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HETEROAROMATIZATION WITH SULPHONAMIDO PHENYL ETHANONE: PART (III)*. SYNTHESIS, REACTIONS AND BIOLOGICAL ACTIVITY OF ENAMINONE CONJUGATED WITH DIMETHYLAMINOSULFONYL MOIETY

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Abstract

4-(3-Dimethylaminoacryloyl)-N,N-dimethylbenzenesulfonamide **(2)** was prepared and used as key intermediate in the synthesis of the title compounds, the structure of these compounds were elucidated on the bases of elemental analysis, IR, ^{1}H-NMR and mass spectra. The Antimicrobial and Antifungal activities of the prepared compounds are also reported.

Keywords: sulfonamido phenyl ethanone; enaminone; pyrazole; triazole; imidazole; pyranone; N,N-dimethylbenzenesulfonamide.

Introduction

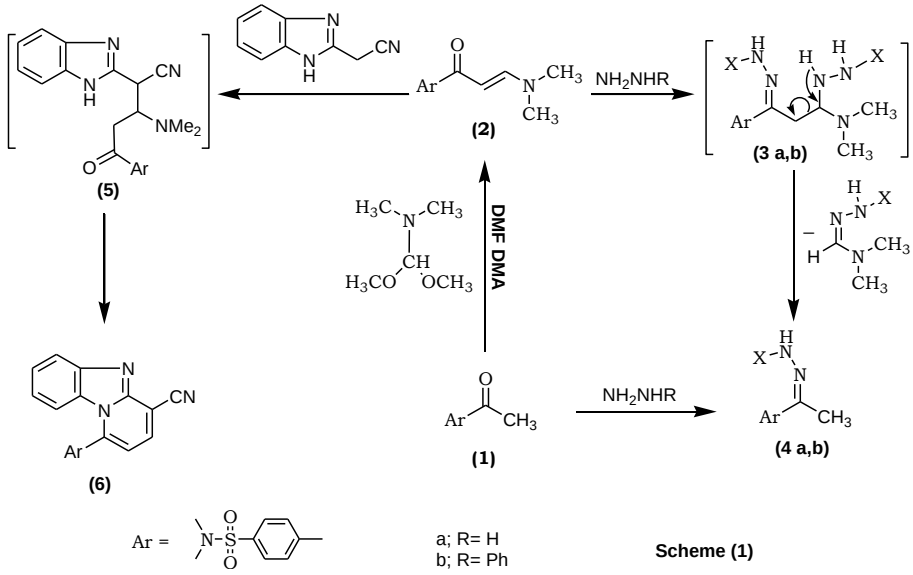
Enaminones constitute an interesting class of compounds that are versatile precursors for the synthesis of several heterocyclic or aromatic compounds[2-8]. Also sulfonamides have a variety of biological activities such as antibacterial[9], insulin releasing[10], carbonic anhydrase inhibitory[11,12], antiflammatory[13] and antitumor activities[14]. Thus, the present investigation deals with the synthesis of some new benzo[4,5]imidazo[1,2-a]pyridine, pyrazolo[1,5-a]pyrimidine, [1,2,4]triazolo[4,3-a]pyrimidine, amino pyrimidine, pyrazolo[3,4-d]pyridazine, pyranone, benzofuran derivatives containing a sulphonamide moiety using 4-(3-dimethylaminoacryloyl)-N,N-dimethylbenzenesulfonamide **(2)** as starting material.

Results and Discussion

4-Acetyl-N,N-dimethylbenzenesulfonamide **(1)** was reacted with N,N-dimethylformamide-dimethylacetal in refluxing xylene to give enaminone **(2)**. The ^{1}H-NMR spectrum of **(2)** revealed two doublet signals of olefinic protons (CH=CH) at 5.6 & 7.8 whose coupling constant ; J =12 Hz which support that the structure in (*E*-form), not (*Z*-form), **(Scheme 1)**.

The reactivity of compound **(2)** towards some nitrogen nucleophile was investigated thus, enaminone **(2)** was treated with hydrazine hydrate or phenylhydrazine in refluxing acetic acid, addition intermediates **(3a,b)** were formed, from which elimination of hydrazone or phenylhydrazone of dimethylformamide afforded acetophenone hydrazones derivative **(4a)** and **(4b)**[15] respectively.

Structure of compound **(4a)** was established on the basis of its elemental analysis and spectral data. A final evidence for the proposed structure, comes from synthesizing compound **(4a)** *via* condensation of compound **(1)** with hydrazine hydrate to afford product identical in all aspects (m.p., TLC, IR, and mass spectra) with those obtained previously from reaction of compound **(2)** with hydrazine hydrate as described before, **(Scheme 1)**.



