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Trichloroisocyanuric Acid-KF as an Efficient Reagent for One-Pot Synthesis of Dialkylfluorophosphates from Dialkylphosphites

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Trichloroisocyanuric Acid–KF as an Efficient Reagent for One-Pot Synthesis of Dialkylfluorophosphates from Dialkylphosphites

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Abstract: Trichloroisocyanuric acid–KF afforded dialkylfluorophosphates from dialkylphosphites at room temperature through a facile electrophilic–nucleophilic metathesis.

Keywords: Dialkylfluorophosphate, dialkylphosphite, KF, trichloroisocyanuric acid

Because of the wide utility of OPFCs and our interest in exploring the effective medicinal and protective countermeasures against such fluoridates, there is a need to develop a rapid and efficient synthetic procedure for these compounds. Several methods have been reported in the literature involving mainly two types of reactions: first, based on halogen metathesis, in which dialkyl chlorophosphates are reacted with metal fluorides in the presence of crown ethers. Chlorine exchange is also reported using sodium tetrafluoroborate, sodium hexafluoro silicate, or hexa flurophosphate.^[1,2] The second approach is based on the replacement of active hydrogen of dialkyl phosphite either with alkali metals or with trimethyl silylchloride, followed by reaction with an activated source of fluorine atom.^[3] The first protocol has drawbacks such as use of an expensive reagent such as crown ethers, excess reagent, high

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temperature (200 °C), and variable yield (12-77%). In the second method, dialkylphosphites were converted to their alkali metal salts followed by reaction with sulfuryl chloride fluoride.^[3] Though this method apparently looks better, it gives a mixture of chloridates and fluoridates, and isolation of pure fluoridates becomes very difficult. Another major drawback of these methods is that they require reaction conditions that are difficult to maintain, such as temperature of -50 °C. In addition, these reactions make use of dialkyl chlorophosphates as starting materials, which in turn need to be prepared from dialkyl phosphites. Recently, the use of solidsupported ion exchange resin Amberlyst A-26 with a fluoride counterion in tetrahydrofuran (THF) at room temperature under an argon atmosphere is also reported.^[4] However, the ion exchange resin Amberlyst A-26 with a fluoride counter ion is a costly affair and ion exchange reactions are reversible; thus formation of products always depends on the concentration of fluoride ions, in ion exchange resin. Furthermore, this process is time consuming; up-scaling is difficult and needs to be done in the argon atmosphere. These limitations prompted us to develop a rapid and efficient synthetic procedure for dialkyl fluorophosphates that involves easy workup and quantitative yields in shorter reaction times by making use of a trichloroisocyanuric acid (TCICA)-KF mixture.

RESULTS AND DISCUSSION

TCICA is a stable, commercially available crystalline compound that provides three active chlorines.^[5] We envisaged that if TCICA-KF is used in combination to react with dialkylphosphites, it would generate corresponding dialkyl flurophosphates via the intermediacy of dialkyl chlorophsphates. To the best of our knowledge, TCICA-KF has not been used so far as a fluorinating agent in organic synthesis. In continuation of our recent efforts to develop new reagents and synthetic procedures for the rapid synthesis of organophosphorus compounds,^[6] herein, we report a rapid, efficient, economic, and easy-to-scale method for the effective conversion of dialkylphosphites to their corresponding dialkyl fluorophosphates at room temperature. Reaction of diisopropylphosphite (1.66 g, 10 mmol) with TCICA (0.76 g, 3.3 mmol) and KF (0.64 g, 11 mmol) was performed at room temperature, and an exothermic reaction was observed, which was monitored by ³¹P NMR. To our surprise, a quantitative conversion of diisopropyl phosphite to diisopropyl fluorophosphate was observed within 25 min. It led us to further explore the generality of this reaction with structurally diverse dialkyl phosphites. The reaction various dialkyl phosphites with of



Scheme 1. Synthesis of dialkylfluorophosphate.

TCICA-KF afforded corresponding dialkyl fluorophosphates in 20– 45 min with excellent yields. The reaction scheme and yields of dialkyl fluorophosphates are depicted in Scheme 1 and Table 1.

