1,5-dioxohexyl)phenol (12) occurred. 12: ^{1}H NMR δ 2.17 (s, 3 H, CH_3), 2.45–2.75 (m, 4 H, 2 × CH_2), 6.87 and 7.50 (dd each, 1 H each, J = 7.3 Hz, H-4 and H-5), 7.00 and 7.95 (d each, 1 H each, J = 8.2 Hz, H-3 and H-6); ^{19}F NMR δ −158.5 (t, $J_{F,H}$ = 21.8 Hz); ^{13}C NMR δ 207.9 (C-5′), 195.4 (d, $^2J_{C,F}$ = 24.4 Hz, C-1′), 169.0 (d, $^2J_{C,F}$ = 25.9 Hz, CO_2H), 163.5 (COH), 137.5, 131.0, 130.8, 119.4, 118.6 (C and CH ar), 97.5 (d, $^1J_{C,F}$ = 198.4, C-2′), 36.7 (C-4′), 29.8 (C-6′), 27.7 (d, $^2J_{C,F}$ = 21.6 Hz, C-3′). Another procedure was therefore employed. The *N*-fluoroimide 1 (480 mg, 1.6 mmol) in chloroform solution (4.0 mL) was added at 0 °C to a vigorously stirred suspension of **9a** (348 mg, 1.5 mmol) and sodium hydrogen carbonate (143 mg, 1.7 mmol) in the same solvent (4.9 mL). After 5 min at room temperature the reaction mixture was washed with water (3 × 3.0 mL), and the residue was dried with anhydrous sodium sulfate, evaporated, and crystallized from diisopropyl ether to give 341 mg (91% yield) of pure 3-fluoro-3-(3-oxobutyl)-2*H*-benzopyran-2,4-dione (**10a**): mp 70–72 °C; ^{1}H NMR δ 2.18 (s, 3 H, C-4′), 2.39 (m, 1 H, Ha-1′), 2.50 (m, 1 H, Hb-1′), 2.78 (t, 2 H, J = 7.2 Hz, H_2-2′), 7.28 (br d, 1 H, J = 8.0 Hz), 7.37 (dm, 1 H, J = 7.5 Hz), 7.75 (ddd, 1 H), 7.93 (dd, 1 H, J = 7.9 Hz); ^{19}F NMR δ −179.4 (t, $J_{F,H}$ = 22.4 Hz); ^{13}C NMR δ 206.0 (C-3′), 187.2 (d, $^2J_{C,F}$ = 18.0 Hz, C-4), 164.7 (d, $^2J_{C,F}$ = 24.0 Hz, C-2), 153.8 (C-O), 137.9, 127.8, 125.8, 118.1, 117.7 (C and CH ar), 95.0 (d, $^1J_{C,F}$ = 204.6, C-3), 35.5 (C-2′), 30.6 (d, $^2J_{C,F}$ = 23.0 Hz, C-1′), 29.83 (C-4′). **3-Fluoro-3-(1-phenyl-3-oxobutyl)-2*H*-benzopyran-2,4-dione (10b).** A solution of the *N*-fluoroimide 1 (965 mg, 3.25 mmol) in chloroform (2.0 mL) was added at room temperature to a suspension of 3-(1-phenyl-3-oxobutyl)-4-hydroxycoumarin (925 mg, 2.70 mmol) in chloroform/water (1:1; 5.0 mL). The resulting heterogeneous system was vigorously stirred for 15 min at 35 °C, water was removed, and the organic phase was washed with water (2 × 5.0 mL). The organic layer was dried with anhydrous sodium sulfate, the solvent was removed under reduced pressure, and the residue was crystallized from diisopropyl ether to give 898 mg (92% yield) of pure 3-fluoro derivative **10b** as a 3:1 mixture of two diastereoisomers: mp 125–127 °C; mass spectrum (CI) *m/e* 327 (M + 1), 147. Major diastereoisomer: ^{1}H NMR δ 2.08 (s, 3 H, CH_3), 3.01 (dd, 1 H, J = 18.4 and 7.7 Hz, H_a-2′), 3.33 (dd, 1 H, $J_{H,H}$ = 18.4 