Supporting Information

Controlling Reactivity Through Additive Selection: The Curious Case of Mechanochemical Fluorination

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General Methods

All chemicals were obtained from commercial sources and used without further purification unless stated otherwise. Dry THF was obtained from a Braun MB SPS-800 solvent purification system fitted with the recommended columns.

¹H, ¹⁹F and ¹³C NMR spectra were obtained on Bruker 300 UltrashieldTM, Bruker 400 MHz and Bruker 500 MHz spectrometers with chloroform-d as deuterated solvent. The obtained chemical shifts δ are reported in ppm and are referenced to the residual solvent signal (7.26 and 77.16 ppm for ¹H and ¹³C respectively). Spin-spin coupling constants *J* are given in Hz and refer to apparent multiplicities rather than true coupling constants. Data are reported as: chemical shift, multiplicity and integration.

High resolution mass spectral (HRMS) data were obtained on a Thermo Scientific LTQ Orbitrap XL by the EPSRC UK National Mass Spectrometry Facility at Swansea University or on a Waters MALDI-TOF mx in Cardiff University. Spectra were obtained using electron impact ionization (EI), chemical ionization (CI), positive electrospray (ES), pneumaticallyassisted electrospray (pNSI) or atmospheric solids analysis probe (ASAP+).

Infrared spectra were recorded on a Shimadzu IR-Affinity-1S FTIR spectrometer.

Melting points were measured using a Gallenkamp apparatus and are reported uncorrected.

The ball mill used was a Retsch MM 400 mixer mill. Unless otherwise stated, mechanochemical reactions were performed in 10 mL stainless steel jars with one stainless steel ball of mass 4 g. The longest time that this mill can be programmed to run for is 99 minutes. In order to run longer reaction times the mill was started, then additional time added to the timer in order to ensure that the mill was running continuously for the desired reaction time.

S2

Synthesis of 1,3-diketones



General Procedure 1 (GP1)

Following a modified literature procedure¹, the corresponding ester (20 mmol, 2 equiv) and NaH (1.2 g, 28 mmol, 2.8 equiv, 60% in mineral oil) were dissolved in dry THF (20 mL) in oven-dried glassware under N₂. A solution of the corresponding ketone (10 mmol) in dry THF (20 mL) was added slowly and the reaction mixture, heated to reflux and stirred overnight. The reaction mixture was quenched with aqueous HCI (25 mL, 1 M) and dichloromethane (50 mL). The aqueous layer was extracted with dichloromethane (2 x 20 mL) and the combined organic phase washed with brine (20 mL). The organic layer was dried (MgSO₄) and the solvent removed under reduced pressure to yield the crude product. This was further purified by recrystallization from EtOH to give the clean product.

1-(4-methoxyphenyl)-3-phenylpropane-1,3-dione²



1,3-bis(4-methoxyphenyl)propane-1,3-dione³



Prepared according to **GP1**, 2.410 g, 8.45 mmol, 85%, yellow crystals. Analytical data is in agreement with the literature.³

¹H NMR (400 MHz, CDCl₃, enol form) δ 7.96 (d, *J* = 8.7 Hz, 4H), 6.98 (d, *J* = 8.7 Hz, 4H), 6.73 (s, 1H, enol), 3.88 (s, 6H).

¹³C NMR (101 MHz, CDCl₃) δ 185.0, 163.0, 129.0, 128.5, 114.0, 91.5, 55.5.

HRMS (EI+) [C₁₇H₁₆O₄]: calc. 284.1049, found 284.1053.

