open a route to various hyperalkylations of cationic C_5Me_5 complexes and of other permethylated π ligands. The dramatic difference between the C_6Me_6 ligand in eq 1 (single branching) and the C_5Me_5 ligand (double branching) arises essentially because of the difference in steric bulk between the C_5 and C_6 rings whose internal angles are respectively 72° and 60°. These internal angles are also responsible for the large difference in rotational barriers of the *i*-Pr groups in **2** and C_6-*i*-Pr_6.[5c]

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Registry No. 1, 126580-33-4; **2**, 126580-35-6; **3**, 126580-37-8.

Supplementary Material Available: Experimental procedures for the synthesis of **2** and **3**, analytical and spectroscopic (^1H, ^{13}C NMR) data for **2** and **3**, mass spectral data and mass spectrum for **4**, and ^1H and [^1H]^{13}C NMR spectra for **2** and **3** (10 pages). Ordering information is given on any current masthead page.

A Direct Total Synthesis of (+)-Longifolene via an Intramolecular Diels–Alder Strategy

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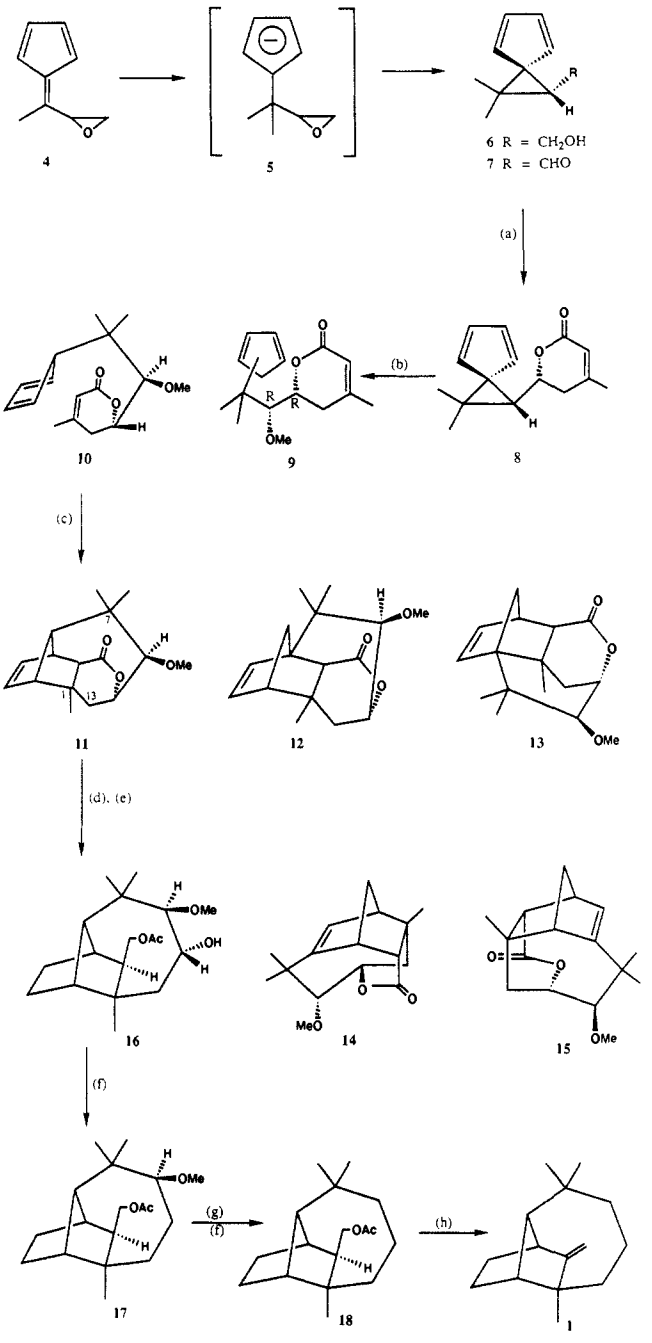
The topological framework represented by the sesquiterpene longifolene (**1**) continues to play an important and historic role in organic chemistry.[1-5] In particular, the longifolene skeleton has served as a subject for synthetic planning and strategy,[3a,5] and the total syntheses reported to date[3] reflect this diversity. From the standpoint of retrosynthetic analysis, the strategic double disconnection of **1** to a triene precursor of type **2** has considerable appeal and as such has been widely noted.[3a,4e,f,5] However, as an early approach to longifolene showed,[4e] the propensity of substituted cyclopentadienes to undergo facile 1,5-sigmatropic rearrangement prior to cyclization takes precedence. Thus for this strategy to succeed, either the rearrangement must be blocked,[6] conditions developed where cyclization can compete efficiently,[7] or alternatively constraints built into the system so the desired cyclization is the preferred one. Unfortunately, blocking the sigmatropic reaction is not necessarily straightforward, since even chlorine migrates prior to cyclization in a related case,[4f,8] although we have demonstrated that the cyclopropane moiety present in a spiro[2.4]heptadiene system can be used effectively for this purpose and as a latent carbon source.[6] Molecular models and molecular mechanics calculations suggest that if the dienophile