This method has allowed us to obtain the quantitative yields of the products in reduced reaction times. The important advantage of this reaction is the occurrence of the reaction at room temperature, and completion of the reaction is indicated by the precipitation of cyanuric acid and KCl within 20–45 min. It was also observed that reaction time increases with increasing the alkyl chain of the substituents. It is probably due to the participation of π -electrons present on the phosphorus atom, which

Entry	R	Time (min)	Yield ^a (%)	Bp °C (mm/Hg)	³¹ P–NMR ^b (ppm)	J _{P-F} (Hz)
1	CH ₃	20	90	65-67/25	-8.39	975.10
2	C_2H_5	20	89	75-77/20	-8.22	970.25
3	C_3H_7	25	90	76-77/15	-8.48	958.14
4	$^{i}C_{3}H_{7}$	20	94	80-82/20	-10.25	968.40
5	ⁿ C ₄ H ₉	30	91	85-87/12	-9.25	971.39
6	ⁱ C ₄ H ₉	30	92	110-112/15	-10.31	968.00
7	Sec-C ₄ H ₉	30	95	95-97/5	-10.71	972.00
8	$C_{5}H_{11}$	35	91	141-142/35	-9.49	962.25
9	$^{i}C_{5}H_{11}$	30	89	142-143/25	-8.99	967.00
10	$C_{6}H_{11}$	35	93	120-121/1.2	-8.98	966.74
11	C_6H_5	45	94	116-117/1.0	-20.25	990.10

Table 1. Preparation of dialkylfluorophosphates from dialkyl phosphites using TCICA and KF in acetonitrile at room temperature

^aisolated yield.

^{b31}P NMR spectra were recorded at 162 MHz in CDCl₃. All the products gave satisfactory IR, NMR, and GC-MS data compared with authentic samples.

Note. Caution! Dialkylfluorophosphates are highly toxic compounds and should be synthesized by trained persons using an efficient fume hood. Great caution should be exercised especially while distilling them, and residue must be properly decontaminated by using 20% alkali solution.

might have reduced the electrophilic character of the phosphorus atom. The formation of cyanuric acid from a heterogeneous reaction medium was confirmed after dissolving the precipitate in acetone followed by filtration to remove undissolved KCl. The by-product (cyanuric acid and KCl) can be removed just by filtration of reaction mixture using suction. Further, to study the up-scaling of such compounds, we carried out a reaction of diisopropylphosphite (1.0 mol) with TCICA (0.34 mol) and KF (1.1 mol), which also gave diisopropyl fluorophosphates with 94% yield. It was also observed that when in situ–generated diisopropylchlorophosphate was isolated and fluorine exchange reaction was performed by the use of KF (1:2), the reaction took 90 min and that under reflux conditions yield is also reduced (74%).

CONCLUSIONS

In conclusion, we have reported an efficient, convenient, and one-pot conversion of dialkylphosphites to dialkylfluorophosphates under mild conditions and in excellent yields.

EXPERIMENTAL

Chemicals purchased from Acros, Sigma-Aldrich, and Merck (India) were used without further purification, and solvents were distilled prior to use. ¹H NMR spectra were recorded on a Bruker Avance 400 (400-MHz) spectrometer (chemical shifts in δ , ppm) against TMS as internal standard and IR spectra were recorded as KBr pellets on a Bruker model Tensor 27 FTIR spectrophotometer (ν , cm⁻¹).

Typical Experimental Procedure

Diisopropylphosphite, 16.6 g (0.10 mol), was added to a stirred suspension of trichlorocyanuric acid (7.6 g, 0.0333 mol) and KF (6.38 g, 0.11 mol) in dry acetonitrile (40 ml) at room temperature in one shot. The resulting mixture was stirred at room temperature, and an exothermic reaction took place, which was periodically monitored by GC and ³¹P NMR. It was then further stirred for 5 min and filtered off to remove the precipitate by suction. The solid precipitate was washed with 2×10 mL of ether. The filtrate and washings were combined. The solvent was removed under vacuum, and product was obtained by distillation under vacuum. Bp 80–82/20 Hg; yield; 17.32 g. (94%).

