JOC The Journal of Organic Chemistry

ARTICLE

pubs.acs.org/joc

Syntheses and Pyrolyses of Furan Analogues of α-Oxo-*o*-quinodimethanes. Formation of Methylenecyclobutenone and 1-Buten-3-yne via a Vinylcarbene−Cyclopropene Rearrangement

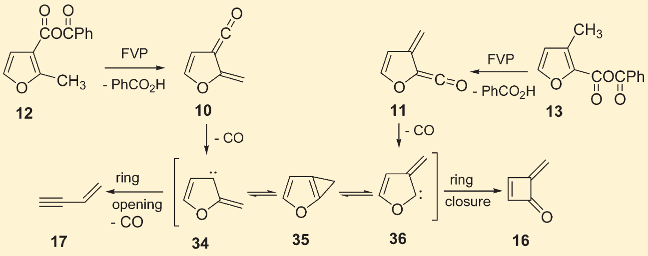
Pen-Wen Tseng,[†] Chen-Yu Kung,[†] Hsing-Yin Chen,[‡] and Chin-Hsing Chou*,[†]

[†]Department of Chemistry, National Sun Yat-Sen University, Kaohsiung, Taiwan 804, Republic of China

[‡]Department of Medicinal and Applied Chemistry, Kaohsiung Medical University, Kaohsiung, Taiwan 807, Republic of China

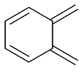
Supporting Information

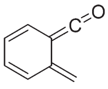
ABSTRACT: Flash vacuum pyrolyses (FVP) of benzoic 2-methyl-3-furoic anhydride (**12**) and benzoic 3-methyl-2-furoic anhydride (**13**) at 550 °C and ca. 10^{-2} Torr both give methylenecyclobutenone (**16**) and 1-buten-3-yne (**17**) as the main products. A mechanism involving generation of furan analogues of α-oxo-*o*-quinodimethane, **10** and **11**, from FVP of **12** and **13**, respectively, followed by elimination of a CO molecule to give the respective carbenes **34** and **36** is proposed. Carbenes **34** and **36** are interconvertible via a cyclopropene intermediate **35**. A ring contraction from **36** will give **16**, whereas a ring-opening of **34** followed by elimination of a CO molecule then leads to **17**. The proposed mechanism is supported by substituent- and deuterium-labeling study on FVP of the derivatives of **12**.

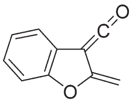


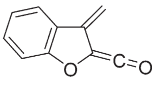
INTRODUCTION

Since Cava and Napier[1] reported the generation of the reactive species *o*-quinodimethane (**1**) in 1957, there have been tremendous efforts put into the study of the preparation, physical properties, and synthetic application of **1** and its derivatives.[2−4]


1


2

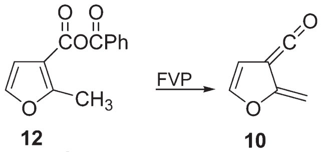

3


4

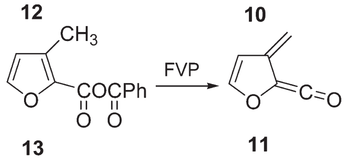
The development of **1** has been extended to α-oxo-*o*-quinodimethane (**2**).[5,6] Recently, in an attempt to synthesize the benzofuran analogues of **2**, (2-methylene-2*H*-benzofuran-3-ylidene)methanone (**3**) and (3-methylene-3*H*-benzofuran-2-ylidene)methanone (**4**), we have studied the pyrolytic chemistry of benzoic 2-methyl-3-benzofurancarboxylic anhydride (**5**) and benzoic 3-methyl-2-benzofurancarboxylic anhydride (**6**), respectively.[7]

Flash vacuum pyrolysis (FVP)[8] of **5** and **6** at 550 °C and ca. 10^{-2} Torr both gave methylenebenzocyclobutenone (**7**) as the major product. A mechanism involving generation of **3** as the primary pyrolysis product from FVP of **5**, followed by elimination of a CO molecule to give carbene **8**, which undergoes a vinylcarbene−cyclopropene rearrangement and a ring contraction of the resulting carbene **9**, is proposed to account for the observed results (Scheme 1).[7]

In order to study the generality of the proposed vinylcarbene−cyclopropene rearrangement, we have extended our study to the syntheses and pyrolyses of the previously unknown furan analogue of **2**, (2-methylene-2*H*-furan-3-ylidene)methanone (**10**) and (3-methylene-3*H*-furan-2-ylidene)methanone (**11**) from FVP of benzoic 2-methyl-3-furoic anhydride (**12**) and benzoic 3-methyl-2-furoic anhydride (**13**), respectively (eqs 1 and 2). The results of our investigation are presented herein.



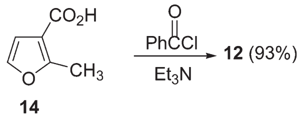
(1)



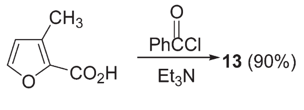
(2)

RESULTS AND DISCUSSION

Anhydrides **12** and **13** were prepared from reactions of benzoyl chloride with the corresponding acids, 2-methyl-3-furoic acid (**14**) and 3-methyl-2-furoic acid (**15**), respectively (eqs 3 and 4). Acids **14** and **15** were prepared by using the methods that have been reported previously.[8,9]



(3)

