A New Method for C–C Coupling of Terminal Alkenes *via* a Sulphonylation–Alkylation–Desulphinylation Sequence: Synthesis of *E*- and *Z*-α-Bisabolenes

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A new method for regiospecific C–C coupling of terminal alkenes based on a sulphonylation–alkylation–desulphinylation process, mediated through allylic sulphinic acids, and its application to the conversion of limonene into *E*- and *Z*-α-bisabolenes, are described.

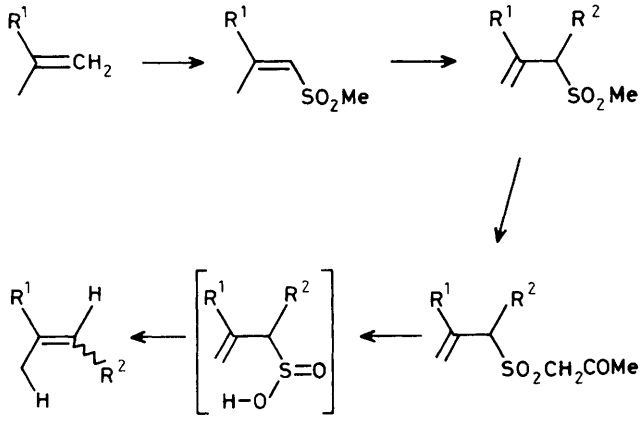
A method of direct C–C extension of terminal alkenes, Scheme 1, would be of value in natural product synthesis since the resulting functionality is common in terpenes. By combining radical sulphonylation of such alkenes with the facile and regiospecific [3,3] sigmatropic desulphinylation of allylic sulphinic acids we have developed a procedure permitting the above extension. Our method is outlined in Scheme 2.† First the alkene is converted into the vinyl methyl sulphone by radical addition of methanesulphonyl iodide and elimination. Next, deprotonation to the *thermodynamic* allylic anion and alkylation provides the C–C bond. The anion of this β,γ-unsaturated sulphone is acylated and the β-ketosulphone is reduced to the allylic sulphinic acid which loses SO_2, *in situ*, thus providing a regiospecifically defined alkene product. We exemplify the method by converting (+)-limonene (**1**) into *E*- and *Z*-α-bisabolenes (which occur in essential oils) (**2a**) and (**2b**), respectively, Scheme 3, for which various stereospecific,[1] chiral auxiliary based,[2] or achiral syntheses[3] have previously been reported.

Thus (*R*)-(+)-limonene (**1**) {$[\alpha]_D^{23}$ +112° (*c* 1, MeOH)} was converted into *E*-vinyl methyl sulphone (**3**)‡ (64—72%) by addition of methanesulphonyl iodide[4] followed by base treatment. Conversion into the thermodynamic anion (**4**) and alkylation gave (**5**) (85%, 1 : 1 mixture of diastereoisomers by ^{13}C n.m.r.). Metallation of (**5**) at −78 °C occurred solely in the sulphonyl methyl group, as was revealed by quenching with

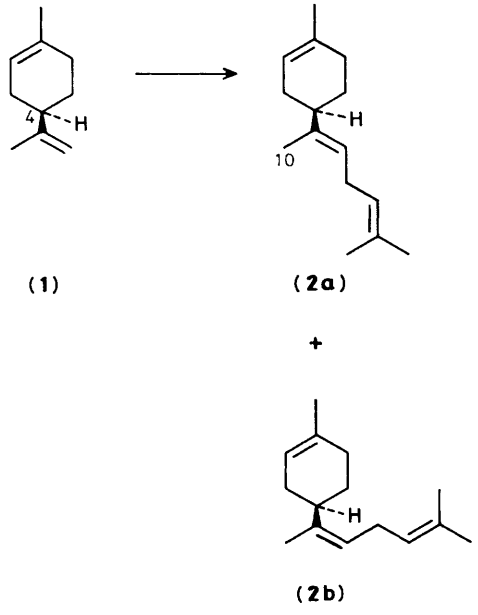
Scheme 1

† The generality of such direct C–C extension of terminal alkenes, as exemplified by the conversion of (*R*)-(+)-limonene to *E*- and *Z*-α-bisobolenes herein, is currently under investigation.

