An Expedient Synthesis of Arene-fused Phthalimides from Morita–Baylis–Hillman Carbonates

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Recently, we reported synthesis of 3,4-diarylidene-N-phenylpyrrolidine-2,5-dione derivatives from Morita–Baylis–Hillman (MBH) carbonates. The compounds have been synthesized from MBH carbonates via the formation of MBH ylides, reaction with phenyl isocyanate to form amide ylides, and a subsequent acid-catalyzed stereoselective Wittig reaction with various aldehydes. More recently, amino-naphthalene has been synthesized from the amide ylide 2a via 6π-electrographic ring closure of the ketenimine intermediate, as shown in Scheme 1. As a continuing study, we reasoned out that 6π-electrocyclization reaction of 3,4-diarylidene-N-phenylpyrrolidine-2,5-dione 1 and a subsequent aerobic oxidation of intermediate II would afford furan fused phthalimide derivative 4a, as also shown in Scheme 1. Various arene-fused phthalimides have been synthesized and found their usefulness in the areas of dual fluorescent dyes as a probe for ratiometric detection of DNA, organic light-emitting devices, and for the synthesis of resonant dyes as a probe for ratiometric detection of DNA, organic light-emitting devices, and for the synthesis of dual fluorescent dyes as a probe for ratiometric detection of DNA.

Encouraged by the successful result, the reactions of 2a with various aromatic aldehydes were examined. We selected five-membered heteroaromatic aldehydes and naphthaldehydes that have small resonance energy, in order to overcome the high activation energy during the 6π-electrocyclization. The results are summarized in Table 1. The reaction of 2a with 2-thiophencarboxaldehyde (3b) afforded 4b in a similar yield (59%). The reactions with 5-methylfurural (3c) and 5-methyl-2-thiophencarboxaldehyde (3d) afforded 4c and 4d, respectively, in moderate yields (59 and 57%). The reaction of 3-furaldehyde (3e) gave 4e in a similar yield (62%). 1-Naphthaldehyde (3f) and 2-naphthaldehyde (3g) also afforded 4f and 4g in moderate yields (56 and 57%), respectively. In addition, other amide ylides 2b and 2c were prepared according to the reported method, and the reactions were also examined. The reactions of 4-chlorophenyl derivative 2b with 3c and 3d also afforded 4h (57%) and 4i (59%) in moderate yields, respectively.

However, the reaction of amide ylide 2c, bearing a 2-thienyl moiety, showed somewhat different result. The reaction of 2c and 3b afforded the desired product 4j in low yield (42%) along with benzo[j]thiophene 5 in appreciable amount (14%), as shown in Scheme 2. A dipolar interaction between the sulfur atom and phosphorous atom in 2c might facilitate an abstraction of amide proton and subsequent elimination of Ph3P=O to form a ketenimine intermediate. The ketenimine underwent 6π-electrocyclization reaction to produce 5, as already reported in our previous report.

It is also interesting to note that the reaction of 2c and 3a afforded a mixture of 4k and 4k’ (1:2, 35%) along with 5 (8%), as shown in Scheme 3. Although the stereochemistry of both double bonds of 3,4-diarylidene-N-phenylpyrrolidine-2,5-dione intermediate I (see Scheme 1) could be controlled under mild conditions (benzene, 80°C, 30 min) in our previous paper, the double bonds might be isomerized in part under the drastic conditions (ODCB, 160°C, 4 h), as shown in Scheme 3. Thus, both double bonds of furan and thiophene could be involved in a following 6π-electrocyclization reaction to produce 4k and 4k’.
Unfortunately, the separation of 4k and 4k’ was impossible and the ratio was determined based on its $^1$H NMR spectrum (see Supporting information). When we used benzaldehyde (3h) in the reaction of 2c, compound 4b was obtained in low yield (38%) along with 5 (11%). Compound 4b’ was not formed in an appreciable amount. The result clearly stated that the double bond of thiophene, that has small resonance energy as compared to that of benzene,\textsuperscript{7} was used preferentially in a $6\pi$-electrocyclization reaction.

As a next trial, the reaction of 2a and benzaldehyde (3h) was also examined. The resonance energy of benzene ring is larger than that of the above heteroaromatic rings (3a–3e) or naphthalene ring (3f and 3g);\textsuperscript{7} however, the reaction afforded 4l\textsuperscript{2} in a reasonable yield (38%) under the typical reaction condition (160 °C, 4 h). The yield of 4l was improved slightly to 44% under refluxing ODCB (180 °C, 4 h) condition, as shown in Scheme 4.

In summary, various arene-fused phthalimides were synthesized via one-pot reaction of amide ylides and aromatic aldehydes in the presence of AcOH in ODCB at 160 °C. The reaction involved $6\pi$-electrocyclization reaction of conjugated triene bearing an aromatic double bond and a following aerobic oxidation process.

