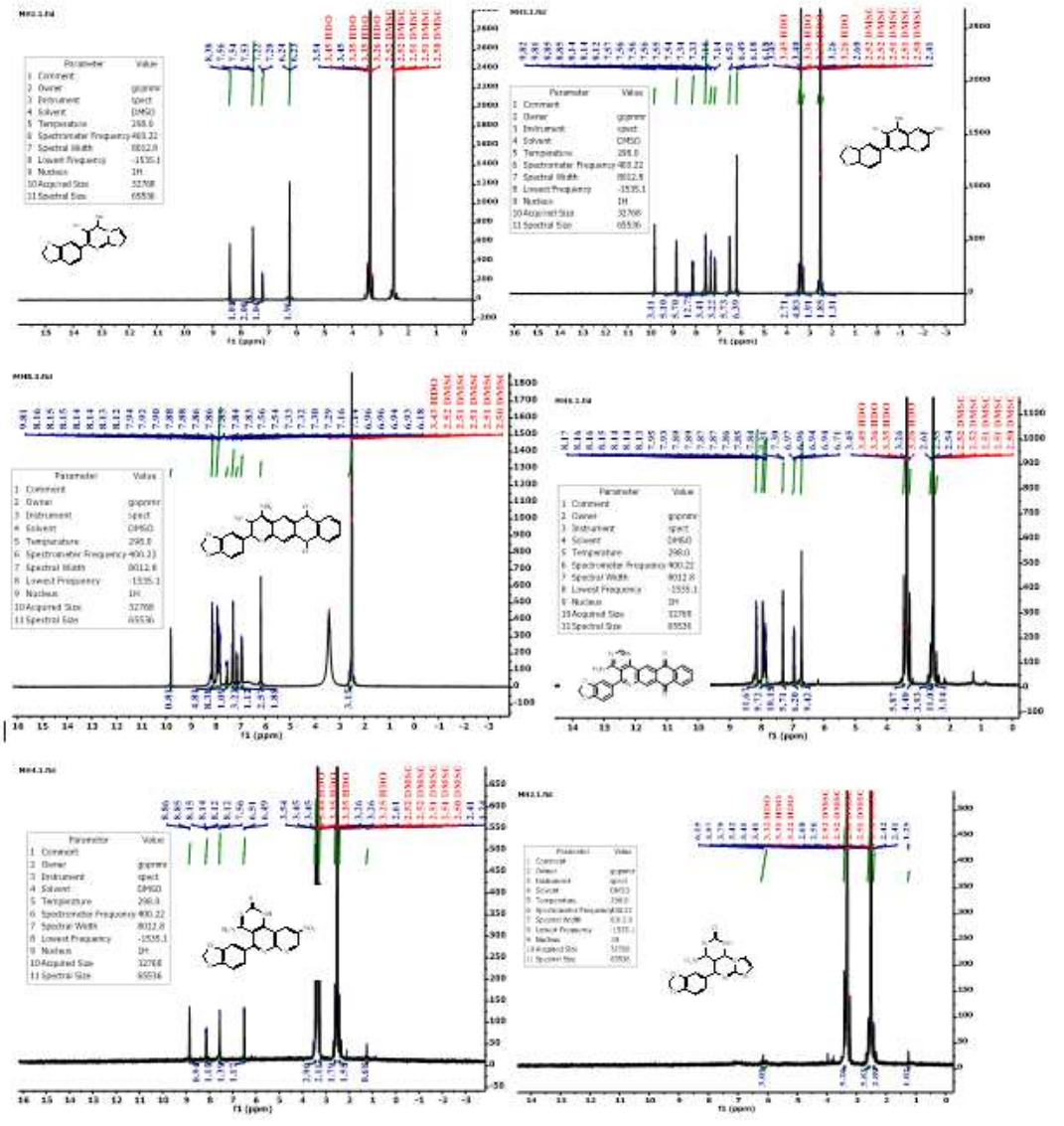
Comp. No.	Structure of Pyrimidine -2-one	FT- IR (cm^{-1})								Others	U.V/MeOH λ max (nm)
		NH_2	NH	=C-H	C=O	C=C	C=N	C-O-C asym.	C-O-C sym.		
3_a		3349,3430	3233	3014	1633	1562	1492	1245	1098	C-S 1033	371,340
3_b		3349,3448	3235	3024	1638	1553	1491	1248	1096	–	341,328
3_c		3295,3352	3199	3085	1636	1598	1512	1283	1083	NO_2 asym. 1483 sym. 1350	343,214
3_d		3390,3434	3064	2914	1672	1591	1508	1274	1031	–	371,340
3_e		3383,3437	3187	3166	1670	1589	1573	1244	1029	–	447,370

Table 4
Spectrum properties of compounds (4_{a-e})

Comp. No	Structure of Pyrimidine -2-thione	FT- IR (cm^{-1})									Others	U.V/MeOH λ max (nm)
		NH_2	NH	=C-H	C=C	C=N	C-O-C asym.	C-O-C sym.	C-O-C	C=S		
4_a		3347,3446	3237	3076	1553	1491	1367	1245	1098		C-S 1033	371,348
4_b		3339, 3440	3227	3030	1565	1489	1369	1245	1096		–	341,329
4_c		3352, 3390	3314	2971	1695	1647	1295	1075	1086		NO_2 asym. 1523 sym. 1380	371,344
4_d		3413, 3435	3347	3072	1635	1591	1273	1037	1076		C=O 1672	370,340
4_e		2395, 3421	3105	3005	1589	1575	1327	1020	1288		C=O 1670	370,340



4 Conclusion

Green chemistry approaches represented by solid phase one-pot multicomponent reaction, grinding and microwave irradiation have been used in the first step under free solvent, catalyst and fusion conditions which lead to afford five novel 4-amino nicotine nitriles ($1_{a\text{-}e}$) in high yield and simple working out. 4-amino nicotine nitriles shown active behavior toward preparing new series of fused pyrimidines derivatives in very simple procedures. As well as thin layer chromatography has an effective and simple role to determining the reaction time and measuring the purity of the prepared compounds.

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