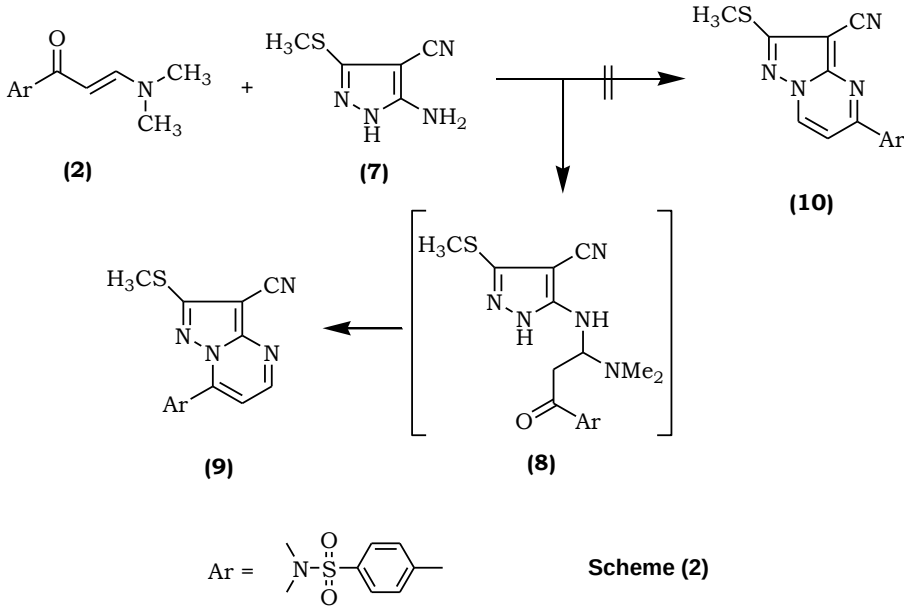
Scheme (1)

Also compound **(2)** reacted with 1H-benzoimidazole-2-yl acetonitrile, in glacial acetic acid to give 4-(4-cyanobenzo[4,5]imidazo[1,2-a]pyridin-1-yl)-N,N-dimethylbenzene-sulfonamide **(6)** via an intermediate **(5) (Scheme 1)**.

On the other hand enaminone **(2)** condensed with 5-amino-3-methylsulfanylpyrazole-4-carbonitrile **(7)**[16-18] to give 7-substituted arylpyrazolo[1,5-a]pyrimidine **(9)** or its 5-substituted isomer **(10)**.

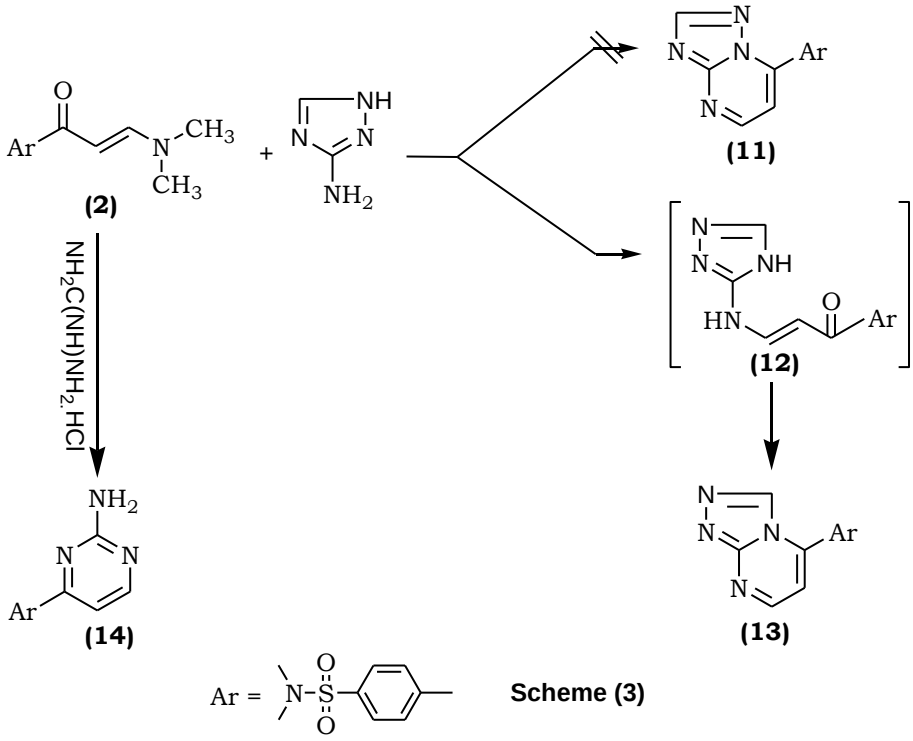
The structure **(9)** was demonstrated on the basis of its ^{1}H-NMR spectrum which showed for pyrimidine ring protons two doublets at 7.6 & 8.8 ppm, whose coupling constant; J = 4.6 Hz has been described as characteristic for the H-5 & H-6 sequence which accepted with the previous work.[19]

The structure **(9)** was assumed to take place via the addition of exoamino group of aminopyrazole to α,β-unsaturated moiety of enaminone **(2)** to yield the corresponding acyclic nonisolable intermediate **(8)** which undergoes cyclization to afford the final product, **(Scheme 2)**.



