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PRELIMINARY NOTE

# Metal Dehalogenation Route To Reactive Fluoroolefins

D.J. BURTON, H.S. KESLING and D.G. NAAE

Department of Chemistry, University of Iowa, Iowa City, Iowa 52242 (U.S.A.)

## SUMMARY

Metal dehalogenation of bromodifluoromethyltriphenylphosphonium bromide with Cd, Zn, or Hg provides a practical route to fluoroolefins that contain an allylic halogen or a pentafluorophenyl group. No SN2' or ring substituted products are observed.

In previous work with fluoromethylenetriphenylphosphorane [1], we described the use of metal dehalogentaion of phosphonium salts as a route to phosphonium ylides [2]. A later report [3] employed a similar strategy in the preparation of some gem-difluoroolefins [4].

The normal mode of generation of difluoromethylene phosphonium ylides from phosphonium salts is via dehalogenation of the requisite phosphonium salt with a second equivalent of a tertiary phosphine [5,6], cf. Method [A] in Scheme 1. The alternative metal dehalogenation method (Method [B] in Scheme 1) can be employed for a variety of reasons:

(a) to minimize the sensitivity of the reaction to the dryness of the solvent [3,7].

(b) to minimize the use of the second equivalent of the expensive tertiary phosphine reagent [8].

(c) to avoid the formation of the phosphorane ($R_3PX_2$) by-product [9,10].

(d) to avoid competitive or destructive side reactions of the carbonyl substrates or products of the reaction with the second equivalent of the tertiary phosphine.

Problem (a) above can be avoided by careful drying and handling of the solvents employed in these reactions. The use of a metal for ylide production facilitates the reaction, but is not absolutely necessary. On a laboratory scale, (b) above is a secondary consideration [12]. Problem (c) is of importance only when the substrate contains a functional group sensitive to the phosphorane [10].

In most cases the only compelling reason for the use of metal dehalogenation is (d). In this report we address this use of the metal dehalogenation method.

We have found that halodifluoromethyl ketones give only low yields of the gem-difluoroolefins via Method [A]. These ketones either react with the tertiary phosphine directly, or the olefin products from these ketones react with the tertiary phosphine. Thus, Method [A] is of limited utility with these substrates (Table 1).

Similarly, aldehydes and ketones that contain the pentafluorophenyl group fail in the Wittig reaction via Method [A]. The aromatic ring appears to be attacked immediately by the tertiary phosphine and either low yields or intractable materials result (Table 1).

However, both of these problems noted above can be avoided via Method [B]. We have surveyed a variety of metals [4] for this method and Cd, Zn, and Hg have shown the best results, and are illustrated with typical examples in Table 1. As noted, good to excellent yields of the gem-difluoroolefins are obtained via Method [B]. For substrates of this type, the choice of method here is absolutely necessary - not merely a choice of convenience as noted in earlier examples.

These reactions can be scaled up without difficulty, if one observes the following precautions:

(1) use of preformed phosphonium salt (1), [13]

(2) aliquot addition of the metal to (1), [14].

Operational details of the experimental procedure are outlined below for the preparation of 2-phenyl-3-chloro-F-propene. Triphenylphosphine (32.8 g, 125 mmoles) was charged into a dry (flamed out) 500 ml three-neck flask equipped with a True-Bore® stirrer, septum port, thermometer, and reflux condenser capped with a nitrogen inlet tee. Triglyme (200 ml) [17] was added via syringe followed by stirring until dissolution of triphenylphosphine was attained. This solution was cooled to 0°C in an ice-bath followed by rapid addition of dibromodifluoromethane (13.7 ml, 150 mmoles). A heavy white precipitate of (1) forms within 30 seconds when the triglyme is dry. The reaction mixture is warmed to room temperature and stirred at

TABLE 1

$$RCOR' + M + [Ph_3\overset{+}{P}CF_2Br]Br^- \xrightarrow[RT]{triglyme} RR'C{=}CF_2 + MBr_2 + Ph_3PO$$

| RCOR' | $RR'C{=}CF_2$[b] | % Yield of olefin[a]<br>Cd | Zn | Hg | % Yield of olefin<br>*via* Method A |
|---|---|---|---|---|---|
| $C_6H_5C(O)CF_2Cl$ | $C_6H_5C(CF_2Cl){=}CF_2$ | 76(60) | 35 | 21 | 25 |
| $C_6F_5C(O)CF_3$ | $C_6F_5C(CF_3){=}CF_2$ | 83(75) | 68 | 71(56) | 0 |
| $C_6F_5CHO$ | $C_6F_5CH{=}CF_2$ | 62(35) | 54 | 41 | 20 |
| $C_6F_5C(O)CF_2Cl$ | $C_6F_5C(CF_2Cl){=}CF_2$ | 72(67) | — | 64 | 0 |
| $p\text{-}MeOC_6H_4C(O)CF_3$ | $p\text{-}MeOC_6H_5C(CF_3){=}CF_2$ | 68(54) | — | 61(54) | 54(36) |

