## COMMUNICATION

# The "kinetic capture" of an acylium ion from live aluminum chloride promoted Friedel–Crafts acylation reactions†

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AlCl$_3$ promoted Friedel–Crafts acylation between 4-*tert*-butylbenzoyl chloride and mesitylene was investigated. The donor–acceptor complex was observed as the major species. Kinetic investigation demonstrated that the reaction was first-order on the donor–acceptor complex and zero-order on ArH, suggesting that the donor–acceptor complex was not the true reactive species. However, the acylium ion was almost invisible with a fairly low concentration under live reaction conditions. It was approved as the true reactive species through kinetic data ("kinetic capture") in the AlCl$_3$ promoted Friedel–Crafts acylation reaction.

Aluminum chloride promoted Friedel–Crafts acylation is a classical textbook reaction.[1–5] It is generally employed as one of the most effective strategies for carbon–carbon bond formation, especially for the synthesis of aryl ketones and heterocyclic aromatic ketones.[6–10] From a mechanistic aspect, the first picture that comes into one's mind is usually a typical electrophilic aromatic-substitution process. However, in such an ancient chemistry, the related mechanistic investigation aiming at AlCl$_3$ promoted Friedel–Crafts acylation is relatively rare.

In textbooks, two pathways were usually presented in the AlCl$_3$ promoted Friedel–Crafts acylation reaction.[3,11,12] As shown in Scheme 1, the key to differentiate one pathway from another is the reactive electrophile. In path I, the donor–acceptor complex **I** is assigned as the reactive electrophile to react with ArH (eqn (1)) and the following step is a deprotonation process (eqn (2)). In path II, acylium ion **II** is regarded as the reactive electrophile instead (eqn (4)).[5,13–16]

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Scheme 1 Deduced rate laws from different pathways in the Friedel–Crafts acylation reaction.

Early research revealed that both **I** and **II** could be formed when AlCl$_3$ reacted with acyl halide.[17–22] In a solvent with a high dielectric constant like nitrobenzene, **I** was the major

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species, whereas **II** could be observed only in a tiny amount. In a low dielectric constant solvent like chloroform, only **I** is present.[18,20] Meanwhile, Susz discovered that **II** was stable and was the major species in solids at low temperature when AlCl₃ reacted with acyl chloride.[19] The existence of the two species was well confirmed, while their reactivities towards ArH were not clear. Hence, it remains problematic to establish which one is the reactive electrophile in the AlCl₃ promoted Friedel–Crafts acylation reaction.

As for the true reactive species in Friedel–Crafts acylation, they were mainly identified relying on a special Lewis acid, acylation reagents and solvents.[16,23,24] For example, from the fluoride method or the silver salt method, an acylium ion crystal has been prepared and was established as the reactive electrophile in $SO_2$ and HF solutions by Olah.[25] Cook proposed that $(PhCO)_2O{\rightarrow}(BF_3)_3$ was the reactive electrophile in $BF_3$ induced Friedel–Crafts acylation with benzoic anhydride.[26,27] In AlCl₃-catalyzed Friedel–Crafts benzoylation of benzene, Brown proposed that both the acylium ion and the donor–acceptor complex **I** could be the reactive electrophile with benzoyl chloride as the solvent.[28] F. Effenberger supported an acylium ion as the reactive electrophile between aromatic compounds and aroyl triflates without the Friedel–Crafts catalyst.[29] However, for AlCl₃ promoted Friedel–Crafts acylation reactions, it remains a challenge to confirm the true active species, especially under live reaction conditions. Herein, we communicate our results in "capturing" the reactive electrophile through a kinetic study from a live AlCl₃ promoted acylation.

Initially, AlCl₃ 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 AlCl₃, 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 methods.[13,17–21,27,30–32] When toluene was added, as shown in Fig. 1, the bands at 1583 cm⁻¹ (C), 1548 cm⁻¹ (D), which were assigned as the AlCl₃ adduct of *p*-methylacetophenone, appeared proportionally (Fig. S1B and S2†). In the 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.[13–15,25,31,33] Therefore, how to distinguish these two high reactive species and "capture" the true reactive electrophile deserved to be further discussed.

