A Probe into Hydrolysis of Nitrile Moiety in 2-Amino-1-methyl-4-oxo-1,4-dihydroquinoline-3-carbonitrile

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ABSTRACT

2-Amino-1-methyl-4-oxo-1,4-dihydroquinoline-3-carbonitrile 2 was prepared by the reaction of N-methylisatoic anhydride 1 with malononitrile via the ring-opening/ring closure pathway. The treatment of this compound with concentrated sulfuric acid at 100 °C gave a mixture of 2-amino-1-methyl-4-oxo-1,4-dihydroquinoline-3-carboxamide 3 and 2-amino-1-methyl-4-oxo-1,4-dihydroquinoline-3-carboxylic acid 4. The NMR analysis showed that the ratio of compound 3 to 4 in the mixture was one to two (1:2). When the later reaction was performed in the presence of NaOH in refluxing H2O:EtOH, the compounds 3 and 4 were not formed, but instead, ring cleavage occurred to give compound 2-(methylamino) benzoic acid 5 in high yield. Density functional theory (DFT) calculations at the M06-2X/6-311+G(d,p) level of theory was also used to compute the 1H NMR chemical shifts of the compounds 3 and 4. Good agreement between the DFT-calculated 1H NMR chemical shifts and corresponding experimental values confirmed the suitability of the optimized geometries for these compounds. Characteristics of the bonding interactions were explored using the atoms in molecules (AIM) analysis.

KEYWORDS

2-Amino-1-methyl-4-oxo-1,4-dihydroquinoline-3-carbonitrile, Hydrolysis

2-(Methylamino)benzoic acid

DFT

AIM
Introduction
Nitrile moiety in heterocyclic compounds is readily available from many simple, straightforward, and cost-effective synthetic methods and can be converted into a range of diverse functional groups [1-5]. Among various transformations, hydration, addition of water, and hydrolysis, addition of water followed by splitting with water, (both terms are normally used here as synonyms) of nitrile motif are of great importance for the preparation of carboxamides and carboxylic acids, respectively, such as acrylamide, nicotinamide, aminoacids, adipic acid, and ibuprofen in view of the industrial applications and pharmacological interest of both classes of these compounds [6,7]. There are a number of different methods for these conversions. Conventionally, these reactions are catalyzed by strong acids and bases at elevated temperature [8,9]. Transition metal catalyzed methods have been also developed for these transformations [10,11]. Furthermore, the conversion of nitriles into carboxylic acids using metal salts, such as sodium perborate and copper salts in heterogeneous medium at high temperatures is also well documented [12]. Under basic conditions, usually, the carboxamide product cannot be isolated because the carboxamide moiety is converted to the corresponding carboxylic acid. Because of a lack of selectivity, chemical methods often give mixtures of carboxamide and carboxylic acid products in many cases. In nature, nitriles are hydrolyzed by enzymes in different biological systems. Nitrilases catalyze the direct hydrolysis of nitriles to afford carboxylic acids, and nitrile hydratases catalyze the conversion of nitriles into carboxamides, which then furnish carboxylic acids via hydrolysis in the presence of amidases [13].

The presence of quinoline motif, either alone or as a fused ring with other heterocyclic moieties, in a number of biological significant molecules has made it prime target for scientific research. Literature reports have already established functionalized quinolines as antioxidant [14], antiviral [15], antiinflammatory [16], antimalarial [17], antinociceptive [18], antifungal [19], anticancer [20], analgesic [21], antihypertensive [22], and antimicrobial [23] agents. Also, a number of compounds with quinoline moiety are known as potential inhibitors of β-glucuronidase [24], α-amylase [25], topoisomerase I [26], COX-2 [27], cholinesterase [28], HIV-1 [29], c-Met kinase [30], nucleotide pyrophosphatase [31], HDAC class I [32], MvFR [33], and VEGFR-II [34]. Furthermore, various derivatives of these compounds are useful as chemotherapeutic agents for leishmaniasis [35].

