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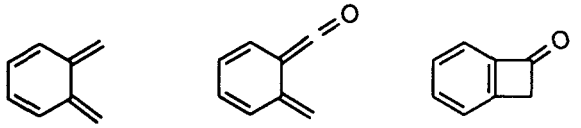
Synthesis of Pyrido[b]cyclobuten-5-one and 1-Azafulvenallene by Flash Vacuum Pyrolysis of 3-Chloroformyl-2-methylpyridine

Chin-Hsing Chou*, Cheng-Chang Wu and Wey-Kao Chen

Department of Chemistry, National Sun Yat-Sen University
Kaohsiung, Taiwan, 80424, China

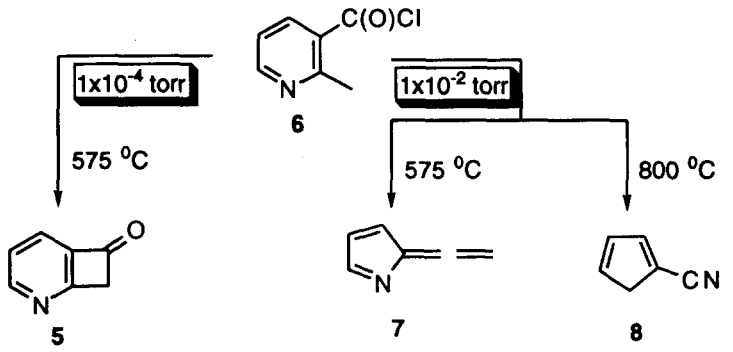
Abstract: The temperature and pressure dependence of products formed on pyrolysis of 3-chloroformyl-2-methylpyridine (**6**) have been studied. Pyrolysis of **6** at 575 ^{0}C and ca. 1x10^{-4} torr gives pyrido[b]cyclobuten-5-one (**5**) in 20% yield. Pyrolysis of **6** at 575 and 800 ^{0}C and under the pressure of ca. 1x10^{-2} torr give 1-azafulvenallene (**7**, 46%) and 1-cyanocyclopentadiene (**8**, 42%), respectively. Irradiation of **5** (λ > 300 nm) in methanol affords 2-methoxy-3-acetylpyridine (**9**) quantitatively.

o-Quinodimethane (**1**) has been shown to be a transient intermediate in many reactions[1] and has been used extensively as a diene in several organic syntheses.[1b-f, i] The development of the chemistry of **1** has led to the study of its ketene derivative, α-oxo-*o*-quinodimethane (**2**). Although **2** has never been isolated successfully, the closed form of **2**, benzocyclobutenone (**3**), has been prepared by several methods.[2] One of the methods is pyrolysis of *o*-toluoyl chloride (**4**) to give **3** as the main product, presumably, involving **2** as the key intermediate.[2h] Based on the same approach, we have synthesized the previously unknown pyridine analogue of **3**, pyrido[b]cyclobuten-5-one (**5**), by the flash vacuum pyrolysis (FVP) of 3-chloroformyl-2-methylpyridine (**6**). We have also studied the chemistry of **5** thermally and photochemically and the results are presented herein.