IR: 1587, 1437, 1256, 1227, 1167, 1110, 1018, 835, 777, 575, 507, 473 cm⁻¹. mp 111 - 113 °C (ethanol)

1,3-di-p-tolylpropane-1,3-dione

Mechanochemical monofluorination of 1,3-diketones

General procedure 2 (GP2)

To a 10 mL stainless steel milling jar was added the 1,3-diketone (1 mmol), Selectfluor (0.708 g, 2 mmol) and acetonitrile (0.125 mL). A stainless steel ball of mass 4.0 g was added and the mixture milled at 30 Hz for 2 hours. The resulting powder was transferred into a flask, washing the residue with chloroform (approximately 40 mL). The insoluble material was removed by gravity filtration. α,α,α -Trifluorotoluene (0.041 mL, 0.33 mmol) was added as an NMR standard (δ = -63 ppm) and ¹⁹F NMR taken of the crude mixture to determine the product ratio and conversion. The solvent and α,α,α -trifluorotoluene were removed under reduced pressure to yield the product. ¹⁹F NMR was measured again to confirm that the ratio of products had not changed after evaporation of the solvent.

2-fluoro-1,3-diphenylpropane-1,3-dione⁴, 2



Prepared according to **GP2**, 236 mg, 0.98 mmol, 98%, 50:1 mono:di, yellow solid

¹H NMR (400 MHz, CDCl₃) δ 8.10 (d, *J* = 8.4 Hz, 4H), 7.65 – 7.59 (m,

2H), 7.53 – 7.45 (d, *J* = 11.0, 4.5 Hz, 4H), 6.54 (d, *J* = 49.2 Hz, 1H).

¹³C NMR (126 MHz, CDCl₃) δ 191.3 (d, J = 20.2 Hz), 134.7, 133.7 (d, J = 2.0 Hz), 130.0 (d, J = 3.5 Hz), 128.9, 96.7 (d, J = 199.0 Hz).

¹⁹F NMR (376 MHz, CDCl₃) δ -186.88 (d, *J* = 48.9 Hz).

IR: 1697, 1672, 1593, 1448, 1282, 1097, 1022, 1001, 966, 867, 779, 705, 680, 553, 457 cm⁻¹ HRMS (EI+): $[C_{15}H_{11}O_2F + NH_4]$ calc. 260.1081, found 260.1083 mp 74-76 °C (chloroform)

2-fluoro-1-phenylbutane-1,3-dione⁴, 4



Prepared according to **GP2**, 180 mg, 0.99 mmol, 99%, 5:1 mono:di, purple oil

¹H NMR (400 MHz, CDCl₃) δ 7.90 (d, *J* = 7.6 Hz, 2H), 7.61 – 7.48 (m, 1H), 7.39 (t, *J* = 7.6 Hz, 2H), 5.86 (d, *J* = 50.0 Hz, 1H), 2.23 (s, 3H).

¹⁹F NMR (376 MHz, CDCl₃) δ -189.58 (d, J = 50.1 Hz). ¹³C NMR (101 MHz, CDCl₃) δ 200.6 (d, J = 23.9 Hz), 190.3 (d, J = 19.0 Hz), 134.6, 133.5 (d, J = 1.3 Hz), 129.7 (d, J = 3.0 Hz), 128.8, 96.5 (d, J = 198.0 Hz), 25.9. IR: 1734, 1692, 1597, 1450, 1360, 1275, 1204, 1179, 1101, 959, 689 cm⁻¹. HRMS (EI+) [C₁₀H₉O₂F] calc. 180.0587, found 180.0589

2-fluoro-1-(4-methoxyphenyl)-3-phenylpropane-1,3-dione, 6



6.51 (d, J = 49.2 Hz, 1H), 3.78 (s, 3H).

¹³C NMR (101 MHz, CDCl₃) δ 191.5 (d, *J* = 20.2 Hz), 189.3 (d, *J* = 19.8 Hz), 164.6, 134.4, 133.6 (d, *J* = 1.9 Hz), 132.3 (d, *J* = 3.6 Hz), 129.7 (d, *J* = 3.3 Hz), 128.7, 126.5 (d, *J* = 2.1 Hz), 114.0, 96.5 (d, *J* = 198.1 Hz), 55.5.

¹⁹F NMR (376 MHz, CDCl3) δ -186.37 (d, *J* = 49.2 Hz).

IR: 1672, 1595, 1510, 1256, 1024, 841, 750, 691 cm⁻¹.

