

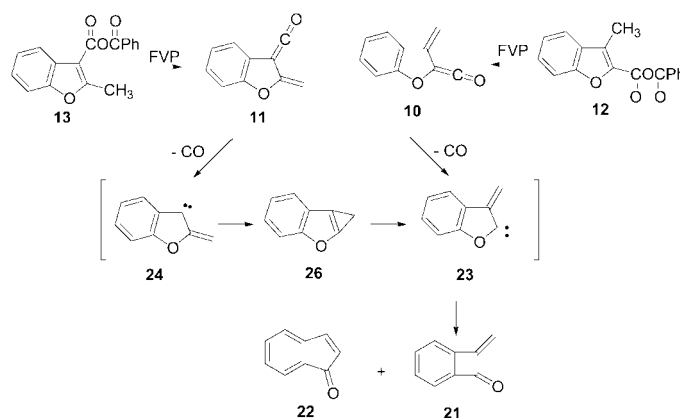
Syntheses and Pyrolyses of Benzofuran Analogues of α -Oxo-*o*-quinodimethane. A Study on Vinylcarbene–Cyclopropene Rearrangement

Pen-Wen Tseng, Su-Wen Yeh, and Chin-Hsing Chou*

Department of Chemistry and Center for Nanoscience and Nanotechnology, National Sun Yat-Sen University, Kaohsiung, Taiwan 804, R.O.C.

ch-chou@mail.nsysu.edu.tw

Received December 20, 2007



Flash vacuum pyrolyses (FVP) of benzoic 3-methyl-2-benzofurancarboxylic anhydride (**12**) and benzoic 2-methyl-3-benzofurancarboxylic anhydride (**13**) at 550 °C and ca. 10^{-2} torr both give methylenebenzocyclobutenone (**21**) as the major product and indenone (**22**) as the minor one. A mechanism involving generation of α -oxo-*o*-quinodimethane **11** as the primary pyrolysis product from FVP of **13**, followed by elimination of a CO molecule to give carbene **24**, which undergoes a vinylcarbene–cyclopropene rearrangement and a ring contraction of the resulting carbene **23**, is proposed to account for the observed results. The proposed mechanism is further supported by a deuterium-labeling study on FVP of (2-benzofuryl)methyl- α,α - d_2 benzoate (**28- d_2**).

Introduction

o-Quinodimethane (**1**), since it was first recognized as a reactive intermediate in 1957,¹ has been actively investigated from theoretical, physical, physical organic, and synthetic organic viewpoints.^{2–4}

The development of **1** has been extended to α -oxo-*o*-quinodimethane (**2**). **2** can be prepared from pyrolysis of either

homophthalic anhydride (**3**)⁵ or *o*-toluyl chloride (**4**),⁶ and once it is generated, **2** converts to the more stable benzocyclobutenone (**5**).

Previously, we have synthesized the benzofuran analogue of **1**, namely, 2,3-dimethylene-2,3-dihydrofuran (**6**), from flash vacuum pyrolysis (FVP) of (2-methyl-3-benzofuryl)methyl benzoate (**7**).⁷ **6** is stable below -40 °C, and at room temperature, **6** dimerized to give a [4 + 2] dimer **8** and a [4 + 4] dimer **9**. The reason for using benzoate instead of acetate as the pyrolysis precursor for our study is that benzoic acid, generated as the byproduct from FVP of **7**, can easily be separated from the target compound **6** by a pyrolysis setup that has been described previously.⁷

On the basis of our work on the preparation of **6**, we anticipated that the previously unknown benzofuran analogues

(7) Chou, C. H.; Trahanovsky, W. S. *J. Org. Chem.* **1986**, *51*, 4208–4212.

* Address correspondence to this author. Fax: +886-7-5253909.

(1) Cava, M. P.; Napier, D. R. *J. Am. Chem. Soc.* **1957**, *79*, 1701–1705.

