Supporting Information

Copper-free Alternatives to Access Ketone Building Blocks from Grignard Reagents

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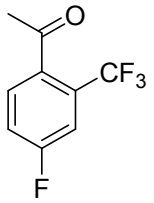
1 Experimental

1.1 General synthetic procedure:

4-Fluoro-2-(trifluoromethyl)phenyl)magnesium bromide (1) (BFBTF-Grignard)

A 2 L reactor was charged at r.t. under N_2 with Mg turnings (40.1 g, 1.65 mol) and THF (1152.24 g) and the obtained suspension was heated to 50˚C. Small quantities of 1-bromo-4-fluoro-2-(trifluoromethyl)benzene (BFBTF) (37.25 g, 0.15 mol) were successively added until an exothermic effect was observed, indicating the start of the Grignard reaction. 1-bromo-4-fluoro-2-(trifluoromethyl)benzene (343.8 g, 1.42 mol) was dosed to the magnesium suspension at 50˚C, under N_2 over 2 h, and then the reaction mixture was further stirred in the same conditions for 3 h (until BFBTF <=0.1 a%). The reaction mixture was cooled to 15˚C and transferred under N_2 flow in storage flasks (storage at 0-5˚C).

1-(4-Fluoro-2-(trifluoromethyl)phenyl)ethan-1-one (3) (FTAP)



Chemical Formula: $C_9H_6F_4O$

Exact Mass: 206.0355

Molecular Weight: 206.1396

Elemental Analysis: C, 52.44; H, 2.93; F, 36.87; O, 7.76

Procedure 1 (AcCl; CuCl):

A 2 L reactor was charged with THF (138 g), acetyl chloride (4.7 g, 0.06 mol), and copper chloride (1.9 g, 0.03 mol) and cooled to -5˚C. The BFBTF-Grignard (**1**) solution (1002.2 g, 1.0 mol) and acetyl chloride (89.5 g, 1.14 mol) were added by parallel dosage over 3h whilst keeping the temperature at -5˚C. The reaction mixture was quenched by addition of water (500 g). Phases were separated and the solvent was removed by distillation. The final product was isolated by distillation in a yield of 93 - 95% and purity > 95% (wt% by 1H-, 19F-NMR; a% GC).

Procedure 2 (Ac_2O; CuCl):

A 2 L reactor was charged with THF (138 g), acetic anhydride (6.1 g, 0.06 mol), and copper chloride (1.9 g, 0.03 mol) and cooled to -5˚C. The BFBTF-Grignard (**1**) solution (1002.2 g, 1.0 mol) and acetic

anhydride (101.1 g, 0.99 mol) were added by parallel dosage over 3h whilst keeping the temperature at -5˚C. The reaction mixture was quenched by addition of water (500 g). Phases were separated and the solvent was removed by distillation. The final product was isolated by distillation in a yield of 93.5% and purity > 95% (wt% by 1H-, 19F-NMR; a% GC).

Procedure 3 (Ac_2O):

A 2 L reactor was charged with THF (138 g) and acetic anhydride (6.1 g, 0.06 mol) and the temperature was adjusted in the range of -5 to 50˚C (see table). The BFBTF-Grignard (**1**) solution (1002.2 g, 1.0 mol) and acetic anhydride (in the range of 0.96 mol – 1.01 mol) were added by parallel dosage over 3h whilst keeping the temperature at the respective temperature of -5˚C to 50˚C. The reaction mixture was quenched by addition of water (500 g). Phases were separated and the solvent was removed by distillation. The final product was isolated by distillation. For yields see table below.

Table S1. Overview of the reaction conditions[a] and experimental results for the Grignard reaction of (1) with Ac_2O (4).

Electrophile (eq)	**T_i** [°C]	**Yield** [%][b]	**SP1** [a%][c]	**SP2** [a%][c]	**SP3** [a%][c]	**Others** [a%][c]
Ac_2O (1.02)	0	95	0.01	n/a[e]	3	2
Ac_2O (1.07)	0	99	n/a[e]	n/a[e]	0.3	0.7
Ac_2O (1.05)	-5	98.5	0.01	n/a[e]	0.35	1.14
Ac_2O (1.05)	0	99.7[d]	n/a[e]	n/a[e]	0.3	0.3
Ac_2O (1.05)	5	99	n/a[e]	n/a[e]	0.31	0.69
Ac_2O (1.05)	25	70	n/a[e]	10	0.45	19.55
Ac_2O (1.05)	50	35	n/a[e]	35	0.61	29.39

[a] Reactions were performed in semi-batch mode by parallel dosage of (**1**) and the respective electrophile. Detailed experimental description is given in the *Supporting Information*.

[b] Isolated yield after distillation.

[c] Calculated based on GC analyses.

[d] Averaged yield over 5 runs.

[e] n/a = compound was not detected in GC analysis.

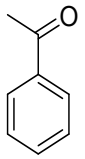
^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.52 (dd, 1H, $^3J_{H,H}$ = 8.5 Hz, $^3J_{H,F}$ = 5.3 Hz), 7.37 (dd, 1H, $^3J_{H,F}$ = 8.9 Hz, $^4J_{H,H}$ = 2.5 Hz), 7.27 (td, 1H, $^4J_{H,F}$ = 2.2 Hz, $^3J_{H,H}$ = 8.0 Hz), 2.53 (s, 3H);

^{13}C NMR (101 MHz, $CDCl_3$) δ: 200.0 (1C), 162.8 (1C, d, $^1J_{C,F}$ = 251.5 Hz), 136.3 (1C, qvart, $^3J_{C,F}$ = 1.5 Hz), 130.0 (1C, d, $^3J_{C,F}$ = 8.5 Hz), 29.4 (1C, qvart d, $^2J_{C,F}$ = 32.8 Hz, $^3J_{C,F}$ = 7.3 Hz), 122.6 (1C, qvart d, $^1J_{C,F}$ = 272.0 Hz, $^4J_{C,F}$ = 2.2 Hz), 118.7 (1C, d, $^2J_{C,F}$ = 21.1 Hz), 114.5 (1C, d qvart, $^2J_{C,F}$ = 24.8 Hz, $^3J_{C,F}$ = 5.1 Hz), 30.1 (1C);

^{19}F NMR (188 MHz, $CDCl_3$) δ: -58.82 (s, 3F), -107.68 (m, 1F)

GC-MS(+) (m/z) found 207.0 $[M+H]^+$, 206.0 [M], 192.0 $[M-CH_3]$, 164.0 $[M-CH_3CO]$; calcd. for $C_9H_6F_4O$ 206.0355. Retention time 8.473 min.