HRMS (EI+): [C₁₆H₁₃O₃F] calc. 272.0849, found 272.0845

mp 37 - 39 °C (chloroform)

2-fluoro-1,3-bis(4-methoxyphenyl)propane-1,3-dione⁵, 8

Prepared according to **GP2**, 295 mg, 0.98 mmol, 98%, 50:1 mono:di, yellow crystals ¹H NMR (400 MHz, CDCl₃) δ 8.08 (d, J = 8.5 Hz, 4H), 6.90 (d, J = 8.5 Hz, 4H), 6.45 (d, J = 49.3 Hz, 1H), 3.81 (s, 6H).

¹⁹F NMR (376 MHz, CDCl₃) δ -185.98 (d, *J* = 49.3 Hz).

¹³C NMR (101 MHz, CDCl₃) δ 189.6 (d, J = 19.9 Hz), 164.6, 132.4 (d, J = 3.5 Hz), 126.6 (d, J = 2.0 Hz), 114.0, 97.8 (d, J = 191.9 Hz), 55.6.

IR: 1667, 1589, 1572, 1508, 1244, 1169, 1096, 1022, 961, 835, 567, 513 cm⁻¹.

HRMS (EI+) [C₁₇H₁₅O₄F] calc. 302.0954, found 302.0961

mp 94 - 95 °C (chloroform)

2-fluoro-1,3-di-p-tolylpropane-1,3-dione, 10



Prepared according to **GP2**, 202 mg, 0.75 mmol, 75%, 29:1 mono:di, yellow solid

¹H NMR (500 MHz, CDCl₃) δ 8.02 (d, *J* = 8.1 Hz, 4H), 7.13 (d, *J* = 8.9 Hz, 4H), 6.50 (d, *J* = 49.2 Hz, 1H), 2.43 (s, 6H).

¹³C NMR (101 MHz, CDCl₃) δ 190.8 (d, J = 20.0 Hz), 145.7, 131.1 (d, J = 1.9 Hz), 130.0 (d, J = 3.4 Hz), 129.5, 96.7 (d, J = 198.3 Hz), 21.8.

¹⁹F NMR (376 MHz, CDCl₃) δ -186.72 (d, J = 49.2 Hz). IR: 1695, 1603, 1287, 1233, 1184, 1090, 959, 876, 824, 752, 556 cm⁻¹. HRMS (EI+): [C₁₇H₁₅O₂F] calc. 270.1056, found 270.1051 mp 88 - 89 °C (chloroform)

Mechanochemical difluorination of 1,3-diketones

General Procedure 3 (GP3)

To a 10 mL stainless steel milling jar was added the 1,3-diketone (1 mmol), Selectfluor (0.708 g, 2 mmol) and sodium carbonate (0.106 g, 1 mmol). A stainless steel ball of mass 4.0 g was added and the mixture milled at 30 Hz for 2 hours. The resulting powder was transferred into a flask, washing the residue with chloroform (approximately 40 mL). The insoluble material was removed by gravity filtration. α , α , α -Trifluorotoluene (0.041 mL, 0.33 mmol) was added as a NMR standard (δ = -63 ppm) and ¹⁹F NMR taken of the crude mixture to determine the product ratio and conversion. The solvent and α , α -trifluorotoluene were removed under reduced pressure to yield the product. ¹⁹F NMR was measured again to confirm that the ratio of products had not changed after evaporation of the solvent.

2,2-difluoro-1,3-diphenylpropane-1,3-dione⁶, 3



Prepared according to **GP3**, 242 mg, 0.93 mmol, 93%, 17:1 di:mono, brown crystals

¹H NMR (400 MHz, CDCl₃) δ 8.09 (d, 4H), 7.70 – 7.61 (m, 2H), 7.50 (d, 4H).

¹³C NMR (126 MHz, CDCl₃) δ 187.5 (t, *J* = 26.8 Hz), 135.2 (t, *J* = 62.7 Hz), 131.8, 130.4 (t, *J* = 2.6 Hz), 129.1, 112.8 (t, *J* = 265.9 Hz).

¹⁹F NMR (376 MHz, CDCl₃) δ -102.66 (s).

