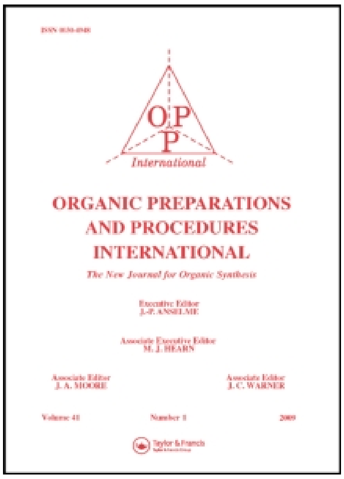

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1,3-DIPOLAR CYCLOADDITIONS OF 3-PHENYLSYDNONE WITH ACETYLENE DICARBOXYLATES IN SUPERCRITICAL CARBON DIOXIDE

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10. The data for product obtained by DDQ oxidation of phenolphthalein hydroxyamide are: ESMS (M + H)+ at 334.2; ^{1}H NMR: δ 11.2 (s, 1H), 9.62 (br, 2H), 7.88 (dd, 1H, J = 7.3, J = 1.8 Hz), 7.51 (m, 3H), 6.83 (d, 4H, J = 8.6 Hz), 6.72 (d, 4H, J = 8.8 Hz), 6.65 (d, 1H J = 7.1 Hz); ^{13}C NMR: δ 162.8, 157.3, 143.4, 132.1, 131.4, 129.8, 128.0, 127.0, 126.4, 126.1, 114.6, 88.1. Although the mass spectrum may be consistent for either the five-membered hydroxyspirolactam or a six-membered oxolactam, the ^{13}C NMR differs from other spirolactams (N-C9 at ~74.0 ppm), in that it shows a C9 resonance at 88.1 ppm, indicative of a C9 substituted with oxygen. In contrast, the N-oxo and N- amino fluorescein spirolactams (reference 6 above) display resonances similar to other N-alkyl species (all show C9 ~64 ppm).

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1,3-DIPOLAR CYCLOADDITIONS OF 3-PHENYLSYDNONE WITH ACETYLENE DICARBOXYLATES IN SUPERCRITICAL CARBON DIOXIDE

Submitted by
(08/04/00)

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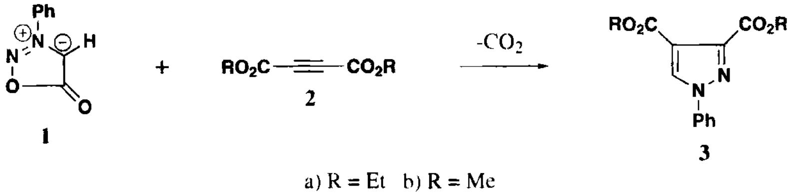
Sydnones undergo 1,3-dipolar cycloadditions with alkynes or alkenes to form pyrazoles or related species.[1] This process is of considerable interest and has been most successful in solvents such as toluene or xylene at temperatures ranging from 110-150° with alkynes bearing electron-withdrawing groups.



With the upsurge of interest in "green" chemistry, we were attracted to the possibility that sydnone cycloadditions could be conducted in a more environmentally benign manner. In this regard, we elected to utilize carbon dioxide as the solvent because of its low toxicity and cost,[2] the ability to manipulate solvent strength by changing temperature and pressure,[2] and the enhanced diffusivity possible in this medium.[3] A supercritical fluid extraction (SFE) apparatus, used in the static mode, served as the batch reactor for this study. A fixed temperature (120°) and pressure (75 atmospheres) were used and each alkyne was allowed to react for one hour. At the end of each run, the products were recovered from molecular sieves on which they had been adsorbed, by extraction with methylene chloride and identification was made by comparison with authentic samples. While methylene chloride is not a "green" solvent, it was chosen to facilitate product isolation in demonstrating proof of concept. The method could be further modified using a "greener" solvent. The product yields were good (65 and 83% for **3a** and **3b**, respectively) and compared favorably with those obtained by the standard method using reflux in toluene (50%[4] and 92%[1]). Since CO_2 is produced in the reactions, product yields are reduced when the reactions are conducted at higher pressures[5] (300 atmospheres), however this effect appears to be minimal at 75 atmospheres. Overall, we have shown the feasibility of conducting 1,3-dipolar cycloaddition reactions using CO_2 as the solvent. We plan to study this approach further in order to assess its scope and limitations.

EXPERIMENTAL SECTION

3-Phenylsydnone [50927-09-8] was prepared by a method previously reported[6] and purified by recrystallization. Pyrazole standards were obtained by reported procedures.[1] Diethyl acetylenedicarboxylate [762-21-0] (95%) and dimethyl acetylenedicarboxylate [762-42-5] (99%) were purchased from Aldrich Chemical Company. Solvents were obtained from commercial sources and used as received. All reactions conducted in CO_2 used helium head pressurized SFE-grade CO_2. A Suprex Prepmaster EL was used to deliver the CO_2 and control pressure and temperature. A 5-mL internal volume, stainless steel SFE extraction vessel served as the reaction vessel. Sodium aluminosilicate molecular sieves (8-12 mesh, 4Å) were obtained from Sigma Chemical Company and were used to disperse the solid 3-phenylsydnone during the reaction. Isolation and purification of 3,4-dicarbomethoxy-1-phenylpyrazole [3198-98-9] was performed on 230-400 mesh Silica Gel 60 [63231-67-4] (TSI Chemical Co.) using methylene chloride-hexane (80:20 v:v) as the eluent. Isolation and purification of 3,4-dicarbethoxy-1-phenylpyrazole [25832-23-9] was performed with the same silica gel using methylene chloride-acetone (90:10 v:v) as the eluent. The fractions containing the desired compounds were combined and the solvents were evaporated under a gentle stream of nitrogen. Identification was by comparison of IR spectra with authentic samples.

General Procedure.- Fifty milligrams (0.30 mmol) of 3-phenylsydnone were dissolved in 5 mL of methylene chloride. The solution was transferred to a beaker containing 3-4 g of molecular sieves and the methylene chloride was allowed to evaporate. The sieves, containing the dispersed 3-phenylsydnone, were transferred to the extraction vessel. With a syringe, 200-250 μL (2-3 mmol) of the corresponding alkyne **2** were added to the sieves inside the extraction vessel. The vessel was sealed and placed inside the SFE unit that was programmed to run at the desired temperature and pressure. The vessel was charged with CO_2 and the static extraction started. After 1 hr, the vessel was cooled to room temperature and the CO_2 was vented. The sieves, containing reaction products and unreacted 3-phenylsydnone, were removed from the vessel and rinsed with methylene chloride. The sieves can be reused. Following isolation, products were identified by comparison with authentic samples.

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