

HYDRIDE TRANSFER INVOLVING GRIGNARD INTERMEDIATES.

A NEW SYNTHESIS OF IRONES III (1).

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(Received 7 July 1964; in revised form 5 October 1964)

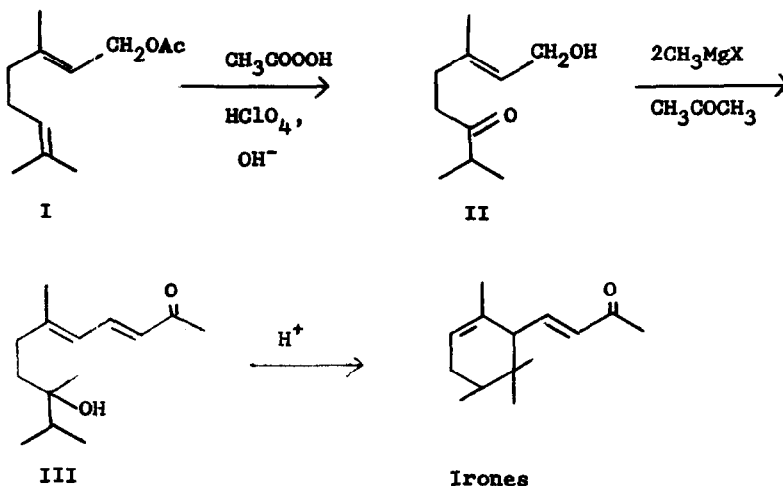
Various synthetic approaches for α -Irone have recently been described (2). The multiplicity of steps involved in some of these syntheses and the relatively poor yields of α -Irone obtained prompted us to seek a shorter synthetic route for α -Irone and its derivatives. We would like to report a novel and shorter synthesis of α -Irones using geranyl acetate (I) as starting material.

Much of the success of our straightforward synthesis was due to the fact that Grignard reaction intermediates, such as IV, possessing hydrogens atoms alpha to the alkoxy group were found to undergo a hydride transfer in the presence of carbonyl compounds acting as acceptors.

A 60% yield of 6-ketodihydrogeraniol (II) was obtained in a single operative step from geranyl acetate (I) when the latter was treated with 40% peracetic acid and the crude intermediate 6,7-epoxydihydrogeranyl acetate (b.p. 110° at 2 mm., n_D^{20} 1.4540) rearranged with perchloric acid to the corresponding 6-ketodihydrogeranyl acetate (b.p. 105° at 1 mm., n_D^{20} 1.4565) and subsequently saponified with aqueous NaOH.

The pure 6-ketodihydrogeraniol (II) (b.p. 115-120° at 1.5 mm., n_D^{20} 1.4695) was then reacted with 2 moles of methyl Grignard and the reaction product treated, in situ, with excess acetone under reflux to yield 6,9,10-trimethyl-9-hydroxyundeca-3,5-dien-2-one (III) (b.p. 140-145° at 1 mm., n_D^{20} 1.5250, 2,4-dinitrophenylhydrazone m.p. 177-178° (EtOH)).

Treatment of hydroxy-ketone III with 85% phosphoric acid afforded a good yield of a mixture of α -Irones (n_D^{20} 1.4980, 4-phenylsemicarbazone m.p. 174-175° (EtOH); the latter gave no melting point depression when mixed with an authentic sample derived from α -neoisoirone) which was identical in composition with that obtained from pseudoirone under similar conditions.



The ability of some magnesium halogen alkoxides to undergo an oxidation-reduction reaction in the presence of certain carbonyl acceptors was described earlier by Schmidlin and Gomberg (3). However, the use of acetone and other ketones both as hydrogen acceptors and condensing agents with Grignard reaction intermediates is novel and of practical value. Under our operating conditions, both primary and secondary alcohols in the form of magnesium halogen alkoxides were found, indeed, to transfer their α -hydrogens to acetone present in a substantial excess. Aldehydes formed from primary alcohols condensed further with acetone, while ketones were usually the final product isolated from secondary alcohols. Thus, benzalacetone was obtained from benzyl alcohol; whereas menthol afforded menthone.

The reaction involved in the hydride transfer of magnesium halogen alkoxides between IV and acetone may find its analogy in the Meerwein-Ponendorf-Oppenauer reaction. The intermediate aldehydo-alkoxide IVa formed, yielded an aldol condensation product upon further reaction with acetone under the catalytic effect of the basic Grignard medium. The water resulting from the dehydration of the aldol compound released the tertiary hydroxyl group and led to the formation of compound III with the concurrent precipitation of the basic magnesium salt. One distinct advantage of our modified Grignard

References

- (1) Parts I and II *J. Am. Chem. Soc.* 81, 2905 (1959);
J. Org. Chem. 26, 3140 (1961).
- (2) M. Mousseron, M. Mousseron-Canet, Ch. Levallois,
Compt. Rend. Ac. Sc. 251, 14 (1960); M. Mousseron-
Canet, Ch. Levallois, *Bull. Soc. Chim.* 993 (1963);
D. H. Barton, M. Mousseron-Canet, *J. Chem. Soc.* 271
(1960); U.S. Pat. 3,117,982 (1964); Belgian Pat.
616,032; W. Kimmel, J. D. Surmatis, J. Weber, G.O.
Chase, N.W. Sax, A. Ofner, *J. Org. Chem.* 22, 1611
(1957); Dorothee Felix, M. Stoll & A. Eschenmoser,
Chimia 5, 174 (1964).
- (3) J. Schmidlin, *Ber.* 39, 4202 (1906); M. Gomberg and
W. E. Bachman, *J. Am. Chem. Soc.* 49, 236 (1927), 52,
4967 (1930); R. V. Shankland & M. Gomberg, *J. Am. Chem.*
Soc. 52, 4973 (1930). Serini, Koster & Strassberger,
U.S.P. 2,379,832 (1945), C.A. 39, 5053 (1945), Oppenauer
U.S.P. 2,384,335 (1945), C.A. 40, 178 (1946).
- (4) *Tetrahedron Letters* 47, 3487 (1964).