Tetrahedron Letters,Vol.27,No.19,pp 2135-2138,1986 0040-4039/86 $3.00 + .00
Printed in Great Britain 

# EFFICIENT CARBON-CARBON BOND FORMATION WITH THERMALLY STABLE 1,1-DIHALO-2,2,2-TRIFLUOROETHYLZINC REAGENT

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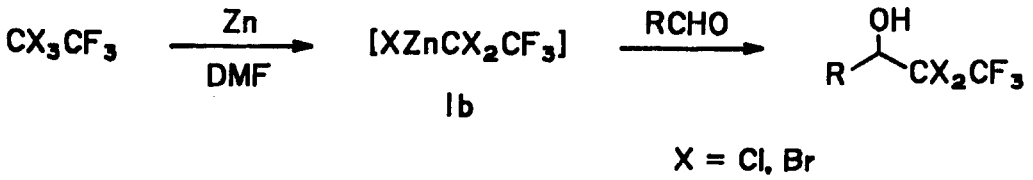
*The zinc carbenoids $CF_3CX_2ZnX$, prepared from $CF_3CX_3$ and zinc powder in dimethylformamide, were found thermally stable to add to aldehyde carbonyls in excellent yields.*

In view of remarkable biological activity of $CF_3$-containing compounds,[1] extensive studies on perfluoroalkylmetals have been made.[2] As synthetic pyrethroids containing $CH=C(Cl)CF_3$ group are recently found highly potent, we explored their synthetic method through employment of a carbenoid reagent, $CF_3CX_2$-Mtl (**1**, X=Cl,Br). The only one example recorded so far is the corresponding Grignard reagent $CF_3CX_2MgX$ (**1a**),[3] which is labile and undergoes carbonyl addition in poor yields even at low temperatures. We report herein that the 2,2,2-trifluoro-1,1-dihaloethylzinc halides (**1b**) are readily prepared from commercially available 1,1,1-trifluoro(trihalo)ethanes and zinc powder in dimethylformamide (DMF) and are thermally stable enough to add to aldehyde carbonyls in good yields without appreciable decomposition.




When 1,1,1-trichlorotrifluoroethane was added to a suspension of small excess of zinc powder[4] in DMF in the presence of CuCl catalyst[5] (5 mol%) at room temperature, exothermic reaction took place, and most of the zinc was consumed within 1 h. Formation of the zinc reagent **1b** (X = Cl) was confirmed by $^{19}F$-NMR analysis.[6] At the expense of the peak of $CCl_3CF_3$ ($\delta$ 81.1), a new peak appeared at $\delta$ 72.3. This peak may be assigned as that of **1b** (X = Cl), since quantitative formation of $CF_3CCl_2H$[7] was observed upon hydrolysis. The

Table 1. Aldehyde addition of $CF_3CX_2ZnX$.[a]

