STUDIES ON TETRAHYDRONAPHTHALENONE-4-SPIROPIPERIDINEDIONE DERIVATIVES

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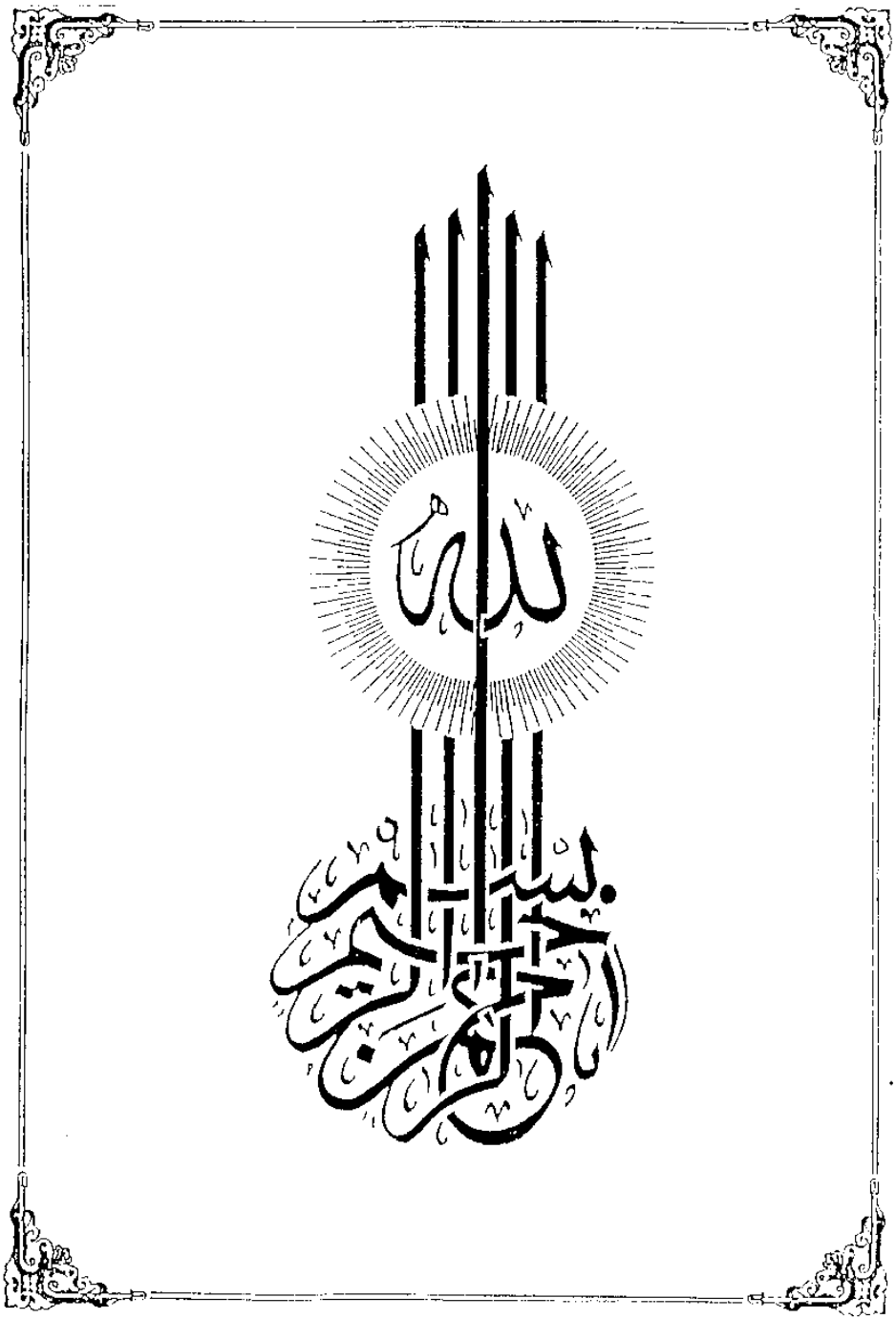

بِسْمِ اللهِ الرحْمَنِ الرحِيمْ

سُبْحَانَكَ لاعِلْمَ لَنَا إلا مَا عَلمْتَنَا إِنكَ أَنْتَ العَلِيمُ الحَكِيم

صدق الله العظيم

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SUMMARY

SUMMARY

When p-tolyl-, p-anisyl-, p-flourophenyl- and 1-naphthyl acetonitrile were allowed to react with acrylonitrile in presence of Triton B, the corresponding trinitrile derivatives were obtained.

