

Short Note

***N*-{2-[3-(3-Formyl-2-oxoquinolin-1(2*H*)-yl)prop-1-ynyl]phenyl}acetamide**

Shylaprasad Durgadas^{1,2}, Khagga Mukkanti¹ and Sarbani Pal^{3,*}

¹ Centre for Chemical Sciences and Technology, Institute of Science & Technology, Jawaharlal Nehru Technological University Hyderabad, Kukatpally, Hyderabad-500085, Andhra Pradesh, India

² MSN Pharmachem Pvt. Ltd., Plot No 212/A,B,C,D, APIICL, Phase-II, Pashamylaram, Patancheru (M), Medak District 502307, Andhra Pradesh, India

³ MNR Degree and PG College, Kukatpally, Hyderabad-500085, Andhra Pradesh, India

* Author to whom correspondence should be addressed; E-Mail: Sarbani277@yahoo.com.

Received: 8 July 2013 / Accepted: 15 August 2013 / Published: 19 August 2013

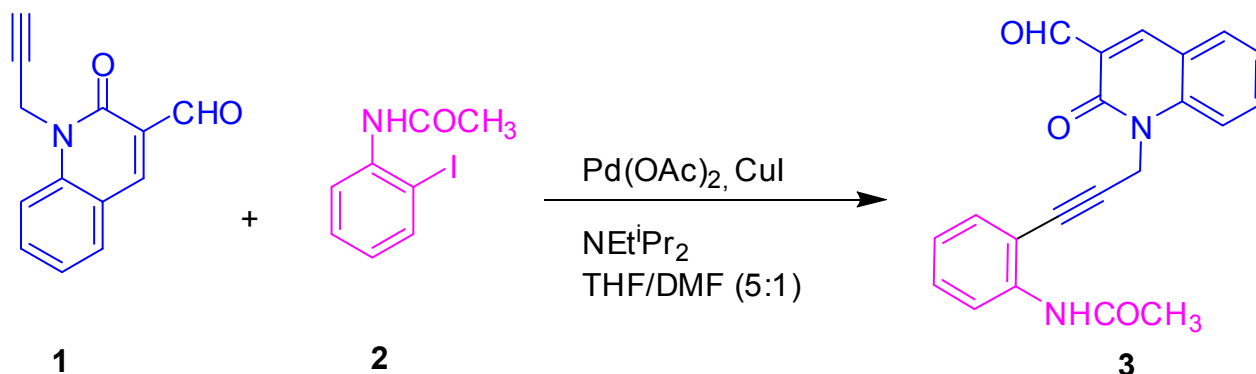
Abstract: The title compound, *N*-{2-[3-(3-formyl-2-oxoquinolin-1(2*H*)-yl)prop-1-ynyl]phenyl}acetamide was synthesized in high yield by Sonogashira cross coupling of 2-oxo-1-(prop-2-ynyl)-1,2-dihydroquinoline-3-carbaldehyde with *N*-(2-iodophenyl)acetamide. The structure of the compound was fully characterized by IR, ¹H-NMR, ¹³C-NMR, Mass spectral analysis and elemental analysis.

Keywords: 2-quinolone; Sonogashira coupling; terminal alkyne

The usefulness of 2-quinolone framework has been well demonstrated in the development of a broad range of pharmacologically active compounds including antibacterial, antiulcer, anti HIV, anti-allergic, anti-inflammatory and antifungal agents [1–7]. In continuation of our efforts to identify novel small molecules of potential pharmacological interest, we have recently reported the synthesis and PDE4 inhibitory properties of 2-quinolone derivatives [8]. In further continuation of our earlier work, we now report the synthesis of a novel analogue *i.e.*, *N*-{2-[3-(3-formyl-2-oxoquinolin-1(2*H*)-yl)prop-1-ynyl]phenyl}acetamide. The alkynylation of iodoarenes *via* C-C bond forming reaction under Pd-Cu catalysis (the Sonogashira coupling) [9] was used in our earlier synthesis [8]. The methodology offered a very convenient, mild and one-step process for the direct coupling of terminal alkynes with iodoarene to provide the desired internal alkynes of medicinal value [10]. We adopted the

same strategy for the preparation of our present target molecule and the corresponding synthesis is shown in Scheme 1.

Scheme 1. Synthesis of the title compound.



Preparation of *N*-{2-[3-(3-formyl-2-oxoquinolin-1(2*H*)-yl)prop-1-ynyl]phenyl}acetamide

To a solution of *N*-(2-iodophenyl)acetamide (**2**) (2.96 g, 11.36 mmol) in THF (20 mL) and DMF (4 mL) were added diisopropylethyl amine (2.44 g, 18.92 mmol), Pd(OAc)₂ (0.21 gm, 0.946 mmol) and copper iodide (0.18 g, 0.946 mmol). The mixture was stirred for 15 min at room temperature. Then the terminal alkyne *i.e.*, 2-oxo-1-(prop-2-ynyl)-1,2-dihydroquinoline-3-carbaldehyde (**1**) [11] (2.0 g, 9.46 mmol) was added. The reaction mixture was heated to reflux for 28 h and the progress of the reaction was monitored by checking TLC (thin layer chromatography) at a regular interval. After completion, the reaction mixture was concentrated under reduced pressure to afford the crude product that was purified by column chromatography using cyclohexane/ethyl acetate (9.5:0.5) to give the title compound **3**.

