Molbank **2005**, M447 http://www.mdpi.net/molbank/

Synthesis of antifungal isoindole (5-methyl-isoxazole-3-yl)-[2-(5-methyl-isoxazol-3-yl)2,3-dihydro-isoindol-1-ylidene]amine

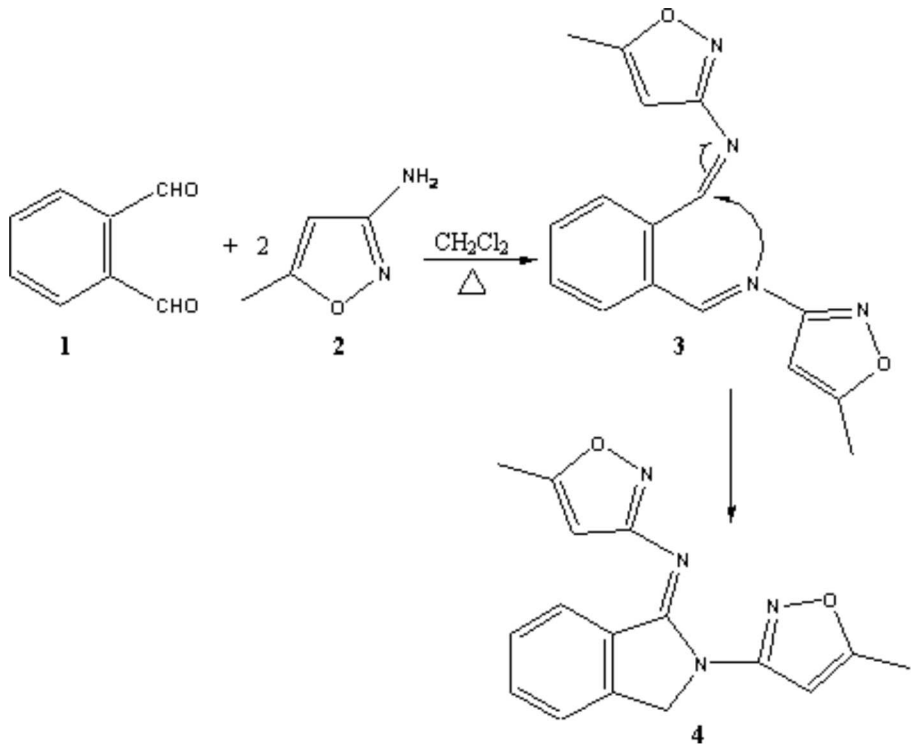
Shar S. Al-Shihry

Department of Chemistry, College of Science, King Faisal University,
P. O. Box 1759 Hofuf 31982 Saudi Arabia
Tel. (+966) 35886435, Fax (+966) 35886437, e-mail: sshihry@kfu.edu.sa

Received: 27 June 2005 / Accepted: 22 September 2004 / Published: 12 December 2005

Keywords: Isoindole, phthalimide, antifungal, Schiff base, isoxazole.

A large number of isoindoline skeletons such as staurosporine, indoprofen, and pazinaclone have been reported to possess biological activities [1-5]. Synthesis and study of the biological activity of isoindoline derivatives are under investigation.



To a stirred solution of *o*-phthalicaldehyde (1) (0.5 g, 3.73 mmol) in dichloromethane (20 ml) a solution of amine 2 (0.73 g, 7.44 mmol) in dichloromethane (20 ml) was added. The reaction mixture was heated under reflux for the 3h, the progress of the reaction was monitored by TLC. The solvent was reduced and left, pale yellow cubic crystals start to form which were filtered off to give the isoindole derivative 4 as colorless cubic crystals (0.75 g, 68 %).

Biological Activity: Compound 4 showed antifungal activity against four species: *Chrysoporium tropicum, Fusarium oxysporum, Geotrichum candidum and Trichoplyton rubrum.*

Melting Point: 191°C.

UV (EtOH; λ_{max} nm; ε ($dm^3.mol^{-1}.cm^{-1}$): 205 (10057); 242 (4583); 277 (4032).

IR (KBr, cm^{-1}): 3099 (CH); 1651 (C=N); 1430 (C-CH_3); 1376 (C-N).

^{1}H-NMR ($CDCl_3$, 400 MHz): d= 7.49 (2H, d, J=7.5 Hz); 7.26-7.24 (2H, m); 7.11 (1H, s); 5.81 (1H, s); 4.96 (2H, s); 2.44 (3H, s); 2.39 (3H, s).

^{13}C-NMR ($CDCl_3$, 100 MHz): d= 170.3; 196.8; 166.8; 159.3; 155.6; 140.9; 132.0; 129.7; 127.9; 126.3; 123.3; 98.2; 96.2; 51.4; 13.0; 12.8.

MS (m/z, %): 294 (M^+, 91.91); 279 (M^+-CH_3, 99.9); 117 (17.25); 116 (C_8H_4N, 100).

Elemental Analysis: Calculated for $C_{16}H_{14}N_4O_2$ (294.31): C, 65.30%; H, 4.79%; N, 19.04%. Found: C, 65.50%; H, 4.94%; N, 18.75%.

Acknowledgment
The author thanks Professor A. H. Moubasher and Professor A. Y. Abdel-Malek, Department of Botany, Assiut University, Assiut, Egypt, for the Biological Activity studies.

References
1. Takahashi, I.; Hatanaka, M. *Heterocycles*, 1997, *45*, 2475.
2. Kundu, N. G.; Khan, M. W.; Mukhopadhyay, R. *J. Indian Chem. Soc*., 2001, *78*, 671.
3. Olmo, E.; Armas, M.; Ybarra, M.; López, J.; Oporto, P.; Giménez, A.; Deharo, E.; Feliciano, A. *Bioorganic & Medicinal Chemistry Letters,* 2003*, 13,* 2769.
4. Takahashi, I.; Miyamoto, R.; Nishiuchi, K.; Hatanaka, M.; Yamano, A.; Sakushima, A.; Sakushima, A. Hosoi, S. *Heterocycles*, 2004, *63*, 1267.
5. Cul, A.; Daïch, A.; Decroix, B.; Sanz, G.; Hijfte, L. *Tetrahedron,* 2004*, 60,* 11029.

Sample Availability: Available from MDPI.