Pergamon

Tetrahedron Letters, Vol. 35, No. 52, pp. 9775-9778, 1994
Elsevier Science Ltd
Printed in Great Britain
0040-4039/94 $7.00+0.00

0040-4039(94)02122-8

Synthesis of Fluorophosphoranes via The Mitsunobu Reaction

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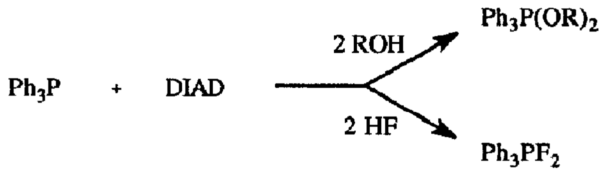
Abstract: Treatment of triphenylphosphine with potassium hydrogen fluoride or hydrogen fluoride-pyridine and diisopropyl azodicarboxylate in acetonitrile or tetrahydrofuran, at room temperature results in the clean formation of difluorotriphenylphosphorane. Analogous results were obtained with other phosphines such as tributylphosphine and tris(dimethylamino) phosphine.

Introduction

Previous work from this laboratory[1-7] and others[8] has shown that the Mitsunobu reaction[9,10] can be used for the synthesis of dialkoxytriphenylphosphoranes, diaryloxytriphenylphosphoranes, and dialkoxytributylphosphoranes (see Scheme 1).

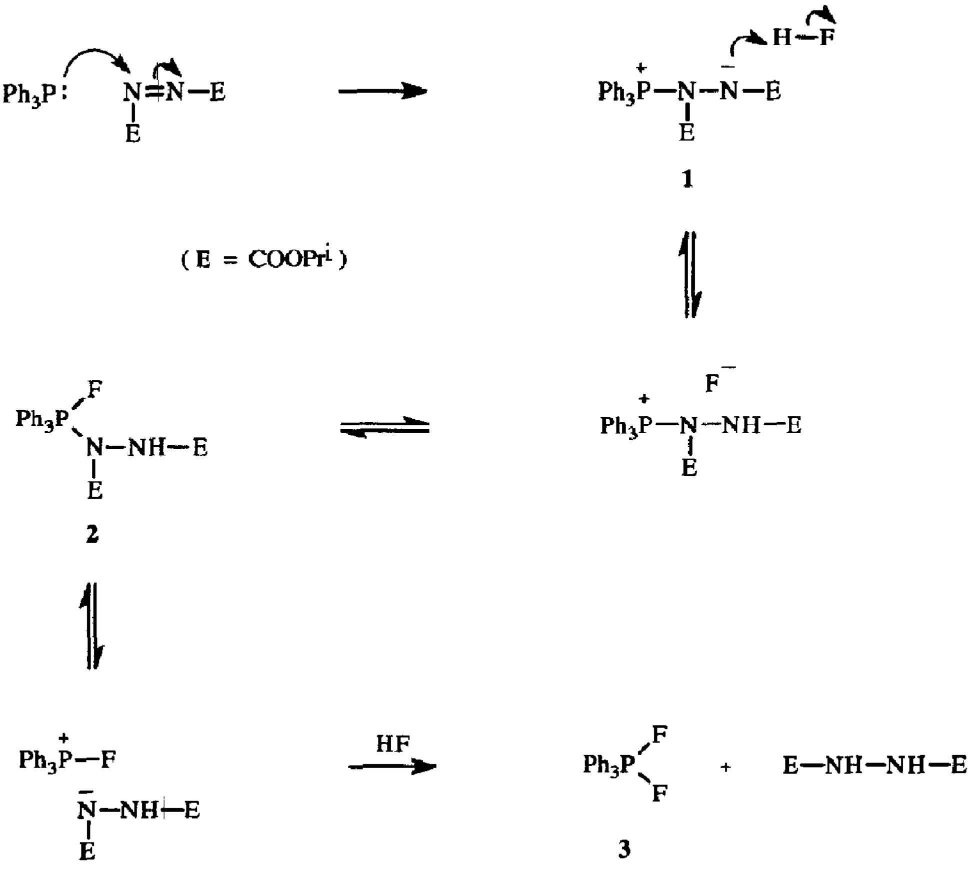


Scheme 1

We now report that the Mitsunobu reaction can be used similarly to prepare difluorotriphenylphosphorane, Ph_3PF_2, from readily available reagents under very mild conditions. Difluorotriphenylphosphorane is a useful reagent for converting primary and secondary alcohols into alkyl fluorides.[11,12] Previous methods of preparation of Ph_3PF_2 have involved use of reagents such as hexafluoroacetone[13], dinitrogen tetrafluoride,[14] sulfur tetrafluoride,[15] phenyl carbamoyl fluoride[16] and difluorodiazirine.[17] The present method employs the cheap, easily handled, and readily available reagent potassium hydrogen fluoride, KHF_2 (hydrogen fluoride-pyridine can also be used).

