NOVEL SYNTHETIC DERIVATIVES OF SYDNONES AND ELUCIDATION OF BIOLOGICAL APPLICATIONS

ABSTRACT

The heterocyclic compounds have been effectively utilised as clinical agents among the various synthesised chemotherapeutic medicines. In synthetic chemistry, several of these are also useful intermediates. Because of their structure, chemical behaviour, and diverse pharmacological characteristics, the "Mesoionic" chemicals have garnered interest among the enormous number of non-benzenoid heterocycles known. The "Sydnones," which are being explored for their pharmacological characteristics and have lately been widely employed as synthons, are the most thoroughly studied class of mesoionic chemicals.Sydnones are one of the most well investigated mesoionic chemicals for cycloaddition processes. Despite their chemical stability and adaptability, only a few research groups have studied their chemistry and applications in organic synthesis. The research was carried out on a variety of sydnones.Theanalyticallaboratory results haverevealed on the synthesis and biological characteristics of a vast number of sydnone derivatives combined with physiologically active heterocycles; however none of them has progressed to the clinical stage. As a result, we attempted to construct various heterocycles on the sydnone ring in order to conducting structure-activity relationship (SAR) research.

1 INTRODUCTION

The sydnones are mesoionic compounds; right off the bat depicted by Earl and Mackney in 1935.The enthusiasm for this class of compounds was created by their incentive as synthons in building heterocyclic complex molecules, just as their pharmaceutical applications. Sydnones are the most contemplated compounds among the mesoionic family because of their fascinating structures, concoction properties, synthetic utility and biological activities.They proposed the development of intertwined 3 and 4-frameworks ring.Item (I) from the activity of acidic anhydride on N-nitrosophenylglycine which was later viewed as off-base by scientists. Hence, Baker and his associate excluded the scaffold bond and suggested an in part fragrant five-membered cyclic (II toV) which was a cross breed of numerous zwitterionic structures.

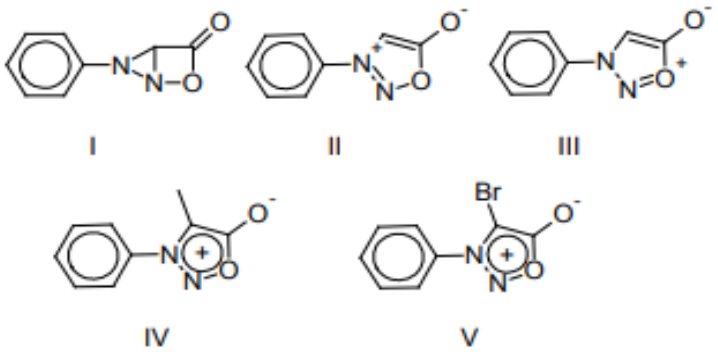


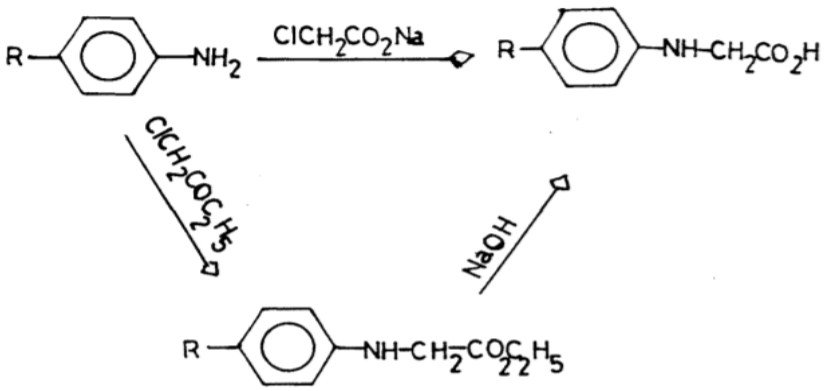
Figure 1.1: Sydnone Structure

2.METHODS AND MATERIALS:

The 3-arylsydnones were synthesized according to the simple procedure which involves the below steps:

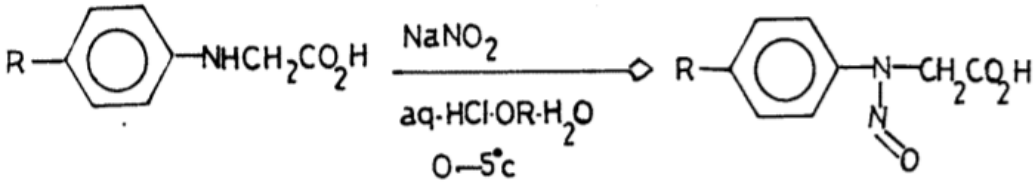
‘Preparation of N-substituted glycines’

Condensation of $C_6H_5NH_2$ with neutralised chloroacetic acid and interaction of anilines with ethylchloroacetate followed by hydrolysis were used to make the aryl glycines.