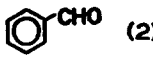
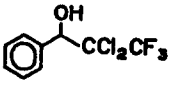
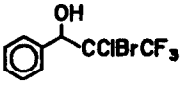
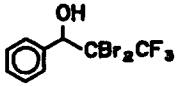
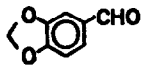
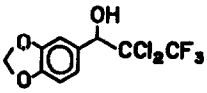
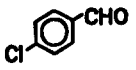
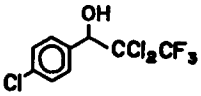
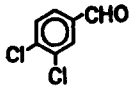
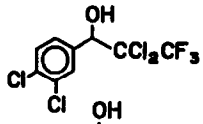
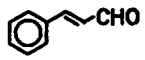
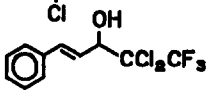
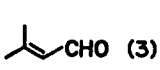
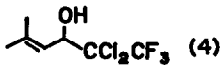
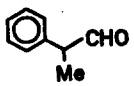
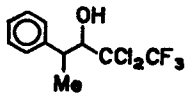
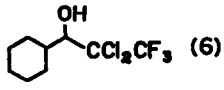
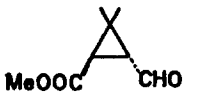
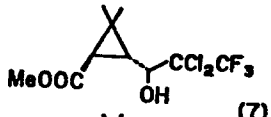
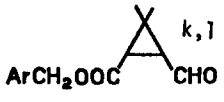
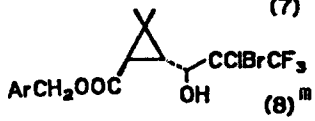
| run | aldehyde | $CX_3CF_3$[b] | conditions | product[c] | % yield[d] |
|---|---|---|---|---|---|
| 1 |  (2) | $CCl_3CF_3$ (1.2) | rt, 3 h – 50 °C, 2 h |  | 86 |
| 2 | 2 | $CClBr_2CF_3$ (1.2) | 0 °C, 0.5 h – 50 °C, 2 h |  | 23[e] |
| 3 | 2 | $CBr_3CF_3$ (1.5) | 0 °C, 0.2 h – rt, 3.5 h |  | 27 |
| 4 |  | $CCl_3CF_3$ (1.2) | 0 °C, 0.2 h – 50 °C, 2 h |  | 80 |
| 5 |  | $CCl_3CF_3$ (1.5) | 0 °C, 0.2 h – 50 °C, 2 h |  | 87 |
| 6 |  | $CCl_3CF_3$ (1.2) | rt, 0.5 h – 50 °C, 4.5 h |  | 96 |
| 7 |  | $CCl_3CF_3$ (1.2) | rt, 1 h – 50 °C, 17 h |  | 82 |
| 8 |  (3) | $CCl_3CF_3$ (1.5) | 60 °C, 12 h |  (4) | 22 |
| 9 | 3 | $CCl_3CF_3$ (1.5) | 50 °C, 8 h[f,g] | 4 | 60 |
| 10 | 3 | $CCl_3CF_3$ (1.5) | 50 °C, 8 h[h] | 4 | 61[e] |
| 11 | | $CCl_3CF_3$ (1.5) | 50 °C, 8 h[i] | 4 | 72[e] |
| 12 | 3 | $CCl_3CF_3$ (1.5) | rt - 50 °C, 3 h[j] | 4 | 83[e] |
| 13 |  | $CCl_3CF_3$ (1.2) | 0 °C, 0.3 h – 50 °C, 12 h |  | 60 |
| 14 |  (5) | $CCl_3CF_3$ (1.2) | 0 °C, 0.3 h – 50 °C, 23 h |  (6) | 16 |

Table 1. (*Continued*)

| | | | | | |
|---|---|---|---|---|---|
| 15 | **5** | $CCl_3CF_3$ (1.5) | 50 °C, 5 h[g] | **6** | 61 |
| 16 |  | $CCl_3CF_3$ (2.0) | rt, 0.3 h – 50 °C, 7 h |  (7) | 75 |
| 17 |  k,l | $CClBr_2CF_3$ (2.0) | rt, 0.6 h – 50 °C, 18 h |  (8)[m] | 35(49)[n] |

[a]The ratio $CX_3CF_3/Zn$ = 1.0-1.2. Reactions were carried out in DMF (1 mL/mmol). [b]Values in the parentheses are mol-equiv. to the aldehyde. [c]All the new compounds gave satisfactory elemental analysis. [d]Isolated yields unless otherwise noted. [e]Glc yield. [f]The aldehyde **3** was added dropwise over 1 h after **1b** was prepared. [g]Employing CuCl catalyst (5 mol%). [h]Employing $PdCl_2(PPh_3)_2$ catalyst (1 mol%). [i]Employing $NiCl_2(PPh_3)_2$ catalyst (1 mol%). [j]Carried out under ultrasonic irradiation (250 W). [k]Ar = 2-methyl-3-phenylphenyl. [l]A mixture of (1R*,3R*)- and (1R*,3S*)-isomers (6 : 1). [m]Only (1R*,3R*)-isomers were isolated. [n]A yield based on the consumed starting material.

reaction with carbon dioxide gave 2,2-dichloro-3,3,3-trifluoropropanoic acid (18 % yield).[8] Thermal stability of **1b** (X = Cl) deserves particular attention: no decomposition of **1b** (X = Cl) was observed in DMF solution after several days at room temperature. The zinc reagent **1b** (X = Cl) was prepared in tetrahydrofuran (THF) solution also in a similar manner.

The synthetic utility of **1b** is demonstrated by aldehyde addition. Zinc powder (22 mmol) was added portionwise to the solution of benzaldehyde (20 mmol) and 1,1,1-trichlorotrifluoroethane (24 mmol) in DMF (20 mL) at room temperature. The reaction mixture was stirred for 3 h at 50 °C. Workup followed by distillation gave 2,2-dichloro-3,3,3-trifluoro-1-phenyl-1-propanol in 86 % yield. Other examples are summarized in Table 1.[9, 10] The reaction with aromatic aldehydes proceeded smoothly in good yields. Though some aliphatic and α,β-unsaturated aldehydes gave low yields, the addition of CuCl, $PdCl_2(PPh_3)_2$, or $NiCl_2(PPh_3)_2$ catalyst or ultrasonic irradiation improved the yields significantly (runs 9-12, and 15). Other 1,1,1-trifluorotrihaloethanes ($CClBr_2CF_3$ and $CBr_3CF_3$) were applicable, though the yields were inferior (runs 2, 3, and 17).