The compound **3** was well characterized by spectral data. In the ¹H-NMR spectrum (DMSO-*d*₆ as a solvent), two characteristic singlets appeared at δ 10.50 and 8.40 ppm due to the aldehyde hydrogen and NH hydrogen respectively. The NH signal was confirmed by its disappearance during D₂O exchange experiment. The methylene and methyl group appeared as two singlets at δ 5.36 and 2.17 ppm respectively. In the BB decoupled ¹³C-NMR spectrum of compound **3**, the two characteristic signals of acetylenic carbon atoms appeared at δ 83.2 and 83.1 ppm. The appearance of a signal at δ 189.7 ppm confirmed the presence of an aldehyde carbonyl group. The formation of the desired compound **3** was also supported by the mass spectrum which showed molecular ion peak (M+1) at *m/z* 344.9.

Description of the compound: Pale yellow crystalline powder.

Yield: 75%.

Mp: 220–225 °C.

R_f: 0.4 (Cyclohexane:EtOAc = 3:2).

IR ν_{max} (KBr cm⁻¹): 3266, 1698, 1648, 1609, 1560.

Mass (ES): *m/z* 344.9 (M+1, 100%).

¹H-NMR (400 MHz, DMSO-*d*₆): δ 10.50 (s, 1H, CHO), 8.4 (s, 1H, NH), 7.78–7.66 (m, ArH, 3H), 7.44–7.32 (m, ArH, 5H), 7.20 (s, 1H, ArH), 4.36 (s, 2H), 2.17 (s, 3H).

¹³C-NMR (100 MHz, DMSO-*d*₆): δ 189.7 (CHO), 168.5, 160.1, 157.0, 142.0, 140.4, 139.8, 134.2, 133.6, 132.2 (2C), 124.7, 123.2, 119.1, 116.1, 115.5, 115.4, 83.2 (acetylenic C), 83.1 (acetylenic C), 54.9 (NCH₂), 24.3 (CH₃).

Anal. calc. for C₂₁H₁₆N₂O₃: C, 73.24, H, 4.68, N, 8.13, O, 13.94; Found: C, 73.21, H, 4.61, N, 8.03.

Acknowledgements

The author (S. Pal) thanks M. N. Raju, the chairman of M. N. R. Educational Trust for his constant encouragement.

Conflicts of Interest

The authors declare no conflict of interest.

References

1. Toube, T.P.; Murphy, J.W.; Cross, A.D. The structure of edulitine and edulinine. *Tetrahedron* **1967**, *23*, 2061–2065.
2. Chung, H.S.; Woo, W.S. A quinolone alkaloid with antioxidant activity from the aleurone layer of anthocyanin-pigmented rice. *J. Nat. Prod.* **2001**, *64*, 1579–1580.
3. Wu, T.-S.; Yeh, J.-H.; Wu, P.-L. The heartwood constituents of tetradium glabrifolium. *Phytochemistry* **1995**, *40*, 121–124.
4. Uchida, M.; Tabusa, F.; Komatsu, M.; Morita, S.; Kanbe, T.; Nakagawa, K. Studies on 2(1*H*)-quinolinone derivatives as gastric antiulcer active agents. Synthesis and antiulcer activity of the metabolites of 2(4-chlorobenzoylamino)-3-[2(1*h*)-quinolinon-4-yl]propionic acid. *Chem. Pharm. Bull.* **1986**, *34*, 4821–4824.
5. Michael, J.P. Quinoline, quinazoline and acridone alkaloids. *Nat. Prod. Rep.* **1997**, *14*, 595–606.
6. Alabaster, C.T.; Belli, A.S.; Campbell, S.F.; Ellis, P.; Henderson, C.G.; Roberts, D.A.; Ruddock, K.S.; Samules, G.M.R.; Stefanisk, M.H. 2(1*H*)-Quinolinones with cardiac stimulant activity. 1. Synthesis and biological activities of (six-membered heteroaryl)-substituted derivatives. *J. Med. Chem.* **1988**, *31*, 2048–2056.
7. Kimura, N.; Fukui, H.; Takagaki, H.; Yonemochi, E.; Terada, K. Characterization of polymorphs of a novel quinolinone derivative, TA-270 (4-hydroxy-1-methyl-3-octyloxy-7-sinapinoylamino-2(1*H*)-quinolinone). *Chem. Pharm. Bull.* **2001**, *49*, 1321–1325.
8. Pal, S.; Durgadas, S.; Nallapati, S.B.; Mukkanti, K.; Kapavarapu, R.; Meda, C.L.; Parsa, K.V.; Pal, M. Novel 1-alkynyl substituted 1,2-dihydroquinoline derivatives from nimesulide (and their 2-oxo analogues): A new strategy to identify inhibitors of PDE4B. *Bioorg. Med. Chem. Lett.* **2011**, *21*, 6573–6576.

9. Sonogashira, K.; Tohda, Y.; Hagihara, N. A convenient synthesis of acetylenes: Catalytic substitutions of acetylenic hydrogen with bromoalkenes, iodoarenes and bromopyridines. *Tetrahedron Lett.* **1975**, *16*, 4467–4470.
10. Durgadas, S.; Chatare, V.K.; Mukkanti, K.; Pal, S. Palladium-mediated synthesis of novel nimesulide derivatives. *Appl. Organometal. Chem.* **2010**, *24*, 680–684.
11. Srivastava, A.; Singh, R.M. Vilsmeier-Haack reagent: A facile synthesis of 2-chloro-3-formylquinolines from N-arylacetamides and transformation into different functionalities. *Indian J. Chem.* **2005**, *44B*, 1868–1875.

© 2013 by the authors; licensee MDPI, Basel, Switzerland. This article is an open access article distributed under the terms and conditions of the Creative Commons Attribution license (<http://creativecommons.org/licenses/by/3.0/>).