A C G publications

*Org. Commun.*3:2 (2010) 30-38

organic communications

Novel 3-[4-(diethylamino)phenyl]-4-substituted-1-ylsulfonyl) sydnones: Synthesis, characterization and antimicrobial studies

Shahrukh T. Asundaria, Nikul S. Patel and Keshav C. Patel*

Department of Chemistry, Veer Narmad South Gujarat University, Udhna-Magdalla Road, Surat. 395007

Gujarat. India

(Received 28 September 16, 2009; Revised March 20 2010; Accepted March 30, 2010)

Abstract: Ten novel 3-[4-(diethylamino)phenyl]-4-substituted-1-ylsulfonyl)sydnones **(8a-j)** have been synthesized. All the synthesized compounds were characterized by IR, ^{1}H NMR, ^{13}C NMR spectroscopy and elemental analysis. Compound 3-[4-(Diethylamino)phenyl]-4-(piperazin-1-ylsulfonyl)sydnone (**8b**) and 3-[4-(Diethylamino)phenyl]-4-[(4-methylpiperazin-1-yl)sulfonyl]sydnone (**8d**) exhibited highest activity against all tested microorganisms. Some compounds were found effectively active against tested organisms.

Keywords: Sydnone; sulfonamide; characterization; antimicrobial.

1. Introduction

Considerable attention has recently been paid to finding applications of the mesoionic compounds in synthesis and pharmacology. The mesoionic compounds possess structural features which have been of considerable interest to medicinal chemists. From literature survey, sydnone derivatives are most important member of the mesoionic category of compounds. Sydnone derivatives have been viewed as exotic structures within the heterocyclic community. With few exceptions, sydnones are stable compounds that exhibit significant polarity[1]. Of the many potential applications of sydnones, the one that has attracted the most interest is their biological properties like antimalarial, antitumor, antibacterial,

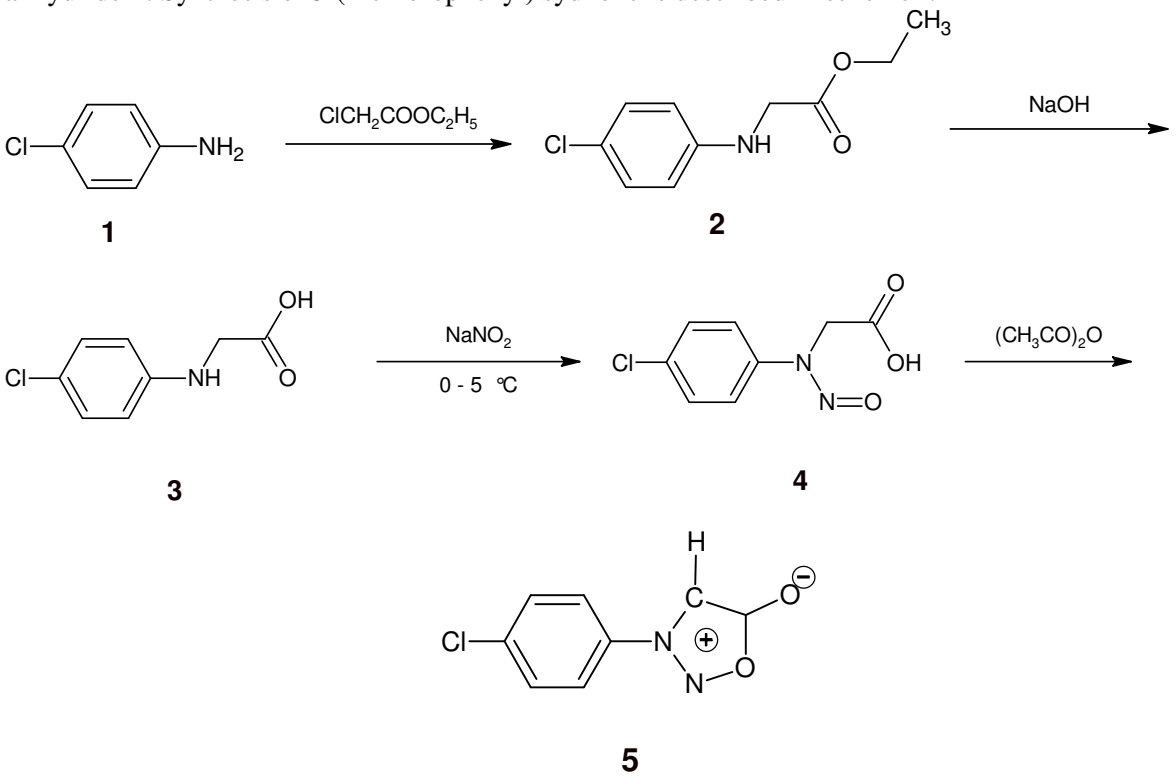
* Corresponding author: E-mail: shahrukh_sun@rediffmail.com

