

One-step Synthesis of Tricyclo[5.3.1.0^{3,8}]undecan-4,11-diones by Three Consecutive Michael Reactions. A Formal Synthesis of (±)-Seychellene

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Divinylketone and the trimethylsilyl enol ethers of cyclohex-2-en-1-ones undergo Lewis acid assisted triple Michael reactions yielding tricyclo[5.3.1.0^{3,8}]undecan-4,11-diones; the application of this reaction enabled a formal synthesis of (±)-seychellene (5).

The efficient construction of polycyclic systems is of great importance in synthetic organic chemistry.¹ Previously we reported a one-step synthesis of tricyclo[3.2.1.0^{2,7}]octan-6-ones, and its application to the total synthesis of (±)-ishwarane, employing successive Michael–Michael–alkylation reactions.² Our continuing interest in the development of a new methodology of forming multiple C–C bonds leads us to our present report: Lewis acid assisted three-fold Michael reactions of divinylketone with trimethylsilyl enol ethers of cyclohex-2-en-1-ones give tricyclo[5.3.1.0^{3,8}]undecan-4,11-diones (equation 1), which form the key framework of several polycyclic natural products such as seychellene (5) or patchouli alcohol.

In a typical procedure, to a stirred solution of Lewis acid in CH₂Cl₂ was added at –80 °C a solution of divinylketone and trimethylsilyl enol ether in CH₂Cl₂ successively. The reaction temperature was gradually raised and stirring was continued at

room temperature overnight. After extractive work-up, the product was isolated by preparative h.p.l.c.†

Among the Lewis acids investigated, satisfactory results were obtained using a mixture of TiCl₄ and Ti(OPrⁱ)₄ (ratio 0.8:1), or Et₂AlCl which gave somewhat higher yields.‡ The results are listed in Table 1.

When the reaction was quenched at –80 °C after 1 h in entry 1 using titanium, the single Michael product (3) and the two-fold Michael product (4)§ were isolated in 9 and 39% yields, respectively. The progress of the reaction could be followed (t.l.c.) by the disappearance of the spots due to these compounds and appearance of the spot due to the three-fold Michael product (2a). From these results, the reaction proceeded *via* the sequential three-fold Michael pathway, not a successive Diels–Alder then Michael reaction pathway.

Since the tricyclic diketone (2b) has previously been transformed into (±)-seychellene (5) by Jung and co-workers,³ the present work constitutes a formal synthesis of this naturally occurring tricyclic sesquiterpene (5).⁴ The spectral data (n.m.r., i.r., and mass) of (2b) matched completely those of an authentic specimen. Since the average yield for each of the three C–C bond forming steps is 75%, the yield is quite satisfactory. Bicycloannulation by the three-fold Michael reaction described above is synthetically useful, since construction of a tricyclic ring system can be achieved in a single step from readily available precursors, although yields are modest.

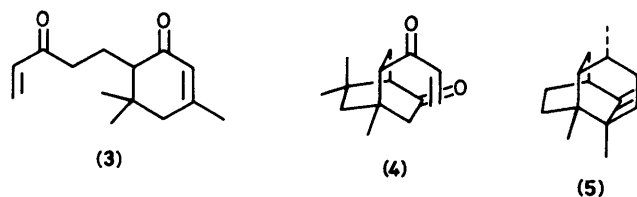
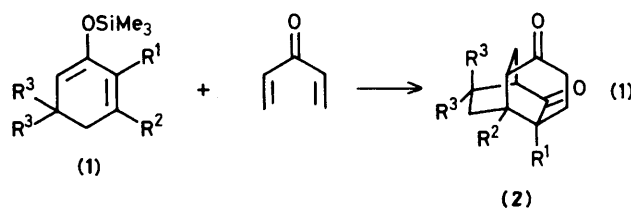
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Table 1. Lewis acid assisted three-fold Michael reaction of the divinylketone with the trimethylsilyl enol ethers of various cyclohex-2-en-1-ones.

Entry	Product	Yield (%)	
		TiCl ₄ /Ti(OPr ⁱ) ₄ ^a	Et ₂ AlCl ^a
1	(2a) (R ¹ = H, R ² = R ³ = Me)	30	34
2	(2b) (R ¹ = R ² = Me, R ³ = H)	20	43 ^b
3	(2c) (R ¹ = Me, R ² = R ³ = H)	5	13
4	(2d) (R ¹ = R ² = H, R ³ = Me)	3	13
5	(2e) (R ¹ = Me, R ² = H, R ³ = –C(Me)=CH ₂ and H)	4	8
6	(2f) (R ¹ = R ² = R ³ = H)	trace	trace

^a Two equivalents of Lewis acid were used. ^b Three equivalents of Et₂AlCl were used.



References

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† Satisfactory ¹H n.m.r., i.r., high resolution mass spectra and/or elemental analyses were obtained for all new compounds.

‡ The reaction of divinylketone with the kinetic enolates generated by cleavage of the trimethylsilyl enol ether by MeLi gave only trace amounts of the desired products.

§ The stereochemistry was tentatively assigned as indicated.