

Facile insertion reaction of arynes into carbon–carbon σ -bonds

Hiroto Yoshida,* Masahiko Watanabe, Joji Ohshita, and Atsutaka Kunai*

*Department of Applied Chemistry, Graduate School of Engineering, Hiroshima University,
Higashi-Hiroshima 739-8527, Japan.*

Supplementary Information

General Remarks. All manipulations of oxygen- and moisture-sensitive materials were conducted with a standard Schlenk technique under a purified argon atmosphere. Nuclear magnetic resonance spectra were taken on a JEOL EX-270 (^1H , 270 MHz; ^{13}C , 67.8 MHz) spectrometer or a JEOL Lambda-400 (^1H , 400 MHz; ^{13}C , 99.5 MHz) spectrometer using residual chloroform (^1H) or CDCl_3 (^{13}C) as an internal standard. High-resolution mass spectra were obtained with a Hitachi M-80B spectrometer. The preparative recycling gel permeation chromatography was performed with GL Science PU 614 equipped with Shodex GPC H-2001L and -2002L columns (chloroform as an eluent). Column chromatography was carried out using Merck Kieselgel 60. Unless otherwise noted, commercially available reagents were used without purification. THF was distilled from sodium/benzophenone ketyl. 18-Crown-6 was recrystallized from distilled MeCN. KF (spray-dried) was vacuum dried at 100 °C for 12 h.

Aryne Precursors. 2-(Trimethylsilyl)phenyl triflate (**1a**),¹ 3-(trimethylsilyl)-2-naphthyl triflate (**1b**),² 4,5-dimethyl-2-(trimethylsilyl)phenyl triflate (**1c**),³ 6-(trimethylsilyl)-5-indanyl triflate (**1d**),³ and 3,6-dimethoxy-2-(trimethylsilyl)phenyl triflate (**1e**),³ 3-methoxy-2-(trimethylsilyl)phenyl triflate (**1f**)⁴ and 4-methyl-2-(trimethylsilyl)phenyl triflate (**1g**)⁵ were prepared according to literature procedures.

β -Dicarbonyl Compounds. All β -dicarbonyl compounds were commercially available, except for **2e** and **2f**, which were synthesized from the corresponding diols and malonyl dichloride by a literature method.⁶

Reaction of Arynes with β -Dicarbonyl Compounds. A General Procedure. To a THF solution (4.0 mL) of 18-crown-6 (0.127 g, 0.48 mmol), **1** (0.24 mmol) and **2** (0.20 mmol) was added KF (0.028 g, 0.48 mmol), and the resulting mixture was stirred at room temperature for the time specified in Schemes 1 and 2. The mixture was diluted with ethyl acetate, filtered through a Celite plug, washed three times with brine and dried over MgSO_4 . Evaporation of the solvent followed by silica-gel column chromatography or gel permeation chromatography gave the corresponding product.

Ethyl 2-(ethoxycarbonyl)phenylacetate (3aa).⁷ Isolated in 71% yield as a pale yellow oil: ¹H NMR (CDCl₃) 1.25 (t, *J* = 7.1 Hz, 3 H), 1.37 (t, *J* = 6.8 Hz, 3 H), 4.01 (s, 2 H), 4.16 (q, *J* = 7.0 Hz, 2 H), 4.33 (q, *J* = 7.2 Hz, 2 H), 7.25 (d, *J* = 7.7 Hz, 1 H), 7.36 (t, *J* = 7.5 Hz, 1 H), 7.47 (t, *J* = 7.5 Hz, 1 H), 8.02 (d, *J* = 7.7 Hz, 1 H); ¹³C NMR (CDCl₃) δ14.1, 14.2, 40.7, 60.7, 60.9, 127.3, 130.1, 130.9, 132.1, 135.8, 167.1, 171.5.

Butyl 2-(butoxycarbonyl)phenylacetate (3ab).⁷ Isolated in 70% yield as a colorless oil: ¹H NMR (CDCl₃) δ0.84-1.08 (m, 6 H), 1.24-1.81 (m, 8 H), 4.02 (s, 2 H), 4.09 (t, *J* = 6.8 Hz, 2 H), 4.27 (t, *J* = 6.8 Hz, 2 H), 7.19-7.57 (m, 3 H), 8.00 (d, *J* = 7.7 Hz, 1 H); ¹³C NMR (CDCl₃) δ13.65, 13.72, 19.0, 19.3, 30.6, 30.7, 40.6, 64.6, 64.8, 127.2, 130.9, 132.10, 132.13, 136.0, 167.2, 171.5.

2-(Benzoylmethyl)benzophenone (3ac).⁸ Isolated in 68% yield as a yellow oil: ¹H NMR (CDCl₃) δ4.62 (s, 2 H), 7.31-7.62 (m, 10 H), 7.83 (d, *J* = 8.5 Hz, 2 H), 7.95 (d, *J* = 8.5 Hz, 2 H); ¹³C NMR (CDCl₃) δ43.1, 126.2, 128.2, 128.5, 130.2, 130.4, 130.9, 132.0, 132.7, 133.0, 134.7, 136.8, 137.9, 138.3, 197.0, 198.3.