Procedure 4: **Synthesis of acetophenone 6**



A 500 mL reactor was charged with Mg turnings (7.0 g, 288 mmol) and dry THF (230.4 g) at r.t. under N2. The obtained suspension was heated to 50˚C and phenylbromide 8 (4.71 g, 29.7 mmol) was added until an exothermic effect was observed. Phenylbromide 8 (41.0 g, 258 mmol) was dosed to the magnesium suspension over 1 h 30 min. The reaction mixture was stirred for 22 h at 50˚C and then cooled to 20˚C.

A 500 mL reactor was charged with acetic anhydride 4a (1.44 g, 14.1 mmol) and dry THF (80.0 g) at r.t. under N2 and the solution was cooled to -10˚C. To this solution, the PhMgBr solution in THF prepared before (231.3 g) and acetic anhydride (27.4 g, 268 mmol) were dosed in parallel over 2 h 20 min at -10˚C. The reaction mixture was stirred for 1 h at -10˚C and for 1 h at 10˚C. The resulting mixture was concentrated under reduced pressure and quenched by temperature-controlled dosage of H2O (116.7 g) at 35˚C over 1 h 20 min. The phases were separated and the organic phase was concentrated under reduced pressure. 6 was isolated as a pale-yellow oil (32.5 g, 248 mmol, 86%) without further purification.

1H NMR (400 MHz, CDCl3, 298 K): δ = 7.89 (m, 2H, 3JH,H = 8.4 Hz), 7.48 (m, 1H, 3JH,H = 7.4 Hz), 7.38 (m, 2H, 3JH,H = 7.4 Hz), 2.51 (s. 3H); 13C NMR (101 MHz, CDCl3, 298 K): δ = 197.6, 136.7, 132.7, 128.2, 127.9, 26.2; GC-MS(+) m/z calcd. for C8H8O: 120.1; found: 121.1 [M+H]+; retention time: 8.885 min.

1.2 Analytical Instrumentation:

1.2.1 NMR:

Measured on a Bruker Avance III 400 MHz NMR spectrometer equipped with a tunable multinuclear BBFO probe

1.2.2 GC-MS:

Measured on a ISQ 7000 Single Quadrupole GC-MS System; Thermo Scientific; GC-Column: ZB-5MSi, 30 m x 0.25 mm x 0.25 µm; Phenomenex

1.3 NMR-Spectra:

1.3.1 1H-NMR-Spectrum:

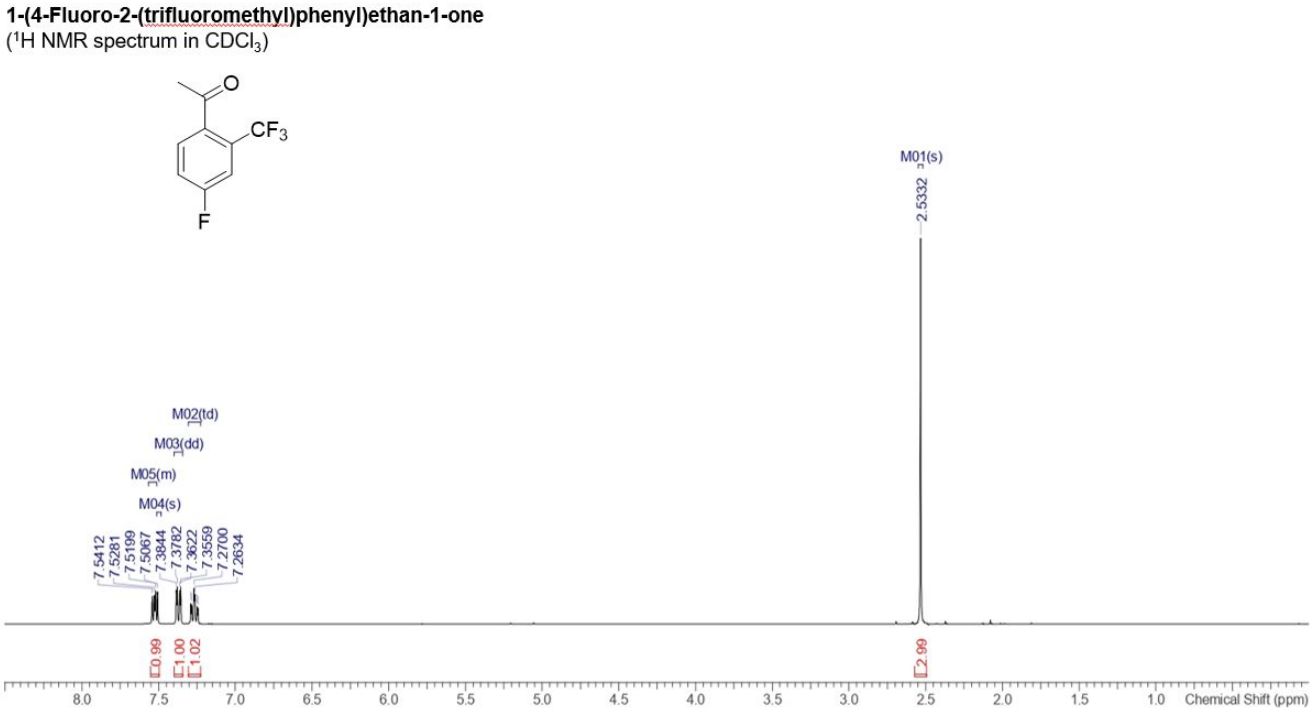


Figure S 1. 1H-NMR spectrum of 1-(4-Fluoro-2-(trifluoromethyl)phenyl)ethan-1-one in $CDCl_3$.

1.3.2 13C-NMR-Spectrum:

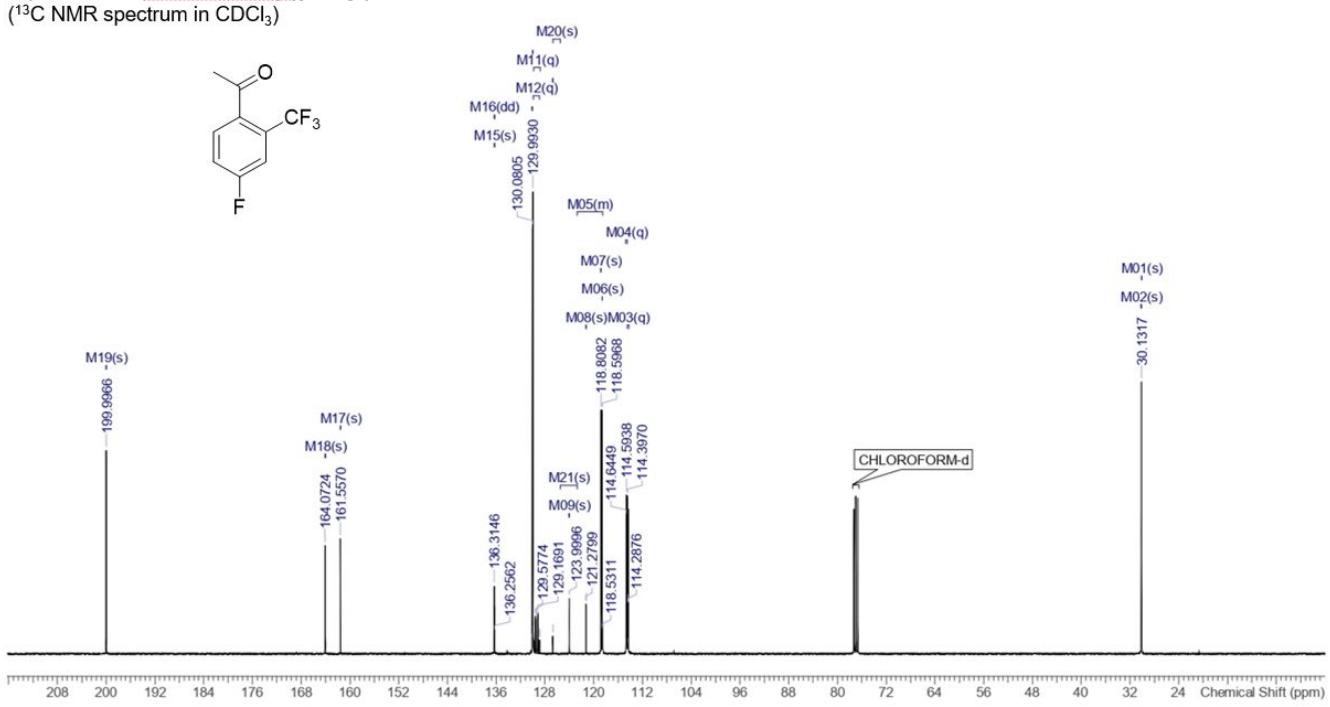


Figure S 2. 13C-NMR spectrum of 1-(4-Fluoro-2-(trifluoromethyl)phenyl)ethan-1-one in $CDCl_3$.

1.3.3 19F-NMR-Spectrum:

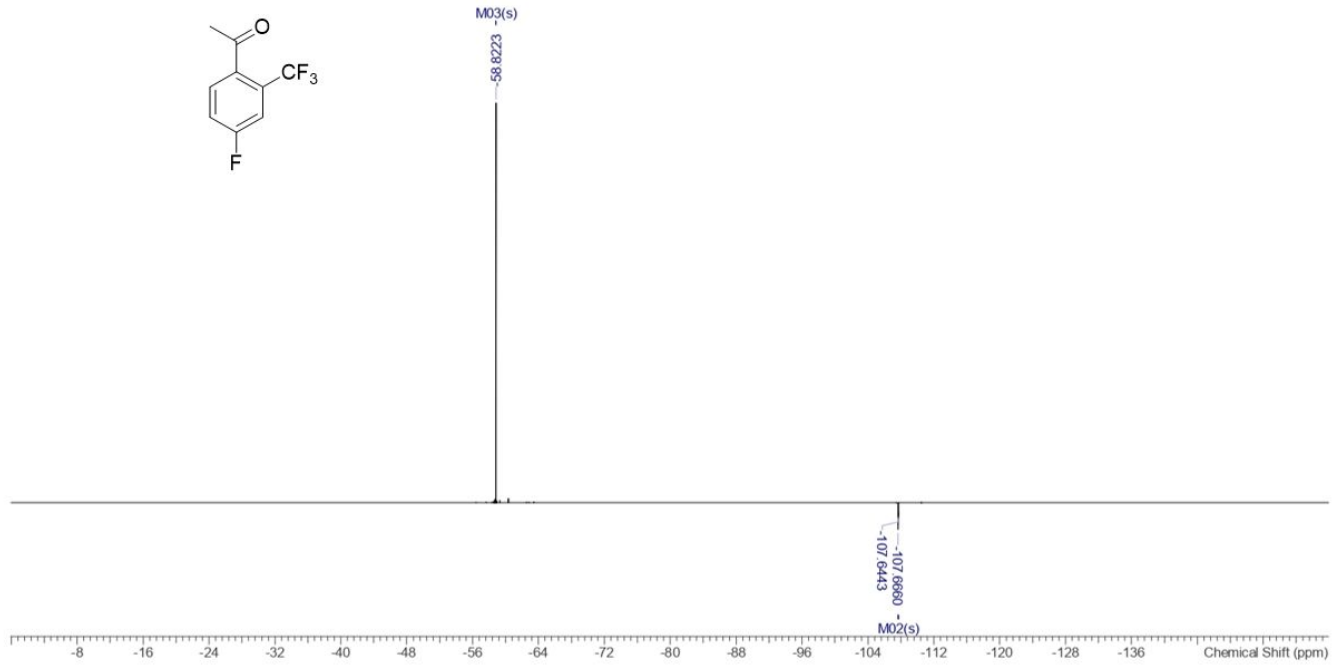


Figure S 3. 19F-NMR spectrum of 1-(4-Fluoro-2-(trifluoromethyl)phenyl)ethan-1-one in $CDCl_3$.

2 4FTM-ACl-2T_add1_c04_THF

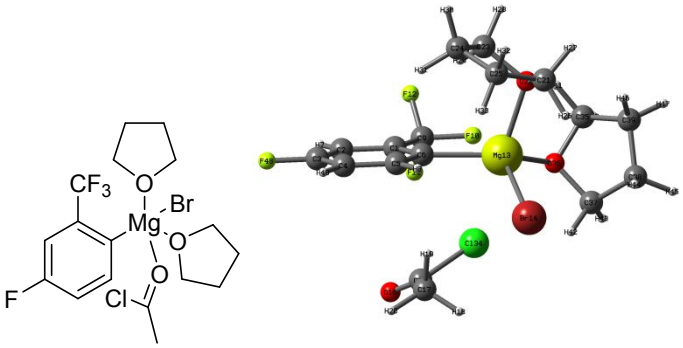


Figure S4. Geometry optimized adduct of the Grignard reagen (1) and acetyl chloride (2) (corresponding to station (A) in Figure 1

Table S2. xyz-coordinates of the Grignard (1) and acetyl chloride (2) adduct of Figure S4