The article was published by Academy of Chemistry of Globe Publications
www.acgpubs.org/OC/index.htm © Published 05/20/2010 EISSN:1307-6175

analgesic, antiinflammatory and other antimicrobial activities [2-6]. Great deal of work has been done to show that sydnones do undergo electrophilic aromatic substitution at the C-4 position of the ring. A large amount of research work and activities has been undertaken to synthesize new derivatives of sydnones having different biological activities. Hence it is interesting to synthesize and characterize novel sydnone derivatives based on diethylaminobenzene.

2. Results and Discussion

Dehydration of an N-alkyl or aryl N-nitroso-α-amino acid is only general route to sydnones. For the formation of sydnones by ring closure of N-substituted N-nitrosoglycines, it is evident that at least one hydrogen atom is required on the α-carbon atom and that the amino nitrogen atom should have a substituent other than hydrogen. However, when an N-alkyl-N-nitroso-α-amino dicarboxylic acid is treated with acetic anhydride, sydnone ring competes with the cyclic acid anhydride formation by dehydration between the two carboxyl groups and the result is rather complicated. In the case of nitrosoiminodiacetic acid, 3-carboxy methyl sydnone is obtained instead of the corresponding cyclic anhydride[7,8]. Synthesis of 3-(4-chlorophenyl) sydnone is described in scheme I.