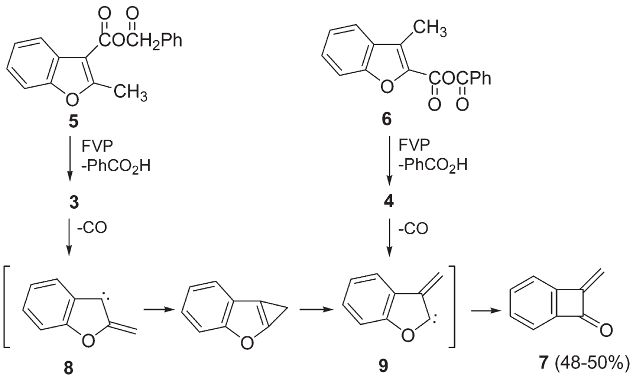


(4)

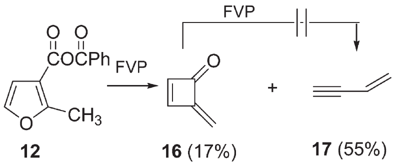
Received: August 23, 2011
Published: September 13, 2011

dx.doi.org/10.1021/jo201743h | *J. Org. Chem.* 2011, 76, 8440–8446

Scheme 1

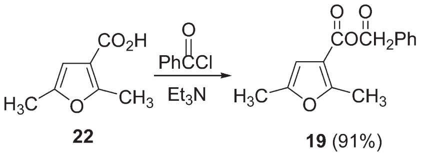


The FVP of **12** was performed at 550 °C and ca. 10^{-2} Torr using the method previously described.[10] Pyrolysis products were collected in $CDCl_3$ from the cold trap. After the solution was warmed to room temperature, quantitative ^{1}H NMR analysis, using dibromomethane as an integration standard, indicated that methylenecyclobutenone (**16**, 17% yield)[11,12] and 1-buten-3-yne (**17**, 55% yield) were obtained as two main products. The pyrolysis temperature at 550 °C and ca. 10^{-2} Torr appeared to be the optimum reaction conditions for our study. FVP of **12** lower than 500 °C or higher than 600 °C all gave lower yields of **16** and **17**. It is noteworthy that FVP of isolated **16** under the same pyrolysis conditions did not give **17**, a result suggesting that **16** and **17** are generated by different pathways from **12** (eq 5).



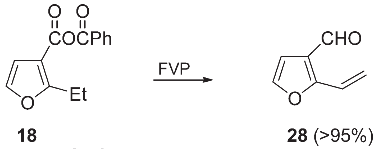
(5)

In order to study the mechanism for the formation of **16** and **17** from FVP of **12**, we have carried out substituent- and deuterium-labeling experiments by synthesizing and pyrolyzing the derivatives of **12**: benzoic 2-ethyl-3-furoic anhydride (**18**), benzoic 2,5-dimethyl-3-furoic anhydride (**19**), and benzoic 5-deuterio-2-methyl-3-furoic anhydride (**20**). Anhydrides **18**−**20** were prepared again from reactions of benzoyl chloride with the corresponding acids, 2-ethyl-3-furoic acid (**21**), 2,5-dimethyl-3-furoic acid (**22**) (eq 6), and 5-deuterio-2-methyl-3-furoic acid (**23**), respectively. Acid **21**[13] was prepared by condensation of ethyl 3-oxopentanonate (**24**)[14] with 2-chloroacetaldehyde followed by hydrolysis of the resulting 2-ethyl-3-furoate (**25**) (Scheme 2). Acid **22** was prepared by a method that has been previously reported.[15] Acid **23** was prepared from refluxing 3-furoic acid (**26**) in basic D_2O solution followed by methylation of the resulting 2,5-dideuterio-3-furoic acid (**27**)[16] (Scheme 3).

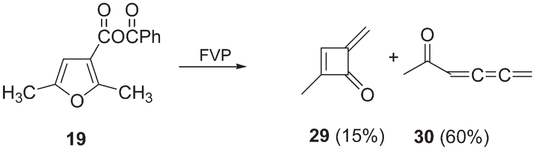


(6)

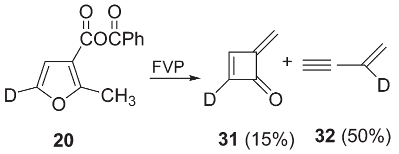
FVP of **18** at 550 °C and ca. 10^{-2} Torr gave 2-vinyl-3-furfural (**28**) as the sole product in quantitative yield (>95% yield) (eq 7). FVP of **19** under the same pyrolysis conditions gave 2-methyl-4-methylenecyclobutenone (**29**, 15% yield) and 3,4,5-hexatrien-2-one (**30**, 60% yield) as the main products (eq 8). In addition, FVP of **20** gave 2-deuterio-4-methylenecyclobutenone (**31**, 15% yield) and 2-deuterio-1-buten-3-yne (**32**, 50% yield) (eq 9).



(7)



(8)



(9)

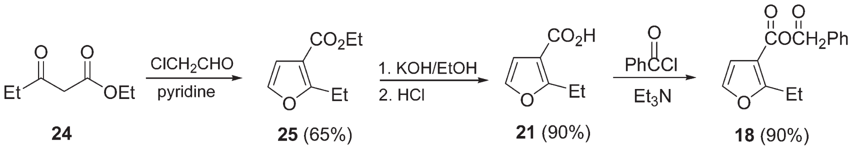
A mechanism to account for the aforementioned results is proposed and shown as Scheme 4.