Nowadays, the computational approaches, such as density functional theory (DFT) calculations, are used as a complementary or alternative method for the experimental ones. The computational chemistry is useful in several aspects of the chemical compounds and chemical reactions such as the optimized geometry, spectral behaviors, kinetics and mechanism of the reactions and so on [36-45].

In light of these facts and due to our interest in the synthesis of heterocyclic compounds [46-56], we here wish to report the results of our investigation in the synthesis and hydrolysis of 2-amino-1-methyl-4-oxo-1,4-dihydroquinoline-3-carbonitrile 2 under acidic or basic reaction conditions (Scheme 1).
Material and methods

All chemicals were purchased from Merck and Aldrich and used without additional purification. Melting points were measured on a Stuart SMP3 melting point apparatus. Fourier transform infrared (FT-IR) spectra were obtained using a Tensor 27 Bruker spectrophotometer as KBr disks. 1H and 13C NMR spectra were recorded on a Bruker 300 FT spectrometer at 300 and 75 MHz frequencies, respectively, in DMSO-d6 as the solvent using tetramethyl silane (TMS) as internal standard.

Computational methods

The DFT calculations were performed by employing the M06-2X functional [57] and 6-311+G(d,p) basis set as implemented in the Gaussian 03 program [58]. All degrees of freedom were optimized for the optimized geometries. The gas phase optimized geometries showed no imaginary frequency of the Hessian. The NMR chemical shifts were computed with respect to tetramethylsilane in DMSO solution by employing the Gauge-Independent Atomic Orbital (GIAO) method [59]. The illustrations were prepared by using the Chemcraft program [60].

The atoms in molecules (AIM) calculations [61] are widely used in identification of the bonding interactions. The basis of the AIM is analysis of the electron density, ρ(r). The ρ(r) value affects several quantities such as strength of a bond, the kinetic energy density (Gρ), the potential energy density (Vρ), the total energy density (Hρ) and the Laplacian of the electron density (∇2ρ) at a bond critical point (BCP). These quantities are significant in reconnoitering nature of the bonding interactions. If (∇2ρ>0, Hρ>0), (∇2ρ>0, Hρ<0) and (∇2ρ<0, Hρ<0), the bonding interaction will be weak, medium and strong, respectively. On the other hand, the – Gρ/Vρ>1, 0.5 < – Gρ/Vρ<1 and – Gρ/Vρ<0.5 values of a bonding interaction are corresponding to the non-covalent, partially covalent and covalent interactions, respectively [62,63]. The AIMALL package [64] was employed for the AIM calculations.

Synthesis of 2-amino-1-methyl-4-oxo-1,4-dihydroquinoline-3-carbonitrile 2

A mixture of N-methylsativic anhydride 1 (1 mmol, 0.177 g) and malononitrile (1 mmol, 0.066 g) in pyridine (2 mL) was heated under reflux for 3 h. Upon completion of the transformation, the solvent was removed under reduced pressure. The residue was washed with diethyl ether (5 mL) and dichloromethane (5 mL) and recrystallized from 96% ethanol to give the pure product 2-amino-1-methyl-4-oxo-1,4-dihydroquinoline-3-carbonitrile 2 in high yield.

Yield 87%. M.p. 328-330 °C. FT-IR (υ, cm⁻¹): 3356 and 3234 (NH₂), 2208 (CN), 1670 (C=O). 1H NMR (δ, ppm): 3.63 (s, 3H, N-CH₃), 7.31-7.36 (m, 1H, Hₐ), 7.60-7.70 (m, 4H, NH₂ and Hₐ), 8.06 (d, 1H, J = 7.5 Hz, Hₐ). 13C NMR (δ, ppm): 33.89, 77.15, 116.66, 117.94, 123.52, 123.72, 125.55, 133.05, 140.25, 157.48, 174.39.