When the trinitrile derivatives boiled with dilute hydrochloric acid (for twenty hours) gave 3-aryl-2,6-piperidinedione-3-propionic acids, which when treated with concentrated sulphuric acid and polyphosphoric acid, ring closure took place with the formation of the cyclic ketones $(I_{a,c})$ and $(I_{b,d})$ respectively.

Treatment of the cyclic ketones (I_{a-d}) with some aromatic aldehydes, which are: benzaldehyde, p-bromo-,p-chloro-, p-nitro-benzaldehyde and p-tolaldehyde, in sodium hydroxide solution (2%) gave arylidene derivatives (II_{a-r}).

Reaction of both of hydrazine hydrate and phenylhydrazine with arylidene derivatives (II_{a-r}) in glacial acetic acid and ethanol respectively, gave the corresponding pyrazoline derivatives (III_{a-r}) and phenylpyrazoline derivatives (IV_{a-r}) respectively.

Also, the reaction of benzoylhydrazine with the arylidene derivatives $(II_{a-f,h,j,l,n,o\&q})$ in glacial acetic acid gave the corresponding benzoylpyrazoline derivatives (V_{a-l}).

Dibromo ketone derivatives (VI_{a-r}) were prepared by the reaction of arylidene derivatives (III_{a-r}) with bromine in glacial acetic acid, compounds (VI_{a-r}) were allowed to stand at room temperature for twenty four hours with secondary amine (morpholine) to give spiro-3-(α-morpholinoarylidene)derivatives (VII_{a-r}).

On the other hand, hydrolysis of arylidene derivatives (II_{a-r}) by boiling with sodium hydroxide solution (20%), the piperidinedione ring was opened to give the dicarboxylic acids ($VIII_{a-r}$).

The dicarboxylic acids ($VIII_{a,c,h,i,l,m,n\&q}$) were converted to the anhydrides (IX_{a-h}) when treated with acetyl chloride.

When the anhydrides ($IX_{b,d,f\&h}$) were allowed to react with benzene in presence of anhydrous aluminium chloride under Friedel-Craft's conditions to give the corresponding mono-carboxylic acids (X_{a-d}).

Whereas action of diazomethane on ($II_{a,f,l\&r}$) gave Δ^1-spiropyrazoline derivatives (XI_{a-d}) which on thermal decomposition gave (XII_{a-d}). Action of alcoholic hydrochloric acid on (XII_{a-d}) gave dinitrophenyl hydrazone derivatives ($XIII_{a-d}$) after treatment with 2,4-DNP.

The structure of the previously mentioned products was discussed on the light of their micro-elemental analysis, infrared, nuclear magnetic resonance and mass spectroscopy.

INTRODUCTION

I- Synthesis and reactions of α,ß-unsaturated carbonyl compounds.

The process for the preparation of α,ß-unsaturated ketones RCH=CHCOMe (R=heterocyclic group, substituted Ph) was carried out by Nakajima et.al.(1), by treating an aldehyde RCHO (same R) with Me_2CO in the presence of perhydroisoindole or pyrrolidine as catalyst in H_2O as a solvent. By adding 4-$(Me_2N)C_6H_4CHO$ to a mixture containing Me_2CO,H_2O and pyrrolidine, pure $Me_2NC_6H_4CH$= CHCOMe (58.7% yield) was obtained.

On the other hand Tsukashima et.al.(2) prepared α,ß- unsaturated ketones R'CH=CHCOMe (R'= α-alkyl aliphatic side chain, heterocyclic group) by the treatment of R'CHO with the alkali metal salt of $MeCOCH_2CO_2M$ (M= alkali metal anion) in the presence of 3- azabicyclo-[3.2.2] nonane as catalyst or a secondary cyclic amine in mixture of H_2O and a water-insoluble organic solvent.
A mixture of aqueous $MeCOCH_2CO_2Na$ (0.20 mol), 3,5-dimethylpiperidine, H_2SO_4(pH 7), $CHCl_3$, and iso-butyraldehyde was heated to 40^o for 5h to give pure

5-methyl-3-hexen-2-one in 86.8% yield.

