药学学报 1959, 7(8) 311-319 DOI: ISSN: CN:

论文

抗结核桿菌化合物的合成Ⅱ. 2-烷氧基-氨基喹啉及其衍生物和2-烷氧基-6-氨基辛可宁酸酰肼

梅放;吴淑云;汪润瑛;高怡生

中国科学院药物研究所,上海

摘要:

1.本文叙述了2-烷氧基-6-(或5-,或7-或8-)氨基喹啉,以及2-正丁氧基-6-乙酰(或二氯乙酰,或二甲)氨基喹啉的合成.2.合成了2-烷氧(甲氧,或乙氧,或正丙氧,或正丁氧)基-6-氨基辛可宁酸酰肼.3.将上述各产物及其中间体均进行了对结核分枝杆菌607及恥垢杆菌的体外抑制作用.结果表示III类型化合物在体外的抗结核杆菌作用仅与联在芳香环上的烷氧基及伯氨基有关,而氨基在喹啉环的苯环部分上的位置则无关.4.加入一个羰肼基于IIIa 及其烷氧基同系物的4-位上对体外抗结核杆菌作用不利.

关键词:

SYNTHESIS OF ANTITUBERCULAR COMPOUNDS, Ⅱ. 2-ALKOXY-AMINOQUINOLINES AND THEIR DERIVATIVES AND 2-ALKOXY-6-AMINOCINCHONINIC ACID HYDRAZIDES

MEI FAN WU SHU-YUN WANG YUEN-YIN KAO YEE-SHENG

Abstract:

The fact that 2-alkoxy-5-aminopyridines(Ⅰ)and 2-alkoxy-6-aminobenzothiazole(Ⅱ)possess high tuberculostatic activities *in vitro* as well as in experimental animals led us to prepare a num- ber of analogous compounds belonging to quinoline series,namely,2-alkoxy(*n*-propoxy,or *n*- butoxy)-6-aminoquinoline(IIIe or IIIa)and its structural isomers,2-butoxy-5-(or 7-,or 8-)- aminoquinoline(IIIb,IIIc,or IIId);and 2-butoxy-6-acetamino-(or dichloroacetamino-,or dimethy- lamino)-quinoline(Ⅳa,or Ⅳb,or Ⅳc) for the purpose of testing their antimycobacterial ac- tivities,and also of studying the relationships between antibacterial activity and chemical structure. Besides,several 2-alkoxy-6-aminocinchoninic acid hydrazides(Ⅳa,Ⅳb,Ⅳc,Ⅳd,Ⅳe),were also prepared.As can be seen from the formula,there is an additional—CONHNH$_2$ group present in the molecule as compared with IIIa and its alkoxy analogues. The results of antimycobacterial activities against mycobacterium *607* and smegmatis activities are listed in tables 1—3. IIIa possesses 1/2—1/4 activity against mycobact.*607* as compared with that of INH,but is comparable to the latter in the case of antismegmatis activity.IIIb,IIIc and IIId possess the similar order of activity as IIIa.2-Hydroxy-6-aminoquinoline and also all the corresponding nitro- compounds of IIIa,IIIb,IIIc,IIId and IIIe are of no significant activity.The acylated and methylated compounds of IIIa are also with much less activities,*p*-Amino-*N*-carbobutoxyaniline (Ⅴ)which was thought to be an open-ring compound of IIIa is also inactive.These facts show that the free amino and alkoxyl groups attached to aromatic structure are necessary for the exhibition of antimycobacterial activity.As to the position of the amino group attached to the benzene moiety of quinoline nucleus seems without practical influence.The introduction of a carbohydrazino group to the 4-position of IIIa or of its alkoxyl analogues is unfavorable to the in vitro antimycobacterial activity. The methods of preparation of compounds of type Ⅲ were by treating at first the 2-chloro- nitroquinolines(Ⅶ)with an appropriate sodium alcoholate to form 2-alkoxy-nitroquinolines (Ⅷ),and then the latter reduced by stannous chloride to give the required products(Ⅲ). The synthesis of the compounds of type Ⅵ was to begin with 2-chloro-6-nitrocinchoninic acid chloride (Ⅸ),which by treating with methyl or ethyl alcohol to give the corresponding methyl or ethyl esters (Ⅹ).The latter were then reacted with the appropriate sodium alcoholates to afford 2-alkoxy-6-nitrocinchoninic acid methyl or ethyl esters(Ⅺ),which were then catalytically reduced in the presence of Pd-C to give the corresponding amino-compounds (ⅩⅢ).The desired pro- ducts(Ⅵ)were obtained by treating the latter with hydrazine hydrate.Ⅺ directly reacted with hydrazine hydrate to give Ⅻ. Solvents of crystallization,melting points,yields of the compounds synthesized in this inves- tigation are summarized in table Ⅳ.

Keywords:

收稿日期 1959-07-30 修回日期 网络版发布日期

DOI:

基金项目:

通讯作者:

作者简介:

参考文献：

本刊中的类似文章

文章评论 (请注意:本站实行文责自负, 请不要发表与学术无关的内容!评论内容不代表本站观点.)

反馈人		邮箱地址	
反馈标题		验证码	7516