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A NEW AND SHORT SYNTHESIS OF DEHYDROELSHOLTZIONE (NAGINATA KETONE) AND ISOEGOMAKETONE

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Summary : 1-Trimethylsilyl 2-methyl 1-propene and 1-trimethylsilyl 3-methyl 1-butene are useful intermediates for the synthesis of furan natural compounds such as Naginata ketone and isoegomaketone.

Since our previous discovery that the substitution of the Me_3Si group by an acyl moiety in vinylsilanes gave α-enones[1], several successful applications of this reaction have been reported by us[2] or others[3,4]. In the course of our investigations in this field, we now report the use of vinylsilanes as convenient intermediates in the synthesis of natural furano terpenic ketones having a side chain attached to the furan ring, either at the -2 or -3 position.

These compounds have been found to occur widely in the nature[5,6], and it was an interesting challenge to look for a new methodology founded on the easy electrophilic substitution of the trimethylsilyl group in vinylsilanes, likely for constituting further entry to more elaborated sesquiterpenes just by choosing the appropriate organosilicon substrate.

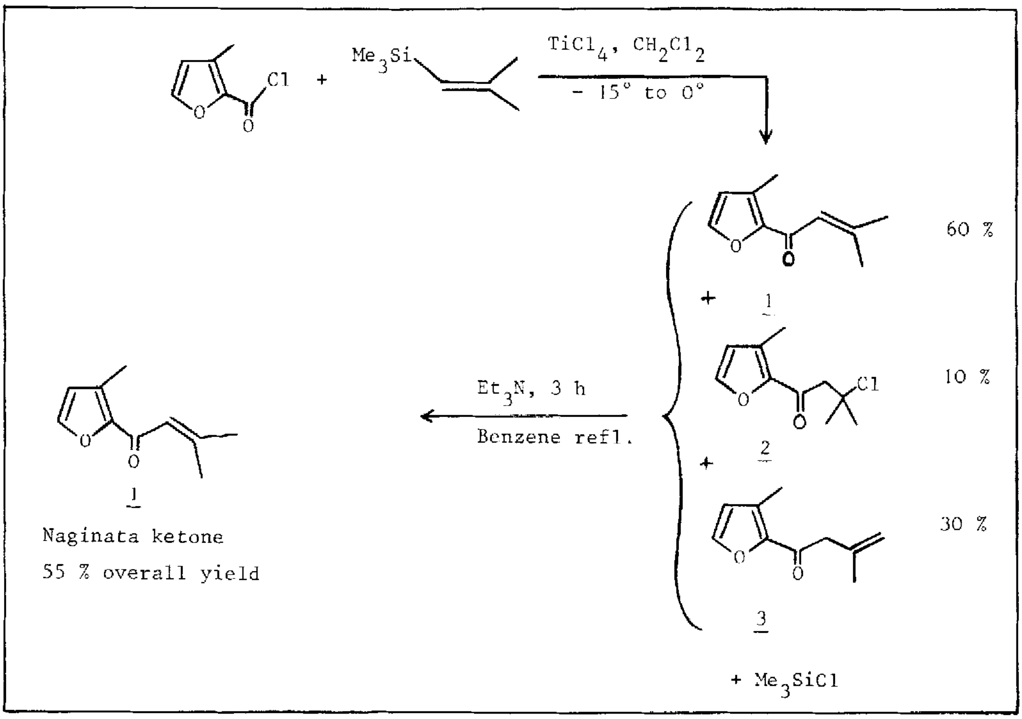
We successfully applied this concept to the preparation in fair yields of Naginata ketone and isoegomaketone, via acylation of respectively 1-trimethylsilyl 2-methyl 1-propene[7] and 1-trimethylsilyl 3-methyl 1-butene[9] by the corresponding and readily available furoic acyl chlorides[10,11] in the presence of $TiCl_4$. These furano monoterpenes were first isolated respectively from *Elsholtzia oldhami* HEMSL[12] and *Perilla frutescens* Britton *var. crispa*[5,13].

Our route to Naginata ketone is summarized in Scheme I.

