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Dehydrogenation of Carboxamidoenamines with Manganese Acetate and Copper Acetate

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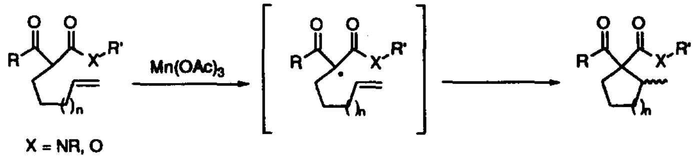
Key words: *Carboxamidoenamines, oxidation, manganese acetate, α,β-unsaturated imines, α,β-unsaturated ketones, substituted aniline derivatives.*

Abstract: *Imine radicals or enamine radicals generated by manganese acetate [Mn(OAc)3] or copper acetate [Cu(OAc)2] can be oxidized by the same metallic salts to produce α,β-unsaturated imines or α,β-unsaturated enones in good yields.*

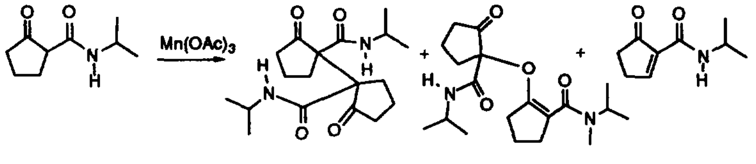
The oxidation of ketoesters[1] and of β-ketoamides[2] by manganese acetate [Mn(OAc)$_3$] produces free radicals. These radicals can react with olefins either intermolecularly to produce the addition products, or intramolecularly (Scheme 1) to produce the corresponding cyclized products.

Scheme 1



In the absence of olefins or of an alkene substituent, the oxidation of ketoesters by Mn(OAc)$_3$ leads to the formation of C-C dimers and C-O dimers [3]. The same behaviour has been observed with N-alkyl-β-ketoamides **1**, which gave the corresponding dimeric compounds **2** (25%) and **3** (47%) together with small amounts of enone **4** (4%). (Scheme 2).

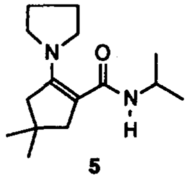
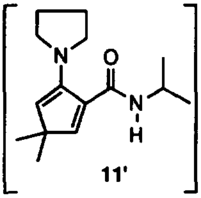
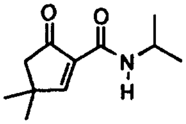
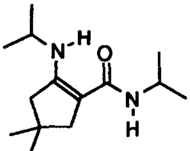
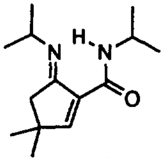
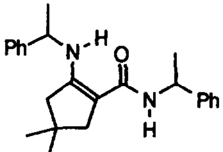
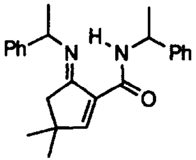
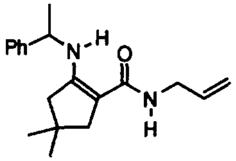
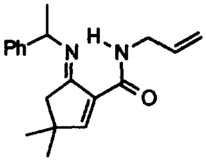
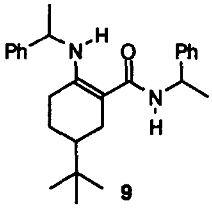
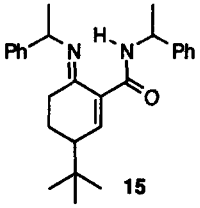
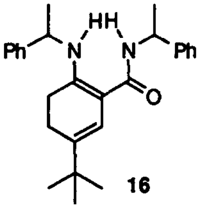
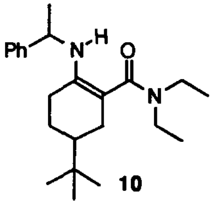
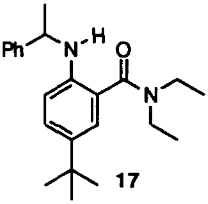
Scheme 2



1 2 3 4

Here we would like to report that when enamines of β-ketoamides are oxidized by Mn(OAc)$_3$ or Cu(OAc)$_2$, the dimerization process is suppressed. Depending on the starting material, unsaturated imines, unsaturated ketones (derived from unsaturated enamines by hydrolysis), or aromatic compounds are obtained in good yields (Table). The recent report by Schultz et al.[4] concerning the dehydrogenation of β-ketoesters and β-ketoamides prompt us to unveil our results.

TABLE: Oxidation of carboxamidoenamines by metallic salts

Enamines	Products	Mn(OAc)$_3$ Yield %	Cu(OAc)$_2$ Yield %
 5	 11'  11	57 (11)	69 (11)
 6	 12	65	68
 7	 13	86	79
 8	 14	74	65
 9	 15  16	72 (15) 5 (16)	- -
 10	 17	67	-

When enamine **5** was treated with 2 equivalents of $Mn(OAc)_3$ or 2 equivalents of $Cu(OAc)_2$, the enone **11** was the sole product isolated in yields up to 55%. The enamine **11'** was detected in the crude reaction mixture by NMR (^1H NMR and ^{13}C NMR spectra). Attempts to isolate this minor compound were not successful.

