Electronic Supplementary Material (ESI) for Organic & Biomolecular Chemistry

The "Kinetic Capture" of Acylium Ion as the Reactive Species from Live Aluminum Chloride Promoted Friedel-Crafts Acylation

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Supporting Information

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Analytical methods and reagents

All reactions and manipulations were performed in a nitrogen-filled self-prepared three-necked micro reactor. IR spectra were recorded on a Mettler Toledo React IR TM 10 spectrometer using a diamond comb. NMR spectra were recorded on a Bruker-BioSpin spectrometers at 400 MHz (^{1}H NMR), 100 MHz (^{13}C NMR). Tetramethylsilane was used as an internal standard. All ^{1}H NMR spectra were reported in delta (δ) units, parts per million (ppm) downfield from the internal standard. Coupling constants are reported in Hertz (Hz). Yields of aryl ketones were obtained by isolating or from GC and diphenyl was added as internal standard. All glasswares were oven dried at 120 ^{o}C for more than 1 hour prior to use. 1, 2-dichloroethane were dried and distilled from CaH_2 under nitrogen. Acetyl chloride and 4-tert-butylbenzoyl chloridewere distilled under nitrogen. Toluene(Sinopharm Chemical Reagent Co.,Ltd), mesitylene(Sinopharm Chemical Reagent Co.,Ltd), benzene-H_6(Sinopharm Chemical Reagent Co.,Ltd), benzene-D_6(ACROS), and $AlCl_3$ (ACROS, stored in glovebox) were commercial available and used without further purification.

$AlCl_3$ promoted Friedel-Crafts acylation reactions between acetyl chloride and toluene

In an oven dried self-prepared three-necked micro reactor with a magnetic stirrer, the reactor was allowed to be vacuumed and purged with nitrogen for three times. 1, 2-dichloroethane (4 mL) and acetyl chloride (142 μL, 2.0 mmol) was added in via a syringe, then $AlCl_3$ (267.0 mg, 2.0 mmol) was added. The mixture was allowed to stir at room temperature and recorded by React IR. The course of the reaction can be observed from the characteristic IR band of acetyl chloride(1803 cm^{-1}). When the acetyl chloride did not decrease anymore and the increasing band (1653 cm^{-1}) was constant, the reaction was cooled to -10 ^{o}C, and toluene (184.0 mg, 2.0 mmol) was added. Band B decreased in a minute in line with the increase of band C and D (Figure S1 (A)). Finally, the reaction was quenched by water and the GC yield was 86 %.

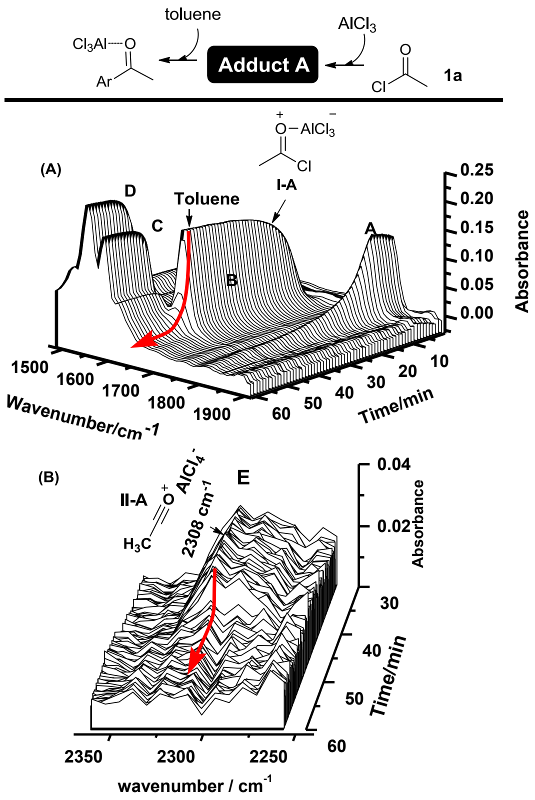


Fig. S1 In situ IR spectra of the reaction of aluminum chloride (0.5 M), acetyl chloride (0.5 M) and toluene (0.5 M) in 1,2-dichloroethane (4 mL) at -10 °C.

$AlCl_3$ promoted Friedel-Crafts acylation between **1a** and toluene was monitored by *in-situ* IR shown in Fig. 1. When **1a** (band A at 1806 cm^{-1}) reacted with $AlCl_3$, adduct **A** was afforded. The band B at 1653 cm^{-1} accumulated and was assigned as the donor-acceptor complex **I-A** according to literature reported. When toluene was added, as shown in Fig. S1, the bands at 1583 cm^{-1} (C), 1548 cm^{-1} (D), which were assigned as the $AlCl_3$ adduct of *p*-methylacetophenone, appeared proportionally (Fig. S2). Meantime, **I-A** decreased quickly. It seemed that **I-A** was the true reactive species. However, when the region at 2250-2350 cm^{-1} was focused, the band E at 2308 cm^{-1}, which was a fairly tiny absorption and almost invisible compared to **I-A**, also disappeared immediately (Fig. 1 (B)). If this band could be assigned to the acylium ion **II-A**, it also might be the active species.

Identification of the product formed in $AlCl_3$ promoted acylation of acylchloride and toluene

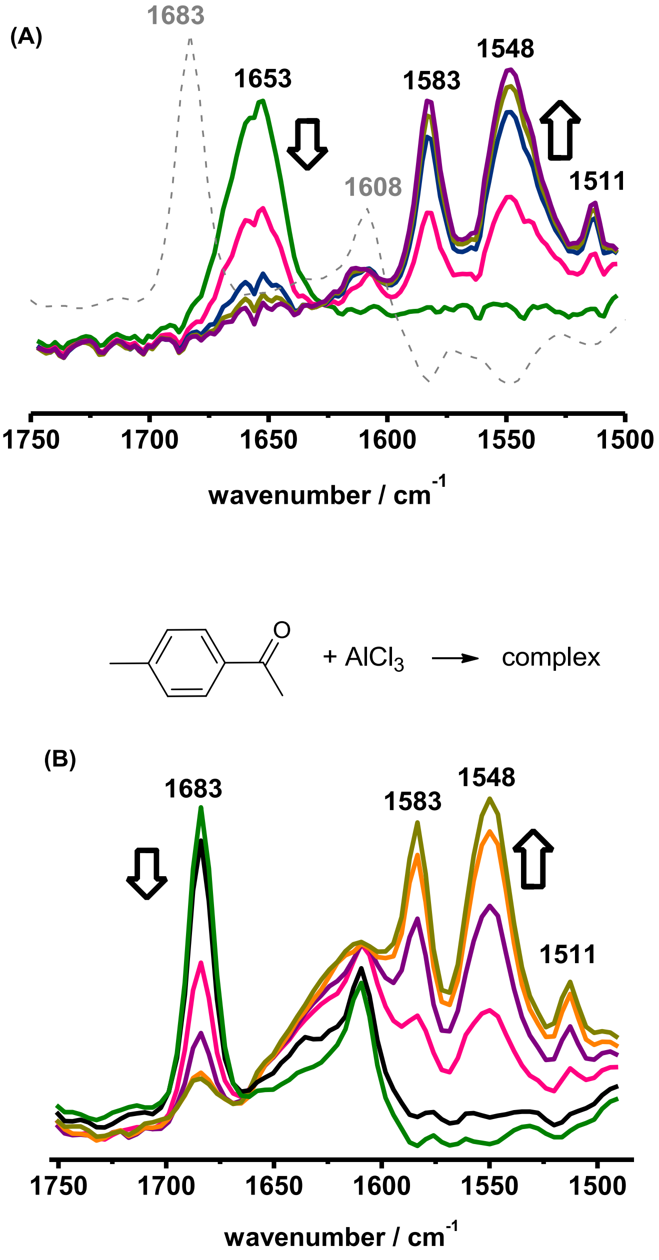
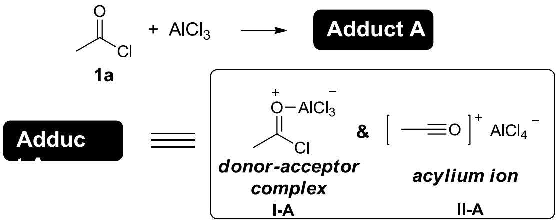