Scheme (2)

Enaminone **(2)** reacted with 3-amino-1H-1,2,4-triazole in acetic acid under reflux to afford [1,2,4]triazolo[4,3-a]pyrimidine derivatives **(13)**. This reaction may be proceed *via* the addition of the exoamino group of aminotriazole to α,β-unsaturated moiety in compound **(2)** to yield the corresponding acyclic nonisolable intermediate **(12)** which undergoes cyclization and aromatization to afford the final product **(13)** not **(11), (Scheme 3)**.



Scheme (3)

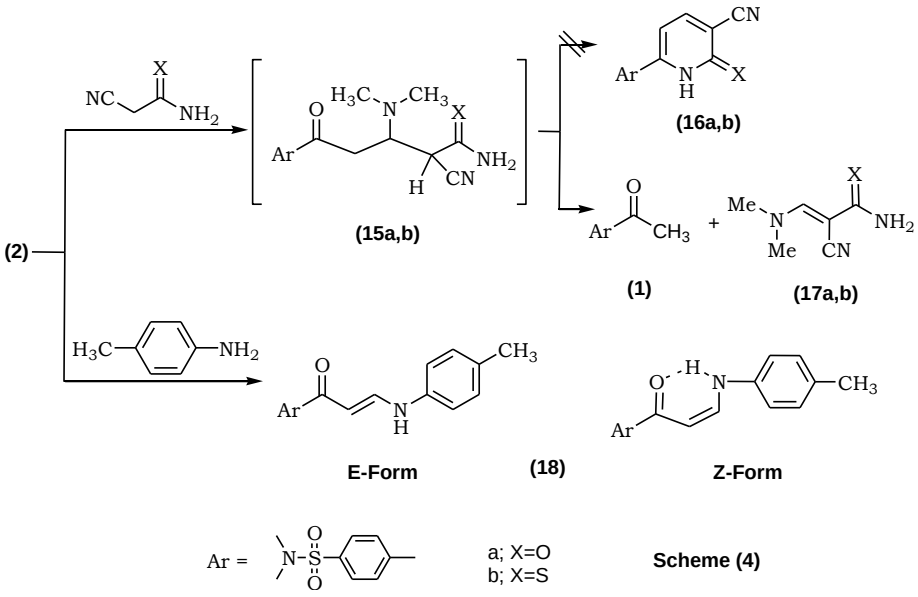
The enaminone **(2)** reacted with guanidine hydrochloride to produce aminopyrimidine derivative **(14)**.

Interaction of enaminone **(2)** with cyanoacetamide or cyanothioacetamide in acetic acid at reflux temperature produce an addition intermediates **(15a,b)** which not cyclized to give the predicted pyridine derivatives **(16a,b)**, this reaction proceed via addition of an active methylene group of cyanoacetamide or cyanothioacetamide to the olefinic bond of enaminone **(2)** followed by elimination of α-cyano-β-dimethylaminoacrylamide or thioacrylamide derivatives **(17a,b)** from the addition intermediates **(15a,b)** to form 4-acetyl-N,N-dimethylbenzenesulfonamide **(1)** (the same m.p., mixed m.p. and spectral data).

Condensation of enaminone **(2)** with *p*-toluidine in a mixture of ethanol/acetic acid at reflux temperature afforded N,N-dimethyl-4-(3-*p*-tolylaminoacrylolyl)benzenesulfonamide **(18)**.

^{1}H-NMR spectrum of compound **(18)** supports that this structure in (Z-form) not in (E-form), while the coupling constant of the doublet signals for olefinic protons

equal to 8.0 Hz. (Z-Form) is stabilized by intramolecular hydrogen bonding **(Scheme 4)**.



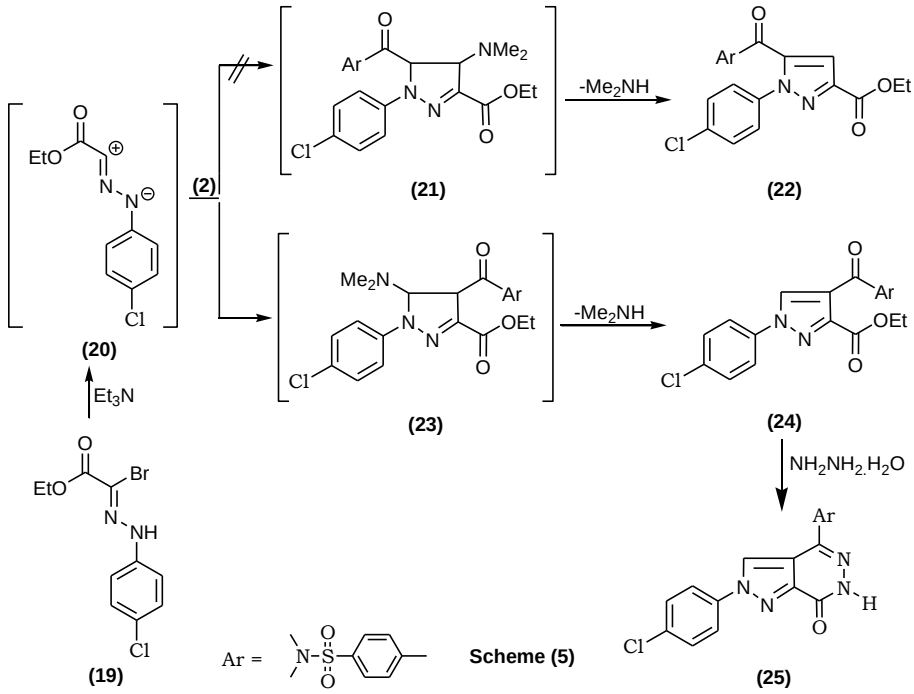
Scheme (4)

