Tetrahedron Letters,Vol.27,No.32,pp 3709-3712,1986 0040-4039/86 $3.00 + .00
Printed in Great Britain Pergamon Journals Ltd.

REGIOSPECIFIC PREPARATION OF α,α-DIHALOFLUOROMETHYL PERFLUOROALKYL KETONES[1]

In Howa Jeong, Donald J. Burton*, and Daryl G. Cox
Department of Chemistry, The University of Iowa
Iowa City, Iowa 52242, U.S.A.

Abstract: Acylation of E-phosphoranium salts with E-acyl chlorides gives the corresponding Z-perfluoro betaine in high yield. Subsequent chlorination or bromination regiospecifically yields the α,α-dihalofluoromethyl perfluoroalkyl ketones.

Although the use of regiospecific enolate chemistry has had a significant impact on synthetic organic chemistry in recent years,[2] concomitant advances in the regiospecific generation and utilization of polyfluorinated enolates in organofluorine chemistry has been exiguous. The lack of general synthetic methods for the preparation of suitable polyfluorinated enolate precursors primarily accounts for the paucity of reports with fluorinated ketones. In this communication we address this problem and outline a new general synthetic route to α,α-dihalofluoromethyl perfluoroalkyl ketones, which *via* Perkow type chemistry can be converted to enol phosphates, silyl ethers, and acetates.[3] Further fluorination of these ketones with SbF_5 will give difluorohalomethyl perfluoroalkyl ketones which can yield perfluoro enol derivatives *via* similar transformations.

There are only limited reports on the synthesis of α,α-dihalofluoromethyl perfluoro alkyl ketones, and these methods either lack regiospecificity,[4,5] utilize toxic reagents,[6] and/or lack generality.[4-7] Recently, work from our laboratory detailed a new approach to fluoroolefin synthesis *via* reaction of E-phosphoranium salts with E-acyl fluorides.[8] In contrast to this facile Wittig olefination with E-acyl fluorides, we find that E-acyl chlorides rapidly acylate (with cleavage) the E-phosphoranium salts (1) in benzonitrile to give the Z-perfluoro betaine (2) in excellent yields (Table I). Subsequent halogenation of (2) with Cl_2 or Br_2 results in the formation of the α,α-dihalofluoromethyl perfluoroalkyl ketones (3) and the dihalophosphorane. In summary this one-pot transformation provides a regiospecific synthesis of α,α-dichloro- and α,α-dibromofluoromethyl-E-ketones in modest yields (Table II) from readily available commercial chemicals[9] or precursors which can be easily prepared in one step from commercially available materials.[10]

Although the E-acyl chlorides function well in the preparation of both dichloro and dibromo ketones, halogen specificity is best controlled *via* use of $CFCl_3/Cl_2$ for the preparation of α,α-dichloroketones and $CFBr_3/Br_2$ for the corresponding α,α-dibromoketones. Otherwise, in the preparation of the E-phosphoranium salt (1) from $CFCl_3$, the dichlorophosphorane by-product can promote halogen exchange reactions to give mixed halogen products on subsequent bromination.[11]