Hydrolysis of 2-amino-1-methyl-4-oxo-1,4-dihydroquinoline-3-carbonitrile 2 using concentrated H₂SO₄

A mixture of 2-amino-1-methyl-4-oxo-1,4-dihydroquinoline-3-carbonitrile 2 (1 mmol, 0.199 g) and excess concentrated H₂SO₄ was heated in an oil bath at 100 °C for 1 h. After this time, the mixture was poured onto cold water and neutralized by 25% ammonia solution. Then, the precipitate was collected and washed with water (7 mL) to afford a mixture of compounds 2-amino-1-methyl-4-oxo-1,4-dihydroquinoline-3-carboxamide 3 and 2-amino-1-methyl-4-oxo-1,4-dihydroquinoline-3-carboxylic acid 4 in 1:2 ratio according to the NMR analysis. The integration ratio of the signals for carboxamide product 3 to carboxylic acid product 4 in 1H NMR was one to two (1:2). Carboxamide product 3: 1H NMR (δ, ppm), 3.63 (s, 3H (the integration ratio in the mixture is 1.5), H₁), 7.29-7.38 (m, 3H (the integration ratio in the mixture was 1.5), H₅, H₆, and H⁷), 7.55-7.73 (m, 4H (the integration ratio in the mixture was 2.0), H² and H³), 8.07 (dd, 1H (the integration ratio in the mixture was 0.5), J = 7.8, 1.5 Hz, H⁴); 1H NMR (δ, ppm, DMSO-d₆ + D₂O), 3.63 (s, 3H (the integration ratio in the mixture was 1.5), H₁), 7.29-7.38 (m, 3H (the integration ratio in the mixture was 1.5), H₅, H₆, and H⁷), 8.06 (dd, 1H (the integration ratio in the mixture was 0.5), J = 7.8, 1.5 Hz, H⁴); Carboxylic acid product 4: 1H NMR (δ, ppm), 3.62 (s, 3H, H¹), 7.21 (d, 1H, J = 4.8 Hz, H²); 7.55-
7.73 (m, 3H, H^5, H^6, and H^7), 8.21 (dd, 1H, J = 7.8, 1.5 Hz, H^4). 10.63 (d, 1H, J = 4.8 Hz, H^3^-); \(^1\)H NMR (δ, ppm, DMSO-d_6 + D_2O), 3.62 (s, 3H, H^3), 7.55-7.73 (m, 3H, H^5, H^6, and H^7), 8.20 (dd, 1H, J = 7.8, 1.5 Hz, H^4). \(^13\)C NMR (δ, ppm) for the mixture of carboxamide product 3 and carboxylic acid product 4: 32.93, 33.90, 93.16, 115.79, 116.69, 117.93, 123.16, 123.54, 123.75, 124.11, 125.58, 126.50, 132.63, 133.08, 139.15, 140.29, 157.50, 158.59, 171.76 (two signals), 174.39, 174.64.

Interation of 2-amino-1-methyl-4-oxo-1,4-dihydroquinoline-3-carbonitrile 2 with NaOH
A mixture of 2-amino-1-methyl-4-oxo-1,4-dihydroquinoline-3-carbonitrile 2 (1 mmol, 0.199 g) and 1 M NaOH (8 mL) in ethanol (4 mL) was heated under reflux for 3 h. Next, the solvent was evaporated in vacuum, the residue was dissolved in water (10 mL) and subsequently neutralized by 1 N HCl. The crude product was collected and recrystallized from 96% ethanol to give compound 2-(methylamino)benzoic acid 5 in high yield. Yield 91%. M.p. 186-188°C. FT-IR (υ, cm\(^{-1}\)): 3387 (NH), 2500-3300 (OH), 1661 (C=O). \(^1\)H NMR (δ, ppm): 2.85 (s, 3H, N-CH_3), 6.54-6.60 (m, 1H, H_α), 6.69 (d, 1H, J = 8.4 Hz, H_α), 7.36-7.43 (m, 1H, H_α), 7.79 (dd, 1H, J = 7.9, 1.8 Hz, H_α), 9.82 (br., 2H, NH and OH). \(^13\)C NMR (δ, ppm): 29.66, 110.35, 111.20, 114.45, 132.05, 134.99, 152.17, 170.40.

