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Regiospecific Replacement of Fluorine by Hydrogen in an Aromatic Ring Induced by a Rare Earth Organometallic

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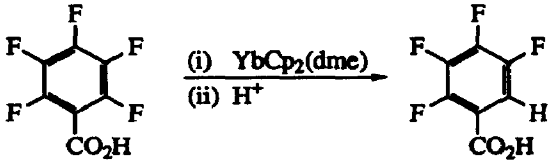
Abstract: Pentafluorobenzoic acid reacts with $YbCp_2(dme)$ to yield, after hydrolysis, 2,3,4,5-tetrafluorobenzoic acid. Conversion is near quantitative with activated magnesium as a coreductant and there is evidence for catalytic turnover in ytterbium on addition of a cyclopentadiene source. Reduction of 2,6-$F_2C_6H_3CO_2H$ to *o*-$FC_6H_4CO_2H$ and of *o*-$FC_6H_4CO_2H$ to $PhCO_2H$ has also been achieved.

Carbon-fluorine bond activation by an organolanthanoid was first observed in the complex redox transmetallation reaction between metallic samarium and bis(pentafluorophenyl)mercury in tetrahydrofuran.[1] Subsequently we have shown that pentafluorobenzoic acid reacts with bis(pentafluorophenyl)ytterbium to give, after hydrolysis, 2,3,4,5-tetrafluorobenzoic acid,[2] and the reaction was extended to other C-halogen bond activations.[3] However, although dehalogenation was regiospecific, the reactions were generally far from quantitative even with excess of the organolanthanoid, necessitating inconvenient separation of reactant and product acids,[2,3] and forcing conditions could not be used owing to the thermal instability of $Yb(C_6F_5)_2$.[4] We now report that regiospecific defluorination of pentafluorobenzoic acid can be achieved with the readily available[5] and thermally stable[6] $YbCp_2$ (Cp = cyclopentadienyl), that the reaction can be made near quantitative by addition of a coreductant, and that catalytic turnover can be achieved by addition of a cyclopentadiene source.

Treatment of pentafluorobenzoic acid with bis(cyclopentadienyl)(1,2-dimethoxyethane)ytterbium(II)[5] in pure, dry tetrahydrofuran under purified N_2 (see Table 1 for amounts of reagents and conditions) gave, after appropriate hydrolytic work up, 2,3,4,5-tetrafluorobenzoic acid.



(1)

The characteristic violet-purple colour of the organolanthanoid was usually discharged rapidly on mixing the reagents. Despite the evident speed of reaction, conversion was incomplete even with a $YbCp_2(dme)$:$C_6F_5CO_2H$ ratio of 4:1 (Table 1). Rapid, but incomplete reaction was also observed at -78°C giving a similar yield to a comparable reaction at room temperature. Although irradiation with white light has been shown to facilitate intermolecular C-F activation between $Ln(C_5Me_5)_2$ (Ln = Sm, Eu or Yb) and hexafluorobenzene in ether,[7] it had no effect on the yields in the present reactions.

Table 1 Reactions of $C_6F_5CO_2H$ with $YbCp_2(dme)$ in tetrahydrofuran[a]

$YbCp_2(dme)$ mmol	$C_6F_5CO_2H$ mmol	Conditions	$2\text{-}HC_6F_4CO_2H$ yield % [b]	$C_6F_5CO_2H$ recovered % [b]
0.5	1.0	RT, 1 min	17	76
1.0	1.0	RT, 1 min	29	59
2.0	1.0	RT, 1 min	45	46
4.0	1.0	RT, 1 h	70	18
1.0	1.0	RT, hv, 30 min	28	57
1.0	1.0	-78°C, hv, 1 h	32	58

[a] Reactions performed in 20 ml of thf, [b] Yields were determined by g.l.c. after conversion of the acids into methyl esters with diazomethane.

In attempts to achieve quantitative conversion, the effects of coreductants, Zn, Yb, Mg, and activated (by I_2) magnesium were investigated. Conversion was improved with the first three reagents, but was still incomplete (e.g. entry 1, Table 2). With activated magnesium as coreductant, near quantitative yields were obtained (Table 2, entries 2, 3) and there was no residual $C_6F_5CO_2H$. Addition of a small amount of iodine directly to a reaction mixture without magnesium led to reduced yield and some loss of selectivity, consistent with the observation[2] that YbI_2 reduces $C_6F_5CO_2H$ to a mixture of *o*-and *p*-$HC_6F_4CO_2H$.

