

*IN THE NAME
OF GOD*



**Shiraz University
Faculty of Science**

M.Sc. Dissertation in Organic Chemistry

**A. Sulfur trioxide pyridine complex as an
efficient reagent for synthesis of Amides and
Nitriles**

**B. Sulfamic acid as an efficient catalyst for
synthesis of pyrazoles**

By

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September 2008



پایان نامه کارشناسی ارشد در رشته شیمی آلی

الف: کمپلکس سولفور تری اکسید پیریدین به عنوان یک
معرف مناسب برای سنتز نیتریلها و آمیدها

و

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FARZANEH DEHGHANI

THESIS

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DEDICATED TO:

My Family

For Their Love and Support

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Farzaneh Dehghani

September 2008

ABSTRACT

A: Sulfur trioxide pyridine complex as an efficient reagent for synthesis of Amides and Nitriles

B: Sulfamic acid as an efficient catalyst for synthesis of pyrazoles

BY

FARZANEH DEGHANI

Our aims in this study were Beckmann rearrangement of a variety of ketoximes and dehydration of aldoximes and primary amides under mild conditions, in the presence of sulfur trioxide pyridine complex in solvent free conditions under heating with excellent yield.

An expeditious room temperature synthesis of pyrazoles by condensation of hydrazines with various 1, 3-diketones is described. This greener protocol was catalyzed by sulfamic acid and proceeded efficiently in solvent free in the absence of any organic solvent with excellent yield.

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Part A

**Sulfur trioxide pyridine complex as an
efficient reagent for synthesis of Amides and
Nitriles**

CHAPTER ONE

INTRODUCTION AND LITERATURE REVIEW

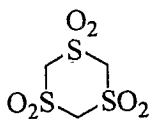
CHAPTER ONE

INTRODUCTION AND LITERATURE REVIEW

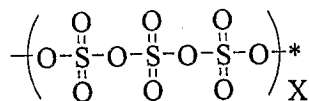
1.1. Sulfur Trioxide Compounds:

Several events have occurred which have led to increased interest in the reactions and derivatives of sulfur trioxide. It was, for the first time, made cheaply available in stabilized liquid form for use as a laboratory and commercial reagent, and it is now so marketed by several companies in various countries. Laboratory research and industrial practice have since established acceptable methods for its handling and use. Secondly, the discovery of its complex with dioxane has led to widespread research on this new approach to modifying the high reactivity of sulfur trioxide in reactions with a variety of organic compounds. Recent study of the older sulfur trioxide-pyridine complex likewise has shown new or broadened uses for it in sulfating dyes, carbohydrates, and sterols, and for sulfonating polycyclic compounds and acid-sensitive heterocyclics. In addition, greatly increased commercial production of certain sulfonates, especially surface active agents and ion-exchange resins, has resulted in a corresponding increase in interest in the stronger, and possibly more efficient, reagents-particularly sulfur trioxide itself.

The chemistry of SO_3 is complicated and only partially known. It exists in the monomeric and in several polymeric forms. The vapor appears to be monomeric. Freshly distilled SO_3 is a water-white liquid, indicated by Raman spectral analysis to comprise approximately 90% of the trimeric, or γ -form (formula I), and 10% monomer¹ or, as reported by others² 20% trimer and 80% monomer.



I



II

If the freshly distilled liquid is exposed to even trace of moisture, or is kept standing in a sealed ampoule at room temperature for a short time, it reverts to solid polymers of various possible chain lengths (formula II) and degrees of cross linking and with correspondingly varied physical properties. Although solid SO_3 has been used to a minor extent in the laboratory for making complexes, and for conversion to SO_3 vapor by heating, it has not been considered a commercially practical compound because of its variability, difficulty in handling, and the high increase in vapor pressure occurring during vaporization.³

1.2. Sulfur Trioxide Complexes:

Sulfur trioxide, being an electron acceptor or Lewis acid, combines with electron donors or Lewis bases, to form coordination compounds, also known as "adducts" or "complexes." The bases employed may be tertiary amines-including those which are fairly strong (*i.e.*, trimethyl- or triethylamines), or considerably weaker (pyridine or dimethylaniline).

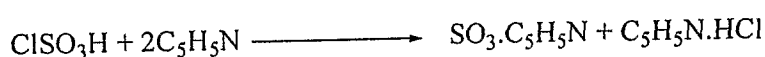
Other even weaker bases used include tertiary amides, ethers and thioethers. The stability of the complex in general varies directly as the strength of the base used. Correspondingly, the reactivity of the complex varies inversely as the strength of the base used. When the adduct is employed for sulfonating an organic compound, the SO_3 is released and the base forms the salt of the new sulfonic acid. Even the weakest complex is a much milder reagent than free SO_3 . It is possible to moderate the reactivity of SO_3 to any desired degree by the correct choice of a complexing basic material.

