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PRELIMINARY NOTE

Preparation, Stability, Reactivity and Synthetic Utility of a Cadmium Stabilized Complex of Difluoromethylene Phosphonic Acid Ester

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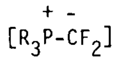
SUMMARY

Diethyl bromodifluoromethylphosphonate reacts readily with cadmium metal to form a stable cadmium complex. Depending on solvent, this functionalized organocadmium reagent exhibits stability for days to months. It reacts with a variety of electrophiles and serves as a synthetically useful source for the introduction of the difluoromethylene phosphonate group into organic compounds.

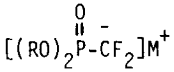
The synthetic utility of a wide variety of fluoromethylene phosphonium ylides has been a major effort in our laboratory over the past several years [1]. The generation and capture of difluoromethylene ylides (1) as a general route to difluoromethylene olefins has been of especial interest to us [2]. In an effort to increase the nucleophilicity of the ylide, we have attempted to prepare the analogous phosphonate ylide (2). Although we have achieved modest success [3] by insitu capture of (2) in the reaction of sodium dialkyl phosphites with diethyl bromodifluoromethylphosphonate (3), attempts to pregenerate (2), either from diethyl difluoromethylphosphonate (4) or (3), have met with little success. (2) appears to have minimal stability even at low temperatures, and scale up processes of synthetic value would seem to be difficult.



$[R_3\overset{+}{P}-\overset{-}{C}F_2]$

(1)

R = Ph, Bu, Me_2N



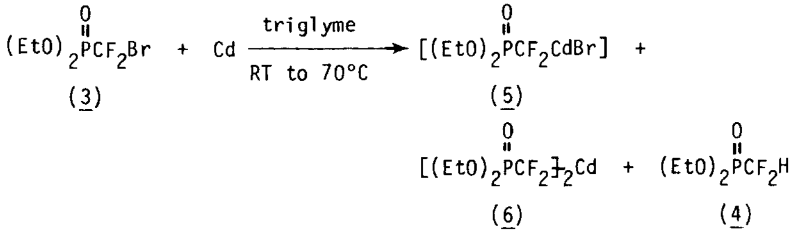
$[(RO)_2\overset{\overset{O}{\|}}{P}-\overset{-}{C}F_2]M^+$

(2)

R = alkyl

Similar stability problems with chlorofluoromethylene tris (dimethylamino) phosphorane were partially overcome by formation of an ylide-metal complex, which enhanced the stability of this unstable ylide [4]. We now wish to report that a similar strategy provides a stable complex of (2)*.

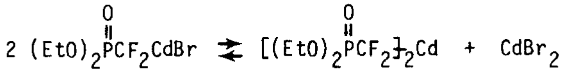
When (3) was reacted with cadmium metal in triglyme at room temperature (14 hrs.) or at 70° (6 hrs.), a stable organocadmium reagent was formed, together with varying amounts of (4). ^{19}F and ^{31}P NMR spectra of the solution showed the presence of two different kinds of organocadmium species, which we tentatively assign to the mono- and bis-organocadmium complex (5) and (6), respectively**. The major cadmium species [assigned as (5)] shows a doublet in the ^{19}F NMR spectrum at Φ^* 118.4 ppm, $J_{P,F}$ = 80.6 Hz with satellite peaks due to ^{111}Cd and ^{113}Cd, ($J^{111}_{F\text{-}Cd} \cong J^{113}_{F\text{-}Cd} \cong$ 256 Hz). The minor cadmium species [assigned as (6)] showed a doublet in the ^{19}F NMR spectrum at Φ^* 120.4 ppm, $J_{P,F}$ = 83 Hz with satellite peaks due to ^{111}Cd and ^{113}Cd ($J^{111}_{F\text{-}Cd} \cong J^{113}_{F\text{-}Cd} \cong$ 198 Hz). In the ^{31}P NMR spectrum the major cadmium species exhibited a triplet at δ -13.5 with satellite peaks due to ^{111}Cd and ^{113}Cd ($J^{111}_{P\text{-}Cd} \cong J^{113}_{P\text{-}Cd} \cong$ 340 Hz). The minor cadmium species showed a triplet at δ -14.0 with satellite peaks due to ^{111}Cd and ^{113}Cd ($J^{111}_{P\text{-}Cd} \cong J^{113}_{P\text{-}Cd} \cong$ 340 Hz). The satellite peaks of (5) and (6) were not well resolved and appeared as partially overlapping peaks.



