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A Radical Clock Reaction in the Photochemistry of an Acylpyrazine

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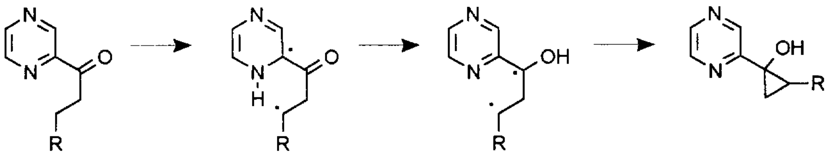
Abstract: Radical clock measurements using the cyclopropyl-substituted acylpyrazine **7** indicate that for the collapse of biradical **9** to **10**, $k \geq 2.8 \times 10^8$ s^{-1}. Copyright © 1996 Elsevier Science Ltd

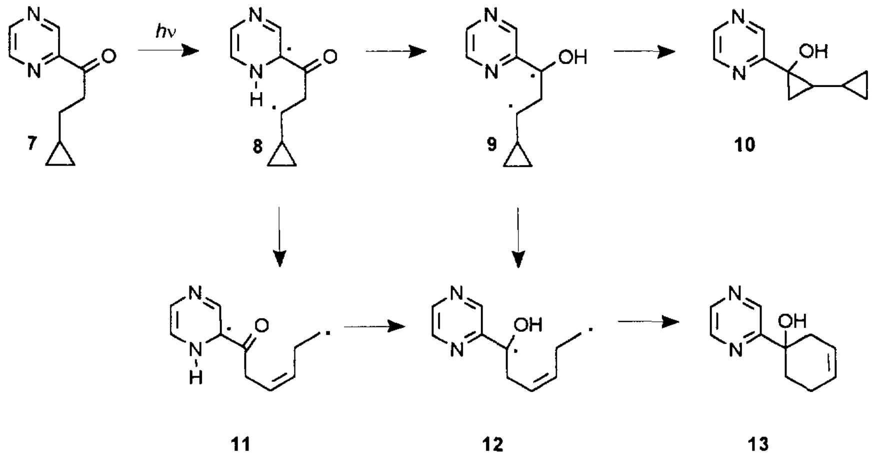
On irradiation, appropriate acylpyrazines such as **1** undergo an efficient photochemical rearrangement that is believed to proceed through abstraction of γ-hydrogen by nitrogen (**2**), rearomatization with transfer of hydrogen from nitrogen to oxygen (**3**), and collapse of the resulting 1,3-biradical to yield the isomeric 1-pyrazylcyclopropanol (**4**).[1] The quantum yield (Φ_P) for formation of **4** (R = H) from **1** (R = H) in *tert*-butyl alcohol-benzene (9:1) is 0.77.[1a] We report here preparation and irradiation of the cyclopropyl-substituted acylpyrazine **7**, in which rearrangement proceeds by way of cyclopropylcarbinyl radicals **8** and **9**. These intermediates can serve as radical clocks[2] to provide information about biradical lifetimes in this reaction.



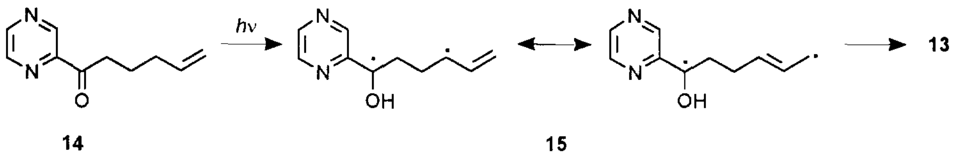
1 **2** **3** **4**

The required ketone **7**[3] was available following a known procedure[1a,4] through addition of the Grignard reagent from 2-cyclopropylethyl bromide to pyrazinecarbonitrile and subsequent hydrolysis. Irradiation of **7** in *tert*-butyl alcohol-benzene (9:1)[1] (λ >340 nm) led to a mixture of **10**[3] (80%) and **13**[3](~1.5%). The amount of **13** formed was estimated from NMR spectra of the crude reaction mixture and independently from analytical gas chromatography. We have previously noted that cyclopropanols such as **4** are unstable,[1a] and

10 underwent significant decomposition on chromatography over either silica gel or neutral alumina and on preparative gas chromatography. With the loss of considerable material, we were able to obtain one diastereomer of **10** pure for characterization. NMR spectra of the two diastereomers of **10** were quite similar in the diastereomeric mixture and did not permit assignment of stereochemistry to the purified isomer. The structures of **10** and **13** rest on the spectroscopic measurements reported[3] and on independent preparation of **13** from **14**,[3] which was available from reaction of 4-pentenylmagnesium bromide with pyrazinecarbonitrile,



following the procedure used for 7. On irradiation, **14** underwent type II reaction to yield biradical **15**, which collapsed to **13**.[5] Other products were formed from **14** as well. The samples of **13** prepared by the two independent routes were essentially indistinguishable both spectroscopically and chromatographically.