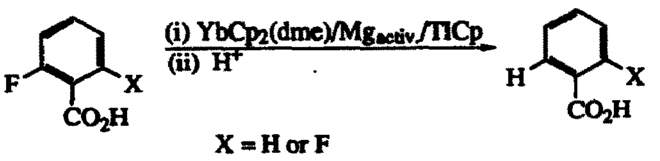
Table 2 Reactions of $C_6F_5CO_2H$ with $YbCp_2(dme)$ and activated Mg in tetrahydrofuran [a]

	$YbCp_2(dme)$ mmol	$C_6F_5CO_2H$ mmol	Mg/I_2 mmol	TlCp mmol	Conditions °C, h	*o*-$HC_6F_4CO_2H$ yield % [b]	$C_6F_5CO_2H$ recovered % [b]
1	1.0	1.0	2.0/-		65, 40	46	44
2	1.5	1.0	2.0/0.02		RT, 0.25	91	-
3	1.0	1.0	2.0/0.02		RT, 0.5	89	-
4	1.0	1.0	-/0.02		65, 40	14 [c]	77
5	-	1.0	2.0/0.02		65, 40	6	85
6	0.5	1.0	2.0/0.02		65, 5	87	-
7	0.2	1.0	2.0/0.02		65, 10	56	31
8	0.2	1.0	4.0/0.05		65, 10	58	30
9	0.2	1.0	2.0/0.02	0.2	65, 5	87	-
10	-	1.0	2.0/0.02	0.2	65, 40	7	85
11	0.2	1.0	2.0/0.02	0.2 (CpH)	65, 7	87	-

[a] Reactions were performed in 20 ml of thf [b] Yields were determined by g.l.c. after conversion of the acids into methyl esters with diazomethane, [c] A trace amount of p-$HC_6F_4CO_2H$ was detected.

Although activated magnesium alone is essentially unreactive (Table 2, entry 5), it enables near quantitative defluorination to be achieved with a YbCp$_2$(dme):C$_6$F$_5$CO$_2$H mole ratio of 0.5:1.0 (Table 2, entry 6), i.e. less than the minimum stoichiometric ratio of 1:1, thereby providing evidence that catalytic turnover of the organolanthanoid species is possible. With a lower YbCp$_2$(dme):C$_6$F$_5$CO$_2$H ratio (0.2:1.0), substantial C$_6$F$_5$CO$_2$H was recovered even with an increase in the amount of activated magnesium (Table 2, entries 7, 8). However, both near quantitative conversion to *o*-HC$_6$F$_4$CO$_2$H and catalytic turnover could be achieved with this ratio (0.2:1.0) of reagents by addition of a cyclopentadiene source, either thallium(I) cyclopentadienide or cyclopentadiene monomer (Table 2, entries 9, 11). There is no significant reaction with activated magnesium and TlCp in the absence of YbCp$_2$(dme) (Table 2, entry 10).

It is also possible to defluorinate *o*-fluorobenzoic acid and remove one fluorine from 2,6-difluorobenzoic acid by reaction with YbCp$_2$(dme) (0.2 mmol/1.0 mmol RCO$_2$H), activated magnesium, and thallous cyclopentadienide. Near quantitative yields of benzoic and *o*-fluorobenzoic acid respectively were obtained, again with evidence for catalytic turnover (Table 3).



(2)

o-Fluorobenzoic acid has only slight reactivity with YbCp$_2$(dme) alone or with activated magnesium and TlCp alone, and is reported to be unreactive towards Yb(C$_6$F$_5$)$_2$.[3] With more vigorous conditions, both fluorines can be removed from 2,6-difluorobenzoic acid (Table 3).