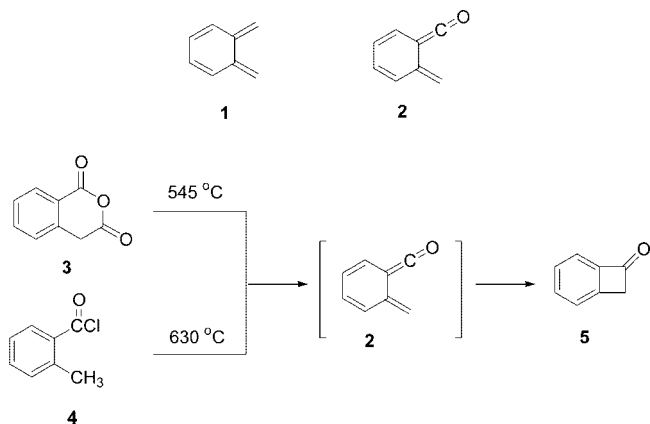
(2) Cava, M. P.; Deana, A. A.; Muth, K. *J. Am. Chem. Soc.* **1959**, *81*, 6458–6460.

(3) Jensen, F. R.; Coleman, W. E. *J. Am. Chem. Soc.* **1958**, *80*, 6149.

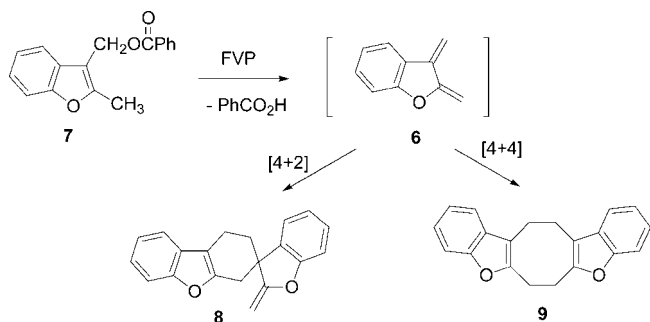
(4) For leading references see: McCullough, J. *J. Acc. Chem. Res.* **1980**, *13*, 270–276.

(5) Spangler, R. J.; Kim, J. H. *Tetrahedron Lett.* **1972**, *13*, 1249–1251.

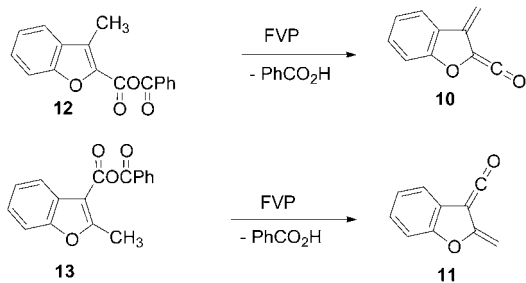
(6) Schiess, P.; Heitzmann, P. *Angew. Chem., Int. Ed. Engl.* **1977**, *16*, 469–470.



of **2**, (3-methylene-3*H*-benzofuran-2-ylidene)methanone (**10**) and (2-methylene-2*H*-benzofuran-3-ylidene)methanone (**11**), could be prepared from FVP of benzoic 3-methyl-2-benzofurancarboxylic anhydride (**12**) and benzoic 2-methyl-3-benzofurancarboxylic anhydride (**13**), respectively.



To study the chemistry of **10** and **11**, we have synthesized and pyrolyzed anhydrides **12** and **13**. The results of this investigation are presented herein.



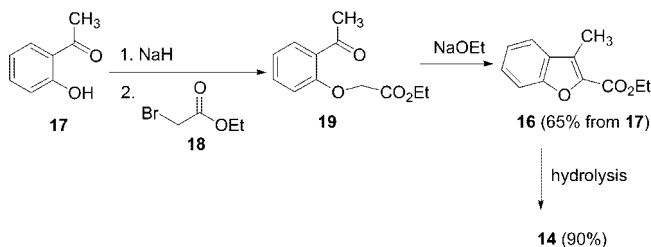
Results and Discussion

Anhydrides **12** and **13** were prepared from reactions of benzoyl chloride with the corresponding acids, 3-methyl-2-benzofurancarboxylic acid (**14**) and 2-methyl-3-benzofurancarboxylic acid (**15**), respectively.

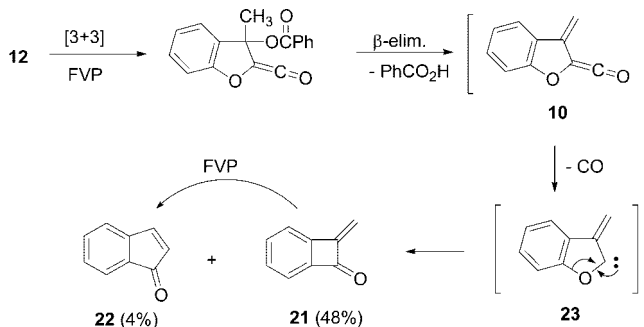
Acid **14** was prepared from hydrolysis of ethyl 3-methyl-2-benzo[*b*]furoate (**16**). **16** was prepared from reaction of 2-hydroxyacetophenone (**17**) with bromoacetate (**18**) followed by intramolecular Aldol-condensation of the resulting **19**⁸ (Scheme 1).