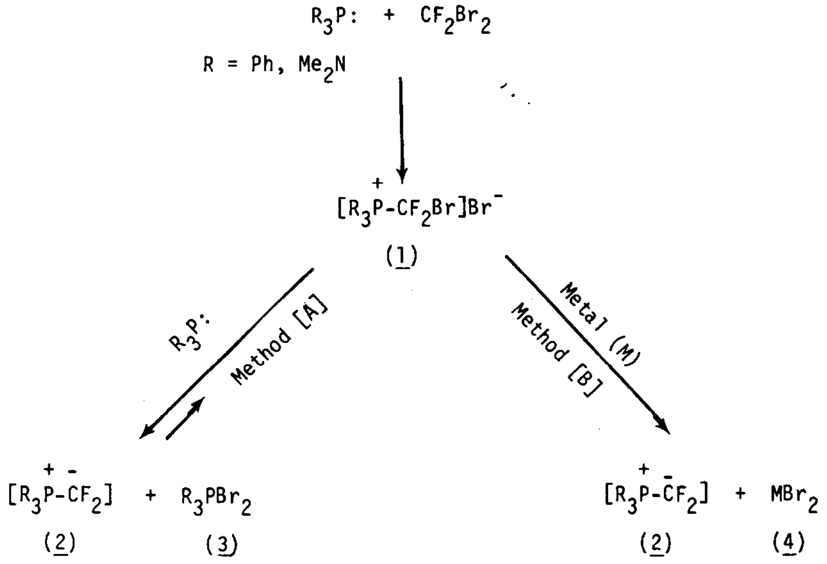
(a) GLPC yield based on starting ketone; (isolated yield).

(b) NMR spectra, mass spectra, IR, and analytical data of all product olefins were consistent with the assigned structures.

room temperature for one hour to ensure total formation of (1). Then, chlorodifluoroacetophenone (19.1 g, 100 mmoles) was added, followed by the addition of cadmium powder [28.1 g, 250 mmoles (325 mesh)] *via* a solids addition tube. The reaction with metal is exothermic, and the metal powder was added at a rate to maintain the temperature of the reaction mixture between 50-70°C. After the addition of the metal powder was completed, the reaction mixture was stirred at 65-70°C for an additional three hours. The 2-phenyl-3-chloro-*F*-propene was isolated *via* flash distillation of the reaction mixture followed by vacuum distillation with a six-inch glass helices column to give 13.5 g (60%) of the olefin, bp 75-76°C/40 mm.

In conclusion the metal dehalogenation method is a convenient synthetic route to some fluoroolefins, although the normal Wittig route (Method [A]) works as well, if the proper precautions are observed. However, with substrates that contain halodifluoromethyl groups or pentafluorophenyl rings, the metal dehalogenation route is the only practical approach to the *gem*-difluoroolefins containing these groups.

We continue to explore this interesting and useful approach to fluoroolefin synthesis and to examine the intermediates formed in this type of reaction. Future reports will elaborate this work in detail.



SCHEME 1

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1 D.J. Burton and P.E. Greenlimb, J. Fluorine Chem., 3 (1973/74) 447.

2 D.J. Burton and P.E. Greenlimb, J. Org. Chem., 40 (1975) 2796.

3 S. Hayashi, T. Nakai, N. Ishikawa, D.J. Burton, D.G. Naae, and H.S. Kesling, Chem. Letters, (1979) 983.

4 For the first report of the use of metals to dehalogenate bromodifluoromethylphosphonium salts, see Ph.D. Thesis of D.G. Naae, University of Iowa, 1972. Both triphenyl and *tris*-(dimethylamino)phosphonium salts are utilized.

5 D.G. Naae and D.J. Burton, J. Fluorine Chem., 1 (1971/72) 123.

6 D.G. Naae and D.J. Burton, Synthetic Comm., 3 (1973) 197.

7 These reactions are believed to proceed through an ylide-metal halide complex, which is less sensitive to moisture than the free basic ylide.

8 See CA 94 (1981) 30324s and 121043r for examples of the utility of this application.

9 Phosphoranes of the type ($R_3PX_2$) will cleave functional groups such as esters, ethers etc., cf. D.J. Burton and W.M. Koppes, J. Org. Chem., 40 (1975) 3026 and references therein.

10 Presumably this is the reason for the use of this method by Suda [11], although in this paper it's not clear whether (a), (b), or (c) is the reason for this choice. Many of the functional groups cleaved by $R_3PX_2$ would also be cleaved by the metal halide formed in the dehalogenation route.

11 M. Suda, Tetrahedron Letters (1981) 1421.

12 On a large scale, the cost of metal and phosphine are comparable.

13 For example, in the examples cited in ref. [8], $CF_2Br_2$ is added to the mixture of phosphine, metal, and carbonyl substrate. If one wishes to avoid competitive or destructive side-reactions by the tertiary phosphine, the metal should be added to the mixture of carbonyl substrate and phosphonium salt.

14 The salt/metal reaction is exothermic. In order to control the reaction on a large scale (1/2 to 1 mole) the metal should be added in portions to control the exotherm and the temperature of the reaction mixture. If the temperature gets too high, fluoride ion is produced [15] and SN2′ reactions will occur. For example, 2-phenyl-*F*-propene will result from the reaction with $C_6H_5C(O)CF_2Cl$ if the temperature gets out-of-hand.

15 As noted earlier [2], it was speculated that the intermediate in this type of reaction is an ylide-metal halide complex. We are exploring the preparation and stability of such an intermediate in this case [16].

16 Work by Y. Inouye in this laboratory.

17 Distilled from sodium benzophenone ketyl.