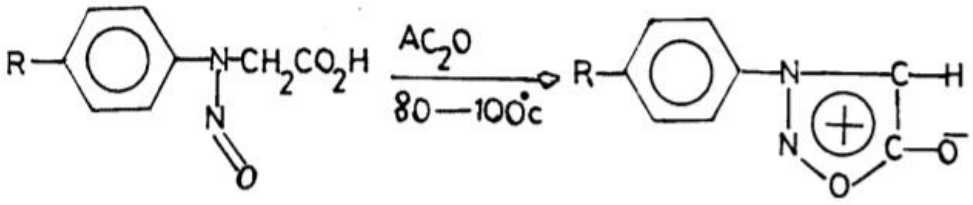
‘Nitrosation of arylglycines to N-nitroso-N-arylglycines’

The addition of sodium nitrite to water or aqueous HCl is used to nitrate the solution.

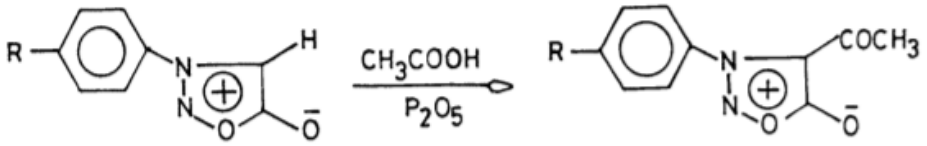


'Cyclisation of N-nitroso-N-arylglycines to N-arylsydnones'

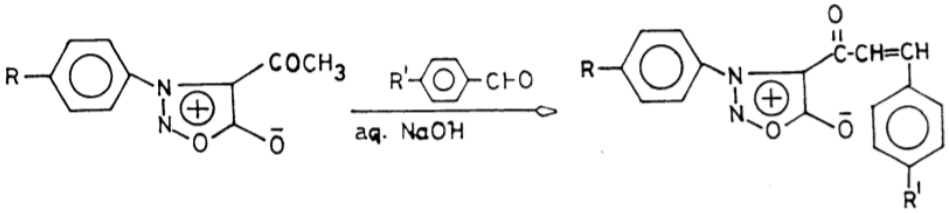
Now N-nitrosoglycines are cyclised to the corresponding sydnones by boiling with acetic anhydride.



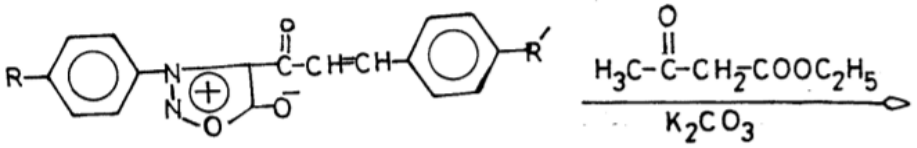
4-acetyl-3-arylsydnones are the initial materials for the synthesis of these intermediates, which are made via acetylation of 3-arylsydnones with CH_3COOH and P_2O_5.

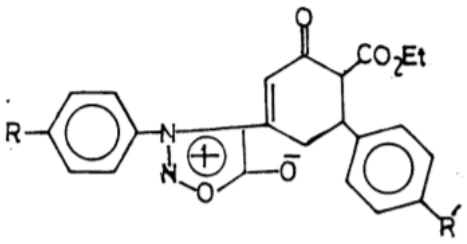


The Claisen-Schmidt reaction converts 4-acetyl-3-arylsydnones to 4-cinnamoyl derivatives. In the presence of an aqueous alkali, the acetyl molecule is condensed with substituted aromatic RCHO to produce-unsaturated ketones (chalcones)



To make the title compounds, the 3-ary1-4-cinnamoylsydnones undergo Michael A addition with ethylacetoacetate in the catalyst of a base, followed by internal Claisen condensation.





Evaluation of antibacterial activity:

- **'Preparation of culture'**

a) 'Preparation of nutrient broth':

Peptone	0.5%
Yeast extract	0.15%
Beef extract	0.15%
NaCl	0.35%
Potassium dihydrogen phosphate	0.13%
Potassium monohydrogen phosphate	0.13%

In dist. H_2O, pH = 7.2, using NaOH solution, sterilised at 15 psi (120°C) for 20 min.

b) 'Preparation of inoculum'

The above-stated02 cultures were injected with 20 ml of nutrient broth the day before testing and incubated overnight at 37°C.

