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CONVENIENT PROCEDURES FOR CONVERSION OF CARBONYL COMPOUNDS TO gem-DIFLUOROOLEFINS AND THEIR SELECTIVE REDUCTIONS TO MONOFLUOROOLEFINS[1)]

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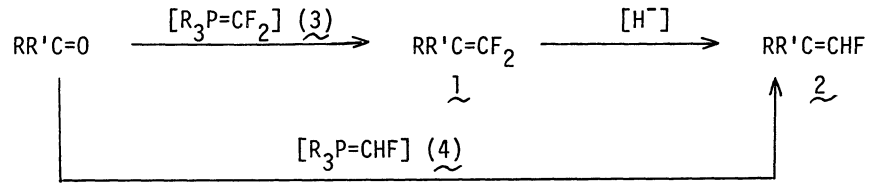
The in situ reaction of dibromodifluoromethane, triphenylphosphine, and aldehydes in the presence of zinc dust affords good yields of gem-difluoroolefins. Reduction of the difluoroolefins gives selectively the corresponding monofluoroolefins in excellent yields. The scope and limitation of these procedures are described and compared with those of previous methods.

In our continuing investigation of new application of organofluorine reagents in "fluorine-free" organic synthesis,[2)] we required facile methods for the preparation of gem-difluoroolefins (1) and monofluoroolefins (2) from carbonyl compounds. In one of our laboratories, considerable efforts have been recently directed to the Wittig olefination reactions with difluoromethylene ylides (3)[3,4)] and fluoromethylene ylides (4).[5)] These methods require extremely dry solvents to obtain satisfactory and reproducible yields, and in the case of (4) the use of the expensive CH_2FI or $CHFI_2$. We now wish to report convenient procedures for the conversion of carbonyl compounds to 1 via a modification of the ylide procedure and for the preparation of 2 via selective hydride reduction of 1.



Difluoromethylenation: Recently, workers in one of our laboratories have reported two methods for the generation of ylide 3 from dibromodifluoromethane (BFM) and tertiary phosphines, such as triphenylphosphine (TPP) (method A)[4a)] and tris(dimethylamino)phosphine (TAP) (method B),[4b)] which offer significant advantages over the sodium chlorodifluoroacetate method.[3,6)] Method B is superior to method A since the former is applicable to both aldehydes and unactivated ketones.

However, both A and B are extremely sensitive to the dryness of the solvent used to obtain good and reproducible yields (compare method A vs. A', B vs. B' in Table 1). In order to avoid this complication we have now studied the Wittig reaction with the ylide 3 in the presence of zinc dust (method C and D, Table 1). The advantageous role of zinc and zinc-copper couple in the Wittig reactions with related halogenated ylides has been the subject of recent papers from one of our laboratories.[5,7]

As illustrated in Table 1, we found that the use of zinc dust in the in situ Wittig reactions expectedly afforded higher olefin yields[8] from aldehydes even in moderately dried N,N-dimethylacetamide (DMAc) as compared with method A. No appreciable difference between TPP and TAP was observed in the olefination of aldehydes (see C vs. D, Table 1).[9] Unfortunately, however, neither C nor D afforded higher olefin yields from unactivated ketones, such as acetophenone, as compared with method B.

Consequently, method C, though applicable only to aldehydes, is the current method of choice for large scale preparation of 1, since this method avoids extensive drying of solvent and permits the use of only one mole of the expensive TPP and TAP. Method B is still the method of choice for the difluoromethylenation of unactivated ketones.

A typical procedure (method C) is described for preparation of 1,1-difluoro-1-octene (1a). A solution of TPP (40 mmol) was added to a mixture of BFM (40 mmol) and heptanal (20 mmol) in DMAc (10 ml) at 0°C over a period of 30 min under nitrogen. The mixture was warmed to room temperature and stirred for 30 min, and then zinc dust (40 mmol) was added in one portion. The resultant mixture was stirred at 100 - 110 °C for 1 hr and then cooled to room temperature. Most of the Ph_3PO was removed by filtration and the filtrate was poured into ice-water and extracted with ether. The extract was washed with water, dried ($MgSO_4$), and distilled to give 1a (1.8 g, 60%), bp 122 - 123 °C (lit.[6] 118 - 120 °C). ^{19}F NMR (neat vs. CF_3CO_2H), δ 13.0 (d, d) and 15.3 (d, d, t); MS, m/e 148 (M^+).

Selective Reduction: In order to avoid the preparation of the expensive CH_2FI or $CHFI_2$ required for the preparation of 4,[5] we have now studied selective hydride reduction of 1 to 2. Although there have been several reports on hydride reductions of polyfluorinated olefins,[10] selective reduction of gem-difluoroolefins have received only scant attention.[11]

We have found that reduction of 1a with lithium aluminum hydride (LAH) in THF was sluggish and impractical. After numerous attempts, however, we found that a commercial benzene solution of sodium bis(2-methoxyethoxy)aluminum hydride (SBAH) easily and selectively reduced 1 to provide excellent isolated yields of the desired monofluoroolefins (2) (Table 1). No over-reduction products were detected.[12] Consequently, the present two-step preparation of 2, though operation-

Table 1. Preparations of gem-Difluoroolefins (1) and Monofluoroolefins (2)

Ylide generation methods : A (A') : CBr_2F_2-Ph_3P (2 equiv)-triglyme* (triglyme**)

