

Short Note

***N*-(9,10-Dioxo-9,10-dihydroanthracen-1-yl)-2-methylbenzamide**

Hamad H. Al Mamari *  and Ahmed Al Sheidi

Department of Chemistry, College of Science, Sultan Qaboos University, Al Khoudh 123, P.O. Box 36, Muscat, Oman

* Correspondence: halmamari@squ.edu.om; Tel.: +968-2414-2471

Received: 24 November 2020; Accepted: 2 December 2020; Published: 4 December 2020



Abstract: In the present Short Note, we report a synthesis for the title compound, *N*-(9,10-dioxo-9,10-dihydroanthracen-1-yl)-2-methylbenzamide by reacting 2-methylbenzoyl chloride (or 2-methylbenzoic acid) with 1-aminoanthraquinone. The synthesized target compound was fully characterized by various spectroscopic methods (¹H-NMR, ¹³C-NMR, IR, GC-MS). The importance of this compound lies its possession of an *N,O*-bidentate directing group, potentially suitable for metal-catalyzed C-H bond functionalization reactions.

Keywords: organic synthesis; bidentate directing groups; benzamides; chelation-assistance; bis-chelates; C-H bond functionalization

1. Introduction

Functionalization of inert nonreactive C-H Bonds [1,2] has emerged as a powerful strategy for expedient chemical bonds. The chemical science avoids prefunctionalized reagents or materials and thus provides rapid access to desired products and synthetic targets. The functionalization of C-H bonds could result in a reduction in waste and saving of materials/chemicals as well as shortening the number of steps in chemical synthesis or step-economy. Therefore, functionalization of C-H bonds could be environmentally benign approach and thus a green science.

The main challenge in functionalization of C-H bonds is controlling which C-H bond would undergo activation or cleavage or site-selectivity [3,4]. One approach to help provide regiocontrol is the use of groups that can direct the reaction to occur at a specific C-H bond. Thus, directing groups have been developed as demonstrated by monodentate [5,6] and bidentate directing groups [7]. The key role of directing groups is chelation-assistance which could promote formation of cyclometallated complexes. The Lewis-basic directing group coordinates the Lewis-acidic metal bringing it in proximity to C-H bonds to be functionalized. The thermodynamic stability of cyclometallated complexes determines which C-H bonds are to be cleaved and thus functionalized. Specifically, relative thermodynamic stability favors formation of five-membered chelates, allowing the formation of mono five-membered-chelate (1, Figure 1) and double-five-membered chelates (2, Figure 1) by using monodentate and bidentate directing groups, respectively (Figure 1) [8].

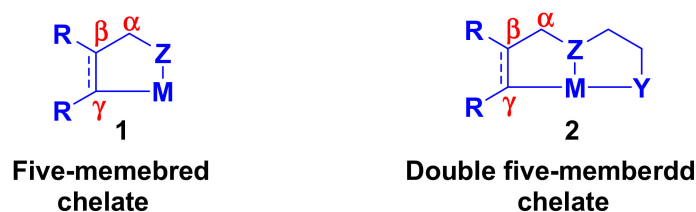


Figure 1. Mono five-membered and double five-membered chelates.

Directing-group-assisted C-H bond functionalization usually occurs at the γ -carbon with respect to the C bearing Z, the first Lewis basic atom. Thus, there is a two-carbon distance between Z and C-H to be cleaved and functionalized. Such structural requirements have triggered design of novel bidentate directing groups represented by modular triazole-based directing. [9,10]

In continuation of our program [11,12] in the design of novel directing groups potentially applicable in metal-catalyzed C-H bond functionalization, we report herein a design-based benzamide bearing 1-aminoanthraquinone (3, Figure 2), a potential *N,O*-bidentate directing groups for metal-catalyzed C-H bond functionalization. The aminodiketone is commercially available from the Aldrich chemical company at a cheap price rate of 0.092 EUR/mmol (0.412 EUR/g).