Hydrazonyl halide **(19)**[20-22] has been reported to add to α,β-unsaturated carbonyl compounds to yield a mixture of isomeric pyrazolines[23,24].

In the present work the reaction of enaminone **(2)** with nitrileimine **(20)** (liberated in situ by the action of triethylamine on the hydrazonoyl bromide **(19)** in refluxing xylene) gave only one isolable product (TLC). From which two proposed structures **(22)** or **(24)** seemed possible **(Scheme 5)**.

^{1}H-NMR spectrum provided a firm support for structure **(24)** and ruled out the other possible structure **(22)**. Thus, ^{1}H-NMR spectrum of **(24)** exhibits a singlet at 8.3 ppm. which indicates the presence of pyrazole H-5 rather than H-4 [25] .

pyrazole derivative **(24)** was assumed to be formed via initial 1,3-dipolar cycloaddition of nitrilimine **(20)** to the activated double bond in compound **(2)** forming nonisolable intermediate **(23)** followed by the loss of dimethylamine, **(Scheme 5)**.

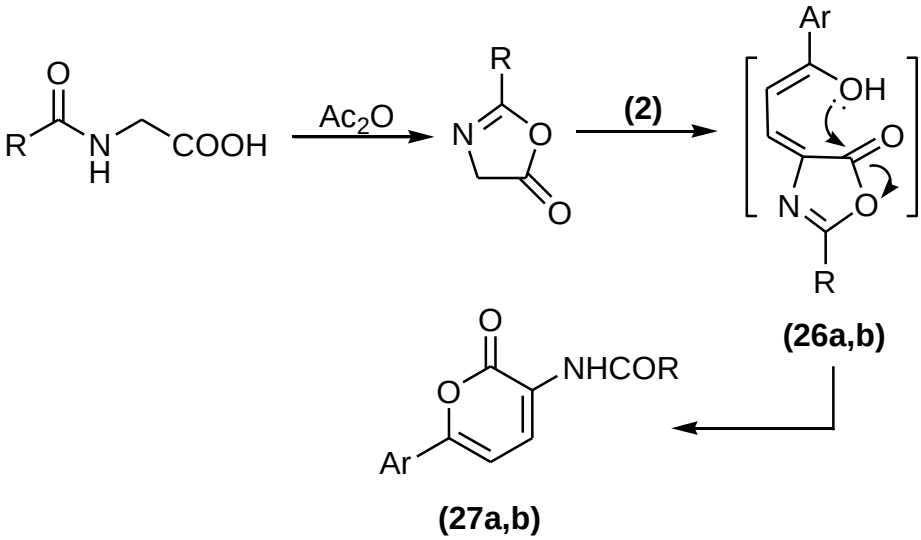


Scheme (5)

Interaction of pyrazole derivative **(24)** with hydrazine hydrate in refluxing absolute ethanol afforded pyrazolo[3,4-d]pyridazine-7-one derivative **(25)**, **(Scheme 5)**.

Enaminone **(2)** reacted with acetylglycine and benzoylglycine in acetic anhydride[23,25] to give a product that was identified as N-[6-(4-dimethylsulfamoylphenyl)-2-oxo-2H-pyran-3-yl]acetamide and N-[6-(4-dimethylsulfamoylphenyl)-2-oxo-2H-pyran-3-yl]benz-amide **(27a,b)** respectively.

Compounds **(27a,b)** were assumed to be formed via initial cyclization of acetylglycine or benzoylglycine into oxazolone derivatives which then add to the activated double bond system of enaminone yielding **(26a,b)** followed by rearrangement to give the final structures **(27a,b)**, this is similar to the well known kepe pyranone synthesis[26], **(Scheme 6)**.