Results and Discussion

Triphenylphosphine (86 mg, 0.33 mmol), finely ground potassium hydrogen fluoride (130 mg, 1.66 mmol), and dry acetonitrile (3 ml) were placed in an nmr tube under a nitrogen atmosphere. The solution was shaken to dissolve the triphenylphosphine, cooled to 0°C and, following the addition of diisopropyl azodicarboxylate (65 µl, 0.33 mmol), placed in a sonic bath for 1-2 hrs. ^{31}P nmr showed clean conversion to difluorotriphenylphosphorane, **3**, δ - 56.5 ppm (triplet, J_{PF} 666 Hz) (Literature[18] value, -56 ppm, J_{PF} 666 Hz). Also present was a small singlet at δ 27.5 ppm, due to triphenylphosphine oxide (this is always seen[1-7] in Mitsunobu reactions and is due to hydrolysis of the initially formed betaine, **1**, by traces of moisture). On standing overnight, large white crystals of the phosphorane **3** were deposited (66 mg, 67 %, m.p 159-162°C) (Literature[13-16] m.p.'s range from 134-142°C to 160°C). When these crystals were dissolved in tetrahydrofuran, ^{31}P nmr showed a clean triplet, (δ - 57.7 ppm, J_{PF} 668 Hz). Addition of a drop of water to this solution resulted in slow hydrolysis and the formation of triphenylphosphine oxide (there was little change after 1 hr. but after 24 hrs., hydrolysis was complete).



Scheme 2

When the reaction was carried out in tetrahydrofuran as solvent and in the absence of sonication, the reaction was much slower and an intermediate could be observed by ^{31}P nmr. Thus, in the early stages of the reaction (1 hr, r.t.) a doublet was observed at δ - 48.5 pm (J_{PF} 560 Hz) as well as the (smaller) triplet (δ - 57.7 ppm, J_{PF} 668 Hz). As the reaction progressed, the doublet decreased while the triplet increased in intensity (50:50 after 24 hrs. at r.t.). Analogous results were obtained when the potassium hydrogen fluoride was replaced by hydrogen fluoride-pyridine, except that the initially formed doublet was converted to the triplet more rapidly (2 hrs., r.t.). We suggest that the intermediate formed is the monofluorohydrazinotriphenylphosphorane, **2**, and a mechanism is outlined in Scheme 2. An analogous intermediate (an O, N-phosphorane) has been proposed (but never observed) in the Mitsunobu reaction with alcohols[1]

In the absence of sonication, the reaction was much slower in both acetonitrile and tetrahydrofuran, presumably due to the insolubility of KHF_2 in organic solvents. When toluene was used as solvent, the reaction was extremely slow [after sonication for 2 hrs., only **1** (95%) and **2** (5%) were present].

The Mitsunobu synthesis of difluorophosphoranes using either KHF_2 or HF-pyridine appears to be general. Thus, tributylphosphine, tris(dimethylamino)phosphine and trimethylphosphite all gave rise to the corresponding difluoro derivatives [however it should be noted that in the case of trimethylphosphite, the yield was much lower (~15%) presumably due to decomposition of the $(MeO)_3P$/DIAD betaine prior to the (slow) reaction with KHF_2]. The results are summarised in Tables 1 and 2.

Product	δ_P (ppm)			J_{PF} (Hz)		
	MeCN	THF	Lit[18]	MeCN	THF	Lit[18]
Ph_3PF_2	-56.5	-57.7	-56	666	668	666
Bu_3PF_2	-11.1	-13.9	-14.5	570	582	585
$(Me_2N)_3PF_2$	-62.6	-64.2	-65.7	700	700	700
$(MeO)_3PF_2$	-70.8	-	-72	717	-	719

Table 1 ^{31}P nmr data for Difluorophosphoranes prepared via the Mitsunobu reaction.

Product	δ_F (ppm)			J_{PF} (Hz)		
	MeCN	THF	Lit[17]	MeCN	THF	Lit[17]
Ph_3PF_2	-39.8	-42.9	-39.8	654	672	664
Bu_3PF_2	-37.6	-	-34.2	568	-	588
$(Me_2N)_3PF_2$	-55.0	-	-53.5	697	-	707
$(MeO)_3PF_2$	-70.8	-	-72.8	722	-	706

Table 2 ^{19}F nmr data for Difluorophosphoranes prepared via the Mitsunobu reaction.

In conclusion, the Mitsunobu reaction employing diisopropyl (or diethyl) azodicarboxylate provides a simple, mild, procedure for the synthesis of difluorophosphoranes, R_3PF_2, from a range of trivalent phosphorus compounds, R_3P.

Acknowledgments. We thank the Australian Research Council and Griffith University for financial support.

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(*Received in UK* 12 *October* 1994; *accepted* 26 *October* 1994)