2-(Acetylmethyl)acetophenone (3ad).⁹ Isolated in 56% yield as a yellow oil: ¹H NMR (CDCl₃) δ2.29 (s, 3 H), 2.58 (s, 3 H), 4.02 (s, 2 H), 7.17 (dd, *J* = 0.9, 7.5 Hz, 1 H), 7.38 (dt, *J* = 1.5, 7.5 Hz, 1 H), 7.47 (dt, *J* = 1.5, 7.5 Hz, 1 H), 7.84 (dd, *J* = 1.4, 7.7 Hz, 1 H); ¹³C NMR (CDCl₃) δ28.6, 30.0, 127.3, 130.2, 132.2, 132.9, 135.1, 136.4, 201.0, 205.7.

7,8,9,10,11,12,13,14-Octahydro-17H-6,15-dioxa-benzocyclopentadecene-5,16-dione (3ae). Isolated in 61% yield as a white solid: ¹H NMR (CDCl₃) δ1.17-1.81 (m, 12 H), 4.00 (s, 2 H), 4.05 (t, *J* = 6.8 Hz, 1 H), 4.06 (t, *J* = 6.5 Hz, 1 H), 4.26 (t, *J* = 7.0 Hz, 1 H), 4.27 (t, *J* = 6.8 Hz, 1 H), 7.24 (d, *J* = 7.5 Hz, 1 H), 7.36 (t, *J* = 6.5 Hz, 1 H), 7.47 (t, *J* = 7.5 Hz, 1 H), 8.00 (d, *J* = 7.7 Hz, 1 H); ¹³C NMR (CDCl₃) δ25.8, 25.89, 25.92, 28.5, 28.56, 28.58, 28.64, 29.07, 29.11, 29.19, 29.21, 41.0, 64.76, 64.83, 65.08, 65.12, 127.3, 130.2, 130.3, 131.0, 132.16, 132.21, 132.22, 135.65, 135.74, 167.3, 167.4, 171.4.

7,8,9,10,11,12,13,14,15,16,17,18-Dodecahydro-21H-6,19-dioxa-benzocyclononadecene-5,20-dione (3af). Isolated in 49% yield as a white solid: ¹H NMR (CDCl₃) δ1.15-1.83 (m, 20 H), 4.00 (s, 2 H), 4.06 (t, *J* = 6.7 Hz, 2 H), 4.26 (t, *J* = 7.0 Hz, 2 H), 7.24 (d, *J* = 7.5 Hz, 1 H), 7.36 (dt, *J* = 1.2, 7.7 Hz, 1 H), 7.47 (dt, *J* = 1.5, 7.5 Hz, 1 H), 8.00 (d, *J* = 7.7 Hz, 1 H); ¹³C NMR (CDCl₃) δ25.8, 25.9, 25.96, 26.00, 28.56, 28.58, 28.60,

28.63, 29.3, 29.4, 29.5, 29.58, 29.61, 29.65, 29.70, 41.0, 64.9, 65.2, 127.3, 130.16, 130.20, 131.0, 132.16, 132.22, 135.68, 135.73, 167.3, 171.5.

3-(Benzoylmethyl)-2-naphthyl phenyl ketone (3bc). Isolated in 71% yield as a white solid: ^1H NMR (CDCl_3) δ 4.85 (s, 2 H), 7.41-8.04 (m, 16 H); ^{13}C NMR (CDCl_3) δ 43.5, 126.5, 127.4, 128.0, 128.2, 128.5, 128.8, 128.9, 130.5, 131.0, 131.1, 131.2, 131.46, 131.53, 132.7, 133.0, 134.3, 136.2, 136.9, 138.1, 197.5, 198.2.

2-(Benzoylmethyl)-4,5-dimethylbenzophenone (3cc). Isolated in 61% yield as a yellow oil: ^1H NMR (CDCl_3) δ 2.26 (s, 3 H), 2.32 (s, 3 H), 4.55 (s, 2 H), 7.12 (s, 1 H), 7.23 (s, 1 H), 7.37-7.58 (m, 6 H), 7.81 (d, $J = 8.3$ Hz, 2 H), 7.97 (d, $J = 8.5$, 2 H); ^{13}C NMR (CDCl_3) δ 19.3, 19.8, 42.8, 128.1, 128.2, 128.4, 130.2, 131.9, 132.4, 132.8, 133.4, 134.5, 135.6, 136.9, 138.4, 140.1, 197.5, 198.3.

