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REACTION OF A CHIRAL CYCLOPROPYL HALIDE WITH ALKALI METALS IN ALCOHOL SOLVENTS. THE SURFACE NATURE OF THE REACTION.[1]

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Abstract: An alcohol solution (methanol, isopropanol or *t*-butanol) of (S)-(+)-1-bromo-1-methyl-2,2-diphenylcyclopropane (**1**) was treated with an alkali metal (lithium, sodium, or potassium). The resultant hydrocarbon. (R)-(-)-1-methyl-2,2-diphenylcyclopropane (**2**), was shown to be optically active and with retained configuration. As in Grignard reagent formation, the reactions are viewed as occurring largely on the surface of metal.

The reaction of alkali metals with organic halides has been a subject of interest and vigorous investigation[2]. The alkali organometallics obtained have found extensive use as reagents in organic syntheses[3]. Our early study[4] on the mechanism of formation of these reagents involved the reaction of lithium metal with chiral 1-X-1-methyl-2,2-diphenylcyclopropane (X=Cl, Br, I) in an aprotic ether solvent. The conclusions that came from this study are as follows:

a) The stronger the carbon-halogen bond the greater the retention of configuration; Cl> Br> I.

b) The greater the surface area (the smaller the particle size) the greater the retention of configuration.

c) Lowering the ionization potential of the lithium surface by increasing the sodium content increased the reactivity as well as the *retention of configuration.*

We proposed[4] the mechanistic scheme shown in Figure 1 with a surface bound intermediate (A) resulting from reaction (1), modified as suggested by Shechter[5], to account for the above observations.

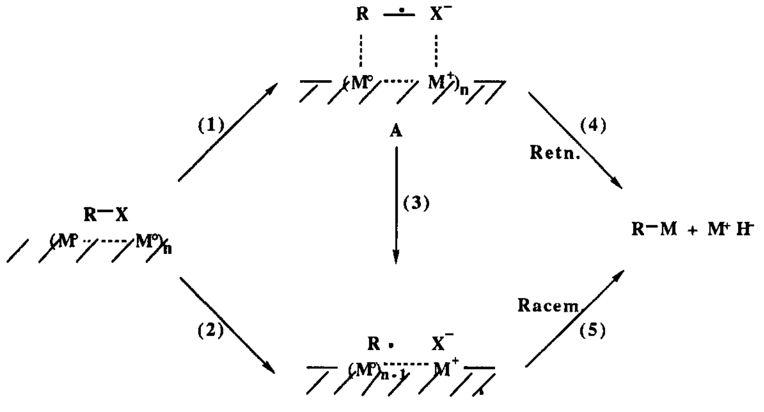
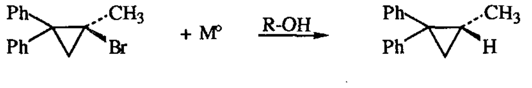


Fig. 1. A Mechanistic scheme for organoalkali metal formation.

Recently, Shechter et al.[5] have reported on their detailed investigation of the reaction of alkyl halides with alkali metals in an alcohol solvent, 2-ethoxyethanol. We now wish to report, **Table 1**, our stereochemical results on the reaction of chiral **1** with alkali metals (Li, Na, K) in alcohol solvents.

Table 1. Treatment of (S)-(+)-**1** with alkali metals in alcohol solvents.



(S)-(+)-**1** (R)-(-)-**2**

M°	R-OH	(R)-(-)-2 Yield, %	$[\alpha]^{25°}_{Hg}$	Opt. Purity[a], %
Li	i-Pr	94	-59	39
Li	*t*-Bu	100	-68	45
Na	Me	100	-71	47
Na	*i*-Pr	100	-70	47
Na	t-*Bu*	100	-69	46
K	*i*-Pr	30	-66	44
K	*t*-Bu	9	-66	44

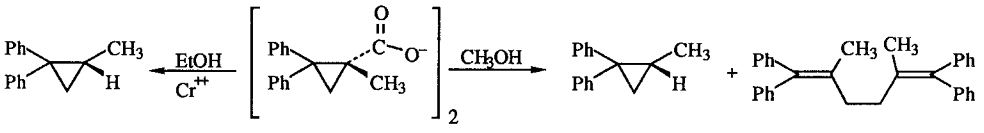
a) Based on $[\alpha]^{25°}_{Hg}$+ 130° for optically pure **1** and $[\alpha]^{25°}_{Hg}$- 150° for **2**.

The reaction of (S)-(+)-**1** with lithium metal in *ether* followed by carbonation yields[4] the corresponding acid with an optical purity of 41-45%. One can see from **Table 1** that irrespective of the solvent or metal used, the optical purities of (R)-(-)-**2** are roughly identical and retained configuration. Moreover, they are almost identical to the result obtained with lithium in ether.

The reason for the low yields of **2** with potassium is that potassium reacts with alcohol solvents much faster than it does with the substrate **2**. On the other hand it is not entirely clear why lithium in methanol resulted in only reaction with solvent and not substrate. Apparently there needs to be a balance in the reactivity of the metal toward solvent and substrate which seems to be met by sodium where you obtain a quantitative yield of product regardless of the alcohol used. From a synthetic point of view sodium is the obvious choice of metal for these Bouveault-Blanc type of reductions.

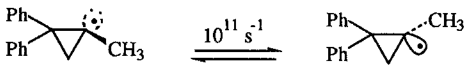
Evidence for the surface nature of the reaction is provided by product analysis and stereochemistry. For example, the reaction of (±)-**1** with sodium in CH_3O-D gave a quantitative yield of (±)-**2** with >95% deuterium incorporated in the 1-position of (±)-**2**. If the radical **5** was in solution as a reactive intermediate then it would be expected to abstract a hydrogen atom from the methyl group of the solvent[6]. The deuterium incorporation is the result of the product R-M being quenched by CH_3O-D.

Also, as we have previously shown[7], when radical **5** is generated in methanol solution a 1:1 mixture of **2** and **4** is obtained. The latter is formed by ring opening of **5** to the allyl radical which dimerizes and this occurs only when the radical has a reasonable lifetime in solution[8]. Significantly, **4** is completely absent in the reaction of alkali metals with **1** in alcohol solvents.



(±)-**2** (R)-(-)-**3** **2** **4**

Finally, the stereochemical result, ~ 45% optical purity or ~ 73% retention of configuration, speaks strongly for a surface bound intermediate since it has been shown by Ingold[9] that radical **5** has an inversion frequency of 10^{11} s^{-1} and hence could not accommodate this radical being free in solution.



5 **5**

We view the mechanism of this reaction as depicted in Fig. 1. Electron transfer from the alkali metal surface to the σ* antibonding orbital of the R-X bond to give the radical anion A on the surface of the metal. The collapse of A leads to the formation of chiral R-M which is quenched by solvent to yield R-H with retention of configuration (pathway 1,4). Alternatively, A can collapse to yield a loose radical pair R· °M adsorbed on the surface (path 3) or the radical pair can be formed directly via path 2. A 180° rotation of R· followed by reaction with the metal to form racemic product.

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