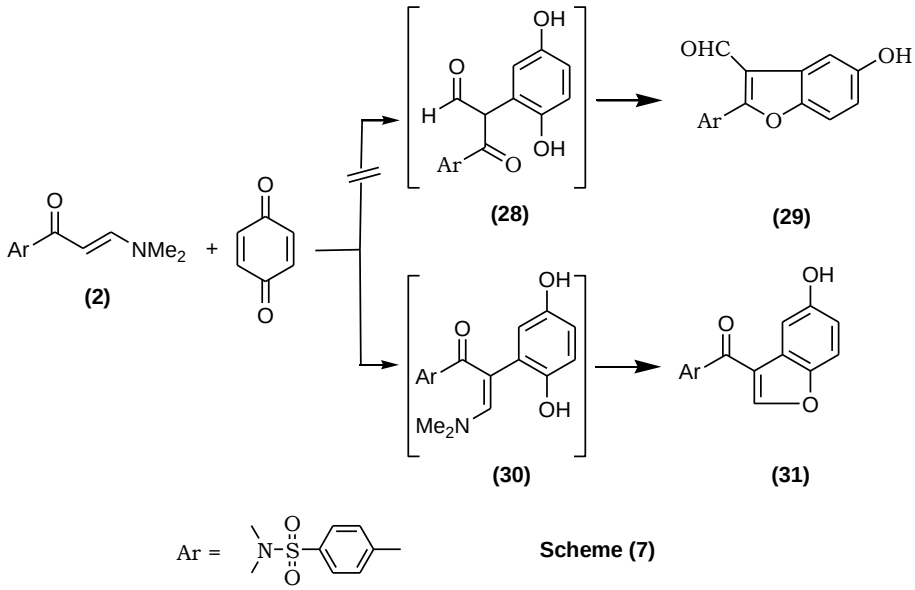


Scheme (6)

Furthermore, the behavior of enaminone **(2)** towards 1,4-benzoquinone was investigated. Thus, compound **(2)** reacted with 1,4-benzoquinone in glacial acetic acid at room temperature to yield a product which formulated as 4-(5-hydroxybenzofuran-3-carbonyl)-N,N-dimethylbenzenesulfonamide **(31)**.

It's believed that electron rich (C-2) in the enaminone **(2)** initially adds to the activated double bond in the quinone yielding acyclic intermediate **(30)** which then cyclizes into **(31)** via dimethylamine elimination[25], and not afforded 4-(3-formyl-5-hydroxybenzofuran-2-yl)-N,N-dimethylbenzenesulfonamide **(29)**.

Elucidation of structure **(31)** and refusing of structure **(29)** was based on ^{1}H-NMR spectrum which indicate the disappearance of aldehydic signal and showed singlet signal at 8.63 ppm for benzofuran H-2, **(Scheme 7).**



Scheme (7)

Antimicrobial and Antifungal Activities

The results of antimicrobial screening (table 2) show that compound **(2, 4a, 18, 24, 25)** are highly active compounds against, Antimicrobial activity, Gram-Positive (B. Subtilis, S. Aureus, S. maxima), Gram-Negative (K. Pneumonia, Salmonella, P. aeruginosa) and Antifungal Activity, Unicellular Fungi (C. Abicans), Filamentous Fungi (Rhizopus, A. Fumigatus), while the compounds **(27a,b, 31)** showed the moderate active, and the remaining compounds **(6, 9, 13, 14)** showed the weak active.

It seems that most activity was exhibited by derivatives with enaminone derivatives.

Experimental Section

Melting points are uncorrected. IR spectra (KBr) were recorded on FT-IR 5300 spectrometer and Perkin Elmer spectrum RXIFT-IR system (ν, cm^{-1}). The ^{1}HNMR spectra were recorded at 300 MHz on a Varian Gemini NMR spectrometer (δ, ppm) using TMS as an internal standard. Mass spectra were obtained on GC Ms-QP 1000 EX mass spectrometer at 70 ev. Elemental analyses were carried out by the Micro analytical Research Center, Faculty of Science, Cairo University and Al-Azhar University.

4-(3-Dimethylaminoacryloyl)-N,N-dimethylbenzenesulfon-amide (2)

A mixture of 4-acetyl-N,N-dimethylbenzenesulfonamide (**1**; 0.01 mol) and DMF-DMA (0.012 mol) in dry xylene (50 ml) was heated under reflux for 4hrs. the separated solid was filtered off, washed with ethanol and recrystallized to give (**2**) (table 1). IR (film) *v* =3100 (CH-arom.), 2916 (CH-aliph.), 1642 (C=O), 1340, 1158 cm^{-1} (SO_2). ^{1}H-NMR ($CDCl_3$): δ =2.70 (s, 6H, $SO_2N(CH_3)_2$), 2.96 and 3.19 (2s, 6H, $N(CH_3)_2$), 5.65 and 7.84 (dd, 2H, olefinic CH=CH; J= 12 Hz), 7.77 and 8.01 ppm. (dd, 4H, AB-ArH; J=8 Hz).

4-(1-Hydrazonoethyl)-N,N-dimethylbenzenesulfonamide (4a)

Method (A):

A mixture of enaminone (**2**; 0.01mol) and hydrazine hydrate (0.01 mol) in acetic acid (30 ml) (1:1) was refluxed for 3hrs. after cooling the solid which formed was collected and recrystallized to give (**4**) (table 1).