‡ Formed as a mixture of *E*- and *Z*-isomers, ratio 9 : 1, from which pure *E*-(**3**) was isolated by recrystallisation (ether/light petroleum), m.p. 51—52 °C, $[\alpha]_D^{20}$ +94° (*c* 1, $CHCl_3$).



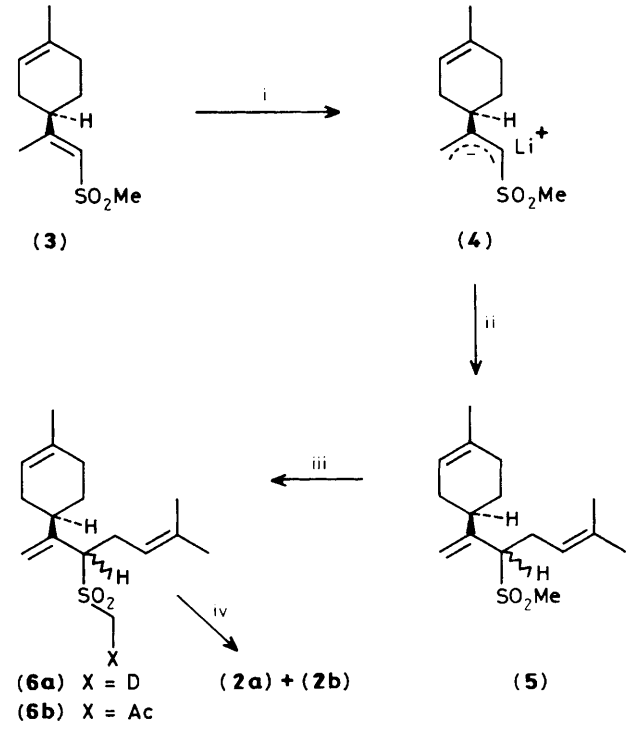
Scheme 2



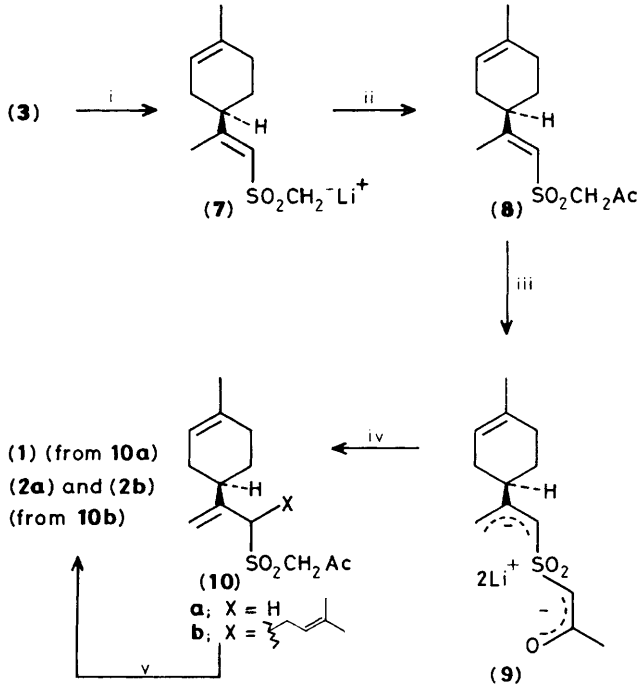
Scheme 3

AcOD [to give (**6a**), 89%] or EtOAc [to give (**6b**), 80%]. Subsequent mild reductive cleavage[5] of (**6b**) gave *E*- and *Z*-α-bisabolenes (**2**) (71%, *E*:*Z* 3:1), purified by preparative g.l.c. (10% Carbowax 20M column, 155 °C) into the separate isomers, Table 1, whose ^{1}H and ^{13}C n.m.r. data were identical with those reported,[1] Scheme 4. Consistent with the intermediacy of the allylic sulphinic acid in this reductive step was the observation that performing the reduction in the presence of D_2O (tetrahydrofuran–D_2O, 9:1) gave bisabolenes containing one deuterium in the C(10) methyl group.[6]

