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Synthesis and Characterization of New Sulfadiazine and Sulfapyridine Derivatives

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ABSTRACT:-

A series of 4-Hydroxybenzosulfadiazine (1, 1a, 1b, 3) and sulfapyridine (2, 2a, 2b, 4) derivatives, were prepared by condensation of appropriate sulfadiazine, sulfapyridine with 4-hydroxybenzoic acid in the presence of molecular sieves followed by 2-amino methylation on hydroxy group.

تحضير وتشخيص مشتقات جديدة للسلفادايزين و للسلفابريدين

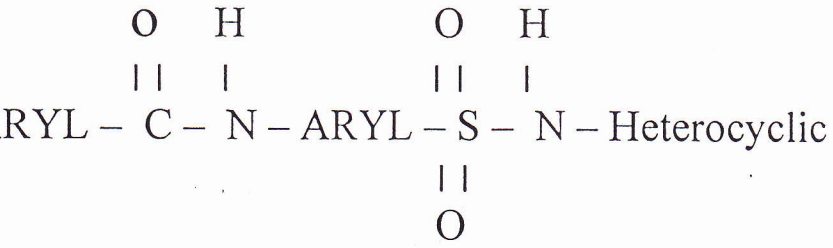
ابتهال قحطان عبد الله

المستخلص:-

سلسلة من مشتقات 4- هيدروكسي بنزوسلفادايزين (1, 1a, 1b, 3) وسلفابريدين (2, 2a, 2b, 4) التي حضرت بواسطة تكاثف السلفادايزين والسلفابريدين مع حامض 4- هيدروكسي بنزويك بوجود سيفس موليكيولر ، يتبعها خطوة المثيلية لمجموعة الهيدروكسي وتحويلها بسلسلة من التفاعلات إلى 2- أمينوأيثوكسي المرتبطة بحلقة البنزين.

INTRODUCTION:-

Sulfadiazine herbicides posses' herbicidal activity at unprecedented levels combined with very low toxicity and desirable environmental properties [1]. The synthesis and SAR-study of a great number of sulfonamide derivatives has shown that maximum herbicidal activity is found in compound having a substituted aryl group with the heterocyclic as pyrimidine or pyridine with methyl or methoxy group in the Y and 6 positions [2].



A comprehensive review of the synthesis of sulfonamide derivatives and their intermediates has been published by Beyer et. al. [3].

EXPERIMENTAL:-

Apparatus: Melting points were recorded by a Gallen Kamp melting point apparatus. Ascending thin Layer chromatography was carried out on PSC-Ferting platlen Kieselgel 60 F245 S (Merck, Barmstadt), and the spots on plats were revealed by using iodine vapor,

Materials: 4-Hydroxybenzoicacid, sulfadiazine, sulfapyridine, 4A° powdered

Synthetic procedures:

(Ethanol : Butanol) (2:2), was used as a solvent. IR. spectra were recorded using apyeVnicam SP3-100 spectrophotometer. U.V. spectra were recorded by :- Gimtra 5GBC UV-Vis-spectrophotometer, (1%) NaHCO3 was used as solvent. molecular sieves, Dichloroethan, Sodium azide, LiH, pd-c.

(1)4-Hydroxybenzo sulfadiazine (1)[4]:- A mixture of 4-hydroxybenzoicacid (0. 15 mole, 20.7gm) and amino sulfadiazine (0.15 mole, 37.5 gm) with 4A° powdered molecular sieves were refluxed at 150C° for 4h. The residue thus obtained was dissolved with ethanol water mixture (2:1, V/V) and recrystalized from ethanol to obtain the product (1). Compound (2) was prepared similarly.

(2) 4- Bromoethoxybenzo sulfadiazine (1a)[5]:- To a solution of compound (1) (0.01 mol, 3.72 gm) in 80ml of THF, was added 100 ml of 10% NaOH at 50C°. The mixture was refluxed for 30 min., the solid was collected by filtration and washed successively with ice-water. To a stirred solution of solid (0.01 mole, 3.8g) in THF with dichloroethane (0.1 mole, 6.3gm). The mixture was refluxed for 2hr, followed by hot filtration. After cooling to 0C° the product was filtered and crystallized from ethanol to give (1a), compound (2a) was prepared similarly.

(3) 4-Azide ethoxybenzo sulfadiazine (1b)[6]:- To a stirred and cooled solution at 0C° of compound (1a) (0-005mol, 2.4g) in 50 ml of butanol was added a drop wise the solution of NaN3 (0.01 mol, 0.65gm) in (40ml) of butanol, over 30 min. The reaction mixture was stirred 1 hr at 50C°, formed compound (1b) was separated by filtration, and crystallized from MeOH. Compound (2b) was prepared similarly.