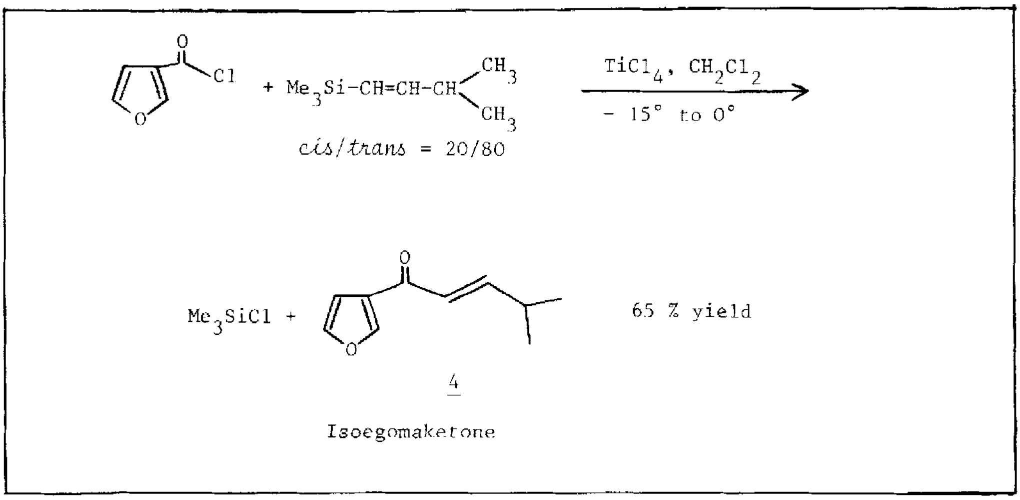
IR and NMR data revealed the crude product was constituted of three ketones, i.e. the isomeric β,γ- and α,β-unsaturated ketones 1, 3 and the chloroketone 2. Refluxing this mixture for 3 h in benzene in the presence of triethylamine gave pure Naginata ketone (via dehydrochlorination of 2 and isomerisation of 3).

Likewise our results concerning isoegomaketone are reported in Scheme II.

Our method appears to be much more convenient than the usual Friedel-Crafts acylation of alkenes. As an example, reaction of isobutene with 3-methyl-2-furoyl chloride in the presence of $SnCl_4$ affords 3 in very poor yields[14]. Moreover we failed in attempts to optimize this preparation of Naginata ketone by using other Lewis acids ($AlCl_3$, $TiCl_4$).



Scheme I



Scheme II

On the other hand, the reaction of alkylsubstituted furans with unsaturated acyl chlorides reveals to be very difficult : although Naginata ketone was obtained from acylation of 3-methyl furan with 3-methylcrotonoyl chloride[15], Büchi reported this result was not reproducible[16]. Moreover, one knows that acylation of furan derivatives occurs in position 2 or 5 and consequently ketones branched at the position 3 are not available : this is the reason why we have not found in the literature synthesis of isoegomaketone by this way. We propose here a more convenient route to this compound than those which have been previously described[17,18].

Both examples illustrate rather well the large possibilities of the methodology involving vinylsilanes as precursors, particularly in the area of terpene derivatives.

Experimental procedure was conducted as follows : $TiCl_4$ (9.49 g, 50 mmol) was added slowly at 0° with vigourous stirring to the furoyl chloride (50 mmol) in freshly distilled dichloromethane (60 ml). The resulting yellow solution was cooled at - 60°C before addition of the vinylsilane (50 mmol in 20 ml of dichloromethane). The reaction medium was allowed to return to 0°C, kept at this temperature during about 1 h and worked up by quenching in ice-cold water containing ammonium chloride. The quenched mixture was decanted and the aqueous layer extracted with petroleum ether. The combined organic layers were stirred overnight with a saturated solution of sodium bicarbonate in order to eliminate unreacted furoic acyl chloride.

After decantation and drying (Na_2SO_4), the solvent was evolved under vacuum (25 mmHg) and the crude product distilled or filtered through a silicagel column (in the case of Naginata ketone, treatment with Et_3N was necessary before purification).

IR and NMR data of the obtained products are in accordance with those given in the literature[16, 17].

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