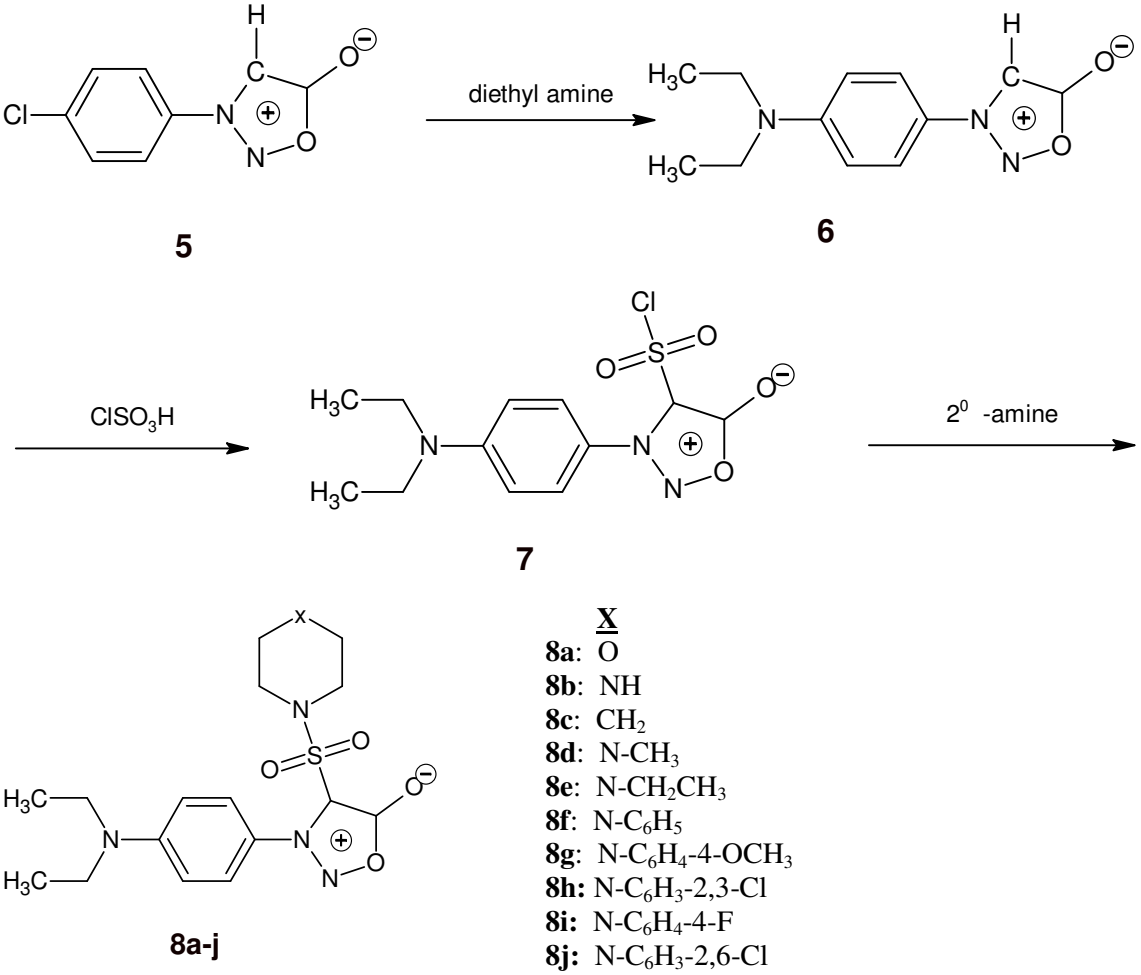


Scheme 1. Synthesis of 3-(4-chlorophenyl) sydnone from 4-chloroaniline

Hydrogen chloride is produced by the reaction between 3-(4-chlorophenyl)sydnone **(5)** and diethyl amine which combines with triethylamine to form triethylammonium chloride, which is required to complete the reaction. Compound **(6)** reacted with chlorosulfonic acid to give corresponding sulfonyl chloride which on condensation with different amines resulted in to final compounds. The new procedure for the synthesis of 3-[4-(diethylamino)phenyl]-4-(substituted-1-yl sulfonyl) sydnone (8a-j) is shown in

scheme II. Yield of the novel compounds were found between 74-89 %, depending upon reactivity of secondary amine. All the compounds gave satisfactorily elemental analysis.

All the compounds were characterized by IR and NMR spectroscopy. The expected spectral features of synthesized compounds have been assigned.



Scheme 2. Synthesis of 3-[4-(diethylamino)phenyl]-4-(substituted-1-yl sulfonyl) sydnone from 3-(4-diethylaminophenyl) sydnone

***Biological activity*:** Antibacterial activity of test compound was assessed against *micrococcus* are *Staphylococcus aureus, Bacillus subtilis, Escherichia coli, and Pseudomonas aeruginosa* by broth dilution method.[9] Ciprofloxacin was used as reference drug. N,N-dimethylformamide (DMF) was used as solvent for this activity. The twofold dilution of the compounds were prepared (128, 64, 32, 16, 8, 4, 2, 1, 0.5, 0.25, 0.125 >) µg/mL in the same solvent for Minimal Inhibitory Concentration (MIC). The compounds were screened under identical conditions at a dose of 200 µg/mL with DMF as solvent.

Compound **8d** with substitution of 4-methylpiperazin showed enhanced activity against *B. Subtilis, E.Coli* and *P. aeruginosa* compared to other compounds. Presence of methyl group at 4th position of piperazine ring could be responsible for enhance activity against these species. The structure variation such as ethyl, phenyl, methoxy, group at para position of piperazine ring result in to decrease in activity. Compound 8e

with substitution of ethyl group at para position of piperazine ring showed highest activity against *S. aureus*. Rest of the compounds showed moderate to good activity. This is an example which shows how biological activities are influenced by minor structure modification.
The observed data on the antimicrobial activity of the compounds **(8a-j)** and the reference drugs are given in Table 1.

Table 1. *In vitro* activity of compounds 3-[4-(diethylamino)phenyl]-4-(substituted-1-ylsulfonyl)sydnone (**8a-j**)

Compound	Gram Possitive Organisms				Gram Negative Organisms			
	S.aureus		*B. Subtilis*		*E.Coli*		*P. aeruginosa*	
	IZ	**MIC**	**IZ**	**MIC**	**IZ**	**MIC**	**IZ**	**MIC**
8a	10	-	18	32	13	64	08	-
8b	12	64	15	64	16	32	18	32
8c	10	-	11	128	09	-	08	-
8d	15	32	21	08	20	08	18	16
8e	18	32	08	-	04	-	05	-
8f	17	32	05	-	11	128	10	-
8g	08	-	12	128	11	128	09	-
8h	05	-	08	-	07	-	08	-
8i	11	128	10	-	12	64	13	64
8j	12	128	11	128	08	-	07	-
Ciprofloxacin	31	01	35	0.5	38	0.25	41	0.125

IZ: Inhibition of zone at 200 µg/mL
MIC: Minimum Inhibitory Concentration

3. Conclusion

Our present investigation is centered on the studies of reactions, synthesis, spectral analysis and biological activities of sydnone sulfonamide derivatives. The procedure proved more profitable than those previously reported in the literature. Some compounds were found effective as antibacterial agents.