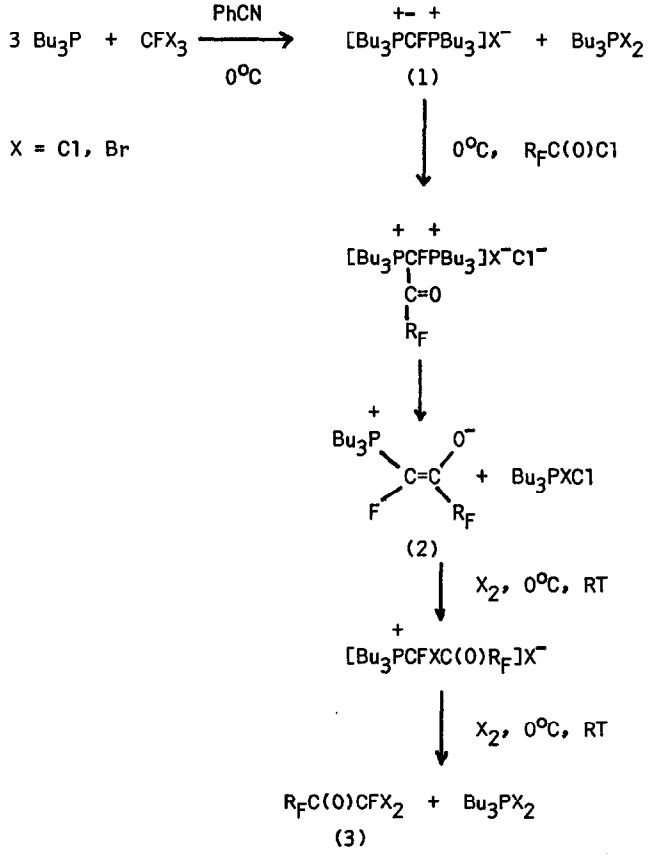

Table I. Preparation of Z-Perfluoro Betaines (2) From (1) + E-Acyl Chlorides

R_F	Yields (%)[a]	
	X = Br[b]	X = Cl[b]
CF_3	85	90
CF_2Cl	72	70
CF_3CF_2	87	91
$CF_3CF_2CF_2$	90	91
$CF_3(CF_2)_5CF_2$	--	90

[a]Yields determined by ^{19}F NMR analysis vs. C_6F_6. [b]Overall yield based on $R_FC(O)Cl$.

$$(\underline{1}) + Bu_3PCl_2 \xrightarrow[2)\ 2\ Br_2]{1)\ C_3F_7C(O)Cl} \underset{53\%}{C_3F_7C(O)CFBr_2} + \underset{27\%}{C_3F_7C(O)CFBrCl} + \underset{20\%}{C_3F_7C(O)CFCl_2}$$

The following experimental procedure for the preparation of 1,1-dichloro-E-pentan-2-one is representative.

A 500 ml three-necked round bottom flask equipped with a stopper, septum, magnetic stir bar, and Dry-Ice/isopropyl alcohol cooled condenser connected to a source of nitrogen was charged with 130 ml of dry benzonitrile and 0.3 mol (60.6 g, 75 ml) of distilled

Table II. Preparation of α,α-Dihalofluoromethyl Perfluoroalkyl Ketones Via Halogenation of (2)

R_F	X	Yield (%)[a,b]
CF_3	Cl	68 (41)
CF_2Cl	Cl	56 (40)
CF_3CF_2	Cl	72 (60)
$CF_3CF_2CF_2$	Cl	75 (62)
$CF_2(CF_2)_5CF_2$	Cl	c (50)
CF_3	Br	68 (42)
CF_2Cl	Br	60 (30)
CF_3CF_2	Br	77 (52)
$CF_3CF_2CF_2$	Br	79 (53)

[a]Yield determined by ^{19}F NMR vs. C_6F_6; yield in parenthesis is isolated yield based on acyl chloride. [b]All products gave satisfactory NMR and MS data. [c]Product is not entirely soluble in the reaction mixture; ^{19}F NMR yield not determined.

tri-n-butylphosphine. After cooling this solution to 0-5°C, 0.1 mol (13.7 g, 9.3 ml) of fluorotrichloromethane was added in one portion. The reaction mixture was stirred at 0-5°C for one hour and then at room temperature for three hours to complete the formation of (1). Then, 0.092 mol (21.4 g) of E-butanoyl chloride was added dropwise with a cooled syringe to this solution keeping the temperature at 0-5°C. After the addition of the acyl chloride was completed, the reaction mixture was stirred at 0-5°C for 0.5 hr. and then at room temperature for one hour, followed by addition of 0.2 mol (14.2 g) of chlorine via the Dry-Ice condenser, again maintaining the reaction mixture at 0-5°C. Upon completion of the chlorine addition, the reaction mixture was stirred at room temperature for one hour, then subjected to flash distillation at 25°C/1 mm, followed by simple redistillation of the flash distillate from an equal volume of conc. H_2SO_4[12] to yield 17.1 g (62%) of 1,1-dichloro-E-pentan-2-one, bp 87-89°C,

