Total Synthesis of (±)-*trans*-Maneonene-B

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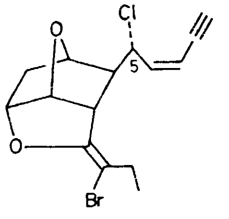
trans-Maneonene-B (**2**) was prepared in four steps from the diacetylenic alcohols (**6**) and (**7**) and was shown to have the relative configuration at C-5 as depicted in structure (**14**).

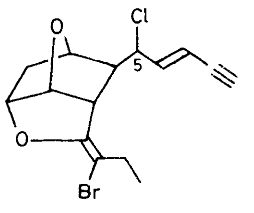
Numerous C-15 halogenated cyclic ethers containing conjugated enyne or halogeno-allene side chains have been isolated from the genus *Laurencia*.[1] We recently reported the synthesis of *cis*-maneonene-B (**1**) and established the relative configuration at C-5 as shown.[2] In this communication a synthesis of *trans*-maneonene-B (**2**)[3] is reported and the relative configuration at C-5 is established.

The silylated diacetylenic alcohols (**4**), (**5**), (**6**), and (**7**) are prepared from the tricyclic lactone acid (**3**) which is readily prepared in three steps from furan and fumaroyl chloride (Scheme 1). For these compounds to be useful in the synthesis of *trans*-maneonenes it was important to know the relative configurations of all the relevant stereocentres. The structure of (**4**) was determined by *X*-ray methods.[2] Compounds (**4**) and (**5**) have the 5-(R^*) configuration (as drawn) because they gave an identical pair of enol ethers on pyrolysis whereas (**6**) and (**7**) have the 5-(S^*) configuration because they gave a different pair of enol ethers on pyrolysis. The methoxy group in (**5**) can be shown to exert a weak nuclear Overhauser effect[4] on the *endo*-H-8 shown on the structure. Therefore (**4**) and (**5**) differ solely in the configuration at C-13. Pyridinium chlorochromate oxidation[5] of (**4**) gave the same diacetylenic ketone as was obtained from oxidation of (**6**). Similarly (**5**) and (**7**) gave a common diacetylenic ketone. Hence (**4**) and (**6**) differ only in the C-5 configuration and similarly for (**5**) and (**7**), whereas (**6**) and (**7**) differ only at C-13.

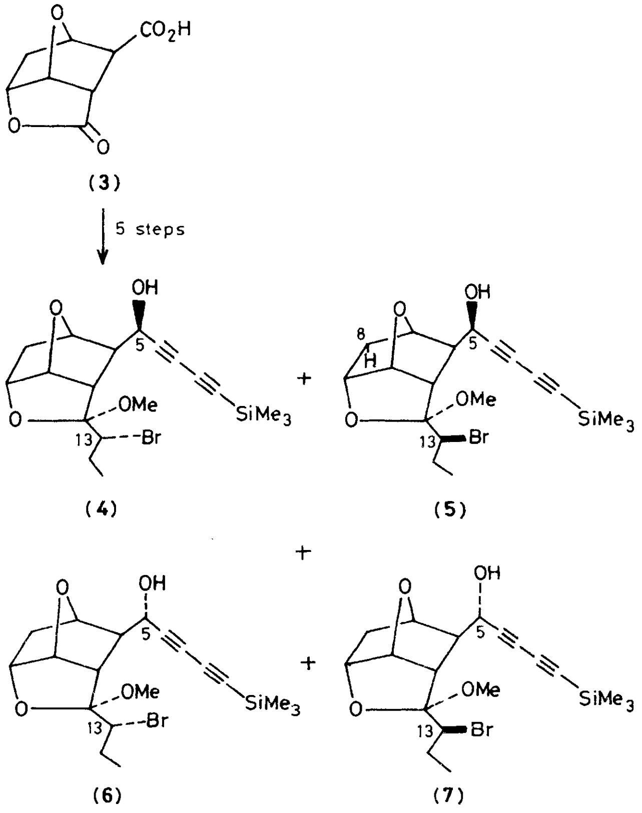
The well known[6] lithium aluminium hydride reduction of prop-2-ynylic alcohols was extended in a model study of the reduction of the diacetylenic alcohol (**8**)[7] to the *trans*-enyne-allylic alcohol (**9**)† (Scheme 2). After our own studies of this reduction were completed, other workers published identical observations.[8]



(**1**)



(**2**)



