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Sonochemical Lactonization of Olefins with Ceric Ammonium Nitrate and Monomethyl Ester of Malonic Acid

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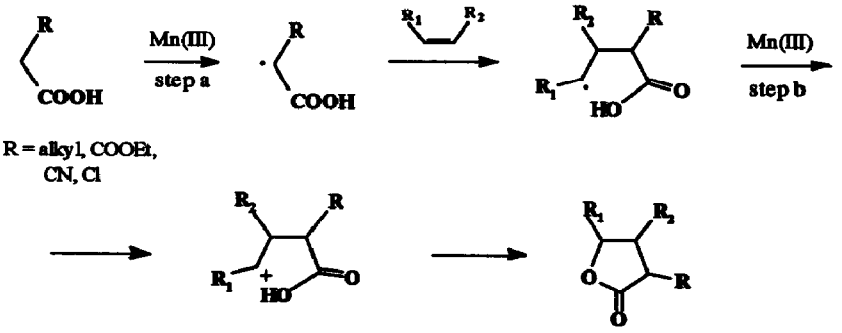
Abstract *- Lactonization of olefins with monomethyl ester of malonic acid and ceric ammonium nitrate was carried out in acetic acid and in acetonitrile under simple mechanical stirring or ultrasound irradiation. Comparative results are reported; for activated olefins a good ultrasonic acceleration was observed.*

Lactonization of olefins promoted by $Mn(OAc)_3$ is a widely used methodology of one-step synthesis of γ-lactones.[1] From a mechanistic point of view, two single electron transfer (SET) steps are involved (see Scheme 1) i.e. the generation of carboxyalkyl radical (step a) and the oxidation to carbocation of the radical adduct formed by addition of the initial radical to olefinic double bond (step b).

Scheme 1

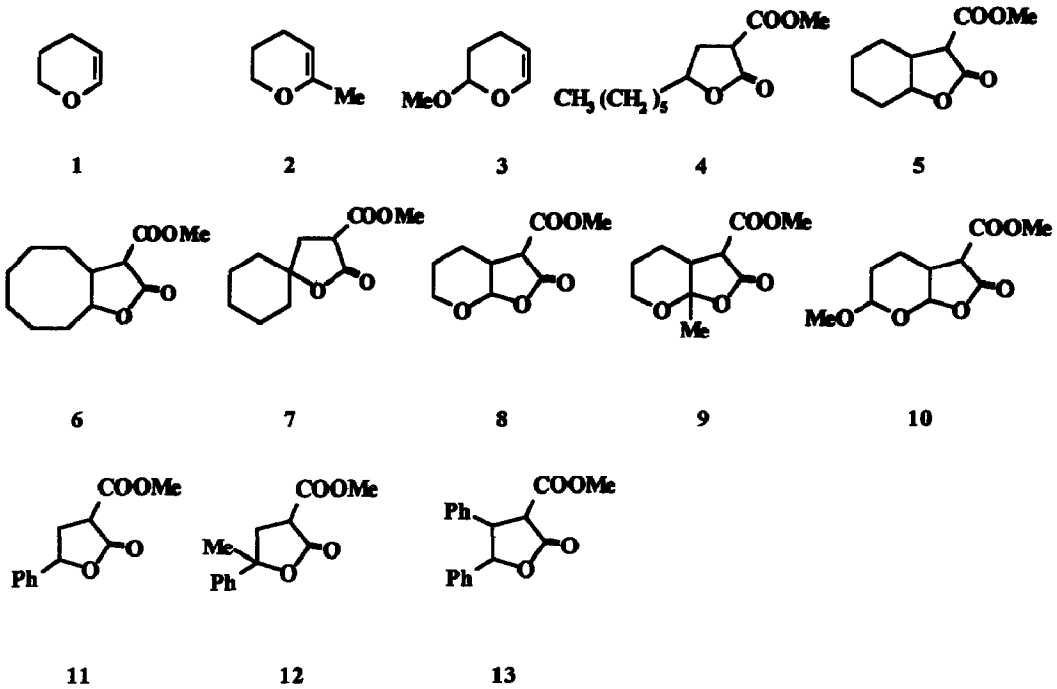


Since electron transfer processes are stimulated by ultrasounds,[2] we have recently studied this reaction under ultrasound irradiation at low temperature. As described in a previous paper,[3] we obtained α-substituted γ-lactones in very short reaction times and in good yields, in most cases higher than those reported in the corresponding "silent" reactions[1] on the same substrates.