In both pathways, deprotonation is the last step (eqn (2) and (5)). KIE experiment (eqn (6)) was performed and $k_D/k_H = 1.1$, revealing that the deprotonation was not the rate-limiting step. Namely, the rate-limiting step should be assigned to the process prior to deprotonation. Regarding the two pathways, if the reaction follows path I and **I** is the reactive species to react with ArH, the rate law would be: rate = $k$[**I**][ArH] (shown in Scheme 1), and the overall reaction will always exhibit a first-order kinetic behavior on [ArH] and first-order on [**I**]. While if the **II** is the reactive intermediate, according to the *Steady-State*
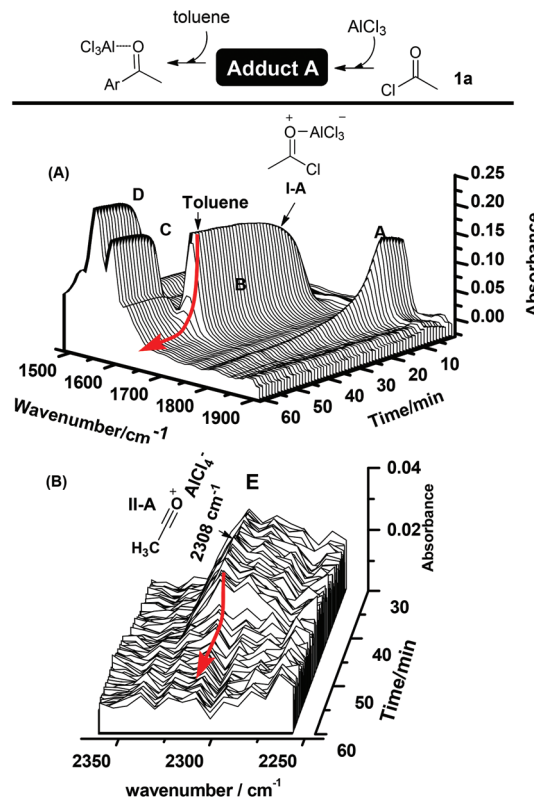


**Fig. 1** 3D-profile of the reaction between AlCl₃ (0.5 M), **1a** (0.5 M) and toluene (0.5 M) in 1,2-dichloroethane (4 mL) at −10 °C through *in situ* IR.

*Approximate Model*, the rate law could be more complicated. If the electrophilic reaction with ArH is the rate-limiting step (Scheme 1, path 2 eqn (4)), which means $k'_{-1} \gg k'_2[\text{ArH}]$, the rate law could be simplified as shown in Scheme 1 (1) and the reaction rate is dependent on [ArH] and [**I**]. If the transformation from **I** to **II** is the rate-limiting step (Scheme 1, path 2 eqn (3)), which means $k'_{-1} \ll k'_2[\text{ArH}]$, the reaction rate will be independent of [ArH] and first-order kinetic on [**I**]. In other words, kinetic differences exist in the two pathways. By choosing proper substrates, the reaction rate law of eqn (3) and (4) could be switched from one kinetic behavior to the other if the reaction follows pathway II.

On the basis of the above understanding, further experiments were carried out in this AlCl₃ promoted acylation between **1a** and toluene. As shown in Fig. 2, plotting $1/(c_0 - c)$ *vs.* $t$ resulted in a line, suggesting that this reaction exhibits a second-order kinetic behavior. The rate law was: rate = $k$[**A**][toluene] (Fig. S3–S7†). As shown in Fig. 1, the major species in **A** was **I-A**, while **II-A** was almost invisible. Namely, [**A**] was approximately equal to [**I-A**]. Therefore, rate ≈ $k$[**I-A**][toluene]. The kinetic result could be fitted well with that of the two pathways. In this case, the two pathways could not be differentiated from each other in this AlCl₃ promoted acylation between acetyl chloride and toluene.

According to the mechanistic discussion, the key to the kinetic differences in the two paths is that the rate-limiting step could be varied when employing different substrates.
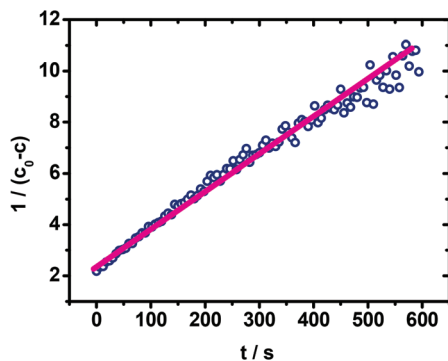
$k_D/k_H = 1.1$



**Fig. 2** 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 ($c_0$: initial concentration of toluene, $c$: concentration of toluene in the process of the reaction).
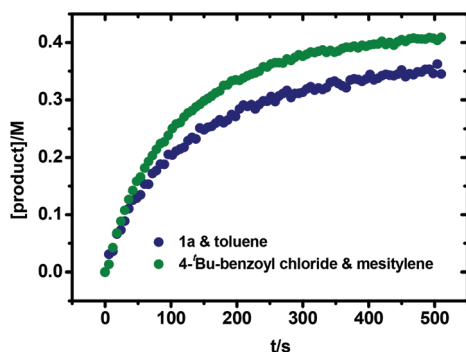


**Fig. 3** AlCl$_3$ promoted Friedel–Crafts acylation of ArH (0.5 M) and RCOCl (0.5 M) in 1,2-dichloroethane (4 mL) at −30 °C.