Fig. S2 (A) IR spectra of the reaction between **A** (0.5 M) and toluene (0.5 M) in 1,2-dichloroethane (4 mL). Dash line: IR spectra of 1-(p-tolyl)ethanone; **(B)**:IR spectra of the reaction between aluminum chloride (0.5 M) and *p*-methylacetophenone (0.5 M) in 1,2-dichloroethane (4 mL).As shown in Figure S1, the increasing bands after toluene was added were 1583 cm^{-1}, 1548 cm^{-1}, 1511 cm^{-1} (Figure S2 (A)). However, the authentic IR spectra of 1-(p-tolyl)ethanone from 1800-1500 cm^{-1} was 1683 cm^{-1} and 1608 cm^{-1} (Figure S2 (A) dash line).

The resutls suggested that the increasing band from the live reaction could not tally with the standard IR spectra of 1-(p-tolyl)ethanone. When $AlCl_3$ and 1-(p-tolyl)ethanone were mixed together and monitorred by react IR, the bands at 1683 cm^{-1} and 1608 cm^{-1} decreased and the bands at 1583 cm^{-1}, 1548 cm^{-1}, 1511 cm^{-1} increased (Figure S2 (B)). This phenomenon indicated that the adduct complex of $AlCl_3$ and *p*-methylacetophenone features the same IR spetra with the compound produced in $AlCl_3$ promoted acylation of acetyl chloride and toluene.

In an oven dried self-prepared three-necked micro reactor with a magnetic stirrer, the reactor was allowed to be vacuumed and purged with nitrogen for three times. 1, 2-dichloroethane (4 mL) was added in via a syringe, then p-methylacetophenone (268.0 mg, 2.0 mmol) and aluminium chloride (267.0 mg, 2.0 mmol) was added. The mixture was allowed to stir at room temperature and recorded by React IR. General prodecure of $AlCl_3$ promoted Friedel-Crafts acylation reactions between acetyl chloride and toluene monitorred by React IR.

Kinetic behavior of $AlCl_3$ promoted Friedel-Crafts acylation reactions between acetyl chloride and toluene



In an oven dried self-prepared three-necked micro reactor with a magnetic stirrer, $AlCl_3$ (75.0 mg, 0.56 mmol), diphenyl (40.1 mg) as the internal standard were added. The reactor was allowed to be vacuumed and purged with nitrogen for three times. 1, 2-dichloroethane (5 mL) and acetyl chloride (40 μL, 0.56 mmol) was added in via a micro syringe. The mixture was allowed to stir at room temperature and monitorred by React IR. When the acetyl chloride did not decrease anymore and the increasing band of **I-A** (1653 cm^{-1}) was steady, the reaction temperature was allowed to be at -10 °C, and toluene (60 μL, 0.56 mmol) was added in. Finally, the reaction was quenched by water and the yield was determined by GC.

The reactions of $AlCl_3$ (0.56 mmol, 0.11 M), CH_3COCl (0.56 mmol, 0.11 M). and different concentrations of toluene(0.11 M, 0.13 M, 0.15M, 0.17M) give excellent GC yields were 95 %, 97 %, 93% and 99 %, respectively. The reactions of toluene (0.85 mmol, 0.17 M) and different concentrations of **A** from 0.08 M, 0.11 M, 0.14 M, 0.17 M also give excellent GC yields were 94 %, 93 %, 96 % and 90 %, respectively. According to the increase of IR absorption of the product vs t and its initial and final concentration, the change of concentration of the product vs t could be calculated, and then the intial rate also could be obtained. Figure S3-S7 were obtained by this method and were farther treated.

The reactions with different concentrations of substrates were carried out (Figure S3 and S5). The kinetic behavior with varied concentrations of toluene and **A** were discussed. Both plotting initial rates *vs* [toluene] (Figure S4) and initial rates *vs* [**A**] and (Figure S6) leaded to linear relationships, suggesting that the reaction was first-order on [toluene] and first-order on [**A**]. Data fits to first or second order of reaction was also shown in Figure S7. Plotting $1/(c_0\text{-}c)$ *vs* t resulted to a line and the value of R is 0.98272 (Figure S7(A)), while Plotting $\ln(c_0\text{-}c)$ vs t obtained a nonlinear behavior and the value of R is 0.92693 (Figure S7(B)). Therefore, this kinetic results established that the reaction exhibits a second order kinetic behavior. This kinetic behavior also provided evidence that the initial rate of the acylation reaction was first-order on [**A**], and first order on [toluene].

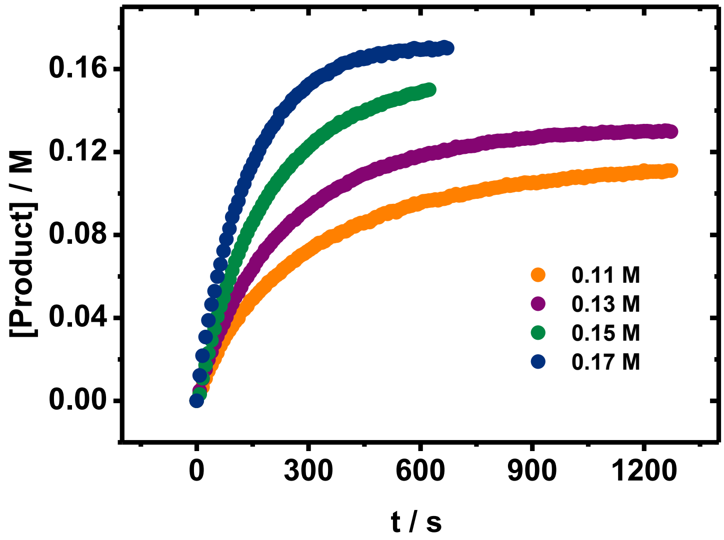


Fig. S3 Kinetic profiles of the reactions with different concentrations of toluene from 0.11 M ~ 0.17M. $AlCl_3$ (0.56 mmol, 0.11 M), CH_3COCl (0.56 mmol, 0.11 M).