These results prompted us to investigate the existence of an ultrasonic improvement of the lactonization process in presence of other transition metal oxidant species. Ceric ammonium nitrate (CAN) is an efficient SET

reagent in various solvents, and it is widely used to generate α-carbonyl alkyl radicals from carbonyl compounds or other easily enolizable species.[4] Nevertheless, only one example of its use in lactonization reactions of alkenes at high temperature is reported.[5]

We started this research studying the efficiency of CAN in the synthesis of α-carbomethoxy γ-lactones from olefins. The first experiments were carried out in acetic acid as solvent using CAN, alkene, and monomethyl ester of malonic acid in a 4:1:5 molar ratio and keeping for two hours the reaction mixture under ultrasound irradiation at 5-10°C or simple mechanical stirring at room temperature. In both these conditions a large amount of side products was observed, probably due to side oxidation processes of radical adduct. This was avoided by adding to the reaction mixture one equivalent of $Cu(OAc)_2$, which is a fast oxidizer of secondary alkyl radicals to carbocations.[6]



As shown in Tab. 1 simple alkyl olefins afforded low to modest yields of γ-lactones in the selected reaction time, while an ultrasonic acceleration could be excluded. With more polar olefins, we had modest to good yields that were enhanced of a 10% or more using sonochemical procedure.

The trend of the reaction in acetonitrile was the same, with a good ultrasonic acceleration for activated olefins. Moreover, simple and acetalic enol ethers underwent the lactonization reaction successfully. This is an important result because the lactonization reaction with Mn(III) in acetic acid was not suitable for these acid sensitive substrates ; furthermore, the particular structure of these lactonization products make them important intermediates in synthesis of fused acetal structures, highly occurring in chemistry of bioactive compounds.[7]

In a typical experimental procedure, 2 mmol of olefin were added to a solution of potassium salt of monomethyl ester of malonic acid (0.9 g, 5.1 mmol) in 30 ml of solvent under an inert atmosphere; then CAN

(2.2 g, 4.0 mmol) was added (plus $Cu(OAc)_2$ (0.4 g, 2 mmol) if the reaction was carried out in acetic acid) and the resulting suspension was stirred at room temperature or sonicated with a probe transducer (equipped with a titanium microtip operating at 200 W/cm^2) in an ice-bath for two hours. Acetonitrile was evaporated under reduced pressure, water (100 ml) was added to the residue and the resulting mixture extracted with CH_2Cl_2 (3x50 ml); the organic phase was then removed "in vacuo" and residue was chromatographed on silica gel with CH_2Cl_2 to afford pure α-carbomethoxy γ–lactone. For reactions carried out in acetic acid, the reaction mixture was poured in water (100 ml), and extracted with CH_2Cl_2. The organic phase was then washed with a saturated $NaHCO_3$ solution (3x50 ml), then with water and finally dried with Na_2SO_4. Removal of the solvent "in vacuo" gave a residue which was chromatographed with CH_2Cl_2 on silica gel to afford pure α-carbomethoxy γ-lactones.

Table 1- Lactonization Reaction of Alkenes with Monomethyl Ester of Malonic Acid and Ceric Ammonium Nitrate

Alkene	Product	acetonitrile Yields[a] (%)		acetic acid Yields[a] (%)		Reaction time (hrs)
		[b]	[c]	[b]	[c]	
1-Octene	4	25	20	8	9	2
Cyclohexene	5	15	25	12	22	2
Cyclooctene	6	34	32	20	23	2
Methylene-cyclohexane	7	43	41	15	21	2
1	8	58	84	55	65	2
2	9	-	-	28	51	2
3	10	73	81	-	-	2
Styrene	11	15	52	38	50	2
α-Methyl Styrene	12	30	49	41	51	2
trans-Stilbene	13	39	58	35	55	2

a) All yields refers to isolated, pure products.
b) Reaction carried out at room temperature under simple mechanical stirring.
c) Reaction carried out at 5-10°C under ultrasound irradiation.

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