- **'Preparation of nutrient agar'**

Bacteriological peptone	0.6%
Yeast extract	0.3%
Beef extract	0.13%
Agar	2.5%

In distilled water, pH = 7.2 and autoclaved at 16 psi (119°C) for 19 minutes.

a) 'Preparation of drug solution'

The specific material (10 mg) was dissolved in 5 ml dimethylformamide, and 1 ml of this resultant was diluted to 200 mg/ml. Antimicrobial activity was tested using 0.1 ml of the solution.

b) 'Testing method'

Nutrient agar was put into sterile petridishes (25 ml each) while hot and allowed to cool to r.t.After 24 hours culture,with a sterilised bent glass rod, 4-5 drops of were dispersed over the surface of the set agar. After that, the cups were produced by punching a sterilised cork orer into the set agar and scooping out the punched area. Each cup had a diameter of 10 mm. aseptically; 0.1 ml (20 ug) of the test chemical solution in dimethyl formamide was applied to these cups.

To aid dispersion, these plates were allowed to cool for hour,and incubated for 24 hours at 37°C. In millimetres, the ZOI was calculated. Two standards were used to compare the results. Norfloxacin and tetracyclic hydrochloride for the aforesaid species, the 'antibacterial activity of the solvent (DMF) was examined by putting aseptically (0.1 ml) into the relevant cup of the agar plates'.

Antifungal activity evaluation:

- **'Preparation of culture'**

a) 'Preparation of fungal broth'

Peptone	1%
Yeast extract	0.6%
Sodium chloride	0.5%
Potassium hydrogen phosphate	0.3%
Glucose	1%

In distilled water,pH = 6.0, sterilised at 15 p.s.i. (120°C) for 20 minutes.

b) 'Preparation of inoculum'

The above-mentioned fungi were introduced into the fungal broth the day before testing and cultured at 37°C for 48 hours.

- **'Preparation of nutrient agar'**

Peptone	4%
Yeast extract	0.6%
Sodium chloride	0.5%
Potassium hydrogen phosphate	0.3%
Glucose	1%

Agar	2.5%

In distilled water and pH = 6. The solution was sterilised at 15 psi (120^0C) for 20 min.

a) Preparation of drug solution

In 5 ml of dimethyl formamide, the test substance (10 mg) was dissolved. To get a concentration of 200 mg/ml, 1 ml of this solution was diluted to 10 ml with dimethyl formamide, and 0.1 ml of this solution was used for the test.

b) Method of testing

Nutrient agar was placed into disinfected petriplates (20 ml each) and kept to cool to room temperature while still hot. 48-hour culture,with a sterile bent glass rod, 4-5 droplets were dispersed over the crust of the set agar. After that, the cups were produced by punching a sterile cork borer into the set agar and scooping out the punctured section. Each cup had a diameter of 10 mm. Aseptically, 0.1 ml (120 mg) of the sample chemical solution in dimethyl formamide was added to these cups.

To aid dispersion, these plates were allowed to normal for sometime thenthey were incubated for 24 hours at 38°C. In millimetres, the inhibitory zone was checked. Griseofulvin, a standard medication, was used to compare the values (antifungal agent). As a solvent control, dimethyl formamide was employed.

3. SYNTHESIS OF SYDNONES DERIVATIVES:

3.1 'Preparation of glycines'

- ✓ **'Condensation of amines with monochloroacetic acid'**

In cool, 100 ml of 2N sodium hydroxide solution was used to neutralise chloroacetic acid 18.9 (0.2mol). The reaction mixture was refluxed with shaking till the aniline had reacted, which took 18.6 g (0.2mol) (appro. for one hr). Cooling separated N-phenylglycine, which was gathered and rinsed with icy water. It was then refined further by dissipating it in a small amount of 10% NaOH solution and extracting it with ether to eliminate any unreacted reactant. To get pure N-phenylglycine, the aqueous stage was treated with norit and acidified with strong HCl.

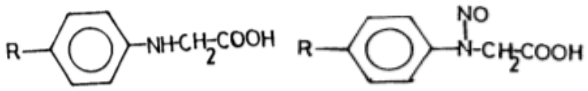
- ✓ Reaction of amines with ethylchloroacetate to produce N-p-chlorophenylglycineethylester.

- ✓ The aforementioned ester is hydrolyzed to provide the equivalent glycine.

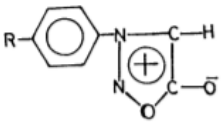
1. In an oil-bath at 125°C, a combination of ethylchloroacetate (31.0 g), p-chloroani1ine (32.0 g), C_2H_5OH (25 ml), and hydrated sodium acetate (30 g) was refluxed for 5 hours. After that, 100 mL of water was added, and the solid ester precipitated was collected, cleaned it.

2. N-p-Chlorophenylglycine ethyl ester (26.5g), ethanol (10 ml), and a NaOH solution (14.5 g) in water (100 ml) were refluxed for 0.5 hrs. The glycine was then collected, filtered & neutralised with strong HCl (23.5 ml).