Result and discussions
The starting material N-methylisatoic anhydride 1 was prepared according to the literature method [65]. This compound was allowed to react with malononitrile in refluxing pyridine. Monitoring of the reaction with thin-layer chromatography (TLC) showed the formation of a product which was isolated from the reaction mixture, as described in Experimental section. The isolated product was identified as 2-amino-1-methyl-4-oxo-1,4-dihydroquinoline-3-carbonitrile 2 and characterized by spectral data. The IR spectrum showed the absorption bands at 3356, 3234, 2208, and 1670 cm\(^{-1}\) for NH\(_2\), CN, and pseudo amidic carbonyl groups respectively, confirming the formation of the product 2. Also, the \(^1\)H NMR spectrum of this compound in DMSO-d_6 showed a singlet at δ = 3.63 ppm for the N-CH\(_3\) group as well as the characteristic signals for the aromatic protons and NH\(_2\) group (overlapped) in aromatic region. Further proof came from \(^13\)C NMR spectrum that showed the characteristic signals at δ 33.89, 77.15, 115.79, 116.66, 117.94, 123.52, 123.72, 125.55, 133.05, 140.25, 157.48, and 174.39 ppm which are in agreement with structure 2.

Hydrolysis of the nitrile moiety in compound 2 under acidic and basic reaction conditions was then investigated. The treatment of this compound with concentrated sulfuric acid at 100 °C for 1 h gave a mixture of two products which were identified as 2-amino-1-methyl-4-oxo-1,4-dihydroquinoline-3-carboxamide 3 and 2-amino-1-methyl-4-oxo-1,4-dihydroquinoline-3-carboxylic acid 4 (Figure 1). Under these conditions, the reaction mixture did not change even upon prolonged heating. The \(^1\)H NMR analysis (Figure 2) showed that the ratio of carboxamide product 3 to carboxylic acid product 4 in the mixture was one to two (1:2). As seen, the characteristic signals for the carboxamide product 3 in \(^1\)H NMR spectrum were observed as a singlet at δ = 3.63 ppm for methyl group (H\(^1\) in Figure 1), a multiplet at δ = 7.29-7.38 ppm belonging to the three aromatic protons (H\(^5\), H\(^6\), and H\(^7\)), a multiplet at δ = 7.55-7.73 ppm for two NH\(_2\) groups (H\(^2\) and H\(^3\)) overlapped with three aromatic protons of the carboxylic acid product 4 (H\(^5\), H\(^6\), and H\(^7\)), and a doublet of doublet at δ = 8.07 ppm for remained aromatic proton (H\(^4\)) that has been deshielded due to carbonyl group. Other signals in Figure 2 are related to carboxylic acid product 4. As can be seen, methyl group in this compound appeared as a singlet at δ = 3.62 ppm (H\(^1\)). Surprisingly, as shown in the expanded view of \(^1\)H NMR spectrum in Figure 2, an AX splitting pattern for two geminal protons in H-N-H group (H\(^2\)= and H\(^2\)=) is seen which appeared as two doublets at δ = 7.21 and δ = 10.63 ppm for H\(^2\)= and H\(^2\)=, respectively. The coupling constants (J values) of two doublets were the same and determined to be 4.8 Hz. These signals along with other signals including a multiplet at δ = 7.55-7.73 ppm for three aromatic protons (H\(^5\), H\(^6\), and H\(^7\)) overlapped with two NH\(_2\) groups of the carboxamide product 3 (H\(^2\) and H\(^3\)), a doublet of doublet at δ = 8.21 ppm for a deshielded aromatic
proton (H⁺) as well as a broad downfield signal at δ = 11.51 ppm belonging to group (H⁺), indicating the formation of carboxylic acid product 4. The D₂O exchange experiment was also performed to prove the presence of the NH₂ and OH protons. In this new ¹H NMR spectrum, all peaks at δ = 7.21, δ = 10.63, and δ = 11.51 ppm belonging to the H₂'a, H₂'b, and H₃' protons were removed and also the integration values at δ = 7.55-7.73 ppm decreased from 5 to 3, confirming the absence of H² and H³ protons.

