



Meerwein arylation with 3-fluorobutenone

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ABSTRACT

3-Fluorobutenone (**7**) reacts with aryl triazenes in the presence of zinc iodide to give 4-aryl-3-fluoro-3-iodo-2-butanones (**9a–9f**) in moderate yields. The products arise from a free radical process that terminated by iodination of an alkyl radical. The process yields unusual geminal iodo-fluoro compounds.

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1. Introduction

Meerwein arylation is a well known process for the addition of an aryl radical to an activated unsaturated function to give both unsaturated and saturated aryl products [1,2] (Scheme 1). An aryl diazonium salt (**1**) reacts with a metal catalyst to generate an aryl radical **A**. The radical reacts with an activated unsaturated system, methyl vinyl ketone (**2**) in this example, to give an alkyl radical **B**. The radical can be terminated by addition of halogen to give the saturated product **3** that can be isolated or can be dehydrohalogenated to give the arylated unsaturated system **4**. Yields are generally moderate to good depending on the ratios of diazonium salt, vinyl compound and catalyst. Sometimes appreciable amounts of aryl halide are formed from a Sandmeyer process.

2. Results and discussion

In 2001 we reported the use of aryl triazines as radical sources for the Meerwein reaction with acrylonitrile to give addition products terminated by iodination as shown in Scheme 2 [3].

Our recent studies on the chemistry of 3-fluorobutenone (**7**) [4–6] led us to investigate the Meerwein arylation of this fluorinated unsaturated system (Scheme 3). Although several non-activated vinyl fluorides have been studied in the Meerwein reaction [7], **7** is

the first activated fluoroalkene. As seen in Scheme 3 several aryl radicals produced from aryl triazines (**8a–8f**) [8] and ZnI_2 were allowed to react with **7** to give the unusual geminal fluoro-iodo products (**9a–9f**) in moderate yields (Table 1).

These reactions do not show any unsaturated products, but products from iododediazotization (Ari) are always observed in 12–15% yields. The rates of aryl addition to **7** (approx. 10^8) and of aryl iodination (approx. 10^{7-8}) should be very similar according to Heinrich [1]. The best way to control the outcome is by varying the amounts of reactants. We found after many attempts that the best ratio of **7**/**8**/ ZnI_2 is 10/1/2. We could not find conditions to stop formation of the iodoaromatic compound.

The geminal fluoro-iodo function is rarely observed. We have only found records of iodo-fluoro methanes and ethanes and some minor products from iodofluorination [9]. In comparison of the F NMR chemical shifts of products **9a–9f** with a similar non-iodinated compound [6], we find that the fluoro-iodo compounds are approximately 67 ppm downfield from hydro-fluoro compound. The large deshielding effect of iodine atoms on proton NMR spectroscopy is reported in the literature and apparently holds also for fluorine NMR [10].

When equivalent amounts of **7** and methyl vinyl ketone, both in excess, were allowed to react with phenyl triazine, equal amounts of phenyl radical products from both substrates were observed. Thus **7** and methyl vinyl ketone show the very similar reactivity in the reaction, with little effect from the fluorine atom of **7**.

3. Experimental procedure

The preparation of **7** [4] and of aryl triazines (**8a–8f**) [9] have been reported.

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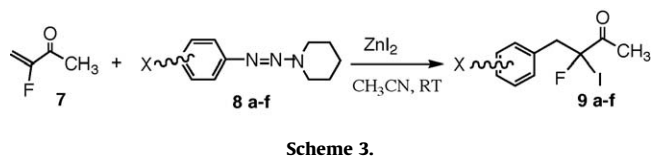
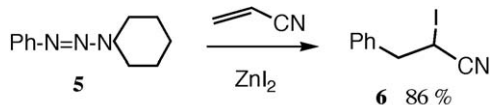
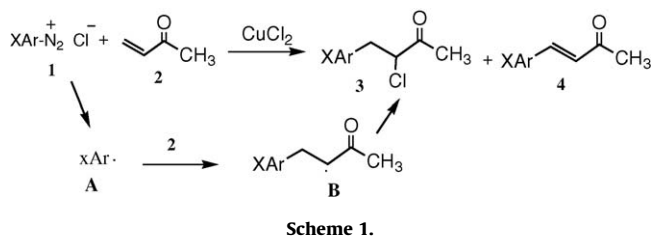


Table 1
Fluoro-iodo products from Meerwein Arylation of 7.

