Molbank **2011**, M740; doi:10.3390/M740

OPEN ACCESS

molbank

ISSN 1422-8599

www.mdpi.com/journal/molbank

Short Note

N-(4-Methylsulfonamido-3-phenoxyphenyl)-9,10-dihydro-9,10-ethanoanthracene-11,12-dicarboximide

Kavitha Kankanala [1], Varsha Prakash [2], Khagga Mukkanti [2], Vangala Ranga Reddy [3] and Sarbani Pal [1,*]

[1] MNR Degree & PG College, Kukatpally, Hyderabad-500085, A. P., India

[2] Centre for chemical Sciences and Technology, Institute of Science & Technology, Jawaharlal Nehru Technological University Hyderabad, Kukatpally, Hyderabad-500085, A. P., India

[3] Reddys Laboratories Limited, IPDO, Bachupally, Hyderabad-500085, India

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

Received: 7 September 2011 / Accepted: 30 September 2011 / Published: 14 October 2011

Abstract: The title compound, *N*-(4-methylsulfonamido-3-phenoxyphenyl)-9,10-dihydro-9,10-ethanoanthracene-11,12-dicarboximide was synthesized in high yield by reaction of *N*-(4-amino-2-phenoxyphenyl)methanesulfonamide and 9,10-dihydroanthracene-9,10-endo-α,β-succinic anhydride in glacial acetic acid. The structure of the compound was fully characterized by IR, ^{1}H and ^{13}C NMR, mass spectral analysis and elemental analysis.

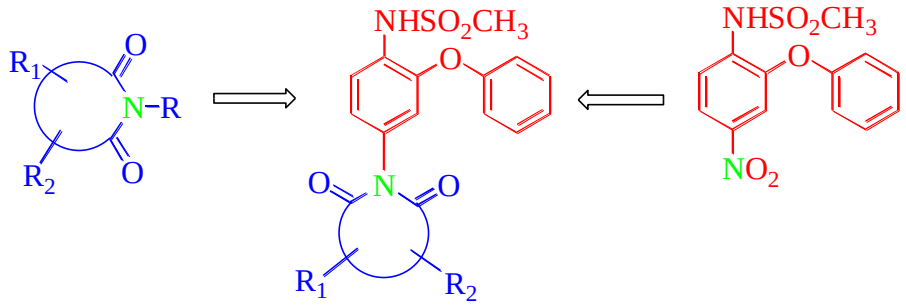
Keywords: sulfonamide; cyclic imide; nimesulide

Cyclic imides **A** (**Scheme 1**) represent an important class of bioactive molecules that shows a wide range of pharmacological activities such as androgen receptor antagonistic, anti-inflammatory, anxiolytic, antiviral, antibacterial, antitumor, antispasmodic, antinociceptive and antineoplastic properties [1-13].

On the other hand *N*-(4-nitro-2-phenoxy phenyl)methane sulfonamide or nimesulide (**B**, Scheme 1), a preferential cyclooxygenase-2 (COX-2) inhibitor is one of the well known non-steroidal anti-inflammatory drugs (NSAIDs) that has been utilized to treat pain and other inflammatory diseases. Because of their common anti-inflammatory properties and our interest in nimesulide (*N*-(4-nitro-2-phenoxy phenyl)methane sulfonamide) derivatives [14-18] as potential anti-inflammatory agents we decided to prepare compound **C** having structural features of both **A** and **B** (Scheme 1).

We estimated that combination of structural features of cyclic imide (**A**) with nimesulide (**B**) in a single molecule (**C**) would provide novel agents possessing potent pharmacological activities.

Scheme 1. Design of hybrid molecule.



