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Studies in 3,4-diaryl-1,2,5-oxadiazoles and their *N*-oxides: Search for better COX-2 inhibitors

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A series of 3,4-diaryl-1,2,5-oxadiazoles and 3,4-diaryl-1,2,5-oxadiazole *N*-oxides were prepared and evaluated for COX-2 and COX-1 binding affinity *in vitro* and for anti-inflammatory activity by the rat paw edema method. *p*-Methoxy (*p*-OMe) substituted compounds 9, 21, 34, 41, 42 showed COX-2 enzyme inhibition higher than that showed by compounds with other substituents. 3,4-Di(4-methoxyphenyl)-1,2,5-oxadiazole *N*-oxide (42) showed COX-2 enzyme inhibition of 54% at 22 μmol L^{-1} and COX-1 enzyme inhibition of 44% at 88 μmol L^{-1}

concentrations, but showed very low *in vivo* anti-inflammatory activity. Its deoxygenated derivative (21) showed lower COX-2 enzyme inhibition (26% at 22 μmol L^{-1}) and higher COX-1 enzyme inhibition (53% at 88 μmol L^{-1}) but, marked *in vivo* anti-inflammatory activity (71% at 25 mg kg^{-1}) *vs.* celecoxib (48% at 12.5 mg kg^{-1}). Molecular modeling (docking) studies showed that the methoxy group is positioned in the vicinity of COX-2 secondary pocket and it also participates in hydrogen bonding interactions in the COX-2 active site. These preliminary studies suggest that *p*-methoxy (*p*-OMe) group in one of benzene rings may give potentially active leads in this series of oxadiazole/*N*-oxides.

Keywords:
1,2,5-oxadiazole; 1,2,5-oxadiazole N-oxide; COX-2 inhibitor

T. D. Warner and J. A. Mitchell, Cyclooxygenases: new forms, new inhibitors, and lessons from the clinic, FASEB J. 18 (2004) 790-804.

E. M. Antman, D. DeMets and J. Loscalzo, Cyclooxygenase inhibition and cardiovascular risk, Circulation 112 (2005) 759-770.

J. J. Li, G. D. Anderson, E. G. Burton, J. N. Cogburn, J. T. Collins, D. J. Garland, S. A. Gregory, H. C. Huang, P. C. Isakson, C. M. Koboldt, E. W. Logusch, M. B. Norton, W. E. Perkins, E. J. Reinhard, K. Seibert, A. W. Veenhuizen, Y. Zhang and D. B. Reitz, 1,2-Diarylcyclopentenes as selective cyclooxygenase-2 inhibitors and orally active anti-inflammatory agents, J. Med. Chem. 38 (1995) 4570-4578.

T. D. Penning, J. J. Talley, S. R. Bertenshaw, J. S. Carter, P. W. Collins, S. Docter, M. J. Graneto, F. J. Lee, J. W. Malecha, J. M. Miyashiro, R. S. Rogers, D. J. Rogier, S. S. Yu, G. A. Anderson, F. G. Burton, J. N. Cogburn, S. A. Gragory, C. M. Koboldt, W. E. Perkins, K. Seibert, A. W. Veenhuizen, Y. Y. Zhang and P. C. Isakson, Synthesis and biological evaluation of the 1,5-diarylpyrazole class of cyclooxygenase-2 inhibitors: Identification of 4-[5-(4-methylphenyl)-3-(trifluoromethyl) -1H-pyrazol-1-yl]benzenesulfonamide (SC-58635, Celecoxib), J. Med. Chem. 40 (1997) 1347-1365.

G. Dannhardt and W. Kiefer, Cyclooxygenase inhibitors - current status and future prospects, Eur. J. Med. Chem. 36 (2001) 109-126.

P. Prasit, Z. Wang, C. Brideau, C. C. Chan, S. Charleson, W. Cromlish, D. Either, J. F. Evans, A. W. Ford-Hutchinson, J. Y. Gauthier, R. Gordon, J. Guay, M. Gresser, S. Kargman, B. Kennedy, Y. Leblanc, S. Leger, J. Mancini, G. P. O'Neil, M. Ouellet, M. D. Percieval, H. Perrier, D. Riendeau, I. Rodger, P. Tagari, M. Therien, P. Vickers, E. Wong, L. J. Xu, R. N. Young, R. Zamboni, S. Boyce, N. Rupniak, M. Forrest, D. Visco and D. Patrick, The discovery of rofecoxib, [MK 966, VIOXX®, 4-(4'-methylsulfonylphenyl)-3-phenyl-2(5H)-furanone], an orally active cyclooxygenase-2 inhibitor, Bioorg. Med. Chem. Lett. 9 (1999) 1773-1778.