Acid **15** was prepared by the methylation of 3-benzofurancarboxylic acid (**20**).⁷ Acid **20** was prepared by a known procedure starting from ethyl phenoxyacetate.^{9,10}

SCHEME 1



SCHEME 2



The FVP of **12** was performed at 550 °C and ca. 10^{-2} torr, using the method previously reported.¹¹ The products were collected in CDCl_3 from the cold trap. Low-temperature ^1H NMR spectroscopy⁷ at -70 °C revealed that no target compound **10** was obtained. After warming the solution to room temperature, quantitative ^1H NMR analysis, using dibromomethane as an integration standard, indicated that methylenebenzocyclobutenone (**21**) was obtained as the major product in 48% yield, along with indenone (**22**) as a minor product in 4% yield, and some polymers. The pyrolysis temperature at 550 °C and ca. 10^{-2} torr appeared to be the optimum reaction conditions for our study. FVP of **12** at temperatures lower than 500 °C would leave unreacted starting materials, whereas FVP of **12** at temperatures higher than 600 °C gave a lower yield of **21**. The formation of **21** and **22** can be rationalized by a mechanism proposed as shown in Scheme 2.

Under the pyrolysis conditions, a [3 + 3] sigmatropic rearrangement from **12** followed by elimination of a benzoic acid molecule is proposed to give the primary pyrolysis product **10**. A sequential elimination of a CO molecule from **10** is proposed to produce carbene **23**, a reaction for which there is good precedent.¹² A 1,2-phenyl shift¹³ from **23** is proposed to give **21**. Rearrangement of **21** under pyrolysis conditions is known to give **22**.⁹

The FVP of **13**, under the same pyrolysis conditions, unexpectedly gave the same pyrolysis products, **21** (50% yield) and **22** (5% yield). Our original expectation was that, as shown in Scheme 3, carbene **24**, generated from the FVP of **13**, would undergo a ring-opening reaction to give triene **25**. However, the formation of **21** and **22** from **13** suggests that carbene **24**, instead of undergoing a process that destroys the aromaticity of

(9) Trahanovsky, W. S.; Amah, A. N.; Cassady, T. J. *J. Am. Chem. Soc.* **1984**, *106*, 2696–2698.

(10) Koelsch, C. F.; Whitney, A. G. *J. Am. Chem. Soc.* **1941**, *63*, 1762.

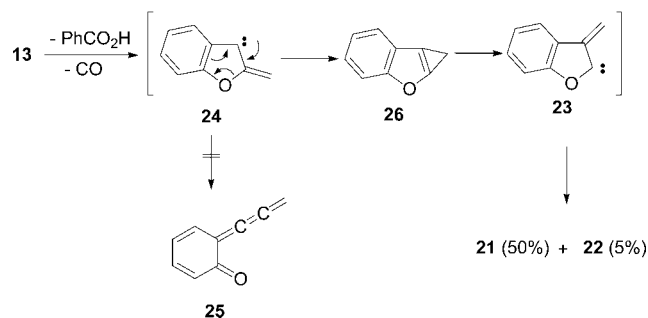
(11) Trahanovsky, W. S.; Ong, C. C.; Pataky, J. G.; Weilt, F. L.; Muellen, P. W.; Clardy, J. C.; Hansen, R. S. *J. Org. Chem.* **1971**, *36*, 3575–3579.

(12) Brown, R. F. C.; Eastwood, F. W.; McMullen, G. L. *Aust. J. Chem.* **1977**, *30*, 179–193.

(13) Brown, R. F. C.; Eastwood, F. W.; Lim, S. T.; McMullen, G. L. *Aust. J. Chem.* **1976**, *29*, 1705–1712.

(8) Foster, R. T.; Robertson, A.; Bushra, A. *J. Chem. Soc.* **1948**, 2254–2260.