and 5.3 Hz, H_b-2′), 4.03 (ddd, 1 H, $J_{H,F}$ = 25.5 Hz, H-1′), 6.7–7.7 (m, 9 H, CH ar.); ^{19}F NMR δ −182.2 (d, $J_{F,H}$ = 25.4 Hz); ^{13}C NMR δ 204.5 (C-3′), 186.1 (d, $^2J_{C,F}$ = 18.3 Hz, C-4), 164.5 (d, $^2J_{C,F}$ = 23.7 Hz, C-2), 153.3, 137.3, 134.6 (C ar.), 128.5, 128.7, 127.1, 117.6 (CH ar.), 98.03 (d, $^1J_{C,F}$ = 209.1 Hz, C-3), 47.0 (d, $^2J_{C,F}$ = 21.4 Hz, C-1′), 42.4 (d, $^3J_{C,F}$ = 3.1 Hz, C-2′), 30.21 (C-4′). Minor diastereoisomer (chemical shifts are given when they are different from those reported above): ^{1}H NMR δ 2.06 (s, 3 H, CH_3), 2.96 (dd, 1 H, $J_{H,H}$ = 18.4 and 7.5 Hz, H_a-2′), 3.31 (dd, 1 H, $J_{H,H}$ = 18.3 and ≃ 6.5 Hz, H-2′), 4.03 (ddd, 1 H, H-1′); ^{19}F NMR δ −181.6 (d, $J_{F,H}$ = 24.5 Hz); ^{13}C NMR δ 204.47 (C-3′), 187.51 (d, $^2J_{C,F}$ = 18.2 Hz, C-4), 163.28 (d, $^2J_{C,F}$ = 24.5 Hz, C-2), 153.76, 137.77, 135.27 (C ar.), 128.66, 128.56, 127.67, 125.50, 118.78, 117.29 (CH ar.), 98.09 (d, $^1J_{C,F}$ = 209.0 Hz, C-3), 46.94 (d, $^2J_{C,F}$ = 21.4 Hz, C-1′), 41.95 (d, $^3J_{C,F}$ = 3.0 Hz, C-2′), 30.15 (C-4′). **3-Fluoro-3-[1-(4-chlorophenyl)-3-oxobutyl]-2*H*-benzopyran-2,4-dione (10c).** The same procedure described above for warfarin (**10b**) was employed. A 2:1 mixture of the two diastereomers was obtained in 90% yield: mp 145–149 °C; mass spectrum (CI) *m/e* 361, 363 (M + 1), 181, 183. Major diastereoisomer: ^{1}H NMR δ 2.10 (s, 3 H, CH_3), 2.97 (dd, 1 H, $J_{H,H}$ = 18.4 and 7.7 Hz, H_a-2′), 3.31 (dd, 1 H, $J_{H,H}$ = 18.5 and 5.1 Hz, H_b-2′), 4.00 (ddd, 1 H, $J_{H,F}$ = 26.2 Hz, H-1′), 6.9–7.7 (m, 8 H, CH ar.); ^{19}F NMR δ −183.2 (d, $J_{F,H}$ = 26.7 Hz); ^{13}C NMR δ 204.15 (C-3′), 185.77 (d, $^2J_{C,F}$ = 18.4 Hz, C-4), 164.08 (d, $^2J_{C,F}$ = 24.0 Hz, C-2), 153.19, 137.59, 134.35, 133.26 (C ar.), 129.95, 128.65, 127.08, 125.78, 119.26, 117.54 (CH ar.), 97.90 (d, $^1J_{C,F}$ = 210.6 Hz, C-3), 46.04 (d, $^2J_{C,F}$ = 21.3 Hz, C-1′), 42.48 (C-2′), 30.02 (C-4′). Minor diastereoisomer (chemical shifts are given when they are different from those reported above): ^{1}H NMR δ 2.07 (s, 3 H, CH_3), 2.91 (dd, 1 H, H_a-2′), 3.29 (dd, 1 H, H_b-2′); ^{19}F NMR δ −182.6 (d, $J_{F,H}$ = 25.4 Hz); ^{13}C NMR δ 187.10 (d, $^2J_{C,F}$ = 18.0 Hz, C-4), 163.00 (d, $^2J_{C,F}$ = 24.7 Hz, C-2), 153.64, 137.82, 134.44, 133.88 (C ar.), 128.86, 127.69, 125.57, 118.49, 117.26 (CH ar.), 97.95 (d, $^1J_{C,F}$ = 208.9 Hz, C-3), 45.92 (d, $^2J_{C,F}$ = 21.3 Hz, C-1′), 41.88 (d, $^3J_{C,F}$ = 2.9 Hz, C-2). Anal. Calcd for $C_{19}H_{14}ClFO_4$: C, 63.26; H, 3.91. Found: C, 63.31; H, 4.03.

