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## PRELIMINARY NOTE

The  $\alpha,\alpha$ -Difluoro Reformatsky Reagent: Pregeneration and Structural Determination

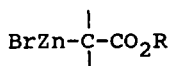
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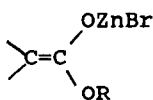
## SUMMARY

The reaction of zinc amalgam with ethyl bromodifluoroacetate in triglyme provides a useful route to a stable  $\alpha,\alpha$ -difluoro zinc reagent.  $^{19}\text{F}$  NMR and  $^{13}\text{C}$  NMR data for this species support the structural assignment of this organo-metallic derivative as a carbon-metallated compound.

A century ago Reformatsky discovered the reaction that bears his name [1]. In the ensuing years Reformatsky reagents have become recognized as key synthons in the construction of organic molecules [2,3,4]. It is well documented that an intermediate zinc reagent is involved in the Reformatsky reaction. However, considerable debate has accompanied the structural assignment of this reagent; both carbon- and oxygen-metallated structures have received support at various times.



carbon-metallated

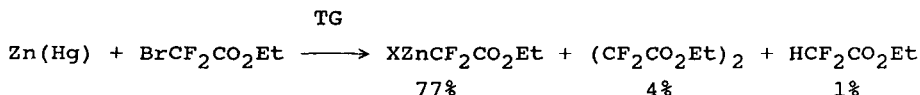


oxygen-metallated

Vaughn and co-workers [5,6] examined this reagent by infrared spectroscopy and based on the absence of a carbonyl group absorption in the IR spectrum, they concluded that the zinc reagent existed in the oxygen-metallated form. However, other workers studied this reagent via  $^1\text{H}$  and  $^{13}\text{C}$  NMR spectroscopy, and concluded that NMR data corroborated the carbon-metallated structure [7,8]. From molecular weight determination and X-ray crystal structure Boersma [9] determined that this reagent exists as a dimer in all but the most polar solvents. In DMSO he concluded that the zinc reagent is a monomeric carbon-metallated species.

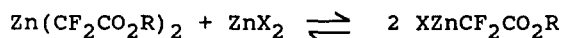
In connection with our current work on fluorine-containing zinc reagents [10-15], we became interested in the fluorinated analog of the Reformatsky reagent. The use of fluorine substituted  $\alpha$ -bromoesters in this reaction is a natural extension of this important reaction, and many examples of the use of alkyl bromodifluoroacetates have been documented [16]. However, these reports utilize the classical one-step method [2], without the description of a detailed pregeneration procedure. Consequently no structural information is available for the  $\alpha,\alpha$ -difluoro Reformatsky reagent.

We have found that this fluorinated analog can be readily generated in triglyme (TG) via the exothermic reaction of zinc amalgam with ethyl bromodifluoroacetate. The zinc reagent is initially formed in 77% yield (by  $^{19}\text{F}$  NMR spectroscopy) and slowly decomposes on standing at room temperature, to the extent of 8.5% decomposition after 20 hours and 23% after 45 hours. This reagent could also be formed in tetrahydrofuran (THF), but it was less stable in this solvent and total decomposition was observed after 20 hours at room temperature.



The  $^{19}\text{F}$  NMR spectrum of the zinc reagent in TG consisted of two singlets at -115.3 and -115.2 ppm downfield from  $\text{CFCl}_3$ .

These signals correspond to the mono (X = Br) and bis (X = CF<sub>2</sub>CO<sub>2</sub>Et) zinc reagents, respectively. Chemical shift assignments of the mono and bis species were facilitated by the addition of zinc halide. The resulting enhancement of the <sup>19</sup>F NMR signal for the mono reagent at the expense of that for the bis reagent was due to the following equilibrium:



The singlets observed for this reagent are in agreement with a carbon-metallated structure. The isomeric oxygen-metallated species would be expected to exhibit an AB pattern in the <sup>19</sup>F NMR spectrum for the two vinylic fluorines. No such pattern is observed for the fluorinated zinc reagent. This type of AB pattern is, however, observed in the <sup>19</sup>F NMR spectrum of the difluoroketene trimethylsilyl acetal [17] and would be expected to be observed in an oxygen-metallated reagent.

Additional evidence for a carbon-metallated structure was obtained by comparison of the <sup>13</sup>C NMR spectrum of the α,α-difluoro Reformatsky reagent with the <sup>13</sup>C NMR spectrum of the oxygen- and carbon-silylated difluoroacetate [17] species (cf. Table I). It should be noted that the carbonyl carbon (C<sub>b</sub>) of the carbon-silylated compound appears at 166.0 ppm, similar to the carbonyl carbon (C<sub>b</sub>) of the fluorinated zinc reagent (170 ppm). This close agreement in chemical shift of C<sub>b</sub> in these two compounds is indicative of the presence of a carbonyl carbon in both species. In contrast to this close agreement, however, the ketene silyl acetal which contains no carbonyl carbon exhibits a chemical shift of 125 ppm for C<sub>b</sub>.

In conclusion, a simple mild preparation of the α,α-difluoro Reformatsky reagent is described \* <sup>19</sup>F NMR and <sup>13</sup>C NMR data support the assignment of a carbon-metallated structure to this compound. Future reports will elaborate on synthetic applications of this reagent and related α-fluoro Reformatsky reagents.

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\* Subsequent to our work a recent report describes a regeneration procedure [18], but no spectroscopic or structural data were given.

TABLE I

 $^{13}\text{C}$  NMR data for difluoroenolate species

Assigned Structure	Chemical Shift (ppm relative to TMS)	Coupling Constant (Hz)
$\begin{array}{c} \text{O} \\    \\ \text{XZnCF}_2\text{COCH}_2\text{CH}_3 \\ \text{a} \quad \text{b} \quad \text{c} \quad \text{d} \\ (\text{X} = \text{Br}) \end{array}$	a 135.18(t)	$J_{\text{F},\text{C}_a} = 291.43$
	b 170.46(t)	$J_{\text{F},\text{C}_b} = 20.92$
	c and d <sup>1</sup>	
$\begin{array}{c} \text{O} \\    \\ (\text{CH}_3)_3\text{SiCF}_2\text{COCH}_2\text{CH}_3 \\ \text{e} \quad \text{a} \quad \text{b} \quad \text{c} \quad \text{d} \end{array}$	a 121.6(t)	$J_{\text{F},\text{C}_a} = 268.0$
	b 166.0(t)	$J_{\text{F},\text{C}_b} = 25.6$
	c, d, and e <sup>2</sup>	
$\begin{array}{c} \text{OSi}(\text{CH}_3)_3 \\ \diagup \quad \diagdown \\ \text{CF}_2=\text{C} \quad \text{e} \\ \diagdown \quad \diagup \\ \text{a} \quad \text{b} \quad \text{OCH}_2\text{CH}_3 \\ \quad \quad \quad \text{c} \quad \text{d} \end{array}$	a 147.9(t)	$J_{\text{F},\text{C}_a} = 270.7$
	b 125.1(t)	$J_{\text{F},\text{C}_b} = 37.7$
	c, d, and e <sup>3</sup>	

1 c 60.11(s); d 14.43(s).

2 c 62.2(s); d 14.2(s); e -5.1(s).

3 c 64.3(s); d 12.9(s); e -2.3(s).

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