4. Experimental

General Procedure: All the melting points reported are uncorrected and were recorded using an electro thermal melting point apparatus. Thin layer chromatography (TLC) was performed on E-Merck pre-coated 60 F254 plates and the spots were rendered visible by exposing to UV light. IR spectra were recorded on Shimadzu FTIR instrument. NMR spectra were recorded on Brucker Avance II NMR spectrometer. Chemical shifts (δ) reported are referred to internal reference tetramethyl silane. Elemental analysis was obtained using a Carlo-Erba CHNS-O EA 1108 Elemental Analyzer.

Preparation of Ethyl *N*-(4-chlorophenyl)glycinate (2) : p-Chloroaniline (1.40 g, 0.01 mol), chloroethyl acetate (1.06 mL, 0.01 mol) in ethanol (10 mL) and anhydrous sodium acetate (1.64 g, 0.02 mol) were refluxed for 5 hours. The mixture was diluted with 10 mL of water and kept in refrigerator for overnight. Recrystalliaztion in ethanol gave yield 81% of pure glycinate. M.p. 115-117 ºC. (lit.[10]m.p. 94 ºC) IR (KBr): 3328, 2951, 2933, 2887, 1757, 1072; ^{1}H NMR (400 MHz, DMSO-d_6): δ 1.21 (t, 3H, $COOCH_2\underline{CH_3}$), 3.76 (s, 1H, NH), 4.29 (s, 2H, CH_2), 4.54 (q, 2H, $COO\underline{CH_2}CH_3$), 6.83-7.21 (m, 4H, Ar-H); ^{13}C NMR (40 MHz, DMSO-d_6): δ 14.67, 44.78, 61.29, 115.12, 123.22, 128.96, 146.26, 172.11.

Preparation of *N*-(4-chlorophenyl)glycine (3): Ethyl *N*-(4-chlorophenyl)glycinate (2.13 g, 0.01 mol) and sodium hydroxide (0.6 g, 0.015 mol) in solution of distilled water and ethanol (18 mL:4 mL) was heated at 80-85 ^{0}C for 0.5 hour. Allowed to cool and acidified with hydrochloric acid. Crystalline white product was obtained. Yield 78%. M.p. 145-147 ºC. (lit.[10] m.p. 144 ºC)
IR (KBr): 3323, 3278-2521, 2954, 2937, 2881, 1705, 1067; ^{1}H NMR (400 MHz, DMSO-d_6): δ 4.33 (s, 2H, CH_2), 6.44 (s, 1H, COOH), 6.52 (s, 1H, NH), 6.88-7.23 (m, 4H, Ar-H); ^{13}C NMR (40 MHz, DMSO-d_6): δ 44.98, 114.32, 123.26, 129.10, 146.07, 172.18.

Preparation of [(4-chlorophenyl)(nitroso)amino]acetic acid (4): To an ice cooled solution of the N-(4-chlorophenyl) glycine (1.86 g, 0.01 mol) in water (40 mL), a solution of sodium nitrite (0.69 g, 0.01 mol) in water (5 mL) was added dropwise with stirring. The reaction mixture was filtered and precipitated by adding concentrated hydrochloric acid to the filtrate. Product obtained as yellowish needles. Yield 78%. M.p. 104-106 ºC. (lit. [11] mp 113 ºC. IR (KBr): 3257-2526, 2925, 2853, 1712, 1571, 1328, 1065; ^{1}H NMR (400 MHz, DMSO-d_6): δ 5.02 (s, 2H, CH_2), 6.93-7.48 (m, 4H, Ar-H), 11.56 (s, 1H, COOH); ^{13}C NMR (40 MHz, DMSO-d_6): δ 49.43, 120.78, 128.31, 130.46, 138.89, 168.24.

