Bicycloannulation leading to the Tricyclo[4.4.0.0^{1,5}]decane Framework and its Congeners

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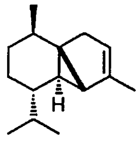
Reactions of the kinetic enolates of 1-acetylcyclohexenes with α-bromo-α,β-unsaturated esters afford 5-methoxycarbonyltricyclo[4.4.0.0^{1,5}]decan-2-ones in one pot syntheses *via* successive Michael–Michael-substitution reactions.

Terpenoids such as the sesquiterpene hydrocarbon, α-cubebene **1** having a tricyclo[4.4.0.0^{1,5}]decane framework have attracted attention due to their unique and unusual structure.[1] The problems of constructing these frameworks have been overcome by means of intramolecular carbenoid addition leading to the synthesis of α-cubebene **1**,[2,3] and by the photochemical rearrangement of a cross conjugated dienone system in the synthesis of (−)-9-anastreptone.[4] As a part of our programme directed towards annulation by successive Michael reactions,[5] we show here an alternative procedure to make the tricyclo[4.4.0.0^{1,5}]decane framework and its congeners *via* successive Michael–Michael-substitution reactions.[6]

Reaction of the kinetic enolate **3** of 1-acetylcyclohexene, generated from the trimethylsilylenol ether **2** by methyllithium in tetrahydrofuran, with methyl α-bromoacrylate **4a** gave 5-methoxycarbonyltricyclo[4.4.0.0^{1,5}]decan-2-one **5a** in 51% yield (see Scheme 1 and Table 1). Similarly, the reaction with methyl (*Z*)-α-bromocrotonate **4b**† afforded 5-methoxycarbonyl-4-methyltricyclo[4.4.0.0^{1,5}]decan-2-one **5b** in 61%



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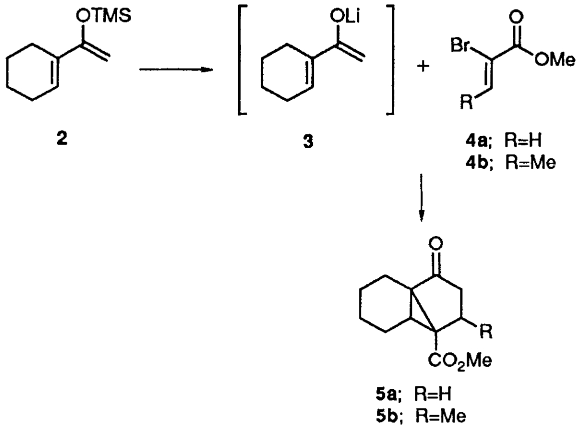

Scheme 1

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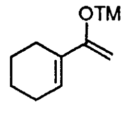
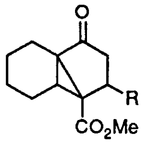
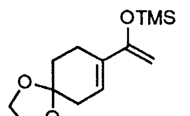
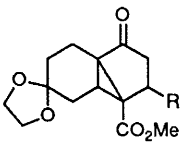
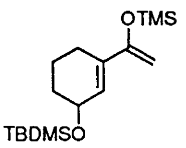
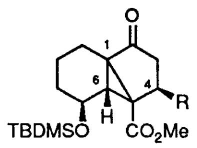
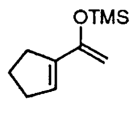
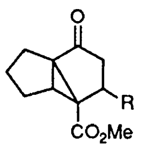
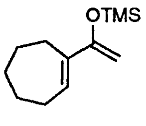
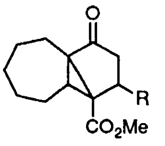
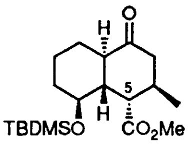
† The geometry of the double bond was determined by comparison of the ^{1}H NMR chemical shift data with those of related compounds. The reaction with methyl (*E*)-α-bromocrotonate led to the recovery of 1-acetylcyclohexene and methyl (*Z*)-α-bromocrotonate.

Table 1 Bicycloannulation of 1-acetylcycloalkene with α-bromo-α, β-unsaturated ester[a]

Entry	Starting material	Product
1	 **2**	 R = H **5a** (51%) R = Me **5b** (61%)
2	 **6**	 R = H **7a** (37%) R = Me **7b** (20%)
3	 **8**	 R = H **9a** (38%) R = Me **9b** (33%)
4	 **10**	 R = H **11a** (52%) R = Me **11b** (51%)
5	 **12**	 R = H **13a** (37%) R = Me **13b** (38%)

[a] TBDMS = $SiMe_2Bu^t$.

yield (see Scheme 1 and Table 1). Addition of hexamethylphosphoric triamide did not improve the yields. The kinetic enolate **3**, generated directly from 1-acetylcyclohexene by treatment with lithium diisopropylamide, resulted in the recovery of the starting enone. The reactions of the enolates generated from the trimethylsilylenol ethers of the substituted 1-acetylcyclohexenes **6** and **8**, 1-acetylcyclopentene **10**, and 1-acetylcycloheptene **12** also gave tricyclic compounds **7a,b**, **9a,b**, **11a,b** and **13a,b**‡ in 20–52% yields, respectively (Table 1). The major by-products in these reactions were 1-acetylcycloalkenes; the brominated compounds were not isolated.



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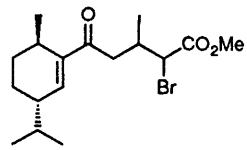

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The tricyclic compounds thus obtained were spectroscopically and chromatographically homogeneous. The phase sensitive NOESY experiment of **9b** showed the nuclear Overhauser effect enhancement between the methyl group at C-4 and the proton at C-6. Treatment of **9b** with lithium in liquid ammonia followed by base catalysed equilibration afforded *trans*-decalone **14** having an axial proton (td, *J* 9.8, 4.3 Hz) on the carbon atom bearing the *tert*-butyldimethylsilyloxy group. Thus, the relative stereochemistry of **9b** was established as shown in Table 1.§

The addition of an equivalent amount of cyclohexene in entry 1 (Table 1, R = Me) provided only the tricyclic compound **5b** in 62% yield. This result along with the isolation of the Michael adduct **15** provides evidence that the present reaction proceeded *via* Michael-Michael-substitution pathway and not a Michael-carbenoid one. The relative stereochemistry of **9b** is explicable by the approach of methyl (*Z*)-α-bromocrotonate **4b** from the opposite side of the *tert*-butyldimethylsilyloxy group of the enolate generated from **8**, and by the intramolecular chelation of the lithium cation between the ketone enolate and the methoxycarbonyl group for the first Michael reaction and then between the ester enolate and the carbonyl group for the second Michael reaction.

In summary, the present reaction offers an easy access to the tricyclo[4.4.0.0^{1,5}]decane and its related frameworks, making two rings by three consecutive C–C bond formations (bicycloannulation) in a one pot synthesis.

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References

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‡ All new compounds gave satisfactory ^{1}H NMR, IR and high resolution mass spectral analyses.

§ The methoxycarbonyl group of **14** stayed in axial (5-H, δ 3.02, $W_{1/2}$ = 8.5 Hz) after base catalysed equilibration. Full stereochemical assignments of **9b** and **14** will be published in due course.