Under the pyrolysis conditions, a [3 + 3] sigmatropic rearrangement from **12** or its derivatives **18**−**20** followed by elimination of a benzoic acid molecule is proposed to give the primary pyrolysis product **33**, a furan analogue of *α*-oxo-*o*-quinodimethane (**2**). A sequential [1,5]H shift from **33** (R = CH_3, R′ = H) will lead to the stable **28**. On the other hand, **33** (R = H) could eliminate a CO molecule to produce carbene **34**, a reaction for which there is good precedent.[17] A ring-opening reaction from carbene **34** (where R′ = H or D) followed by a [1,4]H shift and elimination of a CO molecule then give **17** or **32**. However, when R′ = CH_3, a ring-opening reaction from **34** will give isolable **30**, from which no methyl group migration was observed. Alternatively, a vinylcarbene−cycpopropene rearrangement[7] would convert carbene **34**, involving cyclopropene **35**, to carbene **36**, which then leads to the formation of **16**, **29**, or **31**.

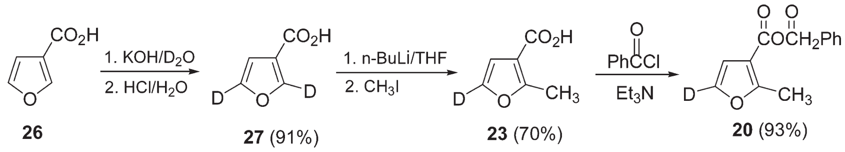
All the pyrolysis products, except **30**, are stable in solution and can be isolated and identified by their respective spectroscopic data. Compound **30** can only survive in solution at −78 °C and polymerized immediately upon warming to room temperature. Nonetheless, the low-temperature ^{1}H and ^{13}C NMR spectral data obtained at −78 °C for the product solution from **19** reveals the formation of **30** as the major product from FVP of **19**.

Additionally, the FVP of **13** performed under the same pyrolysis conditions gave the same pyrolysis products, **16** (15% yield) and **17** (50% yield) (eq 10). The results from FVP of **12** and **13** suggest that, under the reaction conditions, carbenes **34** and **36** are interconvertable via a vinylcarbene−cyclopropene rearrangement and lead to the ring-contraction product **16** and the ring-opening product **17** (Scheme 5). It is noteworthy that the ring-opening process is not observed in the FVP of **5**,[7] the benzofuran analogue of **12** (Scheme 1). This is probably due

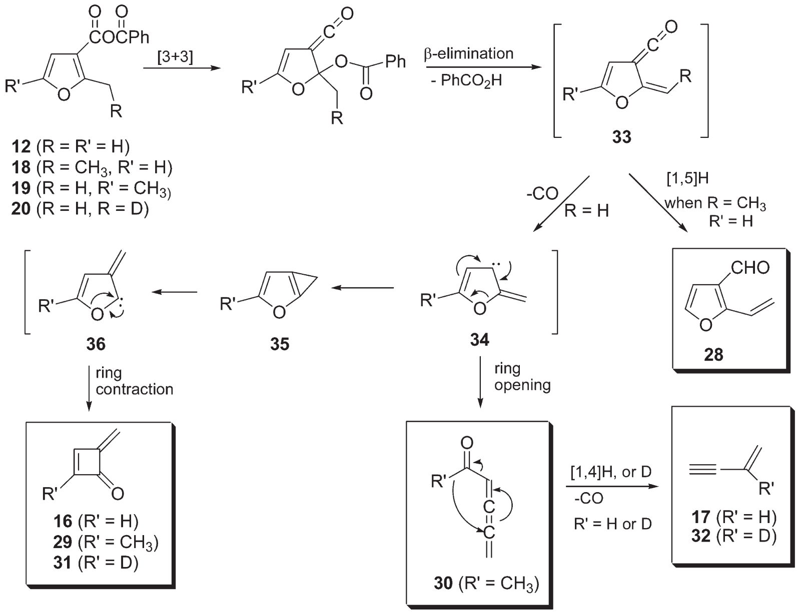
Scheme 2



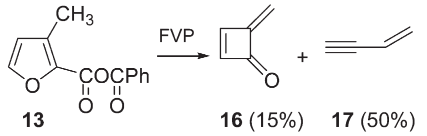
Scheme 3



Scheme 4



to the fact that ring-opening of the resulting carbene intermediate **8** would involve an aromaticity breaking of the fused benzene ring.



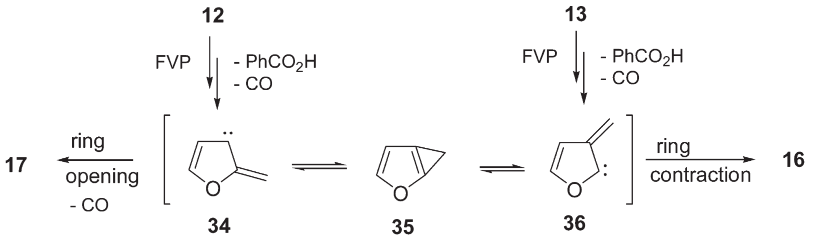
(10)

To provide insight into the pyrolysis behavior from an energetic viewpoint and theoretical basis for the proposed mechanism, the density functional theory method at the B3LYP/6-311++G (3df,2p) level was invoked to calculate the free energy profile, at 823.15 K and 1.0×10^{-5} atm, for the cascade reactions starting from the carbene **34**. The calculated results are presented in Figure 1.

Regarding the cascade reaction leading to the products, 1-buten-3-yne (**17**) and CO (progression to the left from **34** in Figure 1), the process is initiated by a ring-opening of **34** with a very low energetic barrier of 4.5 kcal mol^{-1}, resulting in the formation of low-energy intermediate **30** (26.6 and 29.0 kcal mol^{-1} lower than **34**). The intermediate **30** has two rotamers **30a** and **30b** that are separated by the rotational barriers of 6.9 kcal mol^{-1} for **30a** → **30b** and 9.3 kcal mol^{-1} for **30b** → **30a**. The following [1,4]H shift of **30b** was found to be the rate-determining step in the formation of **17**; the activation energy of this step was calculated to be fairly high with a magnitude of 39.3 kcal mol^{-1}. Once the hydrogen transfer is complete, the dissociation to the final product **17** and CO takes place spontaneously without an energetic barrier. The overall reaction from **34** to **17** is a highly exergonic process with a free energy change of −83.2 kcal mol^{-1}.