Acknowledgment. The partial financial support of this research by the National Science Foundation and the award of a NATO Fellowship (G.R.) are gratefully acknowledged.

Registry No. 1, 108388-06-3; **2a**, 67-52-7; **2b**, 2417-22-3; **2c**, 2518-72-1; **2d**, 1953-33-9; **2e**, 22275-34-9; **2f**, 60703-43-7; **2g**, 7391-67-5; **2h**, 55974-64-6; **2i**, 103858-65-7; **3a**, 55052-01-2; **3b**, 83049-84-7; **3c**, 649-07-0; **3d**, 53162-56-4; **3e**, 53162-61-1; **3f**, 141293-03-0; **3g**, 141293-04-1; **3h**, 141103-65-3; **3i**, 141293-05-2; **5a**, 50-33-9; **5b**, 57-96-5; **6a**, 141293-06-3; **6b**, 141293-07-4; **7**, 83-12-5; **8**, 2625-08-3; **9a**, 104416-34-4; **9b**, 81-81-2; **9c**, 81-82-3; **10a**, 141293-08-5; (*R**,*S**)-**10b**, 141293-09-6; (*R**,*R**)-**10b**, 141293-10-9; (*R**,*S**)-**10c**, 141293-11-0; (*R**,*R**)-**10c**, 141293-12-1; **12**, 141293-13-2.

Calibration of a Fast Benzylic Radical "Clock" Reaction[1]

R. Hollis,[2] L. Hughes, V. W. Bowry,[3] and K. U. Ingold*

Steacie Institute for Molecular Sciences, National Research Council of Canada, Ottawa, Ontario, Canada K1A 0R6

Received January 21, 1992

Radicals which undergo essentially irreversible rearrangements can be used as mechanistic probes and, when the rate of the rearrangement has been determined, can be used to "clock" the rates of radical–molecule reactions.[4] The radical clock approach has proved to be particularly valuable in chemical and biochemical systems which simply are not amenable to more conventional methodologies. For example, the clock technique has been fruitfully applied in investigations of the rates and mechanism(s) of alkane hydroxylation by cytochrome P-450.[5–7] For primary, secondary, and tertiary alkyl radicals there are entire families of "calibrated" clocks, some slow, others extremely fast. There has, however, been no benzylic radical clock. That is, we recently demonstrated[8] that an earlier claim that the α-cyclopropylbenzyl radical underwent a fairly rapid and essentially irreversible ring-opening at 22 °C,[9] reaction 1, was in error. In truth, not only is this reaction reversible but, at ordinary temperatures, the ring-closed form is thermodynamically preferred.[8]

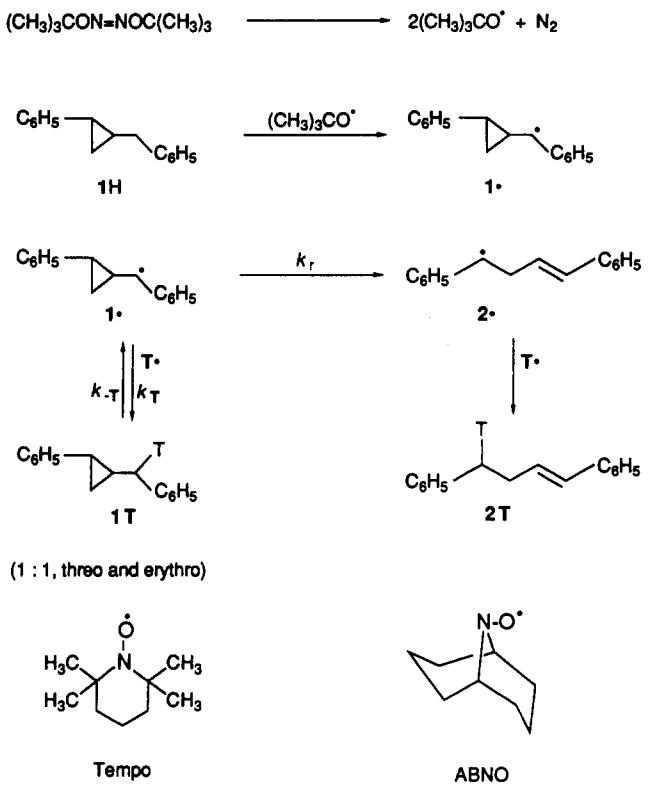
$$C_6H_5\dot{C}HCHCH_2CH_2 \rightleftarrows C_6H_5CH{=}CHCH_2CH_2^{\bullet} \quad (1)$$

Certain fungal enzymes have been shown to be efficient benzylic hydroxylating agents.[10,11] Calibrated, fast benzylic clocks are required to investigate the mechanism of these and other biotransformations which may involve benzyl radicals as intermediates.