These procedures yielded a variety of N-phenylglycines, which were crystallised from hot water:



N-Substututed GlycineN-Nitroso-N-substituted glycine



3-Arylsydnone

3.2 'Nitrosation of H-substituted glycines'

A. 'Nitrosation in water'

Sodium nitrite 6.9 g (0.1 mol) in water 24 ml was applied dropwise over 30 minutes to a stirred suspension of N-phenylglycine 15.1 g (0.1 mol) in water 120 ml at 0°C. After 2 hours, the reaction blend was almost clear, and it was treated with norit to the cold. Using strong HCl, it was filtered and acidified. The N-nitroso-N-phenylglycine that had precipitated was filtered, rinsed,air dried.

B. Aqueous hydrochloric acid nitrosation

At 0.5°C, a mixed suspension of N-p-chlorophenylglycine 18.1 g (0.1mol) in 300 ml of 20% aqueous HCl was added to a solution of sodium nitrite 6.0 g (0.1mol) in water 25 ml. The final mixture was stirred at room temperature for 3 hrs. after the addition was completed. The separated nitrosoglycine was filtered, rinsed carefully with tap

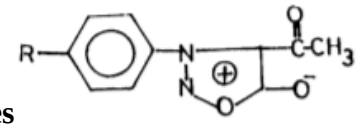
water to remove any acid, and demoisturised in the open air.The nitrosoglycines crystallised from aqueous ethanol using the procedures described above.

3.3'Cyclisation of N-nitroso-N-substituted glycines to sydnones'

On a water bath, 9.09 g (0.05 mol) of N-Nitroso-N-phenylglycine was cooked for 2 hours with 20 ml of acetic anhydride. In ice cold water, the solution was poured. The solid was filtered before being rinsed with water and 5% $NaHCO_3$ solution.Dehydrated and crystallized the solidbyC_6H_6.

3.4'Preparation of 3-phenyl-4-acetylsydnones'

In a 03 necked 250 ml R.B. flask assembled with a reflux condenser and supplied with a $CaCl_2$ drying tube, 8.1 g (0.05mol) of 3-phenylsydnone was added to a suspension of 21.3 g (0.115mol) of P_2O_5in 125 ml of Na dried thiophene free benzene. On water bath, the magnetically swirled mixture was boiled to reflux. Each 10-minutes interval, 2.86 ml (0.05mol) of glacial CH_3COOH was added dropwise by help of a dropping funnel. The stirring reaction mixture was heated for 5 hours, resulting in a blackened clear solution. Benzene was decanted after cooling to ambient temperature, and the black residual was extracted twice by 20 ml of benzene. The decantated and combined wash were evaporated to dryness, a pale-yellow solid yielded by using alcohol to crystallise.

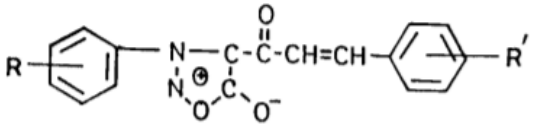


4-Acetyl-3-arylsydnones

3.5 'Preparation of 4-cinnamoyl-3-phenylsydnone (chalcones)'

4-Acetyl-3-phenylsydnone (2.0g, 0.01mol) was suspended in NaOH solution (0.5g, 5ml water, 5 ml EtOH) and benzaldehyde (1.0g, 0.01mole) was added. At the room temperature, the mix was agitated for 30 minutes. The precipitate was quickly collected, thoroughly cleaned with water.Table No.1 lists various cinnamoyl compounds that were synthesized.

Table 1: '4-Cinnamoy1-3-arylsydnones (chalcones)'