Considering the cascade reaction leading to the product of methylenecyclobutenone (**16**) (progression to the right from **34** in Figure 1), the carbene **34** first undergoes a conversion to the intermediate of cyclopropene **35**, which is about 14.2 kcal mol^{-1} higher in energy than **34**. The cyclopropene **35** readily transforms

Scheme 5



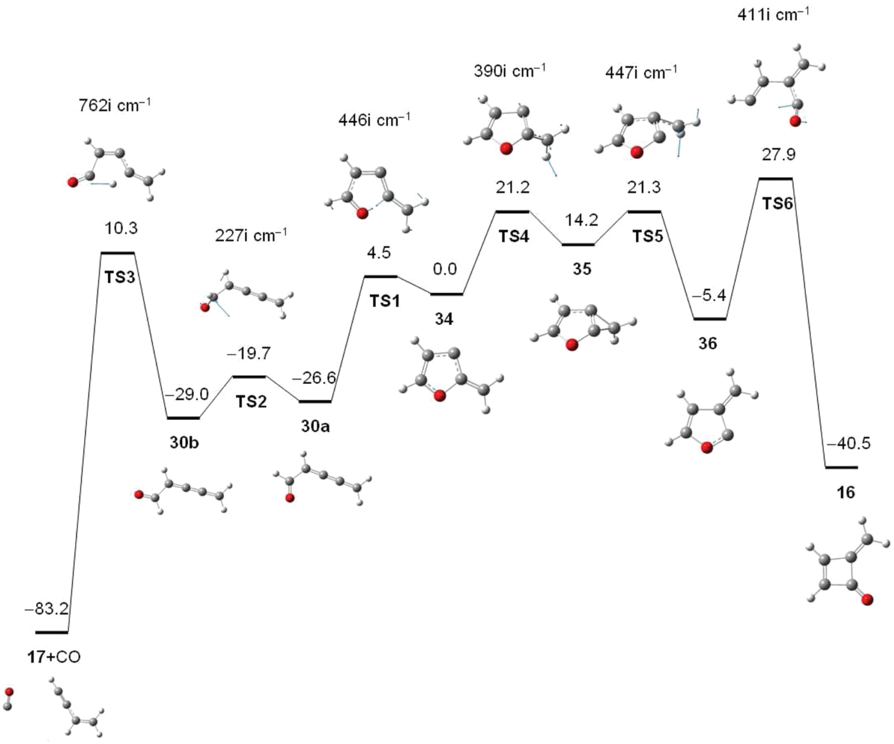


Figure 1. Free energy profile calculated at the CCSD(T)/aug-cc-pVTZ//B3LYP/6-311++G(3df,2p) level of theory. The relative free energies are given in kcal mol^{-1}. The imaginary frequencies and the corresponding vibrational modes are presented for the transition states.

into the carbene **36** with a relatively small activation energy of ca. 7 kcal mol^{-1}. The carbenes **34** and **36** are close in energy with the latter being 5.4 kcal mol^{-1} lower than the former. The subsequent ring-contraction process of **36** is characterized by a fairly high activation energy of 33.3 kcal mol^{-1} and is, thus, the rate-determining step in the production of **16**. The overall reaction from **34** to **16** is also highly exergonic with a free energy change of −40.5 kcal mol^{-1}.

With these computational data in hand, we are now in a position to rationalize the pyrolysis behavior observed in experiment. The computational results show that the activation energy for the rate-determining step for **34** → **17** is about 6 kcal mol^{-1} larger than that for **34** → **16**, which seems to conflict with the experimental observation that product **17** has higher yield than **16**. However, as can be clearly seen from Figure 1, the transformation from **34** to **17** proceeds through the formation of low-lying intermediates (**30a** and **30b**), whereas the intermediates formed in the process **34** → **16** are relatively high in energy (**35** and **36**). Supposing that these intermediates are in equilibrium under the experimental conditions, we can thus rationalize the preference for product **17** by the larger population for intermediate **30b** than for intermediate **36**.

The assumption we just made, that is, the intermediates can be considered in equilibrium, finds support from both theoretical and experimental results. On the theoretical side, the largest energetic barriers for the interconversions **34** ↔ **30** and **34** ↔ **36** are 31.1 kcal mol^{-1} (**30a** → **34**) and 26.7 kcal mol^{-1} (**36** → **35**), respectively. These barriers are significantly smaller than the barriers for the corresponding rate-determining steps of **30b** → **17** and **36** → **16**, implying that the intermediates have time to interconvert and reach equilibrium before transformation into the final products. On the experimental side, the pre-equilibrium of the intermediates is in agreement with and validated by the experimental observation that the FVP of **12** and **13** gives the same distribution of pyrolysis products.

In addition, the reaction of **34** → **17** was found to be more exergonic than the reaction of **34** → **16**, which is consistent with the observation that the dissociation into the **17** and CO is a more favorable channel. The low free energy of state **17** + CO is, in fact, originated from the entropy effect, since it is a dissociation process. On the other hand, if we consider the enthalpy change, **34** → **17** ($\Delta H = -28.8$ kcal mol^{-1}) was calculated to be less exothermic than **34** → **16** ($\Delta H = -38.8$ kcal mol^{-1}). In other words, the product **16** is more stable than the product **17** + CO in terms of enthalpy. This result is not surprising if one recognizes the fact that there are two more carbon−carbon bonds in **16** than in **17** + CO.