B (B') : CBr_2F_2-$(Me_2N)_3P$ (2 equiv)-triglyme* (triglyme**)

C : CBr_2F_2-Ph_3P (1 equiv)-Zn dust (1 equiv)-DMAc**

D : CBr_2F_2-$(Me_2N)_3P$ (1 equiv)-Zn dust (1 equiv)-DMAc**

E : $CHFI_2$-Ph_3P (1 equiv)-Zn (Cu)-triglyme*

* Distilled over sodium benzophenone ketyl just prior to use

** Distilled over sodium hydride and stored under a water-free condition

	Difluoromethylenation			Reduction		
RR'C=O	Product 1[a]	Method	^{19}F NMR Yield (Isolated Yield)	Product 2[a]	Method	Isolated Yield (E : Z)[b]
n-$C_6H_{13}CHO$	n-$C_6H_{13}CH=CF_2$[c]	A	72%			
		A'	9%	n-$C_6H_{13}CH=CHF$[c]	LAH[d]	46% (3 : 1)
		B'	~ 0%		SBAH[e]	78% (5 : 1)
		C	80% (60%)			
		D	77%			
		E	→		→	[54%][f] (4 : 3)
n-$C_{10}H_{21}CHO$	n-$C_{10}H_{21}CH=CF_2$[g]	C	76% (64%)	n-$C_{10}H_{21}CH=CHF$[h]	SBAH[e]	96% (5 : 1)
PhCHO	$PhCH=CF_2$[i]	A	65%			
		C	76% (56%)	PhCH=CHF	SBAH[j]	[91%][f] (13 : 1)
		E	→		→	[52%][f] (3 : 2)
PhCH=CHCHO	$PhCH=CHCH=CF_2$[l]	A	[56%][k]			
		C	33% (30%)			
$PhCOCH_3$	$Ph(CH_3)C=CF_2$[m]	B	[81%][n]			
		B'	~ 0%	$Ph(CH_3)C=CHF$	SBAH[j]	[85%][b] (3 : 1)
		C	< 5%			
		D	43%[o]			
		E	→		→	[12%][f] (4 : 3)

[a] All products exhibited spectral (IR, ^{19}F NMR, and/or MS) data in accord with the assigned structures and/or the reported literature values. [b] Determined by ^{19}F NMR assay. [c] For the physical properties, see the text. [d] Lithium aluminum hydride: the reaction was run in THF under reflux for 57 hr. [e] Sodium bis(2-methoxyethoxy)aluminum hydride; the reaction was run in benzene under reflux for 3 hr. [f] Glc yields taken from ref. 5. [g] Bp 113 - 114 °C/ 28 mmHg. [h] 75 - 76 °C/ 14 mmHg. [i] 62 - 63 °C/ 52 mmHg (lit.[6] 52 - 54 °C/ 40 mmHg). [j] The reaction was carried out at -5 - 0 °C for 30 min (see ref. 12). [k] Glc yield. [l] Bp 87 - 89 °C/ 18 mmHg. [m] Lit.[4b] Bp 155 - 157 °C. [n] Glc yield taken from ref. 4b. [o] 36% Yield in THF.

ally more tedious, circumvents the problems encountered in direct ylide procedure[5] and is the current method of choice for large scale preparation of 2.[13]

A typical procedure is described for the preparation of 1-fluoro-1-octene (2a). A mixture of 1a (6.7 mmol), 70% SBAH (11 mmol), and benzene (3 ml) was refluxed for 3 hr. The resultant mixture was poured into ice-water and acidified with conc. hydrochloric acid. The organic layer was washed with aqueous NaCl solution, dried ($MgSO_4$), and distilled to give 2a (0.68 g, 78%), bp 131 - 134 °C (lit.[5] 135 °C). ^{19}F NMR (neat), δ 52.0 (d, d, t, J = 75.2, 16.9, and 1.9 Hz) and 52.4 (d, d, t, J = 75.2, 37.6, and 1.5 Hz) with ratio of 5 : 1, respectively.

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References and Notes

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8) The notable success can be explained by essentially the same arguments as previously described.[4,5] The olefination proceeds presumably through some type of ylide-zinc halide complex formed via debromination of the initially formed phosphonium slat with zinc (cf. ref. 7 for details).
9) The present ylide-zinc procedure also permits the use of the initially isolated phosphonium bromides, $[R_3\overset{+}{P}CF_2Br]Br^-$, which are quantitatively obtained via reactions of BFM with TPP or TAP in ether or diglyme. These salts can be stored in a desiccator for several months without decomposition. For study of a series of reactions the salts can be prepared in large amounts, stored, and used over a long period of time.
10) F.J. Mettille and D.J. Burton, "Fluorine Chemistry Reviews", Vol. 1, P. Tarrant, ed., Marcel Dekker, New York, 1967, p. 315.
11) A.L. Anderson, R.T. Bogan, and D.J. Burton, J. Fluorine Chem., 1, 121 (1971/72).
12) When the reduction of β,β-difluorostyrene was carried out in benzene under reflux for 3 hr, only styrene (an over-reduction product) was obtained in 86% yield. However, we found that the reaction at -5 - 0 °C gave exclusively the desired monofluoroolefin in an excellent yield (see Table 1).
13) It is worth noting that the hydride reduction method affords predominantly the E isomer of 2 whereas the ylide procedure is less stereoselective (see Table 1).

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