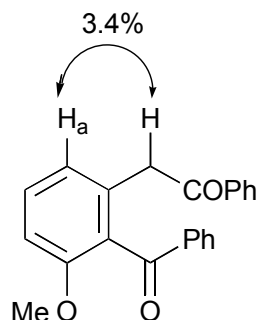
2-(Benzoylmethyl)-4,5-trimethylenebenzophenone (3dc). Isolated in 82% yield as a pale yellow oil: ^1H NMR (CDCl_3) δ 2.12 (quint, $J = 7.6$ Hz, 2 H), 2.90 (t, $J = 7.6$ Hz, 2 H), 2.97 (t, $J = 7.6$ Hz, 2 H), 4.58 (s, 2 H), 7.20 (s, 1 H), 7.30 (s, 1 H), 7.35-7.65 (m, 6 H), 7.81 (d, $J = 6.9$ Hz, 2 H), 7.97 (d, $J = 7.3$ Hz, 2 H); ^{13}C NMR (CDCl_3) δ 25.3, 32.4, 32.9, 43.2, 126.6, 128.1, 128.2, 128.4, 128.6, 130.2, 132.4, 132.87, 132.92, 136.1, 136.9, 138.5, 142.3, 147.9, 197.6, 198.6.

2-(Benzoylmethyl)-3,6-dimethoxybenzophenone (3ec). Isolated in 82% yield as a pale yellow oil: ^1H NMR (CDCl_3) δ 3.62 (s, 3 H), 3.72 (s, 3 H), 4.19 (s, 2 H), 6.87 (d, $J = 8.9$ Hz, 1 H), 6.94 (d, $J = 8.9$ Hz, 1 H), 7.30-7.56 (m, 6 H), 7.80-7.92 (m, 4 H); ^{13}C NMR (CDCl_3) δ 37.1, 56.0, 56.1, 110.5, 111.8, 123.2, 127.9, 128.3, 129.6, 131.0, 132.7, 133.3, 136.8, 137.4, 150.6, 152.1, 196.4, 197.4.

2-(Benzoylmethyl)-6-methoxybenzophenone (3fc). Isolated in 66% yield as a pale yellow oil: ^1H NMR (CDCl_3) δ 3.65 (s, 3 H), 4.21 (s, 2 H), 6.90 (d, $J = 8.0$ Hz, 1 H), 6.92 (d, $J = 7.5$ Hz, 1 H), 7.30-7.59 (m, 7 H), 7.81 (d, $J = 7.5$ Hz, 2 H), 7.83 (d, $J = 7.3$ Hz, 2 H); ^{13}C NMR (CDCl_3) δ 42.2, 55.6, 109.7, 123.1, 128.28, 128.32, 128.4, 129.5, 130.4, 133.0, 133.2, 133.8, 136.4, 137.6, 157.1, 196.8, 197.7.

Structure Determination of 3fc

The structure of **3fc** was determined by NOE in ^1H NMR. As shown below, irradiation of the methylene proton of **3fc** enhanced H_a .



A mixture of 2-(Benzoylmethyl)-4-methylbenzophenone (**3gc**) and 2-(Benzoylmethyl)-5-methylbenzophenone (**3'gc**). Isolated in 76% yield as a pale yellow solid: ^1H NMR (CDCl_3) δ 2.36 (s, major), 2.42 (s, minor) 4.56 (s, major), 4.62 (s, minor), 7.12-7.60 (m), 7.77-7.87 (m), 7.92-8.03 (m); ^{13}C NMR (CDCl_3) δ 21.0, 21.4, 42.7, 43.2, 126.9, 128.1, 128.2, 128.4, 128.7, 128.8, 129.65, 129.70, 130.2, 130.3, 130.7, 130.9, 131.5, 131.6, 131.9, 132.5, 132.7, 132.9, 133.4, 135.0, 135.2, 136.0, 136.8, 137.9, 138.2, 138.3, 141.5, 197.3, 198.2, 198.5.

^1H NMR integration ratio

2.36 (s) : 2.42 (s) : 4.56 (s) : 4.62 (s) : 7.12-7.60 (m) : 7.77-7.87 (m) : 7.92-8.03 (m) = 3.40 : 2.49 : 2.00 : 1.59 : 19.49 : 3.62 : 4.55.

References

- [1] Y. Himeshima, T. Sonoda and H. Kobayashi, *Chem. Lett.*, 1983, 1211.
- [2] H. Yoshida, T. Terayama, J. Ohshita and A. Kunai, *Chem. Commun.*, 2004, 1980.
- [3] H. Yoshida, S. Sugiura and A. Kunai, *Org. Lett.*, 2002, **4**, 2767.
- [4] D. Peña, D. Pérez, E. Guitián and L. Castedo, *J. Am. Chem. Soc.*, 1999, **121**, 5827.
- [5] E. Yoshikawa, K. V. Radhakrishnan and Y. Yamamoto, *J. Am. Chem. Soc.*, 2000, **122**, 7280.
- [6] E. M. Arnett and J. A. Harrelson, Jr., *J. Am. Chem. Soc.*, 1987, **109**, 809.
- [7] S. C. Shim, C. H. Doh, D. Y. Lee, Y. Z. Youn, S. Y. Lee, S. A. Chae, D. H. Oh and H. Oh, *Bull. Korean Chem. Soc.*, 1992, **13**, 45.
- [8] T. Sugimoto, K. Teshima, N. Nakamura, M. Nojima, S. Kusabayashi and K. J. McCullough, *J. Org. Chem.*, 1993, **58**, 135.
- [9] Y. L. Chow and X. Ouyang, *Can. J. Chem.*, 1991, **69**, 423.