The present reaction provides a new practical way for the introduction of $CF_3CCl_2$ group which itself is a partial structure of some precursors of biologically interesting compounds.[11] In particular, the $CF_3CCl_2$ adducts of types **4**, **7**, and **8** are key intermediates of $CF_3$-containing synthetic pyrethroids as is described in the following paper.

**References and Notes**


1. (a) R. Filler and Y. Kobayashi (Eds.) "Biomedical Aspects of Fluorine Chemistry", Elsevier Biomedical Press, Amsterdam, 1982. (b) F. A. Smith, *CHEMTECH*, **1973**, 422. (c) R. Filler, *ibid.*, **1974**, 752.
2. Carbonyl addition of Rf-Mtl compounds: (a) Mtl = Li: O. R. Pierce, E. T. McBee, and G. F. Judd, *J. Am. Chem. Soc.*, **76**, 474 (1954); R. D. Chambers, W. K. R. Musgrave, and J. Savory, *J. Chem. Soc.*, **1962**, 1993; P. G. Gassman and N. J. O'Reilly, *Tetrahedron Lett.*, **26**, 5243 (1985). (b) Mtl = Mg: R. N. Haszeldine, *J. Chem. Soc.*, **1952**, 3423; R. N. Haszeldine, *ibid.*, **1953**, 1748; R. N. Haszeldine, *ibid.*, **1954**, 1273; D. D. Denson, C. F. Smith, and C. Tamborski, *J. Fluorine Chem.*, **3**, 247 (1973/4); C. F. Smith, E. J. Soloski, and C. Tamborski, *ibid.*, **4**, 35 (1974); L. S. Chen, G. J. Chen, and C. Tamborski, *ibid.*, **26**, 341 (1984). (c) Mtl = Zn: T. Kitazume and N. Ishikawa, *Chem. Lett.*, **1981**, 1679; N. Ishikawa, M. Takahashi, T. Sato, and T. Kitazume, *J. Fluorine Chem.*, **22**, 585 (1983); N. J. O'Reilly, M. Maruta, and N. Ishikawa, *Chem. Lett.*, **1984**, 517; T. Kitazume and N. Ishikawa, *J. Am. Chem. Soc.*, **107**, 5186 (1985); S. Benefice, H. Blancou, and A. Commeyras, *Tetrahedron*, **40**, 1541 (1984). (d) Mtl = Ca: G. Santini, M. L. Blanc, and J. G. Riess, *J. Chem. Soc., Chem. Commun.*, **1975**, 678; G. Santini, M. L. Blanc, and J. G. Riess, *J. Organomet. Chem.*, **140**, 1 (1977). (e) Mtl = Mn: K. Kitazume and N. Ishikawa, *Nippon Kagaku Kaishi*, **1984**, 1725.
3. I. Hemer, A. Pošta, and V. Dědec, *J. Fluorine Chem.*, **26**, 467 (1984).
4. Commercially available zinc powder was washed successively with dilute HCl, water, and methanol and dried under reduced pressure.
5. Zinc-copper couple: H. E. Simmon, T. L. Cairns, and S. A. Vladuchick, *Org. React.*, **20**, 1 (1973).
6. Trichlorofluoromethane was employed as the internal standard. Chemical shifts are given as positive value for upfield shift.
7. This compound was directly isolated from the resulting reaction mixture by distillation. [$^{1}$H-NMR ($CDCl_3$) $\delta$ 6.00 (q, $J$ = 4.7 Hz); $^{19}$F-NMR ($CDCl_3$) $\delta$ 77.6 (d, $J$ = 4.7 Hz)].
8. Ger. Offen. 1,900,7588; *Chem. Abstr.*, **73**, 87470g.
9. In tetrahydrofuran solvent, no aldehyde addition took place, though the zinc reagent **1b** was prepared.
10. Attempted reactions of **1b** (X = Cl) with ketones and benzoyl chloride failed.
11. (a) P. Martin, J. Streith, G. Rihs, T. Winkle, and D. Belluš, *Tetrahedron Lett*, **26**, 3947 (1985). (b) US pat. 4,469,896 (1983). (c) US pat. 4,351,961 (1979).


**(Received in Japan 13 March 1986)**