R	R^1	Yield %	M.P.^{0}C	Formula	Results

						C%	H%	N%	Ref
H	H	55	145.7	$C_{17}H_{22}N_2O_3$	Cal/Obs	50.73 (50.70)	5.52 (5.47)	6.96 (6.93)	3
H	CH_3	60	124.6	$C_{18}H_{14}N_2O_3$		70.58 (70.53)	4.50 (4.29)	9.15 (9.07)	3
H	OCH_3	65	185.7	$C_{18}H_{14}N_2O_4$		67.08 (67.05)	4.34 (4.23)	8.69 (8.61)	3
H	Cl	78	150.2	$C_{17}H_{11}N_2O_3Cl$		62.49 (62.41)	3.36 (3.33)	8.57 (8.52)	3
OCH_3	H	50	160.2	$C_{18}H_{14}N_2O_4$		67.08 (67.03)	4.34 (4.29)	8.69 (8.53)	3
OCH_3	CH_3	70	160.2	$C_{19}H_{16}N_2O_4$		67.85 (67.83)	4.76 (4.32)	8.33 (8.30)	3
OCH_3	OCH_3	70	180.90	$C_{19}H_{16}N_2O_5$		64.77 (64.72)	4.54 (4.49)	7.95 (7.90)	3
OCH_3	Cl	67	185.6	$C_{18}H_{13}N_2O_4Cl$		60.67 (60.62)	3.65 (3.61)	7.86 (7.81)	3
CH_3	H	60	180.1	$C_{18}H_{14}N_2O_3$		70.57 (70.53)	4.61 (4.59)	9.14 (9.12)	3
CH_3	CH_3	70	180.1	$C_{19}H_{16}N_3O_2$		71.23 (71.21)	6.03(5.01)	8.74 (8.71)	3
CH_3	OCH_3	65	205.6	$C_{19}H_{16}N_2O_4$		68.25 (68.21)	4.20 (4.01)	8.38 (8.35)	3
CH_3	Cl	70	176.7	$C_{18}H_{13}N_2O_3Cl$		63.44 (63.40)	3.84 (3.79)	8.20 (8.02)	3
Cl	H	60	218.2	$C_{17}H_{11}N_2O_3Cl$		62.49 (62.42)	3.36 (3.31)	8.57 (8.53)	3
Cl	CH_3	80	216.7	$C_{18}H_{13}N_2O_3Cl$		63.44 (63.40)	3.84 (3.80)	8.20 (8.12)	3
Cl	OCH_3	70	220.1	$C_{18}H_{13}N_2O_4Cl$		60.67 (60.62)	3.65 (3.61)	7.86 (7.81)	3
Cl	Cl	68	219.2	$C_{17}H_{10}N_2O_3Cl$		56.52 (56.49)	2.70 (2.30)	7.75 (7.73)	3

3.6 'Preparationof3-phenyl-4-(6-carbethoxy-5-phenyl-cyclohex-2-en-l-one-3yl)sydnones':

4-Cinnamoyl-3-phenylsydnone 2.9g (0.01mole) was dissolved in dry acetone, to which dry K_2CO_3 5.2g (0.04mole) and ethyl acetoacetate 1.3g (0.02mole) were added, and the mixture was agitated for 5 hrs at ambient temperature. The reaction mixture was allowed to sit at surrounding tempature overnight. The filtrate evaporated to dryness after being filtered to remove K_2CO_3. Yellow crystals were formed by crystallising the residue in ethanol. Table No.2 lists different derivatives that made when using this method.

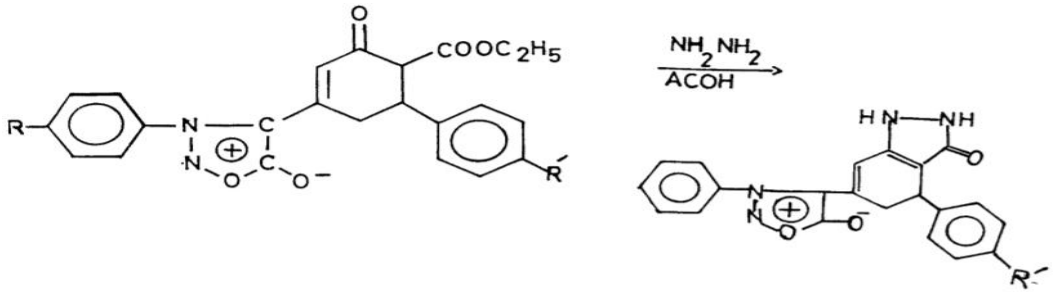
Table 2: '3-Aryl-4-(6-carbethoxy-5-arylcyclohex-2-en-l-one-3-yl) sydnones'

R	R^1	Yield %	M.P.^{0}C	Formula	Analysis			
						C%	H%	N%
H	H	75	165.6	$C_{23}H_{20}O_5N_2$	Cal/Obs	67.30 (58.30)	4.92 (4.95)	6.77 (6.92)

