Synthesis of some fluorinated nitro-olefins

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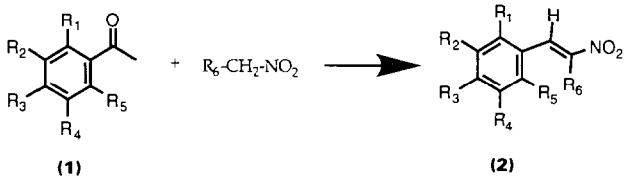
Abstract

The synthesis of fluorinated nitro-olefins from fluorinated benzaldehydes by aldol condensation is described.

Introduction

Nitroalkenes are versatile intermediates in organic synthesis. They are powerful dienophiles in Diels–Alder reactions and also readily undergo Michael additions with a variety of nucleophiles [1–4]. They frequently exhibit insecticidal [5], anti-bacterial [6] and anti-fungal properties [7, 8]. The impetus to our research on nitro-olefins came from the work of Eckstein and co-workers, who reported that nitro-olefins substituted by a fluorinated phenyl ring exhibit insecticidal activity almost equal to that of DDT [9]. Since a variety of fluorinated benzaldehydes are commercially available, we initially targeted fluoro-substituted aromatic nitro-olefins with and without an alkyl group on the β carbon, a prelude to a study of their insecticidal properties.

Commercially available fluorinated benzaldehydes **1** were condensed with nitroalkanes in the presence of acetic acid and ammonium acetate, and the products were further purified by chromatography to give nitrostyrenes **2a–r** in 9%–67% yield. Their identification was confirmed by elemental analysis and ^{1}H NMR spectroscopy.



(1) (2)

Experimental

Melting points were obtained on an Electrothermal 88629 apparatus and are uncorrected. Infrared spectra were recorded on a Perkin-Elmer FT-IR 1750 spectrophotometer. Proton NMR spectra were recorded on Chemagnetic 200 MHz and Varian EM-390 90 MHz spectrometers with TMS as internal standard. Mass spectra were obtained on a Finnigan 3000 instrument at 70 eV by direct insertion and data were processed using the Teknivent system. Elemental analyses for carbon and hydrogen were conducted by Galbraith Laboratories, Inc. (Knoxville, TN).

General preparation of fluorinated nitro-olefins

To a stirred mixture consisting of 2,3-difluorobenzaldehyde (0.5 ml, 4.67 mmol) (**1a**) and nitroethane (1.0 ml, 19.1 mmol) was added ammonium acetate (1.0 g, 12.9 mmol) and acetic acid (15 ml). After reflux for 3 h, the acetic acid was removed under reduced pressure and the mixture quenched with cold water. The organic layer was extracted with dichloromethane. The combined organic phase was dried over anhydrous sodium sulfate and the solvent removed under reduced pressure, leaving yellow crystals that were recrystallized (pentane) to give a 21% yield of **2a**. Table 1 gives details of substituents for compounds **1** and **2** and the percentage yield of compound **2**.

2,3-Difluoro-β-nitrovinylbenzene (**2a**): M.p. 45–48 °C. IR (KBr) (cm^{-1}): 3140; 3100; 3050; 1638; 1628; 1588; 1525; 1350; 1280; 950; 840; 786; 725. ^{1}H NMR ($CDCl_3$) δ: 7.96 (d, 1H, J=15 Hz, CH=); 7.60 (d, 1H, J=15 Hz, CH=); 7.40–6.90 (m, 3H, Ar–H) ppm. MS (*m/e*): 185 (M^+). Analysis: Calc. for $C_8H_5O_2NF_2$: C, 51.90; H, 2.72%. Found: C, 52.31; H, 2.68%.

2,4-Difluoro-β-nitrovinylbenzene (**2b**): M.p. 54–56 °C. IR (KBr) (cm^{-1}): 3100; 3080; 1640; 1618; 1530; 1500; 1345; 1275; 970; 850; 815. ^{1}H NMR ($CDCl_3$) δ: 7.95 (d, 1H, J=13.5 Hz, CH=); 7.58 (d, 1H, J=13.5 Hz, CH=); 7.10–6.66 (m, 3H, Ar–H) ppm. MS (*m/e*): 185 (M^+). Analysis: Calc. for $C_8H_5O_2NF_2$: C, 51.90; H, 2.72%. Found: C, 52.46; H, 2.67%.