SCHEME 3



the benzene ring in **24** to give **25**, undergoes a vinylcarbene–cyclopropene rearrangement,¹⁴ involving cyclopropene **26**, to give carbene **23**, which then leads to the formation of **21** and **22**.

To study the stability of proposed intermediates **23**, **24**, and **26** from FVP of **13**, we have carried out molecular orbital calculations at the B3LYP/6-31G(d) level of DFT for **26**, and carbenes **23** and **24** in multiplicities of both singlet and triplet states. It is desirable to understand the possibility of formation for the intermediates from the computational chemistry. The results of calculation indicate that the ground state carbenes **23** and **24** are singlet, and, as shown in Figure 1, the singlet carbene **23** is indeed 7.07 kcal/mol more stable than the singlet carbene **24**.

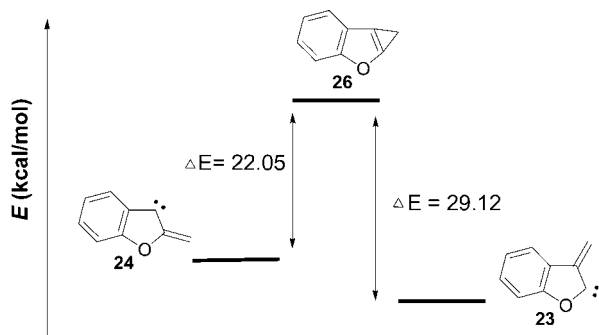


FIGURE 1. Schematic representation of stability of intermediate **26** and singlet carbenes **23** and **24** based on the DFT calculations.

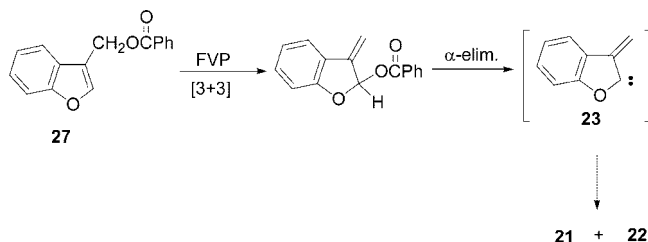
Compound **21** was first prepared by Trahanovsky and co-workers.⁹ They reported that FVP of (3-benzofuryl)methyl benzoate (**27**) gives **21**, presumably involving carbene **23** as the reaction intermediate (Scheme 4).

The involvement of carbene **23** in the FVP of **27**, along with the aforementioned vinylcarbene–cyclopropene rearrangement mechanism for conversion of **24** to **23**, led us to propose that FVP of (2-benzofuryl)methyl benzoate (**28**) would also give **21**.

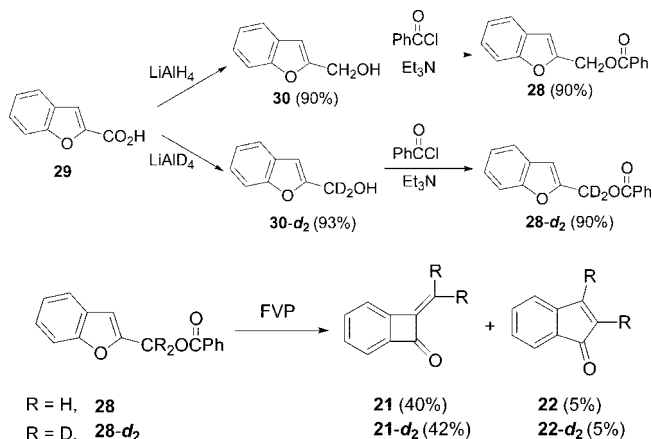
To investigate the pyrolytic chemistry of **28**, the preparations and pyrolyses of **28**, and its deuterated derivative, (2-benzofuryl)methyl- α,α - d_2 benzoate (**28- d_2**) were performed. Compounds **28** and **28- d_2** were prepared by either LiAlH_4 or LiAlD_4 reduction of benzofuran-2-carboxylic acid (**29**)¹⁵ followed by esterification of the resulting alcohol **30** or **30- d_2** with benzoyl chloride in the presence of triethylamine¹⁶ as outlined in Scheme 5.

In agreement with the proposed mechanism, FVP of **28**, at 550 °C and ca. 10^{-2} torr, gave **21** in 40% yield and **22** in 5% yield, whereas FVP of **28- d_2** , under the same pyrolysis conditions, gave α,α - d_2 -methylenebenzocyclobutenone (**21- d_2**) and 2,3-dideuterioindenone (**22- d_2**) in similar yields.