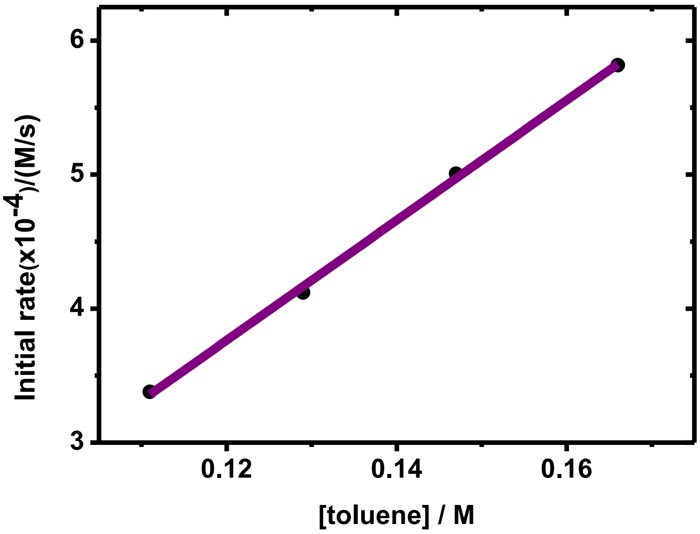


Fig. S4 Kinetic plots of the reactions with different concentrations of toluene from 0.11 M ~ 0.17M. $AlCl_3$ (0.56 mmol, 0.11 M), CH_3COCl (0.56 mmol, 0.11 M).

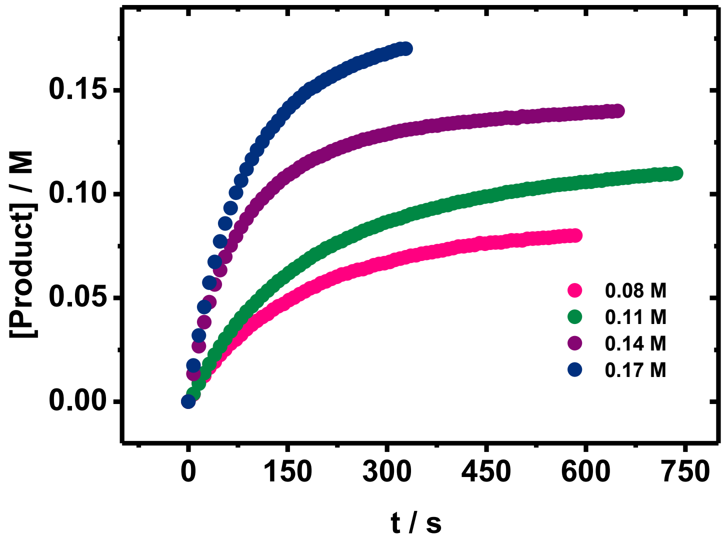


Fig. S5 Kinetic profiles of Friedel-Crafts acylation reactions with different concentrations of **A** from 0.08 M ~ 0.17M, toluene (0.85 mmol, 0.17 M).

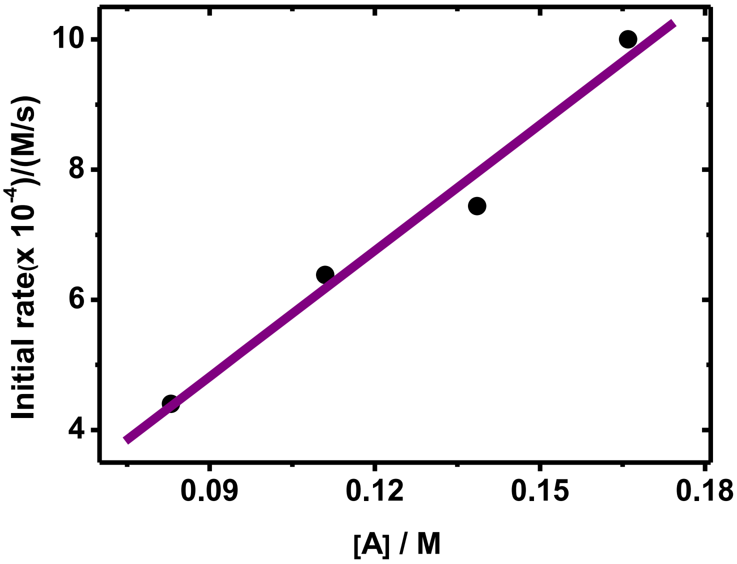


Fig. S6 Kinetic plots of Friedel-Crafts acylation reactions with different concentrations of **A** from 0.08 M ~ 0.17M,toluene (0.85 mmol, 0.17 M).