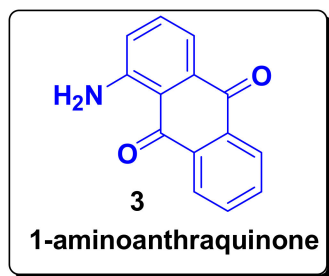
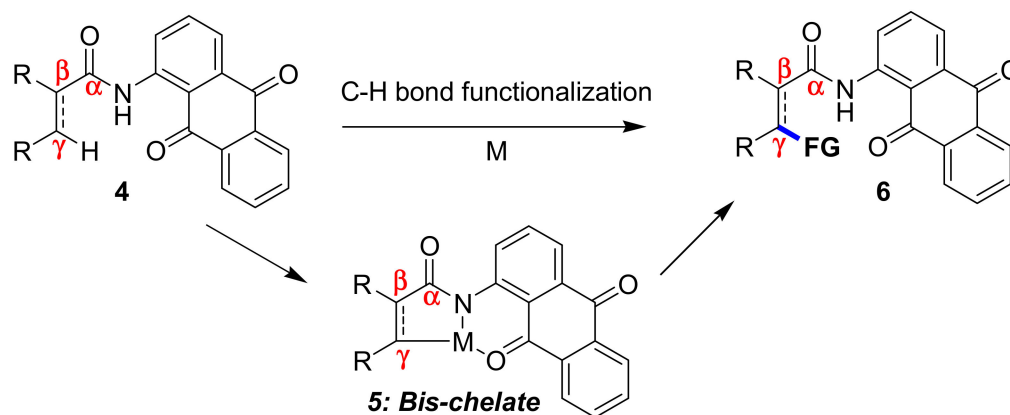


Figure 2. 1-Aminoanthraquinone.

It was envisaged that amides bearing 1-aminoanthraquinone (4, Scheme 1) could undergo metal-catalyzed C-H bond functionalization, to possibly provide functionalized amides (6) via postulated intermediate bis-chelate (5) (Scheme 1). The possession of the 1-aminoanthraquinone amides of *N* and *O* separated by three carbons could promote the functionalization of C-H bonds after C-H bond cleavage at the γ -position, through the bis-chelate shown (5, Scheme 1).



Scheme 1. Potential use of 1-aminoanthraquinone amides in the metal catalyzed C-H bond functionalization reactions.

Toward the end of investigating the use of 1-aminoanthraquinone amides as potential bidentate directing groups in C-H bond functionalization reactions, we have embarked on their synthesis. Thus, herein we describe the synthesis of 1-methylbenzamide bearing 1-aminoanthraquinone, a potential *N,O*-bidentate directing group in metal-catalyzed C-H bond functionalization. Toward that end, the title compound, *N*-(9,10-dioxo-9,10-dihydroanthracen-1-yl)-2-methylbenzamide (7, Figure 3), was synthesized and is reported herein.

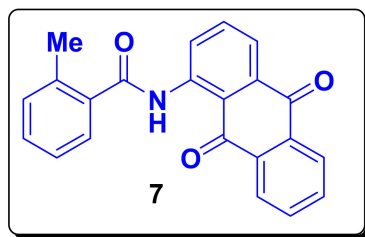
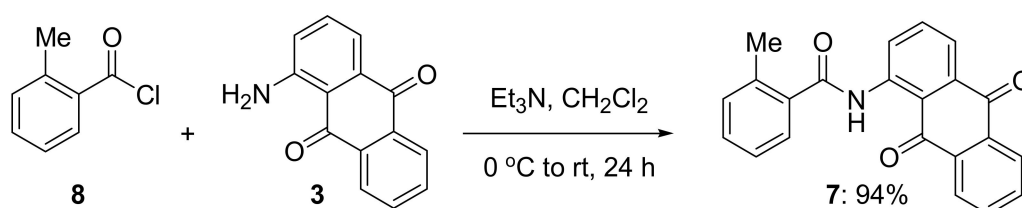


Figure 3. The presented title compound, *N*-(9,10-dioxo-9,10-dihydroanthracen-1-yl)-2-methylbenzamide.

It is noteworthy that the target benzamide does appear on SciFinder search database. However, to the best of our knowledge, its preparation has not been reported or referenced on the database. Accordingly, the present Short Note provides a detailed synthesis of the benzamide and its complete spectral characterization by various spectroscopic methods.