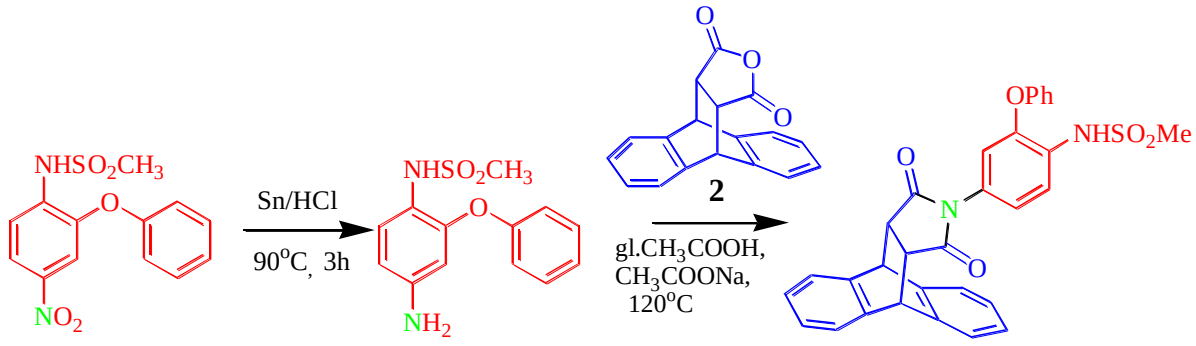
A **C** **B**

R_1,R_2 = Diverse substituents

We report the synthesis *N*-(4-methylsulfonamido-3-phenoxyphenyl)-9,10-dihydro-9,10-ethanoanthracene-11,12-dicarboximide (**3**) as hybrid molecule derived from *N*-(4-nitro-2-phenoxy phenyl)methane sulfonamide, **B**, nimesulide by straight forward condensation of the key intermediate *N*-(4-amino-2-phenoxy-phenyl)-methane sulfonamide (**1**) and 9,10-dihydro anthracene -9,10-endo-α,β-succinic anhydride (**2**).

The starting compound **1** (*N*-(4-amino-2-phenoxy-phenyl)-methane sulfonamide) required for our study was prepared [14] in quantitative yield from *N*-(4-nitro-2-phenoxy phenyl)methane sulfonamide **B**, (nimesulide) *via* reducing its nitro group as shown in **Scheme 2**.

Scheme 2. Synthesis of the title compound **3**.



B **1** **3**

To a mixture of aromatic amine, (*N*-(4-amino-2-phenoxy-phenyl)-methane sulfonamide) **1** (278 mg, 1.0 mmol) and 9,10-dihydroanthracene 9,10-endo-α,β-succinic anhydride (**2**) (276 mg, 1.0 mmol) in glacial acetic acid (3 mL) was added anhydrous sodium acetate (100 mg, 1.2 mmol) and the mixture was allowed to reflux for 20 min. After completion of the reaction (as indicated by TLC) the mixture was added to crushed ice (50 g) and stirred. The solid separated was filtered and dried. The crude product was purified by column chromatography followed by re-crystallization from chloroform.

Description of the compound: White solid.

Yield: 84%.

Mp: 309–311 ℃.

R_f: 0.59 ($CHCl_3$:Ethyl acetate = 9:1).

IR υ_{max} (KBr cm^{-1}): 3155, 1705, 1502, 1331, 1157.

Mass (ES): m/z 538 (M^++1, 100%).

^{1}HNMR (400 MHz, DMSO-d_6): δ 3.0 (s, 3H), 3.31(s, 2H), 4.81(s, 2H), 5.87(d, *J* 2.2 Hz, 1H), 6.29 (dd, *J* 8.6 and 2.2 Hz, 1H), 6.86 (dd, *J* 5.2 and 3.3 Hz, 2H), 7. 0 (d, *J* 7.6 Hz, 2H), 7.14–7.18 (m, 4H), 7.27–7.29 (m, 1H), 7.35 (d. *J* 8.5Hz, 1H), 7.46–7.50 (m, 4H), 9.35 (1H, NH).

^{13}C NMR (75 MHz, $CDCl_3$): δ 30.9 (CH_3), 39.8, 45.9, 47.02, 115.6, 119.4, 120.6, 122.1, 124.3 124.9, 126.9, 127.0, 128.1, 128.2, 130.3, 138.5, 141.0, 147.2, 155.0, 175.8 (CO).

Anal. calc. for $C_{31}H_{24}N_2O_5S$: C, 69.39; H, 4.51; N, 5.22 . Found: C, 69.28; H, 4.46; N, 5.28.

Acknowledgments

The authors (S. Pal and K. Kavitha) thank Mr. M. N. Raju, the chairman of M. N. R. Educational Trust for his constant encouragement.

References and Notes

1. Salvati, M.E.; Balog, A.; Shan, W.; Wei, D.D.; Pickering, D.; Attar, R.M.; Geng, J.; Rizzo, C.A.; Gottardis, M.M.; Weinmann, R.; Krystek, S.R.; Sack, J.; An, Y.; Kish, K. Structure based approach to the design of bicyclic-1H-isoindole-1,3(2H)-dione based androgen receptor antagonists. *Bioorg. Med. Chem. Lett.* **2005**, *15*, 271–276.
2. Sondhi, S.M.; Rani, R.; Roy, P.; Agarwal, S.K.; Saxena, A.K. Microwave-Assisted Synthesis of N-Substituted Cyclic Imides and Their Evaluation for Anticancer and Antiinflammatory Activities. *Bioorg. Med. Chem. Lett.* **2009**, *19*, 1534–1538.
3. Ishizumi, K.; Kojima, A.; Antoku, F. Synthesis and anxiolytic activity of N-substituted cyclic imides (1R*,2S*,3R*,4S*)-N-[4-[4-(2-pyrimidinyl)-1-piperazinyl]butyl]-2,3-bicyclo[2.2.1] heptanedicarboximide (tandospirone) and related compounds. *Chem. Pharm. Bull.* **1991**, *39*, 2288–2300.
4. Shibata, Y.; Shiehita, M.; Sasaki, K.; Nishimura, K.; Hashimoto, Y.; Iwasaki, S. N-Alkylphthalimides: Structural requirement of thalidomidal action on 12-O-tetradecanoylphorbol-13-acetate-induced tumor necrosis factor alpha production by human leukemia HL-60 cells. *Chem. Pharm. Bull.* **1995**, *43*, 177–179.