Scheme I[a]



[a] (a) LDA, THF, −40 °C, $Me_2C{=}CHCO_2Me$, $CdCl_2$, 30 min; 2 h, 0 °C, 73%. (b) $BF_3{\cdot}Et_2O$, MeOH, 4 h, 22 °C, 83%. (c) Toluene, microwave, sealed tube, 2.5 h, 97%. (d) H_2, 5% Pd/C, EtOAc, 30 psi, 4 h; $LiAlH_4$, ether, 0–22 °C, 4 h, 95%. (e) Ac_2O, pyridine, ether, 6 h, 0 °C, 74%. (f) ClC(=S)OPh, pyridine, CH_2Cl_2, 22 °C; nBu_3SnH, AIBN, toluene, 4 h, 110 °C, 71%. (g) NaI, Et_3N, Me_3SiCl, CH_2Cl_2, 22 °C, 1 h (f, 50%). (h) C_6H_6, flow system, 525 °C, 56%.

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(8) As we have pointed out elsewhere (Fallis, A. G.; Breitholle, E. G. International Symposium on Stereochemistry, Kingston, ON, Canada, June 27–July 2, 1976; Abstract M1), an alternative solution employs a "brexane" intermediate followed by a double ring expansion. This approach has been used by Snowden in an imaginative synthesis of sativene (Snowden, R. L. *Tetrahedron Lett.* **1981**, *22*, 101; *Tetrahedron* **1986**, *42*, 3277).

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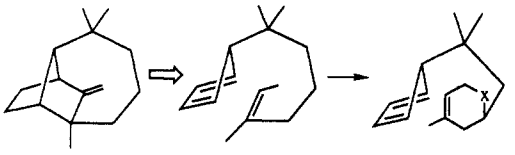
is constrained to a six-membered ring as illustrated in **3**, then the preferred pathway for intramolecular cycloaddition should generate the desired tricyclic nucleus for longifolene directly, and the cyclopentadiene isomers will cease to be a problem. This analysis has been reduced to practice and successfully applied to the total synthesis of (+)-longifolene (**1**) in which one key chiral center induces the relative configuration during the intramolecular cycloaddition and is subsequently removed.



1 2 3

Condensation of 1,2-epoxy-3-butanone with cyclopentadiene in methanol containing pyrrolidine afforded the fulvene **4** (Scheme I) in 86% yield.[9] Addition of methyllithium to **4** generated the cyclopentadienyl anion **5** in situ, which cyclized spontaneously in the favored exo-tet manner to the racemic spiro[2.4]hepta-4,6-diene alcohol **6** (65%). Treatment of this alcohol with (-)-methyl chloroformate (prepared from (-)-methanol and phosgene, toluene, 0 °C) allowed chromatographic separation of the diastereomers and resolution of the *R*-(+) isomer **6** after $LiAlH_4$ reduction.[10] Oxidation of the primary alcohol with active MnO_2 dispersed on carbon provided the aldehyde **7** (81%).

