

Acknowledgments

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Abstract

Arylpropionic acids, or Non-steroidal anti-inflammatory drugs (NSAIDs) are an important class of drugs used to suppress pain and inflammation in cases of rheumatoid arthritis and other inflammatory diseases. Recently, some non-steroidal anti-inflammatory drugs have emerged as a part of a new class of cancer chemotherapeutic and chemopreventive agents. Members of these class characterized by having several common chemical and biological features.

Chapter one of this work covers a concise review of chemistry of NSAIDs including their review of main functional groups dealt with.

Seventeen compounds derived from both sodium-2[2,6-dichlorophenyl-amino]-benzene acetate (I) and 2-(4-isobutylphenyl)propionic acid (XII) were prepared in this work. The synthetic designing of these compounds was worked out through the suitable retrosynthetic analysis and the use of the disconnection approach.

One of the striking features in this work is the synthesis of 1-[2,6-dichlorophenyl]-oxindole (X). This compound is thought to be formed through intramolecular acyl substitution with subsequent ring formation.

Multiple step synthesis was performed as a mean by which the sulphonamide and other acyl derivatives were prepared.

Ring nitration was performed in standard nitration reaction with $\text{H}_2\text{SO}_4/\text{HNO}_3$ followed by reduction with Sn/HCl and functionalization of the resulting amino group in compounds (I) and (XII).

Esterification of both compounds (I) and (XII) resulting in formation of the corresponding alkyl and benzyl esters. The esterification step was performed either with alcohol and acid or with alkyl halide in the presence of K_2CO_3 /acetone. The reactions performed was repeated either

with Sodium salts or with the free carboxylic acid form of starting materials.

The mechanisms of the different reactions and the synthetic pathways in each case were heavily investigated and discussed in chapter three of this work. The reaction course were monitored by TLC technique, recrystallization and TLC were used for purification purposes.

The structures of the prepared compounds were elucidated by spectroscopic means as IR, ^1H - and ^{13}C -NMR, MS, and UV data.

الخلاصة

مركبات أريل حمض البروبيونيك أو المعروف بالـ "الـ ١" استروئيدية المضادة للالتهابات بأنها ذات أهمية في معالجة وتثبيط الألم والالتهابات الناتجة عن الروماتزم وآلام المفاصل وبعض الأمراض الناتجة عن هذه الالتهابات.

في الوقت الحاضر برزت بعض من العقاقير المضادة للالتهابات كجزء من العوامل المساعدة في علاج السرطان أو كعوامل مثبتة له.

أعضاء هذه المجموعة تتميز بأنها تمتلك صفات كيميائية وأخرى حيوية.

الفصل الأول في هذه الدراسة، تناول كيمياء الـ ١ استروئيدات المضادة للالتهابات مع الإهتمام بالمجموعات الوظيفية التي تميزها.

في هذه الدراسة تم اشتقاق وتحضير سبعة عشرة مركباً من كل من المركبين (1) ، (12). حيث صممت عملية تخليق لهذه المركبات عبر عملية التصنيع الضدي التحليلية وباستخدام طريقة التكسير.

أحد الخصائص الهامة في هذه الدراسة هي عملية تخليق المركب (10)، تم تكوين هذا المركب عن طريق الإستبدال داخل الجزيء وبالتالي تكون حلقة. أجريت خطوة تخليق متعددة كوسيلة عن طريقها تم تحضير السلفون-أميد ومشتقات أسيل أخرى.

تمت عملية نترتة الحلقة بواسطة تفاعل النترتة القياسية بحامض النتريك والكبريتيك ومن ثم الاختزال بالقصدير وحامض الهيدروكلوريك ومن ثم توظيف مجموعة الأمين في المركبين (1) ، (12). عملية الأسترة لكل من المركبين (1) ، (12) تكون إسترات الألكيل والبنزيل المقابلة لها. أجريت خطوات الأسترة إما بواسطة الكحول والحامض أو بواسطة هاليد الألكيل في وجود الأستون و كربونات البوتاسيوم.

تفاعلات الأسترة التي أجريت تم تكرارها إما بواسطة أملاح الصوديوم أو الحامض الكاربوكسيلي الحر الناتج من المواد الأولية.

الميكانيكيات المختلفة لهذه التفاعلات والمسارات التخليقية في كل حالة تم بحثها ومناقشتها في الفصل الثالث من هذه الدراسة.

تمت مراقبة هذه التفاعلات عن طريق تقنية كروماتوغرافيا الطبقة الرقيقة ، وإعادة البلورة حيث استخدمت لأغراض التنقية.

استخدمت وسائل طيفية مختلفة وذلك للتعرف على المركبات المحضرة مثل طيف الأشعة تحت الحمراء ، طيف الرنين النووي المغناطيسي ، طيف الكتلة ، وبيانات الأشعة فوق البنفسجية.

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