In situ one pot hemi-synthesis of new 2-pyridone derivatives

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Abstract

New 2-pyridone derivatives were hemi-synthetised in situ using essential oils of endemic Algerian plants; *Ammodaucus Leucotrichus* and *eucalyptus citriodora* as source of chiral aldehydes (perillaldehyde and citronellal respectively). The one pot reaction was carried out in Ethanol including cyanoacetohydrazide, essential oil, and malononitrile. The reaction mixture was catalysed by potassium carbonate. In the present work; two new compounds of highly functionalized 2-pyridones were obtained as privileged medicinal scaffolds. The structures of 2-pyridone derivatives were confirmed by NMR^{1}H, ^{13}C and 2D.

Keywords: one pot; Essential oil; 2-pyridone; Hemi-Synthesis; NMR analysis.

Introduction

. During the last decade, researchers have attached a great importance to hemi-synthesis reactions [1-3], where a new compounds design strategy based on the combination of functional classes and terpene compounds contained as major constituents in essential oils of medicinal plants has been developed. In fact, researchers depend as much as possible in the organic synthesis of their biologically active compounds on the *one-pot* method, to make short effort and time. Several documented studies have revealed that pyridones derivatives possess a range of useful biological activities, being antiviral, anti-HIV and anti-cancer [4-6]. In this context, an efficient and economical method by hemisynthesis reactions; two novel chiral 2-pyridone derivatives: (1) and (2) were synthetised.

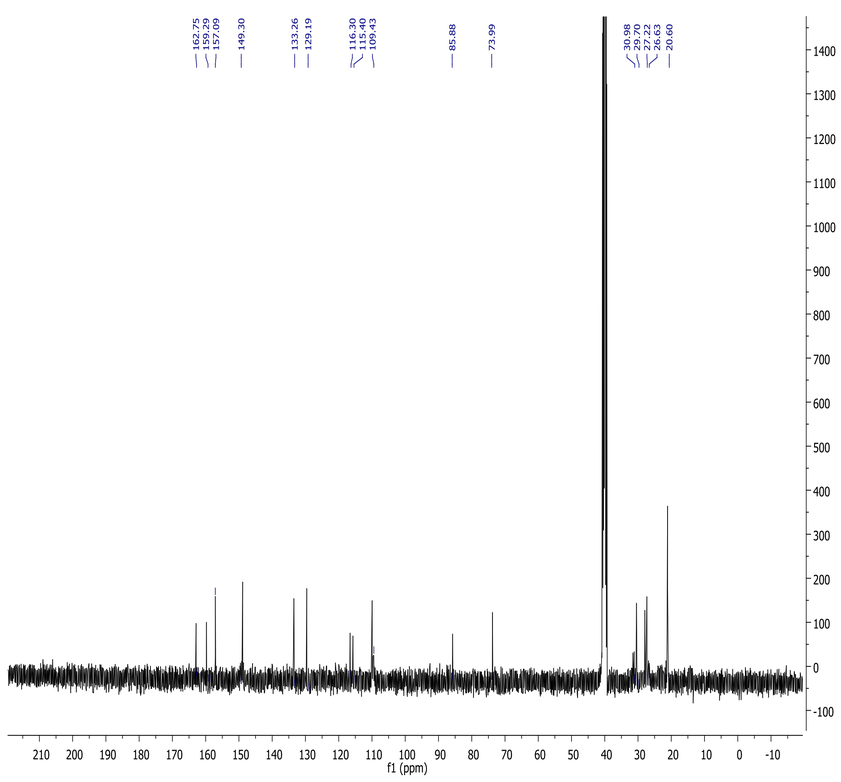
Methods & Materials

The compounds (1) and (2) were prepared from the *Ammodaucus leucotrichus* essential oil (1 mmol of perillaldehyde, 185 mg of the crude oil) or *eucalyptus citriodora* essential oil (1 mmol of citronellal, approximately 0.235 mL of the crude oil) respectevely with malononitrile (66 mg, 1 mmol), cyanoacetohydrazide (99 mg, 1 mmol), and K_2CO_3 (138 mg, 1 mmol), all compounds were mixed and stirred at 80 °C for 4 h in EtOH (7 ml), then when the reaction was completed (monitored by TLC), the reaction mixture was cooled and neutralization with diluted HCl then poured into water. The solid that precipitated was filtered, washed with water, dried and recrystallized in MeOH to afford the product (**1**) and (**2**) (yield 91% and 83% respectively).