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TABLE 1. List of substituents for compounds **1** and **2** and percentage yield for **2**

Compounds **1, 2**	Substituents						% Yield of compound **2**
	R_1	R_2	R_3	R_4	R_5	R_6	
a	F	F	H	H	H	H	21
b	F	H	F	H	H	H	67
c	F	H	H	F	H	H	26
d	F	H	H	H	F	H	39
e	H	F	H	F	H	H	41
f	H	F	OMe	H	H	H	62
g	F	F	H	H	H	Me	39
h	F	H	F	H	H	Me	23
i	F	H	H	F	H	Me	62
j	F	H	H	H	H	Me	53
k	H	F	F	H	H	Me	29
l	H	F	H	F	H	Me	54
m	H	F	OMe	H	H	Me	9
n	F	F	H	H	H	Et	21
o	F	H	F	H	H	Et	9
p	F	H	H	F	H	Et	22
q	F	H	H	H	F	Et	24
r	H	F	F	H	H	Et	19

2,5-Difluoro-β-nitrovinylbenzene (**2c**): M.p. 70–74 °C. IR (KBr) (cm^{-1}): 3118; 3082; 1640; 1525; 1500; 1345; 1275; 972; 845; 825; 766. ^1H NMR ($CDCl_3$) δ: 7.95 (d, 1H, $J=13.5$ Hz, CH=); 7.60 (d, 1H, $J=13.5$ Hz, CH=); 7.33–6.96 (m, 3H, Ar–H) ppm. MS (*m/e*): 185 (M^+). Analysis. Calc. for $C_8H_5O_2NF_2$: C, 51.90; H, 2.72%. Found: C, 52.56; 2.99%.

2,6-Difluoro-β-nitrovinylbenzene (**2d**): M.p. 109–111 °C. IR (KBr) (cm^{-1}): 3140; 3060; 1642; 1625; 1525; 1340; 1010; 848; 790. ^1H NMR ($CDCl_3$) δ: 8.11 (d, 1H, $J=13.5$ Hz, CH=); 7.75 (d, 1H, $J=13.5$ Hz, CH=); 7.58–6.65 (m, 3H, Ar–H) ppm. MS (*m/e*): 185 (M^+). Analysis: Calc. for $C_8H_5O_2NF_2$: C, 51.90; H, 2.72%. Found: C, 52.10; H, 2.62%.

3,5-Difluoro-μ-nitrovinylbenzene (**2e**): M.p. 103–107 °C. IR (KBr) (cm^{-1}): 3130; 3190; 1650; 1600; 1525; 1350; 1296; 1000; 860; 840. ^1H NMR ($CDCl_3$) δ: 7.73 (d, 1H, $J=13.5$ Hz, CH=); 7.40 (d, 1H, $J=13.5$ Hz, CH=); 7.13–6.70 (m, 3H, Ar–H) ppm. MS (*m/e*): 185 (M^+). Analysis: Calc. for $C_8H_5O_2NF_2$: C, 51.90; H, 2.72%. Found: C, 52.31; H, 2.66%.

3-Methoxy-4-fluoro-β-nitrovinylbenzene (**2f**): M.p. 91–92 °C. IR (KBr) (cm^{-1}): 3100; 3040; 2960; 1610; 1510; 1440; 1320; 1270; 810; 755. ^1H NMR ($CDCl_3$) δ: 8.13–7.90 (d, 1H, $J=14$ Hz, CH=); 7.53–7.36 (d, 1H, $J=14$ Hz, CH=); 7.38–6.96 (m, 3H, Ar–H); 4.00 (s, 3H, OCH_3) ppm. MS (*m/e*): 197 (M^+). Analysis: Calc. for $C_9H_8O_3NF$: C, 54.82; H, 4.09%. Found: C, 54.73; H. 4.07%.

2,3-Difluoro-β-methyl-β-nitrovinylbenzene (**2g**): Liquid. IR (KBr) (cm^{-1}): 3080; 3050; 2930; 2850; 1670; 1625; 1590; 1530; 1480; 1435; 1330; 1290; 950; 858; 822; 790; 764; 707. ^1H NMR ($CDCl_3$) δ: 7.93 (s, 1H, CH=); 7.05 (m, 3H, Ar–H); 2.25 (s, 3H, CH_3) ppm. MS (*m/e*): 199 (M^+). Analysis. Calc. for $C_9H_7O_2NF_2$: C, 54.27; H, 3.54%. Found: C, 53.66; H, 3.60%.