(1) Issued as NRCC No. 33296.
(2) NRCC Summer Student, 1991.
(3) Present address: Heart Research Institute, Sydney, Australia.
(4) Griller, D.; Ingold, K. U. *Acc. Chem. Res.* **1980**, *13*, 317–323.
(5) Ortiz de Montellano, P. R.; Stearns, R. A. *J. Am. Chem. Soc.* **1987**, *109*, 3415–3420.
(6) Bowry, V. W.; Ingold, K. U. *J. Am. Chem. Soc.* **1991**, *113*, 5699–5707.
(7) Atkinson, J. K.; Ingold, K. U. Unpublished results.
(8) Bowry, V. W.; Lusztyk, J.; Ingold, K. U. *J. Chem. Soc., Chem. Commun.* **1990**, 923–925.
(9) Masnovi, J.; Samsel, E. G.; Bullock, R. M. *J. Chem. Soc., Chem. Commun.* **1989**, 1044–1045.
(10) Holland, H. L.; Bergen, E. J.; Chenchaiah, P. C.; Khan, S. H.; Munoz, B.; Ninniss, R. W.; Richards, D. *Can. J. Chem.* **1987**, *65*, 502–507.
(11) Holland, H. L.; Chernishenko, M. J.; Conn, M.; Munoz, A.; Manoharan, T. S.; Zawadski, M. A. *Can. J. Chem.* **1990**, *68*, 696–700.

0022-3263/92/1957-4284$03.00/0 Published 1992 by the American Chemical Society

Scheme I



Results

It appeared likely that the unfavorable thermodynamics for ring-opening of the α-cyclopropylbenzyl radicals could be overcome by appropriate resonance stabilization of the ring-opened radical. We therefore synthesized 1-benzyl-*trans*-2-phenylcyclopropane (**1H**) from which the desired benzylic radical **1•** could be produced by hydrogen atom abstraction using *tert*-butoxyl radicals generated by the thermal decomposition of di-*tert*-butyl hyponitrite. The reaction was carried out at 40 °C for both 1 half-life (15 h) and for 10 half-lives of the hyponitrite in deoxygenated cyclopentane containing known concentrations of a nitroxide trap, **T•**. The overall chemistry is shown in Scheme I and the general experimental procedure has been described in earlier publications.[12,13]

Under appropriate conditions both the unrearranged radical **1•** and the rearranged radical **2•** will be trapped by the nitroxide (together with cyclopentyl radicals derived from the solvent). The relative yields of the hydroxylamine products of interest, **1T** and **2T**, can be readily determined by combined liquid chromatography–mass spectrometry (LC-MS).[12] The rate constant k_r for the **1•** → **2•** rearrangement is given by eq I, where k_T is the rate constant

$$k_r = k_T[\mathbf{T}^\bullet]_m([\mathbf{2T}]/[\mathbf{1T}]) \qquad \text{(I)}$$

for the trapping of **1•** by the nitroxide and $[\mathbf{T}^\bullet]_m$ is its mean concentration during the reaction.

We chose Tempo and 9-azabicyclo[3.3.1]nonane-*N*-oxyl (ABNO) as traps. Using laser flash photolysis (LFP), we have previously[8,13] measured k_T for trapping of the α-cyclopropylbenzyl radical by these two nitroxides. This nonrearranging cyclopropylbenzyl radical should be a good "model" for **1•**. The LFP measurements were made at ca. 18 °C in hexane (with Tempo)[8] and in isooctane (with Tempo and ABNO).[13] The very minor changes required for the increase in temperature to 40 °C ($E_T \sim 1.7$ kcal/mol)[14] and for the change in solvent to cyclopentane[15] turn out to be self-cancelling.[16] We therefore take the k_T values actually measured at 18 °C in isooctane for α-cyclopropylbenzyl to be equal to the rate constant for **1•** trapping at 40 °C in cyclopentane, i.e.,[13] for **1•** + Tempo, $k_T = (1.0 \pm 0.1) \times 10^8$ M^{-1} s^{-1}, and for **1•** + ABNO, $k_T = (7.8 \pm 1.2) \times 10^8$ M^{-1} s^{-1}. Since the nitroxide concentrations employed in LFP experiments are very low, we can equate these k_T values with the limiting value of k_T for infinitely dilute concentrations of trap,[17] i.e., $(k_T)_{T\bullet\to 0}$.

