synthesis and reactions of some hetorcyclic compounds containing nitrogen and sulpher and study of some its bilogical effects

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SummaryThe thesis comprises the following:a-Organic synthesis of some new quinoxaline and triazine derivatives.b-Study of biochemical effects of some synthetic compounds. a. The organic synthesisThe project aimed to synthesis some new quinoxaline.Thus the reaction of 4-nitrophenylene diamine with a-diketones namely benzil, 9,10-phenanthraquinone and/or acenaphthenquinone resulted in cyclocondensation affording the corresponding quinoxaline derivative.Scheme 10 0 0II II II Ar-C-CH2-C-CEtX = H; Ar = C6H401(P) X = NO2; Ar = C8H4CI(P)NH2 NH2Summary iiWhen o-phenylenediamine derivatives were allowed to react with aroylpyruvate derivatives resulted in cyclocondensation affording the quinoxaline derivative .N 0 0HScheme 2In the present study it was found that cyclocondensation of 2- chlorobenzylidene pyruvic acid and o-phenylenediamine yielded arylvinylquinoxaline (Scheme 3).NH2 NH2OOHArOHAr = C6H4C1(o) Scheme 3HOT ArN OCOCH3N 0 ArNAr Ac20N OH0 CH3COOH//Ac20Summary iiiarylvinylquinoxaline seamed of appeared to be suitable for further heteroannelation. Thus refluxing quinoxaline derivatives with P2S5 in pyridine yielded thienoquinoxaline.,Ar P2S5N OH N S ArAr = C6H4CI(o)Scheme 4When quinoxaline derivative was allowed to react with Ac20 in acetic acid yielded the ester derivative not furoquinoxaline. The formation of furoquinoxaline was achieved by refluxing of 3a in acetic anhydride. The structure of was proved by the absence of CO absorption band in its IR spectra (Scheme 5).Ar = C61-14C1(P)Scheme 5Hydrazinolysis of quinoxaline derivative using hydrazine hydrate in ethanolic solution yielded 1,2-dihyDROPyridazine[3,4-b]quinoxaline.Summary ivNH2NH2N,N,N N HHAr = C61-14C1(P)Scheme 6The reaction of quinoxaline with semicarbazide affordedpyridazinoquinoxaline.N OH0NH2NHCONH1‘PhNHAr = C61-14C1(P) Scheme 7Chlorolysis of quinoxaline derivatives using POC13 afforded the corresponding chloroquinoxaline derivatives.POCI3a,Ar = - CH2CO C61-14C1(13)b,Ar = CH=CHC6H4C1(o)Scheme 8When 2-chloroquinoxaline was subjected to aminolysis with arylamine namely aniline and/or anthranilic acid in ethanolic solution resulted in dechloroamination affording arylaminoquinoxalines.„ArPOCI3-HO ICI0 N aN3---NCI SummaryNAr N Ar Ar’NH2NCI N NHAr’a;Ar = C6H4CI(o), Ar’ = C6H5b;Ar = C6H4CI(o), = C6H4COOH(o)Scheme 9The author has now studied the intramolecular cyclization reactionof arylaminoquinoxaline. Thus, arylaminoquinoxaline underwent intramolecular cyclodehydration in refluxing

POC13 to give quinazolinoquinoxaline.Ar = C6H4Cl(o) Scheme 10In this study the author investigated the reaction sodium azide with chloroquinoxaline derivative yielded tetrazoloquinoxaline, the structure of compound was proved by the disapperance of azido group in IR spectra.Ar = C6H4Cl(o)Scheme 11C6H5COCl NArN NHNH2 N NHC6H5 CO-NH Summary viHydrazinolysis of chloroquinoxaline yielded the hydrazinoquinoxaline.N Ar+ NH2NH2N Clusing hydrazine hydrateAr = C6H4Cl(o)Scheme 12The author now investigate the reaction of hydrazinoquinoxaline with electrophilic reagents. Thus, the addition of amino function of hydrazinoquinoxaline to the electrophilic carbon of thiocyanate afforded thiosemicarbazide derivative.N Ar n N~~Ar+NH4N=C=SN NHNI-12 N NHNH-C-NH2I ISAr = C6H4Cl(o)Scheme 13hydrazinoquinoxaline was reacted with benzoyl chloride to yieldthe hydrazide derivative.Ar = C6H4Cl(o)Scheme 14The author now investigate the possible cyclization of the hydrazide derivative to triazoloquinoxaline. Thus, refluxing of the hydrazide derivative and POC13 reacted intramolecular cyclodehydration affording triazoloquinoxaline.Summary viiP 0 C IsNC 6H s • C =NScheme 15The author has now investigate the nucleophilic substitution ofchloroquinoxaline using sulphur nucleophile. Thus the reaction of ethyl thioglycolate in basic medium resulted in SN reaction affording mercapto derivative.N ClAr H SC H7CO2EtN SCH2CO2EtAr = C6H4Cl(o)Scheme 16The utilization of benzylidine pyruvic acid derivative for thesynthesis of triazine was also studied. Thus the condensation of benzylidine pyruvic acid with semi and thiosemicarbazide resulted in heterocyclization affording triazine derivative.OH00XH2N —C —NH NH2a,Ar = C6H4C1(0); X = 0b,Ar = C6H4Cl(0); X = S Scheme 17Summary ixb. The biological activity:Numerous publications describe the synthesis of triazines possessing a variety of pharmacological activities The tested compounds 37a and 37b were selected due to the biological activities of triazines.In the toxicity studies, it was found that the tested compounds 37a and 37b were considered to be non lethal to the dose 160 mg/kg. The most effective doses for the inhibition of Ehrlich carcinoma cell EAC growth for 37a and 37b were found 50 mg/kg. Treatment of EAC bearing mice with single dose of the tested compounds 37a and 37b was studied. Single dose induced remarkable decrease by 49.16% (P