SCHEME 4



SCHEME 5



A mechanism to account for the formations of **21** and **22** and their deuterated derivatives **21- d_2** and **22- d_2** from FVP of **28** and **28- d_2** is proposed and shown as Scheme 6.

The deuterium-labeling study not only supports the vinylcarbene–cyclopropene rearrangement, but also rules out the possibility of elimination of a benzoic acid from **28- d_2** as the initial step. For such a mechanism, FVP of **28- d_2** would lead to the formation of a monodeuterated methylenebenzocyclobutenone **21- d** as shown in Scheme 7.

In summary, our results support the involvement of a vinylcarbene–cyclopropene rearrangement in the formation of **21** and **22** from the FVP of **13** and **28** (Scheme 8). We are currently extending our study to the other heteroaromatic systems.

Experimental Section

Benzoic 3-Methyl-2-benzofurancarboxylic Anhydride (12). Anhydride **12** was prepared in 90% yield from reaction of benzoyl chloride with 3-methyl-2-benzofurancarboxylic acid (**14**). **12**: IR (CHCl_3 , cm^{-1}) 1730 (C=O), 1690 (C=O), 1090 (C–O); ^1H NMR (CDCl_3) δ 8.22–7.53 (m, 9H, arom), 2.69 (s, 3H, CH_3); ^{13}C NMR (CDCl_3) δ 162.1 (C), 161.8 (C), 155.4 (C), 154.7 (C), 139.3 (C), 134.4 (C), 134.3 (CH), 130.4 (C), 130.3 (CH), 130.1 (CH), 128.7 (CH), 123.4 (CH), 121.3 (CH), 112.1 (CH), 9.5 (CH_3); high-

(14) Wentrup, C. *Top. Curr. Chem.* **1976**, *62*, 184–187.

(15) Winberg, H. E.; Fawcett, F. S.; Mochel, W. E.; Theobald, C. W. *J. Am. Chem. Soc.* **1960**, *82*, 1428–1435.

(16) Trahanovsky, W. S.; Cassidy, T. J.; Woods, T. L. *J. Am. Chem. Soc.* **1981**, *103*, 6691–6695.

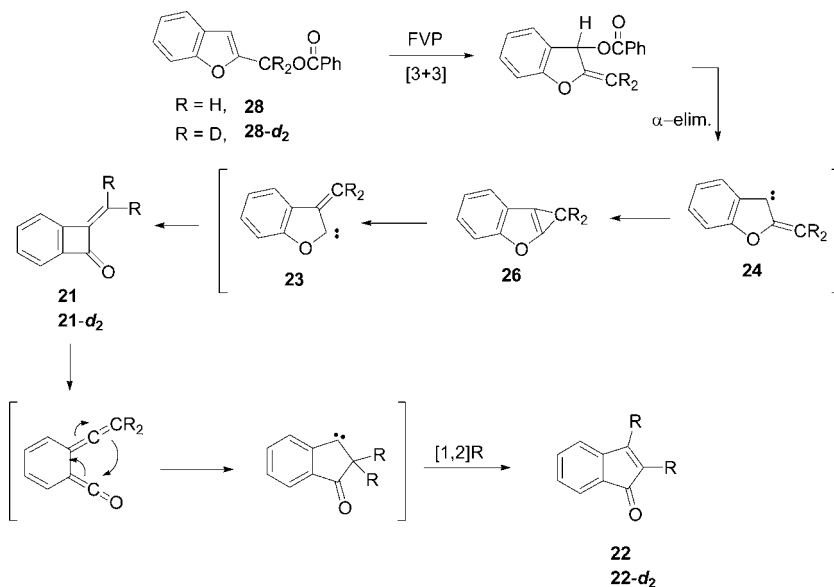
(17) Chou, C. H.; Trahanovsky, W. S. *J. Am. Chem. Soc.* **1986**, *108*, 4138–4144.

(18) Wasson, B. K.; Hamel, P.; Rooney, C. S. *J. Org. Chem.* **1977**, *42*, 4265–4266.