Also α,ß-unsaturated ketones was prepared by Ishiyama et.al.[3] by means of the palladium-catalysed cross-coupling reaction between 9-alkyl-9-borabicyclo-[3.3.1] nonanes (9-R-9-BBN) and 1-halo-1-alkenes under carbon monoxide atmosphere. Thus, treatment of (E) Bu-CH=CHI 9-octyl-9-BBN in dioxane in the presence of $Pd(PPh_3)_4$ and K_3PO_4 under CO gave 98% (E) 5- pentadecen-7-one.

Treatment of 2-morpholino-3-butenenitriles with alkyl halides regioselectively afforded products alkylated on α- position to the nitrile group. Hydrolysis of the α-alkylation products gave the α,ß-unsaturated ketones in good yields, this was investigated by Takahashi **et.al.**[4].

ω-Bromoacetophenone can react with aryl aldehydes in the presence of sodium O,O-diethyl phosphoro-telluroate to give α,ß- unsaturated ketones at room temperature in ethanol with high yields[5]. It was also reported that α-bromoketone reacted with aromatic aldehydes to form α,ß-unsaturated ketones in the presence of dibutyl telluride[6].

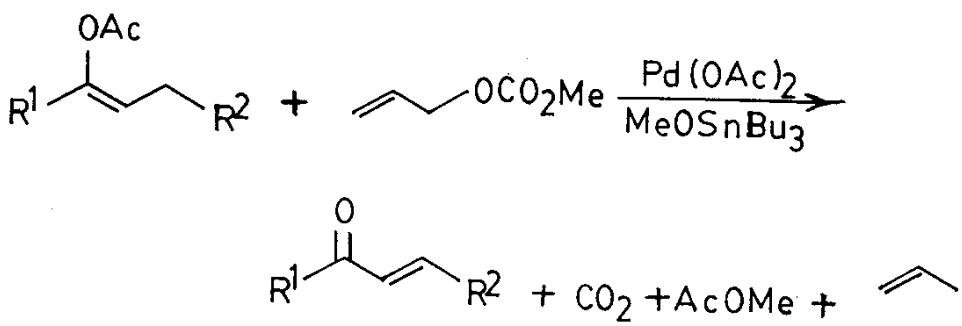
Suzuki[7&8] reported that the synthesis of α,ß-unsaturated esters and nitriles can carried out by using sodium telluride in DMF, but the preparation of sodium telluride needs high temperature, and the reaction requires cooling. A large excess of α-haloesters and nitrile is also necessary.

Other tellurium reagents, such as dibutyl telluride[6], bis(4-methoxy-phenyl) telluroxide[9], and telluronium ylide[10&11], have also been used to synthesize this type of compounds.

The Grignard reaction of ß-(N-alkyl-N-acyl-amino) enones afforded regioselectively α,ß-unsaturated ß-(N-alkyl-N-acylamino)- alcohols, which were converted into α,ß-unsaturated ketones by hydrolysis accompanying dehydration[12].

Conversion of saturated ketones to corresponding α,ß-unsaturated ketones is an important synthetic method . Established methods are based on introduction of hetero atoms (Cl,Br,S,Se) at the α-position, and their elimination with ß-hydrogen [13-15]. Enones were

formed by the palladium-catalyzed decarboxylation-dehydrogenation of allyl ß-keto carboxylates[16] and alkenyl allyl carbonates[17]. Also silyl enol ethers can be converted to enones by the palladium-catalyzed reaction of allylic carbonates[18]. While novel catalytic method was reported for enone formation from enol acetates by the reaction of allyl methyl carbonate using $Pd(OAc)_2$ and tin methoxide as a bimetallic catalyst as expressed by the following scheme:-



Also Tsuji et.al.[18] proved that cyclic enol acetates **(1)** (n=1,2,3,8; R,R' = H,Me) derived from saturated ketones were converted to α,ß-unsaturated cyclic ketones **(2)** by treating **(1)** with $H_2C{=}CHCH_2OCO_2Me$, using a pd-phosphine complex and Bu_3SnOMe.