Mesitylene is usually regarded as a stronger nucleophile which might accelerate the reaction in eqn (4) and 4-*tert*-butylbenzoyl chloride is considered a poorer electrophile which might slow down the reaction in eqn (3). Therefore, the reaction between mesitylene instead of toluene and 4-*tert*-butylbenzoyl chloride instead of **1a** was examined for further kinetic studies. Compared with the acylation between **1a** and toluene (Fig. 3, blue line), the reaction was also performed as a smooth process at −30 °C (Fig. 3, green line). Therefore, the kinetic studies for AlCl$_3$ promoted Friedel–Crafts acylation between 4-*tert*-butylbenzoyl chloride **1b** and mesitylene were performed in detail (Fig. 4).

AlCl$_3$ promoted Friedel–Crafts acylation between **1b** and mesitylene in 1,2-dichloroethane at −30 °C was carried out and monitored through *in situ* IR. Plotting $\ln(c_0 - c)$ *vs.* $t$ obtained a linear relationship, suggesting that this reaction exhibited a first-order kinetic behavior, which was completely different from the kinetic results using toluene and **1a** (Fig. 4). As shown in Fig. 5, plotting initial rate *vs.* [Adduct **B**] showed a linear relationship, indicating that the reaction was first-order
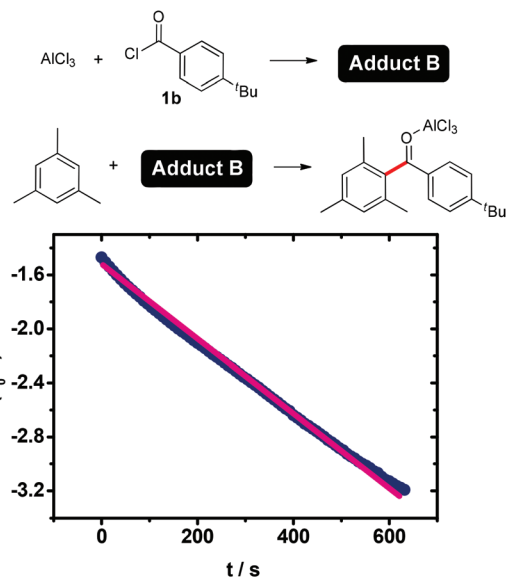




**Fig. 4** Plotting $\ln(c_0 - c)$ *vs.* $t$ for AlCl$_3$ promoted Friedel–Crafts acylation between **1b** (0.23 M) and mesitylene (0.23 M) in 1,2-dichloroethane (4 mL) at −30 °C ($c_0$: initial concentration of mesitylene; $c$: concentration of mesitylene).
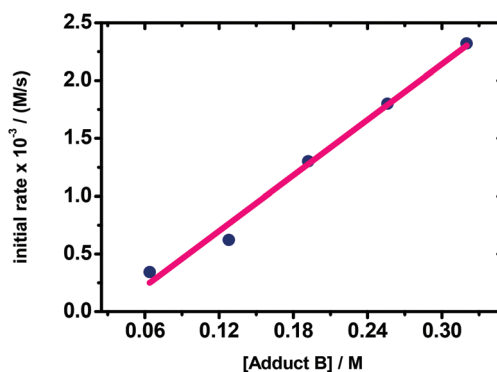


**Fig. 5** Kinetic plots of the reactions of AlCl$_3$ promoted Friedel–Crafts acylation between mesitylene (0.125 M) and different concentrations of **B** in 1,2-dichloroethane (4 mL) at −30 °C (concentrations of **B**: 0.064 M, 0.192 M, 0.128 M, 0.256 M, 0.320 M).

on [**B**]. When the concentration of mesitylene was different, the Friedel–Crafts acylation showed unvaried initial rates (Fig. 6). In other words, [ArH] is not in the rate law!

From the kinetic results above, the reaction rate law can be described as: rate = $k$[**B**]. This result revealed that the reaction between **1b** and mesitylene exhibited different kinetic behavior from the reaction between **1a** and toluene. In other words, employing different substrates could result in different kinetics. Therefore, path I in which the donor–acceptor complex **I** was the reactive electrophile was excluded.