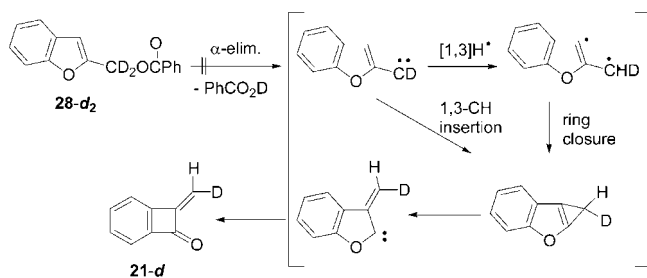
(19) Fieser, L. F.; Fieser, M. *Reagents for Organic Synthesis*; Wiley: New York, 1967; Vol. 1, p 584.

(20) Kundu, N. G.; Pal, M.; Mahanty, J. S.; De, M. *J. Chem. Soc., Perkin Trans. 1* **1997**, *19*, 2815–2820.

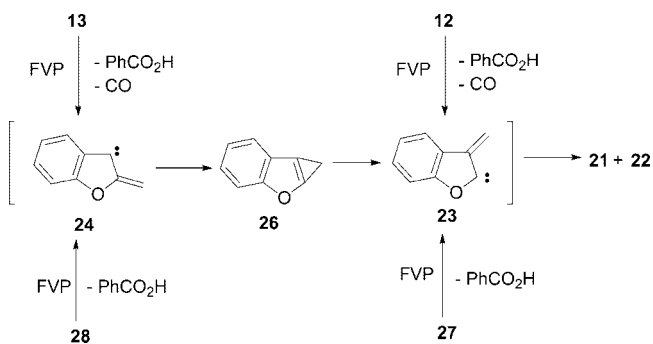
SCHEME 6



SCHEME 7



SCHEME 8



resolution mass spectrum, calcd for $\text{C}_{17}\text{H}_{12}\text{O}_4$ 280.0738, measured 280.0740. Anal. Calcd: C, 72.86; H, 4.29. Found: C, 72.65; H, 4.30.

Benzoic 2-Methyl-3-benzofurancarboxylic Anhydride (13). A procedure described for the preparation of **12** was followed for the reaction of 2-methyl-3-benzofurancarboxylic acid (**15**) and benzoyl chloride to give 92% yield of **13**: IR (CHCl_3 , cm^{-1}) 1725 (C=O), 1683 (C=O), 1105 (C—O); ^1H NMR (CDCl_3) δ 8.19–7.28 (m, 9H, arom), 2.84 (s, 3H, CH_3); ^{13}C NMR (CDCl_3) δ 166.9 (C), 166.7 (C), 162.3 (C), 162.2 (C), 159.5 (C), 153.7 (C), 153.7 (C), 134.5 (CH), 130.5 (CH), 128.9 (CH), 124.9 (CH), 124.4 (CH), 121.3 (CH), 111.1 (CH), 14.9 (CH_3); high-resolution mass spectrum, calcd for $\text{C}_{17}\text{H}_{12}\text{O}_4$ 280.0732, measured 280.0735. Anal. Calcd: C, 72.86; H, 4.29. Found: C, 72.60; H, 4.39.

(2-Benzofuryl)methyl Benzoate (28). Benzoate **28** was prepared in 90% yield by esterification of (2-benzofuryl)methyl alcohol (**30**) with benzoyl chloride. **28**: IR (CHCl_3 , cm^{-1}) 1720 (C=O), 1460 (CH_2), 1150 (C—O); ^1H NMR (CDCl_3) δ 8.08–8.05 (m, 2H, arom),

7.58–7.22 (m, 7H, arom), 6.84 (s, 1H, arom), 5.45 (s, 2H, CH_2); ^{13}C NMR (CDCl_3) δ 166.1 (C), 155.2 (C), 151.9 (C), 133.2 (CH), 129.8 (C), 129.7 (CH), 128.3 (CH), 127.9 (C), 124.8 (CH), 122.9 (CH), 121.3 (CH), 111.4 (CH), 107.0 (CH), 59.0 (CH_2); high-resolution mass spectrum, calcd for $\text{C}_{16}\text{H}_{12}\text{O}_3$ 252.0787, measured 252.0785.

