Synthesis of New (1-alkylamino-4-phenylthio-2-butanol amine) and derivatives.

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Received 24/1/2010 accepted 10/6/2010

Abstract
A new series of (1-alkylamino-4-phenylthio-2-butanol amine) and derivatives, containing two functional groups (phenyl ring and NCS₂) have been prepared from a reaction by 3 steps:
1- In the first step, the preparation of N-phenyl thio 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 derivatives from a reaction between N-3-chloro-2-hydroxy propylamine and epichloro hydrine in methanolic aqueous.
3- In three steps: preparation 1-Alkyl amino -4-phenyl thio-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.

الملخص
تم تحضير سلسلة جديدة من مشتقات (1-الكيل أمين-4-فينيل ثنائي ثابو-2-بيوتانول أمين) الحاوية على مجموعتين قاعدة (حلقة الفينيل و NCS₂) وتتم تحضير هذه المشتقات بتقاطع ثلاث مرحل.
1- المرحلة الأولى: هي تحضير مشتقات N-دي ثابو فينيل كاربمات (A) من خلال فاعلية الإنيلين مع ثنائي كبريتيت الكاربون في وسط قاعدي.
2- تحضير مشتقات N-3-كلورو-2-هيدروكسي بروبيل أمين وبعض من خلال فاعلية 2-هيدروكسي بروبيل أمين ومشتقاته مع أنيبوكلورو هيدريين في محلول الميثانول المائي.
3- تحضير مشتقات 1-الكيل أمين-4-فينيل ثنائي ثابو-2-بيوتانول أمين (I-IV) من خلال فاعلية B,A ومشتقاتهما في الميثانول النقي.

تم تحليل هذه المركبات بواسطة الطرق الورقية UV وIR والتحليل الدقيق للعناصر UV و IRS. وتم تحضير مشتقات جديدة (2-ليوبروتانول أمين المعروف دواني) بتطبيقه للضغط الدم ومعدل ضربات القلب من هذا البحث هو تحسين مشتقات جديدة (2-ليوبروتانول أمين المعروف دواني) بتطبيقه للضغط الدم ومعدل ضربات القلب.
Introduction
Massive work has been reported for the preparation of 2-propanammine. Various substituting were made including aryl (1), substituted aryl (2), N-substituted thiopropanolamine moiety attached to heterocyclic nucleus, & were tested for cardiovascular activity (3). It was also found that the preparation of aryl ethanolamine or arlyoxy propanolamine containing an amide moiety in the side chain confers high degree of cardiac selectivity & beta-adrenergic blocking potency (4). The basic requirement to have cardiovascular & beta-adrenergic blocking effects is the propanamine moiety besides the phenyl or naphthyl group. Changes & substitutions 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-hetro aryalkyl substituted-1-(aryloxi)-2-propanol amine derivative, has been achieved in our previous work(6) these compound were prepared and investigated for electrophysiological activity in isolated canine purkinje fibers and in a anesthetized open-chest-dogs. A formal chemical processing plantin areas importet by accidental releases of IPAC 2-propanol 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 biomediation in highly contaminated field salse(7). It was found that the aryl propanolamines were antagonists at the rate beta 3 receptor,an observation with profound implications for in vitro ratdata(8). Modification reaction of these polymers with lauricesters was conducted in different synthetic approaches. The luryl 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 molecular weight distribution, the observation under lined influence of trans estification 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 SP3 – 100 Spectrophotometer), solid sample were run in KBr disc.

Procedures
Preparation of sodium N- phenyl substituted dithio carbamate: to a solution of 2 gm amline in 50% aqueous ethanol 0.6 gm of sodium hydroxide mass was added. The solution was cooled 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 a mixture of (2 gm,0.086 mole) of 2 propano amine and (1.15gm,0.015 mole) of epichlorohydrine in 50 ml of methanol, then of crushed ice was added to give wise solution of (2 gm,0.058 mole) of hydro chloride acid in 15 ml was added. And the reaction mixture was reflexed for 4-6 hours at 25°C. The solvent was evaporated and the produced substituted amines were ethanol washed with cool 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.

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

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

R=NH₂, NHCH₃
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 Scheme 1. The (II-III) compounds were prepared through treatment of Sodium N-(Phenyl substituted) dithio carbamate with N-(3-chloro-2-hydroxy propyl) substituted amines in a basic medium to prepare the thio propanol amine. Since the (chloro) group in N-(3-chloro-2-hydroxy propyl) substituted amines is a Good leaving group, & the sulfur compounds are good nucleophiles. The 3-chloro group could be replaced easily in this reaction to get the desired compounds. The reaction is typical for the nucleophiles substitution Reaction of thiol compounds.

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, (1135-1115 cm⁻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, (Table 2), 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

<table>
<thead>
<tr>
<th>Com No.</th>
<th>R</th>
<th>R,</th>
<th>Crystallization Solvent</th>
<th>Yield %</th>
<th>M. p.</th>
<th>Formula</th>
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<tr>
<td>I</td>
<td>H</td>
<td>-NH2</td>
<td>Methanol</td>
<td>62</td>
<td>181-182</td>
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<td>H</td>
<td>NHCH3</td>
<td>Ethanol</td>
<td>58</td>
<td>170-172</td>
<td>C11H16N2O2S2</td>
<td>51.56 (50.89)</td>
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<tr>
<td>III</td>
<td>4-CH3</td>
<td>-NH2</td>
<td>Methanol/water</td>
<td>60</td>
<td>224-226</td>
<td>C11H16N2O2S2</td>
<td>51.56 (50.89)</td>
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<tr>
<td>IV</td>
<td>4-CH3</td>
<td>NHCH3</td>
<td>Methanol/water</td>
<td>74</td>
<td>172-174</td>
<td>C11H16N2O2S2CL</td>
<td>45.43 (45.52)</td>
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<tr>
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<td>Methanol</td>
<td>48</td>
<td>148-150</td>
<td>C11H16N2O2S2CL</td>
<td>45.43 (45.52)</td>
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<tr>
<td>VI</td>
<td>3-Cl</td>
<td>NHCH3</td>
<td>Ethanol</td>
<td>52</td>
<td>226-228</td>
<td>C11H16N2O2S2CL</td>
<td>45.43 (45.52)</td>
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Table (2):- Spectral data of compounds (I-IV)

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<tr>
<th>Cpd No.</th>
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<th>IR Absorption Bands Maxima (cm⁻¹)</th>
<th>UV (λ, max nm)</th>
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<tr>
<td></td>
<td></td>
<td></td>
<td>δNH₂</td>
<td>δNH</td>
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References