Preparation of 3-(4-chlorophenyl)sydnone (5): The mixture of [(4-chlorophenyl)(nitroso) amino]acetic acid (2.70 g, 0.0126 mol) and acetic anhydride (15 mL) was stirred at room temperature for 12 hours in dark. The solution was poured slowly into cold water which was very well stirred. The pH of the content was adjusted to 7.0 with 10 % sodium bicarbonate solution. The crude sydnone obtained was washed well with water and dried. Recrystalliaztion from 95 % ethanol afforded yield 98% of light yellow needles, M.p. 140-145 ºC. (lit.[12] m.p. 110-112 ºC). IR (KBr): 3178, 1750, 1056; ^{1}H NMR (400 MHz, DMSO-d_6): δ 7.21 (s, 1H, sydnone), 7.52-8.16 (m, 4H, Ar-H); ^{13}C NMR (40 MHz, DMSO-d_6): δ 124.12, 128.55, 130.63, 135.22, 140.92, 169.19.

Preparation of 3-(4-diethylaminophenyl) sydnone (6): Diethylamine (1.05 mL, 0.01 mol) was added dropwise to the mixture of 3-(4-chlorophenyl) sydnone (1.96 g, 0.01 mol) and triethylamine (1.34 mL, 0.01 mol) in dimethylformamide (DMF) (10 mL) over the period of 30 minute. The reaction mixture heated for about 24 hour at 50 ºC. The solution was poured over the crushed ice. The resulting crystals are filtered. Recrystallized from hot water. Yield obtained was about 78 %. M.p. 160-163 ºC. IR (KBr): 3182, 2956, 2918, 2865, 2823, 1753, 1343; ^{1}H NMR (400 MHz, DMSO-d_6): δ 1.33 (t, 6H, *J*=7 Hz, CH_3), 3.39

(q, 4H, *J*=7 Hz, CH_2), 7.11 (s, 1H, sydnone), 7.18-7.64 (m, 4H, Ar-H); ^{13}C NMR (40 MHz, DMSO-d_6): δ 13.06, 45.13, 116.33, 123.11, 124.43, 140.87, 149.33, 169.24.

Preparation of N-(4-diethylaminophenyl) sydnone sulphonyl chloride (7): Add N-(4-diethylaminophenyl) sydnone (2.33 g, 0.01 mol) in small portion to the mixture of chlororsulphonic acid (0.70 mL, 0.01 mol) and catalytic amount of phosphorous pentoxide. Shake well to ensure thorough mixing. When the addition has been made, heat the reaction mixture at 60-65 ^{0}C for about 1 hour in order to complete the reaction. Allow to cool and pour the mixture over ice. Stir well. Brown solid product was obtained. Filter off the product and wash with cold water. Yield is about 89%. M.p. 195-197 ºC. IR (KBr): 2963, 2923, 2867, 2836, 1747, 1395, 1345, 1178; ^{1}H NMR (400 MHz, DMSO-d_6): δ 1.36 (t, 6H, *J* = 7, CH_3), 3.45 (q, 4H, *J* = 7 Hz, CH_2), 7.13-7.95 (m, 4H, Ar-H); ^{13}C NMR (40 MHz, DMSO-d_6): δ 13.26, 45.35, 115.86, 117.89, 123.10, 140.90, 149.54, 169.22.

Preparation of 3-[4-(diethylamino)phenyl]-4-(substituted-1-yl sulfonyl) sydnone (8a-j): Various 2º - amine (0.005 mol) in acetone (10 mL) was added to N-(4-diethylaminophenyl) sydnone sulphonyl chloride (1.65 g, 0.005 mol) with stirring for 4 hour. Add pyridine (2.0 mL) in portion within this period. Pour the solution to the ice cold water. Products recrystallized in benzene. Similarly other final derivatives were prepared. Yield, Melting point, Elemental analysis of compounds **(8a-j)** are shown in Table 2.

3-[4-(Diethylamino)phenyl]-4-(morpholin-4-ylsulfonyl)sydnone (8a): IR (KBr): 2955, 2928, 2874, 2844, 1743, 1358, 1349, 1187, 1127; ^{1}H NMR (400 MHz, DMSO-d_6): δ 1.29 (t, 6H, *J*=7 Hz, CH_3), 3.37 (q, 4H, *J*=7 Hz, CH_2), 3.54-3.70 (m, 8H, morpholine), 7.10-7.89 (m, 4H, Ar-H); ^{13}C NMR (40 MHz, DMSO-d_6): δ 13.12, 45.21, 42.78, 63.54, 116.76, 123.26, 124.10, 140.92, 150.10, 169.19.