Method (B):

A solution of 4-acetyl-N,N-dimethylbenzenesulfonamide (**1**; 0.01 mol) in ethanol (30 ml) and hydrazine hydrate (0.013 mol) was refluxed for 2hrs. After cooling, the solid product which formed was collected and recrystallized, m.p. and mixed m.p determined with authentic sample gave no depression. IR (film) *v* =3426 and 3295 (NH_2), 3095 (CH-arom.), 2918 (CH-aliph.), 1338, 1158 cm^{-1} (SO_2). MS: m/z (%) =241 (100; M^+), 197 (9.6), 149 (21.8), 133 (27.7), 42 (13.17).

4-(4-Cyanobenzo[4,5]imidazo[1,2-a]pyridin-1-yl)-N,N-dimethyl-benzenesulfonamide (6)

A mixture of enaminone (**2**; 0.01 mol) and 1H-benzoimidazole-2-yl acetonitrile (0.01 mol) in glacial acetic acid (30 ml) was refluxed for 2hrs. The solid product which obtained after cooling was collected by filtration and recrystallized to give **(6)** (table 1). IR (film) *v* =3062 (CH-arom.), 2918 (CH-aliph.), 2226 (CN), 1338, 1168 cm^{-1} (SO_2). MS: m/z (%) =376 (87.9; M^+), 268 (100), 240 (13.5), 134 (3.9).

4-(3-Cyano-2-methylsulfanylpyrazolo[1,5-a]pyrimidin-7-yl)-N,N-dimethylbenzenesulfonamide (9)

A mixture of enaminone (**2**; 0.01mol) and 5-amino-3-methylsulfanylpyrazole-4-carbonitrile (**7**; 0.01 mol) in ethanol (60 ml) was heated under reflux for 7hrs. during the reflux period, a crystalline solid was separated. The separated solid was filtered

off, washed with ethanol and recrystallized to give the compound **(10)** (table 1). IR (film) *v* =3092 (CH-arom.), 2932 (CH-aliph.), 2214 (CN), 1338, 1158 cm^{-1} (SO_2). ^{1}H-NMR (DMSO): δ =2.67 (s, 3H, SCH_3), 2.71 (s, 6H, $N(CH_3)_2$) 7.59 and 8.84 (dd, 2H, pyrimidine ring; $J_{5,6}$= 4.6 Hz), 7.97 and 8.37 ppm (dd, 4H, AB-ArH; J=8 Hz). MS: m/z (%) = 373 (100; M^+), 265 (41.5), 218 (15.9), 92 (6.9), 50 (4.0).

N,N-Dimethyl-4-[1,2,4]triazolo[4,3-a]pyrimidin-5-ylbenzene-sulfonamide (13)

A mixture of enaminone (2; 0.01 mol) and 3-amino-1H-1,2,4-triazole (0.01mol) in acetic acid (30 ml) was refluxed for 5hrs. during the reflux period, a crystalline solid was separated. The separated solid was filtered off, washed with ethanol and recrystallized to give the compound **(13)** (table 1). IR (film) *v* =3134 (CH-arom.), 2916 (CH-aliph.), 1342, 1166 cm^{-1} (SO_2). MS: m/z (%) = 304 (32.0; M^++1), 196 (100), 168 (5.1), 140 (8.8), 113 (12.8), 63 (11.0).

4-(2-Aminopyrimidin-4-yl)-N,N-dimethylbenzenesulfonamide (14)

A mixture of enaminone (**2**; 0.01 mol) and guanidine hydrochloride (0.01 mol) in ethanol (30 ml), anhydrous potassium carbonate (2 gm) was added the resulting mixture was refluxed for 6hrs. and then allowed to room temperature and diluted with water 20 ml the solid product so formed was collected by filtration, washed with water and recrystallized to give the compound **(14)** (table 1). IR (film) *v* =3422, 3322 (NH_2), 3130 (CH-arom.), 2917 (CH-aliph.), 1341, 1168 cm^{-1} (SO_2). MS: m/z (%) =278 (1.3; M^+), 227 (8.5), 148 (6.3), 120 (7.6), 92 (8.3), 44 (100).

N,N-Dimethyl-4-(3-*p*-tolylaminoacryloyl)benzenesulfonamide (18)

A mixture of enaminone (**2**; 0.01mol) and *p*-toluidine (0.01 mol) in a mixture of ethanol/acetic acid (50 ml) (1:1) was heated under reflux for 3hrs. during the reflux period, a crystalline solid was separated. The separated solid was filtered off, washed with ethanol and recrystallized to give the compound (**18**) (table 1). IR (film) *v*=3450 (NH), 3034 (CH-arom.), 2920 (CH-aliph.), 1644 (CO), 1334, 1154 cm^{-1} (SO_2). ^{1}H-NMR ($CDCl_3$): δ =2.33 (s, 3H, CH_3), 2.72 (s, 6H, $N(CH_3)_2$), 5.95 (d, 1H, COCH), 7.5 (m, 1H, CH-NH), 7.0 and 7.1 (dd, 4H, AB-ArH; J=8.56 Hz), 7.85 and 8.05 (dd, 4H, AB-ArH; J=8.5 Hz) 12.20 ppm (d, 1H, NH).

