

Intramolecular Diels–Alder reaction of 2-diphenylphosphinyl-5-(propargyloxymethyl)furans followed by nucleophilic 1,2-rearrangement of the phosphinyl group

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Abstract—The base-catalyzed intramolecular Diels–Alder reactions of 2-diphenylphosphinyl-5-(propargyloxymethyl)furans **2a–e** gave the tetrahydrofuran ring annulated *o*-diphenylphosphinophenols **3a–e** in 70–80% yields, a novel reaction involving an intramolecular Diels–Alder reaction of furan diene with allenyl ether dienophile followed by a nucleophilic 1,2-rearrangement of the diphenylphosphinyl group.

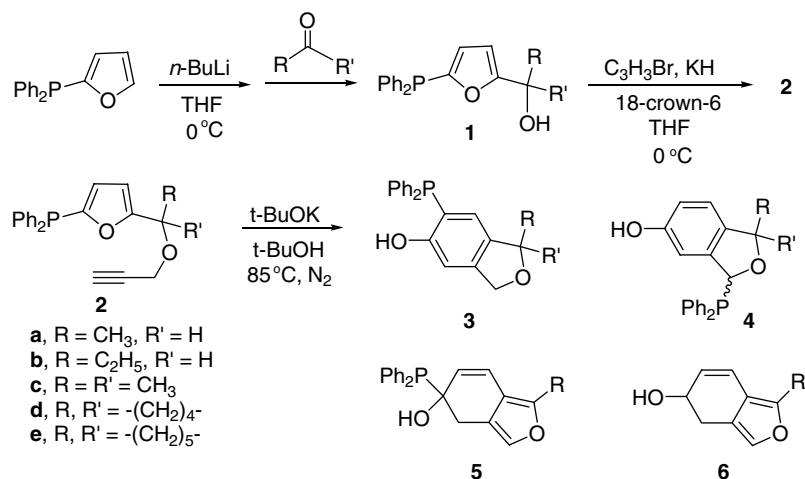
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There is considerable current interest in the intramolecular Diels–Alder reaction, and it has been applied to a number of synthetic objectives with notable success.¹ The vast majority of the work reported in this area has dealt with reactions utilizing ethylenic and acetylenic dienophiles. On the other hand, the intramolecular Diels–Alder reaction of allene has received much less attention.² Two decades ago, Kanematsu et al. demonstrated that the allene unit is a versatile synthon as a dienophile in the intramolecular cycloaddition due to the absence of unfavorable nonbonded interactions in the transition state.³ Afterward, they developed a furan ring transfer reaction via the intramolecular Diels–Alder reaction of furan diene and allenyl ether dienophile and applied this reaction to the synthesis of natural products.⁴ A decade ago, we have also engaged in the investigation of this intramolecular cycloaddition.⁵ In this Letter we report a novel reaction involving an intramolecular Diels–Alder reaction of furan diene with allenyl ether, in which the nucleophilic 1,2-rearrangement of diphenylphosphinyl group is included, to give tetrahydrofuran ring annulated *o*-diphenylphosphinophenols. The prominence of phosphine ligands in the field of organometallic catalysis is a reality for more than three decades.⁶ Therefore, intensive efforts have

been done to produce phosphines with different steric and electronic properties. Main approaches involve stoichiometric reactions between haloarylphosphines and organometallic species, or phosphide anion and organic halides.^{7,8} This Letter provides a new entry for the synthesis of substituted *o*-diphenylphosphinophenols, potential useful bidentate P,O ligands.⁹

Treatment of 2-diphenylphosphinylfuran with *n*-butyllithium in dry tetrahydrofuran (THF) at 0 °C followed by the addition of acetaldehyde, propionaldehyde, acetone, cyclopentanone, and cyclohexanone gave the nucleophilic addition products **1a–e** in 70–85% yields, respectively. Reaction of alcohols **1a–e** with potassium hydride and propargyl bromide in dry THF in the presence of 18-crown-6 at 0 °C gave 2-diphenylphosphinyl-5-(propargyloxymethyl)furans **2a–e** in 65–75% yields. Treatment of **2a–e** with potassium *tert*-butoxide in refluxing *tert*-butyl alcohol (85 °C) under nitrogen for 6 h gave compounds **3a–e** in 70–80% yields, respectively (Scheme 1). No detectable amount of the 1,4-rearrangement^{5b} products **4a–e** was obtained. Also, in the cases of **2a,b** no detectable amount of the furan ring transfer reaction^{4a} products **5a,b** or **6a,b** was obtained. These products were fully characterized by their spectral data.¹⁰ The ¹H and ¹³C NMR spectra of **3a–e** revealed the spin–spin coupling between the phosphorus atom and the aromatic protons and carbons of the newly-formed benzene ring from furan ring since the

