# A Synthesis of (3*S*)-Homomevalonolactone

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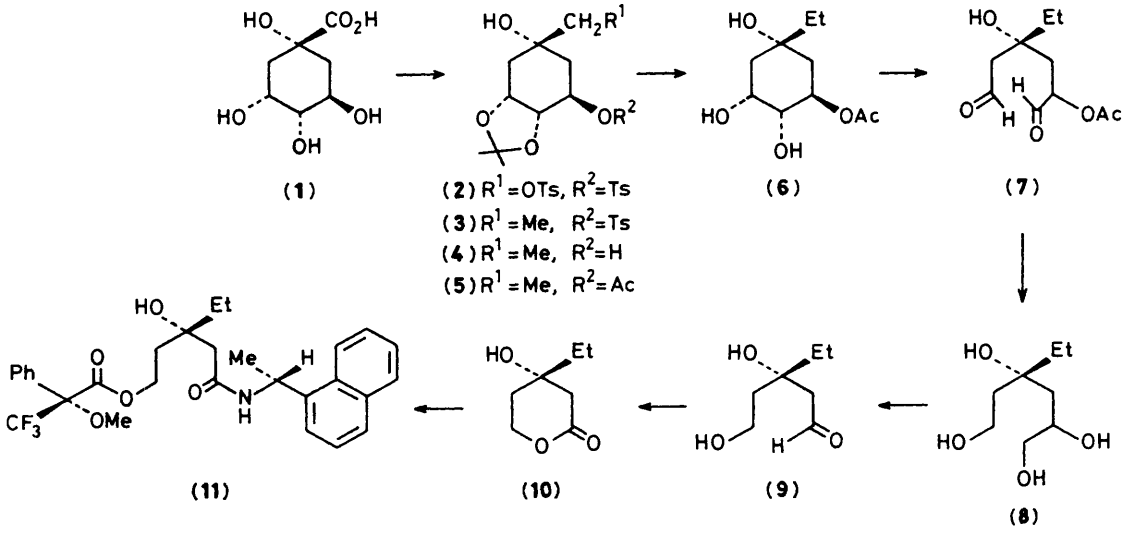
(3*S*)-Homomevalonate was synthesized from quinic acid and used to confirm the (3*R*)-configuration of the biosynthetic enantiomer.

Homomevalonate (HMev) has been implicated as a probable intermediate in insect juvenile hormone biosynthesis.[1] Evidence has suggested that biosynthetic HMev possesses the same (3*R*)-configuration as that of the congeneric Mev. This supposition is based partly on a comparison of the diagnostic n.m.r. resonances of HMev derivatives with those of equivalent Mev derivatives of known configuration, and on induced c.d. studies of both regenerated HMev and Mev lactone.[2] We now report a synthesis of (3*S*)-HMev from quinic acid which should serve as a standard in the assignment of the absolute configuration of the biosynthetic HMev. Quinic acid was previously used by Eberle and Arigoni in the synthesis of (3*S*)-Mev.[3]

The bis-toluene-*p*-sulphonate (**2**) prepared from quinic acid (**1**) by the literature method[3] was treated with lithium dimethyl-




cuprate (3 equiv.) in ether at 0 °C for 30 min. Aqueous work-up gave the toluene-*p*-sulphonate–acetonide (**3**) in 89% yield, the structure of which was confirmed by its n.m.r. spectrum which included typical resonances corresponding to one $MeC_6H_4SO_3$-group [δ 2.40 (3H, s) and 7.52 (4H, ABq)] and a methyl goup [δ 0.87 (3H, t)]. Further transformations followed closely the Arigoni synthesis.[3] Reduction of (**3**) with 5% sodium amalgam in methanol–water yielded the diol (**4**), the acetate (**5**) of which was heated in aqueous acetic acid to generate the triol–acetate (**6**). Treatment of (**6**) with aqueous periodic acid gave the dialdehyde (**7**) which was reduced with $LiAlH_4$ in ether to yield the tetraol (**8**). The tetraol (**8**) was converted into HMev lactone *via* (**9**) by successive treatment with periodic acid and bromine. The n.m.r. spectrum of (**10**) showed a methyl triplet at δ 0.96.

The lactone (**10**) thus synthesized was heated with neat (+)-α-(1-naphthyl)ethylamine and esterified with (+)-α-methoxy-(α-trifluoromethyl)phenylacetyl chloride in pyridine to yield (**11**). The (3*S*)-derivative (**11**) is the faster eluting diastereoisomer on liquid chromatography.† Since the corresponding derivative obtained from the biosynthetic HMev is the slower eluting diastereoisomer, it follows that naturally occurring HMev possesses the (3*R*)-configuration.

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† Zorbax-SIL column, 22 × 0.79 cm, eluted with 20% ethyl acetate in pentane, 75% water-saturated, at 5 ml/min.