Synthesis of New (1-alkylamino-4-phenyldithio-2-bntanol amine) and derivatives.

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Abstract

Anew series of(1-alkylamino-4-phenyldithio-2-bntanol amine) and derivatives,containing two functional groups (pheny ring and NCS2) here been prepared from a reaction by 3steps :-

1-In the first step the preparation of n-phenyl dithio carbamate (A) and derivatives from a reaction between Aniline and carbon disulfide in basic medium.

2-Then , preparation N-3-chloro-2-hydroxy propyl amine " B " and derivativel from reaction between N-3-chloro-2-hydroxy propylamine and epichloro hydrine in methanolic a queous.

3-In three step :-preparation

1-Alkyl amino –4-phenyl dithio-2-butanol amine (I-IV) from reaction between A,B,and derivatives in absolute methanol

The aim :-preparation of new series of propanol amine derivative, these have effect on blood pressure and heart rate .

تحضير سلسلة جديدة من مشتقات ١-الكيل أمينو-٤- فنيل ثنائي ثايو -٢- بيوتانون امين

ابتهـــال قحطان عبدالله

المستخلص

تم تحضير سلسلة جديدة من مشتقات (١-الكيل امنيو -٤- فينل داي ثايو -٢-بيوتانول امين) الحاوية على مجموعتين فعالة (حلقة الفينل و NCS_2) وتم تحضير هذه المشتقات بثلاثة مراحل .

١-المرحلة الاولى :- هي تحضير مشتقات N- داي ثايو فينل كاربامات (A) من خلال مفاعلة الانيلين مع ثنائي كبريتيت الكاربون في وسط قاعدي .

٢-تحضير مشتقات N-٣-كلورو-٢-هيدروكسي بروبيل امين ويحضر من خلال مفاعلة ٢-هيدروكسي بروبيل امين ومشتقاته مع ايبوكلوروهيدرين في محلول الميثانول المائي .

٣-تحضير مشتقات ١-الكيل امنيو-٤-فينيل داي ثايو -٢-بيوتانول امين (I-IV) من خلال مفاعلة B,A ومشتقاتهما في الميثانول النقي .

تم تشخيص هذه المركبات بواسطة الطرق الطيفية I R و UV والتحليل الدقيق للعناصر (C.H.N)

الهدف من هذا البحث هو تحضير مشتقات جديدة ٢-للبروبانول امين المعروف دوائيا" بتثبيطه للضغط الدم ومعدل ضربات القلب

Introduction

Massive work has been reported for the preparation of 2-propanpamine. Various substituting were made including aryl [1],substituted aryl [2], N-substituted thio propanolamine moiety attached to heterocyclic nucleus, & were tested for cardiovascular activity [3]. It was also found that the preparation of aryl ethanolamine or aryloxy propanolamine containing an amide moiety in the side chain confers high degree of cardio selectivity & β-adrenergic blocking potency [4]. The basic requirement to have cardiovascular & β-adrenergic blocking effects is the propane lamine moiety besides the phenyl or naphthyl group. Changes & substitutions are to enhance – reduce the biological activity. An amide group linked to a basic nucleus will potentiate the biological activity [5]. Less active derivatives may be attributed to several major changes(5).synthesis of N-htro arylakyl-substituted-1-(aryloxi)-z-propanol amine deriviateive, has been achieved in our previous work(6) these compound were prepared and investigated for electropysicological activity in isolated canine purkinjefibers and in a nesthetized open-chest-dogs. A formal chemical processing plantin areas imporcted by accidental releases of IPAC 2- prpanol amine oriso propanoamine although their use had ceasedca(7).since IPA exist primarily as cations at the pt of site solis,their persistence apparently results from strong binding to soil,as wellas inhibition of natural biomemediation in highly contaminated field salse(7). It was found that the aryl propanol amines were antagonists at the rate beta 3 receptor,an observation with profound implications for in viro ratdata(8). Modification reaction of these polymers with lauricesters was conducted in different synthetic approaches. The luric ester modified polyester amides obtained from either consecutier or simultaneous poly condensation and lauric acid esterification were found to be quite similar in structure and moleculer weight distribution,the observation under lined influence of trans estrification reactions under the applied conditions

Experimental

Melting point was taken by [Gallen Kamp Melting Point Apparatus]. Elemental analysis run by AL-Mustansiriyah University .UV-VIS Spectra was recorded using [Centra 5 GBC UV-Vis- Spectra Photometer]. Methanol was used as a solvent. IR-Spectra were recorded using (Pye-Unicam SP_3 – 100 Spectrophotometer), solid sample were run in KBr disc.

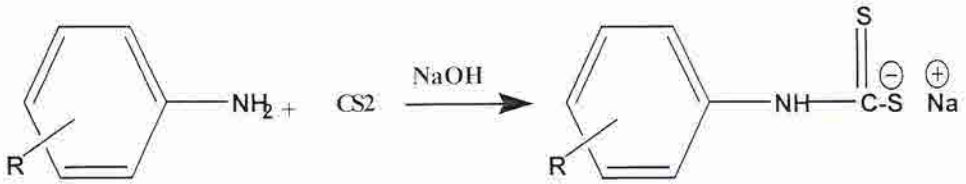
Procedures

Preparation of sodium N- phenyl substituted dithio carbamate: to a solution of 2 gm aniline in 50% aqueous ethanol 0.6 gm of sodium hydroxide mass was added. The solution was coold to 15° C & then 0.9 ml of carbon disulfide was added. Stirring was continued at 15° C for 2 hours. A yellow precipitate was formed. The product was filtered of the crystallized from ethanol and dried [6].