We believe that there are two intramolecular hydrogen bondings in carboxylic acid product 4, as shown in Figure 1. Therefore, as expected and can be seen in Figure 2, H²'b and H₃' appeared in very downfield region in the ¹H NMR spectrum. On the other hands, the integrations of the signals in ¹H NMR spectrum in Figure 2 show that the ratio of carboxamide product 3 to carboxylic acid product 4 in the mixture is one to two (1:2). Moreover, the characteristic signals in ¹³C NMR spectrum are in accordance with the mixture of the products 3 and 4 (Experimental Section).

Figure 1. Numbering of protons in compounds 3 and 4

Finally, to show the possibility of hydrolysis of the nitrile moiety in compound 2 under basic conditions, we allowed this compound to interact with NaOH in refluxing H₂O:EtOH. During monitoring of the reaction mixture with TLC, we unexpectedly observed that a compound with different Rf's of those expected for the products 3 and 4 was formed. As described in the Experimental section, the isolated compound was identified as the product 2-(methylamino)benzoic acid 5 as the result of cleavage of dihydropyridine ring by removing malononitrile from compound 2 (Scheme 1). The structural assignment of the product 5 was based upon spectral data. The IR spectrum was devoid of the CN absorption band of the precursor 2, which showed the removal of malononitrile. The ¹H NMR spectrum in DMSO-d₆ showed a singlet at δ = 2.85 ppm for N-CH₃ group, a broad signal at δ = 9.82 belonging to the NH and OH protons, as well as the characteristic signals in aromatic region in the range of 6.54-7.79 ppm, indicating the formation of compound 5. Furthermore, the ¹³C NMR spectrum data are consistent with the assigned structure 5 (Experimental Section).

A plausible pathway for the formation of compound 5 was proposed as depicted in Scheme 2. As shown, initial deprotonation of amino group in compound 2 followed by protonation afforded the imino intermediate II that then underwent additional deprotonation followed by ring cleavage to give intermediate IV. Final interaction of the later intermediate with hydroxide anion gave the product 5. Under these conditions, attempts to isolate the
intermediates failed even after careful monitoring of the reactions.

**Scheme 2:** A plausible mechanism for the formation of compound 5

**DFT calculations**

DFT calculations were also used to confirm the experimental results in the formation of a mixture of the products 3 and 4 in hydrolysis of compound 2 under acidic conditions. First, geometries of the carboxamide 3 and carboxylic acid 4 species were fully optimized, which are shown in Figure 3 with labeling of atoms. Important structural parameters of these species are demonstrated in Table 1, which are in good agreement with the reported data for the similar compounds. The carboxylic acid 4 species had two intramolecular hydrogen bonds.