In summary, our experimental and computational results support the involvement of a vinylcarbene−cyclopropene rearrangement in the formation of **16** and **17** from the FVP of **12** and **13** (Scheme 5). Some highly functionalized compounds such as **16**, **17**, **29**, and **30** were synthesized from the systems under study. We are currently extending our study to the other heteroaromatic systems.

■ EXPERIMENTAL SECTION

Benzoic 2-Methyl-3-furoic Anhydride (12). A solution of 1.55 g (11.0 mmol) of benzoyl chloride in 20 mL of ether was added over a 10-min period to a stirred solution of 1.26 g (10 mmol) of 2-methyl-3-furoic acid (**14**)[8] and 1.68 mL (12.0 mmol) of triethylamine in 50 mL of ether. The mixture was stirred at room temperature for 10 h, 25 mL of water was added, and the mixture was stirred for an additional 1 h. The organic layer was separated, and the aqueous layer was extracted with ether (3 × 20 mL). The ether layers were combined and washed with 1 M HCl (3 × 30 mL) and saturated NaCl (3 × 30 mL). After drying ($MgSO_4$) and evaporation of the solvent, the crude product was purified by column chromatography on silica gel (5% ethyl acetate in hexanes) to give 2.14 g (9.30 mmol, 93% yield) of **12**: IR ($CHCl_3$, cm^{-1}) 1780 (C═O), 1720 (C═O); ^{1}H NMR ($CDCl_3$) δ 8.18−7.50 (m, 5H), 7.31 (d, *J* = 2.1 Hz, 1H), 6.73 (d, *J* = 2.1 Hz, 1H), 2.66 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 162.5 (C), 162.3 (C), 159.1 (C), 141.0 (CH), 134.5 (CH), 130.5 (CH), 128.9 (C), 128.8 (CH), 112.7 (C), 110.6 (CH), 14.0 (CH_3); HRMS Calcd for $C_{13}H_{10}O_4$: 230.0579. Found: 230.0571. Anal. Calcd: C, 67.83; H, 4.35. Found: C, 68.06; H, 4.43.

Benzoic 3-Methyl-2-furoic Anhydride (13). A procedure described for the preparation of **12** was followed for the reaction of 3-methyl-2-furoic acid (**15**)[9] with benzoyl chloride to give 90% yield of **13**: IR ($CHCl_3$, cm^{-1}) 1780 (C═O), 1720 (C═O); ^{1}H NMR ($CDCl_3$) δ 8.17−8.14 (m, 2H), 7.67−7.50 (m, 4H), 647 (d, *J* = 1.8 Hz, 1H), 2.46 (s, *J* = 7.5 Hz, 3H); ^{13}C NMR ($CDCl_3$) δ 162.2 (C), 154.3 (C), 146.8 (CH), 146.7 (C), 139.2 (C), 135.9 (C), 134.4(CH), 130.6 (CH), 128.8 (CH), 116.0 (CH), 11.9 (CH_3). Anal. Calcd for $C_{13}H_{10}O_4$: C, 67.83; H, 4.35. Found: C, 67.81; H, 4.41.

Ethyl 2-Ethyl-3-furoate (25). To a solution of 11.5 g (100 mmol) of ethyl acetoacetate in 25 mL of THF (dried over $LiAlH_4$), at 0 °C, was added dropwise 4.8 mL (2.2 equiv) of *n*-BuLi. After the solution was stirred at 10 °C for 10 min, 1.52 g (110 mmol) of CH_3I was added, and the resulting mixture was warmed to room temperature and stirred for another 15 min. The mixture was then neutralized with 1 M HCl and extracted with ether (3 × 20 mL). The ether extracts were combined and concentrated to give crude **24**. Without further purification, 25 mL (300 mmol) of pyridine was added, and the solution was stirred for 5 min. An amount of 15.8 mL (110 mmol) of 2-chloroacetaldehyde (a 45% aqueous solution) was added to the pyridine solution, and the resulting mixture was stirred at room temperature for 4 h. After extraction with ether (3 × 30 mL), the ether layers were combined and washed with water (3 × 30 mL) and saturated NaCl (3 × 20 mL). After drying ($MgSO_4$) and evaporation of the solvent, the crude product was purified by column chromatograohy on silica gel (5% ethyl acetate in hexanes) to give 10.9 g (65 mmol, 65% yield) of **25**: IR ($CHCl_3$, cm^{-1}) 1780 (C═O); ^{1}H NMR ($CDCl_3$) δ 7.00 (d, *J* = 1.5 Hz, 1H), 6.43 (d, *J* = 1.5 Hz, 1H), 4.27 (q, *J* = 6.9 Hz, 2H), 2.92 (q, *J* = 7.0 Hz, 2H), 1.33 (t, *J* = 6.9 Hz, 3H), 1.20 (t, *J* = 7.0 Hz, 3H).