$$(EtO)_2\overset{O}{\overset{\|}{P}}CF_2Br + Cd \xrightarrow[\text{RT to 70°C}]{\text{triglyme}} [(EtO)_2\overset{O}{\overset{\|}{P}}CF_2CdBr] + [(EtO)_2\overset{O}{\overset{\|}{P}}CF_2]_2Cd + (EtO)_2\overset{O}{\overset{\|}{P}}CF_2H$$

(3) (5) (6) (4)

The ratio of (5) and (6) was solvent dependent, as expected for an equilibrium of the type:



$$2\ (EtO)_2\overset{O}{\overset{\|}{P}}CF_2CdBr \rightleftarrows [(EtO)_2\overset{O}{\overset{\|}{P}}CF_2]_2Cd + CdBr_2$$

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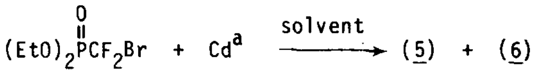
[*] The instability of (2) is presumably due to the known carbanion destabilizing effect of α-fluorine [5,6]

[**] Since there is no evidence to indicate the overall structure of this organometallic reagent, we represent the structures in this way for simplicity.

Table 1 summarizes the formation of (5) and (6) in several solvents. Triglyme, dioxane, and DMF minimize the formation of (4) and appear to be the solvents of choice for further reactions of the cadmium reagent.

TABLE 1

Preparation of (5) and (6)



$$(EtO)_2\overset{\overset{O}{\|}}{P}CF_2Br + Cd^a \xrightarrow{\text{solvent}} (5) + (6)$$

Solvent	Cd Source^c	Rx. Conditions	(5)/(6) Yield^b	Yield (4)^b
Triglyme	MCB	RT, 14 hrs.	48% (60/40)	52%
DMF	MCB	RT, 2 hrs.	89% (50/50)	11%
Dioxane	MCB	75°, 6 hrs.	78% (30/70)	22%
HMPA	MCB	RT, 2 hrs.	68% (100% (5))	15%^{d}
Triglyme	AMCB^e	RT, 13 hrs.	80% (60/40)	20%
DMF	AMCB	RT, 2 hrs.	90% (50/50)	10%
HMPA	AMCB	RT, 2 hrs.	62% (100% (5))	22%^{d}
CH_2Cl_2	AMCB	reflux, 16 hrs.	No reaction	—

a) Unless otherwise indicated, a 10-20% excess of cadmium metal was used.

b) Yield determined by ^{19}F NMR *vs*. $PhCF_3$.

c) Either Matheson Coleman and Bell commercial powder was used directly (MCB) or HCl activated Matheson Coleman and Bell Cadmium (AMCB) was used.

d) In addition to (4), (5), and (6) another component at Φ^* 120.3 ppm (d, d) J = 97.7 Hz and J = 90.3 Hz was also detected.

e) 100% excess of cadmium was used to insure total consumption of (3).

The stability of this reagent is remarkable. In contrast to (2), which is of limited stability, (5) and (6) could be handled with little difficulty in the absence of moisture. In DMF and dioxane the reagent was stable for a few days; in triglyme the reagent exhibited stability for several months. Thermally, the reagent can be used at 70-100°C without extensive decomposition.

The reagent reacts with a wide variety of electrophiles as illustrated in Scheme 1*. With reactive electrophiles, reaction occurs readily at room temperature. With less reactive electrophiles, sodium iodide is required to facilitate the dissociation of the cadmium reagent and capture of (2).