1. Preparation of N- (3 –chloro -2-hydroxypropyl) substituted amines: to amixture of (2.g,0.086 mole) of 2 propanolo amine and (1.15gm,0.015 mole) of epichlorohgdrine in 50 ml of methanol, then of crushed ice was added drope wise asolution of (2gm,0.058 mole) of hydro chloric acid in 15 ml was added. And the reaction mixture was reflexed for 4-6 houres at 25 ° C. The solvent was evaporated and the produced substituded amines were ethanol washed with coold water, the produced substituted amines were used without further purification .

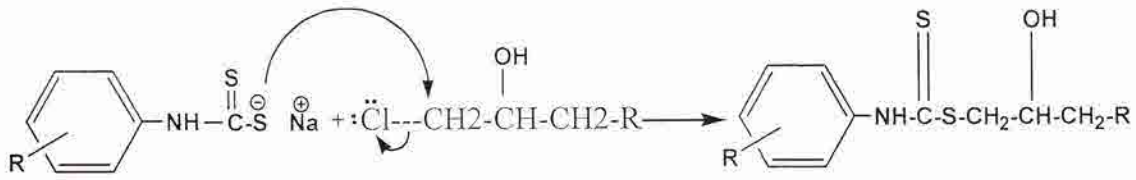
2. Preparation of the object compounds (I-IV): To a stirred solution of sodium N – (phenyl) dithio carbamate (0.017 mol) in

absolutemethanol (50 ml), potassium hydroxide (0.017 mol) & N-(3-chloro-2-hydroxypropyl) substituted amines (0.017 mol) were added & the mixture was heated at 80° C for 3 hours. The reaction mixture was concentrated & the crude product was precipitated by the addition of water, filtered, washed with water, dried & crystallized.



A

(Scheme 1) R=H, 4-Me, 3-Cl



(Scheme 2) R=H, 4-Me, 3-Cl

$R=NH_2$, $NHCH_3$

Results and discussion

Aniline , as a primary aromatic amine , reacts with carbon disulfide in a basic medium at 15°C for 2 hours to give N – (Phenyl substituted) dithio carbamate in a good yield . The reaction is shown in the following Schemel. The (II-III) compounds were prepared through treatment of Sodium N-(Phenyl substituted) dithio carbamate with N-(3-chioro -2- hydroxyl propyl) Substituted amines in a basic medium to prepare The thio propanol amine . Since the (chloro) group in N-(3-chloro -2- hydroxyl propyl) Substituted amines Is a Good leaving group , & the sulfur compounds are good nucleophilics .The 3-chloro group could be replaced Easily in this reaction to get the desired compounds . The reaction is typical for the nucleophilics substitution Reaction of thiol compounds [7].

The Mechanism is believed to be as shown below :

The yield , m. p., molecular formula & CHN Analytical data for all compounds are given in (Table 1) . The IR spectra of these compounds display characteristic bands at certain frequencies . All compounds showed (2920 – 2853 cm^{-1}) due to CH aliphatic , (1520 – 1485 cm^{-1}) due to NH , (1135-1115cm^{-1}) due to C=S& (1040 – 920 cm-1) due to @C=S+@C-N. All these bands are recorded in (Table 2). The UV – Spectra of these compounds , (Table2) , show the following maxima : (260 – 268 nm) due to the aromatic ring , (270 – 300 nm) due to the substituted aryl ring & (310 – 459 nm) due to OH &NH group .

Table (1) :- Chemical Parameters of the synthesized compounds

Com No.	R	R,	Crystallization Solvent	Yield %	M . p.	Formula	Cal. % (Found%)		
							C	H	N
I	H	-NH2	Methanol	62	181-182	C10H14N2OS2	49.58 (49.23)	5.78 (5.69)	11.57 (11.61)
II	H	- NHCH3	Ethanol	58	170-172				
III	4-CH3	-NH2	Methanol/water	60	224-226	C11H16N2OS2	51.56 (50.89)	6.25 (6.30)	10.937 (10.879)
IV	4-CH3	- NHCH3	Methanol/water	74	172-174				
V	3-Cl	-NH2	Methanol	48	148-150	C11H1N2OS2CL	45.43 (45.52)	5.163 (5.200)	9.638 (9.6100)
VI	3-Cl	- NHCH3	Ethanol	52	226-228				

Table (2):- Spectral data of compounds (I-IV)

Cpd No.	R	R,	IR Absorption Bands Maxima (cm-1)					UV (λ max nm)
			δNH2	δNH	δC=S	δC=+δC-N	δ OH	
I	H	-NH2	3450-3500	1485	1135	990	3110-3400	410,361,243
II	H	-NHCH3		1495	1115	920	3100-3350	329,268,210
III	4-CH3	-NH2	3400-3500	1495	1130	1040	3100-3400	454,232,219
IV	4-CH3	-NHCH3		1490	1195	1020	3120-3450	383,256,230
V	3-Cl	-NH2	3400-3450	1520	1115	1040	3110	484,329,253
VI	3-Cl	-NHCH3		1500	1120	1040	3350	303,268,240

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