IR: 1697, 1672, 1595, 1448, 1284, 1097, 968, 939, 867, 707, 680, 553, 457 cm⁻¹ HRMS (EI+): $[M+NH_4^+]$ $[C_{15}H_{14}O_2F_2]$ calc. 278.0987, found 278.0988

mp 58-60 °C (chloroform)

2,2-difluoro-1-phenylbutane-1,3-dione⁷, 5



Prepared according to **GP3**, 185 mg, 0.93 mmol, 93%, >50:1 di:mono, red oil

¹H NMR (400 MHz, CDCl₃) δ 7.94 (d, *J* = 7.4 Hz, 2H), 7.55 (t, *J* = 6.8 Hz, 1H), 7.40 (t, *J* = 7.3 Hz, 2H), 2.31 (s, 3H).

¹⁹F NMR (376 MHz, CDCl₃) δ -108.97 (s).

¹³C NMR (101 MHz, CDCl₃) δ 196.0, 187.6, 135.2, 131.4, 130.1 (t, J = 2.7 Hz), 129.0, 111.3 (t, J = 266.5 Hz), 25.0.

IR: 1753, 1697, 1597, 1450, 1361, 1292, 1111, 1080, 891, 837, 712, 685 cm⁻¹. HRMS (EI+) $[C_{10}H_8O_2F_2]$ calc. 198.0492, found 198.0495

2,2-difluoro-1-(4-methoxyphenyl)-3-phenylpropane-1,3-dione, 7



Prepared according to **GP3**, 270 mg, 0.93 mmol, 93%, >50:1 di:mono, orange solid

¹H NMR (400 MHz, CDCl₃) δ 8.14 – 8.03 (m, 3H), 8.01 - 7.94

(m, 1H), 7.60 (t, *J* = 7.1 Hz, 1H), 7.46 (t, *J* = 7.3 Hz, 2H), 7.00 -

6.88 (m, 2H), 3.83 (s, 3H).

¹⁹F NMR (376 MHz, CDCl₃) δ -102.38 (s).

¹³C NMR (101 MHz, CDCl₃) δ 187.5 (t, J = 26.8 Hz), 185.6 (t, J = 26.6 Hz), 165.1, 134.9,

132.9 (t, *J* = 2.6 Hz), 132.2, 130.3 (t, *J* = 2.5 Hz), 129.4, 128.9, 128.7, 127.0, 114.3, 113.0 (t, *J* = 265.3 Hz), 55.6.

IR: 1589, 1508, 1182, 1092, 1020, 840, 766, 503 cm⁻¹.

HRMS (EI+) [C₁₆H₁₂O₃F₂] calc. 290.0755, found 290.0749.

mp 35 - 36 °C (chloroform)

2,2-difluoro-1,3-bis(4-methoxyphenyl)propane-1,3-dione, 9

_	\sim) L	Ĵ	
MeO		F	F	OMe
		9		

Prepared according to GP3, 219 mg, 0.68 mmol, 68%,

>50:1 di:mono, orange crystals

¹H NMR (400 MHz, CDCl₃) δ 7.96 (d, *J* = 8.4 Hz, 4H), 6.81 (d, *J* = 8.4 Hz, 4H), 3.73 (s, 6H).

¹⁹F NMR (376 MHz, CDCl₃) δ -102.36 (s).

¹³C NMR (101 MHz, CDCl₃) δ 185.7 (t, J = 26.5 Hz), 165.1, 132.9 (t, J = 2.6 Hz), 124.6,

114.3, 113.2 (t, *J* = 264.5 Hz), 55.6.

IR: 1676, 1593, 1508, 1256, 1126, 1020, 847, 781, 573 cm⁻¹.

HRMS (EI+) [C₁₇H₁₄O₄F₂] calc. 320.0860, found 320.0863.

mp 68 - 69 °C (chloroform)

2,2-difluoro-1,3-di-p-tolylpropane-1,3-dione, 11



Prepared according to **GP3**, 274 mg, 0.95 mmol, 95%, 8:1 di:mono, orange crystals ¹H NMR (400 MHz, CDCl₃) δ 7.86 (d, *J* = 7.9 Hz, 4H), 7.14 (d, *J* = 7.9 Hz, 4H), 2.27 (s, 6H).