1-(4-Chlorophenyl)-4-(4-dimethylsulfamoylbenzoyl)-1H-pyrazole-3-carboxylic acid ethyl ester (24)

To a mixture of enaminone (**2**; 0.01 mol) and the hydrazonoyl bromide (**19**; 0.01 mol) in benzene (40 ml) an equivalent amount of triethylamine was added. The

reaction mixture was heated under reflux for 2hrs. the solvent was distilled at reduced pressure and the residual viscous liquid was taken in ethanol then the resulting solid was collected by filtration, washed thoroughly with ethanol, dried and finally recrystallized to give the compound (**24**) (table 1). IR (film) *v* =3088 (CH-arom.), 2978 (CH-aliph.), 1734 (ester CO), 1678 (acetyl CO), 1342, 1162 cm^{-1} (SO_2). ^{1}H-NMR ($CDCl_3$): δ =1.08 (t, 3H, $\underline{CH_3}$-CH_2), 2.72 (s, 6H, $N(CH_3)_2$), 4.13 (q, 2H, $\underline{CH_2}$-CH_3), 7.4 and 7.7 (dd, 4H, AB-ArH; J=8.36 Hz), 7.8 and 8.0 (dd, 4H, AB-ArH; J=8.1 Hz), 8.28 ppm (s, 1H,CH pyrazole).

4-[2-(4-Chlorophenyl)-7-oxo-6,7-dihydro-2H-pyrazolo[3,4-d] pyridazin-4-yl]-N,N-dimethylbenzenesulfonamide (25)

A mixture of pyrazole derivative (**24**; 0.01 mol) and hydrazinehydrate (0.012 mol) in ethanol (50 ml) was heated under reflux for 4hrs. the separated solid was filtered off, washed with ethanol and recrystallized to give (**25**) (table 1). IR (film) *v* = 3450 (NH), 3100 (CH-arom.), 2923 (CH-aliph.), 1681 (C=O), 1334, 1161 cm^{-1} (SO_2). MS: m/z (%) = 429 (60.8; M^+), 321 (40.4), 271 (5.1), 141 (58.9), 97(100), 91 (60.3), 44 (56.8).

General procedure for preparation of (27a,b)

A mixture of enaminone (**2**; 0.01 mol) and acetyl glycine or benzoyl glycine (0.01 mol) in acetic anhydride (30 ml) was heated under reflux for 2hrs. the reaction mixture was concentrated in vacuo. The solid product which formed upon cooling was filtered off then washed with ethanol and recrystallized from the appropriate solvents to give **(27a,b)** respectively, (table 1).

N-[6-(4-Dimethylsulfamoylphenyl)-2-oxo-2H-pyran-3-yl]-acetamide (27a)

IR (film) *v* =3450 (NH), 3099 (CH-arom.), 2925 (CH-aliph.), 1666 and 1656 (2 CO), 1336, 1160 cm^{-1} (SO_2). ^{1}H-NMR (DMSO): δ =2.17 (s, 3H, CH_3), 2.66 (s, 6H, $N(CH_3)_2$), 7.28 and 8.27 (dd, 2H pyranone; J=7.6 Hz) 7.84 and 8.07 (dd, 4H, AB-ArH; J=8.2 Hz), 9.8 ppm (s, 1H, NH).

N-[6-(4-Dimethylsulfamoylphenyl)-2-oxo-2H-pyran-3-yl]-benzamide (27b)

IR (film) *v* =3394 (NH), 3096 (CH-arom.), 2924 (CH-aliph.), 1666 and 1656 (2 CO), 1334, 1158 cm^{-1} (SO_2). MS: m/z (%) = 398 (25.7; M^+), 294 (1.9), 105 (100), 77 (23.4).

4-(5-Hydroxybenzofuran-3-carbonyl)-N,N-dimethylbenzene-sulfonamide (31)

To a stirred solution of enaminone (**2**; 0.01 mol) in glacial acetic acid (30 ml), 1,4-benzoquionone (0.01 mol) was added, Stirring was continued for 3hrs. at room temperature. The reaction mixture was evaporated in vacuo and the solid product was isolated by filtration and recrystallized to give **(31)** (table 1). IR (film) ν =3308 (OH), 3101 (CH-arom.), 2925 (CH-aliph.), 1620 (CO), 1344, 1162 cm^{-1} (SO_2). ^{1}H-NMR (DMSO): δ =2.69 (s, 6H, $N(CH_3)_2$), 6.88 and 7.52 (dd, 2H, H-5,6 benzofuran), 7.55 (s, 1H, H-4 benzofuran), 7.91 and 8.07 (dd, 4H, AB-ArH; J=8.4 Hz), 8.63 (s, 1H, H-2 benzofuran), 9.47 ppm (br s, 1H, OH). MS: m/z (%) = 345 (100; M^+), 284 (13.4), 237 (40.3), 161 (83.6), 105 (28.2), 51 (24.5).

