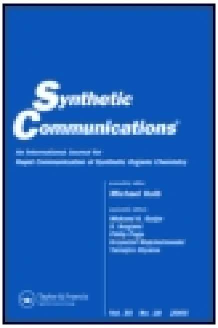

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Reaction of Enol Ethers with Lead Tetraacetate: An Improved Method for the Synthesis of α-Methoxy Ketones

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REACTION OF ENOL ETHERS WITH LEAD TETRAACETATE : AN IMPROVED METHOD FOR THE SYNTHESIS OF α-METHOXY KETONES[#]

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Abstract : The reaction of cyclic enol ethers with lead tetraacetate in methanol in the presence of $BF_3.Et_2O$ at 0°C gives α- methoxy cyclic ketones.

Introduction of a methoxy group at the α- position of carbonyl compounds has been the subject of many investigations. Anodic oxidations of enol ethers[1], enamines[1] and enol acetates[2]; reactions of α- diazoketones with methanol in the presence of BF3.Et2O; displacement of the halo atom in a-halo ketones[3]; thallium nitrate mediated oxidative methoxylations of ketones[4]; and reaction of silyl enol ethers and enamines with MeOF[5] are some of the many reported methods. Moriarty etal. have widely investigated the oxidative transformations of ketones and their silyl enol ethers using phenyl iodosobenzene to prepare α- methoxy and other derivatives[6]. Lead tetraacetate has also been reported to yield α- methoxy ketones in the reaction of

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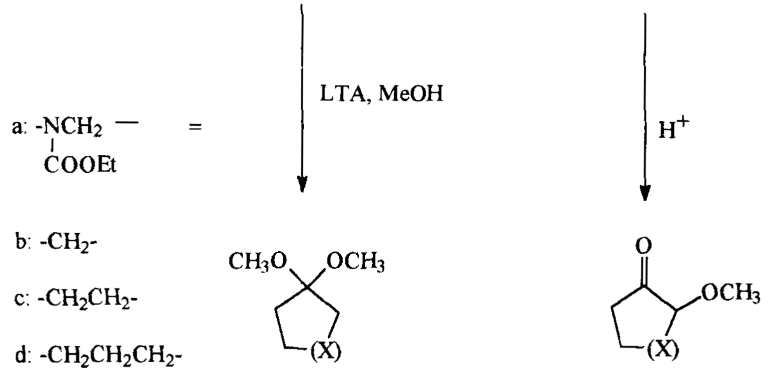
[#] Communication No 5664 from Central Drug Research Institute, Lucknow trimethylsilyl enol ethers[7]. The major drawback of this procedure is the formation of the corresponding α- acetoxy ketones as a major side product. We now report that the reaction of methyl enol ethers in methanol with lead tetraacetate in the presence of $BF_3.Et_2O$ gives α- methoxyketones exclusively.

Thus the methyl enol ethers of some representative cyclic ketones were prepared following the reported protocol [8] using trimethyl orthoformate. Reaction of the methanolic solution of these enol ethers (**I**) with lead tetraacetate in the presence of $BF_3.Et_2O$ gave the α- methoxy dimethyl acetals (**IIa-d**) [9a]. It is interesting to note that a similar reaction in the absence of $BF_3.Et_2O$ did not result in the formation of the desired product **IIa**, and instead the corresponding dimethyl acetal **IIIa** was obtained.



Ia-d **IIa-d** **IIIa**

The reaction mixture of the lead tetraacetate reaction can be directly treated with dilute sulfuric acid to yield the α– methoxy ketones or can be isolated and converted in a separate reaction to the corresponding ketones[9b].

Though it is difficult to define the exact role of $BF_3.Et_2O$ in this reaction, we speculate that $BF_3.Et_2O$ generates HF in methanol which keeps the acetate moiety, generated during the course of the reation, protonated thereby minimising the formation of α-acetoxy compounds.

Typical Reaction procedure

The enol ether **Ia** (18.5g, 100 mmol) was dissolved in anhydrous methanol (250 ml) in a 500 ml round bottommed flask and cooled to 0°C using an ice bath. Lead tetraacetate (88.6g, 200 mmol) was added in portions followed by the addition of BF_3Et_2O (42.6g, 300 mmol). The contents were magnetically stirred at 0°C and for additional 2hr at room temperature . Cold 5% dil. sulfuric acid (150 ml) was then added to the reaction mixture under magnetic stirring. The contents were stirred for 1hr, concentrated partially and poured on to ice cold water (500 ml) . The compound was extracted with CH_2Cl_2 (4x200ml) , the organic layer washed successively with water, dil. sodium bicarbonate,and water, dried (Na_2SO_4) and concentrated. The concentrate was fractionally distilled using an efficient Vigreux column to give the required α- methoxy ketone .

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9. (a) We were not able to affect the complete conversion of the intermediate acetals to the enol ethers and varying ammount of the acetal (5 - 15%) was always

present as contaminant in the enol ethers even after careful fractional distillation.

(b). The reported yields of the α- methoxyketones take into consideration the dimethyl acetal content of the enol ether and have been calculated on the basis of either gas chromatographic data or on the PMR basis. The reason for the low yields may be the facile conversion of **I** to **III** under acid catalysis.

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