Basic strength is not the only factor determining the reactivity of an SO_3 complex, however. Trimethylamine, although equal in basic strength to triethylamine, yields a complex which is more stable and less reactive.⁴

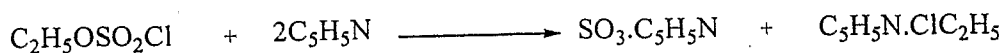
1.3. Sulfur Trioxide-Pyridine:

This complex often has been prepared by direct reaction of SO_3 with the base. A 90% yield was noted by adding pyridine to solid SO_3 suspended in carbon tetrachloride.^{5,6} A quantitative yield of the theoretical assay was obtained with chloroform as solvent.⁷ Addition of pyridine in 1,2-dichloroethane at 0°C to SO_3 dissolved in the same solvent gave a 95% yield.⁸ The Soviet investigator, A. P. Terent'ev, who has worked extensively with this adduct, adds equivalent dry pyridine, with cooling and stirring, to SO_3 in 1,2-dichloroethane; the product is filtered and dried rapidly at 100°C .⁹ Addition of liquid SO_3 to pyridine gives a product of 87% purity.¹⁰ Sulfur trioxide can be vaporized into pyridine.¹¹ The complex also has been prepared by bringing together the two components in equivalent quantities without a solvent, either in a heavy-duty mixer below 20°C ,¹² or as finely divided mists or vapors entrained in dry air.^{13,14}

Reaction of pyridine with ClSO_3H immediately yields SO_3 -pyridine and a mole of pyridinium chloride.^{5,15,16}



Sulfur trioxide and ClSO_3H are reported to form adducts of the same purity (about 92%) and melting point (97 to 100°C).¹⁷ Heating dry sodium pyrosulfate with pyridine for 30 minutes at 95°C also yields the complex.¹⁸ Potassium pyrosulfate, either anhydrous at 115°C ,¹⁹ or in cold aqueous solution²⁰, can also be used. Ethyl chlorosulfonate forms the adduct.^{5,16}



The pyridine complex is a white solid variously reported to melt at 97 °C to 100,¹⁷ 121,⁷ 137,²¹ 155,¹⁶ and at 175°C.⁵ These data all refer to various preparations of crude product, since no method for purifying SO₃-pyridine has as yet been suggested, aside from trituration with ice water to remove pyridinium sulfate.⁵ The lack of purification methods is explainable by its salt-like character, with its consequent low volatility and low solubility in nearly all common solvents, as mentioned below. It is quite stable to, and insoluble in, cold water and cold aqueous alkali, but rapidly decomposes completely upon warming in both media.⁵ It is insoluble (i.e., less than 1% by weight) in pyridine, nitrobenzene, cyclohexane, methylcyclohexane, n-hexane, chloroform, carbon tetrachloride, dioxane, diethyl ether, n-butyl benzenesulfonate, and acetone at 25°C.¹⁰ It is soluble in dimethylformamide,²² and forms at least a 20 weight % solution in liquid SO₂ at -10°C.²² The complex also dissolves in concentrated sulfuric, perchloric, and hydrochloric acids,²³ from all of which it can be precipitated unchanged by dilution with cold water. Sulfur trioxide-pyridine has been used extensively as a laboratory reagent for sulfating alcohols, sterols, and carbohydrates, for sulfamating amines and proteins, and for sulfonating acid-sensitive heterocyclic compounds and alkadienes; these reactions are run at moderate temperatures, usually below 120°C in the presence of excess pyridine or a solvent such as 1,2-dichloroethane. It has been used for sulfating on a semi-micro scale.²⁴ Even upon prolonged heating at 150°C, this complex does not react with paraffins, cycloparaffins, non-terminal olefins, benzene and its homologs, stilbene, anthracene, fluorene, or triphenylethylene.²⁵ Slow reaction occurs with terminal olefins, resulting in a poor yield of sulfonates. At 170°C, it sulfonates naphthalene, phenol, and aniline,²⁶ but these reactions can be effected more

rapidly with other cheaper reagents. It has been used somewhat commercially for sulfating oleyl alcohol and the leuco forms of vat dyestuffs.

Pyridine also forms a complex with two moles of SO_3 . It has been prepared by the addition of SO_3 to pyridine dissolved in liquid SO_2 ,²⁷ or by the addition of SO_3 to SO_3 -pyridine suspended in 1,2-dichloroethane.²⁸ The second mole of sulfur trioxide is much more reactive than the first. Work with this adduct has been very limited; the Soviet group headed by A. P. Terent'ev has employed it for sulfonating heterocyclic compounds. The complex is designated herein as "2 SO_3 -pyridine."

1.4. Applications of Sulfur Trioxide-Pyridine Complex

1.4.1. Reaction with Alcohols:

Ethanol²⁶ and 2-butanol²⁹ react with SO_3 -pyridine at 25°C in an hour or less to give good yields of the sulfates. Optically active 2-butanol also has been sulfated with the same reagent in 1 hour at 100°C in 90% yield,³⁰ with retention of optical purity and configuration. Alcohols from oxidized petroleum fractions have been sulfated semi-commercially with SO_3 -pyridine at 50 to 95°C using a 30-minute reaction time.³¹

1.4.2. With Sterols:

A ternary solvent mixture (benzene, pyridine, and acetic anhydride) is reported to give quantitative sulfation using SO_3 -pyridine at 50 °C to 60°C in 20 minutes with cholesterol, ergosterol, and lanosterol.³² Sulfation on a semi-micro scale is effected by heating with SO_3 -pyridine in excess pyridine for two minutes.