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A NOVEL YLIDE-ANION FORMATION RESULTING FROM NUCLEOPHILIC ADDITION. SYNTHESIS OF TRANS-α-TRIFLUOROMETHYL ALLYLIC ALCOHOLS

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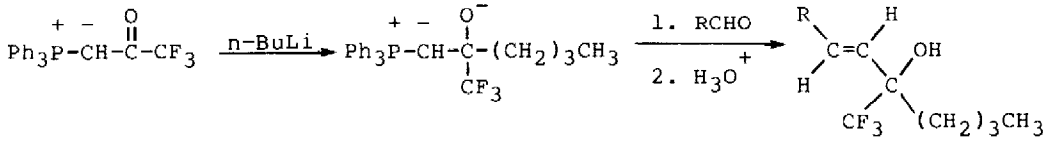
Summary. A novel ylide-anion formation resulting from nucleophilic addition of n-butyllithium and its application to the synthesis of trans-α-trifluoromethyl allylic alcohols are described.

Allylic alcohols are employed as useful intermediates in organic synthesis particularly for the synthesis of biologically active compounds.[1] Therefore reactions leading to the formation of allylic alcohols, especially fluoro species, have attracted much attention. Numbers of methods to prepare allylic alcohols are known,[2] but the synthesis of α-trifluoromethyl allylic alcohols has not been reported previously.

Ylide-anion with higher reactivity was first reported by Corey and Kang using sec-butyllithium or tert-butyllithium as a base to deprotonate the ylide, methylenetriphenylphosphorane, and was applicable with unreactive substrates such as epoxides or hindread ketones.[3] However its use as synthetic reagents was still limited.[4] Usually ylide-anion was generated by deprotonation of ylide with a base. Alternatively, we now wish to report a novel ylide-anion formation resulting from nucleophilic addition to carbonyl group neighbouring to the perfluoroalkyl group and its application to the synthesis of trans-α-trifluoromethyl allylic alcohols.

The reaction sequence is shown as follows:



1 **2** **3**

Due to the strong electron-withdrawing effect of trifluoroacetyl group, trifluoroacetylmethylenetriphenylphosphorane (1), or even more reactive arsorane was very stable and unable to react with aldehydes.[5] Attempt to activate this phosphorane by nucleophilic addition of n-butyllithium to the carbonyl group has succeeded, because the reactivity of the carbonyl group neighbouring to the trifluoromethyl one is enhanced. In this case the n-butyllithium as a nucleophile rather than a base attackes 1 to give an ylide-anion **2** which reacts with aldehydes to afford , after hydrolysis, trans-α-trifluoromethyl allylic alcohols in 46-55% yields (2 steps). The aldehydes may contain double bonds. The double bond conjugated with a carbonyl group does not interfere with the reaction, the attack being at the carbonyl carbon.

In a general procedure n-butyllithium (1 mmol) is added dropwise with stirring to a solution of trifluoroacetylmethylenetriphenylphosphorane (**1**)[6] (1 mmol) in absolute diethyl ether (10 ml) at -70°C under nitrogen. The reaction mixture is stirred for 1 h at -70°C, allowed to warm to 0°C and the aldehyde (1 mmol) is slowly added. After stirring at 0°C for 4 h, 5% aqueous hydrochloride solution (2 drops) and water (40 ml) are added. The mixture is extracted with diethyl ether (3 X 10 ml). The organic layer is collected, washed with water until neutral and dried. Evaporation of the solvent gives a residue which is purified by column chromatography on silica gel eluting with petroleum ether (b.p.60-90°C)/ethyl acetate (9:1) to afford product (**3**).

The results are shown in Table 1. All products are new and characterized by microanalyses, IR, NMR and mass spectroscopy. Neither MeLi nor PhLi could be used in this reaction, no product was obtained in both cases. Unfortunately aliphatic aldehydes resulted in a resinous product.

Table 1.

Compound	R	B.P.(°C/0.5 mmHg)	Yield(%)
3a	C_6H_5	100	54
3b	4-$CH_3C_6H_4$	120-122	51
3c	4-ClC_6H_4	120	48
3d	4-FC_6H_4	122-124	55
3e	4-$NO_2C_6H_4$	140	46
3f	4-$CH_3OC_6H_4$	128-130	49
3g	2,4-$Cl_2C_6H_3$	138-140	49
3h	$C_6H_5CH=CH$	136-138	46

This one-pot synthesis of α-trifluoromethyl allylic alcohols is quite convenient, giving the trans-isomer exclusively as judged on the basis of their ^1H NMR spectra, should be useful in the synthesis of biologically active compounds.

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