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A SIMPLE SYNTHESIS OF α,β-UNSATURATED CARBONYL COMPOUNDS BY TRAPPING THE MICHAEL ADDITION-ENOLATE ANION WITH METHANESULFINYL CHLORIDE

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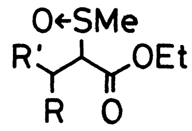
Trapping of an enolate anion, formed by the Michael addition, with methanesulfinyl chloride and subsequent desulfinylation is found to be a useful method for the synthesis of various α,β-unsaturated carbonyl compounds. Synthetic utility of this method is demonstrated in the synthesis of geraniol, nerol, farnesol, and dihydrojasmone.

Although many synthetic methods for α,β-unsaturated carbonyl compounds have been developed, the most direct approach involves an introduction of double bond into the corresponding saturated carbonyl compounds. One of the most simple and widely applicable methods developed recently by Trost et al.[1] involves elimination of sulfinic acid from α-sulfinyl carbonyl compounds after introduction of sulfenyl group into an α-position of the saturated carbonyl compounds and an oxidation. But the application to the compounds with functions sensitive to the oxidation have somewhat troublesome. We wish to describe here a simple synthesis of α,β-unsaturated carbonyl compounds *via* α-sulfinylated carbonyl compounds produced by trapping the Michael addition-enolate anions with methanesulfinyl chloride, and the application to the synthesis of several natural products.

The key step for this method is a continuous operation of the Michael addition of the Grignard reagents to easily available α,β-unsaturated carbonyl compounds and subsequent α-sulfinylation. A typical procedure is as follows; ethyl crotonate was treated with butylmagnesium bromide in the presence of a catalytic amount of copper (I) chloride (2 mol%) in ether at -30 °C for 40 min, and then the reaction solution was added into a solution of methanesulfinyl chloride[2,3] in ether at -78 °C, and then allowed to warm slowly to 0 °C to provide α-sulfinyl ester (**1**, R = Me, R' = Bu).[4] Ethyl 3-methyl-2-heptenoate (**2**, R = Me, R' = Bu, E:Z = 1:1)[4] was obtained in an overall yield of 64% by refluxing **1** in toluene in the presence of calcium carbonate for 7 h. Similarly, ethyl acrylate could also be converted to ethyl 2-heptenoate (**2**, R = H, R' = Bu) in an overall yield of 60%.

This simple method of α,β-unsaturated ester synthesis appeared to offer an attractive method for the synthesis of some terpenes such as geraniol (E-**4**, R = H), nerol (Z-**4**, R = H), and farnesol (**4**, R = Prenyl). Indeed, geraniol and nerol were



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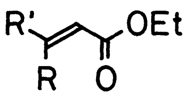

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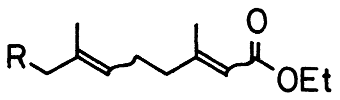

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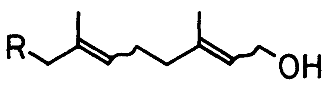

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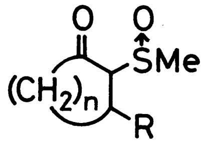
synthesized *via* ethyl geranate (3, R = H) from ethyl crotonate and homoprenylmagnesium bromide. By the same treatment and work up as described above, α-sulfinyl citronellate (1, R = Me, R' = Homoprenyl) was obtained in a yield of 80%. Then the thermal desulfinylation gave ethyl geranate (3, R = H, E:Z = 1:1) in a yield of 88%. A 1:1 mixture of geraniol (E-4, R = H) and nerol (Z-4, R = H) was obtained in a yield of 81% by the reduction of the geranate with lithium aluminum hydride. In a similar manner, the trapping of enolate anion, formed by the Michael addition of the Grignard reagent prepared from homogeranyl bromide (E:Z = 72:28) into ethyl crotonate in the presence of copper(I) chloride, with methanesulfinyl chloride gave α-sulfinylated ester (1, R = Me, R' = Homogeranyl) in a yield of 76%. After the desulfinylation, ethyl farnesoate (3, R = Prenyl, ZZ:ZE:EZ:EE = 14:14:36:36, yield 86%) was converted into farnesol (4, R = Prenyl) by the reduction with lithium aluminum hydride in a yield of 85%.

This method can be applied not only to α,β-unsaturated ester, but also to α,β-unsaturated ketones. Namely, the Michael addition of butylmagnesium bromide to 2-cyclohexenone in the presence of copper(I) chloride in ether and subsequent treatment with methanesulfinyl chloride gave 3-butyl-2-methanesulfinylcyclohexanone (5, n = 3, R = Bu), which gave 3-butyl-2-cyclohexenone (6) in an overall yield of 76% by refluxing in toluene in the presence of calcium carbonate.



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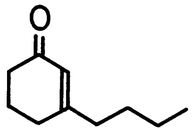

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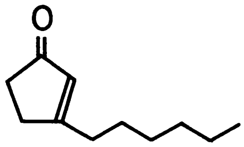

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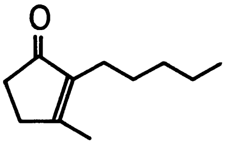

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Dihydrojasmone (8) could also be synthesized in only three steps from 2-cyclopentenone. 3-Hexyl-2-cyclopentenone (7) was obtained in an overall yield of 53% by the thermal desulfinylation of 3-hexyl-2-methanesulfinylcyclopentanone (5, n = 2, R = Hexyl), which was prepared by the reaction of 2-cyclopentenone and hexylmagnesium bromide in the presence of copper(I) iodide in ether and subsequent treatment with methanesulfinyl chloride. According to the procedure of McCurry et al.,[5] dihydrojasmone (8) was obtained by refluxing 7 in 2% NaOH aq solution in a yield of 83%.

As mentioned above, utilizing the trapping of the Michael addition-enolate anions with methanesulfinyl chloride, α,β-unsaturated carbonyl compounds were synthesized in good yields in two steps. This method consists of carbon homologation and introduction of double bond, thus this procedure should have a wide applicability to the synthesis of a variety of natural products by the combination of various α,β-unsaturated carbonyl compounds and the Grignard reagents.

References

1. B. M. Trost, T. N. Salzmann, and K. Hiroi, *J. Am. Chem. Soc.*, 98, 4887 (1976).
2. I. B. Douglass and R. V. Norton, *Org. Synth.*, Coll. Vol. V, 709 (1973); I. B. Douglass and D. R. Poole, *J. Org. Chem.*, 22, 536 (1957).
3. The best result was obtained in the use of 2 equivalents of the sulfinyl chloride. The yield of the sulfinylation decreased, when methanesulfinyl chloride was added into the solution of the enolate anion.
4. All products were isolated by distillation or preparative TLC, and the structures were verified by compatible spectral data.
5. P. M. McCurry, Jr. and R. K. Singh, *J. Org. Chem.*, 39, 2317 (1974).

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