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Flexible Approach for Stereoselective Synthesis of Functionalized *Cis*-Hydrindanes: Potential Building Blocks for Natural Product Synthesis♠

Suresh Chander Suri

Hughes-STX Corporation, C/O Phillips Laboratory/RKS
10 East Saturn Blvd., Edwards Air Force Base, CA 93524-7680

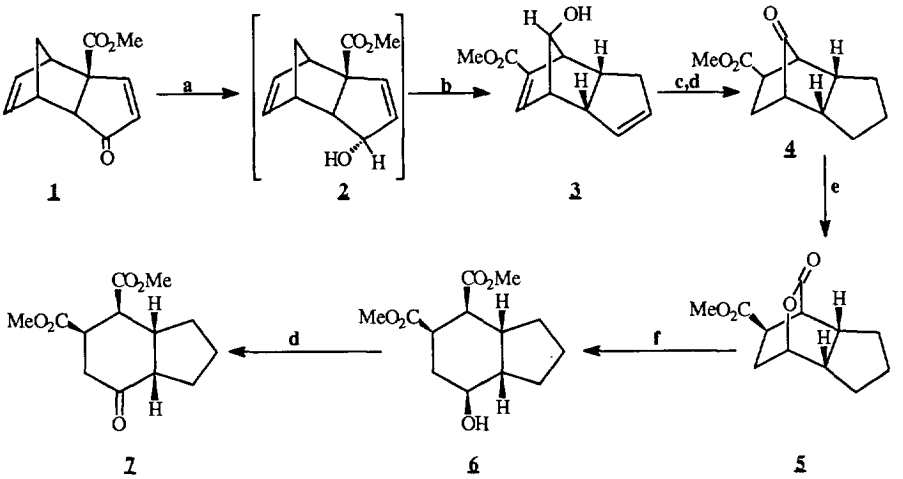
Abstract: Functionalized cis-hydrindanes are conveniently prepared from 2-*exo*-carbomethoxytricyclo-[5.2.1.$0^{2,6}$]dec-3,8-dien-5-ones. Copyright © 1996 Elsevier Science Ltd

Nature is enriched with biologically active polycarbocyclic compounds having entirely or as a core unit *cis*-hydrindane carbon skeleton.[1] It has also been used as a building block for synthesis of a wide variety of natural products. The synthesis of functionalized hydrindanes generally involves an annulation of cyclopentanones[2]/cyclohexanones[3], intramolecular Diels-Alder cyclization of trienes[4] or anionic oxy-Cope rearrangement[5] in bicyclo[2.2.1]systems. The *cis*-hydrindane carbon skeleton is imbedded within 2-*exo*-carbomethoxytricyclo[5.2.1.$0^{2,6}$]dec-3,8-dien-5-ones (**1**)[6] that can be a viable precursor for functionalized *cis*-hydrindanes. Owing to rigid configuration, the chemical transformations of **1** occur in a stereoselective manner. The stereo- and regiochemistry of the substituents in *cis*-hydrindane can be derived from the stero- & regiochemistry of the corresponding substituents in tricyclodecadiene **1**. In this communication, the general approach for the synthesis of functionalized *cis*-hydrindanes from 2-*exo*-carbomethoxytricyclo[5.2.1.$0^{2,6}$]dec-3,8-dien-5-ones (**1**) is described.

The successful strategy to transform **1** into functionalized bicyclo[4.3.0]nonane system (hydrindane) requires dissection[7] of one of the bond between C_1-C_{10}-C_7 carbons. It can only be accomplished by functionalization of C_{10} position in **1**. The functionalization of C_{10} position in **1** is conveniently achieved by Cope rearrangement[6] of the corresponding allylic alcohol **2** which is obtained by Luche reduction ($NaBH_4/CeCl_3/MeOH$)[8] of **1**. The 8-carbomethoxytricyclo[5.2.1.$0^{2,6}$]deca-3,8-diene-10-ol (**3**) on catalytic hydrogenation (10% Pd-C/H_2) furnished saturated hydroxy ester which was converted to corresponding keto ester **4** in 88% yield on exposure to an oxidizing agent tetrapropylammonium perruthenate(VII)/N-methylmorpholine N-oxide (TPAP/NMO).[9] The subsequent oxidation of **4** with peracid (MCPBA/CH_2Cl_2) led to a regioselective lactone[10] in 84% yield. The lactone was assigned structure **5** on the basis of ^{1}H NMR

♠ Dedicated to my mentor Professor Goverdhan Mehta

decoupling experiments. The bridged lactone can be opened by different nucleophilic reagents to furnish variety of substituted cis-hydrindanes. The methanolysis (MeOH/PTS) of lactone furnished single hydroxy diester **6** (82% yield). Conversion of alcohol into keto group with TPAP/NMO furnished the corresponding ketone **7** in 87% yield.



Reagents: (a) $NaBH_4/CeCl_3/MeOH$; (b) distillation; (c) 10% Pd-C/H_2; (d) TPAP/NMO/CH_2Cl_2/molecular sieves; (e) m-CPBA/CH_2Cl_2/0°C; (f) PTSA/dry MeOH

It is noteworthy that this methodology provides *cis*-hydrindane **6** with five contiguous assymmetric centers and is loaded with functionalities which can be elaborated to variety of natural products. Further studies are in progress.

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