2-Ethyl-3-furoic Acid (21). To a solution of 1.68 g (10 mmol) of **25** in 50 mL of EtOH was added 10 mL of a saturated aqueous solution of KOH. The mixture was stirred at room temperature for 10 h and then neutralized with 1 M HCl. The reaction mixture was extracted with ether (3 × 20 mL). The ether exatracts were combined and washed with saturated NaCl (3 × 20 mL) and dried with $MgSO_4$. After evapovation of the solvent, **21** was obtained in 90% yield (1.12 g, 9.0 mmol). **21**: mp 84−85 °C; IR ($CHCl_3$, cm^{-1}) 1690 (C═O); ^{1}H NMR ($CDCl_3$) δ 7.02 (d, *J* = 1.5 Hz, 1H), 6.45 (d, *J* = 1.5 Hz, 1H), 2.92 (q, *J* = 7.0 Hz, 2H), 1.21 (t, *J* = 7.0 Hz, 3H). [Lit.[13] mp 84−85 °C; ^{1}H NMR ($CDCl_3$) δ 7.02 (d, *J* = 1.5 Hz, 1H), 6.45 (d, *J* = 1.5 Hz, 1H), 2.92 (q, *J* = 7.0 Hz, 2H), 1.21 (t, *J* = 7.0 Hz, 3H)].

Benzoic 2-Ethyl-3-furoic Anhydride (18). A procedure described for the preparation of **12** was followed for the reaction of 2-ethyl-3-furoic acid with benzoyl chloride to give 90% yield of **18**: IR ($CHCl_3$, cm^{-1}) 1780 (C═O), 1720 (C═O); ^{1}H NMR ($CDCl_3$) δ 8.17−8.10 (m, 2H), 7.68−7.63 (m, 1H), 7.55−7.49 (m, 2H), 7.32 (d, *J* = 1.8 Hz, 1H), 6.71 (d, *J* = 1.8 Hz, 1H), 3.08 (q, *J* = 7.5 Hz, 2H), 1.29 (t, *J* = 7.5 Hz, 3H); ^{13}C NMR ($CDCl_3$) δ 167.3 (C), 162.3 (C), 159.0 (C), 141.0 (CH), 134.5 (CH), 130.5 (CH), 128.9 (C), 128.7 (CH), 111.7 (C), 110.5 (CH), 21.4 (CH_2), 11.8 (CH_3); HRMS Calcd for $C_{14}H_{12}O_4$:244.0732. Found: 244.0751. Anal. Calcd for $C_{14}H_{12}O_4$: C, 69.85; H, 4.92. Found: C, 69.61; H, 4.95.

Benzoic 2,5-Dimethyl-3-furoic Anhydride (19). A procedure described for the preparation of **12** was followed for the reaction of 2,5-dimethyl-3-furoic acid[15] with benzoyl chloride to give 91% yield of **19**: IR ($CHCl_3$, cm^{-1}) 1770 (C═O), 1715 (C = O); ^{1}H NMR ($CDCl_3$) δ 8.18−8.14 (m, 2H), 7.67−7.62 (m, 1H), 7.55−7.48 (m, 2H), 6.28 (s, 1H), 2.60 (s, 3H), 2.27 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 162.4 (C), 161.1 (C), 159.3 (C), 150.8 (C), 134.2 (CH), 130.3 (CH), 128.9 (C), 128.7 (CH), 113.2 (C), 105.9 (CH), 13.9 (CH_3), 13.1 (CH_3); HRMS Calcd for $C_{14}H_{12}O_4$:244.0732. Found: 244.0738. Anal. Calcd for $C_{14}H_{12}O_4$: C, 69.85; H, 4.92. Found: C, 69.65; H, 5.04.

2,5-Dideuterio-3-furoic Acid (27). To a solution of 5.00 g (44.6 mmol) of 3-furoic (**26**) in 50 mL of D_2O was added 10.0 g (92.6 mmol) of KOH. The solution was heated to reflux for 10 h. After being cooled to room temperature, the resulting mixture was neutralized with 1 M HCl and extracted with ether (4 × 50 mL). The ether extracts were combined, dried ($MgSO_4$), and concentrated to give 4.62 g (41. mmol, 91% yield) of **27**: IR ($CHCl_3$, cm^{-1}) 1675 (C═O); ^{1}H NMR ($CDCl_3$) δ 10.50−9.50 (br, 1H), 6.78 (s, 1H); ^{13}C NMR ($CDCl_3$) δ 168.6 (C), 149.0 (CD), 144.0 (CD), 118.6 (C), 109.8 (CH); LRMS (*m*/*z*, rel intensity) 114 (M$^+$, 100).

5-Deuterio-2-methyl-3-furoic Acid (23). To a solution of 4.50 g (39.5 mmol) of **27** in 100 mL of THF (dried over $LiAlH_4$) was added 2.2 equiv of *n*-BuLi in hexanes dropwise at −78 °C under nitrogen. After the reaction mixture was stirred at −78 °C for 30 min, a 3.73 g (26.3 mmol) quantity of CH_3I was added, and the mixture was allowed to warm to room temperature and stirred for another 3 h. The mixture was then poured into 100 mL of water. After separation, the aqueous layer was extracted with ether (3 × 30 mL), and the combined organic layers were dried ($MgSO_4$) and evaporated. The crude product was purified by recrystallization from hexanes to give 3.51 g (27.6 mmol, 72% yield) of **23**: mp 101−102 °C; IR ($CHCl_3$, cm^{-1}) 1700 (C═O); ^{1}H NMR ($CDCl_3$) δ 12.00−11.00 (br, 1H), 6.68 (s, 1H), 2.60 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 170.0 (C), 160.9 (C), 140.6 (CD), 112.9 (C), 110.6 (CH), 13.8 (CH_3); LRMS (*m*/*z*, rel, intensity) 127 (M$^+$, 100).