(4) 4- Aminoehtoxybenzosulfadazine (2)[7]:- A mixture of compound (1b) (0.005 mol, 2gm) with LiH (0.1 mol, 0.7gm) in 100ml of (10% pd-c), was refluxed for 2h. after distillation of MeOH, the residue was diluted with water. The compound (2) was filtrated and recrystallized from EtOH. Compound (3) was prepared similarly.

RESULTS AND DISCUSSIONS:-

The sulfadiazine and sulfapyridine were reacted with 4-Hydroxybenzoicacid the presence of powdered 4A' molecular sives at 150C° for 3 to 5h, to produces 4-Hydroxybenzo sulfadiazine (1) and 4-Hydroxybenzosulfapyridine (2). Reaction of 4-Hydroxybenzoicacid with thionylchloride followed by sulfadiazine provide amides (1) in similar yields, but this procedure was less convenent than that of using molecular sieves without solvent. This is identified by their melting point, and their CHN elemental analysis tables (1), and (2) respectively. The IR spectra of these compounds (1,2), table (3), show the following absorption bands :- (OH) at (3400-3450) cm^{-1}, (C=O) at (1690-1700) cm^{-1}, (NH) at (3320-3300) cm^{-1}, (S=O) at (1370-1330) cm^{-1}, (C=N) at (1635-1630) cm^{-1}. The U.V. spectra of these compounds, table (3), show the following maxima :- (270-294) nm due to the aromatic ring, (323-408) nm due to (C=0), (NH), (NH2) and (S=0) groups. For introduction of aminemethyl group on the phenolic hydroxyl group of (1) and (2) compounds, sodium salts of (1) and (2) were reacted with 1,2 – dichloroethan in tetrahydrofuran heated at reflux to generate chlorides in 80 , 90% yields. Compounds (1a, 2a) are identified by their melting points and their C.H.N elemental analysis, table (1) and (2). The IR. spectra of these compounds, table (3), show the following absorbtion bands :- disappearance of band at (3340-3450) cm^{-1} due to the reaction of (OH) group and the appearance of a band at 1220 cm^{-1} due to (O-CH2) and band at (778-780) cm^{-1} due to (C-C1). The chlorides (1a, 2a) were converted to corresponding a zides (1b, 2b) in the presence of NaN3 and catalytic amounts of Bu-NH2, compounds (1b,2b) are identified by their melting points and their C.H.N elemental analysis, tables (1) and (2) respectively. The IR spectra of these compounds, table (3) show:- disappearance of band at (778-780) cm^{-1} due to (C-C1) converted to azides, and appearce band at (1435-1450) cm^{-1} due to a zides group. The U.V spectra of these compounds, table (3) show the following maxima :- (285-300) nm due to the aromatic ring, and (342-430) nm due to a zide group. The azides (1b, 2b) were reduced to amines (3,4) in better than 9% yields. Compounds (3,4) also, identified by their melting points and their CHN elemental analysis tables (1) and (2) .The IR spectra of these compounds, table (3), show the appearance of band at (3400-3410) cm^{-1} due to (NH2) and disappearance band at (1435-1450) cm^{-1} due to disappearance a zides group. The U.V.

spectra of these compounds, table (3) show the following maxima :- (270-300) nm due to the aromatic ring and (340-415) due to (C=0, NH2, S=0) groups.

Table (1) Physical Data of Compounds (1, 1a, 1b, 3, 2, 2a, 2b, 4)

No. Compound	M. P C°	%	RF
1	169-170	83	0.77
2	183-185*	85	0.74
1a	152-154	90	0.90
2a	148-150	88	0.81
1b	160-162*	60	0.76
2b	144-146	22	0.79
3	117-118	50	0.88
4	192-194	48	0.85

*Decomp.

