

CARBOLACTONIZATION OF OLEFINS UNDER MILD CONDITIONS BY  
CYANOACETIC AND MALONIC ACIDS PROMOTED BY MANGANESE (III) ACETATE

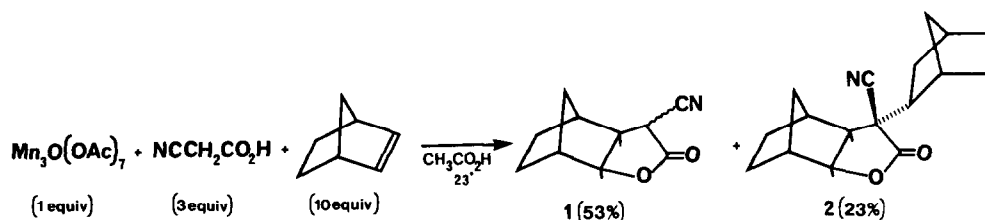
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**Summary:** A variety of olefins can be converted to  $\gamma$ -lactones with good efficiency by intermolecular carbolactonization using cyanoacetic acid or malonic acid derivatives in the presence of Mn (III) at 23°.

The formation of  $\gamma$ -lactones from the reaction of olefins and manganese (III) acetate in acetic acid at reflux, formally the cycloaddition of  $-\text{CH}_2(\text{C}=\text{O})\text{O}-$  to a double bond, has been used in synthesis only sporadically partly because of the vigorous conditions required.<sup>1</sup> Recently a mild and efficient intramolecular version of this process has been described involving the concurrent formation of two rings starting from an olefinic  $\beta$ -keto acid.<sup>2</sup> It was demonstrated that electron withdrawing groups alpha to the carboxylic acid function accelerate the carbolactonization sufficiently to allow rapid reaction at 25° or below. Reported herein are the results of studies aimed at enhancing the utility of the intermolecular Mn (III)-promoted carbolactonization reaction by the use of more reactive carboxylic substrates, cyanoacetic acid, ethyl hydrogen malonate, and ethyl hydrogen chloromalonate. These substrates can serve as reactive equivalents of acetic acid in carbolactonization.


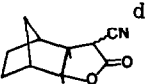

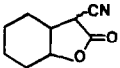

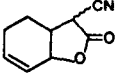

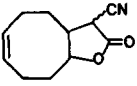
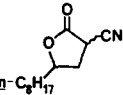
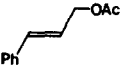
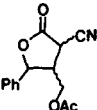
Cyanoacetic acid reacts rapidly with Mn (III) and olefins at room temperature to form  $\alpha$ -cyano  $\gamma$ -lactones.<sup>2,3</sup> A detailed study of this reaction with norbornene revealed that using excess norbornene and cyanoacetic acid at 23°, the yield of cyanolactone 1 reaches a maximum in just 15 min because of a further reaction of 1 with Mn (III) and olefin to form 2, that reaction being sufficiently fast to produce



measurable amounts of 2 after a reaction time of 1-2 min. As shown in Table I excellent yields (based on Mn (III)) of  $\alpha$ -cyano lactones could be obtained with a variety of olefins in excess simply by monitoring the reactions and limiting reaction time. When only 1 equiv of olefin was utilized moderate yields of  $\gamma$ -lactone

were possible if the reaction time was limited.

TABLE I  
REACTION OF  $Mn_3O(OAc)_7$  WITH CYANOACETIC ACID AND OLEFINS


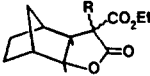

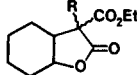

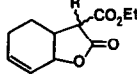

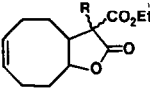
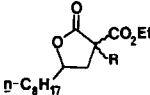

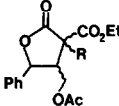
Olefin	Product	xs olefin <sup>a, c</sup> 1-3 hr	Yield xs olefin <sup>a, c</sup> 15 min	1 equiv <sup>b, c</sup> olefin, 15 min
		55 %	81 %	49 %
		51 %	79 %	57 %
		69 %	78 %	60 %
		54 %	82.5 %	55 %
$n-C_8H_{17}CH=CH_2$		—	85 %	55 %
		—	77 %	63 %

<sup>a</sup>Reaction of olefin (5-10 equiv),  $NCCH_2CO_2H$  (3 equiv) and Mn (III) acetate (1 equiv) in acetic acid at 23°; <sup>b</sup>Reaction of olefin (1 equiv),  $NCCH_2CO_2H$  (3 equiv), and Mn (III) acetate (2.4 equiv) in acetic acid at 23°; <sup>c</sup>Yields based on requirement of 2/3 mol equiv of  $Mn_3O(OAc)_7$  to produce 1 equiv of  $\gamma$ -lactone; <sup>d</sup>No  $\delta$ -lactone formation was detected by gas chromatography.