¹³C NMR (101 MHz, CDCl₃) δ 186.9 (t, J = 26.7 Hz), 146.5, 130.4 (t, J = 2.6 Hz), 129.7,

129.2, 112.9 (t, *J* = 265.6 Hz), 21.9.

¹⁹F NMR (376 MHz, CDCl₃) δ -102.65 (s).

IR: 1688, 1603, 1244, 1159, 1125, 1094, 939, 880, 766, 573, cm⁻¹.

mp 84 °C (chloroform)

Mechanochemical monofluorination of β -ketoester

General Procedure 4 (GP4)

To a 10 mL stainless steel milling jar was added the ethylbenzoylacetate (1 mmol), Selectfluor (0.708 g, 2 mmol), sodium chloride (twice the total mass of substrate and Selectfluor) and acetonitrile (0.25 mL). A stainless steel ball of mass 4.0 g was added and the mixture milled at 30 Hz for 2 hours. The resulting powder was transferred into a flask, washing the residue with chloroform (approximately 40 mL). The insoluble material was removed by gravity filtration. α,α,α -Trifluorotoluene (0.041 mL, 0.33 mmol) was added as a NMR standard (δ = -63 ppm) and ¹⁹F NMR taken of the crude mixture to determine the product ratio and conversion. The solvent and α,α,α -trifluorotoluene were removed under reduced pressure to yield the product. ¹⁹F NMR was measured again to confirm that the ratio of products had not changed after evaporation of the solvent.

ethyl 2-fluoro-3-oxo-3-phenylpropanoate⁴, 13



Prepared according to **GP4**, 201 mg, 0.96 mmol, 96%, 13:1 mono:di, dark red liquid

¹H NMR (400 MHz, CDCl₃) δ 8.04 (d, J = 7.8 Hz, 2H), 7.64 (t, J = 7.4 Hz, 1H), 7.51 (t, J = 7.7 Hz, 2H), 5.86 (d, J = 48.9 Hz, 1H), 4.30 (q, J =

6.8 Hz, 2H), 1.26 (t, J = 7.1 Hz, 3H).

¹³C NMR (101 MHz, CDCl₃) δ 189.7 (d, J = 20.2 Hz), 165.1 (d, J = 24.2 Hz), 134.7, 133.5, 129.7 (d, J = 3.4 Hz), 129.0, 90.2 (d, J = 197.7 Hz), 62.7, 14.1. ¹⁹F NMR (376 MHz, CDCl₃) δ -190.29 (d, J = 48.8 Hz). IR: 2983, 1759, 1693, 1597, 1448, 1371, 1242, 1095, 686 cm⁻¹ HRMS (ASAP+) [C₁₁H₁₁O₃F + H] calc. 211.0770, found 211.0773

Mechanochemical difluorination of β -ketoester

General Procedure 5 (GP5)

To a 10 mL stainless steel milling jar was added the β -ketoester (1 mmol), Selectfluor (0.708 g, 2 mmol), sodium carbonate (0.106 g, 1 mmol) and sodium chloride (twice the total mass of substrate and Selectfluor). A stainless steel ball of mass 4.0 g was added and the mixture milled at 30 Hz for 2 hours. The resulting powder was transferred into a flask, washing the residue with chloroform (approximately 40 mL). The insoluble material was removed by gravity filtration. α,α,α -Trifluorotoluene (0.041 mL, 0.33 mmol) was added as a NMR standard (δ = -63 ppm) and ¹⁹F NMR taken of the crude mixture to determine the product ratio and conversion. The solvent and α,α,α -trifluorotoluene were removed under reduced pressure to yield the product. ¹⁹F NMR was measured again to confirm that the ratio of products had not changed after evaporation of the solvent.