Antimicrobial and Antifungal screening

The prepared compounds were evaluated for their antimicrobial activity using the agar diffusion technique.[27,28] A mg/ml solution in DMF was used. The test organisms were gram-positive Bacillus subtilis (NCTC-1040), Staphylococcus aureus (NCTC-7447), sarcina maxima (ATCC-33910); gram-negative Klebsiella peneumonia (NCIMB-9111), Salmonella, Pseudomonas aeruginosa (ATCC-10145), and Antifungal activity, unicellular fungi Candida abicans (IMRU-3669); filamentous fungi Rhizopus, Asperigillus fumigatus. DMF showed no inhibition zones. The reference antibiotics were Ampicillin (AMD) and Calforan. The inhibition zones (IZ) of these compounds are listed in (table 2).

TABLE(1): Physical and Analytical Data for the Newly Prepared Compounds

Comp.	m.p.°C (Solvent of recrystallization)	Colour (Yield%)	M.formula (M.Wt.)	Calculated / Found (%)					
				C	H	N	O	S	Cl
2	160 (Et.)	Orange (85)	$C_{13}H_{18}N_2O_3S$ (828)	55.30 55.10	6.43 6.22	9.92 9.70	17.00 16.80	11.36 11.32	…..
4a	130 (Et.)	Yellow (88)	$C_{10}H_{15}N_3O_2S$ (241)	49.77 49.66	6.27 6.17	17.41 17.40	13.26 13.24	13.29 13.27	…..
6	345 (Et./B.)	Yellow (78)	$C_{20}H_{16}N_4O_2S$ (376)	63.81 63.77	4.28 4.25	14.88 14.78	8.50 8.44	8.52 8.51	…..
9	246 (Et./B.)	Yellow (79)	$C_{16}H_{15}N_5O_2S_2$ (373)	51.46 51.44	4.05 4.10	18.75 18.65	8.57 8.48	17.17 17.16	…..
13	230 (Et./B.)	Yellow (80)	$C_{13}H_{13}N_5O2S$ (303)	51.47 51.36	4.32 4.30	23.09 23.05	10.55 10.45	10.57 10.55	…..
14	180 (Et./B.)	White (70)	$C_{12}H_{14}N4O_2S$ (278)	51.78 51.87	5.07 5.03	20.13 20.03	11.50 11.32	11.52 11.36	…..
18	205 (Et.)	Yellow (66)	$C_{18}H_{20}N_2O_3S$ (344)	62.77 62.74	5.85 5.74	8.13 8.12	13.94 13.89	9.31 9.26	…..
24	161 (Et.)	Brown (70)	$C_{21}H_{20}ClN_3O_5S$ (461)	54.60 54.48	4.36 4.34	9.10 9.08	17.32 17.29	6.94 6.93	7.68 7.66
25	280 (Et./B.)	White (89)	$C_{19}H_{16}ClN_5O_3S$ (429)	53.09 53.05	3.75 3.78	16.29 16.25	11.17 11.15	7.46 7.45	8.25 8.32
27a	270 (Et./B.)	Yellow (90)	$C_{15}H_{16}N_2O_5S$ (336)	53.56 53.66	4.79 4.78	8.33 8.29	23.78 23.77	9.53 9.51	…..
27b	247 (Et./B.)	Brown (80)	$C_{20}H_{18}N_2O_5S$ (398)	60.29 60.25	4.55 4.48	7.03 7.10	20.08 20.10	8.05 8.12	…..
31	231 (Et.)	White (89)	$C_{17}H_{15}NO_5S$ (345)	59.12 59.23	4.38 4.39	4.06 4.08	23.16 23.19	9.28 9.31	…..

(B.; benzene, Et.; ethanol).

Table 2: Antimicrobial activity & Antifungal Activity; Inhibition zone diameter (mm)

Compd. No.	Gram-Positive			Gram-Negative			Unicellular Fungi	Filamentous Fungi	
	B. Subtilis (NCTC-1040)	S. Aureus (NCTC-7447)	S. maxima (ATCC-33910)	K. Pneumonia (NCIMB-9111)	Salmonella	P. aeruginosa (ATCC-10145)	C. Abicans (IMRU-3669)	Rhizopus	A. Fumigatus
2	20	21	19	19	18	20	18	17	18
4a	19	17	16	20	21	17	19	19	20
6	13	12	15	15	13	11	17	13	11
9	16	15	17	18	11	10	11	10	12
13	12	13	14	17	18	16	10	10	15
14	18	16	15	13	12	17	11	12	11
18	19	20	20	21	18	17	19	19	20
24	20	21	20	22	19	20	18	19	19
25	19	21	20	18	17	22	19	20	18
27a	17	19	16	20	21	18	17	19	15
27b	18	18	19	20	18	15	17	13	14
31	16	17	19	13	17	18	12	19	20
Ampicillin (AMD)25mg Calforan 30 mg.	26	25	27	27	26	25	24	25	25

24-20 mm: high active,
19-18 mm: moderate active,
17-12 mm: weak active.

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