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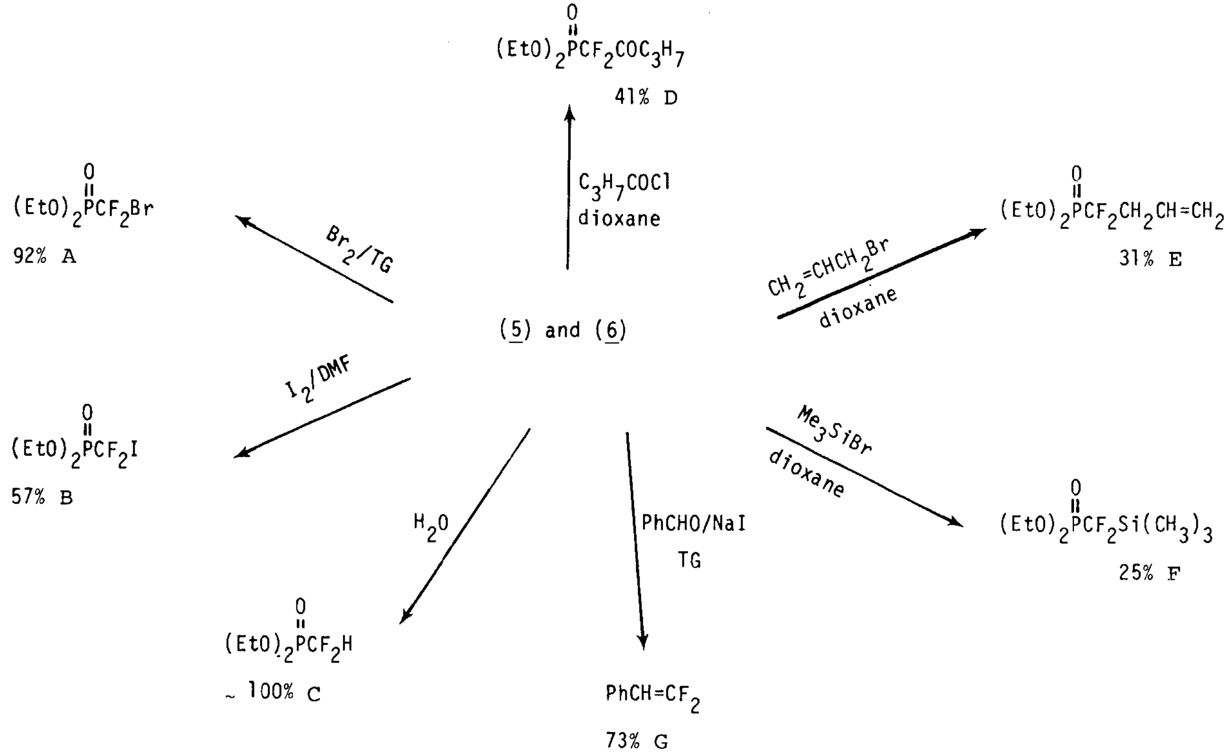
* Both (5) and (6) react with the electrophiles noted in Scheme 1.



SCHEME 1

(Key for A-G on facing page)

A ^{19}F NMR yield *vs*. PhCF$_3$; identified by spiking with an authentic sample of ($\underline{3}$).

B Isolated yield; bp 59-60°/0.13 mm Hg; ^{19}F NMR (CDCl$_3$) Φ^* 58.6 (d), $J_{P,F}$= 87.9 Hz; ^{31}P NMR (CDCl$_3$) δ 2.5 (t); ^{1}H NMR (CDCl$_3$) δ 1.4 (CH$_3$, t) J = 7.2 Hz and δ = 4.4 (CH$_2$, m).

C ^{19}F NMR yield *vs*. PhCF$_3$; identified by spiking with an authentic sample of ($\underline{4}$).

D Isolated yield; bp 110-115°/0.8 mm Hg; ^{19}F NMR (CDCl$_3$) Φ^* 118.4 (d), $J_{P,F}$ = 97.1 Hz; ^{31}P NMR (neat) δ -2.89 (t); ^{1}H NMR (CDCl$_3$) δ 0.96 (t) [$\underline{\mathrm{CH_3}}\mathrm{CH_2CH_2}$-] J = 7 Hz; δ 1.4 (t) [$\underline{\mathrm{CH_3}}\mathrm{CH_2O}$-] J= 7 Hz; δ 1.57 (sextet) [-$\mathrm{CH_2}\underline{\mathrm{CH_2}}\mathrm{CH_3}$] J = 7 Hz; δ 2.8 (t) [-$\underline{\mathrm{CH_2}}\mathrm{CH_2CH_3}$] J= 7 Hz, and δ 4.35 (pentet) [$\mathrm{CH_3}\underline{\mathrm{CH_2}}\mathrm{O}$-], J = 7 Hz.