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49
4FTM-ACl-2T_c04
C          2.10773        0.43583        0.85201
C          3.45696        0.76882        0.67858
C          3.80320        1.36740       -0.52481
C          2.87837        1.64220       -1.53603
C          1.54963        1.29027       -1.31890
C          1.16787        0.68336       -0.12630
H          4.20151        0.56607        1.44841
H          0.81055        1.49628       -2.09600
C          1.69173       -0.20200        2.13884
F          0.38816       -0.46604        2.24230
F          2.28107       -1.36834        2.41084
F          1.94505        0.53574        3.22590
Mg        -0.86154        0.13480        0.04672
Br        -1.74631       -0.40748       -2.40897
C          2.00064       -2.49674       -1.16084
O          3.01152       -2.95155       -0.75029
C          1.58419       -1.99370       -2.46332
H          0.75429       -2.58439       -2.90247
H          1.21460       -0.94599       -2.42325
H          2.41217       -2.00977       -3.19871
C         -2.71809        2.40649       -0.29420
O         -1.92818        1.81524        0.75935
C         -0.99224        2.82744        1.19823
C         -0.67174        3.68043       -0.02874
C         -1.76759        3.32785       -1.05483
H         -3.13059        1.56276       -0.87227
H         -3.54465        2.94730        0.19963
H         -1.50151        3.38697        2.00174
H         -0.13119        2.27944        1.62329
H         -0.66736        4.75614        0.21319
H          0.33563        3.45977       -0.42699
H         -2.28155        4.22515       -1.43641
H         -1.33766        2.82681       -1.94135
Cl         0.64832       -2.40244        0.05634
C         -2.61847       -0.51518        2.29324
O         -1.75644       -1.19953        1.35842
C         -2.57210       -2.17176        0.66764
C         -3.97433       -1.57268        0.57669
C         -3.99448       -0.45187        1.63516
H         -2.60378       -1.12029        3.21796
H         -2.14786        0.46530        2.49278
H         -2.08134       -2.35541       -0.30390
H         -2.52723       -3.08927        1.28213
H         -4.18364       -1.17343       -0.43093
H         -4.75416       -2.32942        0.76584
H         -4.17740        0.53378        1.17161
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H	-4.80595	-0.59163	2.36853
F	5.07408	1.69786	-0.72619
H	3.18701	2.11611	-2.46722

3 4FTM-ACl-2T_TS5_THF

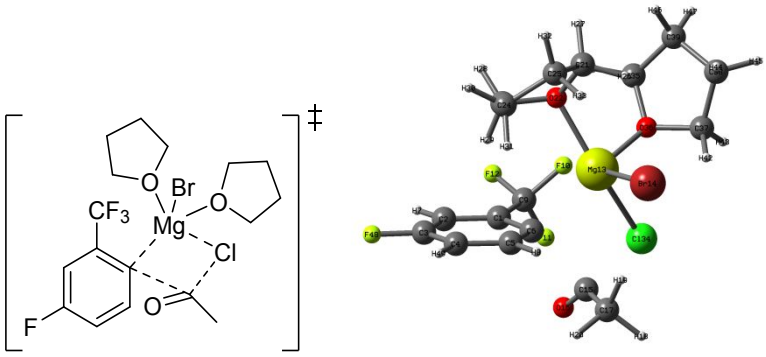

Figure S 5. Transition state structure of the reaction of the Grignard reagent (**1**) with acetyl chloride (**2**) (corresponding to station (B) in Figure 1.

Table S3. xyz-coordinates of the transition state structure of the reaction of the Grignard reagent (1) and acetyl chloride (2) of Figure S5.

49
4FTM-ACl-2T_TS5_THF

C	-2.29302	-0.48567	-0.56582
C	-3.41316	0.17401	-1.06750
C	-3.79562	1.34519	-0.41131
C	-3.11270	1.87150	0.68280
C	-2.00942	1.16305	1.16569
C	-1.62096	-0.01920	0.55557
H	-3.97482	-0.19135	-1.92811
H	-1.46739	1.55126	2.03219
C	-1.74358	-1.69887	-1.26069
F	-0.41066	-1.63341	-1.39029
F	-1.97008	-2.86809	-0.67120
F	-2.15913	-1.88971	-2.51493
Mg	0.61773	-0.07268	0.14721
Br	1.84888	1.26914	2.07680
C	-1.42901	-1.49653	2.02502
O	-2.31001	-2.19881	1.67738
C	-1.07846	-0.79259	3.25694
H	-0.77266	-1.51779	4.04132
H	-0.24747	-0.06960	3.17333
H	-1.94913	-0.23611	3.65937
C	2.02311	2.00719	-1.41699
O	0.84677	1.17355	-1.53206
C	-0.26365	2.05438	-1.79597
C	0.01929	3.32309	-0.99982
C	1.55641	3.36516	-0.89375
H	2.71452	1.45787	-0.75254
H	2.44889	2.06205	-2.43573
H	-0.27663	2.21540	-2.88976
H	-1.16720	1.50086	-1.49777
H	-0.38747	4.22164	-1.49184
H	-0.44691	3.28596	0.00199
H	1.98255	4.19300	-1.48536
H	1.87974	3.54256	0.14641
Cl	0.31525	-2.20014	1.33028
C	2.37767	-1.21722	-2.14130
O	1.99865	-1.35910	-0.76443
C	3.17722	-1.62631	0.01432

C	4.34211	-0.96861	-0.71970
C	3.85175	-0.81436	-2.17108
H	2.19138	-2.20792	-2.59659
H	1.69097	-0.47183	-2.57994
H	2.98258	-1.22008	1.02253
H	3.25706	-2.72796	0.06441
H	4.59975	0.01070	-0.27983
H	5.26053	-1.57652	-0.65907
H	3.98949	0.21798	-2.53548
H	4.42838	-1.45184	-2.86328
F	-4.86034	1.99500	-0.86312
H	-3.42823	2.80177	1.15469

4 4FTM-ACl-2T_IRC5_THF

An IRC calculation was conducted at the PM7 level of theory using the SMD solvation model. The transition state 4FTM-Ac-TS5 was used as starting point. Following intrinsic reaction coordinate was obtained:

