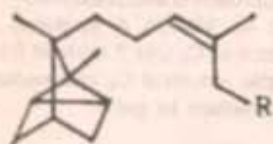


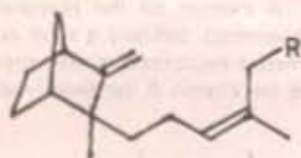
S.a.c.8 UNNIKRISHNAN, P.A.—Studies on the synthesis of  $\beta$ -Santalenes,  $\beta$ -Santalols and related compounds—1989—  
Dr. Paul A. Vatakencherry.

The main components responsible for the fragrance of East Indian Sandal

Wood [*Santalum album*(Linn)] oil are  $\alpha$ - and  $\beta$ -Santalols. The corresponding hydrocarbons namely  $\alpha$ - and  $\beta$ -santalenes constitute the major hydrocarbons present in this very valuable oil. It must also be possible to convert these hydrocarbons to the more valuable santalols by suitable synthetic manipulations. Their structural characteristics i.e. presence of bicyclo [2.2.1] heptane system, geometry of the double bond in the side chain,



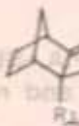
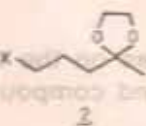
R = -H - santalene  
R = -OH - santalol



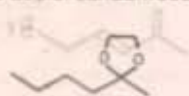
R = -H  $\beta$ -santalene  
R = -OH  $\beta$ -santalol

and orientation of substituents in  $\beta$ -santalenes and  $\beta$ -santalols, as well as the perfumery properties especially that of  $\beta$ -santalols have stimulated active synthetic studies on these and related compounds.  $\beta$ -Santalenes and santalols have been synthesized in connection with structure elucidation studies. Because of their commercial importance many new methods and routes have been developed to synthesize these and related compounds of perfumery value.

The thesis describes studies on the synthesis of  $\beta$ -santalenes,  $\beta$ -santalols and related compounds. It is divided into three chapters. Chapter - I is an introduction which is an upto date review of the synthesis of  $\alpha$ - and  $\beta$ -santalenes and santalols. Chapter - II discusses the scope of the work and the synthetic strategy involved in the present study. The basic strategy involved in the work is the elaboration of suitably functionalised bicyclo [2.2.1] heptane (1) skeleton to  $\beta$ -santalenes and  $\beta$ -santalols. A suitably functionalised  $C_5$  unit (2) that can be easily prepared which after attaching to bicyclo [2.2.1] heptane system is transformed to  $\beta$ -santalenes,  $\beta$ -santalols and related compounds, is employed to yield key synthons 3 and 4. These are transformed into the required  $\beta$ -santalenes  $\beta$ -santalols and related compounds. Synthesis of 3 and 4 and the various procedures described in the thesis allow synthetic manipulations of these to yield not only  $\beta$ -santalenes and  $\beta$ -santalols but also a variety of compounds of interest for studying structure-odour relationships for drawing structural parameters required for a molecular skeleton and functionality that will have useful sandalwood like fragrance and olfactory properties.



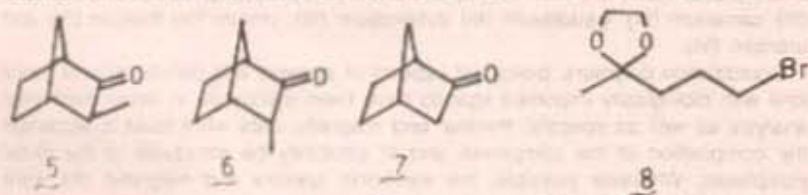
2, R<sub>1</sub>



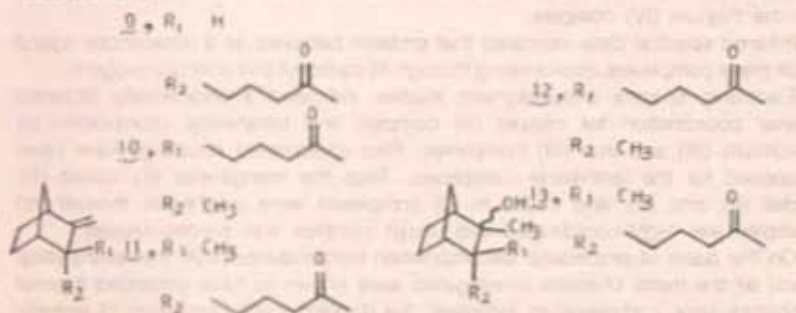
R<sub>2</sub> (CH<sub>3</sub>)  
R<sub>2</sub> (CH<sub>3</sub>)  
R<sub>2</sub>



Methyl derivatives 5 and 6 were prepared from 7 using two different methodologies. The  $\alpha$ -bromoketal (8) was prepared in a two step process in high yields. Alkylation of 5 and/or 6 with 8 is described to get the synthon 3 suitably functionalised for further elaboration to the target molecules. A reverse sequence of reactions to get 4 and an approach to get 3 through through 9 by a different route are also described. Subjecting 10 and 11, obtained from 3 and 4 to a sequence of reactions namely with excess of  $\text{CH}_3\text{MgI}$  followed by  $\text{SOCl}_2/\text{pyridine}$  and alternatively with  $\text{CH}_3^+ \text{P Ph}_3\text{Br}^-$  at the carbonyl functions and attempts to rearrange the terminal olefin at the side chain completes the approach for  $\beta$ -santalenes. The compounds 3 and 4 when converted to 12 and



13 give potential synthons for more valuable  $\beta$ -santalols. Procedures for effecting this and allied conversions are described. This divergent approach is expected to yield  $\beta$ -santalenes,  $\beta$ -santalols and other molecules of interest having  $\beta$ -santalene skeleton easily.



Chapter-III deals with experimental procedures and Chapter-IV is a discussion of results obtained and conclusions based on the work. The list of references is given at the end of the thesis.