The experimental ¹H-NMR chemical shifts (δ) of the carboxamide 3 and carboxylic acid 4 species together with the corresponding DFT-calculated chemical shifts are listed in Table 2. The atom positions are numbered as shown in Figure 3. Except for the H², H²', and H³ protons, the DFT-predicted chemical shifts are in relatively good agreement with the experimental results, indicating suitability of the optimized geometries for these species. Engagement in intermolecular H-bonds affects chemical environment of the mentioned protons, which changes their chemical shifts. These protons are rigid in the optimized geometries. But, rotations around the C7-N2 and C11-N3 change positions of the H² as well as the H³ protons, respectively. The experimental chemical shifts were obtained from the DMSO solution, while the DFT values were predicated for the isolated molecule in vacuum.
The energy gap, the energy difference between the HOMO and LUMO orbital is mainly localized on carbonyl group. As seen, the HOMO orbital of both species is localized on the C8 atom. But, their LUMO orbital is mainly localized on carbonyl group. The energy gap, the energy difference between the occupied and unoccupied molecular orbital (LUMO) of 3 and 4 species were determined using Natural Bond Orbital (NBO) analysis as shown in Figure 4. As seen, the HOMO orbital of both 3 and 4 species is localized on the C8 atom. But, their LUMO orbital is mainly localized on carbonyl group.

Table 1: Important structural parameters of the carboxamide 3 and carboxylic acid 4 species

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<th>Bond length (pm)</th>
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<th>4</th>
<th>Angle (°)</th>
<th>3</th>
<th>4</th>
<th>Dihedral angle (°)</th>
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<th>4</th>
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<td>C1-C2-C3</td>
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<td>121.0</td>
<td>C1-C2-C3-C4</td>
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<td>0.9</td>
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<td>140.4</td>
<td>C6-N1-C7</td>
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Table 2: The comparison of the experimental (Exp.) 1H NMR chemical shifts data (δ, ppm) with those obtained from the DFT-calculated (Cal.) values for the compounds 3 and the 4

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<th>Atom position</th>
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HOMO and LUMO frontier orbitals plays a critical role in many properties of the chemical compounds, such as the electronic spectra, photochemical reactions and electric properties. The calculated energy gaps for the 3 and 4 species are 4.06 and 4.47 eV, respectively. These large energy gaps demonstrate high stability of the investigated species [66-69].

**Figure 4:** The HOMO and LUMO frontier orbitals of the 3 and 4 species

The AIM molecular graphs of the Acid and Amide species are also shown in Figure 5, where the small green and red spheres correspond to the BCPs and RCPs, respectively. The computed \( \rho(r) \), \( \nabla^2 \rho(r) \), \( H_b \), \( G_b \), \( V_b \) and \( \frac{G_b}{V_b} \) values at BCPs are pointed out in Table 3. In the carboxylic acid 4 species, Mulliken charge (q(e)) on the C7, C8, C9 and C11 atoms are +0.94, -0.06, +0.87 and +1.53, respectively. The C11 has the highest positive charge in the molecule, which is the most suitable position for nucleophilic attack. On the other hand, the most negative charge is localized on the N2 atom. In the structure of carboxamide 3 species, the C11 and O2 atoms involve the most positive and the most negative charge, respectively.

Due to engagement in intramolecular H-bond, in the carboxylic acid 4 species, the N2-H2'b bond is weaker than that of the N2-H2'a. The \( \nabla^2 \rho>0 \), \( H_b<0 \) and \( 0.5<\frac{G_b}{V_b}<1 \) values demonstrate that both of the O2-H2'b and O1-H3'b interactions are medium and partially covalent H-bonds. The energy value of a hydrogen bond is calculated by \( E_{HB}=V_b/2 \) equation [70]. In the carboxylic acid 4 species, energy value of the O2-H2'b and O1-H3'b bonds are 41.54 and 100.03 kJ.mol\(^{-1}\), respectively. There are four rings in the structure of carboxylic acid 4 species. The benzene ring, dihydropyridine ring and two rings result from the O1...H3'b and O2...H2'b intramolecular H-bonds. The calculated \( \rho(r) \) values for these rings are +0.020995, +0.018835, +0.021498 and +0.015945 C.Bohr\(^{-3}\), respectively. The highest electron density is therefore attributed to the six-membered ring formed by the O1...H3'b H-bond.