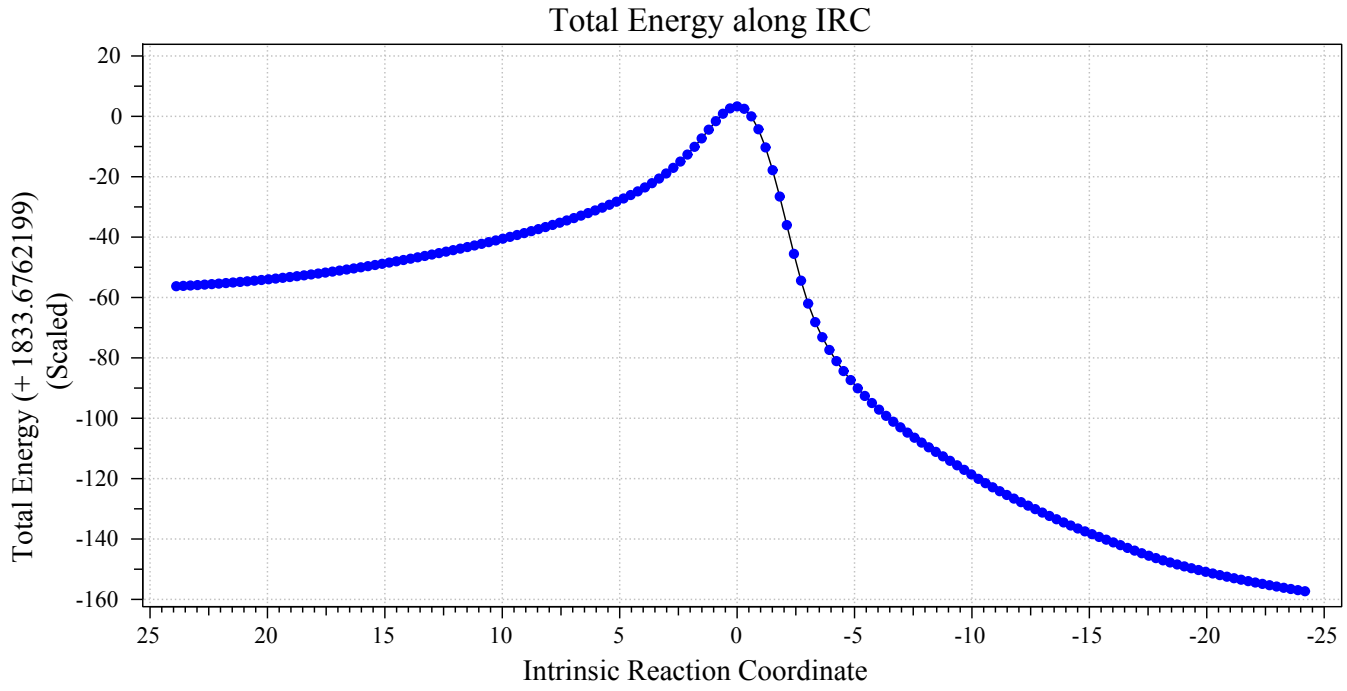

Figure S 6. Intrinsic reaction coordinate (IRC) of the reaction between the Grignard reagent (**1**) and acetyl chloride (**2**). The electronic energy is referenced to the individually calculated energies of the materials (Grignard reagent (**1**) and acetyl chloride (**2**)).

Table S4. Total Energy along IRC: X-Axis: Intrinsic Reaction Coordinate; Y-Axis: Total Energy (+ 1833.6762199) (Scaled)

#	X	Y
	-24.1827300000	-157.2998949891
	-23.8804000000	-156.9359172927
	-23.5781000000	-156.5535345709
	-23.2758000000	-156.1531990109
	-22.9734800000	-155.7364595343
	-22.6711500000	-155.3046675910
	-22.3688100000	-154.8611571407
	-22.0664600000	-154.4104078849
	-21.7641000000	-153.9508022164
	-21.4617300000	-153.4781101422
	-21.1593700000	-152.9889002179
	-20.8570100000	-152.4812328106

-20.5546500000	-151.9560304476
-20.2522900000	-151.4152945292
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-19.6475500000	-150.2746991287
-19.3452600000	-149.6782834677
-19.0430000000	-149.0680264805
-18.7407200000	-148.4341876042
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-17.8337800000	-146.3237723167
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0.0000000000	3.3000000027
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6.9518400000	-33.6974192797
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7.8588200000	-35.9639567294
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8.4634500000	-37.3571635439
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10.8824000000	-42.2263559484
11.1848000000	-42.7686730978
11.4872000000	-43.2975469390
11.7896000000	-43.8144536567
12.0920000000	-44.3196442933
12.3944000000	-44.8143509775
12.6968000000	-45.2997168496
12.9992000000	-45.7752342033
13.3016000000	-46.2414177706
13.6040000000	-46.6989444160
13.9064000000	-47.1468551728
14.2088000000	-47.5849878824
14.5112000000	-48.0136015030
14.8136000000	-48.4319008312
15.1160000000	-48.8400720804
15.4184000000	-49.2386678765
15.7207900000	-49.6272120350
16.0231900000	-50.0060917885
16.3255900000	-50.3758694244
16.6279900000	-50.7354925452
16.9303900000	-51.0846419690
17.2327900000	-51.4232848138
17.5351900000	-51.7502678027
17.8375900000	-52.0658675609
18.1399900000	-52.3711044312
18.4423900000	-52.6655683813
18.7448000000	-52.9491313028
19.0471900000	-53.2218587359
19.3495900000	-53.4830952271
19.6519900000	-53.7335663360
19.9543800000	-53.9744315176
20.2567800000	-54.2052647425

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20.5591700000      -54.4263403124
20.8615600000      -54.6386399489
21.1639600000      -54.8416318414
21.4663500000      -55.0361234204
21.7687400000      -55.2234908758
22.0711300000      -55.4027444229
22.3735200000      -55.5736481423
22.6759200000      -55.7360422460
22.9783100000      -55.8872395006
23.2806900000      -56.0263409533
23.5830600000      -56.1534841042
23.8854100000      -56.2671245239
```

5 4FTM-ACl-2T_Pr2_c03_THF

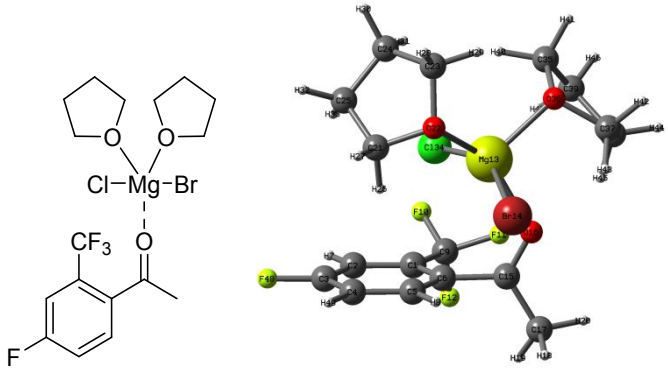

Figure S 7. Geometry optimized product structure of the reaction between the Grignard reagent (**1**) and acetyl chloride (**2**) corresponding to station (C) in Figure 1.

Table S5. xyz-coordinates of the Geometry optimized product structure of the reaction between the Grignard reagent (1) and acetyl chloride (2) in Figure S7.

