

التخليق والتقييم الفارماكولوجي الأولي لبعض مشتقات الترايزول

سلسل كمال عبد الرحمن
كلية بغداد للصيدله -باب المعظم

الخلاصة

اعتمادا على نتائج المعلومات السابقة التي تم الحصول عليها من الدراسة النظرية للأدوية التي لها فعالية بيتا -
ادرينيرجييه حضرت سلسله من مشتقات 2-بروبانول امين تحتوي على حلقة ترايازول وتم تقييم فعالية وتأثير هذه المشتقات في
أوعية القلب . وهذه المركبات اختبرت على ادينات القلب النابضة المأخوذه من الجرذان البيضاء .

Synthesis and Preliminary Pharmacological Evaluation of Some New Triazole Derivatives

S . K Abdul-Rahmann

Baghdad college of pharmacy —Baghdad-bab almoadam

Abstract

On the basis of the results which was previously obtained from the structural and the theoretical studies on α -adrenergic drugs, a series of 2-propanolamine derivatives containing triazole moiety have been prepared and evaluated for their cardiovascular activity . These derivatives were tested by using spontaneously-beating right atria of albino rats.

Introduction

1,2,4 —Triazole is one of a class of organic heterocyclic compounds containing a five member di-unsaturated ring structure composed of three nitrogen atoms and two non adjacent carbon atoms.

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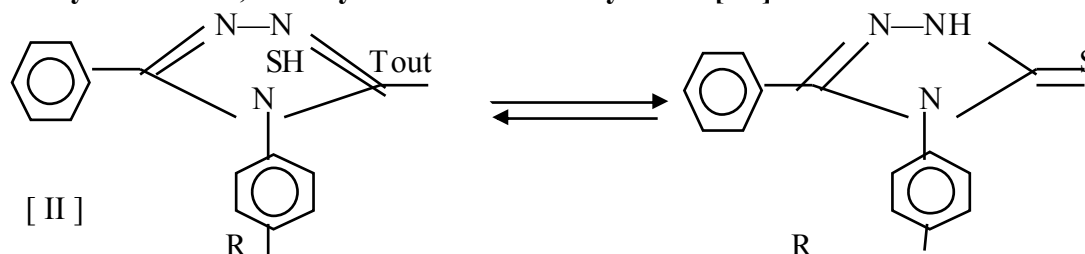
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Experimental

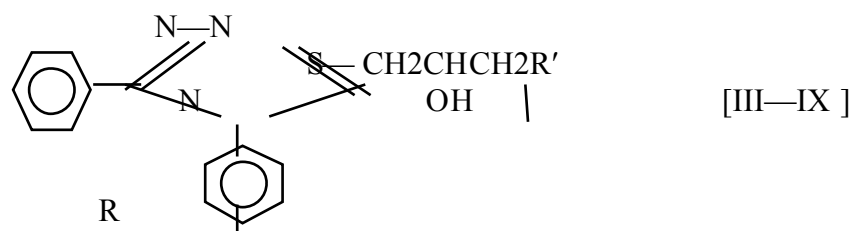
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A mixture of 1-substituted-4-arylthiosemicarbazide [I], 8% sodium hydroxide in ethanol was heated under reflux for 5hr. After concentration and cooling the solution was filtered and neutralized with 10% acetic acid solution (8) The solid product that formed was filtered and recrystallized from ethanol.

Synthesis of 1,2,4-triazole derivatives [III – IX]



General procedure

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(b) Spontaneously-beating right atria.

Rats were stunned & hearts were quickly removed. Right atria were dissected out & were suspended in a 20 ml, double jacketed organ bath containing krebs physiological solution of the following composition [gm/l]: NaCl 5.5, KCl 0.35, MgSO₄ 7 H₂O 0.11, CaCl₂ 0.14, KH₂PO₄ 0.16, NaHCO₃ 2.10, glucose 2.0, PH 7.4 maintained at 37°C ± 1°C & continuously bubbled with a stream of 5% CO₂-95% O₂ mixture.

Initial tension [Resting tension] of 1.0gm was applied, the tissue was allowed to equilibrate for a period of 45-60 min. and during this time, the bathing fluid was changed every 15 min(9), spontaneous contractions of the right atria were isometrically recorded by using a force transducer [UFI], coupled to a lectromed recorder physiographe. The results were registered at least 3 in 6 different experiments & in different preparations.