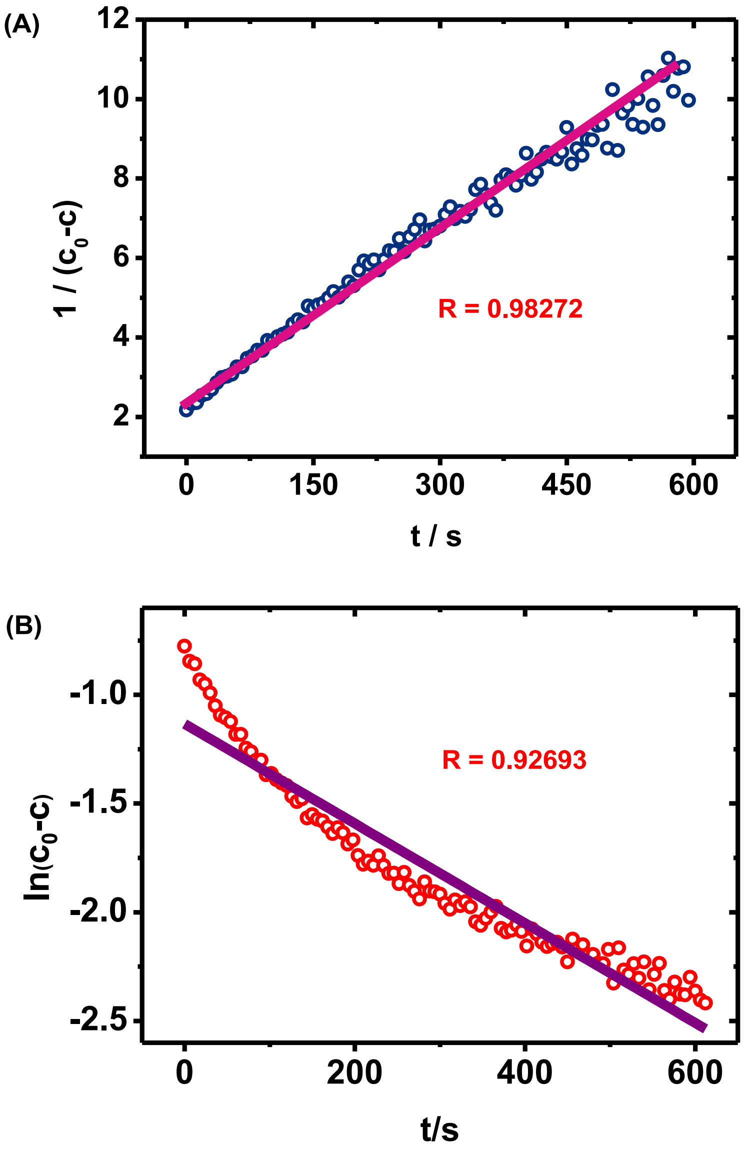


Fig. S7 (A): Plotting 1/(c_0-c) *vs* t when the reaction of **A** (0.5 M) and toluene (0.5 M) was carried out in 1,2-dichloroethane (4 mL) at -30 °C; (**B**): Plotting ln(c_0-c) vs t of $AlCl_3$ promoted Friedel-Crafts acylation reaction between **A** (0.5 M) and toluene (0.5 M) in 1,2-dichloroethane (4 mL) at -30 °C. (c_0: initial concentrate of toluene, c: concentrate of toluene in the process of reaction.)

Kinetic behavior of $AlCl_3$ promoted Friedel-Crafts acylation reactions by using different substrates

In an oven dried self-prepared three-necked micro reactor with a stirrer bar, $AlCl_3$ (267.0 mg, 2.0 mmol) was added. The reactor was allowed to be vacuumed and purged with nitrogen for three times. 1, 2-dichloroethane (4 mL) and acyl chloride (2.0 mmol) was added in via a syringe. The mixture was allowed to stir at room temperature and recorded by React IR. When the acyl chloride did not decrease anymore and the increasing band was steady, the temperature was allowed to be -30 °C, and the arene (2.0 mmol) was added. Finally, quenched the reaction by water, the yield was obtained by chromatography and NMR spectra data of all the products are presented below.

As shown in Figure S8, the reaction between 4-tert-butylbenzoyl chloride and mesitylene in 1,2-dichloroethane at -30 °C was a proper model reaction for the kinetic investigation.

p-Methylacetophenone

Isolated yield: 76 %.^{1}H NMR (400 MHz, $CDCl_3$) δ 7.86 (d, *J* = 8.1 Hz, 2H), 7.25 (d, *J* = 8.8 Hz, 2H), 2.57 (s, 3H), 2.41 (s, 3H).^{13}C NMR (100 MHz, $CDCl_3$) δ 197.90, 143.89, 134.68, 129.24, 128.44, 26.54, 21.64.

[4-(1,1-Dimethylethyl)phenyl](2,4,6-trimethylphenyl)-benzophenone

Isolated yield: 86 %. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.73 (d, *J* = 8.3 Hz, 2H), 7.44 (d, *J* = 8.7 Hz, 2H), 6.89 (s, 2H), 2.33 (s, 3H), 2.09 (s, 6H), 1.34 (s, 9H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 200.52, 157.35, 138.30, 137.17, 134.74, 134.15, 129.41, 128.25, 125.74, 35.20, 31.10, 21.18, 19.39.

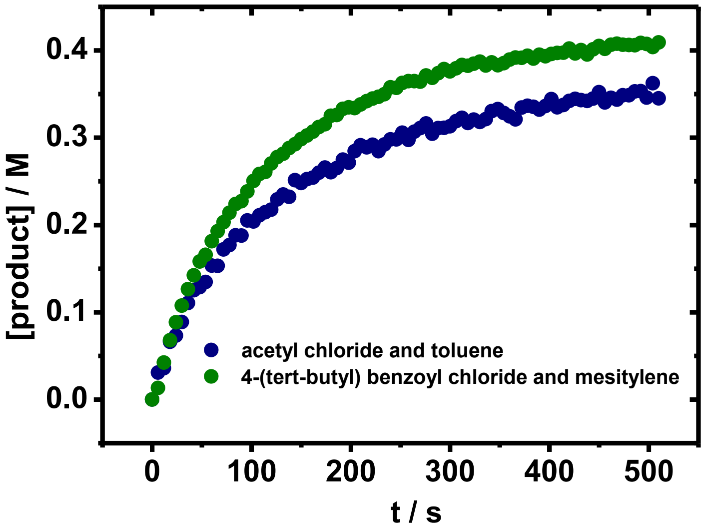
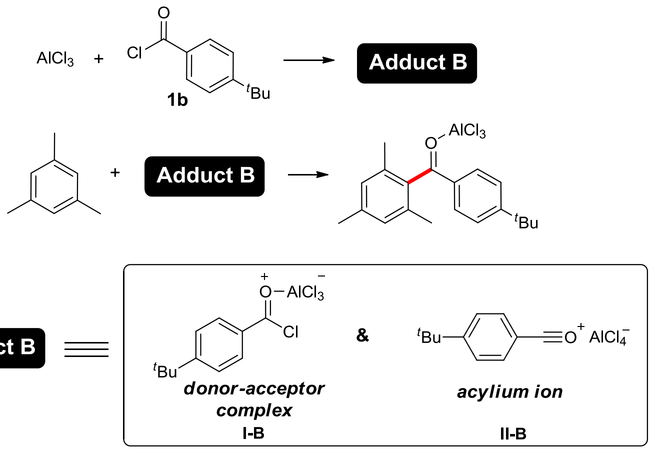


Fig. S8 $AlCl_3$ promoted Friedel-Crafts acylation reactions of ArH (0.5 M) and RCOCl (0.5 M) in 1,2-dichloroethane (4 mL) at -30 °C.

Kinetic behavior of $AlCl_3$ promoted Friedel-Crafts acylation reactions between 4-tert-butylbenzoyl chloride and mesitylene



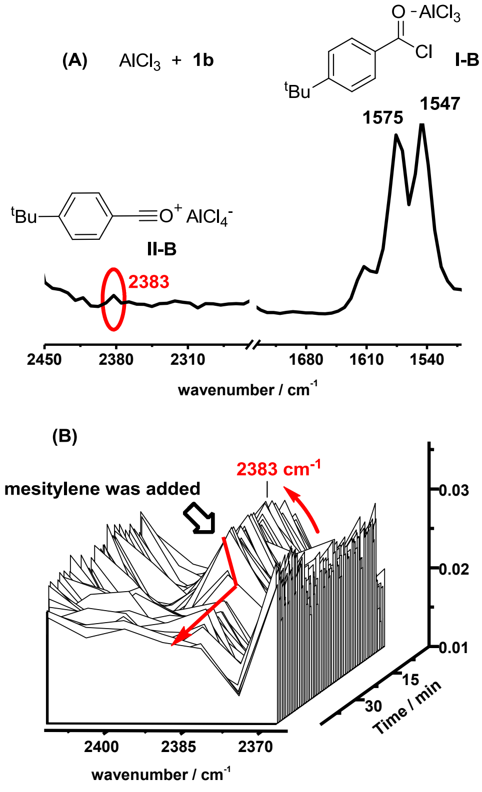


Fig. S9 (A): IR absorption of mixture of $AlCl_3$ and **1b**; **(B)**: 3D-profile of the reaction between $AlCl_3$ (0.23 M), **1b** (0.23 M) and mesitylene (0.23 M) in 1,2-dichloroethane (4 mL) at -30 °C through in-situ IR.