```
49
4FTM-ACl-2T_Pr2_c03
C          -2.58405       -0.30055        0.01064
C          -3.34014        0.72609       -0.54777
C          -3.22240        1.99762        0.01546
C          -2.40204        2.27405        1.10653
C          -1.65899        1.22826        1.64812
C          -1.74663       -0.05211        1.10102
H          -4.00157        0.55557       -1.40223
H          -1.00588        1.41567        2.50934
C          -2.70953       -1.68327       -0.57468
F          -2.85015       -1.74376       -1.89599
F          -1.70243       -2.51303       -0.30590
F          -3.78478       -2.33555       -0.11436
Mg          1.22839        0.00110       -0.03325
Br          1.93939        1.01520        2.31604
C          -0.89574       -1.11959        1.69470
O           0.23774       -1.30323        1.28275
C          -1.44250       -1.93435        2.80004
H          -1.24125       -1.44833        3.77612
H          -2.53276       -2.07930        2.74569
H          -0.97888       -2.93526        2.86048
C           0.71227        2.81727       -0.65472
O           1.84105        1.96480       -0.36642
C           2.73859        2.04025       -1.49170
C           1.86169        2.24383       -2.72381
C           0.59018        2.92129       -2.17537
H          -0.15541        2.34903       -0.15760
H           0.93778        3.78187       -0.16757
H           3.41203        2.89327       -1.29337
```

H	3.32768	1.10675	-1.47640
H	2.35942	2.85742	-3.49146
H	1.61824	1.28191	-3.21071
H	0.51379	3.97086	-2.50408
H	-0.32049	2.42084	-2.54727
Cl	-0.30428	-0.24457	-1.66782
C	2.74954	-1.63695	-1.87828
O	2.89847	-1.09938	-0.54339
C	2.97627	-2.22900	0.35853
C	2.09415	-3.31821	-0.24728
C	1.94049	-2.92308	-1.73099
H	2.26402	-0.84187	-2.47325
H	3.77546	-1.80380	-2.25284
H	4.04482	-2.50409	0.40737
H	2.64969	-1.85045	1.34607
H	2.54250	-4.31866	-0.13324
H	1.10981	-3.37297	0.25196
H	2.30241	-3.71465	-2.40695
H	0.87726	-2.76932	-1.99170
F	-3.92875	2.98472	-0.51421
H	-2.33525	3.28003	1.53025

6 4FTM-Ac-2T_Add1_c01_THF

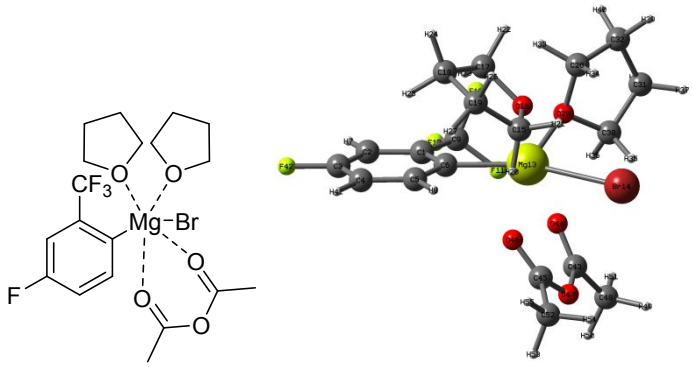

Figure S 8. Geometry optimized adduct of the Grignard reagen (1) and acetic anhydride (4) (corresponding to station (A) in Figure 1

Table S6. xyz-coordinates of the Grignard (1) and acetic anhydride (4) adduct of Figure S8

55
4FTM-Ac-2T_Add1_THF

C	2.55705	-0.79779	-0.70737
C	3.91720	-0.63283	-0.99875
C	4.40751	0.66419	-0.96573
C	3.61645	1.77669	-0.66156
C	2.27627	1.56048	-0.36249
C	1.74901	0.27067	-0.37652
H	4.56615	-1.47343	-1.23828
H	1.63669	2.41057	-0.11644
C	1.92591	-2.15113	-0.75776
F	1.74151	-2.72517	0.43321
F	0.71897	-2.15368	-1.32313
F	2.58841	-3.08645	-1.44894
Mg	-0.30824	0.08718	0.12828
Br	-2.92120	0.92324	0.59108
C	-0.24474	2.38915	2.14958
O	-0.01325	0.97253	2.13369
C	1.22250	0.66203	2.79288
C	1.98406	1.96732	3.00590
C	0.90504	3.05523	2.90546
H	-0.31303	2.71271	1.09444
H	-1.22410	2.50505	2.64315
H	0.93018	0.17472	3.73984

H	1.74761	-0.05854	2.13922
H	2.50597	1.98869	3.97597
H	2.76513	2.10689	2.23676
H	0.58663	3.39582	3.90534
H	1.27414	3.95383	2.38481
C	-0.81407	-1.88296	2.26553
O	-0.70127	-1.88158	0.83214
C	-1.85617	-2.55405	0.29817
C	-2.27296	-3.59175	1.34453
C	-1.53776	-3.17909	2.63261
H	0.23241	-1.83137	2.61090
H	-1.37863	-0.98516	2.58067
H	-2.64477	-1.80953	0.10066
H	-1.50487	-2.99052	-0.64956
H	-3.36619	-3.60786	1.48430
H	-1.99461	-4.61299	1.03574
H	-2.23372	-3.03481	3.47469
H	-0.82876	-3.96060	2.95438
H	4.03635	2.78063	-0.65596
F	5.69320	0.86323	-1.24044
C	-1.97473	-0.16518	-2.48387
O	-1.24551	-0.66721	-1.66346
C	-1.47280	2.14161	-1.91653
O	-0.54527	1.88396	-1.19216
O	-2.12822	1.18058	-2.64570
C	-2.81757	-0.88333	-3.46131
H	-3.89157	-0.65813	-3.32308
H	-2.57456	-0.60529	-4.50367
H	-2.69868	-1.97926	-3.37842
C	-2.02770	3.46977	-2.24059
H	-1.88622	3.72876	-3.30640
H	-3.11564	3.52253	-2.05091
H	-1.55078	4.26591	-1.64060

7 4FTM-Ac-2T_TS1_c02_THF

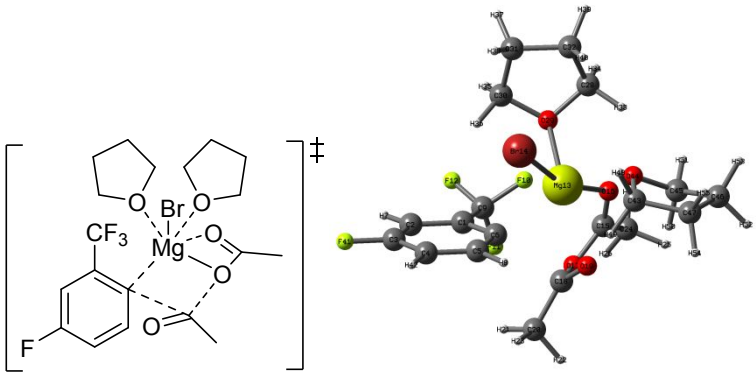

Figure S 9. Transition state structure of the reaction of the Grignard reagent (**1**) with acetic anhydride (**4**) (corresponding to station (B) in Figure 1.

Table S7. xyz-coordinates of the transition state structure of the reaction of the Grignard reagent (1) and acetic anhydride (4) of Figure S9.

55
4FTM-Ac-2T_TS1_c02_THF

C	-2.51486	0.12244	-0.09168
C	-3.62620	-0.71046	-0.27588
C	-3.53601	-1.65870	-1.28766
C	-2.42537	-1.79204	-2.12284
C	-1.35431	-0.92594	-1.91476
C	-1.39625	0.01032	-0.88598
H	-4.52386	-0.62933	0.33474
H	-0.48273	-0.97839	-2.57496
C	-2.57116	1.18312	0.96416

F	-1.42398	1.40538	1.60441
F	-2.92612	2.38783	0.50752
F	-3.43333	0.97004	1.96411
Mg	0.73308	-0.06579	-0.01723
Br	1.01953	-2.71270	-0.46768
