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PHENYLTETRAFLUOROPHOSPHORANE AS A SELECTIVE FLUORINATION AGENT FOR ALCOHOLS

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A recent communication by KOOP and SCHMUTZLER[1] prompts us to report our own results on the evaluation of fluorophosphoranes as selective fluorination agents for hydroxyl groups. Earlier reports by SCHMUTZLER[2,3] mentioned his failure to prepare the alkoxy substituted fluorophosphorane RPF_3OR' (R = Ethyl; R' = i-Propyl) by reacting the fluorophosphorane with the trimethylsilyl ether of the alcool $(CH_3)_3SiOR'$. Instead, he obtained their decomposition products $RP(O)F_2$ and R'F. We undertook to apply this observation to the selective fluorination of hydroxyl groups which, so far, has not received a fully adequate solution.

Phenyltetrafluorophosphorane ($R = C_6H_5 = Ph$) was selected as a convenient compromise between reactivity and stability when compared to diphenyltrifluorophosphorane and ethyltetrafluorophosphorane[3], and for its greater availability. Both the direct reaction of $PhPF_4$ on the alcools, and the alternative route through their silyl ethers were investigated.

The direct reaction gave poor results (low conversion ratio, predominant elimination products), although some C-F compound was generally formed. A comparable attempt by other workers[4], using diphenyltrifluorophosphorane in rather drastic conditions (12hrs, 120°C), did not meet with more success.

On the contrary, the reaction of $PhPF_4$ with the silyl ethers, according to :

$$R'OH \xrightarrow[\text{Pyridine}]{ClSi(CH_3)_3} R'OSi(CH_3)_3 \xrightarrow{PhPF_4} [R'OPF_3Ph] \longrightarrow R'F + PhP(O)F_2$$

could be performed in very mild conditions, at or below room temperature, although in some cases heating was needed to accomplish the last step.

The method was tested on over 20 alcohols. The formation of the trimethylsilyl ethers was generally quantitative. Their conversion was always complete. The formation of the expected fluorinated compound has been observed in most cases. However, there appears to be some disagreement with KOOP and SCHMUTZLER on the importance of olefin formation through elimination reactions, which, in our hands, was observed each time that it was possible, including for example with primary alcools.

Typical conversion ratio in fluorination and elimination products, obtained when the silyl ether was dropwisely added into an equivalent quantity of ice-cooled fluorophosphorane so as to maintain an excess of the fluorophosphorane throughout the reaction, are as follows (% fluorination / % elimination) : 1-pentanol (50/50); 2-pentanol (60/40); 3-pentanol (60/40); t-butanol (90/-); cyclopentanol (40/60); cyclohexanol (30/70); cholesterol (90/-); 2-chloroethanol (>95/-); 3-chloropropanol (95/5); 4-chlorobutanol (75/25). The extent of elimination could, as yet, not be significantly reduced by operating at lower temperature, nor by dilution with CCl_4 or CH_3CN, nor by using an excess $PhPF_4$.

Special attention was given to the selectiveness of the reagent. Thus the substitution of the chlorine atoms was never observed during the fluorination of the chloro-alcools $Cl(CH_2)_nOH$, CCl_3CH_2OH and $PhCH(OH)CH_2Cl$. 3β-fluoro-5-cholestene was isolated in 90% yield; no addition of fluorine atoms on the double bond was detected. In the case of 2-bromoethanol however, the main reaction product was 1,2-dibromoethane (40%) along with 1-bromo-2-fluoroethane (10%).

An electron attracting R' rest strongly stabilizes the intermediate phenylalkoxytrifluorophosphorane. Its temperature of decomposition to the C-F compound increases markedly along the series $Cl(CH_2)_n$- from n = 4 to 2 while the extent of elimination decreases. With R' = CCl_3CH_2- the alkoxyfluorophosphorane became too stable to allow the recovery of the C-F compound.

The new phenylalkoxytrifluorophosphoranes $PhPF_3OR'$ with R' = $ClCH_2CH_2$- and CCl_3CH_2- were isolated and identified through NMR and mass spectrometry.

1-chloro-2-fluoroethane was prepared in 80% yield when the silyl ether was added into the phosphorane and the intermediate alkoxyfluorophosphorane was heated to 150°C. When the order of addition was inverted all the silyl ether was consumed and the expected amount of $FSi(CH_3)_3$ was collected well before than the equivalent amount of $PhPF_4$ had been added to the silyl ether. In this case significant amounts of the ether $(ClCH_2CH_2)_2O$ and of $PhP(O)F_2$ were present, already at 0°C, besides the expected alkoxyfluorophosphorane, thus indicating that further reaction takes place between the alkoxyfluorophosphorane and the silyl ether.

Benzyl alcohol on the other hand was converted to a polymer whereas benzhydrol always gave benzhydryl ether (80%) and some $Ph_2CHCHPh_2$ (~20%), with no C-F compound present. Partial fluorination (~60%) was again achieved when benzyl alcohol was substituted by the chloromethyl group in $PhCH(OH)CH_2Cl$.

Separation of the C-F compounds was performed through distillation for the lower boiling terms. For the others, distillation was preceded by alcaline hydrolysis and solvent extraction. Further separation was then achieved through distillation or adsorption chromatography. When necessary the ethylenic compounds were bromated or oxidized in order to allow an easier recovery of the C-F compound.

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