As shown in Fig. 7, the bands at 1575 cm$^{-1}$ and 1547 cm$^{-1}$ were assigned as **I-B** which was the major species in **B**. Moreover, a band at 2383 cm$^{-1}$ was also observed which might be characteristic absorption of 4-*tert*-butylbenz-acylium ion **II-B**. **II-B** was almost invisible compared with **I-B**. Therefore, [**B**] ≈ [**I-B**] and rate ≈ $k$[**I-B**]. The kinetic data could be fitted
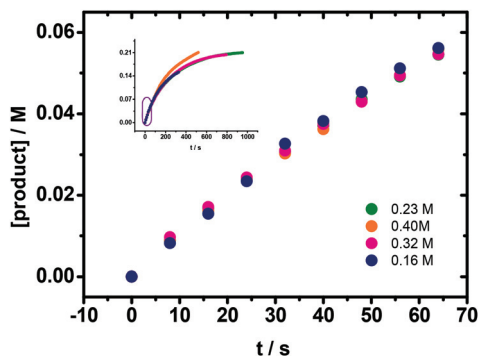
**Fig. 6** Kinetic plots of the reactions of AlCl₃ promoted Friedel–Crafts acylation between **B** (0.23 M) and different concentrations of mesitylene in 1,2-dichloroethane (4 mL) at −30 °C ([mesitylene]: 0.16 M, 0.23 M, 0.32 M, 0.40 M).
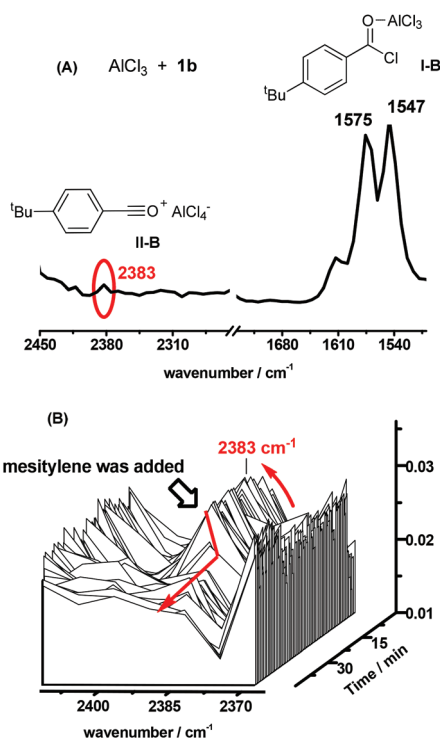


**Fig. 7** A: IR absorption of a mixture of AlCl₃ and **1b**; B: 3D-profile of the reaction between AlCl₃ (0.23 M), **1b** (0.23 M) and mesitylene (0.23 M) in 1,2-dichloroethane (4 mL) at −30 °C through *in situ* IR.

well with path II in Scheme 1 (2). The rate-limiting step was assigned to eqn (3), in which the donor–acceptor complex **I** was isomerized to the acylium ion (Scheme 1, Path II). Namely, the steady state might be **I-B** in the overall reaction. And indeed, **I-B** decreased smoothly with the formation of the product. However, **II-B** disappeared instantly when mesitylene was added (Fig. 7(B)). This phenomenon supported that **II-B** is an active electrophile to react with mesitylene in a facile process. Once the **II-B** was formed, it would be consumed immediately and its concentration limited the detection by IR. Consequently, pathway II in this transformation was favored.

Above all, both the acylium ion (at 2308 cm⁻¹ for **1a** or 2383 cm⁻¹ for **1b**) and the donor–acceptor complex **I** (at 1653 cm⁻¹ or 1575 cm⁻¹) were detected in our model reactions. Compared with the donor–acceptor complex **I**, the acylium ion existed in a fairly low concentration. As an almost invisible species, it was supported as the true active species.

## Conclusions

AlCl₃ promoted Friedel–Crafts acylation reactions were monitored by *in situ* IR. The donor–acceptor complex **I** could be observed as the major species. With the reaction between **1b** and mesitylene in 1,2-dichloroethane as a model, kinetic studies were performed. First order on [**I-B**] and zero order kinetic on [mesitylene] were identified. The kinetic results established that [ArH] is not involved in the rate law and the donor–acceptor complex **I** was ruled out to be an active electrophile to directly react with ArH. Almost invisible acylium ions **II** were narrowly observed and were also approved ("capture") by kinetic studies as a real active species. Remarkably, this "kinetic capture" strategy allows the first acquisition of direct kinetic evidence to support the reactive electrophile in this AlCl₃ promoted Friedel–Crafts acylation reaction.