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REFERENCES

- 1. (a) Gerstenberger, M. R. C.; Haas, A. Methods of fluorination in organic chemistry. Angew Chem. Int. Ed. 1981, 20, 647; (b) Farooq, O. Fluorination of organochlorophosphorus compounds with alkali metal salts of perfluorinated complex anions, part 2. New J. Chem. 2000, 24, 81; (c) Farooq, O. Fluorination of organodichlorophosphorus compounds with sodium hexafluorosilicate, Part 1. J. Chem. Soc. Perkin Trans. 1 1998, 1, 839; (d) Wozniak, L. A.; Chworos, A.; Pyzowski, J.; Stec, W. J. Base-dependent regioselective and P-stereocontrolled hydrolysis of nucleoside 3'-O-(O-2,4,6-trimethylbenzolyl methane-phosphonothioates)s. J. Org. Chem. 1998, 63, 9109; (e) Chworos, A.; Wozniak, L. A. A facile conversion of thio- and selenophosphoric acids and their derivatives into fluoridates by means of reaction with silver fluoride. Tetrahedron Lett. 1999, 40, 9337.
- (a) Schmutzler, R. Chemie der Phosphorfluoride, XII: Uber Phenyldifluoropfosphin. *Chem. Ber.* **1965**, *98*, 552; (b) Roesky, H. W. Dialkylaminochlorofluorophosphine und bis-diathylamino-fluorophosphin. *Inorg. Nucl. Chem. Lett.* **1969**, *5*, 891; (c) Heuer, L.; Sell, M.; Schmutzler, R.; Schomberg, D. Preparation of *ortho*-substituted aryldifluoro-phosphines, 2-XC₆H₄PF₂ (X = MeO or Me₂N), and some of their derivatives: X-ray crystal structure determination of (2-MeOC₆H₄P)₄ and of the platinum complex, Cl₂Pt-(2-MeOC₆H₄PF₂)₂. *Polyhedron* **1987**, *6*, 1295; (d) Heuer, L.; Jones, G.; Schmutzler, R.; Schomburg, D. Tetrakis(organodifluorophosphine)platinum(O) and bis(arylphosphonofluoridite-bis(arylphosphonofluoridous acid)-platinum(II) complexes. *New J. Chem.* **1990**, *14*, 891.
- Dabkowski, W.; Cramer, F.; Michalski, J. A new synthesis of phosphorofluoridates of biological interest: The reaction of phosphoroazolides with benzoyl fluoride. *Tetrahedron Lett.* 1987, 28, 3561.
- Sierakowski, T.; Kiddle, J. J. Rapid and efficient solid-supported reagent synthesis of fluorine derivatives of phosphorus (V) compounds. *Tetrahedron Lett.* 2005, 46, 2215.
- (a) Juenge, E. C.; Spangler, P. L.; Duncan, W. P. The reaction of 1,3,5-trichloro-2,4,6-trioxo-hexahydro-s-triazine with tetrahydrofuran and related cyclic ethers. J. Org. Chem. 1966, 31, 3836; (b) Juenge, E. C.; Beal, D. A. Direct conversion of ethers to esters by trichloroisocyanuric acid. Tetrahedron Lett. 1968, 9, 5819; (c) Juenge, E. C.; Beal, D. A.; Duncan, W. P. Chlorination of aromatic systems with trichloroisocyanuric acid under polar and free-radical conditions. J. Org. Chem. 1970, 35, 719.
- Shakya, P. D.; Dubey, D. K.; Pardasani, D.; Palit, M.; Gupta, A. K. N,N'-Dichloro bis-(2,4,6-trichlorophenyl) urea (CC-2): An efficient reagent for

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synthesis of dialkyl chlorophosphates. J. Chem. Res. 2005, 821; (b) Acharya, J.; Shakya, P. D.; Pardasani, D.; Palit, M.; Dubey, D. K.; Gupta, A. K. Surface-mediated solid phase reactions: A simple, efficient, and base-free synthesis of phosphonates and phosphates on Al₂O₃. J. Chem. Res. 2005, 3, 194; (c) Shakya, P. D.; Dubey, D. K.; Pardasani, D.; Palit, M.; Gupta, A. K. A solid supported, rapid and mild synthesis of CWC related phosphoramidates. Catal. Commun. 2005, 6, 669; (d) Gupta, A. K.; Palit, M.; Pardasani, D.; Shakya, P. D.; Shrivastava, R. K.; Dubey, D. K. Micro-synthesis and electron ionization mass spectral analysis of O-alkyl N,N-dialkylphosphoramidocyanidates. Eur. J. Mass Spectrom. 2005, 10, 309; (e) Gupta, A. K; Acharya, J.; Dubey, D. K; Kaushik, M. P. Efficient and convenient one-pot synthesis of phosphoramidates and phosphates. Synth. Commun. 2007, 37, 3403.