## **Reversible** ArS<sub>E</sub> Aroylation of Naphthalene Derivatives

Akiko Okamoto and Noriyuki Yonezawa\*

Department of Organic and Polymer Materials Chemistry, Tokyo University of Agriculture and Technology, 2-24-16 Naka-machi, Koganei, Tokyo 184-8588

(Received July 2, 2009; CL-090624; E-mail: yonezawa@cc.tuat.ac.jp)

Reversible  $ArS_E$  aroylation has been observed in the reaction of 2,7-dimethoxynaphthalene (1) with 4-chlorobenzoic acid/acid chloride 2 with the aid of discrete acidic mediators. The reaction readily gives 1-aroylated-, 3-aroylated-, and 1,8-diaroylated products. The product distribution clearly shows dependence on the kind and strength of the acidic mediators and the time-course of the distribution manifests dearoylation of the productive aroylnaphthalenes. These reaction behaviors including acid-strength-dependent reversibility are well interpreted from the viewpoint of highly congested noncoplanar geometry of the polyaromatic ketone products.

Electrophilic aromatic substitution  $(ArS_F)$  is one of the most effective protocols for C-C bond formation in addition to metalcatalyzed coupling methods. The Friedel-Crafts C-C bond formation<sup>1</sup> is a representative  $ArS_E$  reaction and still receives continued interests.<sup>2</sup> This well-known reaction is divided into two distinct types, i.e., alkylation and acylation. The latter is further categorized as alkanoylation giving alkyl aryl ketones and aroylation affording diaryl ketones. Reactivity and successibility in Friedel-Crafts reactions are recognized to depend substantially on the electronic stability of the cationic intermediate and electron density of the aromatic substrates. The rather stable acylium ions slowly undergo acylation and the resulting ketones are almost inert to prolonged acylation due to the strong electronwithdrawing effect of the ketonic carbonyl group introduced. This behavior is distinct from alkylation. On the other hand, there is another dichotomy of regio-descrimination in ArS<sub>E</sub> reactions as observed for the  $\alpha$ - and  $\beta$ -substitution of naphthalene derivatives, which is concerned with a reversible substitution process to some extent. Gore and his co-workers have proposed that the Friedel–Crafts  $\alpha$ -alkylation of naphthalene is essentially reversible.<sup>3</sup> Contrarily, reversible alkanoylation has been little observed except for acetyl group transfer<sup>4,5</sup> and the reversible aroylation has been seldom reported.<sup>5,6</sup> The virtual irreversibility of aroylation is probably due to the large resonance stabilization by conjugation of the aryl-aryl ketone linkage.<sup>7-9</sup>

In the course of the authors' investigation to achieve consecutive and regioselective dual  $ArS_E$  aroylation utilizing the electronic and steric characteristics of polyaromatic molecules,<sup>10</sup> a unique feature of  $ArS_E$  aroylation of a naphthalene core is disclosed.

In this letter, the authors wish to introduce hitherto-unknown reversible aroylation behavior in the acid-mediated reaction of 2,7-dimethoxynaphthalene (1) and 4-chlorobenzoic acid/acid chloride 2 and discuss the reaction governing factors from the aspect of noncoplanar and highly congested structure of the produced molecules.

Table  $1^{11}$  shows the results of the reaction of **1** and **2** with several acidic mediators such as a typical Friedel–Crafts cata-

Table 1. ArS<sub>E</sub> aroylation of 2,7-dimethoxynaphthalene (1) with 4-chlorobenzoic acid derivatives  $2^{a}$ 

MeO	$\frac{\text{ArCOX } X = \text{Cl } (2a)}{\text{Acidic media}}$ $\frac{\text{ArCOX } X = \text{Cl } (2a)}{\text{Arcidic media}}$ $\frac{\text{ArCOX } X = \text{Cl } (2a)}{\text{Arcidic media}}$	), OH ( <b>2b</b> ) ator M <sub>6</sub> H <sub>4</sub>	eO 3–5	OMe 3 R <sup>3</sup> 4 5	R <sup>1</sup> ArCO ArCO H	R <sup>8</sup> H ArCO H	R <sup>3</sup> H H ArCO
Entry	Acidic	Acyl-	Temp	Time	Yield <sup>b</sup> /%		/%
	mediator	donor	$/^{\circ}C$	/h	3	4	5
$1^{c}$	AlCl <sub>3</sub> (3 equiv) <sup>d</sup>	2a	0	2	7	0	0
2 <sup>e</sup>	AlCl <sub>3</sub> (3 equiv) <sup>d</sup>	2a	0	2	70	12	0
3°	AlCl <sub>3</sub> (1 equiv) <sup>d</sup>	2a	0	6	80	5	0
$4^{\mathrm{f}}$	PPA	2b	70	2	0	1	7
$5^{\rm f}$	PPA	2b	100	2	0	0	10
6 <sup>g</sup>	P <sub>2</sub> O <sub>5</sub> -MsOH	2b	60	2	0	75	23
7 <sup>h</sup>	TfOH (3 equiv) <sup>d</sup>	2a	50	24	0	58	39