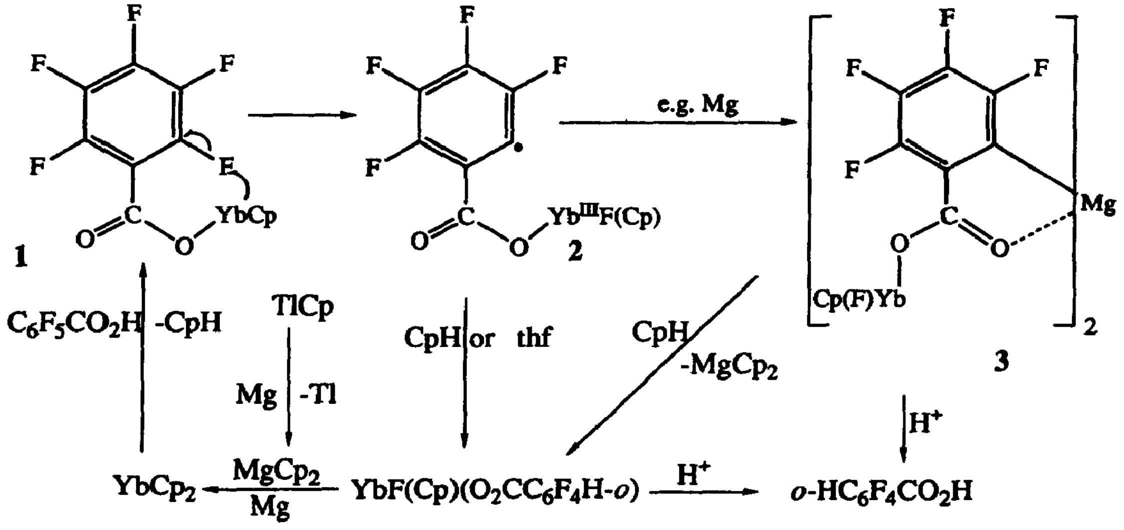
Table 3 Reactions of RCO$_2$H (R = *o*-FC$_6$H$_4$ or 2,6-F$_2$C$_6$H$_3$) with YbCp$_2$(dme), activated magnesium and TlCp in tetrahydrofuran [a]

YbCp$_2$(dme) mmol	RCO$_2$H (1.0 mmol) R	Mg/I$_2$ mmol	TlCp mmol	Conditions °C/h	Product R'CO$_2$H		Recovered RCO$_2$H	
					R'	yield(%)[b]	R	(%)[b]
0.2	*o*-FC$_6$H$_4$	2.0/0.02	0.2	65/10	Ph	87	*o*-FC$_6$H$_4$	0
1.0	o-FC$_6$H$_4$	-	-	65/48	Ph	2	*o*-FC$_6$F$_4$	87
-	*o*-FC$_6$F$_4$	2.0/0.02	1.0	65/48	Ph	2	*o*-FC$_6$F$_4$	90
0.2	2,6-F$_2$C$_6$H$_3$	2.0/0.02	0.2	65/8	*o*-FC$_6$H$_4$	89	2,6-F$_2$C$_6$H$_3$	0
2.0	2,6-F$_2$C$_6$H$_3$	2.0/0.02	0.2	65/7	Ph	87	2,6-F$_2$C$_6$H$_3$	0

[a] 20 ml in all cases

[b] Yields determined by g.l.c. after conversion of the acids into methyl esters with diazomethane.

The regiospecificity of the defluorination (1) can be explained by initial acidolysis giving cyclopentadienylytterbium(II) pentafluorobenzoate, which then undergoes intramolecular electron transfer and fluoride abstraction in a favourable cyclic six membered transition state 1. The resulting radical 2 can abstract an hydrogen atom from cyclopentadiene or thf giving a 2,3,4,5-tetrafluorobenzoate ligand. Alternatively, 2 may undergo further reduction, especially in the presence of the coreductant activated magnesium, to give a highly carbanionic organometallic 3, which can be protonated by CpH, or on hydrolysis.



In summary, $YbCp_2(dme)$ can induce regiospecific C-F activation, which is quantitative with activated magnesium as a coreductant, and can be catalytic in the organoytterbium reagent with an added cyclopentadiene source.

ACKNOWLEDGMENT

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REFERENCES

1. Deacon, G. B.; Koplick, A. J.; Raverty, W. D.; Vince, D. G. *J. Organomet. Chem.* **1979**, *182*, 121.
2. Deacon, G. B.; MacKinnon, P. I.; Tuong, T. D. *Aust. J. Chem.* **1983**, *36*, 43.
3. Deacon, G. B.; MacKinnon, P. I. *Tetrahedron Lett.* **1984**, *25*, 783.
4. Deacon, G. B.; Raverty, W. D.; Vince, D. G. *J. Organomet. Chem.* **1977**, *135*, 103.
5. Deacon, G.B.; Pain, G. N.; Tuong, T. D. *Inorg. Synth.* **1990**, *28*, 291.
6. Calderazzo, F.; Pappalardo, R.; Losi, S. *J. Inorg. Nucl. Chem.* **1966**, *24*, 987.
7. Watson, P. L.; Tulip, T. H.; Williams, I. *Organometallics* **1990**, *9*, 1999.

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