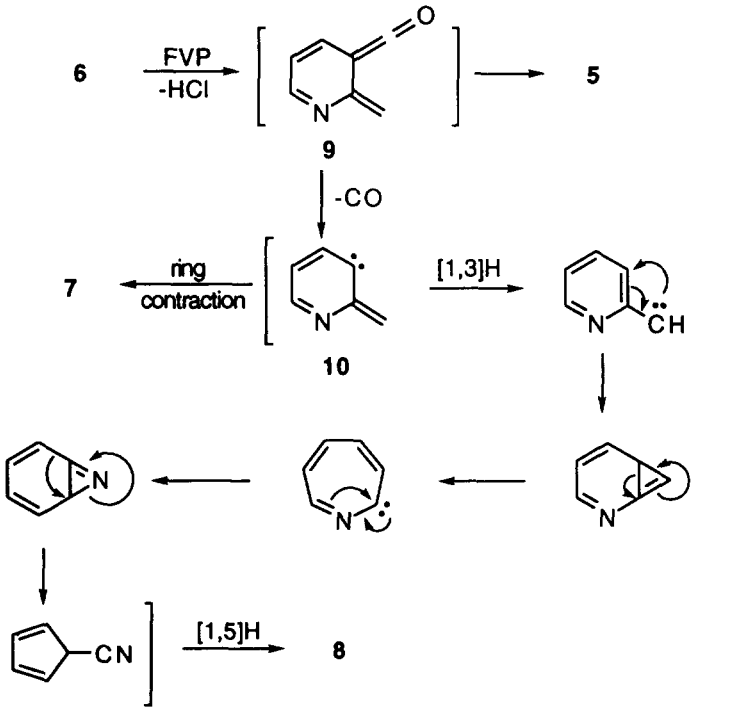
1 **2** **3**

FVP of **6**[3] at 575 ^{0}C and ca. 1x10^{-4} torr by the previously described procedure[4] gave **5** as the only identifiable product along with substantial amounts of polymers. Purification of the product mixture by flash column chromatography on silica gel (EtOAc-hexane, 1:2) afforded **5** in 20% yield.[5] When the pressure was raised to ca. 1x10 $^{-2}$ torr, FVP of **6** at 575 ^{0}C gave 1-azafulvenallene (**7**) as the main pyrolysis product in 46% yield,[6] whereas at 800 ^{0}C FVP of **6** gave 1-cyanocyclopentadiene (**8**) in 42% yield.[7]



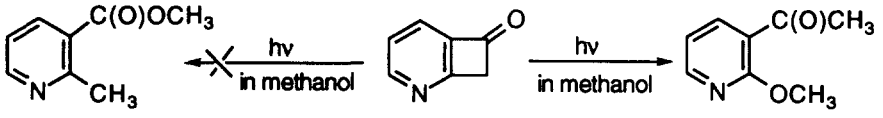
FVP of **6** is expected to give 3-carbonyl-2-methylene-2,3-dihydropyridine (**9**) as the primary pyrolysis product by 1,4-elimination of HCl from **6**. Under high vacuum condition, i.e. at ca. $1x10^{-4}$ torr and 575 °C, **9**, due to short contact time in the hot zone, survives under the reaction condition and cyclizes to give the more stable product **5**. When the pyrolysis is performed under lower vacuum condition, i.e. at ca. $1x10^{-2}$ torr, **9** eliminates a CO molecule to give the carbene intermediate **10**, which, at 575 °C, undergoes ring contraction to give **7**, or, at 800 °C, proceeds through a series of rearrangement to give **8**. A possible reaction mechanism for the formation of **8** from **6** is proposed as shown in Scheme 1.

Scheme 1



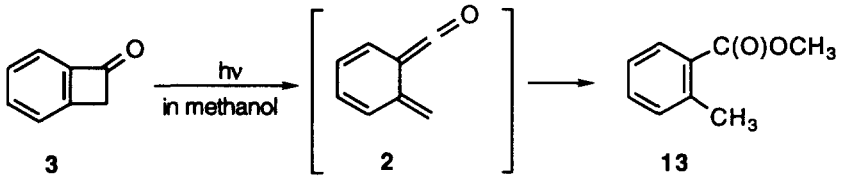
It is noteworthy that FVP of the isolated **7** at 800 °C and ca. $1x10^{-2}$ torr does not give **8**. A result indicates that **7** is not an intermediate leading to the formation of **8**, and supports the mechanism shown above.

Irradiation of **5** ($\lambda > 300$ nm) in methanol afforded 3-acetyl-2-methoxypyridine (**11**) quantitatively, whereas irradiation of **5** ($\lambda > 300$ nm) in benzene only resulted in complete decomposition of **5**. The formation of **11** instead of the expected methyl 2-methylnicotinate (**12**), from irradiation of **5** in methanol, might result from an attack of a methanol molecule at the bridgehead carbon atom adjacent to the nitrogen atom in the pyridine ring of **5** and suggests that no open form of **5**, i.e. compound **9**, is involved.