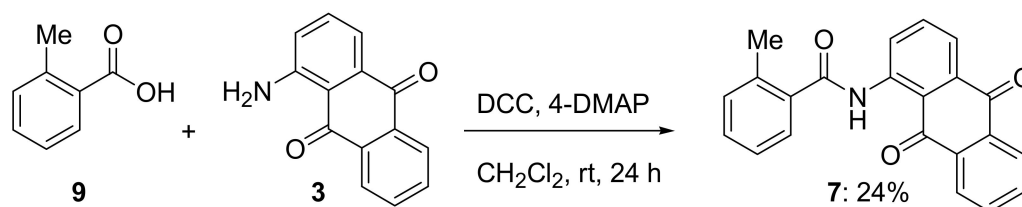
2. Results and Discussion

In order to synthesize amides bearing 1-aminoanthraquinone, the corresponding acid chloride were treated with the amine. The synthesis of the title compound, *N*-(9,10-dioxo-9,10-dihydroanthracen-1-yl)-2-methylbenzamide (7), was achieved by reacting *o*-toluoyl chloride (2-methylbenzoyl chloride) (8, Scheme 2) with 1-aminoanthraquinone (3, Scheme 2) under standard amide formation reaction conditions to afford the corresponding target benzamide (7) in 94% yield.



Scheme 2. Synthesis of *N*-(9,10-dioxo-9,10-dihydroanthracen-1-yl)-2-methylbenzamide from 2-methylbenzoyl chloride.

For comparison purposes, the synthesis of the target compound (7) was carried out by coupling the corresponding, relatively cheaper carboxylic acid with 1-aminoanthraquinone. Thus a mixture of 2-methylbenzoic acid (9, Scheme 3) and 1-aminoanthraquinone (3) was treated with the coupling agent; DCC (dicyclohexylcarbodiimide) in the presence of DMAP (4-*N,N*-dimethylaminopyridine) to give the desired title compound, *N*-(9,10-dioxo-9,10-dihydroanthracen-1-yl)-2-methylbenzamide (7), in 24% yield.



Scheme 3. Synthesis of *N*-(9,10-dioxo-9,10-dihydroanthracen-1-yl)-2-methylbenzamide (7) from 2-methylbenzoic acid.

Consequently, the synthesis of the target amide is better achieved using the acid chloride method illustrated above (Scheme 2). The amide product was characterized by various spectroscopic methods; $^1\text{H-NMR}$, $^{13}\text{C-NMR}$, IR and GC-MS analysis.

3. Materials and Methods

3.1. General Methods

All chemicals, reagents and solvents were purchased from chemical companies (Sigma-Aldrich Chemie GmbH, Taufkirchen, Germany) and were used as received without prior purification. Reactions that required dry conditions were performed in an inert atmosphere with Ar gas. Syringes and needles for the transfer of reagents were oven dried and cooled in a desiccator over silica gel before use. The reaction's progress was monitored by thin-layer chromatography (TLC) on glass plates pre-coated with Merck silica gel. TLC plates were examined under UV lamplight (UVGL-58 Handheld 254/365 nm, UVP, Upland, CA, USA). Büchi-USA rotary evaporators (Büchi, Flawil, Switzerland) were used to evaporate solvents using appropriate temperatures. Flash column chromatography was performed using silica gel (Kieselgel) (70–230) (Merck KGaA, Darmstadt, Germany) mesh as an adsorbent. The purified products were characterized using analyses NMR (^1H -NMR, ^{13}C -NMR), IR, mass spectra and melting points. Melting points were recorded on the Gallenkamp-MPd350.bm2.5 melting point apparatus (Gallenkamp, Kent, UK). Attenuated total-reflectance IR spectra were recorded on pure samples on Agilent Technologies Cary 630 FTIR (Agilent, Santa Clara, CA, USA). ^1H -NMR spectra were recorded in CDCl_3 on JEOL ECX-400 spectrometers (JEOL Ltd., Tokyo, Japan). ^1H -NMR chemical shifts (δ) were assigned in part per million (ppm) downfield using an internal standard trimethylsilane (TMS) and were referenced to CDCl_3 , $\delta = 7.24$. Abbreviations s, d, t, q, quin, sept and m refer to singlet, doublet, triplet, quartet, quintet, septet and multiplet, respectively. Chemical shifts in ^{13}C spectra (175 MHz) (JEOL Ltd., Tokyo, Japan). were quoted in ppm and referenced to the central line of the CDCl_3 triplet, $\delta \text{ C } 77.0$. Coupling constants (J) were recorded in hertz (Hz). GC-MS spectra were obtained using an Agilent mass spectrometer (Agilent, Santa Clara, CA, USA) (Supplementary Materials).

