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Research Article

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# Synthesis and reaction of 1,2-bis-(2/oxocyclohexyl)ethane and its rearrangement to spiroketone

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## ABSTRACT

*1,2-Bis-(2/oxocyclohexyl) ethane has been prepared by the condensation between cyclohexanone and 1,2 dibromoethane. It was then coverted to dihydroxy perhydrophenantrene and subsequently to a sweet smelling oil when treated with concentrated sulphuric acid by the loss of one molecule of water. Treatment of the 1,2-Bis-(2/oxocyclohexyl)ethane with $BF_3$-acetic acid gave another sweet smelling liquid (m/z 204) identified as spirocyclohexane-2-one. All the structures were assigned by mass, pmr and ir spectra.*

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## INTRODUCTION

Spirocompounds can be defined as cyclic molecules containing at least two rings joined together by a single carbon atom. This unique structural feature has been observed in natural products and has also been the target of methodological studies and syntheses. Spiro compounds having cyclic structures fused at a central carbon are of recent interest due to their interesting conformational features and their structural implications on biological systems. The asymmetric characteristic of the molecule due to the chiral spiro carbon is one of the important criteria of the biological activities. The retention of neurotoxic properties of perhydrohistrionicotoxin, an analogue of a natural product, is clear evidence of the role of the spiro carbon in steering the biological activity [1].The spiro functionality has been known for a long time to be present in phytochemicals either in alkaloids, lactones or terpenoids. The spirocyclic alkaloid (K)-histrionicotoxin isolated from skin extracts of the poison dart frog, *Dendrobats histrionius,* found in Columbia, is a very potent nicotinic receptor antagonist [2]. Therefore, suitably substituted spiroketones may serve as promising lead compound in pharmaceutical research. But the present literature is lack about the simple method of their synthesis.

Condensation of α,ω-dihalo compounds with cyclic ketones is one of the methods of synthesis of spirans [3-4]. A review of this and other reactions leading to carbocyclic spiro compounds have been reported in literature [5-7]. Cristol have reported [4] that the di and tetra-alkylation of ketonic substrates with α,ω-dihaloalkanes yields spiro compounds whereas the alkylation of cyclohexanone with 1,3-dibromo propane led to 2-allylcyclohaxanone. But there was no such kind of reaction with dibromoethane, but with other α,ω-dihalo compounds like 1,4-dibromobutane and 1,5-dibromopentane spiro compounds was obtained. It was felt that 1,2-dibromoethane with cyclic ketone will undergo similar kind of reaction.

In this communication we are reporting our recent work about the synthesis and reaction of 1,2-bis-(2/oxocyclohexyl)ethane and its rearrangement to spiroketone via simple steps.

## EXPERIMENTAL SECTION

*General*
All melting and boiling points are uncorrected. All the compSolvents are dried over anhydrous sodium sulphate.

*1,2-Bis-(2-oxocyclohexyl)-ethane (I)*
A mixture of cyclohexanone (98 g, 1 mole) and 1,2 – dibromoethane (94 g, 0.5 mole) was added in one lot to sodium ethoxide (prepared from 300ml absolute alcohol and 23g sodium) and refluxed on water bath for 6 hours. Excess alcohol was removed under reduced pressure and the reaction mixture carefully acidified with dilute hydrochloric acid. The reaction was extracted with benzene, washed dried and concentrated. The gummy residue on saturation with petroleum ether gave white solid (**I**) (50g) m.p. 156 $^{o}$C.