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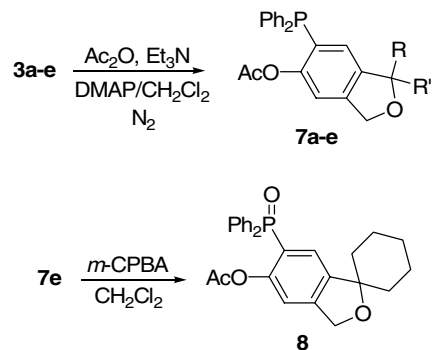


Scheme 1.

phosphorus atom has a I value 1/2. For example, the $^3J_{P-H}$ and $^4J_{P-H}$ coupling constants between the phosphorus atom and the newly-formed aromatic protons of **3c** are 4.2 Hz and 5.4 Hz.

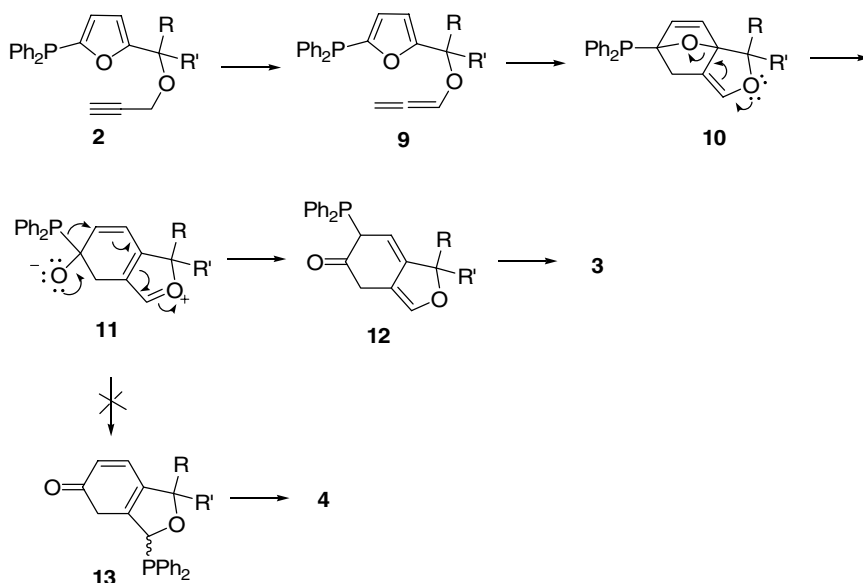
Compounds **3a–e** were not very stable when exposed in the air atmosphere and might be oxidized. Reaction of the crude compounds **3a–e** with acetic anhydride and triethylamine in the presence of a catalytic amount of 4-dimethylaminopyridine (DMAP) in dichloromethane at room temperature under nitrogen for 4 h gave acetates **7a–e** (Scheme 2). Compounds **7a–e** were very stable in air. Treatment of **7e** with *m*-chloroperoxybenzoic acid (*m*-CPBA) in dichloromethane at room temperature for 1 h gave compound **7** in 80% yield.

A mechanism is proposed for the intramolecular cycloaddition of **2a–e** (Scheme 3). The intramolecular Diels–Alder reactions of **2a–e** gave **3a–e**, respectively,



Scheme 2.

presumably via the corresponding allenyl ethers **9a–e** and the initial cycloadducts **10a–e**. Under the reaction conditions, the initial cycloadducts **10a–e** easily undergo ring opening of the oxygen bridge to form zwitterions



Scheme 3.

11a–e as the reaction intermediates. Nucleophilic 1,2-rearrangement of the diphenylphosphinyl group, caused by the alkoxide anion repelling the phosphinyl group, gave intermediates **12a–e**, which undergo aromatization to give the phenolic derivatives **3a–e**, respectively. Since no detectable amount of the 1,4-rearrangement products **4a–e** was obtained, the accessibility of repelling the diphenylphosphinyl group by the alkoxide anion followed by 1,4-shift of the diphenylphosphinyl group to give the rearranged intermediates **13a–e** was precluded. In the cases of **2a** and **2b**, which possess a proton on the furfurylic position ($R' = H$), no detectable amount of the furan ring transfer reaction products **5a** and **5b** or **6a** and **6b** was obtained. These results may imply that the reaction rates of 1,2-rearrangement are much faster than that of the furan ring transfer reaction from zwitterion intermediates **11**.