Benzoic 5-Deuterio-2-methyl-3-furoic Anhydride (20). A procedure described for the preparation of **12** was followed for the reaction of 5-deuterio-2-methyl-3-furoic acid with benzoyl chloride to give 93% yield of **19**: IR ($CHCl_3$, cm^{-1}) 1800 (C═O), 1720 (C═O); ^{1}H NMR ($CDCl_3$) δ 8.17−8.10 (m, 2H), 7.70−7.60 (m, 1H), 7.55−7.40

(m, 2H), 6.70 (s, 1H), 2.65 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 162.3 (C), 162.2 (C), 159.0 (C), 141.0 (CD), 134.4 (CH), 130.4 (CH), 128.8 (C), 128.7 (C), 112.6 (C), 110.3 (CH), 14.0 (CH_3); HRMS Calcd for $C_{13}H_9O_4D$: 231.0639. Found: 231.0634.

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 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. 50 °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 $CS_2/CDCl_3$ solution was deposited into the trap through a side arm. 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 2-Methyl-3-furoic Anhydride (12). **12** (850 mg, 3.70 mmol) was pyrolyzed at 550 °C and ca. 10^{-2} Torr in the normal manner for 3 h. One milliliter of $CDCl_3$ and a weighed amount of dibromomethane as an integration standard were added to the product trap. ^{1}H NMR analysis of this mixture showed the presence of **16** (50.2 mg, 0.630 mmol, 17%) and **17** (106 mg, 2.04 mmol, 55%). **16** and **17** can be separated by low-pressure distillation. **16**: ^{1}H NMR ($CDCl_3$) δ 8.73 (d, *J* = 2.7 Hz, 1H), 7.08 (d, *J* = 2.7 Hz, 1H), 5.10 (d, *J* = 0.9 Hz, 1H), 4.82 (d, *J* = 0.9 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 188.6 (C), 172.5 (CH), 157.6 (C), 153.3 (CH), 98.0 (CH_2). [Lit.[10] **16**: ^{1}H NMR ($CDCl_3$) δ 8.66, 7.16, 5.01, 4.78]. **17**: ^{1}H NMR ($CDCl_3$) δ 5.80−5.40 (m, 3H), 2.82 (s, 1H); ^{13}C NMR ($CDCl_3$) δ 128.8 (CH_2), 116.3 (CH), 82.2 (C), 77.8 (CH). [Lit.[17] **17**: ^{1}H NMR ($CDCl_3$) δ 5.8−5.4 (m, 3H), 2.88 (s, 1H); ^{13}C NMR ($CDCl_3$) δ 128.6, 116.4, 82.3, 77.8].

Pyrolysis of Benzoic 3-Methyl-2-furoic Anhydride (13). A 900 mg (3.91 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 45.9 mg (0.587 mmol, 15%) of **16** and 102 mg (1.96 mmol, 50%) of **17**.

Pyrolysis of Benzoic 2-Ethyl-3-furoic Anhydride (18). A 310 mg (1.27 mmol) quantity of **18** was pyrolyzed at 550 °C and ca. 10^{-2} Torr in a procedure described for the FVP of **12** to give **28** in 96% yield (149 mg, 1.27 mmol). **28**: IR ($CHCl_3$, cm^{-1}) 1680 ($C{=}O$); ^{1}H NMR ($CDCl_3$) δ 10.05 (s, 1H), 7.37 (d, *J* = 1.8 Hz, 1H), 7.00 (dd, *J* = 17.4, 11.4 Hz, 1H), 6.77 (d, *J* = 1.8 Hz, 1H), 6.07 (dd, *J* = 17.4, 0.9 Hz, 1H), 5.60 (dd, *J* = 11.4, 0.9 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 184.4 (CH), 158.6 (C), 142.8 (CH), 122.7 (C), 122.2 (CH), 119.7 (CH_2), 109.1 (CH). HRMS Calcd for: $C_7H_6O_2$: 122.0368. Found: 122.0368.

Pyrolysis of Benzoic 2,5-Dimethyl-3-furoic Anhydride (19). A 650 mg (3.91 mmol) quantity of **19** was pyrolyzed at 550 °C and ca. 10^{-2} Torr in a procedure described for the FVP of **12** to give 37.6 mg (0.40 mmol, 15%) of **29** and 150 mg (1.60 mmol, 60%) of **30**. **29**: ^{1}H NMR ($CDCl_3$) δ 8.46 (d, *J* = 0.9 Hz, 1H), 4.84 (s, 1H), 4.57 (d, *J* = 0.9 Hz, 1H), 1.95 (s, 3H, CH_3). ^{13}C NMR ($CDCl_3$) δ 192.8 (C), 176.0 (CH), 168.3 (C), 155.0 (C), 94.0 (CH_2), 10.2 (CH_3). HRMS Calcd for: C_6H_6O: 94.0419. Found: 94.0412. **30**: ^{1}H NMR ($CS_2/CDCl_3$ = 1:1, −78 °C) δ 6.09 (dd, *J* = 8.4, 7.8 Hz, 1H), 5.93 (dd, *J* = 8.7, 7.8 Hz, 1H), 5.86 (dd, *J* = 8.7, 8.4 Hz, 1H), 2.27 (s, 3H); ^{13}C NMR ($CS_2/CDCl_3$ = 1:1, −78 °C) δ 196.0 (C), 177.5 (C), 166.3 (C), 110.6 (CH), 105.5 CH_2), 25.8 (CH_3). Low-temperature atmospheric pressure ionization MS at −78 °C (*m*/*z*, rel intensity) 95 (MH^+, 100).[18]

Pyrolysis of Benzoic 5-Deuterio-2-methyl-3-furoic Anhydride (20). A 350 mg (1.52 mmol) quantity of **20** was pyrolyzed at 550 °C and ca. 10^{-2} Torr in a procedure described for the FVP of **12** to give 18.4 mg (0.23 mmol, 15%) of **31** and 40.2 mg (0.76 mmol, 50%) of **32**. **31**: ^{1}H NMR ($CDCl_3$) δ 8.73 (s, 1H), 5.10 (s 1H), 4.82 (s, 1H); ^{13}C NMR ($CDCl_3$) δ 188.6 (C), 157.6 (C), 153.3 (CH), 98.0 (CH_2). **32**: ^{1}H NMR ($CDCl_3$) δ 5.70−5.40 (m, 2H), 2.82 (s, 1H); ^{13}C NMR ($CDCl_3$) δ 128.9 (CH_2), 82.8 (C), 77.8 (CH).