Fluoro-iodo products (9)	% yield	δ F 19 (CFCl ₃)
H 9a	45	-122.1
<i>p</i> -CH ₃ 9b	51	-122.0
<i>p</i> -OCH ₃ 9c	78	-122.2
<i>m</i> -CH ₃ 9d	46	-121.7
<i>p</i> -Cl 9e	35	-123.3
<i>p</i> -F 9f	27	-123.2
		-115.3 <i>p</i> -F

3.1. General procedure for the ZnI₂ catalyzed Meerwein arylation of 7

1-Phenyl-2-(piperidin-1-yl)diazene (**8a**) (1.14 mmol, 215.7 mg), ZnI₂ (2.28 mmol, 727.7 mg), and 3-fluorobutanone (**7**) (11.4 mmol, 1 g) in 10 mL of acetonitrile were placed in a clean dry 25 mL round bottom flask. The flask was degassed and sealed under argon. The flask was stirred vigorously overnight. Acetonitrile and excess 3-fluorobutanone (**7**) were removed by vacuum evaporation followed by filtration on a short plug of silica gel to remove excess ZnI₂. The crude product was purified by flash column chromatography using hexane/ethyl acetate solvent gradient. An oily compound (**9a**) was obtained in 45% yield. Compounds **9a–9f** were all obtained as amber oils.

3.2. Analytical data for 9a–9f

F NMR spectra are reported in Table 1 with a reference of CFCl₃.

3-Fluoro-3-iodo-4-phenylbutan-2-one (**9a**): ¹H NMR (CDCl₃, TMS) δ 2.30 (d, *J* = 4.6 Hz, 3H, CH₃), δ 3.70–3.80 (dq, *J*_{H–H} = 14.7 Hz, *J*_{H–F} = 10.0 Hz, *J*_{H–I} = 2.1 Hz, 2H, CH₂), δ 7.26–7.32 (m, 5H aromatic); ¹³C NMR (CDCl₃, TMS) δ 23.4 (d, *J* = 2.0 Hz, CH₃), δ 47.80 (d,

J = 19.1 Hz, CH₂), δ 88.0, 91.6 (d, *J* = 271.9 Hz, CFI), δ 128.0–134.0 (m, aromatic), δ 201.1 (d, *J* = 28.7 Hz, CO). Anal. Calcd for C₁₀H₁₀FIO: *m/e* 291.976. Found, 291.977.

3-Fluoro-3-iodo-4-*p*-tolylbutan-2-one (**9b**): ¹H NMR (CDCl₃, TMS) δ 2.30 (d, *J* = 4.6 Hz, 3H, CH₃), δ 2.32 (s, 3H, Ph-CH₃), δ 3.67–3.77 (dq, *J*_{H–H} = 14.7 Hz, *J*_{H–F} = 10.0 Hz, *J*_{H–I} = 2.0 Hz, 2H, CH₂), δ 7.12 (s, 4 H aromatic); ¹³C NMR (CDCl₃, TMS) δ 21.4 (s, Ph-CH₃), δ 23.6 (d, *J* = 4.0 Hz, CH₃), δ 48.4 (d, *J* = 19.1 Hz, CH₂), δ 88.8, 92.4 (d, *J* = 271.9 Hz, CFI), δ 129.3–137.7 (m, aromatic), δ 201.5 (d, *J* = 28.7 Hz, CO). Anal. Calcd for C₁₁H₁₂FIO: *m/e* 305.991. Found, 305.989.

3-Fluoro-3-iodo-4-(4-methoxyphenyl)butan-2-one (**9c**): ¹H NMR (CDCl₃, TMS) δ 2.29 (d, *J* = 4.9 Hz, 3H, CH₃), δ 3.65–3.78 (dq, *J*_{H–H} = 15 Hz, *J*_{H–F} = 8.5 Hz, *J*_{H–I} = 1.5 Hz, 2H, CH₂), δ 3.79 (s, 3H, OCH₃), δ 6.82–7.23 (dm, 4 H aromatic); ¹³C NMR (CDCl₃, TMS) δ 23.6 (d, *J* = 3.0 Hz, CH₃), δ 48.0 (d, *J* = 19.1 Hz, CH₂), δ 55.5 (s, OCH₃), δ 88.5, 91.5 (d, *J* = 271.9 Hz, CFI), δ 114.0–159.3 (m, aromatic), δ 201.7 (d, *J* = 28.7 Hz, CO). Anal. Calcd for C₁₁H₁₂FIO₂: *m/e* 321.986. Found, 321.984.