In conclusion, we found a novel reaction involving an intramolecular Diels–Alder reaction of furan diene with allenyl ether dienophile followed by a nucleophilic 1,2-rearrangement of diphenylphosphinyl group of zwitterion intermediate **11** to give tetrahydrofuran ring annulated *o*-diphenylphosphinophenols. This reaction provides a new entry for the synthesis of potential useful bidentate P,O ligands.

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References and notes

- For reviews see: (a) Oppolzer, W. *Angew. Chem., Int. Ed. Engl.* **1977**, *16*, 19; (b) Briger, G.; Bennett, J. N. *Chem. Rev.* **1980**, *80*, 63; (c) Fallis, A. G. *Can. J. Chem.* **1984**, *62*, 183; (d) Ciganek, E. *Org. React.* **1984**, *32*, 1; (e) Weinreb, S. M.; Staib, R. R. *Tetrahedron* **1982**, *38*, 3087; (f) Weinreb, S. M. *Acc. Chem. Res.* **1985**, *18*, 16; (g) Craig, D. *Chem. Soc. Rev.* **1987**, *16*, 187; (h) Denmark, S. E.; Thorarensen, A. *Chem. Rev.* **1996**, *96*, 137; (i) Winkler, J. D. *Chem. Rev.* **1996**, *96*, 167; (j) Kappe, C. O.; Murphree, S. S.; Padwa, A. *Tetrahedron* **1997**, *53*, 14179; (k) Takao, K.; Munakata, R.; Tadano, K. *Chem. Rev.* **2005**, *105*, 4779.
- For some examples of the intramolecular Diels–Alder reactions of allenic dienophiles, see: (a) Bartlett, A. J.; Laird, T.; Ollis, W. D. *J. Chem. Soc., Perkin Trans. 1* **1975**, 1315; (b) Himbert, G.; Diehl, K.; Mass, G. *J. Chem. Commun.* **1984**, 900; (c) Harrison, R. M.; Hobson, J. D.; Midgley, A. W. *J. Chem. Soc., Perkin Trans. 1* **1973**, 1960; (d) Saxton, H. M.; Sutherland, J. K.; Whaley, C. *J. Chem. Soc., Chem. Commun.* **1987**, 1449; (e) Hayakawa, K.; Yasukouchi, T.; Kanematsu, K. *Tetrahedron Lett.* **1986**, *27*, 1837; (f) Hayakawa, K.; Nagatsugi, F.; Kanematsu, K. *J. Org. Chem.* **1988**, *53*, 860; (g) Hayakawa, K.; Yasukouchi, T.; Kanematsu, K. *Tetrahedron Lett.* **1987**, *28*, 5895; (h) Yasukouchi, T.; Kanematsu, K. *Tetrahedron Lett.* **1989**, *30*, 6559; (i) Yoshida, M.; Hiromatsu, M.; Kanematsu, K. *Heterocycles* **1986**, *24*, 881; (j) Hayakawa, K.; Ohsuki, S.; Kanematsu, K. *Tetrahedron Lett.* **1986**, *27*, 947.
- Hayakawa, K.; Yodo, M.; Ohsuki, S.; Kanematsu, K. *J. Am. Chem. Soc.* **1984**, *106*, 6735.
- (a) Hayakawa, K.; Yamaguchi, Y.; Kanematsu, K. *Tetrahedron Lett.* **1985**, *26*, 2689; (b) Yamaguchi, Y.; Hayakawa, K.; Kanematsu, K. *J. Chem. Soc., Chem. Commun.* **1987**, 515; (c) Yamaguchi, Y.; Yamada, H.; Hayakawa, K.; Kanematsu, K. *J. Org. Chem.* **1987**, *52*, 2040; (d) Yamaguchi, Y.; Tatsuta, N.; Hayakawa, K.; Kanematsu, K. *J. Chem. Soc., Chem. Commun.* **1989**, 470; (e) Kanematsu, K.; Soejima, S. *Heterocycles* **1991**, *32*, 1483.