ethyl 2,2-difluoro-3-oxo-3-phenylpropanoate⁷, 14



Prepared according to GP5, 227 mg, 0.99 mmol, 99%, 7:1 di:mono,

yellow-green liquid

¹H NMR (400 MHz, CDCl₃) δ 8.08 (d, *J* = 7.9 Hz, 2H), 7.68 (t, *J* = 7.4 Hz, 1H), 7.53 (t, *J* = 7.5 Hz, 2H), 4.39 (q, *J* = 7.1 Hz, 2H), 1.32 (t, *J* =

7.2 Hz, 3H).

¹³C NMR (101 MHz, CDCl₃) δ 185.6 (t, J = 30.3 Hz), 162.0 (t, J = 30.6 Hz), 135.2, 131.2, 130.1 (t, J = 2.7 Hz), 129.1, 109.9 (t, J = 264.6 Hz), 63.9, 14.0.

¹⁹F NMR (376 MHz, CDCl₃) δ -107.61 (s).

IR: 1770, 1697, 1597, 1450, 1371, 1307, 1255, 1155, 1097, 1001, 921, 684, 582 cm⁻¹ HRMS (ASAP+) [C₁₁H₁₀O₃F₂ + H] calc. 229.0676, found 229.0680

Study of yield against time with and without LAG

We considered that the reactions with and without LAG could proceed at different rates for the mono- and difluorination. This could cause one reaction to be complete before the other. A single snap-shot in time may lead to an incorrect conclusion of the selectivity. We have therefore run both reactions under varying time conditions and found that the monofluorination of dibenzoylmethane is faster in the absence of LAG. However, at the point where both reactions have just converted all starting material there is a superior selectivity for mono- versus difluorinated in the case where LAG is used. The following describes the methods used to study the yield of mono- and difluorinated products at different time points with and without LAG.

Neat grinding conditions

To a 10 mL stainless steel grinding jar was added Selectfluor (0.142 g, 0.2 mmol), dibenzoylmethane (0.045 g, 0.2 mmol) and a stainless steel ball (mass 4.0 g). The ball mill was run at 30 Hz for the appropriate time. The contents of the tube were transferred to a flask, washing with chloroform. α,α,α -Trifluorotoluene (0.041 mL, 0.33 mmol) was added and the mixture filtered through a plug of cotton wool into an NMR tube. ¹⁹F NMR was taken and the yield determined by comparing the integrals of the products to the integrals of trifluorotoluene. This process was repeated for each jar over different time intervals (Table 1).

Time / min	Yield Mono / %	Yield Di / %
5	7	0
30	53	4
45	78	9
60	87	11
90	76	24
120	61	38
180	57	43

 Table 1 Neat grinding kinetic results

Liquid-Assisted-Grinding (LAG) conditions

To a 10 mL stainless steel grinding jar was added Selectfluor (0.142 g, 0.2 mmol), dibenzoylmethane (0.045 g, 0.2 mmol), acetonitrile (0.125 mL) and a stainless steel ball (mass 4.0 g). The ball mill was run at 30 Hz for the appropriate time. The contents of the tube were transferred to a flask, washing with chloroform. α,α,α -Trifluorotoluene (0.041 mL, 0.33 mmol) was added and the mixture filtered through a plug of cotton wool into an NMR tube. ¹⁹F NMR was taken and the yield determined by comparing the integrals of the products to the integrals of trifluorotoluene. This process was repeated for each jar over different time intervals (Table 1).

Time / min	Yield Mono / %	Yield Di / %
5	12	0
45	47	0
90	75	0
120	100	0
180	95	3

Table 2 LAG kinetic results



Figure 1 Yields of mono- and difluorinated products at different times a) without and b) with acetonitrile

Conventional solution phase reactions

Monofluorination general procedure

To a solution of Selectfluor (0.708 g, 2 mmol) in acetonitrile (20 mL) was added the 1,3-dicarbonyl (1 mmol). α , α , α -Trifluorotoluene (0.041 mL, 0.33 mmol) was added as an NMR standard (δ = -63 ppm) and the reaction mixture was stirred at room temperature, monitoring by ¹⁹F NMR. When the reaction was complete, the solvent was removed under reduced pressure. Water (20 mL) and dichloromethane (20 mL) were added and the aqueous layer further extracted with dichloromethane (20 mL). The combined organic layers were dried (MgSO₄), filtered and the solvent removed to yield the product. ¹⁹F NMR was measured again to confirm that the ratio of products had not changed during extraction.