In an oven dried self-prepared three-necked micro reactor with a magnetic stirrer, $AlCl_3$ (122.8 mg, 0.92mmol), diphenyl (33.0 mg) as the internal standard were added. The reactor was allowed to be vacuumed and purged with nitrogen for three times. 1, 2-dichloroethane (4 mL) and **1b** (180.8mg, 0.92 mmol) was added in via a syringe. The mixture was allowed to stir at room

temperature and recorded by React IR. When **1b** did not decrease anymore and the increasing band was steady, the temperature was allowed to be -30 ^{o}C, and mesitylene (110.4 mg, 0.92 mmol) was added. Finally, quenched the reaction by water and the yield was determined by GC. The GC yield was 92 %.
And a band at 2383 cm^{-1}, which might be characteristic absorption of **II-B** was also observed when $AlCl_3$ was mixed with **1b** and compared with **I-B**, acylium ion **II-B** existed in a fairly low concentration (Figure S9 (A)). Moreover, it disappeared instantly when mesitylene was added as shown in Figure S9 (B).

Other reactions followed the same procedure under different reaction conditions.

The reactions of **B** (0.23 M) and different concentrations of mesitylene(0.16 M, 0.23 M, 0.32 M, 0.40 M) give excellent GC yields, were 99 %, 91 %, 92 % and 98 %, respectively. The yield of reactions between mesitylene (0.125 M) and different concentrations of **B**(0.064 M, 0.128 M, 0.192 M, 0.256 M, 0.320 M) were 50 %, 80 %, 99 %, 99 % and 98 %, respectively. According to the increase of IR absorption of the product vs t and its initial and final concentration, the change of concentration of the product vs t could be calculated, and then the intial rate also could be obtained. Figure S10-S13 were obtained by this method and were farther treated.

The reactions with different concentrations of substrates were carried out. The kinetic behavior on mesitylene and **B** were discussed. The kinetic profiles with varied concentrations of mesitylene overlapped perfectly, further suggesting that the initial rates of this acylation reaction was independent on the concentrations of mesitylene (Figure S10). Plotting initial rates *vs* [**B**] showed a linear relationship, indicating that the reaction was first-order kinetic on [**B**] (Figure S12). Data fits to first or second order of reaction was also shown in Figure S13. Plotting ln(c_0-c) *vs* t obtained a linear relationship and the value of R is 0.99810 (Figure S13(A)), while Plotting 1/(c_0-c) *vs* t resulted to a nonlinear relationship and the value of R is 0.96886 (Figure S13(B)). Therefore, this kinetic results suggesting that this reaction exhibited a first-order kinetic behavior. In other words, [ArH] is not in the rate law!

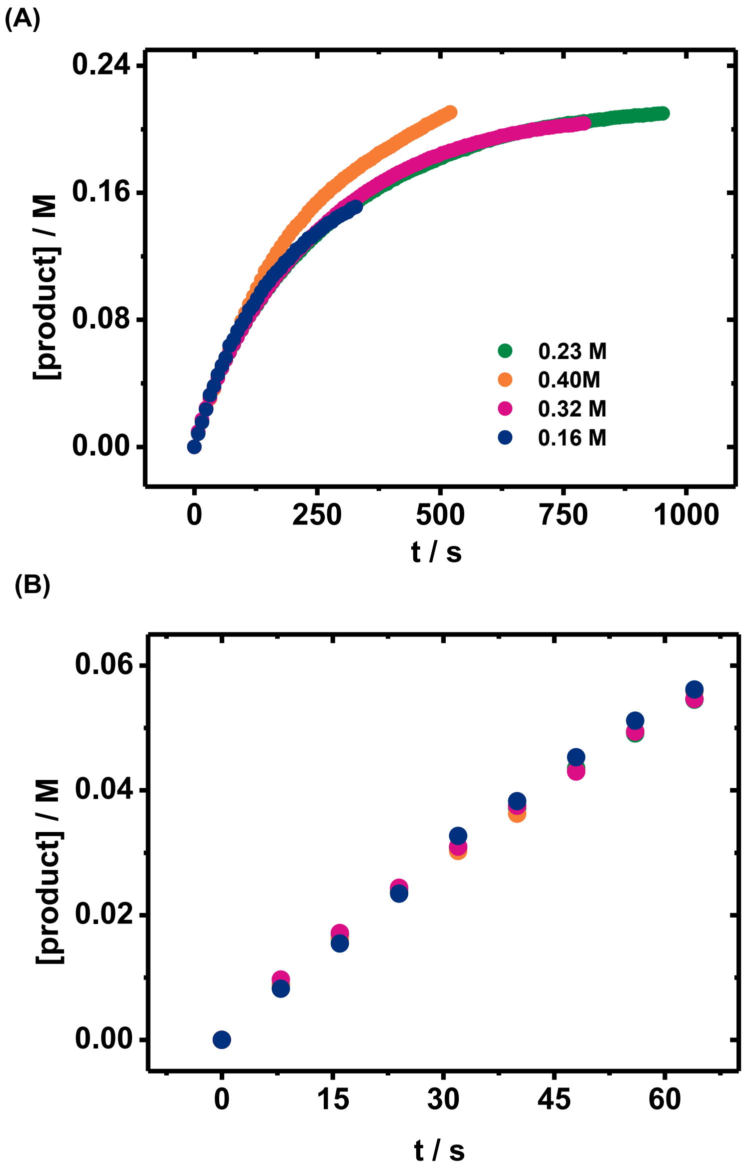


Fig. S10 Kinetic plots of the reactions of $AlCl_3$ promoted Friedel-Crafts acylation between **B** (0.23 M) and different concentrations of mesitylene in 1,2-dichloroethane (4 mL) at -30 ^{o}C. (concentrations of mesitylene: 0.16 M, 0.23 M, 0.32 M, 0.40 M)

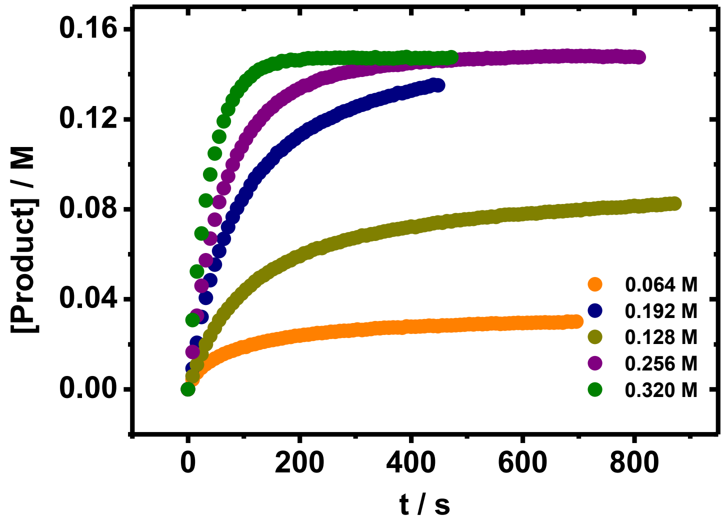


Fig. S11 Kinetic profiles of the reactions of $AlCl_3$ promoted Friedel-Crafts acylation between 1b (0.125 M) and different concentrations of **B** in 1,2-dichloroethane (4 mL) at -30 °C. (concentrations of **B**: 0.064 M, 0.192 M,0.128 M, 0.256 M, 0.320 M).