12 **5** **11**

A result that is different from irradiation of benzene analogue, **3**, in methanol, from which methyl 2-methylbenzoate (**13**) is obtained as the major product, presumably, involve **2** as the intermediate.[2e] The structure of **11** was confirmed by comparing NMR spectral data of **11**[8] with that of **12**, prepared from an reaction of **6** wih methanol.[9]



3 **2** **13**

We are currently applying this approach to the preparation of other heterocyclic analogues of α-oxo-*o*-quinodimethanes.

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References and Notes

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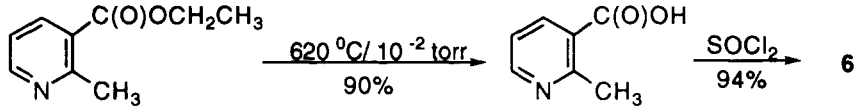
3. Compound **6** was prepared as follows.



4. Chou, C. H.; Trahanovsky, W. S. *J. Am. Chem. Soc.***1986**, *108*, 4138-4144.
5. **5**: pale yellow solid, m.p. 54-56 °C; IR ($CDCl_3$, cm^{-1}) 1796, 1768, 1572, 1472, 1394; ^1H NMR ($CDCl_3$) δ 8.69 (dd, *j* = 5.1, 1.2 Hz, 1H), 7.62 (dd, *j* = 7.5, 1.2 Hz, 1H), 7.37 (dd, *j* = 7.5, 5.1 Hz, 1H), 4.17 (s, 2H); ^{13}C NMR ($CDCl_3$) δ 186.10 (C), 170.24 (C), 156.38 (CH), 141.46 (C), 128.85 (CH), 124.53 (CH), 55.69 (CH_2); HRMS Calcd for C_7H_5NO: 119.0371. Found: 119.0376.
6. **7**: IR ($CDCl_3$, cm^{-1}) 1928, 1717, 1607, 1457, 1378; ^1H NMR ($CDCl_3$) δ 6.75 (m, 1H), 6.35 (m, 1H), 5.15 (m, 3H); ^{13}C NMR ($CDCl_3$) δ 215.83 (C) 146.59 (CH), 116.30 (C), 96.57 (CH), 91.86 (CH), 77.62 (CH_2); MS, m/z (rel intensity) 92 (9), 91 (M^+, 100), 65 (14), 64 (43), 63 (32), 62 (13), 61 (10).
7. (a) **8**: IR ($CDCl_3$, cm^{-1}) 2928, 2905, 2220, 1620, 1395, 1198; ^1H NMR ($CDCl_3$) δ 7.32 (t, *j* = 1.5 Hz, 1H), 6.69 (m, 1H), 6.61 (m, 1H), 3.33 (dd, *j* = 2.7, 1.5 Hz, 2H); ^{13}C NMR ($CDCl_3$) δ 147.18 (CH), 139.23 (CH), 132.22 (CH), 116.81 (C), 114.35 (C), 44.24 (CH_2); MS, m/z (rel intensity) 92 (7), 91 (m^+, 100), 65 (13), 64 (61), 63 (26), 62 (10), 52 (21), 50 (10), 41 (10), 40 (11).(b) Wentrup, C.; Crow, W. D. *Tetrahedron* **1970**, *26*, 4375-4386.
8. **11**: ^1H NMR ($CDCl_3$) δ 8.77 (br s, 1H), 8.54 (br s, 1H), 7.56 (br s, 1H), 3.99 (s, 3H), 3.04 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 164.91 (C), 158.20 (C), 147.86 (CH), 142.27 (CH), 127.14 (C), 122.53 (CH), 52.87 (CH_3), 22.33 (CH_3).
9. **12**: ^1H NMR ($CDCl_3$) δ 8.62 (dd, *j* = 4.8, 1.8 Hz, 1H), 8.20 (dd, *j* = 8.1, 1.8 Hz, 1H), 7.22 (dd, *j* = 8.1, 4.8 Hz, 1H), 3.93 (s, 3H), 2.85 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 166.94 (C), 159.86 (C), 151.77 (CH), 138.39 (CH), 125.34 (C), 120.84 (CH), 52.21 (CH_3), 24.74 (CH_3).

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