IR at 1700 and 1440 cm$^{-1}$; PMR in $\delta$ 1.0 (s, 8H), 1.2 (d, 4H J = ) 1.6 (m, 4H), 2.0 (s, 4H), 2.2 (m, 2H); Mass m/z 222, 204,186,96

*Reduction of (I) with sodium amalgam.*
To sodium amalgam ( prepared from 1.8 g clean sodium and 10.0 ml Hg ) warmed to 50 $^{o}$ C was added the diketone (**I**) (2 g) dissolved in 20 ml absolute alcohol in atmospheric nitrogen with stirring. After the addition the reaction mixture was stirred for one hour at room temperature and refluxed for one hour on water bath. The mixture was cooled, mercurry separated and the residue concentrated and diluted with water. The aqueous solution was extracted with benzene, washed dried and concentrated. The dihydroxyperhydrophenanthrene (**II**) separated as a white solid (1.3 g) when recrystallised from benzene-petrolium ether. m.p. 140 $^{o}$C.

IR in 3400 (broad), 1400 and 1370 cm$^{-1}$; PMR in $\delta$ 0.8 (s, 8H), 0.9 (m, 4H), 1.3 (m, 4H), 1.6 (s, 4H), 1.7 (m, 2H) and 3.8(s, 2H); Mass m/z 224, 206, 188, 173, 150, 149, 108.

*Action of conc. Sulphuric acid on (II): Attempted Pinacol-Pinacolone rearrangement*
The diol (**II**) (1 g) was treated with conc. Sulphuric acid (5 ml) and the reaction mixture stirred at room temperature for half an hour. An intence blood red colour developed. The stirring was continued for two hours and the reaction left over night at room temperature. The next day the reaction was diluted with ice cold water, extracted with benzene washed free of acid, dried and concentrated. The residue on distillation gave a sweet smelling oil (500 mg) (**III**) b.p 138/1.5 Torr.

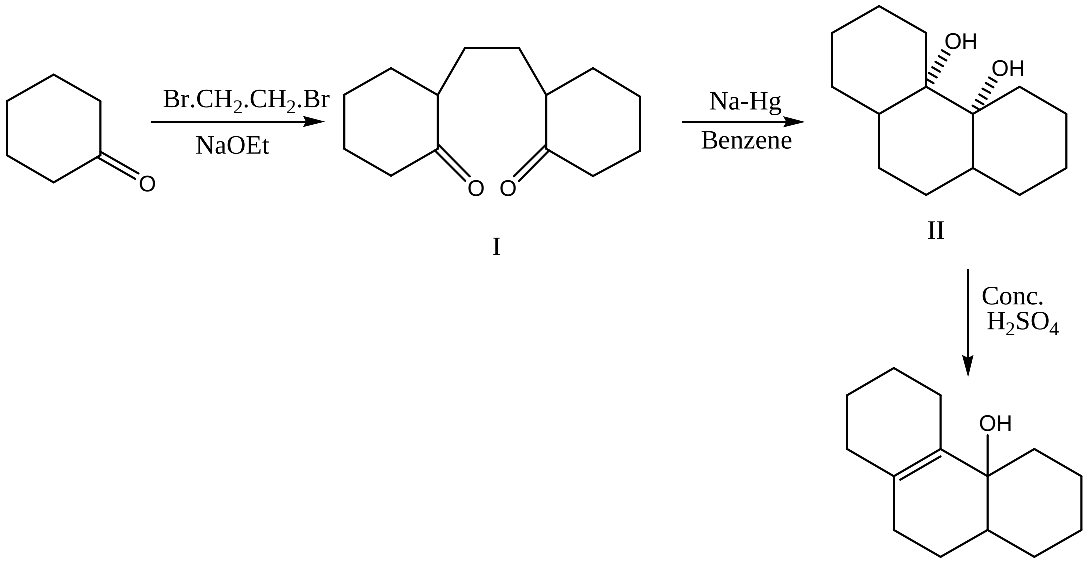
IR in (liquid film) 3400, 1450 and 1070 cm$^{-1}$; PMR in $\delta$ 0.9 (s, 8H), 1.1 (m, 4H), 1.5 (s, 4H), 1.8 (m, 1H), 2.0 (m, 4H), 3.8 (s, 1H); Mass m/z 206, 188, 173,159.

