SYNTHESIS OF 1,4-DICARBONYL COMPOUNDS BY THE CERIC AMMONIUM NITRATE PROMOTED REACTION OF KETONES WITH VINYL AND ISOPROPENYL ACETATE

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<u>Summary</u>: 1,4-diketones and 4-ketoaldehydes dimethylacetals can be prepared in good yields (65%-82%) by the cerium(IV) ammonium nitrate promoted reaction of ketones with isopropenyl acetate and vinyl acetate, respectively.

In recent years the addition of carbonyl compounds to alkenes promoted by one electron oxidants has attracted the attention of several research groups as a very efficient method for the synthesis of a variety of compounds (eq. 1, where M^{n+} is a metal ion and X^{-} is a ligand or a nucleophile present in the medium).¹ The reactive species is most probably an

$$\operatorname{RCOCH}_{3} + 2 \operatorname{M}^{n+} + x^{-} + \operatorname{CH}_{2} = \operatorname{CHR}' \xrightarrow{} \operatorname{RCOCH}_{2} \operatorname{CH}_{2} \operatorname{CHXR}' + 2 \operatorname{M}^{(n-1)+}$$
(1)

 α -ketoalkyl radical (in some case still bonded in some way to the metal²) which forms in the reaction of the carbonyl compound with the oxidant. This radical attacks the alkene to give another free radical species which is further oxidized by the metal into the final addition product. One of the most interesting applications of this process is due to Dessau and Heiba. These authors, in one of their pionering works on the subject, have carried out the one step synthesis of 1,4-diketones by reacting a ketone with isopropenyl acetate in the presence of Mn(OAc)₃.³ The yields were however quite modest, in the 20-35% range. Moreover, with 2--alkanones practically no regioselectivity was observed.

We wish now to report that this kind of synthesis can be made much more efficient and its scope enlarged when $Mn(OAc)_3$ is replaced by cerium(IV) ammonium nitrate (CAN) as the one electron oxidant. Much higher yields are observed and moreover the reaction can also be used for the synthesis of 4-ketoaldehydes dimethylacetals by replacing isopropenyl acetate with vinyl acetate. Another significant advantage of CAN reactions with respect to those promoted by $Mn(OAc)_3$ is the regiospecificity with 2-alkanones. 5358

<u>Synthesis of 1,4-diketones</u>. CAN (10 g) is dissolved in a mixture made up by MeOH (40 mL) and the reacting ketone (20 mL) containing 5 mL of isopropenyl acetate. After disappearance of the CAN colour (20-25 min at room temperature) a solution of NaHCO₃ (1.5 g) in 25 mL of H_2O is added and the mixture heated at 40°C for <u>ca.</u> 45 min under strong stirring. After cooling the mixture is poured into water and extracted with CHCl₃. The organic phase is evaporated and the product separated by vacuum distillation after removing of MeOH and the unreacted ketone.

Synthesis of 4-ketoaldehyde dimethylacetals. For the cyclic ketones the procedure was the same than that described for 1,4-diketones except that vinyl acetate was used in the place of isopropenyl acetate and that a suspension of NaHCO₃ (0.3 g) in 50 mL of MeOH was added at the end of the reaction. The resulting mixture was refluxed for 2.5 h and then worked up as above. With acyclic ketones (which compete with vinyl acetate for CAN less efficiently than cyclic ketones) it was necessary to use a greater ketone: vinyl acetate ratio. Thus for these compounds CAN was dissolved in a mixture made up by 50 mL of ketone, 10 mL of MeOH and 5 mL of vinyl acetate. The procedure was then the same as in the other cases. All results are collected in the table.

Carbonyl compound	Product, yield (%) ^a	
	Reaction with MOAC	Reaction with AOAc
Y o	O Me O Me O Me 70	
\sim	O Me 73	74
Å	O Me 77	70
Å	O Me 69	65 0
Meo	MeO O Me MeO O Me O Me	Me O O O 82

TABLE. The CAN-Promoted Reaction of Carbonyl Compounds with Vinyl and Isopropenyl Acetate

 ⁽a) Yield of isolated product calculated with respect to CAN. All the known products had NMR and mass Spectra in agreement with literature data. The unknown compounds (the products from dimethyl malonate, and the diketone derived from cyclopentanone) had the expected spectra and correct C,H analyses.

The yields are quite good ranging from 65 to 82%, with most of them over 70%; with 2-butanone the reaction is practically regiospecific affording, with both isopropenyl and vinyl acetate, only the product involving attack from the more substituted side of the ketone

Acetone is too slow to react, but the reaction can satisfactorily be extended to a dicarbonyl compound like dimethyl malonate, using MeOH is the solvent (last entry in the Table).

In this reaction the first formed product is the nitrate adduct (1) $\stackrel{5}{\sim}$ whose formation is easily rationalized on the basis of the equations 2 and 3 (R and R' = alkyl, R" = alkyl, H).



Thus, heating of the reaction mixture with water or methanol has been carried out to convert 1 into the final products as shown in the scheme.



Attempts to extend this reaction to 2-alkyl substituted vinyl acetates failed when a ketone was used as the carbonyl reactant. In contrast, the reaction was succesful with 1,3-dicarbonyl compounds. Thus from dimethyl malonate and 1-heptenyl acetate 70% yield of 2 was obtained.



This observation further widens the scope of the process, and in this respect it is interesting to note that with $Mn(OAc)_3$ the enol acetates do not undergo any oxidative addition, no even when dicarbonyl compounds are used.^{la}

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- 4. An attempt was carried out to get free aldehydes in the place of the acetals by running the reaction in ketone water mixtures. However the reaction was slower and the yields very poor. Some improvement was observed when the reaction was run in a solvent made up by 50 mL of ketone and 5 mL of MeOH, a solution of NaHCO₃ in water was added at the end of the reaction and the mixture refluxed for 30 min. Under these conditions it was possible to prepare the free 4-ketoaldehydes, albeit in modest yields (25-40%).
- 5. At the end of the reaction the unreacted ketone is removed under vacuum and the residue is extracted with CHCl₃. Removing CHCl₃ a product is obtained which has been assigned the structure of 1 by NMR analysis.

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