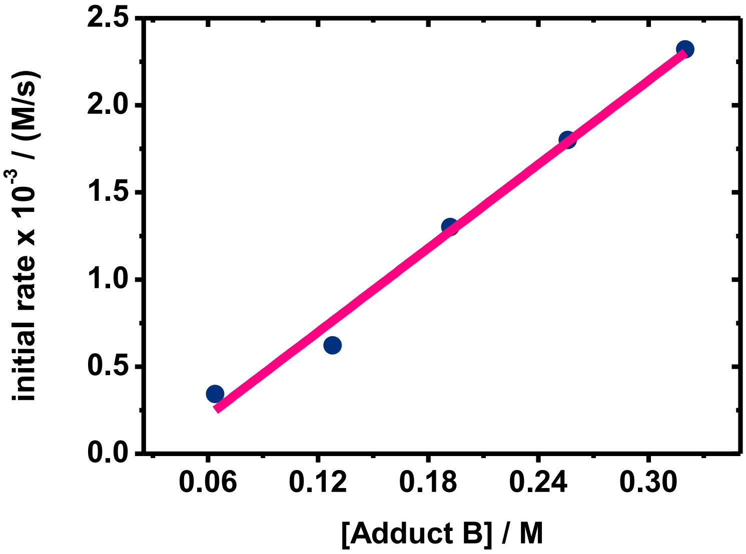


Fig. S12 Kinetic plots of the reactions of $AlCl_3$ promoted Friedel-Crafts acylation between 1b (0.125 M) and different concentrations of **B** in 1,2-dichloroethane (4 mL) at -30 °C. (concentrations of **B**: 0.064 M, 0.192 M,0.128 M, 0.256 M, 0.320 M).

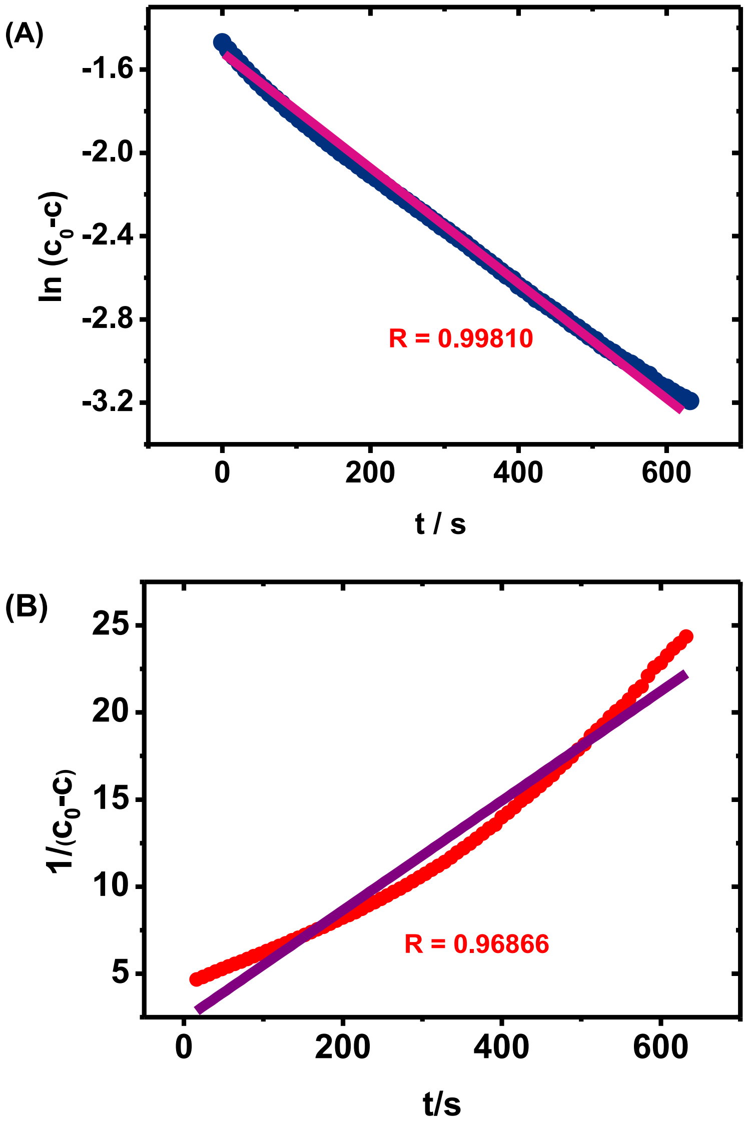
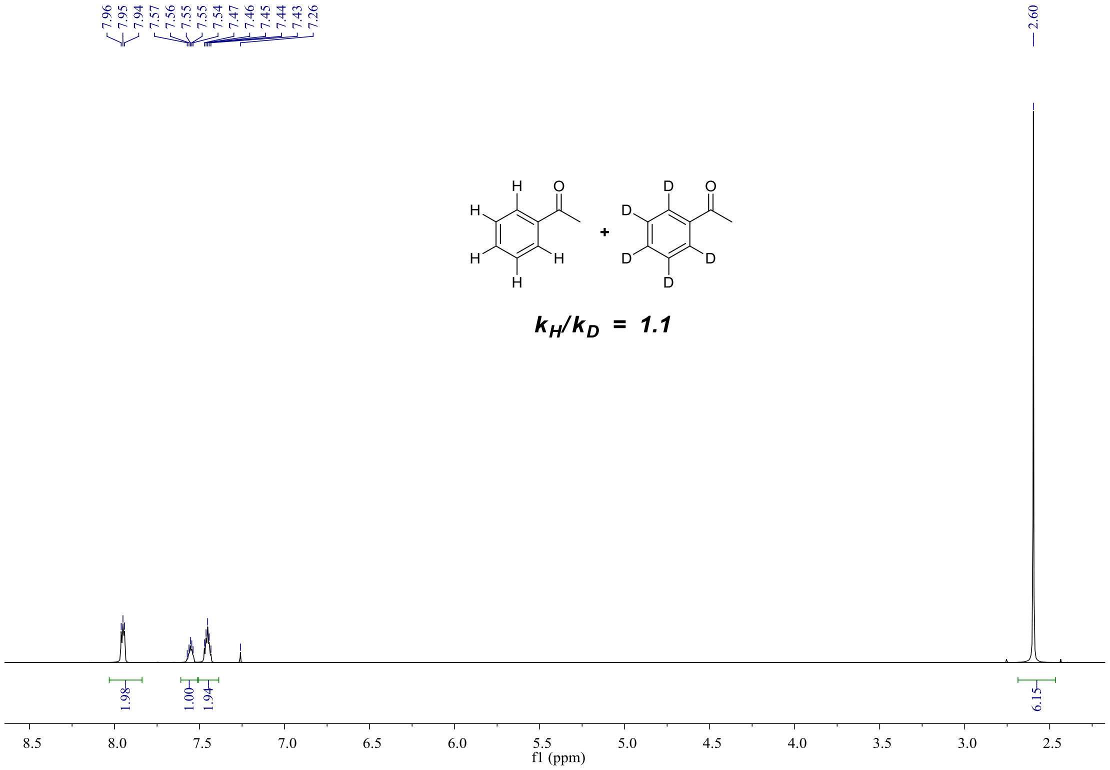
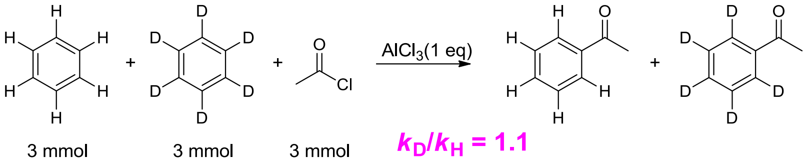