(2-Benzofuryl)methyl- α,α - d_2 Benzoate (28- d_2). Benzoate **28- d_2** was prepared in 90% yield by esterification of (2-benzofuryl)-methyl- α,α - d_2 alcohol (**30- d_2**) with benzoyl chloride. **28- d_2** : IR (CHCl_3 , cm^{-1}) 1710 (C=O), 1250 (CD_2), 1180 (C—O); ^1H NMR (CDCl_3) δ 8.81–8.05 (m, 2H, arom), 7.58–7.22 (m, 7H, arom), 6.84 (s, 1H, arom); ^{13}C NMR (CDCl_3) δ 166.1 (C), 155.2 (C), 151.9 (C), 133.2 (CH), 129.8 (C), 129.7 (CH), 128.3 (CH), 127.9 (C), 124.8 (CH), 122.9 (CH), 121.3 (CH), 111.4 (CH), 107.1 (CH); high-resolution mass spectrum, calcd for $\text{C}_{16}\text{H}_{10}\text{D}_2\text{O}_3$ 254.0912, measured 254.0916.

General Pyrolysis Procedure. A tube furnace was used for our study. The pyrolysis temperature was measured at the center of the pyrolysis tube. The furnace was maintained at 550 °C. A sample of the anhydride or ester in a Pyrex boat was placed into the sample chamber and the system was evacuated to ca. 10^{-2} torr. The sample chamber was heated to ca. 100 °C during the pyrolysis. A condenser inserted between the furnace and the liquid-nitrogen-cooled trap to collect the benzoic acid formed as byproduct was cooled to ca. 0 °C. During the pyrolysis, a 1:1 ratio of $\text{CS}_2/\text{CDCl}_3$ solution was deposited into the trap through a sidearm. Upon completion of the pyrolysis nitrogen was introduced into the system and the trap was warmed to -78 °C and collected in NMR tubes, maintained at -78 °C, for low-temperature NMR measurements. The product solution was then warmed to room temperature and the products were purified for identification.

Pyrolysis of Benzoic 3-Methyl-2-benzofurancarboxylic Anhydride (12). **12** (930 mg, 3.32 mmol) was pyrolyzed at 550 °C and ca. 10^{-2} torr in the normal manner for 3 h. 1 mL of CDCl_3 and a weighed amount of dibromomethane as an NMR integration standard were added to the product trap. ^1H NMR analysis of this mixture showed the presence of **21** (207 mg, 1.60 mmol, 48%) and **22** (17.3 mg, 0.133 mmol, 4%). To separate **21** from **22**, an amine-acid method⁹ was employed: 1 mL of anhydrous ether was added to the product. To the mixture was added 10.0 mg (0.15 mmol) of pyrrolidine in anhydrous ether. After 30 s 8.97 mg (0.15 mmol) of acetic acid in ether was added to the mixture. After 2 min 1.0 g (11.9 mmol) of NaHCO_3 was added to the mixture, and the mixture was stirred at room temperature for 2 h. The mixture was then separated by thin-layer chromatography with a mixture

of 5% ethyl acetate in hexanes as an eluent to give **21** (80.0 mg, 19%) as a yellow oil: IR (CDCl₃, cm⁻¹) 3010 (CH₂), 1770 (C=O), 1730 (C=C); ¹H NMR (CDCl₃) δ 7.50–7.30 (m, 4H, arom), 5.47 and 5.24 (ABd, *J* = 1.5 Hz, 2H, CH₂); ¹³C NMR (CDCl₃) δ 186.1 (C), 159.0 (C), 156.4 (C), 156.1 (C), 135.0 (CH), 130.2 (CH), 121.6 (C), 120.2 (CH), 102.1 (CH₂); high-resolution mass spectrum, calcd for C₉H₆O 130.0419, measured 130.0414. [Lit.⁹ **21**: IR (CDCl₃, cm⁻¹) 3010, 1770, 1740; ¹H NMR (CDCl₃) δ 7.5–7.3 (m, 4H), 5.47 (d, *J* = 1.47 Hz, 1H), 5.24 (d, *J* = 1.46 Hz, 1H); ¹³C NMR (CDCl₃) δ 186.1, 159.6, 156.4, 156.1, 135.0, 130.2, 121.6, 120.2, 102.1.]