3-[4-(Diethylamino)phenyl]-4-(piperazin-1-ylsulfonyl)sydnone (8b): IR (KBr): 3225, 2961, 2926, 2870, 2830, 1751, 1373, 1342, 1185; ^{1}H NMR (400 MHz, DMSO-d_6): δ 1.28 (t, 6H, *J*=7 Hz, CH_3), 2.61 (s, 1H, NH), 3.25-3.56 (m, 8H, piperazine), 3.39 (q, 4H, *J*=7, CH_2), 7.12-7.89 (m, 4H, Ar-H); ^{13}C NMR (40 MHz, DMSO-d_6): δ 13.42, 41.57, 45.23, 45.37, 116.73, 123.28, 124.61, 150.36, 140.83, 169.15.

3-[4-(Diethylamino)phenyl]-4-(piperidin-1-ylsulfonyl)sydnone (8c): IR (KBr): 2985 (CH_3), 2934, 2875, 2825, 1765, 1370, 1347, 1182; ^{1}H NMR (400 MHz, DMSO-d_6): δ 1.33 (t, 6H, *J*=7 Hz, CH_3), 1.54-1.60 (m, 6H, piperidine), 3.40 (t, 4H, *J*=11 Hz, piperidine), 3.45 (q, 4H, J=7 Hz, CH_2), 7.12-7.84 (m, 4H, Ar-H); ^{13}C NMR (40 MHz, DMSO-d_6): δ 13.32, 23.47, 25.32, 45.21, 45.63, 116.66, 123.35, 124.12, 140.92, 150.31, 169.36.

3-[4-(Diethylamino)phenyl]-4-[(4-methylpiperazin-1-yl)sulfonyl]sydnone (8d): IR (KBr): 2989, 2977, 2875, 2852, 1746, 1382, 1363, 1174, 1095; ^{1}H NMR (400 MHz, DMSO-d_6): δ 1.26 (t, 6H, *J*=7 Hz, CH_3), 2.38 (s, 3H, N-CH_3), 2.83 (t, 4H, *J*=4 Hz, piperazine), 3.38 (q, 4H, *J*=7 Hz, CH_2), 3.58 (t, 4H, *J*=5 Hz, piperazine), 7.10-7.88 (m, 4H, Ar-H); ^{13}C NMR (40 MHz, DMSO-d_6): δ 13.37, 42.45, 45.27, 45.73, 52.78, 116.54, 123.72, 124.09, 150.57, 140.78, 169.16.

Table 2. Analysis of 3-[4-(diethylamino)phenyl]-4-(substituted-1-ylsulfonyl)sydnone (**8a-j**)

	RMol. Formula	Yield (Mol. Weight)	%	M.P ^{0}C	Analysis Calcd/found				
					%C	%H	%O	%N	%S
8a	morpholine	$C_{16}H_{22}N_4O_5S$ (382.43)	87	204-206	50.25 (50.35)	5.80 (5.86)	20.92 (21.14)	14.65 (14.62)	5.47 (5.56)
8b	piperazine	$C_{16}H_{23}N_5O_4S$ (381.45)	89	185-187	50.38 (50.26)	6.08 (5.98)	16.78 (16.49)	18.36 (18.12)	5.48 (5.55)
8c	piperidine	$C_{17}H_{24}N_4O_4S$ (380.46)	82	224-226	53.67 (53.96)	6.36 (6.54)	16.82 (16.96)	14.73 (14.87)	5.50 (5.58)
8d	N-methyl piperazine	$C_{17}H_{25}N_5O_4S$ (395.48)	78	195-197	51.63 (51.87)	6.37 (6.68)	16.18 (16.26)	17.71 (17.78)	5.23 (5.31)
8e	N-ethyl piperazine	$C_{18}H_{27}N_5O_4S$ (409.50)	76	243-245	52.79 (52.54)	6.65 (6.96)	15.63 (15.72)	17.10 (16.98)	5.00 (4.90)
8f	N-phenyl piperazine	$C_{22}H_{27}N_5O_4S$ (457.55)	79	210-212	57.75 (57.69)	5.95 (6.03)	13.99 (13.91)	15.31 (15.56)	4.35 (4.43)
8g	N-4-methoxyphenyl-piperazine	$C_{23}H_{29}N_5O_5S$ (487.57)	74	201-203	56.66 (56.76)	6.00 (6.13)	16.41 (16.33)	14.36 (14.28)	4.02 (4.11)
8h	N-2,3-dichlorophenyl-piperazine	$C_{22}H_{25}Cl_2N_5O_4S$ (526.44)	82	173-175	50.19 (50.32)	4.79 (4.86)	12.16 (12.28)	13.30 (13.22)	3.67 (3.61)
8i	N-4-florophenyl-piperazine	$C_{24}H_{26}FN_5O_4S$ (475.54)	81	215-217	55.57 (55.68)	5.51 (5.65)	13.46 (13.41)	14.73 (14.86)	4.15 (4.09)
8j	N-2,6-dichlorophenyl piperazine	$C_{22}H_{25}Cl_2N_5O_4S$ (526.44)	74	238-240	50.19 (50.02)	4.79 (5.01)	12.16 (12.31)	13.30 (13.42)	3.67 (3.74)