Fig. S13 (A): Plotting ln(c_0-c) vs t of $AlCl_3$ promoted Friedel-Crafts acylation reaction between **1b** (0.23 M) and mesitylene (0.23 M) in 1, 2-dichloroethane at -30 °C; **(B)**: Plotting 1/(c_0-c) *vs* t when the $AlCl_3$ promoted Friedel-Crafts acylation reaction of **1b** (0.23 M) and mesitylene (0.23 M) was carried out in 1, 2-dichloroethane (4 mL) at -30 °C. (c_0: initial concentrate of mesitylene, c: concentrate of mesitylene.)

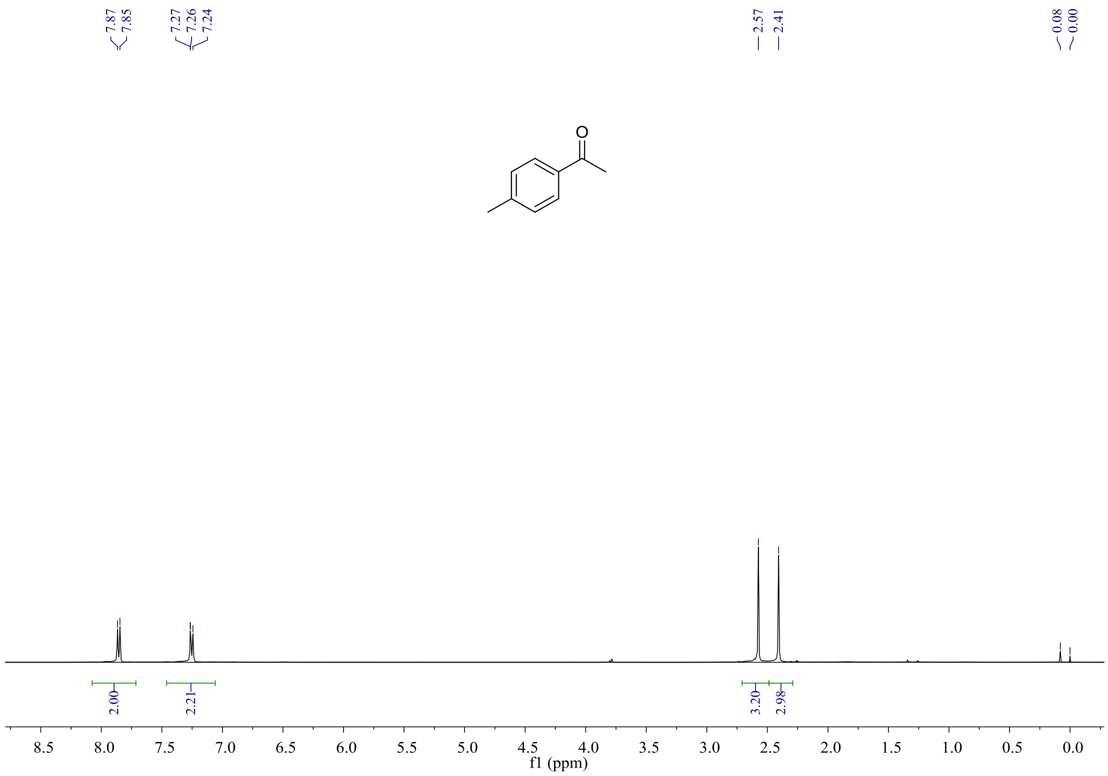
Kinetic Isotope Effect Experiments





In an oven dried schlenk tube with a magnetic stirrer, $AlCl_3$ (534.0 mg, 4.0 mmol) was added and then was allowed to be vacuumed and purged with nitrogen for three times. 1, 2-dichloroethane (4 mL) and acetyl chloride (284 μL, 4.0 mmol) was added in via a syringe, then the mixture was allowed to stir at room temperature for 30 min to lead the adduct (1 mol/L, 4 mL). 3 mL adduct was added in another oven dried schlenk tube in which contained a mixture of benzene-H_6 (234.0 mg, 4 mmol), benzene-D_6 (252.0 mg, 4 mmol) and 1, 2-dichloroethane (1 mL). This mixture was stirred for 4 hours at room temperature under nitrogen. After completion of the reaction, the reaction mixture was quenched and extracted with ethyl acetate (10 mL×3). The organic layers were combined, dried over Na_2SO_4 and concentrated under reduced pressure, and then purified by silica gel chromatograph to yield the desired product. The product distribution (k_H/k_D = 1.1) was analyzed by ^1H NMR.