3-Fluoro-3-iodo-4-*m*-tolylbutan-2-one (**9d**): ¹H NMR (CDCl₃, TMS) δ 2.31 (d, *J* = 4.9 Hz, 3H, CH₃), δ 2.34 (s, 3H, Ph-CH₃), δ 3.67–3.77 (dq, *J*_{H–H} = 14.6 Hz, *J*_{H–F} = 9.3 Hz, *J*_{H–I} = 1.5 Hz, 2H, CH₂), δ 7.04–7.24 (m, 4 H aromatic); ¹³C NMR (CDCl₃, TMS) δ 23.61 (d, *J* = 3.0 Hz, CH₃), δ 48.70 (d, *J* = 19.1 Hz, CH₂), δ 88.70, 92.30 (d, *J* = 272.5 Hz, CFI), δ 128.06–157.15 (m, aromatic), δ 201.10 (d, *J* = 28.2 Hz, CO). Anal. Calcd for C₁₁H₁₂FIO: *m/e* 305.991. Found, 305.990.

4-(4-Chlorophenyl)-3-fluoro-3-iodobutan-2-one (**9e**): ¹H NMR (CDCl₃, TMS) δ 2.33 (d, *J* = 4.9 Hz, 3H, CH₃), δ 3.66–3.76 (dq, *J*_{H–H} = 14.7 Hz, *J*_{H–F} = 10.3 Hz, *J*_{H–I} = 3.2 Hz, 2H, CH₂), δ 7.13–7.27 (dm, 4 H aromatic); ¹³C NMR (CDCl₃, TMS) δ 23.42 (d, *J* = 2.0 Hz, CH₃), δ 48.80 (d, *J* = 19.1 Hz, CH₂), δ 87.98, 91.59 (d, *J* = 271.9 Hz, CFI), δ 128.04–134.0 (m, aromatic), δ 200.87 (d, *J* = 28.2 Hz, CO). Anal. Calcd for C₁₀H₉ClFIO: *m/e* 325.937. Found, 325.927.

3-Fluoro-4-(4-fluorophenyl)-3-iodobutan-2-one (**9f**): ¹H NMR (CDCl₃, TMS) δ 2.32 (d, *J* = 4.9 Hz, 3H, CH₃), δ 3.66–3.76 (dq, *J*_{H–H} = 15 Hz, *J*_{H–F} = 10.3 Hz, *J*_{H–I} = 3.2 Hz, 2H, CH₂), δ 6.97–7.26 (dm, 4 H aromatic); ¹³C NMR (CDCl₃, TMS) δ 26.74 (d, *J* = 4.5 Hz, CH₃), δ 37.47 (d, *J* = 20.1 Hz, CH₂), δ 94.66, 97.16 (d, *J* = 188.3 Hz, CFI), δ 115.48–163.92 (m, aromatic), δ 208.0 (d, *J* = 28.2 Hz, CO). Anal. Calcd for C₁₀H₉F₂IO: *m/e* 309.967. Found, 309.968.

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References

- [1] M.R. Heinrich, Chem. Eur. J. 15 (2009) 820.
- [2] C.S. Rondstvedt Jr., Org. React. 24 (1976) 225.
- [3] T.B. Patrick, T. Juehne, E. Reeb, D. Hennessy, Tetrahedron Lett. 42 (2001) 3553.
- [4] T.B. Patrick, T.Y. Agboka, K. Gorrell, J. Fluorine Chem. 129 (2008) 983.
- [5] T.B. Patrick, H. Li, J. Fluorine Chem. 130 (2009) 544.
- [6] T.B. Patrick, U.P. Dahal, J. Fluorine Chem. 130 (2009) 470.
- [7] C.S. Rondstvedt Jr., J. Org. Chem. 42 (1977) 2618.
- [8] D.F. Shellhamer, V.L. Heasley, Adv. Org. Synth. 2 (2006) 43.
- [9] T.B. Patrick, R.P. Willaredt, D.J. Degonia, J. Org. Chem. 50 (1985) 2232.
- [10] R.J. Abraham, M.A. Warne, L. Griffiths, J. Chem. Soc., Perkin Trans. 2 (1997) 215.