2,4-Difluoro-β-methyl-β-nitrovinylbenzene (**2h**): M.p. 44–47 °C. IR (KBr) (cm^{-1}): 3090; 3070; 2920; 2850; 1660; 1610; 1595; 1515; 1495; 1430; 1318; 1275; 980; 865; 830. ^1H NMR ($CDCl_3$) δ: 7.93 (s, 1H, CH=); 7.46–6.60 (m, 3H, Ar–H); 2.33 (s, 3H, CH_3) ppm. MS (*m/e*): 199 (M^+). Analysis: Calc. for $C_9H_7O_2NF_2$: C, 54.72; H, 3.54%. Found: C, 54.62; H, 3.49%.

2,5-Difluoro-β-methyl-β-nitrovinylbenzene (**2i**): M.p. 40–45 °C. IR (KBr) (cm^{-1}): 3080; 2920; 2850; 1663; 1592; 1530; 1490; 1430; 1328; 1280; 1000; 820; 740. ^1H NMR ($CDCl_3$) δ: 7.93 (s, 1H, CH=); 7.36–6.70 (m, 3H, Ar–H); 2.33 (s, 3H, CH_3) ppm. MS (*m/e*): 199 (M^+). Analysis: Calc. for $C_9H_7O_2NF_2$: C, 54.27; H, 3.54%. Found: C, 54.53; H, 3.51%.

2,6-Difluoro-β-methyl-β-nitrovinylbenzene (**2j**): M.p. 60–65 °C. IR (KBr) (cm^{-1}): 3080; 2060; 2920; 2825; 1675; 1623; 1590; 1520; 1455; 1400; 1320; 1000; 980; 870; 785; 748; 714. ^1H NMR ($CDCl_3$) δ: 7.70 (s, 1H, CH=); 7.50–6.66 (m, 3H, Ar–H); 2.21 (s, 3H, CH_3) ppm. MS (*m/e*): 199 (M^+). Analysis: Calc. for $C_9H_7O_2NF_2$: C, 54.27; H, 3.54%. Found: C, 54.62; H, 3.57%.

3,4-Difluoro-β-methyl-β-nitrovinylbenzene (**2k**): M.p. 46–50 °C. IR (KBr) (cm^{-1}): 3080; 3060; 2932; 2850; 1432; 1320; 1280; 990; 860; 816; 750. ^1H NMR ($CDCl_3$) δ: 7.83 (s, 1H, CH=); 7.40–6.86 (m, 3H, Ar–H); 2.41 (s, 3H, CH_3) ppm. MS (*m/e*): 199 (M^+). Analysis: Calc. for $C_9H_7O_2NF_2$: C, 54.27; H, 3.54%. Found: C, 54.55; H, 3.52%.

3,5-Difluoro-β-methyl-β-nitrovinylbenzene (2l): Liquid. IR (KBr) (cm^{-1}): 3090; 3062; 2930; 2850; 1665; 1620; 1592; 1525; 1435; 1315; 990; 850. ^1H NMR ($CDCl_3$) δ: 7.86 (s, 1H, CH=); 7.36–6.46 (m, 3H, Ar–H); 2.40 (s, 3H, CH_3) ppm. MS (*m/e*): 199 (M^+). Analysis: Calc. for $C_9H_7O_2NF_2$: C, 54.27; H, 3.54%. Found: C, 54.79; H, 3.91%.

3-Methoxy-4-fluoro-β-methyl-β-nitrovinylbenzene (**2m**): M.p. 50–56 °C. IR (KBr) (cm^{-1}): 3030; 2842; 1580; 1520; 1440; 1310; 1280; 1130; 1000; 760. ^1H NMR ($CDCl_3$) δ: 7.80 (s, 1H, CH=); 7.26–6.73 (m, 3H, Ar–H); 3.86 (s, 3H, $-OCH_3$); 2.40 (s, 3H, CH_3) ppm. MS (*m/e*): 211 (M^+). Analysis: Calc. for $C_{10}H_{10}O_3NF$: C, 56.87; H, 4.77%. Found: C, 56.89; H, 5.10%.

