

Annellation of 1,3-Dicarbonyl Compounds with β -Vinylbutenolide

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Summary With β -vinylbutenolide 2-methylcyclohexane-1,3-dione or 2-ethoxycarbonylcyclohexanone undergoes 1,6-Michael addition and subsequent cyclisation yielding the annellation product.

THE synthesis of sesquiterpene lactones has received attention recently owing to their biological activity. We have found that the reaction of β -vinylbutenolide with some 1,3-dicarbonyl compounds such as 2-methylcyclohexane-1,3-dione gives annellation products, which are attractive intermediates for sesquiterpene lactone synthesis.

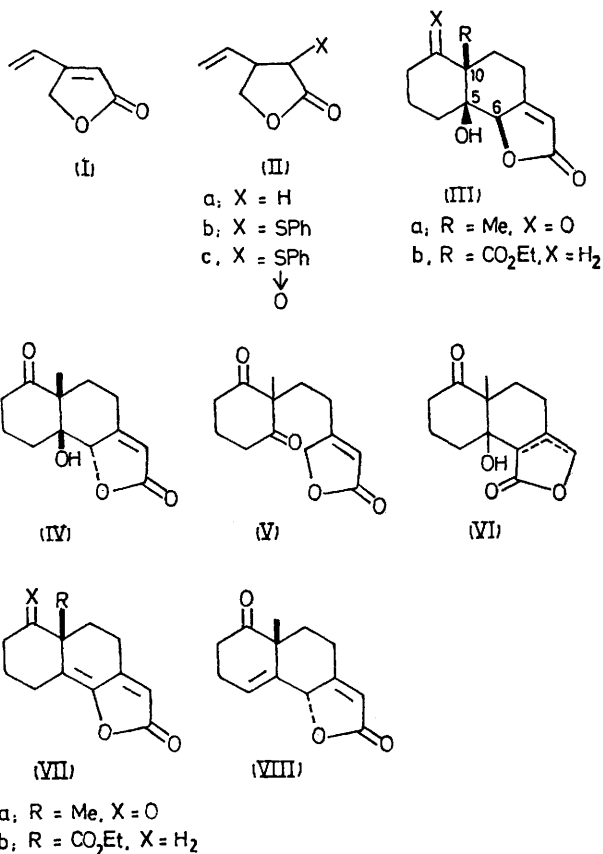
β -Vinylbutenolide (I) was conveniently prepared from β -vinylbutyrolactone¹ (IIa) as follows: after metallation of (IIa) with lithium di-isopropylamide, the resulting enolate was sulphenylated with diphenyl disulphide to give (IIb) (50%). *m*-Chloroperoxybenzoic acid oxidation of (IIb) followed by pyrolysis of the resulting (IIc) in refluxing toluene produced (I)^{2†} (90% from IIb).

When a mixture of (I) and the enolate of 2-methylcyclohexane-1,3-dione, prepared from 2 mol. equiv.‡ thereof and 1 mol. equiv. of sodium dispersion in tetrahydrofuran, was refluxed for 15 h, two products (IIIa) [m.p. 176–177°; ν_{\max}

† Relatively unstable neat. Use of (IIc) is more convenient for storage.

‡ When 1 mol. equiv. of the dione was used, much lower yields were obtained.

1780 and 1750 cm^{-1} ,³ δ 5.75 (1H)] and (IV) [m.p. 171°; ν_{max} 1783 and 1750 cm^{-1} ,³ δ 5.89 (1H)] were obtained in the ratio 11:1 (47% total). The formation of the Michael adduct (V) was observed at the initial reaction stage.



Spectral data of these annelation products excluded alternative structures such as (VI). Dehydration of (IIIa) and (IV) with thionyl chloride in pyridine selectively yielded (VIIa) (m.p. 145–146°) and (VIII) (oil) in almost quantitative yields, respectively. N.O.E. experiments on (IV) demonstrated a *cis*-relationship between the angular methyl group and the C(6)-proton. The above results and the well documented stereochemical course of Robinson annelations⁴ led us to conclude the stereochemistry of these annelation products (IIIa) and (IV) as depicted. The regiospecific dehydration obviously suggests the considerable conformational preference of these *cis*-fused decalin lactones.

Similarly the sodium salt of 2-ethoxycarbonylcyclohexanone yielded the annelation product (IIIb) (m.p. 169–170°) as the major product (40%), and dehydration of (IIIb) with thionyl chloride in pyridine gave (VIIb) (45%).

Upon treatment with KOBu^t in tetrahydrofuran or Bu^tOH either of the annelation products (IIIa) or (IV) provided the same equilibrium mixture consisting of both the lactones in the ratio of *ca.* 7:2. Three pathways are possible in this equilibration: (a) simple epimerisation of the 6-H through the conjugated butenolide system, (b) retroaldol fission between the 5- and 6-positions followed by recyclisation with stereochemical inversion at the 6-position, and (c) fragmentation of the C(10)—C(5) bond by retroaldolisation in the 1,3-ketol system giving a cyclodecadiene derivative, followed by epimerisation at the 6-position and by subsequent cyclisation into the original decalin system. Pathways (b) and (c) may be excluded, as they proceed *via* intermediates involving more than four enolisable hydrogen atoms. Treatment of (IIIa) with KOBu^t in Bu^tOD afforded a tetradeuteriated product (mass spectrum) as expected *via* pathway (a).

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² This compound has also been synthesised by an alternative route. K. Iwai, H. Kosugi, and H. Uda, *Chemistry Letters*, 1974, 1237.

³ Y. S. Rao, *Chem. Rev.*, 1964, 64, 353.

⁴ T. A. Spencer, K. K. Schmiegell, and K. L. Williamson, *J. Amer. Chem. Soc.*, 1963, 85, 3785; J. A. Marshall and W. I. Fanta, *J. Org. Chem.*, 1964, 29, 2501.