These results permit a semiquantitative estimate of the rate of cyclization of **9** to **10**, since this reaction proceeds in competition with the alternative opening of **9** to **12**. From earlier work,[2] the rate constant for opening of a secondary cyclopropylcarbinyl radical such as **9** may be estimated at ~7.0 × 10^7 s^{-1} at 37 °C, the approximate temperature of irradiation of 7. However, the observed yields of **10** and **13** only approximately reflect the rates in question. Owing to the inevitable loss of the trans isomers of radicals **11** and **12**, the observed yield ratio for **10** and **13** (80/1.5 ~ 53) is undoubtedly too large. The lower limit (but an unlikely value) for this ratio is 80/20 = 4, which would obtain only if all material that remains unrecovered originated from rearranged biradicals **11** and **12**. A further limitation on interpretation of the product ratio is the fact that there are two paths for competitive ring opening (**8** → **11** and **9** → **12**). The existence of this alternative path (**8** → **11**) precludes using the upper limit ratio of 53 to set an upper limit for the rate constant for closure of **9** to **10**. However, since all **10** is formed by way of **9**, the lower limit product ratio of 4 requires a lower limit of $k \geq 2.8 \times 10^8$ s^{-1} for this reaction. Greater precision in this value must await further experimentation.[6]

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3. These new compounds were characterized by IR and NMR spectra and by measurement of their molecular ions in high resolution mass spectra. For **7**: ^{1}H NMR ($CDCl_3$, 300 MHz): δ 9.18 (d, 1H, *J* = 1.5 Hz), 8.73 (d, 1H, *J* = 2.4 Hz), 8.62 (dd, 1H, *J* = 2.4, 1.5 Hz), 3.26 (t, 2H, *J* = 7.2 Hz), 1.60 (q, 2H, *J* = 7.2 Hz), 0.75 (m, 1H), 0.39 (dm, 2H, *J* = 5.1 Hz), 0.04 (m, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 201.3, 147.6, 143.6, 143.4, 37.9, 28.9, 10.6, 4.6; IR (neat): 3001,1701 cm^{-1}; HRMS *m/z* 176.0951 $[(M)^+$, calcd for $C_{10}H_{12}N_8O$ 176.0950]. For **10** (one diastereomer): ^{1}H NMR ($CDCl_3$, 300 MHz): δ 8.85 (d, 1H, *J* = 1.2 Hz), 8.37 (dd, 1H, *J* = 2.4, 1.5 Hz), 8.31 (d, 1H, *J* = 2.7 Hz), 4.25 (bs, 1H), 1.48 (dd, 1H, *J* = 9.6, 5.1 Hz), 1.32 (dt, 1H, *J* = 9.6, 6.9 Hz), 1.08 (dd, 1H, *J* = 6.9, 5.1 Hz), 0.96-0.87 (m, 1H), 0.58 dq, 2H, *J* = 7.8, 2.1 Hz), 0.41-0.35 (m, 1H), 0.25-0.19 (m, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 159.6, 143.1, 141.1, 140.7, 59.2, 33.6, 23.1, 8.3, 4.5, 3.7; IR (neat): 3290,3080, 3002 cm^{-1}; HRMS *m/z* 176.0956 $[(M)^+$, calcd for $C_{10}H_{12}N_2O$ 176.0950]. For **13**: ^{1}H NMR ($CDCl_3$, 300 MHz): δ 8.76 (d, 1H, *J* = 1.2 Hz), 8.45-8.42 (m, 2H), 5.82-5.69 (m, 2H), 3.95 (s, 1H), 2.62 (dm, 1H, *J* = 18.0 Hz), 2.38-2.28 (m, 1H), 2.22 (dm, 1H, *J* = 18.6 Hz), 2.06-1.96 (m, 2H), 1.82-1.75 (m, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 160.7, 143.0, 142.6, 141.9, 126.9, 124.1, 71.5, 37.9, 33.9, 22.5; IR (neat): 3388, 3027 cm^{-1}; HRMS *m/z* 176.0951 $[(M)^+$, calcd for $C_{10}H_{12}N_2O$ 176.0950]. For **14**: ^{1}H NMR ($CDCl_3$, 300 MHz): δ 9.15 (d, 1H, *J* = 1.5 Hz), 8.68 (d, 1H, *J* = 2.4 Hz), 8.57 (dd, 1H, *J* = 2.4, 1.0 Hz), 5.75 (ddt, 1H, *J* = 17.1, 10.2, 6.6 Hz), 5.01-4.89 (m, 2H), 3.13 (t, 2H, *J* = 7.5 Hz), 2.09 (m, 2H), 1.78 (quintet, 2H, *J* = 22.8; IR (neat): 3076,1701 cm^{-1}; HRMS *m/z* 176.0951 $[(M)^+$, calcd for $C_{10}H_{12}N_2O$ 176.0950].

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5. For earlier study of type II abstraction of allylic hydrogen and subsequent cyclization, see Cormier, R. A.; Agosta, W. C. *J. Am. Chem. Soc.* **1974**, *96*, 1867

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