Category

Synthesis of Heterocycles

Key words

sulfonylpyrazoles

nitroalkenes

diazosulfones

withasomnine

R. KUMAR, I. N. N. NAMBOOTHIRI* (INDIAN INSTITUTE OF TECHNOLOGY, BOMBAY, INDIA)

Regioselective Synthesis of Sulfonylpyrazoles via Base Mediated Reaction of Diazosulfones with Nitroalkenes and a Facile Entry into Withasomnine

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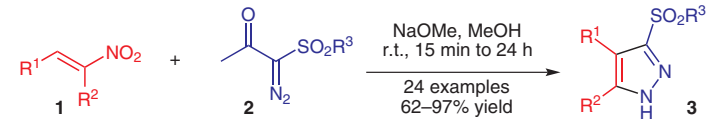
Sulfonylpyrazoles via Base-Mediated Reaction of Diazosulfone with Nitroalkenes

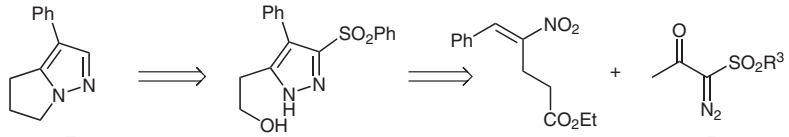


1 **2** **3**

R^1 = 4-$MeOC_6H_4$, Ph, 4-ClC_6H_4, 3-BrC_6H_4, 4-MeC_6H_4, 3,4-di$MeOC_6H_3$, 3,4,5-tri$MeOC_6H_2$, 2-$O_2NC_6H_4$, 3-$O_2NC_6H_4$, 4-$O_2NC_6H_4$, 2-furyl, 2-thienyl, Cy, morpholino, CH=CHPh, 4-$MeOC_6H_4CH$=CH

R^2 = Me, CH_2OH, CO_2Et

R^3 = Tol, Ph



7 **Withasomnine** 5 steps **6** **4** **5**

Significance: Based on a previous report (R. Muruganantham, S. M. Mobin, I. N. N. Namboothiri *Org. Lett.* **2007**, *9*, 1125), the synthesis of sulfonylpyrazoles **3** from α-diazo-β-ketosulfone **2** and nitroalkene **1** via a 1,3-dipolar cycloaddition is reported. Optimized conditions require the presence of nucleophilic base such as NaOMe to achieve the deacylation of **2**, which precedes the [2+3] cycloaddition. Various aryl, heteroaryl, alkyl, hydroxymethyl and hydrazinyl pyrazoles were thus prepared by the appropriate choice of nitroalkene. However, when α,β-disubstituted nitroethylenes are used, the synthesis of the corresponding 3,4,5-trisubstituted pyrazoles **3** needed longer time and they were formed in lower yields. The potent analgesic agent withasomnine (H.-B. Schröter, D. Neumann, A. R. Katritzky, F. J. Swinbourne *Tetrahedron* **1966**, *22*, 2895) was prepared by this methodology in five steps.

Comment: Pyrazole is an important scaffold found in many pharmaceutical products such as Celecoxib (antiarthritic), Viagra and Thiomethisosidenafil. Similarly, the sulfonyl group is an important pharmacophore found also in many drugs, for example, Bicalutamide (anticancer agents) and Dapsone (antileprosy). In spite of this significance, the synthesis of sulfonyl pyrazoles has received limited attention (D. Gao, H. Zhai, M. Parvez, T. G. Back *J. Org. Chem.* **2008**, *73*, 8057). The present work is an extension of a previous report in which the Bestmann–Ohira reagent, α-diazo-β-keto phosphonate was applied in [2+3]-cycloaddition chemistry (R. Muruganantham, S. M. Mobin, I. N. N. Namboothiri *Org. Lett.* **2007**, *9*, 1125).

SYNFACTS Contributors: Victor Snieckus, Cédric Schneider
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