

Preparation of Methylcycloalkenyl Ketones. A Couple of Cycloalkanes with Acid Chlorides in the Presence of Aluminum Chloride

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2-Methylcycloalkenyl ketones are considered to be convenient synthetic blocks for various purposes such as dienophiles in the Diels-Alder reactions¹ and intermediates in the generation of quaternary center via organocuprate addition-alkylation sequences.² α - and γ -positions of this compound are also activated to be functionalized.³ α, β -Unsaturated ketones are easily accessible by various routes. However, α -exo-carbonyl- β -methylcycloalkenes are relatively rare entity. Such compounds were synthesized with cycloalkene with acid anhydride in the presence of zinc chloride.⁴ On the other hand, only limited preparation of such compounds has been known for some time.^{5,6} These methods are extended here to several acid chlorides and cycloalkanes. Even though yields are quite low for reasons, easy access, handy operations and cheapness of cycloalkanes make it attractive for large scale laboratory preparation.

Typical reaction procedure is as follows. Acid chloride (140 mmol) was added to aluminum chloride (70 mmol) in 70 ml of chloroform and the mixture was stirred for 10 min, at which time cycloalkane (70 mmol) was added. The mixture was heated at reflux for 2 hours and then allowed to stir for 2 days at room temperature. The mixture was poured onto ice/HCl mixture and the layers were separated. Aqueous layer was washed with methylene chloride and the combined layer was concentrated. The resulting material was dissolved in 30 ml of methanol, 3 grams of potassium hydroxide was added and the mixture was stirred for 2 hours. After removal of methanol the residue was dissolved in ether. The ethereal layer was washed with water and brine, dried, and concentrated. The reaction product was purified by distillation and (or) chromatography.

According to the mechanism proposed by Tabushi⁵ and Akhrem⁷ hydride ion abstraction from cycloalkane from acid chloride/aluminum chloride complex initiate the reaction to generate carbonium ion which undergoes further rearrangement to more stable tertiary ion. Then methylcycloalkyl carbonium ion is deprotonated to methyl cycloolefin at which stage the alkylation occurs. (Scheme) The acylated tertiary carbonium ion is deprotonated to give α, β - and β, γ -unsaturated acylated methylcycloalkene which was equilibrated to give more stable α, β -unsaturated product. Following this

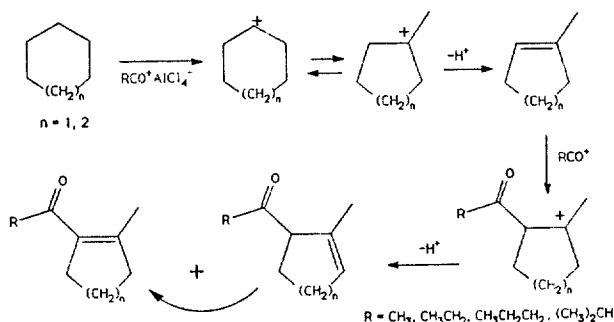




Table. Methylcycloalkenyl ketones from Cycloalkanes and Acid Chlorides in the presence of Aluminum Chloride

Cycloalkane	Acid Chloride	Yield ^{a,b} (%)
 n = 1	Acetyl	36
	Propionyl	35
	Butyryl	39
	Isobutyryl	42
 n = 2	Acetyl	23
	Propionyl	29
	Butyryl	33
	Isobutyryl	31

^aAll products were identified by IR, ¹H NMR, and mass spectra.

^bYields are based on purified products and have not been optimized.

procedure each of cyclohexane and cycloheptane with acid chloride gives 1-acyl-2-methylcyclopentene and 1-acyl-2-methyl cyclohexene. (Table) This mechanism was further supported by generation of 1-acetyl-2-methylcyclopentene from the reaction of methylcyclopentene with acetyl bromide in the presence of aluminum chloride.⁸ In case of cyclooctane the yield was too low to be used for synthetic purpose. Poor yield of this scheme is deemed to be mostly due to the condensation of various carbonium ions with olefins, indicated by lower boiling hydrocarbon and higher boiling by-products remained in the distillation residue.

In conclusion, we have found that this reaction is useful to obtain large amount of synthetically useful 1-acyl-2-methylcyclopentenes and cyclohexenes. Synthetic application of these compounds is under progress.

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