Angular Alkylation *via* Carbenoid Intermediates

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WE report the simple, efficient preparation of the tricyclododecenediones (VIII) and (XI), key intermediates in the total synthesis of tetracyclic diterpenes. Our method employs an intramolecular angular alkylation sequence based on carbenoid intermediates arising from the copper(II)-catalysed decomposition of suitably functionalised bicyclic diazomethyl ketones. This approach, essentially the logical extension of recently reported studies,[1] seems generally applicable, as illustrated in the following synthesis.

Reduction of 6-methoxy-2-naphthoic acid[2] under Birch–Dryden conditions[3] afforded the 1,2,3,4,5,8-hexahydroderivative† (87%, m.p. 131—133·5°) which, on dissolution in benzene–methanol containing a trace of toluene-*p*-sulphonic acid[4] was rapidly converted into the $\beta\gamma$-unsaturated acetal acid (I) (95%, m.p. 101—103·5°). Conversion into the diazomethyl ketone was effected by the dropwise addition of oxalyl chloride (1 mole) to a rapidly stirred, ice-cold solution of the acid (1 mole) in dry benzene containing pyridine (1·1) mole), and quickly filtering the resulting suspension into an excess of ethereal diazomethane. This procedure did involve some anhydride formation and hence contamination of the diazo-ketone by methyl ester, but alternative methods based on inverse addition lead to attack on the labile methyl acetal group. Other acyl activating functions,[5] *e.g.* ethoxycarbonyloxy,[6] required at least 10 days for complete reaction with the weakly nucleophilic diazomethane. Decomposition of a 0·05M-solution of the crude diazo-ketone in refluxing cyclohexane over anhydrous copper(II) sulphate yielded the cyclopropyl ketone (IV) (48%, m.p. 118—120°) which, when hydrolysed in weakly acidic aqueous acetone, underwent concomitant fragmentation to the substituted bicyclo[3,2,1]octanone derivative (VIII) (85%, m.p. 88—90°).

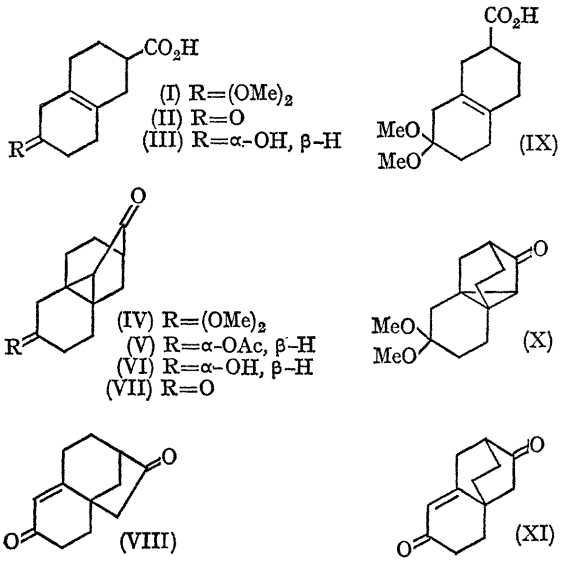
A similar sequence beginning with 1,2,3,4-tetrahydro-2,7-methoxynaphthoic acid,‡ m.p. 122—123·5°, gave, respectively, 1,2,3,4,5,8-hexahydro-7-methoxy-2-naphthoic acid (m.p. 107—109°), ketal acid (IX) (m.p. 110—111°), cyclopropyl ketone (X) (m.p. 103—107°), and finally, the bicyclo[2,2,2]octanone derivative (XI) (m.p. 80—82°).

† Satisfactory C and H analyses were obtained for all crystalline compounds; all compounds reported had spectroscopic properties in accord with the structures assigned.

‡ This compound was prepared by sequential hydrogenolysis and hydrolysis of ethyl 1,2,3,4-tetrahydro-7-methoxy-1-oxo-2-naphthoate, obtained by the procedure of J. H. Hunter and K. Korman, *J. Amer. Chem. Soc.*, 1947, **69**, 2124.

A slightly longer, but equally efficient, procedure which rendered the elaboration of the diazomethylcarbonyl function a routine and higher-yield operation is illustrated in the following sequence. The $\beta\gamma$-unsaturated keto-acid (II) (m.p. 121—124°) obtained from mildly acidic hydrolysis of the 1,2,3,4,5,8-hexahydro-6-methoxy-2-naphthoic acid was reduced by lithium tri-t-butoxyaluminium hydride (2·1 mole, tetrahydrofuran, 0°) to the *trans*-hydroxy-acid (III)§ (90%, m.p. 172—173°), the acetate of which was converted by standard procedures[7] into the oily cyclopropyl keto-acetate (V) in 45% overall yield from the keto-acid (II). Mild alkaline hydrolysis of the acetate gave the crystalline keto-alcohol (VI) [m.p. 121—123°, ν_{max} (Nujol) 3300, 1705, 895 cm.$^{-1}$] which, on careful oxidation,[8] was transformed into the diketone (VII) [m.p. 129—130°, ν_{max} 1715—1705, 896 cm.$^{-1}$] and thence into (VIII) on brief treatment in aqueous acetone with a trace of mineral acid. The isomeric diketone (XI) was also prepared by an equivalent sequence of reactions.

Despite the only moderate recovery of useful products from the insertion reactions, the complete procedure compares very favourably in overall yield and brevity with published procedures.[9]



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§ The relative stereochemistry of this compound is based on *a priori* considerations of reagent approach to the preferred ground-state conformation of the keto-acid (II). *Cf.* S. G. Levine, N. H. Eudy, and C. F. Leffler, *J. Org. Chem.*, 1966, **31**, 3995.

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