Unsaturated imines **12-13** were obtained when the corresponding N-alkyl-β-carboxamidoenamines **6-7** were treated with $Mn(OAc)_3$ or $Cu(OAc)_2$. The hydrolysis of these imines with aqueous acetic acid (50%) led to the corresponding enones in quantitative yield. We have to point out that, contrary to the oxidation of unsaturated N,N-dialkyl-β-carboxamidoenamines[5], no cyclized products were detected when the enamine **8** was treated with Mn(III) or Cu(II) salts. The extension of this reaction to 6-membered ring β-carboxamidoenamines **9** and **10** was realized. The oxidation of **9** with two equivalents of $Mn(OAc)_3$ or $Cu(OAc)_2$ allowed isolation of the imine **15** (72%) and the diene **16** (5%), after chromatography on alumina. When the purification was performed on silica gel, **16** was the only product isolated. It thus appears that under slighly acidic conditions **15** was transformed into **16**. When **10** was treated with 2 equivalents of Mn(III) or Cu(II) the aromatic compound **17** was isolated in a yield of 51%, together with ca. 30% of unreacted starting material. When 3 equivalents of $Mn(OAc)_3$ were used, the conversion of **10** was complete, and **17** was obtained in a 67% yield.

The formation of the unsaturated ketone **11**, of the unsaturated imines **12-15**, and of the aromatic compound **17** can be interpreted in terms of electron transfer between the metallic salts and the enamines (Scheme 3).

Complexation of enaminocarboxamides with metallic salts (M^nX) is expected to produce complexes of type **A**. Electron transfer (ET_1) can occur between M^nX and the enamine producing cation radicals of type **B** – **B'**. These intermediates can then undergo deprotonation, generating the free-radical **D** or **D'**. In radicals **D** and **D'** (R_1 = H, R_2 = alkyl) intramolecular hydrogen bonding between the two nitrogen atoms is possible. **D** or **D'** can then be oxidized by a second equivalent of M^nX (ET_2) to produce the cations **E**, **E'**, respectively, the deprotonation of which leads to the corresponding unsaturated imines or enamines. In the six-membered ring derivatives the unsaturated imine can isomerize into a diene which can be isolated in the case of the oxidation of **9**. Alternatively, the cyclohexadiene **F''** (R_1 = alkyl, R_2 = alkyl), which comes from the isomerization of enamine **F'**, can undergo another electron transfer (ET_3) and can be transformed to an aromatic compound as is observed in the case of the oxidation of **10** into **17**.

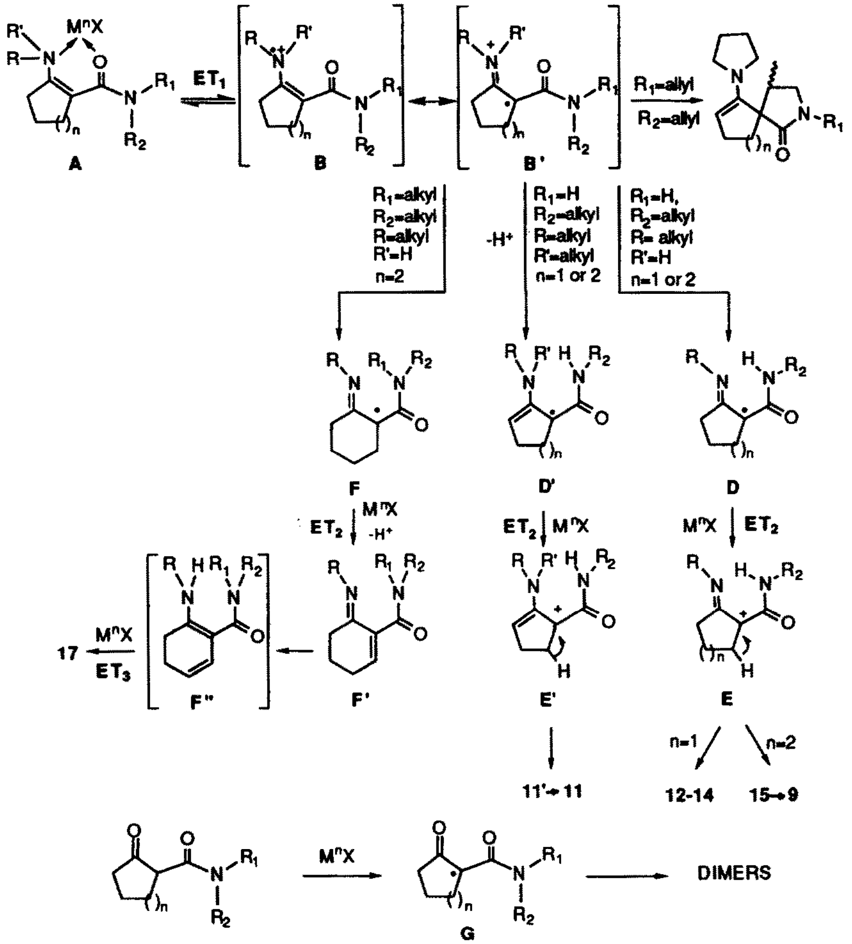
The absence of cyclized products during the oxidation of **8** by metallic salts is probably due to unfavorable conformations made rigid by intramolecular hydrogen bonding.

In the case of β-ketoamide **1** a second electron transfer to **G** is probably a slow process. It may be retarded because of the electronegativity of the ketone moiety. The radical **G** can react with a second molecule of β-ketoamide to produce **2** and **3**.

Our study has revealed that Mn(III) and Cu(II) oxidation of carboxamidoenamines can lead easily and efficiently in a one step procedure to α,β-unsaturated imines, ketones or substituted anilines.

Experimental part: A solution of $Mn(OAc)_3$ or $Cu(OAc)_2$ (2 equiv) in ethanol (5×10^{-2} M) was added to a solution of enamine (1 equiv) in ethanol (5×10^{-2} M). After stirring for 20 min at 20° C[6] [when $Mn(OAc)_3$ was used] or heating under reflux for 20 min when [$Cu(OAc)_2$ was used], the ethanol was evaporated. The crude reaction mixture was diluted with ethyl acetate, filtered on Celite, evaporated, and purified by flash column chromatography on alumina.

Scheme3



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