

A General Method for the Preparation of Cis-Annulated Rings

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The ability of certain bridged bicyclic olefins to undergo the Cope rearrangement¹ or a formal oxy-Cope rearrangement² suggested a general approach to 5/6, 6/6 and 5/7 cis-fused ring systems which occur in numerous naturally occurring terpenoids.³ This approach involves the Cope rearrangement (1+2) of the vinylbicycloolefins (1; X=CH₂) which provides cis-bicyclic products (2) with unsaturated functionality capable of further useful modification.

The vinyl bicycloolefins (1; X=CH₂; m=1, n=1 or 2) were readily available by Wittig reaction from the corresponding ketones (1; X=O) which were, in turn, prepared by Diels-Alder reactions of cyclopentadiene and cyclohexadienes with vinyl ketones. Diels-Alder reactions involving cyclopentadiene gave predominately (>80%) the endo-adducts (1; X=O, m=n=1, R=Me, i-Pr, t-Bu and Ph) which, on base catalysed equilibration (NaOMe/MeOH) gave values of K_{exo/endo} ranging from 0.98 (1; X=O, m=n=1, R=Me)[†] to 2.96 (1; X=O, m=n=1, R=t-Bu). The steric requirements of the system (1; X=O, m=n=1) resulted in an inefficient Wittig reaction, in most cases, when ether or tetrahydrofuran was used as solvent. Wittig reactions in DMSO gave better yields but resulted in exo-endo equilibration.^{††}

[†]This value differs from that previously reported.⁴

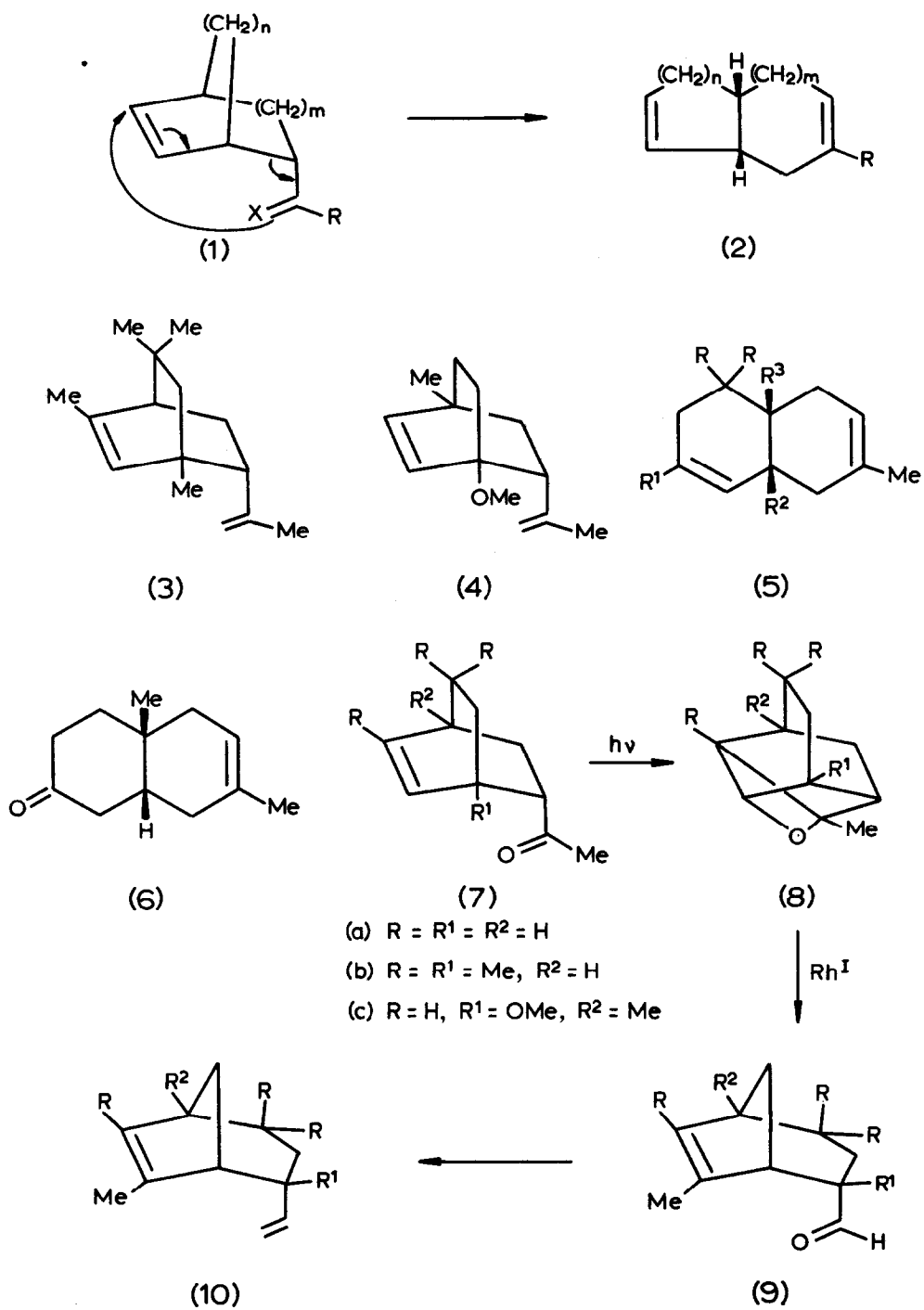
^{††}Such epimerisation problems need not present insurmountable synthetic problems and may be overcome by replacing the epimerisable hydrogen by a suitable substituent.