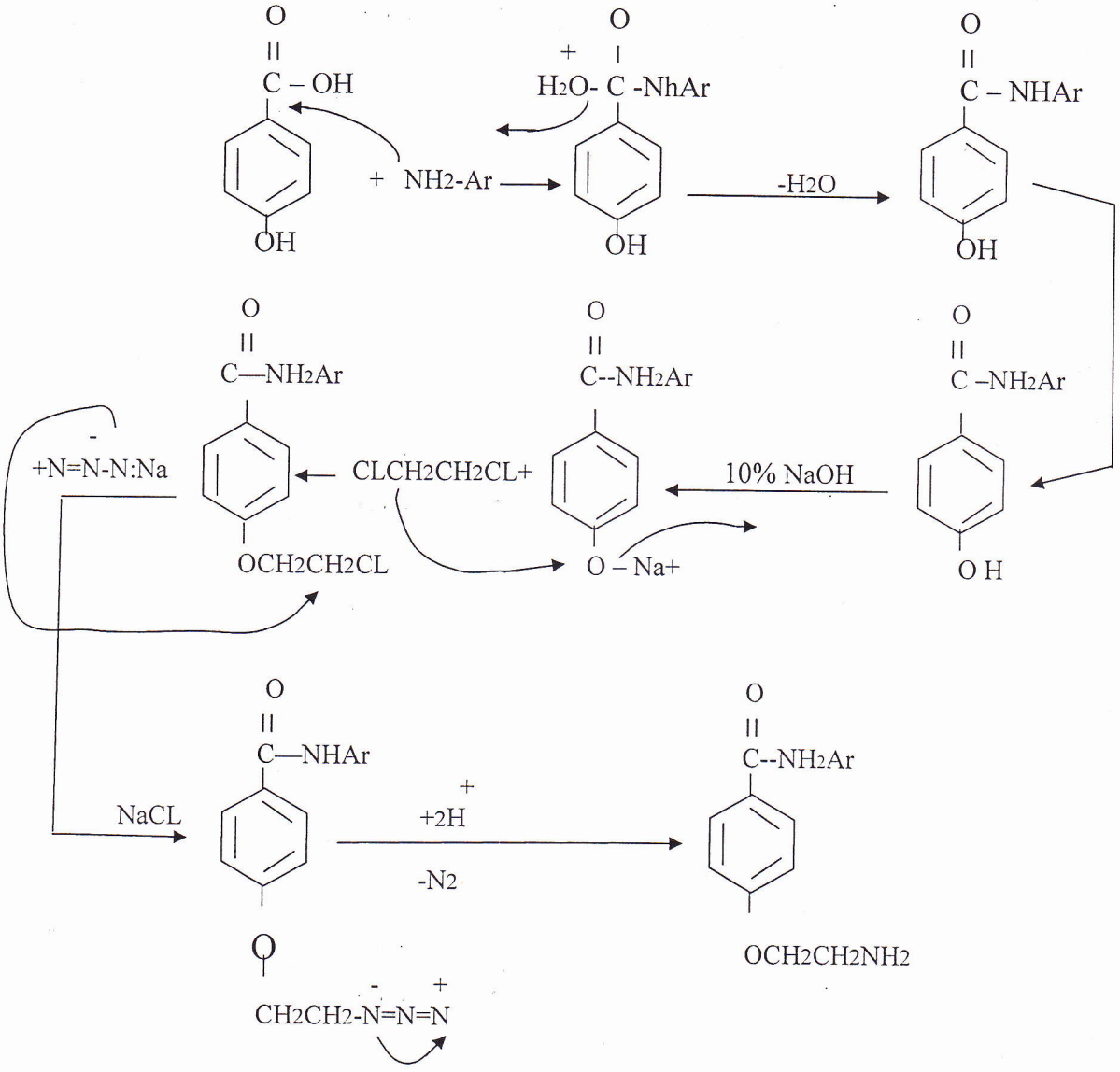
Table (2) (C.H.N) Analysis of compounds (1, 2, 3, 4)

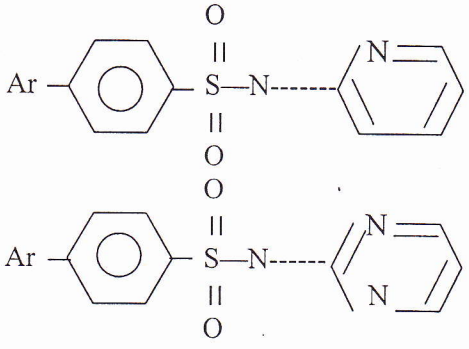
No. Compound	Formula	C-H.N
1	C17H15N4O4S	Calc. 55.135, 4.05, 18.24 Fou. 55.01, 4.03, 17.87
2	C18H16N3O4S	Calc. 60.50, 4.48, 11.79 Fou. 59.45, 4.39, 11.75
3	C19H20N5O4S	Calc. 52.53, 4.60, 16.12 Fou. 52.50, 4.29, 16.00
4	C22H21N4O4S	Calc. 57.00, 4.75, 13.30 Fou. 56.87, 4.68, 13.00

Table (3) Spectral Data for Data Compounds (1, 1a, 1b, 3, 2, 2a, 2b, 4)

No. Compound	U.V Ama/ nm	I-R. absorption bands max/cm^{-1} KBr disk					
		-OH	C=0	-NH	S=0	C=N	Others
1	270, 323:395	3450	1700	3300	1370-1350	1630	arom(1580)
2	294, 342:408	3400	1690	3320	1360-1330	1630	arom(1600)
1a	300, 395:420		1690	3300	1370-1340	1635	(c-c1) (780)
2a	287, 397:430		1695	3300	1365-1330	1630	(c-c1) (778)
1b	300, 342:400		1685	3200	1370-1340	1640	-N3 (1435)
2b	286, 335:430		1700	3250	1370-1350	1635	-N3 (1450)
2	270, 340:390		1680	3200	1360-1330	1630	-NH2 (3400)
3	300, 345:415		1690	3300	1365-1340	1630	-NH2(34100)

Scheme (I) : The Chemical Reactions





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