C	0.22398	2.80437	0.42582
O	0.94202	1.89235	0.79711
O	-0.61073	2.68597	-0.63082
C	-0.39236	1.78379	-1.68311
O	0.71669	1.28471	-1.81529
C	-1.39162	2.07374	-2.74107
H	-2.42191	2.17181	-2.36247
H	-1.15133	3.03057	-3.24046
H	-1.39501	1.28913	-3.51747
C	0.12343	4.12539	1.07478
H	0.92455	4.79762	0.71139
H	-0.83233	4.64277	0.88190
H	0.24145	4.05008	2.17167
C	1.56023	-0.25872	2.77810
O	0.32113	-0.25093	2.04799
C	-0.45136	-1.39963	2.44348
C	0.50612	-2.41930	3.06105
C	1.87821	-1.71983	3.07733
H	2.29867	0.25433	2.13345
H	1.38441	0.34868	3.68287
H	-1.19439	-1.01770	3.16533
H	-0.96233	-1.74645	1.52773
H	0.18764	-2.70801	4.07655
H	0.54168	-3.35331	2.47396
H	2.39557	-1.84290	4.04159
H	2.54734	-2.14702	2.30865
F	-4.56792	-2.47367	-1.47897
H	-2.39411	-2.54248	-2.91013
C	3.31927	-0.53457	-1.54251
O	2.86554	0.05816	-0.31197
C	3.42087	1.37944	-0.22150
C	4.79700	1.28334	-0.88106
C	4.61927	0.17643	-1.93500
H	3.46679	-1.59685	-1.28191
H	2.51666	-0.41491	-2.29277
H	2.76166	2.08707	-0.75569
H	3.43838	1.59048	0.86004
H	5.10939	2.23933	-1.32860
H	5.57940	1.02024	-0.14969
H	4.55701	0.59538	-2.95322
H	5.47866	-0.51351	-1.94652

8 4FTM-Ac-2T_IRC1_THF

An IRC calculation was conducted at the PM7 level of theory using the SMD solvation model. The Transition state 4FTM-Ac-TS1_c02 was used as starting point. Following intrinsic reaction coordinate was obtained:

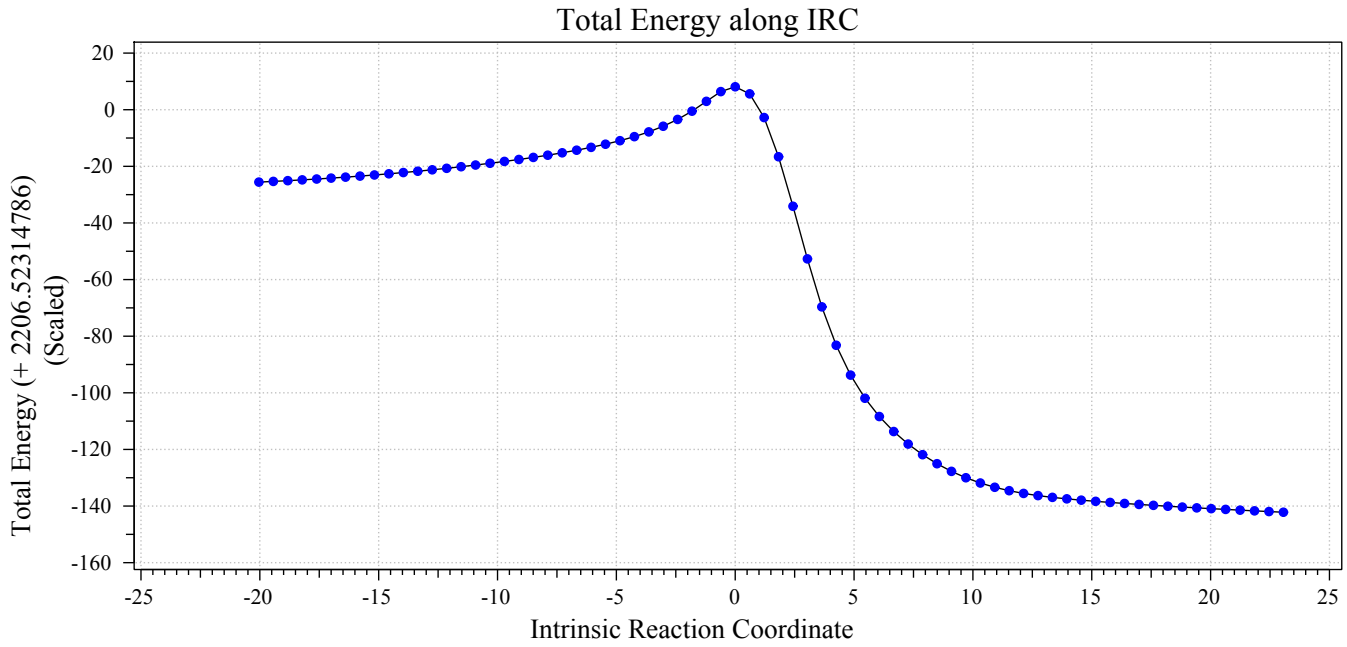

Figure S 10. Intrinsic reaction coordinate (IRC) of the reaction between the Grignard reagent (**1**) and acetic anhydride (**4**). The electronic energy is referenced to the individually calculated energies of the materials (Grignard reagent (**1**) and acetic anhydride (**4**)).

Table S8. Total Energy along IRC: X-Axis: Intrinsic Reaction Coordinate; Y-Axis: Total Energy (+ 2206.52314786) (Scaled)

#	X	Y
	-20.0397500000	-25.5686426405
	-19.4321000000	-25.3253123534
	-18.8244500000	-25.0648498779
	-18.2168000000	-24.7846072714
	-17.6091000000	-24.4827964817
	-17.0014000000	-24.1596001832
	-16.3937000000	-23.8141484139
	-15.7860000000	-23.4466291727
	-15.1782900000	-23.0553180417
	-14.5705800000	-22.6384647445
	-13.9628800000	-22.1963473240
	-13.3551800000	-21.7268490577
	-12.7474800000	-21.2290469116
	-12.1397800000	-20.6994174121
	-11.5320800000	-20.1361635988
	-10.9244000000	-19.5421421969
	-10.3167300000	-18.9180146303
	-9.7090900000	-18.2657128887
	-9.1014700000	-17.5797969048
	-8.4939000000	-16.8500134840
	-7.8863500000	-16.0677220639
	-7.2788400000	-15.2209947616
	-6.6714100000	-14.3006603985
	-6.0641100000	-13.2945705313
	-5.4570100000	-12.1866780516
	-4.8500700000	-10.9439391069
	-4.2432200000	-9.5144941201
	-3.6363900000	-7.8367712831
	-3.0297800000	-5.8385201387
	-2.4238000000	-3.4355015666
	-1.8184400000	-0.5115636885
	-1.2128600000	2.9532899128
	-0.6069200000	6.3965084620
	0.0000000000	8.0999999961
	0.6074600000	5.6017546152
	1.2149100000	-2.7702092239
	1.8223800000	-16.6152355925

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 2.4297800000      -34.1055746288
 3.0368400000      -52.6937367301
 3.6429000000      -69.6359512577
 4.2473400000      -83.2082265138
 4.8521600000      -93.7440159348
 5.4572800000     -101.9170877650
 6.0618000000     -108.3790494011
 6.6680800000     -113.6774454469
 7.2748400000     -118.1015587226
 7.8819500000     -121.8550814753
 8.4892700000     -125.0455539723
 9.0966700000     -127.7474312639
 9.7040500000     -130.0039966235
10.3113000000     -131.8594735951
10.9183500000     -133.3669824368
11.5251500000     -134.5758668587
12.1316900000     -135.5395514037
12.7379700000     -136.3091581459
13.3440800000     -136.9328703926
13.9503500000     -137.4576185861
14.5570700000     -137.9177775998
15.1642200000     -138.3355188096
15.7716200000     -138.7220247584
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16.9866300000     -139.4262018615
17.5942100000     -139.7512188339
18.2018000000     -140.0621242243
18.8094000000     -140.3589418119
19.4170000000     -140.6431169842
20.0246300000     -140.9179239156
20.6322800000     -141.1853032210
21.2399500000     -141.4462778816
21.8476100000     -141.7000785919
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23.0629100000     -142.1832132772
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9 4FTM-Ac-2T_Pr4_c01_THF

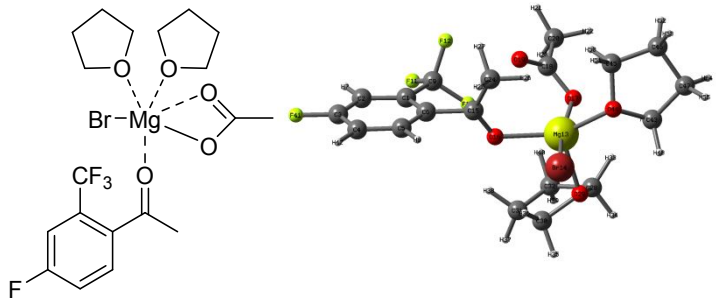

Figure S 11. Geometry optimized product structure of the reaction between the Grignard reagent (**1**) and acetic anhydride (**4**) corresponding to station (C) in Figure 1.

Table S9. xyz-coordinates of the Geometry optimized product structure of the reaction between the Grignard reagent (1) and acetic anhydride (4) in Figure S11.