E Isolated yield; bp 90-92°/0.25 mm Hg; ^{19}F NMR (CDCl$_3$) Φ^* 112.1 ppm (d, t), $J_{P,F}$ = 107 Hz and $J_{H,F}$ = 19 Hz; ^{31}P NMR (neat) δ -6.4 (t); ^{1}H NMR (CDCl$_3$) δ 1.4 (t) [$\underline{\mathrm{CH_3}}\mathrm{CH_2O}$-] J = 7 Hz; δ 4.3 (pentet) (-$\mathrm{O}\underline{\mathrm{CH_2}}\mathrm{CH_3}$), J = 7 Hz; δ 2.85 (t,t) (-$\mathrm{CF_2}\underline{\mathrm{CH_2}}$-), J = 7 Hz and J = 19 Hz; δ 5.1 to 6.3 (m) (-$\underline{\mathrm{CH}}$=$\underline{\mathrm{CH_2}}$).

F Isolated yield; bp 47-50°/0.04 mm Hg; ^{19}F NMR (CDCl$_3$) Φ^* 131.0 ppm (d), $J_{P,F}$= 89.2 Hz; ^{31}P NMR (neat) δ -8.61 (t); ^{1}H NMR (CDCl$_3$) δ 1.39 (t) ($\underline{\mathrm{CH_3}}\mathrm{CH_2O}$-) J = 7 Hz; δ 4.29 (pentet) ($\mathrm{CH_3}\underline{\mathrm{CH_2}}\mathrm{O}$-) J= 7 Hz, δ 0.29 (s) ($\mathrm{Si}(\underline{\mathrm{CH_3}})_3$).

G ^{19}F NMR yield *vs*. PhCF$_3$; identified by spiking with an authentic sample.

Thus, stabilization of ($\underline{2}$) can be readily accomplished by attachment of the ylide to cadmium ** . Scale-up of the reaction to synthetically useful quantities presents no problems *. This organometallic reagent readily serves as a source of ($\underline{2}$) by further reactions with electrophiles and permits the facile introduction of the difluoromethylenephosphonate group into a variety of organic compounds.

Our work continues to explore these interesting reagents as well as the examination of related substrates and metals. Future reports will detail these extensions.

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* Reactions of 50 to 200 mmoles can be routinely carried out.

** These phosphonate-cadmium reagents exhibit much greater solution stability than simple fluorinated cadmium reagents, such as bis (trifluoromethyl) cadmium [7]

We wish to thank the Air Force Office of Scientific Research, the Office of Army Research, and the National Science Foundation for support of our programs.

1 For illustrative examples, cf. to M.J. Van Hamme and D.J. Burton, J. Fluorine Chem., 10 (1979) 407; D.J. Burton and P.E. Greenlimb, J. Org. Chem., 40 (1975) 2796; R.W. Vander Haar, D.J. Burton, and D.G. Naae, J. Fluorine Chem., 1 (1971/72) 381; and D.J. Burton and H.C. Krutzsch, J. Org. Chem., 35 (1970) 2125.

2 D.G. Naae and D.J. Burton, Syn. Comm., 3 (1973) 197; D.G. Naae and D.J. Burton, J. Fluorine Chem., 1 (1971) 123; F.E. Herkes and D.J. Burton, J. Org. Chem., 32 (1967) 1311; G.A. Wheaton and D.J. Burton, Tetrahedron Letts. (1976) 895; and D.J. Burton, Y. Inouye, and J.A. Headley, J. Amer. Chem. Soc., 102 (1980) 3980.

3 D.J. Burton and R.M. Flynn, J. Fluorine Chem., 15 (1980) 263.

4 M.J. Van Hamme and D.J. Burton, J. Organometallic Chem., 169 (1979) 123

5 R.D. Chambers, "Fluorine In Organic Chemistry", Wiley-Interscience, New York (1973), pg 84-93.

6 D.J. Burton, S. Shin-ya, and R.D. Howells, J. Amer. Chem. Soc., 101 (1979) 3689.

7 L.J. Krause and J.A. Morrison, Chem. Comm. (1980) 671.