## Notes and references

1  G. A. Olah, *Friedel–Crafts and Related Reactions*, Interscience Publishers, New York, 1963.

2  R. Bruckner, *Advanced Organic Chemistry: Reaction Mechanisms*, Harcourt/Academic Press, San Diego, 2002.

3  J. McMurry, *Organic Chemistry*, Thomson Brooks/Cole, Belmont, CA, 7th edn, 2008.

4  R. T. Morrison and R. N. Boyd, *Organic Chemistry*, Prentice Hall, Englewood, Cliffs, N.J., 6th edn, 1992.

5  G. A. Olah, *Friedel–Crafts Chemistry*, Wiley, New York, 1973.

6  Z. Wang and B. Gao, *J. Mol. Catal. A: Chem.*, 2010, **330**, 35–40.

7  C. Friedel and J. M. Crafts, *Compt. Rend.*, 1877, **84**, 1450–1454.

8  T.-X. Liu, F.-B. Li and G.-W. Wang, *Org. Lett.*, 2011, **13**, 6130–6133.

9  G. A. Olah, O. Farooq, S. M. F. Farnia and J. A. Olah, *J. Am. Chem. Soc.*, 1988, **110**, 2560–2565.

10  R. A. Wolf, *Org. Process Res. Dev.*, 2008, **12**, 23–29.

11  F. P. DeHaan, W. D. Covey, G. L. Delker, N. J. Baker, J. F. Feigon, D. Ono, K. D. Miller and E. D. Stelter, *J. Org. Chem.*, 1984, **49**, 3959–3963.

12  P. H. Gore, *Chem. Rev.*, 1955, **55**, 229–281.

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*Org. Biomol. Chem.*, 2013, **11**, 1810–1814 | **1813**

13 D. Cassimatis, J. P. Bonnin and T. Theophanides, *Can. J. Chem.*, 1970, **48**, 3860–3871.

14 G. A. Olah, W. S. Tolgyesi, S. J. Kuhn, M. E. Moffatt, I. J. Bastien and E. B. Baker, *J. Am. Chem. Soc.*, 1963, **85**, 1328–1334.

15 M. G. Davlieva, S. V. Lindeman, I. S. Neretin and J. K. Kochi, *New J. Chem.*, 2004, **28**, 1568–1574.

16 M. G. Davlieva, S. V. Lindeman, I. S. Neretin and J. K. Kochi, *J. Org. Chem.*, 2005, **70**, 4013–4021.

17 F. Seel, *Z. Anorg. Chem.*, 1943, **250**, 351.

18 B. P. Susz and I. Cooke, *Helv. Chim. Acta*, 1954, **37**, 1273–1280.

19 B. P. Susz and J. J. Wuhrmann, *Helv. Chim. Acta*, 1957, **40**, 971–980.

20 D. Cook, *Can. J. Chem.*, 1959, **37**, 48–53.

21 L. K. Tan and S. Brownstein, *J. Org. Chem.*, 1983, **48**, 302–306.

22 B. Chevrier and R. Weiss, *Angew. Chem., Int. Ed. Engl.*, 1974, **13**, 1–10.

23 M. M. T. Anous, M. M. El-Banna and A. M. Ahmed, *Proc. Pak. Acad. Sci.*, 1992, **29**, 27–37.

24 I. Hashimoto, *Nippon Kagaku Kaishi*, 1982, 1179–1186.

25 G. A. Olah, S. J. Kuhn, W. S. Tolgyesi and E. B. Baker, *J. Am. Chem. Soc.*, 1962, **84**, 2733–2740.

26 D. Cook, *Can. J. Chem.*, 1961, **40**, 480–485.

27 D. Cook, *Can. J. Chem.*, 1961, **40**, 445–448.

28 H. C. Brown and F. R. Jensen, *J. Am. Chem. Soc.*, 1958, **80**, 2291–2296.

29 F. Effenberger, J. K. Eberhard and A. H. Maier, *J. Am. Chem. Soc.*, 1996, **118**, 12572–12579.

30 S. Csihony, H. Mehdi, Z. Homonnay, A. Vertes, O. Farkas and I. T. Horvath, *J. Chem. Soc., Dalton Trans.*, 2002, 680–685.

31 S. Csihony, H. Mehdi and I. T. Horvath, *Green Chem.*, 2001, **3**, 307–309.

32 S. Csihony, A. Bodor, J. Rohonczy and I. T. Horvath, *J. Chem. Soc., Perkin Trans. 1*, 2002, 2861–2865.

33 F. P. Boer, *J. Am. Chem. Soc.*, 1968, **90**, 6706–6710.