```
55
4FTM-Ac-T_Pr4_c01_THF
C          3.44415        0.28758       -0.29936
C          4.82976        0.16326       -0.21961
C          5.37277       -1.11993       -0.28103
C          4.59614       -2.26839       -0.42219
```

C	3.21759	-2.11527	-0.52165
C	2.64419	-0.84243	-0.46973
H	5.48827	1.03163	-0.11586
H	2.58103	-3.00085	-0.63843
C	2.82237	1.65678	-0.21757
F	1.71421	1.71478	0.51481
F	3.60013	2.59103	0.33913
F	2.50735	2.17373	-1.40308
Mg	-1.51680	-0.10283	0.33039
Br	-1.88109	-2.75403	0.07089
C	1.15743	-0.76199	-0.60968
O	0.51039	-0.50843	0.39420
O	-1.59158	1.80651	0.06526
C	-0.70493	2.24175	-0.75807
O	0.05608	1.46602	-1.33927
C	-0.67914	3.72309	-0.96122
H	-0.07898	4.00471	-1.83562
H	-1.69256	4.12527	-1.09834
H	-0.24886	4.22401	-0.08173
C	0.59294	-1.08190	-1.93730
H	0.77754	-2.13284	-2.21953
H	-0.50014	-0.91775	-2.00622
H	1.03199	-0.44511	-2.72818
C	-2.31363	1.13215	2.80341
O	-2.13625	-0.22044	2.32591
C	-1.03848	-0.78837	3.07738
C	-0.08957	0.36516	3.40506
C	-0.91427	1.64223	3.14330
H	-2.81910	1.67569	1.98140
H	-2.98366	1.07026	3.67733
H	-1.48773	-1.25389	3.97068
H	-0.60268	-1.57386	2.43132
H	0.27012	0.31562	4.44541
H	0.81322	0.33677	2.76994
H	-0.91825	2.31874	4.01117
H	-0.49063	2.22233	2.30116
F	6.68847	-1.24911	-0.20026
H	5.05048	-3.26261	-0.45815
C	-4.32898	0.21708	-0.27126
O	-3.19702	-0.42928	-0.88098
C	-3.05336	0.06119	-2.22556
C	-4.42510	0.57849	-2.66611
C	-5.30977	0.49909	-1.40787
H	-4.67635	-0.52391	0.46979
H	-3.99360	1.14437	0.23324
H	-2.27747	0.84935	-2.23616
H	-2.70898	-0.82721	-2.78259
H	-4.35989	1.61184	-3.04707
H	-4.84350	-0.02201	-3.49025
H	-5.87408	1.43101	-1.24155
H	-6.06168	-0.30293	-1.49975