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TRIFLUOROMETHYLATION OF CARBONYL COMPOUNDS WITH TRIFLUOROMETHYLZINC IODIDE UNDER ULTRASONIC IRRADIATION

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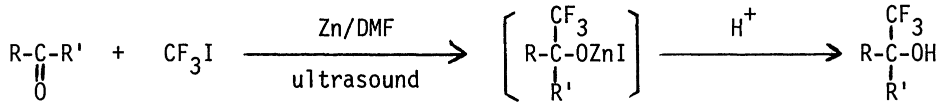
The trifluoromethylation of carbonyl compounds with trifluoromethylzinc iodide, prepared from trifluoromethyl iodide with ultrasonically dispersed zinc, smoothly proceeded to give corresponding α-trifluoromethyl carbinols in good yields.

A number of studies have been made on the biologically unique properties of trifluoromethylated organic compounds,1) and several synthetic methods for these compounds have been developed in recent years. Reported indirect routes involve, 1. a halogen-exchange of CCl_3 with $HF\text{-}SbCl_5$,2) and 2. fluorination of CO_2H by SF_4,3) as practical methods. Meanwhile, a direct route for the introduction of a perfluoroalkyl group into an aromatic ring by the Ullmann-type reaction between R_fI and ArI using copper powder was reported.4,5) The trifluoromethylation by this method has been developed by Y. Kobayashi and his co-workers not only for aromatic, but also for heterocyclic and aliphatic compounds.6) On the other hand, perfluoroalkylzinc compounds are known to be much more stable than the corresponding magnesium or lithium compounds and the preparation of heptafluoro-1-methylethylzinc iodide and its reactions with acyl halides or acid anhydrides, affording heptafluoro-1-methylethyl aryl ketones, were reported by our group.7)

In our continuing studies on the introduction of a perfluoroalkyl group to an organic molecule with perfluoroorganometallic compounds,8) we now wish to report a novel trifluoromethylation of carbonyl compounds with trifluoromethyl iodide by ultrasonically dispersed zinc in N,N-dimethylformamide. This ultrasonic technique was hinted by the J-L. Luche and his co-worker's report on the formation of the organometallic compounds.9) Aliphatic and aromatic aldehydes and ketones were converted into the trifluoromethylated carbinols in less than 1 h at room temperature.



$$\underset{\underset{O}{\parallel}}{R\text{-}C\text{-}R'} + CF_3I \xrightarrow[\text{ultrasound}]{Zn/DMF} \left[\overset{CF_3}{\underset{R'}{R\text{-}C\text{-}OZnI}}\right] \xrightarrow{H^+} \overset{CF_3}{\underset{R'}{R\text{-}C\text{-}OH}}$$

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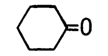
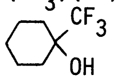
Technical grade N,N-dimethylformamide or tetrahydrofuran dried over molecular sieve (4A) can be used in this reaction, though the former was more preferable. Without the aid of ultrasonic irradiation, the reaction did not proceed at all.

Based on these results, we believe that this method provides a readily achieved and practical one-pot trifluoromethylation as it takes place by having the carbonyl compounds react with trifluoromethyl iodide in N,N-dimethylformamide in the presence of zinc at room temperature (Table 1).

TABLE I. Physical Properties of α-Trifluoromethyl Carbinols

RCHO or RCOR'	Product[a)]	Reaction Time (h)	Yield[b)] (%)	Bp (°C/mmHg)	^{19}F NMR[e)] CF_3
PhCHO	$PhCH(CF_3)OH$	0.5	72 (86)[c)]	105-108/16 (105/17)[d)]	-0.3
$C_5H_{11}CHO$	$C_5H_{11}CH(CF_3)OH$	0.5	61	96-97/18	0.6
MeCH=CHCHO	$MeCH=CHCH(CF_3)OH$	0.5	62	92-95/105	0.7
PhCH=CHCHO	$PhCH=CHCH(CF_3)OH$	0.5	68 (81)	86-88/5	0.4
PhCOMe	$PhC(CF_3)(Me)OH$	1	55	81-83/3	-0.1
		1.5	48 (61)	93-95/24	-1.3
$CH_2=CHCH_2COMe$	$CH_2=CHCH_2C(CF_3)(Me)OH$	1	45	94-97/65	3.2

a) Structures were confirmed by means of IR and NMR spectra. b) Isolate yield. c) The figures in parentheses give the yields based on the relative intensities of ^{19}F NMR signals, using $PhCF_3$ as an internal standard. d) D.M.Feigl and H.S.Mosher, J. Org. Chem., 33, 4242 (1968). e) δ ppm upfield from ext. CF_3CO_2H.

A typical procedure of the reaction with benzaldehyde is as follow: A flask containing commercial available zinc powder (1.30 g, 0.02 g-atom), trifluoromethyl iodide (2.15 g, 11 mmol) and benzaldehyde (1.06 g, 10 mmol) in N,N-dimethylformamide (25 ml) was irradiated in the water bath of an ultrasound laboratory cleaner (35 W, 32 KHz) for 30 min. Then, the solution was poured into a 2% HCl solution and an oily material was extracted with diethyl ether. After the ethereal solution was dried over magnesium sulfate, the solvent was removed. Distillation gave phenyltrifluoromethylcarbinol in a yield of 72 % (1.27 g), bp 105-108°C/16 mmHg. ^{19}F NMR(CCl_4) ; δ -0.3 (CF_3, d, J_{CF_3-H} = 5.6 Hz) from ext. CF_3CO_2H : ^{1}H NMR(CCl_4) ; τ 5.00(CH,q), 6.22(OH) and 7.50(Ar-H).

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