Condensation of the aldehyde **7** with the anion derived from methyl 3-methylcrotonate (LDA mediated by cadmium chloride, -40–0 °C, 2 h, 73%)[11] initially resulted in the γ substitution product, which cyclized spontaneously to the lactone **8**. The crowded environment of the carbonyl center resulted in attack from the less hindered *re* face (away from the *gem*-dimethyl substituents) to form the $C_5(R)$ enantiomer preferentially (9:1). The cyclopropyl bonds in **8** are strained and polarized, with the negative dipole toward the cyclopentadiene ring, rendering them susceptible to acid-catalyzed cleavage. Consequently, treatment of **8** in methanol containing $BF_3{\cdot}Et_2O$ at 22 °C resulted in the formal addition of methanol to form the $C_5(R),C_1'(R)$-substituted cyclopentadiene **9** (83%) as a mixture of diene isomers. The triene **9** was heated in a sealed glass tube in toluene in a microwave oven for 2.5 h, to afford a single adduct (97%).[12] This material displayed two olefinic hydrogen signals at δ 6.24 and 6.32 in its ^1H NMR spectrum and clearly rules out the Bredt olefin structures **14** and **15**. In contrast to **11**, adducts **12** and **13** contain two methylene and three quaternary carbons (excluding the carbonyl).

The ^{13}C NMR spectrum of the Diels–Alder product displayed a single signal at δ 41.5 due to the ring methylene carbon at C_{13} and only two quaternary carbon signals at 40.4 (C_7 *gem*-dimethyl) and 56.3 (C_1). These features are only consistent with structure **11**, which must have arisen from the exo transition state **10** as illustrated, and excluded the other possible adducts **12–15**. The arrangement in **10** is the only geometry that can be achieved readily due to the chirality of C_5 and the restricted rotation that also controls the development of the additional chiral centers in the adduct. This represents the first direct preparation of a cycloheptane in a bridged ring system from a carbocyclic precursor in preference to a cyclohexane bridge.[13] However, in this instance, because of the constrained nature of the dienophile, the competing pathways to the cyclohexane systems **12–15** are less favorable. This fact is reflected in the ratios of the relative energies of these adducts **11**:**12**:**13**:**14**:**15** (1:7:4.7:3.6:4.1).[14] The twisted nature of **12** is apparent by inspection while its isomer **13**, which would arise from addition to the opposite face, has the cyclohexane side chain in a boat conformation and also contains a methyl–hydrogen bowsprit interaction.

Selective functional-group manipulations completed the synthesis in the following manner. Hydrogenation of the double bond (Pd/C, 30 psi, 99%), reduction of the lactone ($LiAlH_4$, 96%), and selective acetylation (Ac_2O, Py, 0 °C, 74%) afforded **16**. The chiral secondary alcohol, having fulfilled its role, was removed under free-radical conditions (ClCSOPh, AIBN, nBu_3SnH),[15] the methyl ether cleaved (NaI, TMSCl, Et_3N),[16] and the resulting alcohol similarly removed, to give the acetate **17**. Pyrolysis of this acetate in a flow system at 525 °C provided (+)-longifolene (56%), which was identical with an authentic sample of natural (+)-longifolene by ^1H NMR, ^{13}C NMR, infrared, and high-resolution mass spectral comparison.

In conclusion, a carefully selected [4 + 2] cycloaddition step, in which competing pathways are energetically unfavorable, has resulted in a direct total synthesis of (+)-longifolene. The sequence required 12 steps from cyclopentadiene in 8.2% overall yield from aldehyde **7**. This general strategy may be extended to other pericyclic reactions for the synthesis of diverse natural product skeletons.

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Supplementary Material Available: Spectroscopic data for compounds **1**, **6–9**, **11**, and **16–18** (3 pages). Ordering information is given on any current masthead page.

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(12) We have found microwave heating to be a very useful technique for a variety of thermal transformations. The sample is enclosed in a glass pressure tube equipped with a threaded Teflon cap which extends through a small hole in the top of the oven. The base of the tube rests in a beaker packed with vermiculite. Under these conditions, cyclizations that proceed in <20% in *o*-dichlorobenzene over 48–72 h afforded yields of 75–100% in 2–3 h. Toluene is the solvent of choice. See also: Gedye, R.; Smith, F.; Westaway, K.; Ali, H.; Baldisera, L.; Laberge, L.; Rousell, J. *Tetrahedron Lett.* **1986**, *27*, 279. Giguere, R. J.; Bray, T. L.; Duncan, S. M.; Majetich, G. *Tetrahedron Lett.* **1986**, *27*, 4945.

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(16) Et_3N is essential for the success of this reaction to avoid concomitant cleavage of the acetate.