Results and Discussion

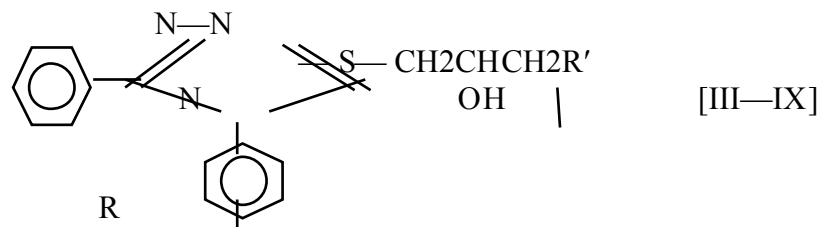
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4,5-diaryls-1,2,4-triazole [II] was obtained by the oxidative cyclization appropriate 1-substituted-4-

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Compound [II] was identified by m.p. and IR spectra which showed the following characteristic absorption band (Nujol). The IR showed an appearance band at $(1640)\text{cm}^{-1}$ due to stretching vibration of $(\text{C}=\text{N})$, also an appearance of a very weak band of $(2400-2700)\text{cm}^{-1}$ due to the (SH) group and $(3100-3060)\text{cm}^{-1}$ due to (C-H aromatic) which also showed an appearance band at $(1980-2853)\text{cm}^{-1}$ due to (C-H aliphatic) .

The new 1.2. 4-triazole derivative [III – IX]



They were synthesized by stirring aqueous methanolic solution 80% (10ml) with 4,5-diaryle-1,2,4-triazole [II] and N-(3-chloro-2-hydroxypropyl) substituted amine (1 mM) for 24hr at room temperature. The product was recrystallized from methanol/water.

The compound [III-IX] was identified by IR spectrum which showed the disappearance of absorption band at $(2400-2700)\text{cm}^{-1}$ due to (S-H) group and appearance of band at $(3500-3440)\text{cm}^{-1}$ due to (O-H) group. This is strong evidence to present this reaction. Also an appearance band at $(3400-3200)\text{cm}^{-1}$ due to stretching vibration of (N-H) group, $(3100-3060)\text{cm}^{-1}$ is due to (C-H aromatic) , $(1640)\text{cm}^{-1}$ $(\text{C}=\text{N})$ and $(1600-1500)\text{cm}^{-1}$ is due to $(\text{C}=\text{C aromatic})$.

Pharmacological results:

Experiments were carried. Several & different concentrations of compounds [III-IX] were tested on the spontaneous contractions of the right atria of albino rats to detect their behavior & to determine the median effective dose of each compound. Compounds with concentration 1 mg/ml showed a negative inotropic effect on the right atria except compounds [IV & VIII] which needed more concentration to produce a similar activity. The increasing of the concentration in organ bath of these experiments showed calcium antagonistic activity. The median effective dose of compounds [III-IX] on the spontaneous contractions of the right atria of albino rats, is shown in table (2).

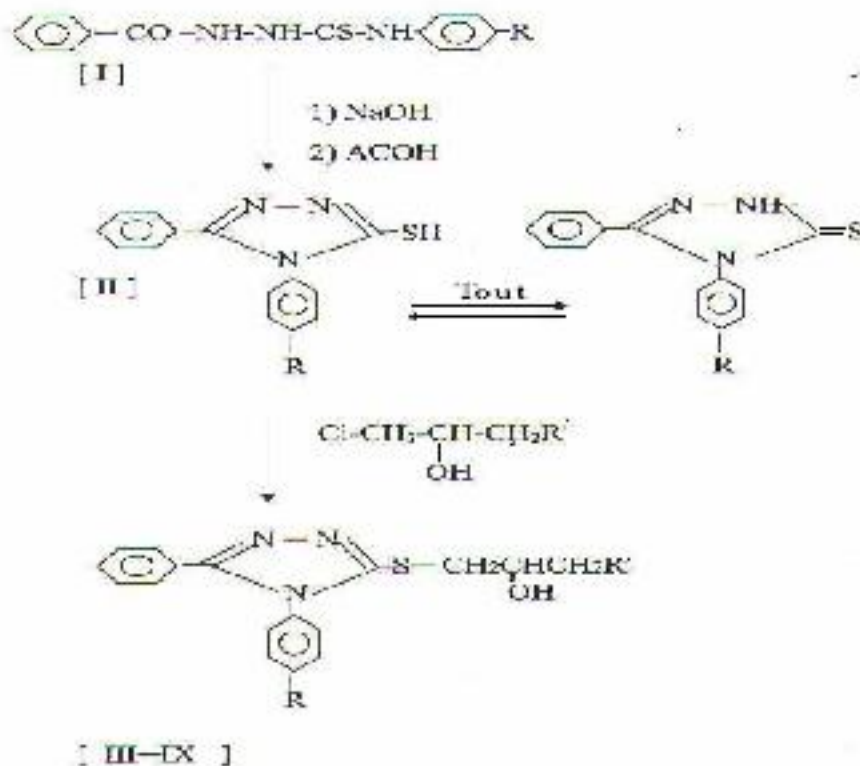
These results are promising and more work should be continued before landing at the precise mechanisms for cardiovascular effects in order to have the correct decision for the usage of these compounds for medicinal purposes.