When **12** (510 mg, 1.82 mmol) was pyrolyzed at 700 °C and ca. 10⁻² torr in the normal manner for 2 h, **22** was obtained as the main product. Purification of the pyrolysis product by thin-layer chromatography with a mixture of 10% ethyl acetate in hexanes as an eluent gave **22** as a yellow oil (94.6 mg, 40%): IR (CDCl₃, cm⁻¹) 3010 (phenyl C–H), 1710 (C=O), 1630 (phenyl C=C), 1510 (phenyl C=C); ¹H NMR (CDCl₃) δ 7.57 (dd, *J* = 6.2, 0.9 Hz, 1H, vinyl), 7.44 (d, *J* = 7.2 Hz, 1H, arom), 7.34 (dd, *J* = 6.6, 0.9 Hz, 1H, arom), 7.25 (d, *J* = 6.6 Hz, 1H, arom), 7.07 (d, *J* = 7.2 Hz, 1H, arom), 5.90 (d, *J* = 6.2 Hz, 1H, vinyl); ¹³C NMR (CDCl₃) δ 198.4 (C), 149.8 (CH), 144.6 (C), 133.7 (CH), 130.4 (C), 129.2 (CH), 127.2 (CH), 122.7 (CH), 122.2 (CH). [Lit.²¹ ¹H NMR (200 MHz, CDCl₃) δ 7.56 (d, *J* = 5.9 Hz, 1H), 7.45–7.04 (m, 4H), 5.89 (d, *J* = 5.9 Hz, 1H); ¹³C NMR (50 MHz, CDCl₃) δ 200.2, 151.6, 146.7, 135.6, 132.4, 131.1, 129.2, 124.6, 124.2.]

Pyrolysis of Benzoic 2-Methyl-3-benzofurancarboxylic Anhydride (13). A 900 mg (3.21 mmol) quantity of **13** was pyrolyzed at 550 °C and ca. 10⁻² torr in a procedure described for the FVP of **12** to give 209 mg (1.61 mmol, 50%) of **21** and 20.9 mg (0.16 mmol, 5%) of **22**.

Pyrolysis of (2-Benzofuryl)methyl Benzoate (28). A 300 mg (1.19 mmol) quantity of **28** was pyrolyzed at 550 °C and ca. 10⁻²

torr in the normal manner for 3 h. Quantitative NMR analysis with dibromomethane as an integration standard indicated that a 40% yield of **21** and a 5% yield of **22** were obtained.

Pyrolysis of (2-Benzofuryl)methyl- α,α -d₂ Benzoate (28-d₂). A 250 mg (0.984 mmol) quantity of **28-d₂** was pyrolyzed at 550 °C and ca. 10⁻² torr in the normal manner for 3 h. Quantitative NMR analysis with dibromomethane as an integration standard indicated that a 42% yield of **21-d₂** and a 5% yield of **22-d₂** were obtained. **21-d₂**: IR (CDCl₃, cm⁻¹) 1770 (C=O), 1730 (C=C); ¹H NMR (CDCl₃) δ 7.50–7.30 (m, 4H, arom); high-resolution mass spectrum, calcd for C₉H₄D₂O 132.0419, measured 132.0414. **22-d₂**: IR (CDCl₃, cm⁻¹) 1710 (C=O), 1630 (phenyl C=C), 1510 (phenyl C=C); ¹H NMR (CDCl₃) δ 7.44 (d, *J* = 7.2 Hz, 1H, arom), 7.34 (d, *J* = 6.6 Hz, 1H, arom), 7.25 (d, *J* = 6.6 Hz, 1H, arom), 7.07 (d, *J* = 7.2 Hz, 1H, arom); high-resolution mass spectrum, calcd for C₉H₄D₂O 132.0419, measured 132.0415.

Computational Details. Density function theory (DFT) calculations at the B3LYP level were performed to obtain the total energies of intermediate **26**, and carbenes **23** and **24** in multiplicities of both triplet and singlet states. The basis set used for C, O, and H atoms was 6-31G(d). We have generated the theoretical geometry of **23**, **24**, and **26** by optimization. All the calculations were made with the use of Gaussian 03.

Acknowledgement. We thank the National Science Council of the Republic of China for financial support.

Supporting Information Available: Experimental procedures for the syntheses of **12**, **14**, **15**, **16**, **28**, **28-d₂**, **30**, and **30-d₂**, computational details of **23**, **24**, and **26**, and spectroscopic data for **12**, **13**, **28**, **28-d₂**, **21**, **21-d₂**, **22**, and **22-d₂**. This material is available free of charge via the Internet at <http://pubs.acs.org>.

JO702704E

(21) Zengin, M.; Dastan, A.; Balci, M. *Synth. Commun.* **2001**, *13*, 1993–1999.