3.2. Synthesis of *N*-(9,10-Dioxo-9,10-dihydroanthracen-1-yl)-2-methylbenzamide (7)

2-Methylbenzoyl chloride (**8**) (1.30 mL, 9.86 mmol) was added dropwise under an atmosphere of N_2 into a cold (0°C ice-water bath) solution of 1-aminoanthraquinone (**3**) (1.10 g, 5.00 mmol), in CH_2Cl_2 (20 mL). Et_3N (1.40 mL, 10.0 mmol) was then added to the 0°C mixture under N_2 . The mixture was stirred for 1 h at 0°C , allowed to warm up to room temperature and then stirred for an additional 23 h. To the reaction mixture, water (30 mL) was added, followed by aqueous saturated NaHCO_3 solution (30 mL). The mixture was extracted with CH_2Cl_2 (3×30 mL). The combined organic extracts were washed with water (50 mL) and brine (50 mL) and then dried over anhydrous MgSO_4 and filtered. Recrystallization of the crude product from CH_2Cl_2 :hexane, gave the title compound (**7**) as a yellow solid (1.60 g, 94%); $R_f = 0.37$ (hexane/EtOAc, 1:2). $\text{Mp} = 187.5\text{--}188.7^\circ\text{C}$. ^1H -NMR (400 MHz, CDCl_3) δ 9.29 (d, $J = 8.7$ Hz, 1H), 8.30–8.22 (m, 2H), 8.04 (d, $J = 7.3$ Hz, 1H), 7.92 (d, $J = 6.4$ Hz, 2H), 7.77 (t, $J = 7.1$ Hz, 4H), 7.46–7.39 (m, 2H), 2.48 (s, 3H); ^{13}C -NMR (101 MHz, CDCl_3) δ 187.6, 182.7, 166.8, 142.5, 138.9, 136.0, 134.5, 134.4, 134.1, 133.2, 132.8, 131.8, 130.9, 128.9, 128.6, 127.5, 127.1, 126.3, 124.6, 122.7, 117.9, 21.6; IR (film): $\nu_{\text{max}}/\text{cm}^{-1}$: 3424, 3198, 1690, 1662, 1576. MS (EI) m/z (relative intensity): 341 (18), 281 (45), 262 (24), 207 (95), 191 (18), 147 (18), 119 (100), 91 (64). Elemental analysis, calculated: C (77.41), H (4.43), N (4.10), found: C (77.39), H (4.40), N (4.06).

4. Conclusions

In our continuing program of the design of directing groups suitable for metal-catalyzed C-H bond functionalization reactions, a synthesis of a design-based amide, bearing *N,O*-directing group bearing the commercially cheap 1-aminoanthraquinone is reported. Thus, the target title compound, *N*-(9,10-dioxo-9,10-dihydroanthracen-1-yl)-2-methylbenzamide, was synthesized in 94% yield from 2-methylbenzoyl chloride and 1-aminoanthraquinone. The compound was characterized by various spectroscopic methods (^1H -NMR, ^{13}C -NMR, IR, and GC-MS analysis). With bearing 1-aminoanthraquinone in hand, work is currently underway to investigate their *N,O*-bidentate directing group-potential in metal-catalyzed C-H bond functionalization reactions.

Supplementary Materials: The following are available online. Figure S1: ^1H -NMR of *N*-(9,10-Dioxo-9,10-dihydroanthracen-1-yl)-2-methylbenzamide. Figure S2. ^{13}C -NMR of *N*-(9,10-Dioxo-9,10-dihydroanthracen-1-yl)-2-methylbenzamide. Figure S3. IR NMR of *N*-(9,10-Dioxo-9,10-dihydroanthracen-1-yl)-2-methylbenzamide. Figure S4. GC-MS of *N*-(9,10-Dioxo-9,10-dihydroanthracen-1-yl)-2-methylbenzamide.