H	CH_3	60	178.9	$C_{24}H_{22}O_5N_2$		68.90 (68.99)	5.30 (5.20)	6.70 (6.68)
H	OCH_3	75	168.9	$C_{24}H_{22}O_6N_2$		66.36 (66.31)	5.10 (4.87)	6.43 (6.45)
H	Cl	80	168.9	$C_{23}H_{19}O_5N_2\,CI$		62.94 (62.90)	4.36 (4.30)	6.38 (6.35)
CH_3	H	85	145.6	$C_{24}H_{22}O_5N_2$		68.87 (68.83)	5.29 (5.17)	6.70 (6.49)
CH_3	CH_3	80	160.1	$C_{25}H_{24}O_5N_2$		69.42 (69.39)	5.60 (5.00)	6.47 (6.43)
CH_3	OCH_3	75	171.2	$C_{25}H_{24}O_6N_2$		66.95 (66.91)	5.16 (5.15)	6.24 (6.21)
CH_3	CI	8	180.2	$C_{23}H_{19}O_5N_2\,CI$		62.94(62.90)	4.36 (4.32)	6.38 (6.34)
OCH_3	H	75	163.4	$C_{24}H_{21}O_6N_2$		66.34 (66.23)	5.10 (5.02)	6.44 (6.41)
OCH_3	CH_3	80	179.0	$C_{25}H_{24}O_6N_2$		66.95 (66.97)	5.39(5.29)	6.24 (6.08)
OCH_3	OCH_3	80	185.6	$C_{25}H_{24}O_7N_2$		64.64 (64.57)	5.20 (5.12)	6.03 (6.01)
OCH_3	Cl	75	158.9	$C_{24}H_{23}O_5N_2\,Cl$		61.47 (61.39)	4.51(4.08)	5.03 (5.01)
Cl	H	80	161.2	$C_{23}H_{19}O_5N_2\,Cl$		62.94 (62.87)	4.36 (4.31)	6.38 (6.34)
Cl	CH_3	85	168.9	$C_{24}H_{21}O_5N_2\,Cl$		69.05 (69.02)	4.89 (4.82)	6.71 (6.63)
Cl	OCH_3	70	172.3	$C_{24}H_{21}O_6N_2\,Cl$		61.47 (61.43)	4.50 (4.46)	5.97 (5.90)
Cl	Cl	75	195.6	$C_{23}H_{18}O_5N_2\,Cl_2$		58.48 (58.41	3.81 (3.43)	5.93 (5.87)

3.7'Preparation of 3-Aryl-4(4,5-dihydro-3-oxo-indazolin-6-yl) sydnones'

Condensation of 3-aryl-4 (6-carbethoxy-5-aryl-2-en-l-one-3-yl) sydnones with hydrazine hydrate in AcOH yields these chemicals.



On a water bath, the 3-phenyl-4-(6-carbethoxy-5-pheny1-2-en-1-one-3-yl)sydnone 4.0 g (0.01 mole) and hydrazine hydrate 0.5 g (0.01 mole) were refluxed for 4 hours in CH_3COOH 1.3 ml (0.02 mole) and ethyl alcohol (100 ml). After cooling, the residue was filtered and crystallised from ethanol to produce saffron colour crystals.Table No.3 lists the several oxoindazole derivatives that have been made:

Table 3: '3-Ary1-4-(4,5-dihydro-4-ary1-(3H)-3-oxo-indazolin-6-yl)sydnones'

R	R^1	Yield %	M.P.^{0}C	Formula	Analysis			
						C%	H%	N%

H	H	80	290.1	$C_{21}H_{16}N_4O_3$	Cal/Obs	67.73 (67.70)	4.33 (4.30)	15.04 (15.01)
H	CH_3	85	294.5	$C_{22}H_{18}N_4O_3$		68.38 (68.33)	4.69 (4.65)	14.50 (14.47)
H	OCH_3	70	280.1	$C_{22}H_{18}N_4O_4$		65.66 (65.61)	4.50 (4.46)	13.92 (13.87)
H	Cl	75	198.2	$C_{21}H_{15}N_4O_3Cl$		61.99 (61.92)	3.71 (3.67)	13.77 (13.73)
CH_3	H	80	285.6	$C_{22}H_{18}N_4O_3$		68.38 (68.38)	4.69 (4.64)	14.49 (14.45)
CH_3	CH_3	85	292.3	$C_{23}H_{20}N_4O_3$		68.98 (68.93)	5.03 (5.01)	13.92 (13.89)
CH_3	OCH_3	70	285.7	$C_{23}H_{20}N_4O_4$		66.34 (66.29)	4.84 (4.80)	13.45 (13.41)
OCH_3	H	80	304.5	$C_{22}H_{18}N_4O_4$		65.67 (65.62)	4.50 (4.47)	13.92(13.89)
OCH_3	CH_3	75	285.6	$C_{23}H_{20}N_4O_4$		66.33(66.30)	4.84 (4.80)	13.45(13.39)
OCH_3	OCH_3	85	286.8	$C_{23}H_{17}N_4O_5$		63.88 (63.83)	4.66 (4.62)	12.95 (12.91)
CH_3	Cl	75	290.2	$C_{22}H_{17}N_4O_4Cl$		60.48 (60.42)	3.92 (3.89)	12.82 (12.79)
Cl	H	75	304.5	$C_{21}H_{15}N_4O_3Cl$		61.99 (61.93)	3.71(3.69)	13.77(13.75)
Cl	OCH_3	80	306.7	$C_{22}H_{27}N_4O_4Cl$		60.48 (60.43)	3.92(3.89)	12.82 (12.79)
Cl	CH_3	75	310.1	$C_{22}H_{77}N_4O_3Cl$		62.78(62.74)	4.07(4.03)	13.30 (13.09)
Cl	Cl	70	303.4	$C_{22}H_{14}N_4O_3Cl_2$		55.88 (55.85)	5.35 (5.31)	12.41 12.39)