<sup>a</sup>Reaction conditions: 2,7-dimethoxynaphthalene (1, 0.2 mmol), acyl-donor **2** (0.4 mmol), N<sub>2</sub> atmosphere. <sup>b</sup>Isolated yield. <sup>c</sup>In CH<sub>2</sub>CH<sub>2</sub>Cl<sub>2</sub> (2.0 mL). <sup>d</sup>Against 0.4 mmol of acyl-donor **2**. <sup>e</sup>In nitrobenzene (2.0 mL). <sup>f</sup>PPA (6.4 g). <sup>g</sup>P<sub>2</sub>O<sub>5</sub>–MsOH (0.8 mL). <sup>h</sup>In CH<sub>2</sub>CH<sub>2</sub>Cl<sub>2</sub> (0.5 mL).

lyst, a direct condensation reagent, and a Brønsted superacid. When **1** was allowed to react with **2a** in the presence of AlCl<sub>3</sub>, **3** was formed with high selectivity (Entries 1–3). Polyphosphoric acid (PPA)-mediated reaction of **1** with **2b** gave a mixture of **4** and **5** or solely **5** in low conversions, respectively (Entries 4 and 5). On the other hand, both phosphorus(V) oxide–methanesulfonic acid mixture ( $P_2O_5$ –MsOH)<sup>12</sup> and trifluoromethanesulfonic acid (TfOH) achieved sufficient conversion of **1** into the aroylated products **4** and **5** with appreciably different product distributions (Entry 6 vs. 7).

The time-course of the product distributions in the aroylation reaction with different Brønsted acid strengths also shows a characteristic feature of this transformation (Figure 1).<sup>11</sup> With 5% TfOH–95% TFA, the fraction of **3** maintains high conversion throughout the reaction and further aroylation scarcely proceeds (Figure 1a). With 50% TfOH–50% TFA, **4** increases rapidly at the early stage followed by abrupt decrease and **5** increases with time, whereas **3** is produced only in the early period and decreases simply afterward (Figure 1b). In the presence of TfOH, **4** and **5** increase gradually in a constant ratio with steady decrease of **3** that is formed rapidly at the quite early stage (Figure 1c).

These results clearly manifest the reversibility of this  $ArS_E$  aroylation, i.e., progress of dearoylation of **3** and **4** (Scheme 1). The increase of acid strength essentially accelerates dearoylation of **3** and **4**, whereas that of **4** is depressed under superacidic conditions.

The ready formation of the congested polyaromatic molecule of **4** and the dynamic interconvertibility of  $ArS_E$  aroylation of these molecules are well interpreted from electronic and steric factors. In the X-ray crystal structures of **3**<sup>13</sup> and **4**, <sup>14</sup> the aroyl groups are twisted almost perpendicularly but a little tiltedly to-



Figure 1. The time-courses of the distribution of the aroylated products by different Brønsted acid strengths ( $\diamond$ : 1,  $\blacksquare$ : 3,  $\blacktriangle$ : 4, and  $\diamond$ : 5): a) 5% TfOH–95% TFA, b) 50% TfOH–50% TFA, c) TfOH.



Figure 2. X-ray crystal structures of 1-monoaroylnaphthalene 3 (left) and 1,8-diaroylnaphthalene 4 (right).

ward exo sides against the naphthalene rings with far larger torsion angles than the  $\beta$ -substituted isomer of  $3^{15}$  (Figure 2).<sup>11</sup> Precisely, the torsion angle between the carbonyl groups and the naphthalene ring in 4 is somewhat smaller than that of 3 and two aroyl groups in 4 are approximately antiparallel to each other, which suggests appreciable steric hindrance in 4. Hence, successive progress of second peri-aroylation of 3 affording 4 is plausibly enabled at least by the same electronically activated state of the 8-position of 3 with that of 1. As a consequence, the electron-withdrawing effect of the 1-aroyl group of 3 scarcely functions through the almost perpendicularly twisted ketone.

Simultaneously, the absence of the coplanar geometry of aromatic ketone moiety presumably gives little conjugation stabilization so that the Brønsted acid-mediated dearoylation promptly progresses. The susceptibility to dearoylation of 3 and 4 and the acid-strength dependent behavior are also explained from the viewpoint of structural characteristics. Contrary to expectation of larger susceptibility to dearoylation of 4 with apparently greater congestion than that of 3, dearoylation of 4 is depressed in the strong acidic-superacidic region, whereas that of 3 is accelerated with acid strength. In the superacidic region, diprotonated species of 4 presumably have dual chelation of MeO oxygen...H<sup>+</sup>...carbonyl oxygen, which makes two chlorophenyl groups lean conrotatory toward the endo direction of the naphthalene plane. This conformational fixation plausibly retards reversion to  $\sigma$ -complex then to  $\pi$ -complex, resulting in suppression of departure of aroylium ion.