Since there were discrepancies between our observed rotations for (−)-*Z*-α-bisabolenes and those reported[1] we have checked the configurational integrity of C-4 in limonene during these transformations. Thus kinetic deprotonation of (**3**) (Bu^{n}Li, 1.1 equiv., −78 °C) gave anion (**7**) which was acylated (EtOAc) to β-ketosulphone (**8**) (83% overall) and then converted into the dianion (**9**) [LiN(SiMe$_3$)$_2$, 3.5 equiv.], Scheme 5. Quenching with AcOH gave (**10a**), 82%, and with prenyl bromide (**10b**), 63%. Reduction, as before gave, from (**10a**), (*R*)-(+)-limonene {$[\alpha]_D^{23}$ +108° (*c* 1, MeOH), 58%} and from (**10b**) the same mixture of *E*- and *Z*-α-bisabolenes (*E*:*Z* 3:1, 68%) with identical optical rotation of the major *E*-isomer as was obtained in the first sequence, Table 1.



Scheme 4. *Reagents*: i, Bu^{n}Li, 1.0 equiv., 0 °C (2 h), 0 to 20 °C (1 h), 20 °C (1 h), tetrahydrofuran (THF), argon; ii, prenyl bromide, 3.1 equiv., −78 to 20 °C, THF, argon, 4 h, then AcOH [85% from (**3**)]; iii, Bu^{n}Li, 1.1 equiv., −78 °C, THF, argon, 1 h and then either AcOD, −78 °C (**6a**, 89%) or EtOAc, 3—4 equiv., −78 to 0/20 °C, THF, argon, 2—2.5 h then AcOH (**6b**, 80%); iv, Al/Hg, 10 equiv. (Al), 20 °C, THF/H_2O (9:1), 4—24 h (**2a** and **2b**, 71%).



Scheme 5. *Reagents*: i, Bu^{n}Li, 1.1 equiv., −78 °C, THF, argon, 1 h; ii, EtOAc, 3.0 equiv., −78 to 20 °C, THF, argon, 3 h then AcOH [70% isolated, 83% based on consumed (**3**)]; iii, LiN(SiMe$_3$)$_2$, 3.5 equiv., −72 to 20 °C, THF, argon, 3 h; iv, either AcOH, 20 °C (**10a**, 82%) or prenyl bromide, 3—5 equiv., −78 to 20 °C, THF, argon, 2.5 h, then AcOH [(**10b**), 63%]; v, Al/Hg, 10.0 equiv. (Al), 20 °C, THF/H_2O (9:1), 4 h [(**1**), 58% or (**2a**) and (**2b**), 71%].

Table 1. Comparison of optical rotation data for (**2**).

	(+)-(*R*)-(*E*)-(**2**)	(−)-(*R*)-(*Z*)-(**2**)	
Obs. $[\alpha]_D^{20}$	+64° [a]	−1° [b]	(*c* 1, EtOH)
Lit.[1] $[\alpha]_D^{20}$	+55.9°	−12.4°	(1% in EtOH)
Lit.[1] $[\alpha]_D^{20}$	—	+3.8° [c]	

[a] From Scheme 4 or 5. [b] From Scheme 4. [c] For (+)-(*S*)-(*Z*)-(**2**).

In conclusion, we have demonstrated that allylic β-ketosulphones are convenient precursors of allylic sulphinic acids. These sulphinic acids, *via* their facile [3,3] sigmatropic loss of sulphur dioxide,[7] provide regiochemical control of double bonds resulting from desulphinylation procedures. This is to be contrasted with the widely used desulphonylation of aryl sulphones which results in most cases in regioisomeric mixtures of alkenes.

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