J. J. Tally, D. L. Brown, J. S. Carter, M. J. Graneto, C. M. Koboldt, J. L. Masferrer, W.

E. Perkins, R. S. Rogers, A. F. Shaffer, Y. Y. Zhang, B. S. Zweifel and K. Seibert, 4-[5-Methyl-3-phenylisoxazol-4-yl]-benzenesulfonamide, valdecoxib: A potent and selective inhibitor of COX-2, J. Med. Chem. 43 (2000) 775-777.

J. J. Tally, S. R. Bertenshaw, D. L. Brown, J. S. Carter, M. J. Graneto, M. S. Kellogg, C. M. Koboldt, J. Yuan, Y. Y. Zhang and K. Seibert, N[[(5-Methyl-3-phenylisoxazol-4-yl)-phenyl]sulfonyl]propanamide, sodium salt, parecoxib sodium: A potent and selective inhibitor of COX-2 for parenteral administration, J. Med. Chem. 43 (2000) 1661-1663.

D. Riendeau, M. D. Percieval, C. Brideau, S. Charleson, D. Dube, D. Ethier, J. P. Falgueyret, R. W. Friesen, R. Gordon, G. Greig, J. Guay, J. Mancini, M. Ouellet, E. Wong, L. J. Xu, S. Boyce, D. Visco, Y. Girard, P. Prasit, R. Zamboni, I. W. Rodger, M. Gresser, A. W. Ford-Hutchinson, R. N. Young and C. C. Chan, Etoricoxib (MK-0663): Preclinical profile and comparison with other agents that selectively inhibit cyclooxygenase-2, J. Pharmacol. Exp. Ther. 296 (2001) 558-570.

M. R. Yadav, R. Giridhar and H. B. Prajapati, A Process for Preparation of 3-[-o-/m-/p-Mono/DisubstitutedPhenyl]-4-[o-/p-Substitutedphenyl]furazans and Furoxans, Indian Patent Appl. No. 109/MUM/2004, Feb. 2004.

H. Cerecetto and W. Porcal, Pharmacological properties of furoxans and benzofuroxans: Recent developments, Mini-Rev. Med. Chem. 5 (2005) 57-71.

V. G. Granik and N. B. Grigor, Nitric oxide synthase inhibitors: Biology and Chemistry, Russ. Chem. Bull. 51 (2002) 1973-1995.

C. Velazquez, P. N. P. Rao, R. McDonald and E. E. Knaus, Synthesis and biological evaluation of 3,4-diphenyl-1,2,5-oxadiazole-2-oxides and 3,4-diphenyl-1,2,5-oxadiazoles as potential hybrid COX-2 inhibitor/nitric oxide donor agents, Bioorg. Med. Chem. 13 (2005) 2749-2757.

J. S. Buck and W. S. Ide, Mixed benzoins. I, J. Am. Chem. Soc. 52 (1930) 220-224.

J. S. Buck and W. S. Ide, Mixed benzoins. II, J. Am. Chem. Soc. 52 (1930) 4107-4109.

S. T. Shirude, P. Patel, R. Giridhar and M. R. Yadav, An efficient and time saving microwave assisted selenium dioxide oxidation of 1,2-diarylethanones, Indian. J. Chem. 45B (2006) 1080-1085.

H. Sano, T. Noguchi, A. Tanatani, Y. Hashimoto and H. Miyachi, Design and synthesis of subtype-selective cyclooxygenase (COX) inhibitors derived from thalidomide, Bioorg. Med. Chem. 13 (2005) 3079-3091.

C. A. Winter, E. A. Risley and G. W. Nuss, Carrageenin-induced edema in hind paw of the rat as an assay for antiinflammatory drugs, Proc. Soc. Exp. Biol. Med. 111 (1962) 544-547.

SYBYL Molecular modeling system, version 6.9, Tripos, Inc., St. Louis, USA, (2003).

R. A. Friesner, J. L. Banks, R. B. Murphy, T. A. Halgren, J. J. Klicic, D. T. Mainz, M. P. Repasky, E. H. Knoll, M. Shelly, J. K. Perry, D. E. Shaw, P. Francis and P. S. Shenkin, Glide: A new approach for rapid, accurate docking and scoring. 1. Method and assessment of docking accuracy, J. Chem. 47 (2004) 1739-1749.

M. Clark, R. D. Crammer and N. van Opdenbosh, Validation of the General-Purpose Tripos 5.2 force field, J. Comput. Chem. 10 (1989) 982-1012.

J. H. Boyer, R. F. Reinisch, M. J. Danzig, G. A. Stoner and F. Sahhar, The transformation of -o-dinitroso aromatic compounds into o-nitroaryl amines, J. Am. Chem. Soc. 77 (1955) 5688-5690.

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