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Cyanomethylation of 2,3,4,9-tetrahydro-1H-carbazol-1-one based on using two different reagents: Antioxidant activity and DFT studies

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ABSTRACT

C-2 and C-6 monoalkyl nitrile substituted reactant **(1)**, which constitute the tricyclic framework of carbazole derivatives along with the substructure of the *Strychnos* alkaloids family, have been synthesized by using different bases to produce substitution reactions. In addition, the antioxidant capacity of the synthesized compound by the CUPRAC (cupric reducing antioxidant capacity) method was evaluated and the obtained TEAC (Trolox equivalent antioxidant capacity) coefficient implied that product **(2)** has antioxidant feature. The B3LYP/6-311G(d,p) level calculations were performed in the gas phase, and the optimized geometries obtained from these calculations were used for the solvation media calculations. The SMD variation of the IEFPCM (polarized continuum model) was used to conduct the quantum chemical calculations in the solvent environment such as $CHCl_3$, CH_3OH, and H_2O (water, ε=78.4). Also, the NMR chemical shifts of the products were calculated using GIAO (Gauge-Independent Atomic Orbital) approach and compared with the corresponding experimental data. The TD-DFT calculations disclosed that the observed peaks for both products were attributed to the n$\rightarrow \pi^*$ and $\pi \rightarrow \pi^*$ excitations. Moreover, NBO analysis revealed that the n$\rightarrow \pi^*$ and $\pi \rightarrow \pi^*$ interactions have a great importance for lowering the stabilization energy for all compounds. Also, the FMO (Frontier Moleular Orbital) analyses implied that the product **P2** would prefer the intermolecular interactions would rather than the intramolecular interactions.

1. Introduction

Carbazole and carbazole derivatives are encountered in a very large number of groups of heterocyclic compounds. They represent one of the most valuable ring systems, which are widely recognized versatile biological activities such as antiviral [1] anti-inflammatory [2] antioxidant [3,4] and anticancer activities [5]. Carbazole-based compounds have taken a gerat attention by the medicinal chemists because of their promising biological properties [6]. In this context, the biological properties of such compounds have been developed for the construction of the carbazole framework and its derivatives [7–13]. In view of the above consideration, we have been involved in the development of carbazole derivatives and also developed the synthesis of substituents at two different positions on the carbazole main structure. The reaction also involved a monoalkyl nitrile side chain at the C-6 position and developed a new method. This method could be a useful method for syntheses of these species of carbazole and other similar syntheses [14–16]. In this respect, the novel pathways to synthesis of the *sytrochinos* type compounds [17,18] from the carbazole-cored molecules as well as to synthesis of the carbazole type [19–22] compounds have been introduced.

The main goal of this work is to provide a novel route to the synthesis of carbazole-based molecules by using two different reagents and pathways. For this purpose, the synthesized products were confirmed by analytical tools (FT-IR, NMR, UV–vis, elemental analysis). Then, the possible antioxidant activities of both products were explored by the CUPRAC method and evaluated in light of the results obtained from quantum chemical calculations. In this respect, the geometry optimizations of both the reagent and products were performed by B3LYP functional and all stable structures of the compounds were confirmed by performing the frequency calculations. After FT-IR, NMR, and UV–vis spectroscopic data were compared with the observed values, the intramolecular interactions and the possible reactivity routes of each compound were evaluated by using the results obtained from NBO and FMO studies. The results obtained from both experiments and computations are hoped to provide useful information in further research to the synthesis of the carbazoles and their possible reactivity behaviors.

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