Scheme 1

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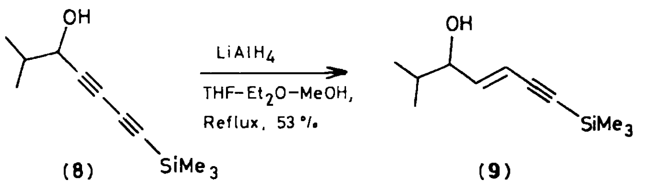
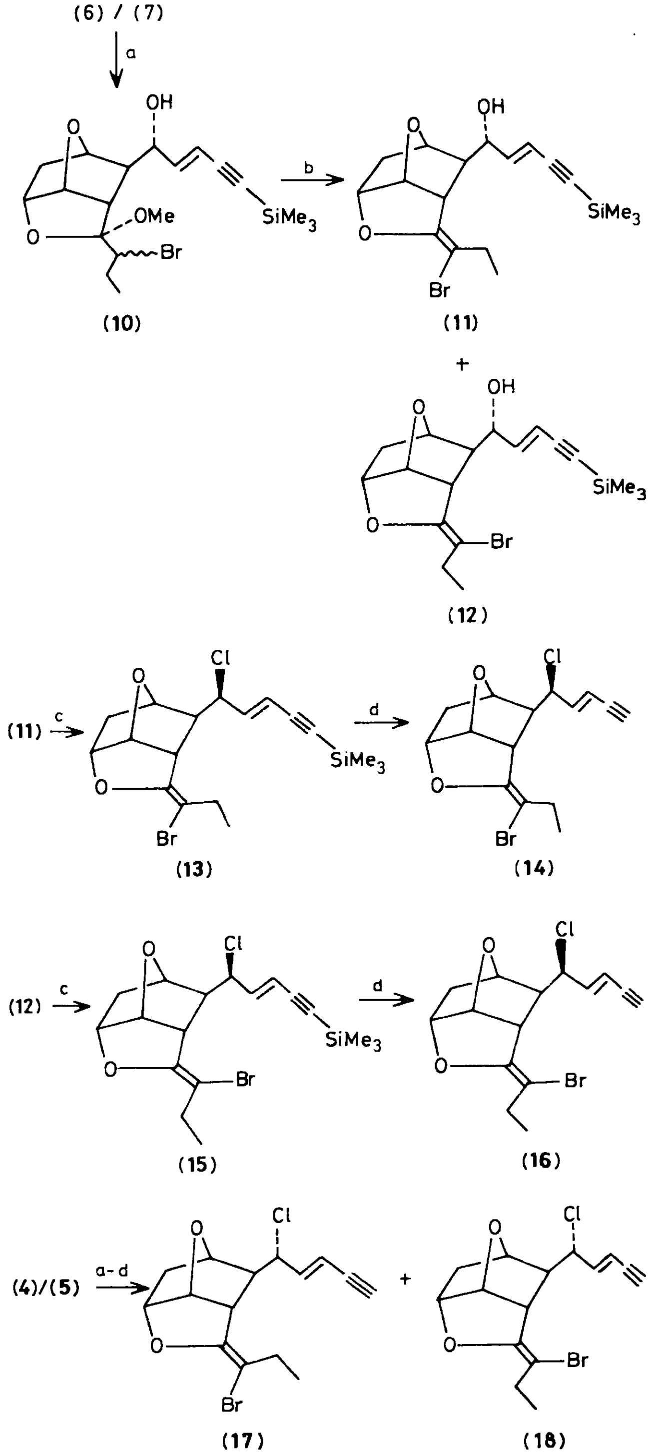
† All new compounds exhibited spectroscopic and analytical data consistent with the assigned structure.



Scheme 2



Scheme 3. *Reagents:* a, LiAlH$_4$, tetrahydrofuran (THF), reflux, 90 min (65—80%); b, *N,N*-dimethylacetamide, reflux, 30 min (52—65%); c, Me$_2$NC(Cl)=CMe$_2$, CH$_2$Cl$_2$, propylene oxide, 0 °C to room temp., 45 min (55—65%); d, Bu$_4$NF, THF-H$_2$O (99 : 1), 0 °C, 30 min (35—50%).

For the synthesis of *trans*-maneonene-B each of the diacetylenic alcohols (**4**), (**5**), (**6**), and (**7**) was taken through the reactions shown in Scheme 3. Compounds (**6**)/(**7**) were reduced to the corresponding *trans*-allylic alcohols (**10**)† which were then pyrolysed to give the enol ethers (**11**)† and (**12**).† These were converted into the corresponding chloro-compounds (**13**)† and (**15**)† using Ghosez's[9] α-chloro-enamine method.‡ Tetra-n-butylammonium fluoride desilylation[11] caused unexpected rearrangement to an allenic compound. This was circumvented by moderating the desilylation with a small amount (1%) of water,[12] and ultimately led to the successful preparation of the diastereoisomeric *trans*-maneonenes (**14**)† and (**16**)† [from alcohols (**6**)/(**7**)] and (**17**)† and (**18**)† [from alcohols (**4**)/(**5**)] (Scheme 3). No authentic sample of (**2**) was available for comparison, and the ^{1}H n.m.r. data[3] had been recorded at 60 MHz, thus making comparison difficult. Ultimately, comparison of ^{13}C n.m.r. data for authentic *trans*-maneonene-B (**2**)[3] with the synthetic compounds established unambiguously that *trans*-maneonene-B has structure (**14**). The conclusion that the relative configuration at C-5 is (R^*) in the *cis*-series and (S^*) for *trans*-maneonene-B (as drawn) is interesting and may be related to the double bond configuration of the appropriate alkene precursor in the biosynthesis of (**1**) and (**2**).

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‡ An α-chloro-enamine reagent has recently been used in a completely different way to promote nucleophilic displacement of allylic alcohols with carbon nucleophiles.[10]