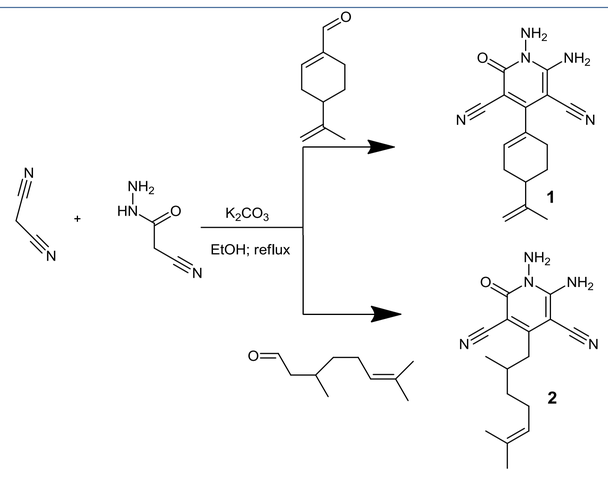
Results & discussions

We hemi synthesized in a single step (*one pot*) two new 2-pyridone derivatives containing a terpene moiety according to the method used by Ramadan A.M. *and all* [7], from three compounds malononitrile, cyanoacetohydrazide and an essential oil containing mainly oxygenated terpene (an aldehyde in this Case).The structures of compounds **1** and **2** were characterized from their ^{1}H NMR and ^{13}C NMR spectroscopic data scheme 3 and 4.

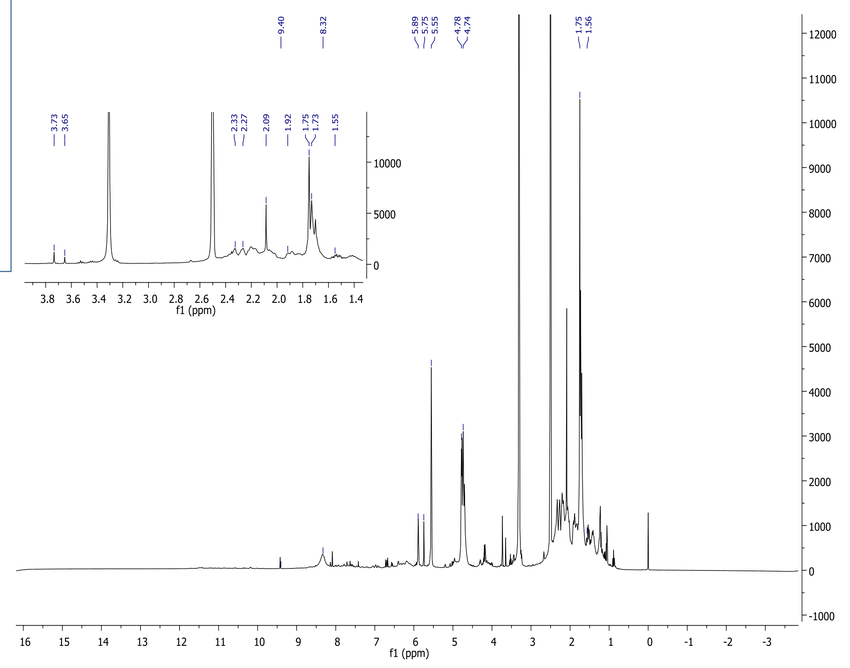
The investigation of the ^{1}H NMR spectra to the product **1** showed that, signals at δ 5.55 and 8.33 ppm confirmed the presence of N–NH_2 and NH_2 amino group protons respec-tively. A singlet appeared at δ 1.75 ppm is assigned to methyl group protons CH_3. The proton =CH intra cyclic and extra cyclic of the terpene moieties reflect signals at (δ 5.75-5.88 ppm, doublet) and at δ 4.74 ppm respectively. ^{13}C NMR spectra showed signals at 159, 157 and 162 ppm assigned to the carbons C-NH_2, C-4, and the carbonyl group in the pyridone ring respectively.



Scheme 3. ^{13}C NMR spectra of 2-pyridone derivatives **1**



Scheme 1. Formation of pyridone derivatives **1** and **2**



Scheme 2. ^{1}H NMR spectra of 2-pyridone derivatives **1**

Conclusion

In summary, we have reported the first *one pot* hemi-synthesis of new pyridone derivatives using essential oils as source of chiral aldehydes, the reactions were carried out in situ without any prior isolation or purification. This method is advantageously applicable to generate chiral compounds avoiding the use of expensive chiral catalyst and isolated natural compounds. In many molecules of biological and pharmaceutical fields, pyridones can be synthesized by different chemical protocols. From our point of view, it will be interesting to continue the investigation in the results of hemisynthesis by carrying out the biological activity of the obtained compounds, according to the results of the bibliography.

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