3-[4-(Diethylamino)phenyl]-4-[(4-ethylpiperazin-1-yl)sulfonyl]sydnone (8e): IR (KBr): 2978, 2964, 2870, 2857, 1757, 1388, 1368, 1177, 1087; ^{1}H NMR (400 MHz, DMSO-d_6): δ 1.23 (t, 3H, *J*=7 Hz, CH_3), 1.47 (t, 6H, *J*=6 Hz, CH_3), 2.88 (q, 2H, *J*=4 Hz, CH_2), 2.91 (t, 4H, *J*= 4 Hz, piperazine), 3.45 (q, 4H, *J*=7 Hz, CH_2), 3.73 (t, 4H, *J*=5 Hz, piperazine), 7.18-7.84 (m, 4H, Ar-H); ^{13}C NMR (40 MHz, DMSO-d_6): δ 11.48, 13.25, 41.33, 45.27, 50.63, 51.75, 116.76, 123.25, 124.26, 140.74, 150.33, 169.54

3-[4-(Diethylamino)phenyl]-4-[(4-phenylpiperazin-1-yl)sulfonyl]sydnone (8f): IR (KBr): 2979, 2974, 2878, 2858, 1741, 1368, 1375, 1171, 1083; ^{1}H NMR (400 MHz, DMSO-d_6): δ 1.35 (t, 6H, *J*=7 Hz, CH_3), 3.47 (q, 4H, *J*=6 Hz, CH_2), 3.76-3.83 (m, 8H, piperazine), 6.82-7.76 (m, 9H, Ar-H); ^{13}C NMR (40 MHz, DMSO-d_6): δ 13.53, 45.25, 45.54, 50.35, 116.88, 117.00, 120.24, 123.35, 124.42, 129.42, 140.66, 150.37, 153.46, 169.43.

3-[4-(Diethylamino)phenyl]-4-{[4-(4-methoxyphenyl)piperazin-1-yl]sulfonyl}sydnone (8g): IR (KBr): 2990, 2977, 2876, 2852, 1747, 1364, 1382, 1239, 1174, 1087, 1023; ^{1}H NMR (400 MHz, DMSO-d_6): δ 1.41 (t, 6H, *J*=7 Hz, CH_3), 3.33 (q, 4H, *J*=7 Hz, CH_2), 3.69-3.75 (m, 8H, piperazine), 3.71 (s, 3H, OCH_3), 6.85-8.76 (m, 8H, Ar-H). ^{13}C NMR (40 MHz, DMSO-d_6): δ 13.34, 45.24, 45.67, 50.83, 54.96, 114.63, 116.56, 119.58, 123.27, 124.51, 140.73, 145.65, 150.13, 154.74, 168.68.

3-[4-(Diethylamino)phenyl]-4-{[4-(2,3-dichlorophenyl)piperazin-1-yl]sulfonyl}sydnone (8h): IR (KBr): 2968, 2945, 2852, 2861, 1756, 1374, 1359, 1172 , 1092, 1090; ^{1}H NMR (400 MHz, DMSO-d_6): δ 1.27 (t, 6H, *J*=7 Hz, CH_3), 3.38 (q, 4H, *J*=7 Hz, CH_2), 3.79-3.85 (m, 8H, piperazine), 6.95-7.84 (m, 7H, Ar-H); ^{13}C NMR (40 MHz, DMSO-d_6): δ 13.53, 45.23, 45.43, 51.44, 116.62, 118.34, 122.23, 123.18, 123.81, 124.31, 129.58, 136.28, 140.35, 147.87, 150.53, 169.26.