5. Jindal, D.P.; Bedi, V.; Jit, B.; Karkra, N.; Guleria, S.; Bansal, R.; Palusczak, A.; Hartmann, R.W. Synthesis and study of some new N-substituted imide derivatives as potential anticancer agents. *Il Farmaco* **2005**, *60*, 283–290.
6. Wang, J.J.; Wang, S.S.; Lee, C.F.; Chung, M.A.; Chern, Y.T. *In vitro* antitumor and antimicrobial activities of N-substituents of maleimide by adamantane and diamantane. *Chemotherapy* **1997**, *43*, 182–189.
7. Machado, A.L.; Lima, L.M.; Arau ĵo, J.X., Jr.; Fraga, C.A.M.; Koatz, V.L.G.; Barreiro, E.J.I. Design, synthesis and antiinflammatory activity of novel phthalimide derivatives, structurally related to thalidomide. *Bioorg. Med. Chem. Lett.* **2005**, *15*, 1169–1172.
8. Kenji, S.; Hideko, N.; Yoshihiro, U.; Yoshikazu, S.; Kazuharu, N.; Motoji, W.; Konstanty, W.; Tadafumi, T.; Tetsuji, A.; Yuji, Y.; Kenji, K.; Hitoshi, H. Napthalimidobenzamide DB-51630: A novel DNA binding agent inducing p300 gene expression and exerting a potent anti-cancer activity. *Bioorg. Med. Chem.* **2005**, *13*, 4014–4021.
9. Mayer, A.; Neuenhofer, S. Luminescent labels - more than just an alternative to radioisotopes. *Angew. Chem. Int. Ed.* **1994**, *33*, 1044–1072.
10. Miguel, F.B.; Gema, D.; Beatriz, S.; Cynthia, R.; Simmon, R.; Teresa, B. Synthesis and antitumour activity of new dendritic polyamines–(imide–DNA-intercalator) conjugates: potent Lck inhibitors. *Eur. J. Med. Chem.* **2002**, *37*, 541–551.
11. Miyachi, H.; Azuma, A.; Ogasawara, A; Uchimura, E.; Watanabe, N.; Kobayashi, Y.; Kato, F.; Kato, M.; Hashimoto, H. Novel biological response modifiers: Phthalimides with tumor necrosis factor-alpha production-regulating activity. *J. Med. Chem.* **1997**, *40*, 2858–2865.
12. Mederski, W.W.K.R.; Baumgarth, M.; Germann, M.; Kux, D.; Weitzel, T. A Convenient Synthesis of 4-Aminoaryl Substituted Cyclic Imides. *Tetrahedron Lett.* **2003**, *44*, 2133–2136.
13. Cremlyn, R.; Swinbourne, F.; Nunes, R. Diels Alder Reactions using N-(p-Chlorosulfonyl)-Maleimide a dienophile. *Phosphorous Sulfur Relat. Elem.* **1987**, *33*, 65.
14. Pericherla, S.; Mareddy, J.; Rani, D.P.G.; Gollapudi, P.V.; Pal, S. Chemical Modifications of Nimesulide. *J. Braz. Chem. Soc.* **2007**, *18*, 384–390.
15. Reddy, L.V.; Nakka, M., Suman, A.; Ghosh, S.; Helliwell, M.; Mukkanti, K.; Mukherjee, A.K.; Pal, S. Synthesis of Novel Quinoline Analogues of Nimesulide: An Unusual Observation. *J. Heterocycl. Chem.* **2011**, *48*, 555–562.
16. Durgadas, S.; Chatare, V.K.; Mukkanti, K.; Pal, S. Palladium-mediated synthesis of novel nimesulide derivatives. *Appl. Organomet. Chem.* **2010**, *24*, 680–684.
17. Kankanala, K.; Reddy, V.R.; Mukkanti, K.; Pal, S. Lewis Acid Free High Speed Synthesis of Nimesulide-Based Novel *N*-Substituted Cyclic Imides. *J. Braz. Chem. Soc*. **2010**, *21*, 1060–1064.
18. Reddy, L.V.; Kethavath, M.; Nakka, M., Beevi, S.S.; Mangamoori, L.N.; Mukkanti, K.; Pal, S. Design and Synthesis of Novel Cytotoxic Agents Based on Combined Framework of Quinoline and Nimesulide. *J. Heterocycl. Chem.* **2011**, doi:10.1002/jhet.801.