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SELENOESTERS IN ORGANIC SYNTHESIS. 2. SYNTHESIS OF α,β-UNSATURATED KETONES.

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Abstract. An efficient synthesis of α,β-unsaturated ketones based on reaction of alkenylcopper(1)reagents with selenoesters (or acylchlorides) has been elaborated.

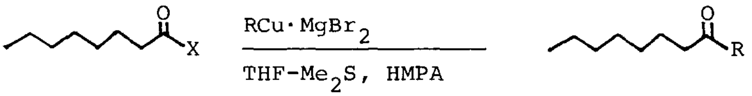
One of the most direct and convenient syntheses of ketones is based on reaction of organometallics with activated acyl derivatives. Unfortunately, there are only a very few examples of application of this approach to enone synthesis, namely reactions of alkenyl derivatives of magnesium[1], manganese[2], mercury[3] with anhydrides or chloroanhydrides of carboxylic acids, alkenyllithium reagents with carboxylic acid salts[4,5] and some specific cases of organocopper(1)reagents reactions with acyl halides[6] to produce the enones in fair to good yields.

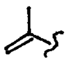
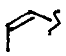
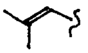
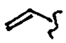
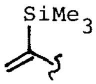
The considerable achivements in alkenylcopper(1)reagents synthesis by stereospecific carbometallation of acetylenes[6] make this compounds the most attractive candidates for α,β-unsaturated ketones synthesis. However, the reaction is contaminated with undesirable conjugate addition of organocopper(1)reagents to arising enones, particularly in cases of β-unsubstituted vinylketones.

We now wish to report the convenient and efficient synthesis of α,β-unsaturated ketones using organocopper(1)reagents.

Alkenylcopper(1)reagents were found to react with selenoesters in presence of HMPA to produce enones in excellent yield. Special investigation has shown that the critically important for success is amount of HMPA which not only increases the rate of process but also progressively suppresses the conjugate addition of alkenylcopper to arising enones. Actually, in presence of 5÷6 mol of HMPA per mol of alkenylcopper(1)reagent (generated in THF-Me_2S(1:1) mixture) the yield of conjugate addition product in most cases does not exceed 5 percent even at -10° and can be further decreased by lowering of reaction temperature. The results are presented in the Table.

Table



R	X	T °C	Time (hours)	Yield,%a)	Bp (torr)
	SeMe	-25	3	96	79-81° (2.5)
	Cl	"	5	87	
	SeMe	"	2	87	56° (1)
	Cl	"	4	82	
	SeMe	"	2	95	68-71° (1)
	Cl	"	2	89	
	SeMe	"	4	33	55-58° (2)
	Cl	"	4	62	
	SeMe	-50	2	96	78-82° (1.5)
	Cl	-50	3	85	

a) isolated yield; the yield determined by GLC in most cases is nearly quantitative.

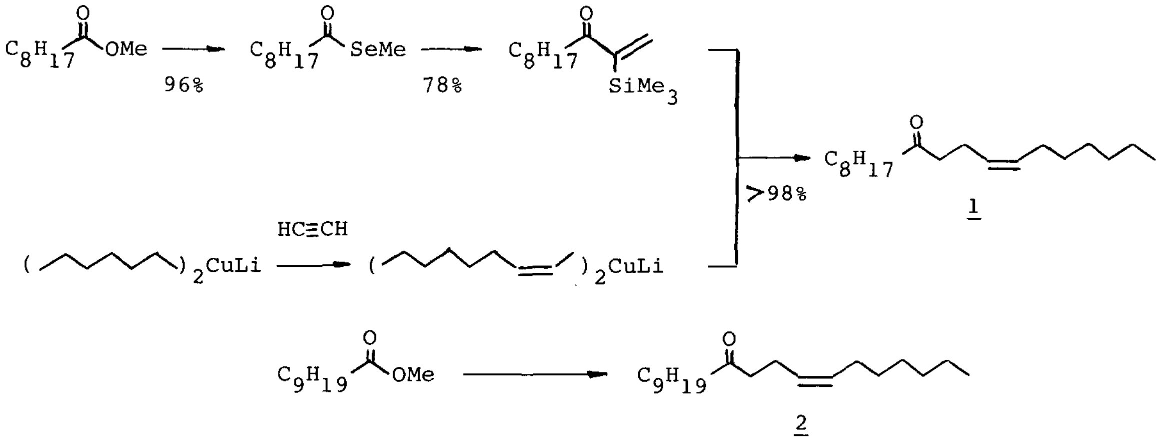
The choice of reaction temperature is a compromise between desired reaction rate and purity of enone obtained. In most cases temperature -(25÷30)° is suitable, exept for α-(trimethylsilyl)vinylcopper when reaction should be carried out at <-50° on account of a high tendency of α-(trimethylsilyl)vinylketones to undergo 1.4-addition. Acylchlorides also can be used as acyl transfer reagents, but selenoesters have the advantages in rate and purity of reaction.

General procedure. To a solution of 2.5 mmol of CuBr·Me$_2$S in Me$_2$S (2.5 ml) and THF (2.5 ml) cooled to -(45÷50)° (partial precepitation) was added 2.5 ml of 1.0 molar solution of alkenylmagnesium bromide in THF. The obtained dark (brown to black) mixture was stirred at this temperature for 10 min, and 2.5 ml of HMPA was introduced. After additional 10 min a solution of 2.0 mmol of selenoester (or acylchloride) was added and the mixture was stirred at appropriate temperature. After the reaction was complete (GLC control) reaction mixture was quenched by saturated NH_4Cl solution and participated between ether and aqueous ammonia. The mixture was filtered through celite, layers were separated and aqueous phase was extracted by ether. Combined ether extracts were washed with ammonia, water, brine and dried (Na_2SO_4). After removal of solvent the crude enone was purified by short-path distillation or by chromatography[8].

Alkenylcopper(1)reagents of various structural types can be employed in the reaction; the only exception is unsubstituted vinylcopper, probably due to its low solubility. In this case the yield of ketone is low, but use of acylchloride gives some improvement in this respect.

If the desired vinylketone must be used further as a Michael acceptor (conjugate addition,annelation) this difficulty can be overcame by the employment of α-(trimethylsilyl)vinylketones[7] easily synthesized by proposed method.

For illustration we reported synthesis of (Z)-12-nonadecen-9-one (1) and (Z)-13-eicosen-10-one (2), the components of the pheromone of peach fruit moth *Carposia niponensis*:



Selenoester obtained from methyl nonanoate ($Me_2AlSeMe$, Et_2O,r.t.,5 min) was converted into α-(trimethylsilyl)vinylketone (-60°,3 hrs) as described above. After chromatographic purification it was treated with (Z)-(octen-1-yl)cuprate[9] (Et_2O,-78°,5 min,quenching by KF/MeOH) to afford pure 1 (>99%,GLC) in nearly quantitative yield.

Compound 2 was synthesized similarly.

This synthesis of 1 and 2 seems to be superior over those published[10] due to high yields and garantied purity (>99.9%) of (Z)-configuration of a double bond[9].

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