Annelation 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 annelation 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 annelation products, which are attractive intermediates for sesquiterpene lactone synthesis.

β-Vinylbutenolide (I) was conveniently prepared from β-vinylbutyrolactone[1] (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}

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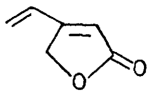
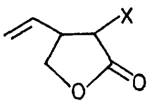
† Relatively unstable neat. Use of (IIc) is more convenient for storage.

‡ 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.

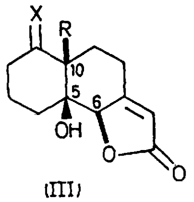


(I)



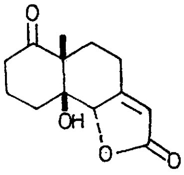
(II)

a; X = H
b; X = SPh
c, X = SPh
$\downarrow$
O

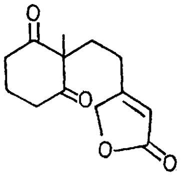


(III)

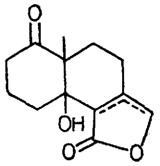
a; R = Me, X = O
b, R = CO_2Et, X = H_2



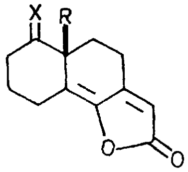
(IV)



(V)

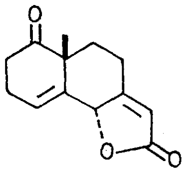


(VI)



(VII)

a; R = Me, X = O
b; R = CO_2Et, X = H_2



(VIII)

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 annelations[4] 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^{t}OH 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 cyclodecadione 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^{t}OD afforded a tetradeuteriated product (mass spectrum) as expected *via* pathway (a).

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[1] K. Kondo and F. Mori, *Chemistry Letters*, 1974, 741.
[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. Schmiegel, and K. L. Williamson, *J. Amer. Chem. Soc.*, 1963, **85**, 3785; J. A. Marshall and W. I. Fanta, *J. Org. Chem.*, 1964, **29**, 2501.