A parallel series of studies were carried out with ethyl hydrogen malonate, Mn (III) and various olefins in the hope that the further reaction of the  $\gamma$ -lactone resulting from carbolactonization would be less likely than for the corresponding cyanoacetic acid products. In addition it is apparent that  $\alpha$ -carboethoxy- $\gamma$ -lactones are more suitable for further synthetic elaboration than the corresponding cyano lactones. Ethyl hydrogen malonate is readily available from diethyl malonate by reaction with 1 equiv of potassium hydroxide in ethanol.<sup>4</sup> Reaction of manganese (III) acetate (2.2 equiv), ethyl hydrogen malonate (3-5 equiv) and various olefins (1 equiv) in acetic acid at 23° led to complete consumption of manganese (III) in 4-6 hr with the formation of the desired  $\alpha$ -carboethoxy- $\gamma$ -lactones. As expected, the further reaction of these  $\gamma$ -lactones with another molecule of olefin did not occur to a significant extent, making possible the higher yields recorded in Table II.

TABLE II

REACTION OF  $Mn_3O(OAc)_7$  WITH ETHYL HYDROGEN MALONATE AND VARIOUS OLEFINS

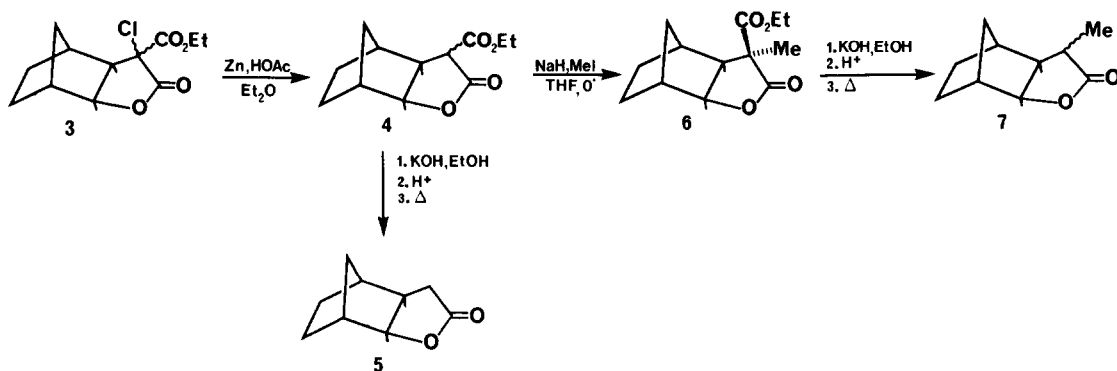
Olefin	Product	R = H <sup>a</sup>	Yield	R = Cl <sup>b</sup>
		73%		88%
		75%		< 5%
		76%		82%
		58% <sup>c</sup>		—
$n-C_8H_{17}CH=CH_2$		74%		40%
		78%		71% <sup>d</sup>

<sup>a</sup> Standard conditions: olefin (1 equiv),  $Mn_3O(OAc)_7$  (0.75 equiv),  $C_2H_5OOCCH_2COOH$  (3.5 equiv) in acetic acid at 23°; <sup>b</sup> Standard conditions: olefin (1 equiv),  $Mn_3O(OAc)_7$  (3.3 equiv),  $C_2H_5OOCCHClCOOH$  (5 equiv) in acetic acid at 23°; <sup>c</sup> In addition ca. 15% of bis adduct was obtained; <sup>d</sup> Yield was 91% based on recovered olefin.

The use of ethyl hydrogen chloromalonate as the carboxylic component in the carbolactonization of olefins was also investigated. Reaction of excess manganese (III) acetate and  $EtO_2CCHClCO_2H$  with norbornene (1 equiv) gave an 88% yield of the desired lactone. However, the use of the less reactive cyclohexene under these conditions gave only very poor yields. Whereas ethyl hydrogen malonate did not react appreciably with Mn (III) acetate in the absence of an olefin the ethyl hydrogen chloromalonate underwent rapid decarboxylation. Because of this competing reaction, only reactive olefins afforded good yields of the desired lactones (Table II) with the chloromalonate.<sup>5</sup>

The  $\gamma$ -lactones described above can be utilized in synthesis in a number of ways as illustrated for the case of chloro lactone 3. Treatment of 3 with zinc (5 equiv) in acetic acid (10 equiv) - ether at 23° afforded ester lactone 4 in 93% yield. Saponification of 4 followed by acidification and warming to 65° produced pure exo lactone 5 in 94% yield. Methylation of 4 to form 6 was effected using sodium hydride (1.2 equiv) and methyl iodide (2.5 equiv) in tetrahydrofuran at 0° for 1 hr. Saponification of 6 using ethanolic potassium

hydroxide followed by acidification and heating gave a mixture of the two methyl-epimeric exo lactones 7 in 82% yield.



The results described above show that the carbolactonization of olefins promoted by Mn (III) can be a useful synthetic process with a variety of olefins when suitable activated acetic acid equivalents such as ethyl hydrogen malonate are used. Preliminary studies carried out with dichloroacetic acid, benzenesulfonyl acetic acid and acetoacetic acid indicated that these substrates were less satisfactory. The first was unreactive at 23°, the second reacted only slowly at 40°, and the last reacted extremely rapidly at 0° but afforded major by-products.<sup>6</sup>

#### References and Notes

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- Ethyl hydrogen chloromalonate was prepared in 75% yield by the reaction of ethyl hydrogen malonate with chlorine (2 equiv) in methylene chloride at 23° until starting material has been consumed (tlc analysis using 10% methanol in ethyl acetate). The product is isolated by removal of methylene chloride, addition of water, storage at 23° for 6 hr (to allow decarboxylation of any dichloro acid), and isolation of the acidic product.
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