>98% GLPC purity with the following spectroscopic properties: $CF_3^dCF_2^cCF_2^bC(O)CCl_2F^a$: ^{19}F NMR ($CFCl_3$), F^a (tt) at -71.0 ppm; F^b (dq) at -113.3 ppm; F^c (d) at -124.7 ppm; and F^d (t) at -80.2 ppm; $J_{a,b}$ = 12 Hz; $J_{a,c}$ = 7 Hz; and $J_{b,d}$ = 10 Hz; MS: M^+-Cl (265,263).

Acknowledgement. We thank the National Science Foundation (CHE-85-16380) and the Air Force Office of Scientific Research (AFOSR-85-0009) for financial support of this work.

References and Notes

1. Presented in part at the 190th ACS National Meeting, Chicago, Illinois, September 1985, Abstract FLUO 19.
2. D.A. Evans, J.V. Nelson, and T.R. Taber, Topics in Stereochemistry, Vol. 13, 1-115 (1982).
3. Work in progress with Mr. I.H. Jeong. For related work with F- -haloketones see: (a) D.W. Wiley and H.E. Simmons, J. Org. Chem., 29, 1876 (1964); (b) R.A. Bekker, G.G. Melikyan, E.P. Lur'e, B.L. Dyatkin, and I.L. Knunyants, Dokl. Akad. Nauk SSSR, 217, 1320 (1974); R.A. Bekker, G.G. Melikyan, B.L. Dyatkin, and I.L. Knunyants, Zh. Org. Khim., 11, 1370 (1975); A.F. Ermolov, A.F. Eleev, A.P. Kutepov, and G.A. Sokol'skii, Zh. Org. Khim., 18, 1846 (1982).
4. H.R. Nychka and C. Woolf, Fr. Pat. 1,369,785 (1964); CA 62, 3940 (1965).
5. L.A. Saloutina, A.Ya. Zapevolov, M.J. Kodess, I.P. Kolenko, and L.S. German, Izv. Akad.Nauk SSSR, Ser. Khim., 1434 (1983).
6. E.T. McBee, O.R. Pierce, and H.W. Kilbourne, J. Am. Chem. Soc., 75, 4091 (1953).
7. R.A. Shepard and A.A. Loiselle, J. Org. Chem., 23, 2012 (1958).
8. D.G. Cox and D.J. Burton, J. Am. Chem. Soc., 105, 650 (1983).
9. Bu_3P, $CFCl_3$, $CFBr_3$, and several F-acyl chlorides are available from Aldrich, SCM, or Fluorochem. Ltd.
10. $CFBr_3$ can also be easily prepared from CBr_4 (Aldrich) via the literature method (J.M. Birchall and R.N. Haszeldine, J. Chem. Soc., 13 (1959), and F-acyl halides are conveniently prepared from the commercially available F-acids and benzoyl chloride or phosphorus pentachloride.
11. The dichlorophosphorane presumably can supply chloride ion via the following equilibrium: $Bu_3PCl_2 \rightleftharpoons [Bu_3PCl]^+Cl^-$. In a control experiment, LiCl in triglyme with $C_3F_7C(O)CFBr_2$ gave 60% $C_3F_7C(O)CFCl_2$ and 21% $C_3F_7C(O)CFBrCl$ after 24 hrs. at room temperature.
12. The product is distilled from conc. H_2SO_4 to convert any hydrate formed in work-up to the anhydrous ketone.

(Received in USA 24 March 1986)