*Treatment of the (**I**) with the Boron trifluoride in acetic acid : Formatiom of spiro compound (**V**)*
The diketone (**I**, 2 g) was dissolved in glacial acetic acid (5 ml) and treated with freshly distilled boron trifluoride in acetic acid (5 ml) and gently refluxed for one hour. The reaction mixture was diluted with water and extracted with benzene. The extract was thoroughly washed free of acid, dried and concentrated. The residue on distillation gave pleasant smelling oil (800 mg) b.p. 120/1.5 Torr.

IR at 1720, 1450, 1250 and 1100 cm$^{-1}$; PMR in $\delta$ 1.2 (m, 8H), 1.5 (m, 4H), 1.8 (m, 4H), 2.2 (m, 2H), 2.5 (m, 2H); Mass m/z 204, 176,148.

## RESULTS AND DISCUSSION

Cyclohexanone with 1,2-dibromoethane in presence of sodium ethoxide in ethanol yields appreciable amounts of white crystalline solid with melting point 156 $^{o}$C. A study of the MASS, PMR and IR spectra clearly indicate the structure of the compound is **I**, 1,2-bis(2$^{/}$-oxocyclohexyl)-ethane. Interestingly such kind of compound (**IV**) was prepared in a nine step sequence starting from cyclohexanone.

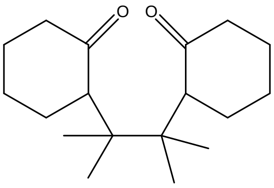


I

II

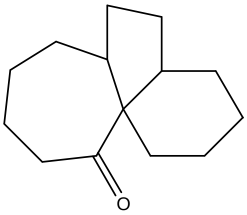
III

Our aim is to study the conversion of the diketone (**I**) to the perhydrophenanthrene diol (**II**) and the study the action of acid on the resulting diol and to convert the diketone (**I**) to a spiro system by acid and base catalyzed aldol condensation reaction.



IV

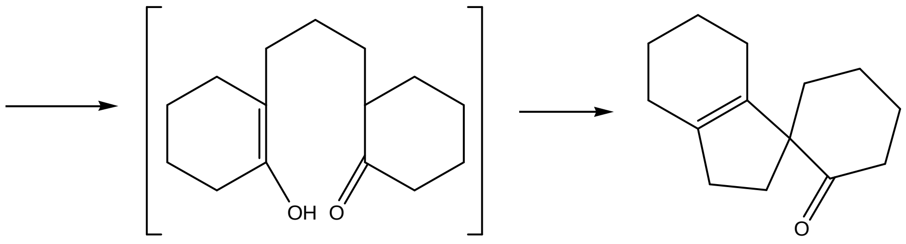
1,2-bis(2$^{/}$-oxocyclohexyl)-ethane was treated with sodium amalgam in benzene under nitrogen for three hours to give a white crystalline compound of melting point 145 $^{o}$C which in IR showed a band at 3400 cm$^{-1}$ indicating the presence of a hydroxyl group. The mass spectrum (m/z 224) indicates that the compound is the unreported perhydrophenanthrenediol (**II**). We hoped that the diol would rearrange to the tricyclic ketone (**V**) under the influence of acids. When the diol was treated with concentrated sulfuric acid, an intense blood red colour developed. The reaction mixture on work up gave pleasant smell oil. The molecular weight (m/z 206) along with the IR spectrum (presence of a band at 3400 cm$^{-1}$) indicates that the compound (**III**) was formed by the loss of one molecule of water.



V

It was thought that acid catalyzed aldol condensation might form a spiro compound. Treatment of doketone (**I**) with BF$_3$-acetic acid gave a sweet smelling liquid (m/z 204) by elimination of one molecule of water from the diketone. The IR (1720 cm$^{-1}$) and PMR spectrum indicate the structure of the compound was **VII** through the intermediacy of **VI**.

I



VI

VII

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