Author Contributions: A.A.S. carried out all experimental work under the supervision of H.H.A.M. All authors have read and agreed to the published version of the manuscript.

Funding: The research work is funded by Sultan Qaboos University Internal Grant (IG/SCI/CHEM/15/02).

Acknowledgments: The support of Sultan Qaboos University is gratefully acknowledged.

Conflicts of Interest: Authors declare no conflict of interest.

References

- Shilov, A.E.; Shul'pin, G.B. Activation of C-H bonds by metal complexes. *Chem. Rev.* **1997**, *97*, 2879–2932. [[CrossRef](#)] [[PubMed](#)]
- Ryabov, A. Mechanisms of intramolecular activation of carbon-hydrogen bonds in transition-metal complexes. *Chem. Rev.* **1990**, *90*, 403–424. [[CrossRef](#)]
- Dick, A.R.; Sanford, M.S. Transition metal catalyzed oxidative functionalization of carbon-hydrogen bonds. *Tetrahedron* **2006**, *11*, 2439–2463. [[CrossRef](#)]
- Li, J.; De Sarkar, S.; Ackermann, L. *Meta*- and *para*-selective C-H functionalization by C-H activation. *Top. Organomet. Chem.* **2016**, *55*, 217–257. [[CrossRef](#)]
- Sato, T.; Yoshida, T.; Al Mamari, H.H.; Ilies, L.; Nakamura, E. Manganese-catalyzed directed methylation of $\text{C}(\text{sp}^2)\text{-H}$ bonds at 25 °C with high catalytic turnover. *Org. Lett.* **2017**, *19*, 5458–5461. [[CrossRef](#)] [[PubMed](#)]
- Sambiagio, C.; Schönbauer, D.; Blicke, R.; Dao-Huy, T.; Pototschnio, G.; Schaaf, P.; Wiesinger, T.; Zia, M.F.; Wencel-Delord, J.; Besset, T.; et al. A Comprehensive review of directing groups applied in metal-catalyzed C-H functionalization chemistry. *Chem. Soc. Rev.* **2018**, *47*, 6603–6743. [[CrossRef](#)] [[PubMed](#)]
- Rouquet, G.; Chatani, N. Catalytic functionalization of $\text{C}(\text{sp}^2)\text{-H}$ and $\text{C}(\text{sp}^3)\text{-H}$ bonds by using bidentate directing groups. *Angew. Chem. Int. Ed.* **2013**, *52*, 11726–11743. [[CrossRef](#)] [[PubMed](#)]
- Omae, I. Intramolecular five-membered ring compounds and their applications. *Coord. Chem. Rev.* **2004**, *248*, 995–1023. [[CrossRef](#)]
- Al Mamari, H.H.; Diers, E.; Ackermann, L. Triazole-assisted ruthenium-catalyzed C-H arylation of aromatic amides. *Chem. Eur. J.* **2014**, *20*, 9739–9743. [[CrossRef](#)] [[PubMed](#)]
- Gu, Q.; Al Mamari, H.H.; Graczyk, K.; Diers, E.; Ackermann, L. Iron-catalyzed $\text{C}(\text{sp}^2)\text{-H}$ and $\text{C}(\text{sp}^3)\text{-H}$ arylation by triazole assistance. *Angew. Chem. Int. Ed.* **2014**, *53*, 3868–3871. [[CrossRef](#)] [[PubMed](#)]
- Al Mamari, H.H.; Al Awaimri, N.; Al Lawati, Y. *N*-Benzo[*c*][1,2,5]thiazol-4-yl-3—trifluoromethylbenzamide. *Molbank* **2019**, 2019, M1075. [[CrossRef](#)]
- Al Mamari, H.H.; Al Lawati, Y. *N*-(2-Hydroxy-1,1-dimethylethyl)-3-methylbenzamide. *Molbank* **2020**, 2020, M1099. [[CrossRef](#)]

Publisher's Note: MDPI stays neutral with regard to jurisdictional claims in published maps and institutional affiliations.



© 2020 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 (CC BY) license (<http://creativecommons.org/licenses/by/4.0/>).