3-[4-(Diethylamino)phenyl]-4-{[4-(4-fluorophenyl)piperazin-1-yl]sulfonyl}sydnone (8i): IR (KBr): 2989, 2973, 2872, 2854, 1752, 1378, 1386, 1227, 1162, 1077; ^{1}H NMR (400 MHz, DMSO-d_6): δ 1.22 (t, 6H, *J*=7 Hz, CH_3), 3.40 (q, 4H, *J*=7 Hz, CH_2), 3.67-3.75 (m, 8H, piperazine), 7.00-8.23 (m, 8H, Ar-H); ^{13}C NMR (40 MHz, DMSO-d_6): δ 13.33, 45.26, 45.34, 51.21, 115.86, 116.47, 116.56, 123.15, 124.64, 140.36, 149.12, 150.35, 156.48, 169.30.

3-[4-(Diethylamino)phenyl]-4-{[4-(2,6-dichlorophenyl)piperazin-1-yl]sulfonyl}sydnone (8j): IR (KBr): 2975, 2964, 2877, 2856, 1766, 1384, 1358, 1176, 1095, 1084; ^{1}H NMR (400 MHz, DMSO-d_6): δ 1.31 (t, 6H, *J*=7 Hz, CH_3), 3.36 (q, 4H, *J*=7 Hz, CH_2), 3.79-3.85 (m, 8H, piperazine), 6.95-7.50 (m, 7H, Ar-H); ^{13}C NMR (40 MHz, DMSO-d_6): δ 13.14, 45.24, 45.33, 51.43, 116.76, 123.22, 124.12, 126.33, 128.45, 136.77, 140.66, 143.54, 150.17, 169.22.

Acknowledgements

The authors express their sincere gratitude to Dr. P. Bahadur, Head of the Department of Chemistry, Veer Narmad South Gujarat University, Surat for providing necessary research facilities.

References

[1] Baker, W; Ollis, W. D. Meso-ionic compounds. *Quart. Rev*. **1957**, 11, 15-29.

[2] Popoff, I. C.; Singhal, G. H. Antimalarial agents. I. Reduction of sydnone derivatives. *J. Med. Chem.* **1968**, *11*(3), 631–633.

[3] Kier, L. B.; Roche, E. B. Medicinal chemistry of the mesoionic compounds. *J. Pharm. Sci.* **1967**, 56, 149-168.

[4] Kier, L. B; Dhawan, D. Synthesis of sydnones as potential therapeutic agents. *J. Pharm. Sci.* **1962**, 51, 1058-1061.

[5] Pattanashetti, P. P; Tikare, R. K; Dambal, D. B; Badami, B. V.; Puranik, G. S. Syntheses and biological activities of 3-[4-(alkoxycarbonyl)phenyl]sydnones and their derivatives. *Arch. Pharm*. **1984**, 317, 59-63.

[6] Kamble, R. R.; Latthe, P. R; Badami, B. V. 3/4-phenylene bisheterocycles from ring transformation reaction of sydnone derivatives: Synthesis of 3-[3/4-heterocyclyl]phenyl-5-methyl-3H-[1,3,4]-oxadiazol-2-ones from 3/4- acetylphenylsydnones and their biological properties. *Heteroat. Chem.* **2007**, 18, 50-54.

[7] Stewart, F. H. C. Competitive reactions involving formation on sydnones and cyclic anhydrides. *J. Chem. Soc.* **1963**, 701-706.

[8] Stewart, F. H. C. The chemistry of sydnones. *Chem. Rev.* **1961**, 64, 129-147.

[9] Stalons, D. R.; Thornsberry, C. Broth-dilution method for determining the antibiotic susceptibility of anaerobic bacteria. *Antimicrob. Agents Chemother*. **1975**; 7, 15-21.

[10] Bryson, A.; Davies, N.R.; Serjeant, E.P. The ionization constants of N-(Substituted-phenyl)-glycines .J. *Am. Chem. Soc.* **1963**, 85, 1933-1938.

[11] Baker, W.; Ollis, W. D.; Poole, V. D. Cyclic meso-ionic compounds. I. The structure of the sydnones and related compounds. *J. Chem. Soc*. **1949**, 307-314.

[12] N. N. Chitiyo, Lithiation reactions of 3-(4-chlorophenyl) sydnone and 3-(4- methylphenyl) sydnone. M.S. Thesis, Wright State University, **2009**.