2,3-Difluoro-β-ethyl-β-nitrovinylbenzene (**2n**): M.p. 43–44 °C. IR (NaCl) (cm^{-1}): 3100; 3060; 1660; 1630; 1590; 1525; 1370; 1340; 1260; 980; 790; 710. ^1H NMR ($CDCl_3$) δ: 7.95 (s, 1H, CH=); 7.29–7.03 (m, 3H, Ar–H); 2.93–2.56 (q, 2H, $J=7.2$ Hz, CH_2-); 1.33–1.07 (t, 3H, $J=7.2$ Hz, CH_3) ppm. MS (*m/e*): 213 (M^+). Analysis: Calc. for $C_{10}H_9O_2NF_2$: C, 56.35; H, 4.27%. Found: C, 56.43; H, 4.33%.

2,4-Difluoro-β-ethyl-β-nitrovinylbenzene (**2o**): M.p. 44–45 °C. IR (NaCl) (cm^{-1}): 3145; 3090; 3000; 2960; 2900; 1660; 1620; 1520; 1490; 1475; 1460; 1435; 1390; 1335; 1280; 1130; 975; 920; 870. ^1H NMR ($CDCl_3$) δ: 8.00 (s, 1H, CH=); 7.45–6.90 (m, 3H, Ar−H); 2.85–2.71 (q, 2H, $J=8.0$ Hz, CH_2-); 1.35–1.15 (t, 3H, $J=7.0$ Hz, CH_3) ppm. MS (*m/e*): 213 (M^+). Analysis: Calc. for $C_{10}H_9O_2NF_2$: C, 56.35; H, 4.27%. Found: C, 56.33; H, 4.34%.

2,5-Difluoro-β-ethyl-β-nitrovinylbenzene (**2p**): M.p. 52–53 °C. IR (NaCl) (cm^{-1}): 3190; 3000; 2960; 2890; 1670; 1600; 1560; 1520; 1490; 1470; 1440; 1380; 1342; 1290; 1250; 1200; 980; 918; 835. ^1H NMR ($CDCl_3$) δ: 8.01 (s, 1H, CH=); 7.28–7.00 (m, 3H, Ar−H); 3.00–2.64 (q, 2H, $J=7.0$ Hz, CH_2-); 1.37–1.13 (t, 3H, $J=7.0$ Hz, CH_3) ppm. MS (*m/e*): 213 (M^+). Analysis: Calc. for $C_{10}H_9O_2NF_2$: C, 56.35; H, 4.27%. Found: C, 56.22; H, 4.32%.

2,6-Difluoro-β-ethyl-β-nitrovinylbenzene (**2q**): M.p. 46–47 °C. IR (NaCl) (cm^{-1}): 3110; 3080; 2960; 2890; 2940; 1670; 1622; 1590; 1520; 1460; 1440; 1370; 1335; 1270; 1230; 1000; 975; 945; 905; 870; 810; 780. ^1H NMR ($CDCl_3$) δ: 7.65 (s, 1H, CH=); 7.51–6.80 (m, 3H, Ar−H); 2.72–2.35 (q, 2H, $J=7.0$ Hz, CH_2-); 1.19–0.95 (t, 3H, $J=7.0$ Hz, CH_3) ppm. MS (*m/e*): 213 (M^+). Analysis: Calc. for $C_{10}H_9O_2NF_2$: C, 56.35; H, 4.27%. Found: C, 56.37; H, 4.31%.

3,4-Difluoro-β-ethyl-β-nitrovinylbenzene (**2r**): M.p. 67–69 °C IR (NaCl) (cm^{-1}): 3080; 2995; 1655; 1610; 1555; 1520; 1450; 1375; 1350; 1280; 930; 830. ^1H NMR ($CDCl_3$) δ: 7.80 (s, 1H, CH=); 7.23–7.00 (m, 3H, Ar−H); 2.89–2.5 (q, 2H, $J=7.0$ Hz, CH_2); 1.29–1.04 (t, 3H, $J=7.0$ Hz, CH_3) ppm. MS (*m/e*): 213 (M^+). Analysis: Calc. for $C_{10}H_9O_2NF_2$: C, 56.35; H, 4.27%. Found: C, 56.27; H, 4.30%.

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