4. RESULTS & DISCUSSION:

Table 4: 'Antibacterial and Antifungal Activity of 3-Arylsydnones'

Compound no.	R	R_1	Zone of inhibition (ZOI)in mm			
			Antibacterial		Antifungal	
			B. aureus	E. coli	A. niger	C. albicans
1	H	H	++	++	-	+
2	H	CH_3	-	-	-	-
3	H	OCH_3	-	-	-	+
4	H	Cl	++	++	-	+
5	CH_3	CH_3	++	++	-	++
6	CH_3	H	-	-	-	+
7	CH_3	OCH_3	-	-	-	+
8	OCH_3	Cl	++	++	-	+
9	OCH_3	H	+	++	-	++
10	OCH_3	OCH_3	-	-	+	+
11	OCH_3	CH_3	++	+	-	+
12	Cl	H	++	++	-	++
13	Cl	CH_3	++	++	-	++
14	Cl	OCH_3	++	++	-	-
15	Cl	Cl	-	-	-	+

ZOI in mm: 12-14 (+), 15-17 (++), 18-21 (+++)

- ✓ **Antibacterial:**With the exception of compounds 2,3,6,7,10,15 all of the fifteen derivatives tested for antibacterial function had only little action opposed E. coli and B. aureus.
- ✓ **Antifungal:**Only entities 5,9,12 and 13 have been found to exhibit anti-C-albicans and none of the substances have demonstrated anti-A-niger action.

Table 5: 'Antibacterial and Antifungal Activity of Aryl-4(4,5-Dihydro-4-Aryl 3h)-3-oxo-indazolin-6-yl) Sydnones'

Compound no.	R	R_1	Z.O.I.in mm			
			Antibacterial		Antifungal	
			B. aureus	E. coli	A. niger	C. albicans
1	H	H	++	++	-	+
2	H	CH_3	-	++	+	+
3	H	OCH_3	+	++	-	+
4	H	Cl	+	++	-	++
5	CH_3	CH_3	+	++	-	-
6	CH_3	H	++	++	-	-
7	CH_3	OCH_3	-	-	-	+
8	OCH_3	H	++	++	-	-
9	OCH_3	CH_3	+	++	-	++
10	OCH_3	OCH_3	+	++	+	+
11	OCH_3	Cl	++	++	-	++
12	Cl	H	++	++	-	+
13	Cl	CH_3	++	++	-	-
14	Cl	OCH_3	++	++	-	++
15	Cl	Cl	++	-	-	+

ZOI in mm.: 12-14 (+), 15-17 (++), 18-21 (+++).

- ✓ **Antibacterial:** With a few exceptions, all of these chemicals have proven action against E. coli. Only a few chemicals have exhibited limited anti-B-aureus action.
- ✓ **Antifungal:** Only compounds 4,9,11,14 have been found to exhibit anti-C-albicans and nil substances demonstrated anti-A-niger action.

5. CONCLUSION

Mesoionic compounds are a form of heterocycle that belongs to the non-benzenoid aromatics category. Due of its peculiar geometry, chemical characteristics, fabrication

value, sydnone, the typical mesoionic substance, has been intensively explored. In heterocyclic synthesis, sydnone is a flexible synthon.

Owe to ease of synthesis from basic amines and the fact that it is the single mesoionic ring that witnesses a large variety of reagent reactions of synthetic use, the Sydnone ring is the most intensively researched of complete mesoionic compounds known. This lactone, a 1,2,3-oxadiazole-5-one heterocycle, was given the name Sydnone in honour of the (University of **Sydn**ey + lact**one**), where Earl and Mackney originally manufactured it in 1935.

Sydnones are dipolar compounds having delocalized positive and negative charges that belong to the class of mesoionic heterocycles. According to the IUPAC definition, mesoionic compounds are composed of five-member ring heterocyclici.e.incapableto accurately represent by anequal or only one polar frame, requiring numerous canonical structures to be specified. Planar conjugated entities, known as sydnones, are aromatic. The aromaticity of sydnones is supported by their planar structure, delocalized charges, and high resonance energy.

Sydnones are a new type of meso-ionic molecule having unusual chemical and physical compounds. Sydnone derivatives have been discovered to disclose a wide spectrum of biological features, like antioxidant activity, liquid crystalline qualities. Biological activities have been documented for a variety of meso-ionic compounds. Antibacterial, antifungal, antimalarial, anti-inflammatory, analgesic, anticonvulsant, antihyertensive, antithrombotic, antitumor, and other biological actions have been claimed for sydnones. In vivo, sydnone cephalosporin derivatives show anti-streptococcal and anti-staphylococcal activity. Molsidomine has antianginal and antischemic properties, whereas sydnofen and sydnocarb have depressive properties.