Reference

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Compound	Median effective dose ED ₅₀
III	2mg / ml (5.4×10^{-3} M)
IV	1mg / ml (2.7×10^{-3} M)
V	1mg / ml (2.6×10^{-3} M)
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$\text{R} = \text{H}, \text{Cl}$
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Scheme (I)

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مجلة ابن الهيثم للعلوم الصرفة والتطبيقية المجلد 22 (3) 2009

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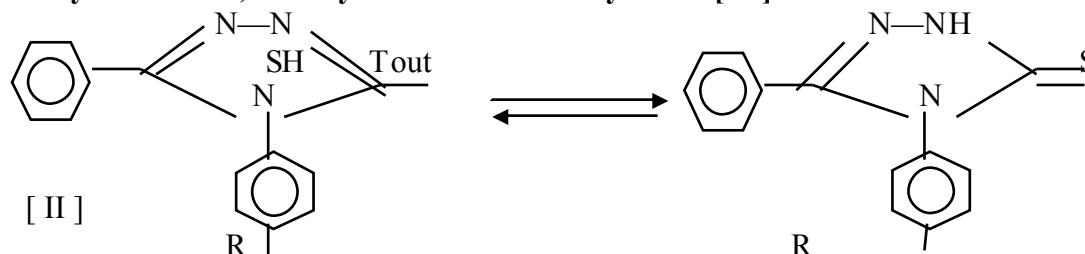
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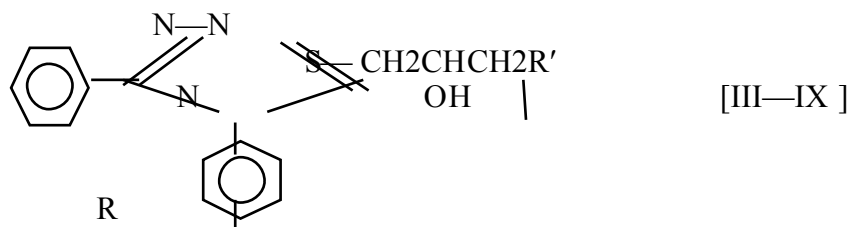
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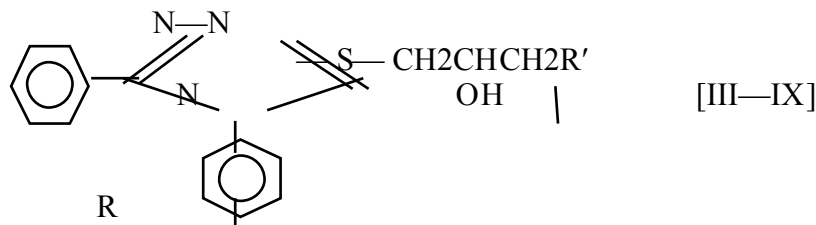
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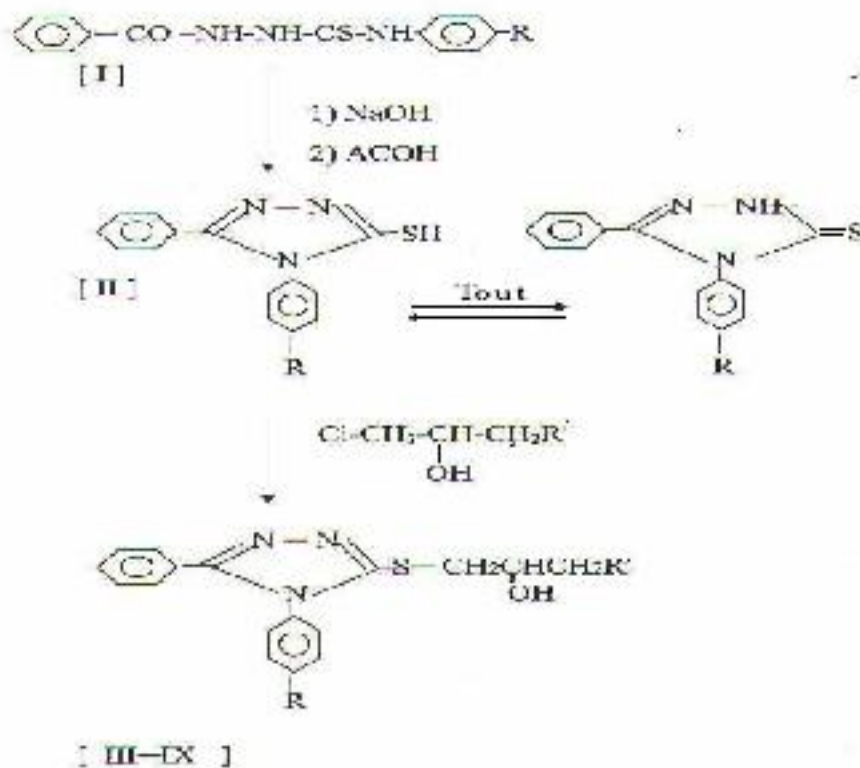
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