Spectrum: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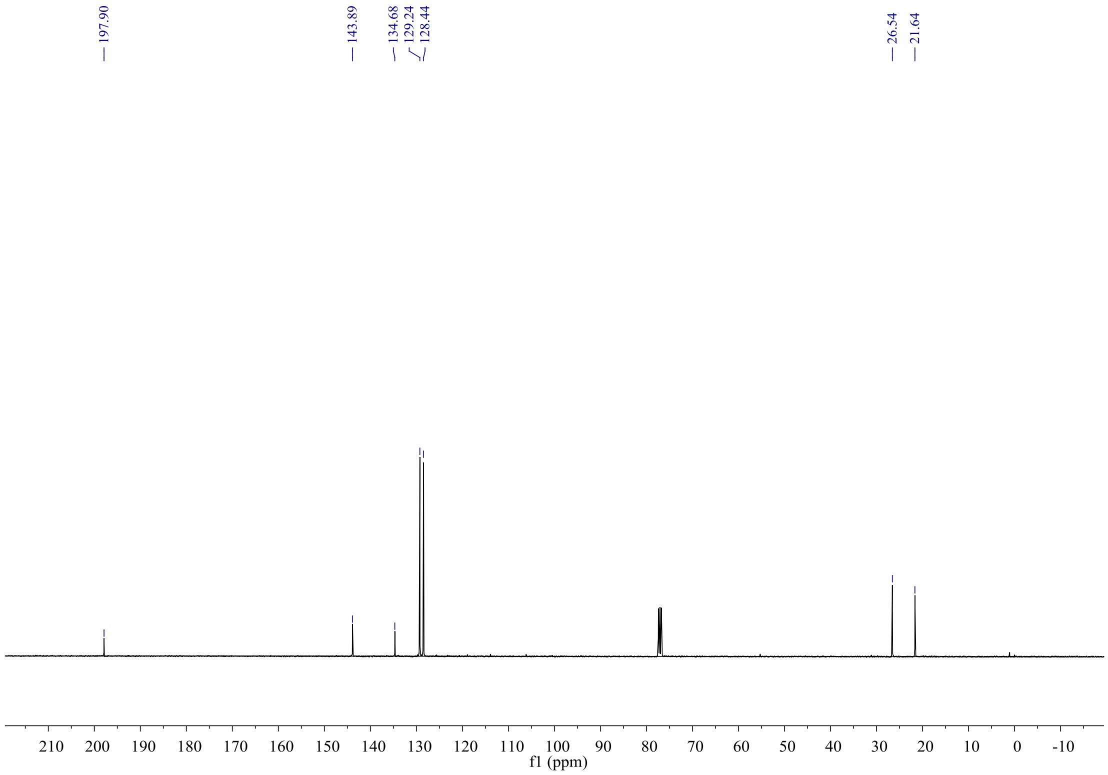
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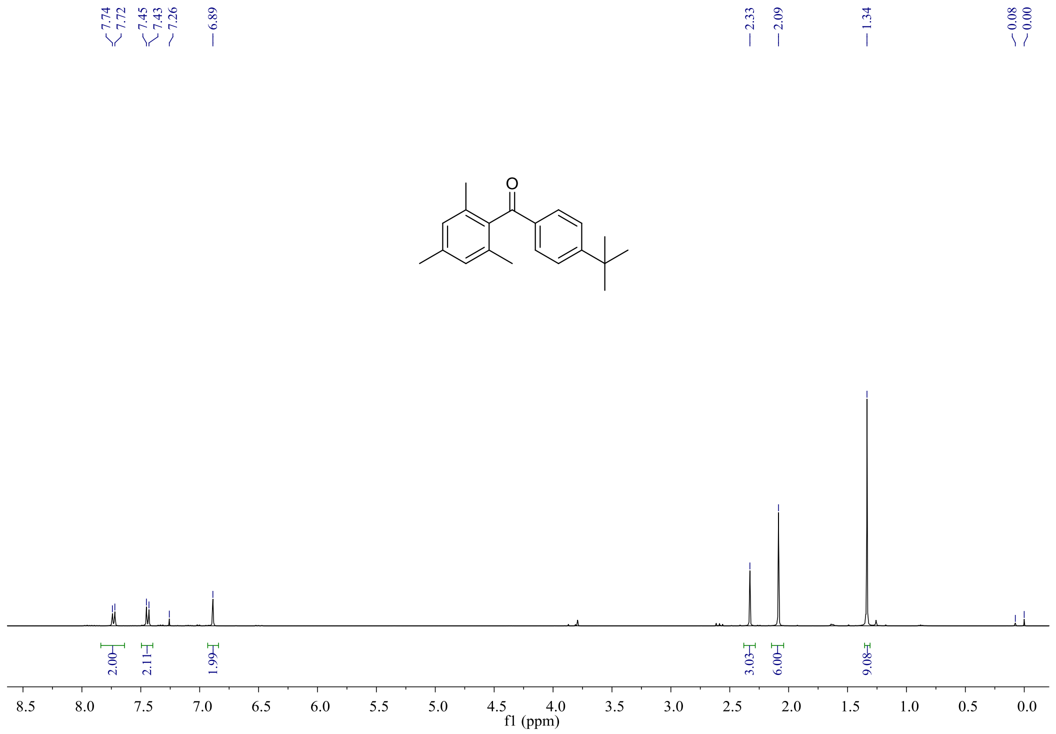
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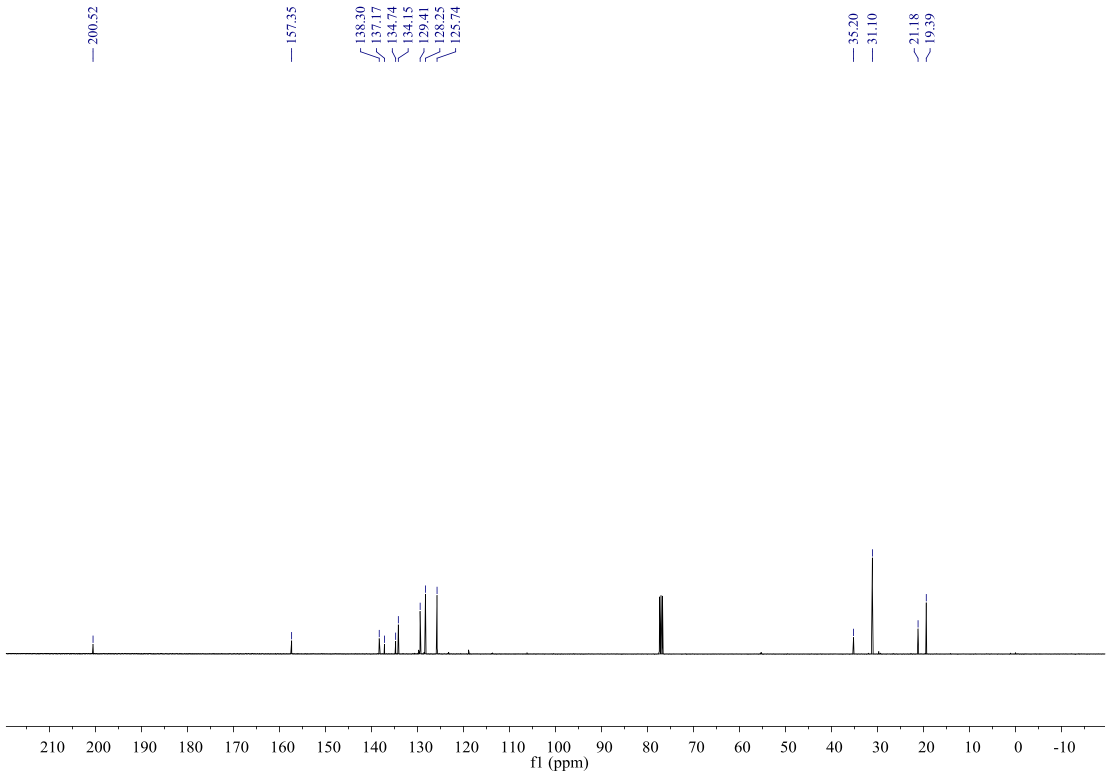
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