Difluorination general procedure

To a solution of Selectfluor (0.708 g, 2 mmol) in acetonitrile (20 mL) was added the 1,3-dicarbonyl (1 mmol) and sodium carbonate (0.106 g, 1 mmol). α , α , α -Trifluorotoluene (0.041 mL, 0.33 mmol) was added as an NMR standard (δ = -63 ppm) and the reaction mixture was stirred at room temperature, monitoring by ¹⁹F NMR. When the reaction was complete, the solvent was removed under reduced pressure. Water (20 mL) and dichloromethane (20 mL) were added and the aqueous layer further extracted with dichloromethane (20 mL). The combined organic layers were dried (MgSO₄), filtered and the solvent removed to yield the product. ¹⁹F NMR was measured again to confirm that the ratio of products had not changed during extraction.

Difluorination of 2,2,6,6-tetramethyl-3,5-heptanedione

Mechanochemically

To a 10 mL stainless steel milling jar was added 2,2,6,6-tetramethyl-3,5-heptanedione (0.184 g, 1 mmol), Selectfluor (0.708 g, 2 mmol), sodium carbonate (0.106 g, 1 mmol) and sodium chloride (1.78 g). A stainless steel ball of mass 4.0 g was added and the mixture milled at 30 Hz for 2 hours. The resulting powder was transferred into a flask, washing the residue with chloroform (approximately 40 mL). The insoluble material was removed by gravity filtration. 2,2,2-Trifluoroethanol (0.024 mL, 0.33 mmol) was added as an NMR standard (δ = -77.03 ppm) and ¹⁹F NMR taken of the crude mixture to determine the product ratio and conversion as 59% difluorinated product and 0% monofluorinated product.

In solution

To a solution of Selectfluor (0.708 g, 2 mmol) in acetonitrile (20 mL) was added 2,2,6,6tetramethyl-3,5-heptanedione (0.184 g, 1 mmol) and sodium carbonate (0.106 g, 1 mmol). α,α,α -Trifluorotoluene (0.041 mL, 0.33 mmol) was added as an NMR standard (δ = -63 ppm) and the reaction mixture was stirred at room temperature, monitoring by ¹⁹F NMR. After 9 days, the conversion was 62% difluorinated product and 7% monofluorinated product.

Spectroscopic Data

Monofluorinated 1,3-diketones

2-fluoro-1,3-diphenylpropane-1,3-dione, 2





2-fluoro-1-phenylbutane-1,3-dione, 4





2-fluoro-1-(4-methoxyphenyl)-3-phenylpropane-1,3-dione, 6





2-fluoro-1,3-bis(4-methoxyphenyl)propane-1,3-dione, 8





2-fluoro-1,3-di-p-tolylpropane-1,3-dione, 10





Difluorinated 1,3-diketones

2,2-difluoro-1,3-diphenylpropane-1,3-dione, 3





2,2-difluoro-1-phenylbutane-1,3-dione, 5





2,2-difluoro-1-(4-methoxyphenyl)-3-phenylpropane-1,3-dione, 7





2,2-difluoro-1,3-bis(4-methoxyphenyl)propane-1,3-dione, 9

2,2-difluoro-1,3-di-p-tolylpropane-1,3-dione, 11

Monofluorinated β-ketoester

ethyl 2-fluoro-3-oxo-3-phenylpropanoate, 13

Difluorinated β -ketoester

ethyl 2,2-difluoro-3-oxo-3-phenylpropanoate, 14


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Mechanochemical difluorination of 2,2,6,6-tetramethyl-3,5-heptanedione, 15 4,4-difluoro-2,2,6,6-tetramethyl-3,5-heptanedione, 16
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Solution difluorination of 2,2,6,6-tetramethyl-3,5-heptanedione (15)

4,4-difluoro-2,2,6,6-tetramethyl-3,5-heptanedione, 16

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