Similar results were obtained in the bicyclo [2.2.2] octene series (1; X=O or CH₂, n=2, m=1) but in this case the endo isomers predominated on equilibration.

The endo-isomers (1; X=CH₂, m=n=1, R=Me, Et, i-Pr or Ph) were all cleanly and quantitatively isomerised at ca. 150° to the corresponding 5/6 systems (2; m=n=1, R=Me, Et, i-Pr or Ph). In all cases the corresponding exo-alkenyl compounds remained unchanged under the same conditions.

Similar results were obtained with the bicyclo [2.2.2] octenes (1; X=CH₂, m=1, n=2, R=Me), (3) and (4) which rearranged to the corresponding 6/6 systems (2; m=1, n=2, R=Me), (5; R=R¹=R²=Me, R³=H) and (5; R=R²=H, R¹=OMe, R³=Me). The enol ether (5; R=R²=H, R¹=OMe, R³=Me) was readily hydrolysed to the corresponding ketone (6) in the course of chromatography on silica. Temperatures required to effect the Cope rearrangement in the bicyclo [2.2.2] octene series were typically 220-255° and although the exo-isomers of (3) and (4) were unchanged under the conditions required to rearrange their endo-isomers, the exo-isomer of (1; X=CH₂, m=1, n=2, R=Me) was slowly consumed at 225°⁵. N.m.r. spectra were particularly useful in monitoring the reactions, e.g. the characteristic olefinic proton pattern of (4; τ, 5.02, q, 2H, J_{AB}=9Hz, and terminal methylene protons as a broad singlet at τ 5.29) was replaced by that of (5; R=R²=H, R¹=OMe, R³=Me; broad singlet (1H) at τ 4.78 and vinyl ether proton as a broad triplet at τ 5.67).

Our approach to the synthesis of the 5/7 bicyclic system takes advantage of the ready availability of endo-2-acylbicyclo [2.2.2] oct-5-enes previously utilised for the construction of the 6/6 bicyclic systems. Photo-chemical 2+2 cycloaddition (Paterno-Buchi reaction)^{6,7} of (7; a-c) gave the corresponding



oxetanes (8; a-c) in high yield. Cleavage of these oxetanes with $\text{Rh}_2(\text{CO})_4\text{Cl}_2$ gave the endo-2-formylbicyclo [3.2.1] oct-6-enes (9; a-c).⁷ Two of these (9; a and b) have, thus far, been converted by Wittig reaction to the corresponding vinyl derivatives (10; a and b). Thermal rearrangement of (10a) occurred at 232° (14 h., neat liquid) to give one principal product and a considerable amount of unchanged starting material (55:45). G.l.c. analysis also revealed ca. 10% of minor products. A similar result was obtained at 260° in benzene solution. In contrast (10b) was unchanged at 300°. The product from (10a) is currently under investigation.

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