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BIS(1-TRIFLUOROMETHYL-2,2,2-TRIFLUOROETHOXY)TRIPHENYLPHOSPHORANE. A NEW ROUTE TO TRIFLUOROMETHYLATED HETEROCYCLES

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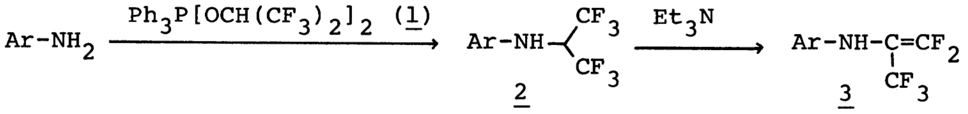
Bis(1-trifluoromethyl-2,2,2-trifluoroethoxy)triphenylphosphorane(1) readily reacted with anilines to form N-hexafluoroisopropylated products(2). By the dehydrofluorination of 2, 2-arylamino-1,1,3,3,3-pentafluoropropenes(3) were obtained. Furthermore, when anilines with *o*-functional group were used as nucleophile, benzo-1,4-dihetero-six membered rings that have CF_3 group at N-α-position were obtained.

Phosphoranes with fluoroalkoxy group as ligand are known to be remarkable compounds as to the stereochemistry for phosphorus atom.[1)] However, little other utilities of these compounds in the synthesis of organofluorine compounds have been studied.[2)]

On the other hand, heterocyclic compounds with trifluoromethyl group are attracting attention owing to their biological unique properties in these days.[3)]

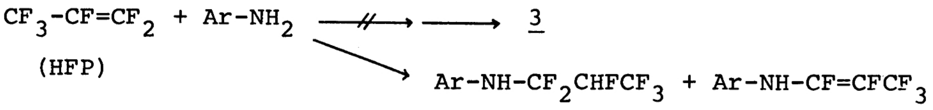
In our continuing study of phosphoranes,[4-6)] we have found a new route to introduce the trifluoromethyl group into a desired position of heterocycles.

Bis(1-trifluoromethyl-2,2,2-trifluoroethoxy)triphenylphosphorane(1) was readily reacted with anilines to produce the corresponding N-hexafluoroisopropylated derivertives(2). This fact shows the remarkable contrast to analogous phosphorane, i.e., bis(2,2,2-trifluoroethoxy)triphenylphosphorane, which was inert to N-nucleophiles.[6)] Resulting N-hexafluoroisopropylanilines were dehydrofluorinated to form very interesting 2-arylamino-1,1,3,3,3-pentafluoropropenes(3) by base, e.g., triethylamine, potassium tert-buthoxide, etc. However, it is impossible to obtain these compounds(3) directly from the reaction of hexafluoropropene(HFP) with anilines, because HFP is attacked on the terminal CF_2 group by the nucleophiles.[7)]



$$\text{Ar-NH}_2 \xrightarrow{\text{Ph}_3\text{P[OCH(CF}_3)_2]_2\ (\underline{1})} \underset{\underline{2}}{\text{Ar-NH-CH(CF}_3)_2} \xrightarrow{\text{Et}_3\text{N}} \underset{\underline{3}}{\text{Ar-NH-C(CF}_3)\text{=CF}_2}$$

2a(Ar = Ph)	46%	3a	76%
2b(Ar=tolyl)	58%	3b	81%

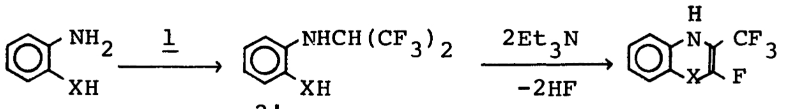


$$\underset{\text{(HFP)}}{\text{CF}_3\text{-CF=CF}_2} + \text{Ar-NH}_2 \not\longrightarrow \underline{3}$$

$$\longrightarrow \text{Ar-NH-CF}_2\text{CHFCF}_3 + \text{Ar-NH-CF=CFCF}_3$$

We also found that wider variety of anilines with *o*-functional group underwent the addition-elimination reaction to afford the trifluoromethylated heterocycles(4).

In conclusion, we believe that bis(1-trifluoromethyl-2,2,2-trifluoroethoxy)-triphenylphosphorane is useful intermediate to introduce the trifluoromehtyl group into a desired position of heterocycles, and that this procedure provides a practical and convenient route to heterocycles.



2'

4

2'a(X = NH)	62%	4a	73%
2'b(X = O)	64%	4b	69%
2'c(X = S)	66%	4c	60%

In a typical procedure, *o*-phenylenediamine(1.80g, 10mmol) was added into a solution of 1 in dichloromethane(40ml)-diethyl ether(10ml) which was prepared from triphenylphosphine dibromide(4.22g, 10mmol) and sodium 1-trifluoromethyl-2,2,2-trifluoroethoxide(3.80g, 20mmol) in situ.[6)] After 1h of stirring, precipitates(NaBr) were centrifuged from the reaction mixture, and the solvent was removed. then distillation gave N-hexafluoroisopropylated product(2'a, 1.51g) in a yield of 62%, b.p.84.0-85.0°C/7mmHg. ^{1}H nmr($CDCl_3$) : δ4.40(NH), 4.50(NH_2), 5.40(sep, J_{H-F}=6.1Hz, 1H), 6.20-6.75(4H). ^{19}F nmr($CDCl_3$) : δ+1.22(d, CF_3) from CF_3COOH as an ext. standard. MS : m/e 258(M^+).

The mixture of 2'a(1.22g, 5mmol), triethylamine(1.50g, 15mmol) and tetrahydrofuran(30ml) was refluxed for 1h, and then worked-up as usual. 2-Fluoro-3-trifluoromethyl-1,4-dihydroquinoxaline(4a, 0.80g) was obtained by column chromatography on silica gel using chloroform as eluent in 73% yield, m.p.89.5-91.0°C. ^{1}H nmr($CDCl_3$) : δ 4.40(2H), 6.10-6.90(4H). ^{19}F nmr($CDCl_3$) : δ -15.9(d, J_{CF_3-F}=16.2Hz, CF_3), -19.1(q, CF) from CF_3COOH as an ext. standard. MS : m/e 238(M^+).

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