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An Expedient Cyclopentenone Annulation Protocol

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Abstract: A short and efficient procedure of general applicability for $\underline{1} \longrightarrow \underline{2}$ annulation is described.

Annulation process $\underline{1} \rightarrow \underline{2}$ has considerable synthetic value as the structural fragment $\underline{2}$ is present in many terpenic natural products; moreover the reduced and deoxygenated form $\underline{3}$ of $\underline{2}$ is of even more wide occurrence, particularly among sesquiterpenes, Chart 1.¹ While numerous cyclopentenone annulation methodologies are currently available,² we are not aware of any that directly generate the 5,5-dimethyl-cyclopentenone molety $\underline{2}$ from a carbonyl precursor. In the context of our interest in the synthesis of terpenes displayed in Chart 1, we have developed a convenient and efficient procedure for the transformation of $\underline{1} \rightarrow \underline{2}$ and representative examples of successful cyclopentenone annulation of cyclic ketones $\underline{5-8}$ are shown in Scheme 1.



Our annulation procedure basically consists of three steps <u>viz</u>. Barbier-type addition of 3-lithio-2,2-dimethylpropyl-tert-butyldimethyl-silylether $\underline{4}^3$ to the alkanone and deprotection of the TBDMS group, clean and highly efficient oxidation of the resulting diol with Griffith-Ley reagent (tetra-n-propylammonium perruthenate, TPAP)⁴ to the γ -lactone and the rearrangement of the lactone to the <u>gem</u>-dimethylcyclo-pentenone molety in P₂O₅-methanesulphonic acid milieu.⁵ The whole sequence is carried out under mild conditions, is tolerant of other functional groups (e.g. carbonyl) and is short enough to be implemented in a long working day.

General Procedure: Ketones 5-8 (1-2 mmol) in dry ether were introduced into an ethereal solution of 4^3 (2-3 equiv.) in dry ether (5 ml), with stirring and under N₂, at 5-10°. After 15 min, the reaction was guenched with moist ether and the



crude product was dissolved in THF and treated with an excess of tetra-nbutylammonium fluoride to furnish diols 9-12, respectively, in 75-85% yield. The diols 9-12 (1-2 mmol) were dissolved in 10% acetonitrile-CH₂Cl₂ (5 ml) and TPAP (0.08 equiv.) and N-methylmorpholine oxide (2-3 equiv.) were added under N 2 . Standard work-up after 30 min stirring and filtration through a short silica gel column gave lactones 13-16, respectively, in 90-96% yield. Lactones 13-16 (1-2)mmol) were placed under N₂ blanket and P_2O_5 -CH₃SO₂OH reagent (0.5-1 ml)⁵ was introduced. After heating at 80° for 1h under stirring, the reaction was workedup to furnish corresponding enones <u>17-20</u> in 74-80% yield.⁰

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