**Figure 5:** The AIM molecular graphs of the carboxamide 3 and carboxylic acid 4 species (small green and red spheres correspond to the BCPs and RCPs, respectively)
Table 3. Important topological parameters of the Carboxamide 3 and carboxylic acid 4 species in a.u.

<table>
<thead>
<tr>
<th>Bond</th>
<th>ρ(r)</th>
<th>ρ(r)</th>
<th>Vb</th>
<th>Gb</th>
<th>Hb</th>
<th>(\sim G_b/V_b)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carboxamide 3</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>N2-H2</td>
<td>0.340028</td>
<td>-1.64813</td>
<td>-0.52195</td>
<td>0.054958</td>
<td>-0.46699</td>
<td>0.105294</td>
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<tr>
<td>N3-H3</td>
<td>0.330503</td>
<td>-1.55078</td>
<td>-0.49077</td>
<td>0.05154</td>
<td>-0.43923</td>
<td>0.105018</td>
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<tr>
<td>C7-N2</td>
<td>0.330281</td>
<td>-0.96978</td>
<td>-0.6934</td>
<td>0.225477</td>
<td>-0.46792</td>
<td>0.325176</td>
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<tr>
<td>C11-O2</td>
<td>0.381794</td>
<td>-0.51986</td>
<td>-1.11457</td>
<td>0.492304</td>
<td>-0.62227</td>
<td>0.441697</td>
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<tr>
<td>C9-O1</td>
<td>0.376757</td>
<td>-0.44885</td>
<td>-1.1085</td>
<td>0.498144</td>
<td>-0.61036</td>
<td>0.449385</td>
</tr>
<tr>
<td>C11-N3</td>
<td>0.325992</td>
<td>-0.90634</td>
<td>-0.70466</td>
<td>0.239038</td>
<td>-0.46562</td>
<td>0.339224</td>
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<td>Carboxylic acid 4</td>
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<td>N2-H2’a</td>
<td>0.342421</td>
<td>-1.84868</td>
<td>-0.56053</td>
<td>0.049178</td>
<td>-0.51135</td>
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<td>N2-H2’b</td>
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<td>-0.53654</td>
<td>0.045181</td>
<td>-0.49136</td>
<td>0.084209</td>
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<tr>
<td>O2… H2’b</td>
<td>0.037231</td>
<td>0.125932</td>
<td>-0.03168</td>
<td>0.031582</td>
<td>-0.00001</td>
<td>0.996844</td>
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<tr>
<td>O3… H3’</td>
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<td>-1.60361</td>
<td>-0.5561</td>
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<tr>
<td>O1… H3’</td>
<td>0.07576</td>
<td>0.158519</td>
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<tr>
<td>C11-O2</td>
<td>0.392255</td>
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<td>-0.90702</td>
<td>0.406012</td>
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Conclusion
In summary, we have reported the results of our investigation in the synthesis and hydrolysis of 2-amino-1-methyl-4-oxo-1,4-dihydroquinoline-3-carbonitrile 2 under acidic or basic reaction conditions. Under acidic conditions using concentrated sulfuric acid, a mixture of two products carboxamide 3 and carboxylic acid 4 were isolated. The NMR analysis showed that the ratio of compound 3 to 4 in the mixture is one to two (1:2). In the presence of aqueous ethanolic NaOH as basic medium, however, ring cleavage occurred, giving the product 2-(methylamino)benzoic acid 5 in high yield. Good consistency between the experimental \(^1H\) NMR chemical shifts and the corresponding DFT-calculated values approves suitability of the optimized geometry of the carboxamide 3 and carboxylic acid 4 compounds. Based on the AIM results, two intermolecular H-bonds in structure of the species 4 are medium in strength and partially covalent. These H-bonds stabilize structure of species 4 significantly. Also, the six-membered ring formed by the O1…H3’ H-bond involves the highest electron density.

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Conflict of Interest
We have no conflicts of interest to disclose.

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