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REARRANGEMENT OF α,α-DICHLOROALKYLARYLKETONES WITH GRIGNARD REAGENTS : SYNTHESIS OF HIGHLY STERICALLY HINDERED ALCOHOLS

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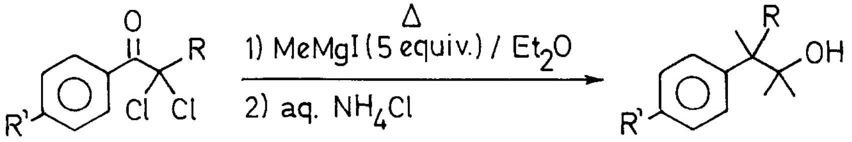
α,α-Dichloroalkylarylketones 1 are a class of α-halogenated ketones which have not been studied extensively. Recently, we reported two syntheses of compounds 1[2,3] and it was shown that they were versatile starting materials for the synthesis of 1-aryl-1,2-alkanediones.[4] We wish to report now the conversion of α,α-dichloroketones 1 into the highly sterically hindered alcohols 2 on treatment with methylmagnesium iodide.



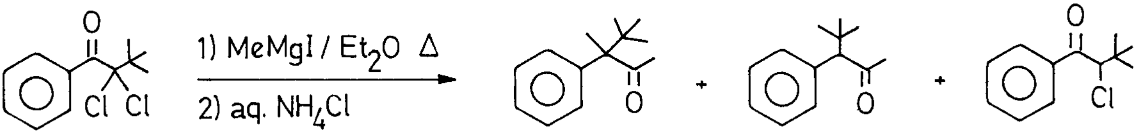
1 2

The rearrangement of α-chloroketones[5,6,7] and α-haloaldehydes[8] with organomagnesium reagents to afford carbonyl compounds is well documented in the literature. The reaction proceeds by initial addition of the Grignard reagent at the carbonyl function followed by rearrangement of the halomagnesium salt of the halohydrin. Accordingly, the rearrangement of the magnesium salts of halohydrins has found wide application in the synthesis of α-substituted carbonyl compounds[9,10,11] while the method was applied to effect ring enlargements[12] and introduction of angular methyl groups.[13,14]

According to our knowledge no reactions of α,α-dichloroketones, e.g. compounds 1, with organomagnesium reagents were reported hitherto.

Treatment of 1-aryl-2,2-dichloropropiophenones 1 (R=Me) with 5 equivalents methylmagnesium iodide in diethylether under reflux (1-2 hr) afforded 3-aryl-

2,3-dimethyl-2-butanol derivatives 2 (R=Me) as the sole product. Higher substituted derivatives 1 (R=Et, n-Pr) yielded tertiary alcohols 2 in similar way, while the bulky 2,2-dichloro-3,3-dimethyl-1-phenyl-1-butanone 1 (R=t-Bu; R'=H) gave a complex reaction mixture, which consisted of 39 % 4,4-dimethyl-3-phenyl-2-pentanone 3, 17 % 3-phenyl-3,4,4-trimethyl-2-pentanone 4 and 14 % 2-chloro-3,3-dimethyl-1-phenyl-1-butanone 5 as revealed by GLC.



1 (R=t-Bu; R'=H) 4 3 5

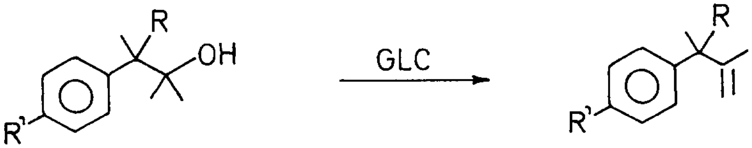
Table I gives a survey of the synthesis of alcohols 2.

TABLE I : Synthesis of 3-Alkyl-3-aryl-2-methyl-2-butanol Derivatives 2

R	R'	Yield	B.p.
Me	H	86 %	51- 52°C/0.05 mmHg[a]
Me	Cl	85 %	105-110°C/0.5 mmHg
Me	Br	75 %	84- 92°C/0.006 mmHg
Et	H	86 %	56- 58°C/0.05 mmHg
n-Pr	H	70 %	70- 76°C/0.02 mmHg

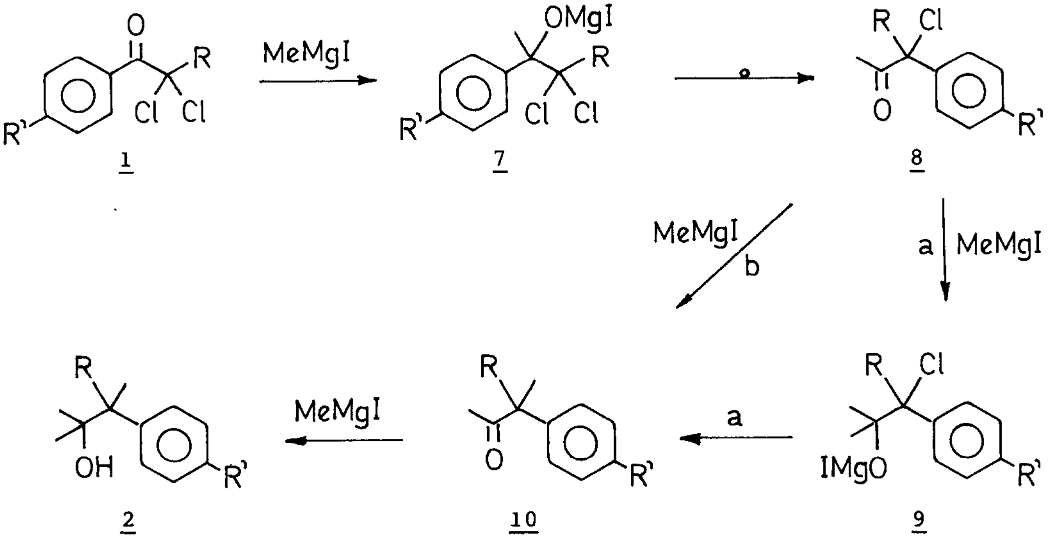
[a] Lit. bp 123-126°C/16 mmHg (ref. 15)

Compounds 2 were isolated by high vacuum distillation. Gas chromatographic analysis of these compounds gave partial dehydration into the corresponding alkenes 6.



2 6

From the mechanistic point of view, it is well established[9,16] that compounds 1 are initially attacked at the carbonyl function followed by rearrangement of the resulting halohydrin salt 7, involving a pseudo pinacol rearrangement or a rearrangement via an intermediate epoxide, into α-chloroketone 8 (aryl migration). The latter compound again is susceptible to addition of the Grignard reagent at the carbonyl function and subsequent rearrangement of halohydrin salt 9 to yield ketone 10 (path a, involving methyl migration). An alternative route consists of a substitution reaction (path b). In view of the deviating migratory aptitude of the aryl group in preference of the methyl group, work is in progress to distinguish between the two plausible pathways a and b. Finally, ketone 10 is converted into alcohol 2 by simple Grignard addition to the carbonyl function.



The reported method for the conversion of easily accessible[2,3] 1-aryl-2,2-dichloro-1-alkanones 1 into the highly sterically hindered alcohols 2 hides several possibilities which are currently under research. In our opinion, the synthesis of crowded compounds 2 described in this paper may be regarded as useful in view of the continuing interest in sterically crowded organic molecules.[17]

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