- (a) Wu, H. J.; Lin, S. H.; Lin, C. C. *Heterocycles* **1994**, *38*, 1507; (b) Wu, H. J.; Shao, W. D.; Ying, F. H. *Tetrahedron Lett.* **1994**, *35*, 729; (c) Wu, H. J.; Ying, F. H.; Shao, W. D. *J. Org. Chem.* **1995**, *60*, 6168; (d) Lin, C. C.; Chen, L. H.; Wu, H. J. *J. Chin. Chem. Soc.* **1991**, *38*, 613; (e) Wu, H. J.; Yen, C. H.; Chuang, C. T. *Tetrahedron Lett.* **1996**, *37*, 7395; (f) Wu, H. J.; Yen, C. H.; Chuang, C. T. *J. Org. Chem.* **1998**, *63*, 5064; (g) Chuang, C. T.; Yen, C. H.; Wu, H. J. *J. Chin. Chem. Soc.* **1998**, *45*, 789.
- Noyori, R. *Asymmetric Catalysis in Organic Synthesis*; John Wiley and Sons Ltd: New York, 1994.
- Gilheany, D. G.; Mitchell, C. M. In *The Chemistry of Organophosphorus Compounds*; Hartley, F. R., Ed.; John Wiley and Sons: Chichester, UK, 1990; Vol. 1, pp 151–190.
- (a) Rauchfuss, T. B. *Inorg. Chem.* **1997**, *16*, 2966; (b) Cope, S. J.; Dawson, G. J. *Synlett* **1993**, 509; (c) Abrunhosa, I.; Delain-Bioton, L.; Gaumont, A. C.; Gulea, M.; Masson, S. *Tetrahedron* **2004**, *60*, 9263; (d) Sprinz, J.; Helmchen, G. *Tetrahedron Lett.* **1993**, *34*, 1769; (e) Peer, M.; de Jong, J. C.; Kiefer, M.; Langer, T.; Rieck, H.; Schell, H.; Sennhenn, P.; Sprinz, J.; Steinhagen, H.; Wiese, B.; Helmchen, G. *Tetrahedron* **1996**, *52*, 7547; (f) Müller, C.; Ackerman, L. J.; Reek, J. N. H.; Kamer, P. C. J.; van Leeuwen, P. W. N. M. *J. Am. Chem. Soc.* **2004**, *126*, 14960; (g) Mino, T.; Tanaka, Y.; Hattori, Y.; Yabusaki, T.; Saotome, H.; Sakamoto, M.; Fujita, T. *J. Org. Chem.* **2006**, *71*, 7346; (h) Whelligan, D. K.; Bolm, C. *J. Org. Chem.* **2006**, *71*, 4609; (i) Baillie, C.; Xiao, J. *Tetrahedron* **2004**, *60*, 4159.
- (a) Bianchi, A.; Russo, A.; Bernardi, A. *Tetrahedron: Asymmetry* **2005**, *16*, 381; (b) Bianchi, A.; Bernardi, A. *J. Org. Chem.* **2006**, *71*, 4565; (c) Uozumi, Y.; Tanahashi, A.; Lee, S. Y.; Hayashi, T. *J. Org. Chem.* **1993**, *58*, 1945; (d) Suárez, A.; Pizzano, A. *Tetrahedron: Asymmetry* **2001**, *12*, 2501; (e) Nandi, M.; Jin, J.; RajanBabu, T. V. *J. Am. Chem. Soc.* **1999**, *121*, 9899.
- Compound **3c**: IR (neat): 3600–3200 cm^{-1} ; ^1H NMR (CDCl_3) δ 7.40–7.32 (m, 10H), 6.70 (d, $J = 4.2$ Hz, 1H), 6.63 (d, $J = 5.4$ Hz, 1H), 4.97 (s, 2H), 1.33 (s, 6H); ^{13}C NMR (75 Hz, CDCl_3) δ 158.85 (d, C), 142.11 (2C), 139.01 (d, C), 135.45 (d, C), 133.27 (d, 4CH), 128.65 (d, 4CH), 128.44 (d, 2CH), 125.98 (d, CH), 120.79 (d, C), 107.88 (CH), 85.67 (C), 70.19 (CH_2), 28.38 (2 CH_3); LRMS m/z (rel inten) 348 (M^+ , 37), 255 (100). Compound **7c**: IR (CHCl_3): 1740, 1110 cm^{-1} ; ^1H NMR (CDCl_3) δ 7.24–7.14 (m, 10H), 6.85 (d, $J = 3.6$ Hz, 1H), 6.44 (d, $J = 4.2$ Hz, 1H), 4.92 (s, 2H), 1.83 (s, 3H), 1.23 (s, 6H); ^{13}C NMR (75 Hz, CDCl_3) δ 168.98 (C), 151.98 (d, C), 144.67 (d, C), 141.01 (2C), 135.46 (d, C), 133.72 (d, 4CH), 129.02 (d, 2CH), 128.50 (d, 4CH), 125.34 (d, CH), 115.40 (CH), 85.43 (C), 70.16 (CH_2), 28.27 (2 CH_3), 20.42 (CH_3); HRMS (EI): calcd for $\text{C}_{24}\text{H}_{23}\text{O}_3\text{P}$, 390.1385; found, 390.1389.