Computational Methods. Density functional theory method at the B3LYP/6-311++G(3df,2p) level were applied to optimize the stationary structures. Vibrational frequency calculations were subsequently carried out at the same level of theory for two purposes: (i) identification of the nature of the optimized structures (all positive frequencies for a minimum and one imaginary frequency for a transition state) and (ii) thermochemical corrections to obtain enthalpies and free energies. All transition states were checked to connect the proper minima by intrinsic reaction coordinates (IRC) calculations. To simulate the experimental conditions, thermochemical corrections were performed at 823.15 K and 1.0×10^{-5} atm instead of standard conditions. In order to obtain more accurate energies, single-point calculations using a high-level correlated coupled cluster method with single, double, and noniterative triple excitations, CCSD(T), combined with the aug-cc-pVTZ basis set were performed on the B3LYP/6-311++G(3df,2p) optimized structures. Our preliminary calculations at the B3LYP/6-311++G(d,p) level indicate that the singlet state is more stable than the triplet state for carbenes **34** and **36** by 8.7 kcal mol^{-1} and 18.5 kcal mol^{-1}, respectively; we therefore consider only the singlet carbenes in the following computational study on the reaction mechanism. All calculations were accomplished with the Gaussian 09 program.[20]

■ ASSOCIATED CONTENT

Ⓢ **Supporting Information.** Spectroscopic data for **12**, **13**, **16**, **17**, **18**, **19**, **20**, **28**, **29**, **30**, **31**, and **32**, computational details of **16**, **17**, **30**, **34**, **35**, and **36**. This material is available free of charge via the Internet at http://pubs.acs.org.

■ AUTHOR INFORMATION

Corresponding Author

*Fax: +886-7-5253909. E-mail: ch-chou@mail.nsysu.edu.tw.

■ ACKNOWLEDGMENT

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

■ REFERENCES

(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* **1972**, *13*, 1249–1251.

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

(7) Tseng, P. W.; Yet, S. W.; Chou, C. H. *J. Org. Chem.* **2008**, *73*, 3481–3485.

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

(9) Sherman, E.; Amstutz, E. D. *J. Am. Chem. Soc.* **1950**, *72*, 2195–2198.

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

(11) Trahanovsky, W. S.; Park, M. G. *J. Am. Chem. Soc.* **1973**, *95*, 5412.

(12) Trahanovsky, W. S.; Park, M. G. *J. Org. Chem.* **1974**, *39*, 1448–1449.

(13) Knight, D. W.; Nott, A. P. *J. Chem. Soc., Perkin Trans. 1* **1981**, 1125–1131.

(14) Huckin, S. N.; Weiler, L. *J. Am. Chem. Soc.* **1974**, *96*, 1082–1087.

(15) Hurd, C. D.; Wilkinson, K. *J. Am. Chem. Soc.* **1948**, *70*, 739–741.

(16) Knight, D. W. *Tetrahedron Lett.* **1979**, *5*, 469–472.

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

(18) Aitken, R. A.; Atherton, J. I. *J. Chem. Soc., Perkin Trans. 1* **1994**, *11*, 1281–1284.

(19) Wang, W. S.; Tseng, P. W.; Chou. C. H.; Shiea, J. T. **1998**, *Rapid Commun. Mass Spectrom.* **1998**, *12*, 931-934.

(20) Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M. A.; Cheeseman, J. R.; Scalmani, G.; Barone, V.; Mennucci, B.; Petersson, G. A.; Nakatsuji, H.; Caricato, M.; Li, X.; Hratchian, H. P.; Izmaylov, A. F.; Bloino, J.; Zheng, G.; Sonnenberg, J. L.; Hada, M.; Ehara, M.; Toyota, K.; Fukuda, R.; Hasegawa, J.; Ishida, M.; Nakajima, T.; Honda, Y.; Kitao, O.; Nakai, J.; Vreven, T.; Montgomery, J. A., Jr.; Peralta, J. E.; Ogliaro, F.; Bearpark, M.; Heyd, J. J.; Brothers, E.; Kudin, K. N.; Staroverov, V. N.; Kobayashi, R.; Normand, J.; Raghavachari, K.; Rendell, A.; Burant, J. C.; Iyengar, S. S.; Tomasi, J.; Cossi, M.; Rega, N.; Millam, J. M.; Klene, M.; Knox, J. E.; Cross, J. B.; Bakken, V.; Adamo, C.; Jaramillo, J.; Gomperts, R.; Stratmann, R. E.; Yazyev, O.; Austin, A. J.; Cammi, R.; Pomelli, C.; Ochterski, J. W.; Martin, R. L.; Morokuma, K.; Zakrzewski, V. G.; Voth, G. A.; Salvador, P.; Dannenberg, J. J.; Dapprich, S.; Daniels, A. D.; Farkas, O.; Foresman, J. B.; Ortiz, J. V.; Cioslowski, J.; Fox, D. J. *Gaussian 09, Revision A.02*; Gaussian, Inc., Wallingford, CT, 2009.