From the point of synthesis of peri-aroylnaphthalenes, the highest efficiency of yield of **4** from **1** was achieved by the  $P_2O_5$ -MsOH-mediated direct condensation. In this system, the aroylium ion equivalent acid-anhydride-like species as electrophile attacks on the naphthalene ring at electronically activated peri-carbons. This extended electrophile conveniently receives strong electronic direction achieving the high peri-regioselectivity. At the same time, the bulkiness of the electrophile gives a certain amount of **5**. On the other hand, dearoylation of **3** and **4** is retarded owing to the rather weak Brønsted acidic function of  $P_2O_5$ -MsOH. On the whole, kinetic peri-aroylated product is preferentially obtained.

The selective formation of **3** by treatment with excess AlCl<sub>3</sub> is explained by predominant electrophilic attack at the 1-position of **1** followed by precipitation of complex with AlCl<sub>3</sub> before dearoylative equilibrium. The apparently conventional result of sole formation of  $\alpha$ -monoaroylated product by treatment of **1** with a typical Friedel–Crafts catalyst might have disturbed the findings of this facile dual peri-aroylation and quite unique Brønsted acid-mediated dearoylation behavior in the modified Friedel–Crafts acylation employing direct condensation reagent or superacid.

In conclusion, the authors have found 1) dual  $ArS_E$  aroylation on peri-carbons in a naphthalene core, 2) Brønsted acidmediated dearoylation of  $\alpha$ -naphthyl aryl ketones, and 3) depression of dearoylation of 1,8-diaroylated naphthalene in the superacidic region. These behaviors are well interpreted from the viewpoint of structural characteristics of the noncoplanar peri-aroylated products and the unique functionalities of the acidic mediators employed.

## **References and Notes**

- G. A. Olah, *Friedel–Crafts and Related Reactions*, Wiley-Interscience, New York and London, **1963–1964**, Vol. I–IV.
- a) A. Zarei, A. Hajipour, L. Khazdooz, *Tetrahedron Lett.* 2008, 49, 6715.
   b) M. Sarvari, H. Sharghi, J. Org. Chem. 2004, 69, 6953.
- 3 a) P. H. Gore, ref 1, Vol. I, p. 25. b) P. H. Gore, Chem. Rev. 1955, 55, 229.
- a) P. H. Gore, M. Jehangir, J. Chem. Soc., Perkin Trans. 1 1979, 3007. b) C.
   Giordano, M. Villa, R. Annunziata, Synth. Commun. 1990, 20, 383. c) L.
   Levy, S. Pogodin, S. Cohen, I. Agranat, Lett. Org. Chem. 2007, 4, 314.
- 5 S. Pivsa-Art, K. Okuro, M. Miura, S. Murata, M. Nomura, J. Chem. Soc., Perkin Trans. 1 1994, 1703.
- 6 a) I. Agranat, D. Avnir, J. Chem. Soc., Chem. Commun. 1973, 362. b) I. Agranat, Yu. S. Shih, Y. Bentor, J. Am. Chem. Soc. 1974, 96, 1259.
- 7 C. A. Buehler, D. E. Pearson, Survey of Organic Syntheses, Wiley-Interscience, New York, 1970, p. 653.
- 8 R. O. C. Norman, R. Taylor, *Electrophilic Substitution in Benzenoid Compounds*, Elsevier, Amsterdam, **1965**, p. 174.
- 9 N. L. Allinger, M. P. Cava, D. C. De Jongth, C. R. Johnson, N. A. Lebel, C. L. Stevens, *Organic Chemistry*, Worth, New York, **1971**, p. 358.
- a) N. Yonezawa, T. Ikezaki, H. Nakamura, K. Maeyama, *Macromolecules* 2000, 33, 8125. b) N. Yonezawa, S. Miyata, T. Nakamura, S. Mori, Y. Ueha, R. Katakai, *Macromolecules* 1993, 26, 5262. c) N. Yonezawa, S. Mori, S. Miyata, Y. Ueha-Anyashiki, S. Wu, K. Maeyama, *Polym. J.* 2003, 35, 998. d) A. Okamoto, M. Yamazaki, K. Maeyama, H. Oike, H. Saito, Y. Murakami, N. Yonezawa, *React. Funct. Polym.* 2008, 68, 340.
- 11 Supporting Information is available electronically on the CSJ-Journal Web site, http://www.csj.jp/journals/chem-lett/index.html.
- 12 P. E. Eaton, G. R. Carlson, J. T. Lee, J. Org. Chem. 1973, 38, 4071.
- 13 R. Mitsui, K. Nakaema, K. Noguchi, A. Okamoto, N. Yonezawa, Acta
- Crystallogr., Sect. E 2008, 64, o1278.
  K. Nakaema, A. Okamoto, K. Noguchi, N. Yonezawa, Acta Crystallogr., Sect. E 2007, 63, o4120.
- 15 K. Nakaema, A. Okamoto, M. Imaizumi, K. Noguchi, N. Yonezawa, Acta Crystallogr., Sect. E 2008, 64, o612.