New compounds have been discovered, demonstrating that sydnones may be used to make a wide range of heterocycles. The majority of the novel compounds were discovered to have antibacterial, antifungal, and anti-helmintic applications, as well as being effective in the treatment of cancer. The mesoionic structures made it possible to use it as a solvent for ionic processes or as a component in electrical devices. Despite the fact that sydnones have been around for a long time, their applications continue curiositypiqued of organic chemists and others.

REFERENCES:

1. Ranjana Dubey "Study of mesoionic compounds: Synthesis and Pharmacological Evaluation of Several 2-[{(4-Substituted-1-Sulphonyl) Sydnon-3-Yl}]-1,3,4-Thiadiazino(6,5-B)Indoles as antimicrobial, insecticidal and antihelmintic agents" Volume 30, Number 1 2010.

2. Patel YM, Patel KC. Synthesis and biological evaluation of new sydnone based derivatives. J Saudi Chem Soc 2015;19:193-9.

3. Nithinchandra, Kalluraya B, Aamir S, Shabaraya AR. Regioselective reaction: synthesis, characterization and pharmacological activity of some new mannich and schiff bases containing sydnone. Eur J Med Chem 2012;54:597-604.

4. Savaliya PP, Akbari VK, Modi JA, Patel KC. Synthesis, characterization, and antimicrobial screening of some mannich base sydnone derivatives. Med Chem Res 2013;22:5789-97.

5.Ganem, B. (2019). Strategies for innovation in multicomponent reaction design. *Accounts of Chemical Research, 42*, 463-472.

6. Denisa Elena Dumitrescu "Synthesis of 1-(2-Fluorophenyl) pyrazoles by 1,3-Dipolar Cycloaddition of the corresponding Sydnones" Molecules 26(12):3693 2021.

7. Deshpande SR, Pai KV, Pai RS. Design and synthesis of certain mesoionic sydnonyl styrylketones as potential nonsteroidal antiinflammatory agents. Arzneimittel-Forschung/Drug Res 2011;61:180-5.

8. Bizetto EL, Noleto GR, Echevarria A, Canuto AV, Cadena SM. Effect of sydnone SYD-1 on certain functions of LPS-stimulated macrophages. Mol Cel Biochem 2012;360:15-21.

9. Browne DL, Harrity JP. Recent developments in the chemistry of sydnones. Tetrahedron 2010;66:553-68.

10.Asundaria ST, Patel KC. Synthesis, characterization and antimicrobial activity of thiazole, benzothiazole and pyrimidine derivatives bearing sydnone moieties. Pharm Chem J 2012;45:725-31.

11. Abdualrahman Mohammed Abdualkader “MESOIONIC SYDNONE: A REVIEW IN THEIR CHEMICAL AND BIOLOGICAL PROPERTIES” International Journal of Pharmacy and Pharmaceutical Sciences 9(8):2017.

12. Taj, Tasneem & Raikar, Shraddha & Kamble, Ravindra. (2011). Synthetic utility of sydnones to couple pharmacologically important heterocycles for antitubercular activity. Arabian Journal of Chemistry. 7. 10.1016/j.arabjc.2011.01.029.

13. Tegginamath G, Kamble RR, Taj T, Kattimani PP, Meti GY. Synthesis of novel imidazo[2,1-B][1,3,4]thiadiazoles appended to sydnone as anticancer agents. Med Chem Res 2013;22:4367-75.

14. Sachin Bhosale “Mesoionic Sydnone Derivatives: An Overview” Journal of Chemical and Pharmaceutical Research 4(2):1185-1199 2012.

15. Gududuru, V., Hurh, E., Dalton, J. T., & Miller, D. D. (2014). Synthesis and antiproliferative activity of 2-aryl-4- oxo-thiazolidin-3-yl-amides for prostate cancer. *Bioorganic and Medicinal Chemistry Letters, 14*, 5289-5293.

16. Patel, Yogesh & Patel, Keshav. (2012). Synthesis and biological evaluation of new sydnone based derivatives. Journal of Saudi Chemical Society. 16. 10.1016/j.jscs.2012.02.005.

17.Nils Ahlburg “Functionalization of Sydnones with Donor/Acceptor Cyclopropanes, Cyclobutanes and Michael Acceptors” European Journal of Organic Chemistry 2021.

18. Muhammad Taher “Mesoionic Sydnone: A Review in their Chemical and Biological Properties” International Journal of Pharmacy and Pharmaceutical Sciences Vol 9, Issue 8, 2017.

19. N. O. Cornelli “Screening of Heterocyclic Substituted Sydnones for Potential Biological Activity” Farmacia 66(4): 2018.