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Conjugate Addition of Lithiotrimethylsilylacetate. A Simple Synthesis of Methyl Jasmonate via Vicinal Double Alkylation

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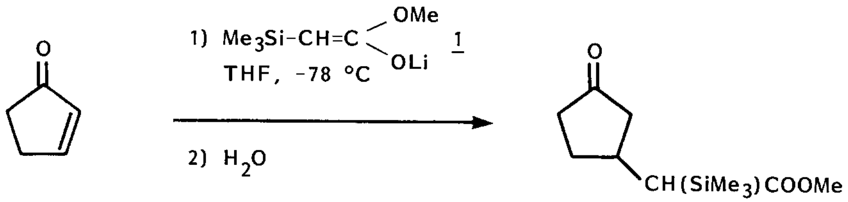
Abstract: Exceptional conjugate addition of methyl lithiotrimethylsilylacetate to cyclopentenone has been found and can be applied to a convenient synthesis of methyl jasmonate by sequential vicinal double alkylation via successful stannyl enolate trapping.

Conjugate addition of functionalized carbanions to enones has vast utility in synthetic chemistry, so that many variants has been developed.[1] Among them, acetate anion equivalents, such as silylketene acetals,[2] were tacitly designed to depress the inherent nature of 1,2-addition for naked ester enolates.[3] We incidentally found an exeptional conjugate addition of methyl lithiotrimethylsilylacetate 1 to cyclopentenone, although the reaction of the lithium ester enolate was already reported but resulted in exclusive 1,2-aditions for unsaturated carbonyls.[4] We report here the exceptional conjugate addition of 1 as a simple acetate anion derivative and the successful vicinal double alkylation in jasmonate synthesis.

Addition of 2-cyclopentenone (1.0 mmol) to an excess (1.25 mmol) of methyl lithiotrimethylsilylacetate 1, which was generated by treatment of methyl trimethylsilylacetate (1.25 mmol) with lithium diisopropylamide (1.25 mmol) in THF (3 mL) at -78 °C, followed by hydrolysis gave the ketoester 2 in 85% yield (a mixture of the stereoisomers, 3:1).[5]



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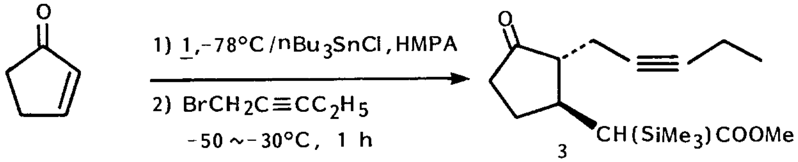
The reaction of 2-cyclohexenone, however, gave cyclohexenylideneacetate derived from 1,2-addition as a major product (64%) and 1,4-adduct (19%) in THF at -78 °C. Addition of HMPA and rise of the reaction temperature (-78 → -10 °C) made no serious change in the product ratios.[6] Benzalacetone in THF at -78 °C gave only 3-methyl-5-phenylpentadienoate in 61% yield (a mixture of cis and trans isomers).[4]

Exclusive conjugate addition of 1 to 2-cyclopentenone, even though a limited case, has much potential versatility in cyclopentanoid synthesis. We, therefore, demonstrate a short step synthesis of methyl jasmonate by the combination of the conjugate addition and the effective sequential α-alkylation via a stannyl enolate trapping, as recently disclosed by us.[7] After the conjugate addition, the lithium enolate intermediate was treated with tri-n-butyltin chloride (1.0 equiv. to 1) at -78 °C. After addition of HMPA (0.7 mL/1 mmol of 1), the stannyl enolate was alkylated with 1-bromo-2-pentyne (1.5 equiv. to 1) to give the desired silyketoester 3 in 54% yield as a mixture of the stereoisomers (3:1; Rf = 5.0 and 4.5, SiO_2, hexane-ether = 1:1).[8] The mixture was treated with n-$Bu_4N \cdot F(H_2O)_n$ in CH_2Cl_2 at room temperature for 5 h to give *d,l*-methyl dehydrojasmonate 4[9], as a single product in 91% yield, which was hydrogenated with Pd-$BaSO_4$ and quinoline in MeOH to give *d,l*-methyl jasmonate 5 in 95% yield.[10]



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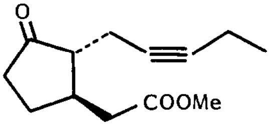

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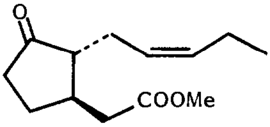

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These findings show a new aspect of synthetic approach to cyclopentanoids and a usefulness of silylacetate. Further studies on its scope and limitations are currently under way.

References and Notes.

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5. 2: ^1H NMR(90 MHz, $CDCl_3$, $CHCl_3$)δ 0.06, 0.10(s×2, Si-CH_3), 3.60, 3.63(s×2, 3:1, 3 H, $COOCH_3$) ppm. See, ref. 2(a).
6. In Et_2O in place of THF; the former (13%) and the latter (44%) at -78 °C; 48% and 22% at -78 → -10 °C for 2 h, respectively.
7. H. Nishiyama, K. Sakuta, and K. Itoh, Tetrahedron Lett., 25, 223 (1984).
8. 3: ^1H NMR(90 MHz, $CDCl_3$, TMS)δ 0.02(s, 9 H), 0.89(t, 3 H), 1.7-3.0(m, 11 H), 3.45 (s, 3 H)ppm. Cis isomer (12%) and 2 (20%) were obtained. No addition of n-Bu_3SnCl gave complicated products.
9. 4: IR; 2230, 1738 cm^{-1}. ^1H NMR(90 MHz)δ 1.08(t, 3 H), 1.4-3.0(m, 11 H), 3.71(s, 3 H), See, H.J. Monterio, J. Org. Chem., 42, 2325 (1977).
10. 5: ^1H NMR(90 MHz)δ 0.96(t, 3 H), 1.4-2.8(m, 12 H), 3.69(s, 3 H), 5.10-5.70(m, 2 H). ^{13}C NMR(22.5 MHz, $CDCl_3$, TMS) 13.0, 20.6, 25.7, 27.2, 37.6, 38.2, 38.9, 51.5, 54.1, 125.1, 134.0, 172.4, 218.4 ppm. See, S. Torii, H. Tanaka, and T. Mandai, J. Org. Chem., 40, 2221 (1975). S. Torii, H. Tanaka, and Y. Kobayashi, Ibid., 42, 3473 (1977)

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