### Experimental

#### Typical Procedure for the Synthesis of 4a

To a stirred mixture of amide ylide 2a (278 mg, 0.5 mmol) and 2-furaldehyde (3a, 72 mg, 0.75 mmol) in ODCB (1.5 mL) was added two drops of AcOH, and the reaction mixture was heated to 160 °C for 4 h under O$_2$ balloon atmosphere.
After removal of ODCB and column chromatographic purification process (hexanes/CH$_2$Cl$_2$, 1:1) compound 4a was obtained as a pale yellow solid, 104 mg (61%). Other compounds were synthesized similarly, and the selected spectroscopic data of 4a, 4d, 4e, and 4j are as follows.

**Compound 4a.** Yield 61%; pale yellow solid, mp 196–197°C; IR (KBr) 1717, 1373 cm$^{-1}$; $^1$H NMR (CDCl$_3$, 500 MHz) δ 6.89 (dd, $J = 2.3, 0.9$ Hz, 1H), 7.35–7.39 (m, 1H), 7.40–7.42 (m, 7H), 7.59–7.62 (m, 2H), 7.86 (d, $J = 2.3$ Hz, 1H), 8.08 (d, $J = 0.9$ Hz, 1H); $^{13}$C NMR (CDCl$_3$, 125 MHz) δ 107.4, 107.9, 122.0, 126.8, 128.1, 128.3, 129.1 (2C), 129.7, 129.9, 131.9, 133.5, 133.9, 136.0, 149.1, 157.3, 166.8, 167.0; ESIMS $m/z$ 340 [M$^+$$H$]. Anal. Calcd for C$_{22}$H$_{13}$NO$_3$: C, 77.87; H, 3.98; N, 3.95. Found: C, 77.74; H, 3.98; N, 3.95.

**Compound 4d.** Yield 57%; pale yellow solid, mp 233–234°C; IR (KBr) 1712, 1369 cm$^{-1}$; $^1$H NMR (CDCl$_3$, 500 MHz) δ 2.61 (s, 3H), 7.02 (s, 1H), 7.32–7.38 (m, 1H), 7.40–7.47 (m, 4H), 7.48–7.55 (m, 5H), 8.33 (s, 1H); $^{13}$C NMR (CDCl$_3$, 125 MHz) δ 16.7, 117.7, 122.8, 123.3, 126.8, 127.0, 127.9, 128.2, 128.7, 129.8, 132.0, 135.0, 136.1, 144.6, 144.8, 146.7, 166.9, 167.2; ESIMS $m/z$ 370 [M$^+$$H$]. Anal. Calcd for C$_{22}$H$_{14}$NO$_3$: C, 74.78; H, 4.09; N, 3.79. Found: C, 74.91; H, 4.33; N, 3.92.

**Compound 4e.** Yield 62%; white solid, mp 217–219°C; IR (KBr) 1715, 1373 cm$^{-1}$; $^1$H NMR (CDCl$_3$, 500 MHz) δ 7.05 (d, $J = 2.1$ Hz, 1H), 7.34–7.40 (m, 1H), 7.43–7.57 (m, 7H), 7.68–7.74 (m, 2H), 8.77 (d, $J = 2.1$ Hz, 1H), 8.20 (s, 1H); $^{13}$C NMR (CDCl$_3$, 125 MHz) δ 108.4, 116.9, 123.5, 126.6, 126.8, 128.0, 128.1, 129.2, 129.4, 130.3, 130.6, 132.0, 132.9, 149.5, 155.9, 166.8, 167.1; ESIMS $m/z$ 340 [M$^+$$H$]. Anal. Calcd for C$_{22}$H$_{14}$NO$_3$: C, 77.87; H, 3.86; N, 4.13. Found: C, 77.79; H, 4.04; N, 4.08.

**Compound 4j.** Yield 42%; pale yellow solid, mp 214–215°C; IR (KBr) 1717, 1368 cm$^{-1}$; $^1$H NMR (CDCl$_3$, 500 MHz) δ 7.22 (dd, $J = 5.1$, 3.6 Hz, 1H), 7.35–7.40 (m, 2H), 7.43–7.50 (m, 4H), 7.57 (dd, $J = 5.1$, 1.2 Hz, 1H), 7.62 (dd, $J = 5.6$, 0.8 Hz, 1H), 7.74 (d, $J = 5.6$ Hz, 1H), 8.47 (d, $J = 0.8$ Hz, 1H); $^{13}$C NMR (CDCl$_3$, 125 MHz) δ 118.7, 124.3, 125.3, 126.8, 127.2, 127.7, 127.9, 128.1, 129.1, 129.88, 129.91, 131.6, 131.9, 134.3, 144.6, 144.8, 166.4, 166.8; ESIMS $m/z$ 362 [M$^+$$H$]. Anal. Calcd for C$_{22}$H$_{14}$NO$_3$: C, 66.46; H, 3.07; N, 3.88. Found: C, 66.81; H, 3.34; N, 3.69.

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**Supporting Information.** Additional supporting information is available in the online version of this article.

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