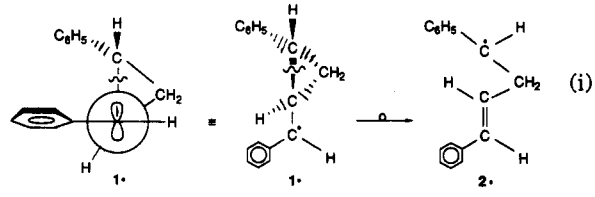
Our LC-MS analyses showed that **1•** was trapped by both nitroxides as a surprisingly well-resolved (retention times differed by ca. 4%), ca. 1:1 mixture of erythro and threo **1T** hydroxylamine isomers (see Scheme I). The **2T** rearranged hydroxylamine eluted in each case as a single peak which we would predict to be mainly the trans isomer.[18] If the cis isomer is present it either coelutes with the trans isomer or is a very minor product.

To overcome the problem caused by the fact that at the high nitroxide concentrations required for the trapping of at least some unrearranged **1•**, the effective values of k_T are smaller than the LFP measured values [which were obtained at low (1–20 mM) nitroxide concentrations],[17] we rewrite eq I in the form

$$\frac{[\mathbf{2T}]}{[\mathbf{1T}]}\cdot[\mathbf{T}^\bullet]_m = \frac{k_r}{k_T} = \left(\frac{k_r}{k_T}\right)_{T\bullet\to 0} + a[\mathbf{T}^\bullet]_m \qquad \text{(II)}$$

Plots of the ratio of the yields of rearranged to unrearranged hydroxylamines multiplied by the mean trap concentration against the mean trap concentration yield good straight lines.[12,13] Extrapolation to $[\mathbf{T}^\bullet]_m = 0$ yields $(k_r/k_T)_{T\bullet\to 0}$ for which the appropriate value of k_T is $(k_T)_{T\bullet\to 0}$, i.e., it is the LFP measured value. Furthermore, the slope/intercept ratios obtained from such plots are expected to depend mainly on the nature of the nitroxide trap (i.e., whether or not it is sterically hindered) and only to a lesser extent on the nature of the carbon radical which is rearranging and being trapped.[19] That is, the slope/intercept ratio is given by

(12) Bowry, V. W.; Lusztyk, J.; Ingold, K. U. *J. Am. Chem. Soc.* **1991**, *113*, 5687–5698.
(13) Bowry, V. W.; Ingold, K. U. *J. Am. Chem. Soc.* In press.
(14) Chateauneuf, J.; Lusztyk, J.; Ingold, K. U. *J. Org. Chem.* **1988**, *53*, 1629–1632.
(15) Beckwith, A. L. J.; Bowry, V. W.; Ingold, K. U. *J. Am. Chem. Soc.* In press.
(16) A 20% increase in k_T for the increase in temperature is nicely balanced by an equivalent decrease for the change in solvent from isooctane[13] to cyclopentane.
(17) Values of k_T decrease as **T•** concentrations increase both because of the increased polarity of the solvent[15] and, for ABNO, because dimerization, $2\mathbf{T}^\bullet \rightleftarrows \mathbf{T}_2$, reduces the effective **T•** concentration.
(18) The expected transition state for the **1•** → **2•** reaction, viz. eq i, implies that the trans isomer should be the sole reaction product.



(i)

(19) For all nitroxides the value of $(k_T)_{T\bullet\to 0}$ depends on the degree of steric crowding and extent of resonance stabilization of the carbon radical.[12-15] However, the relative change in the effective value of k_T at high $[\mathbf{T}^\bullet]$ is expected to be rather similar for different carbon radicals. This is because the effective trap concentration differs from the measured trap concentration at high $[\mathbf{T}^\bullet]$[17] and hence the percentage change in apparent k_T at high $[\mathbf{T}^\bullet]$ should be more-or-less unrelated to the nature of the radical which is trapped. Exact equality of slope/intercept values for different carbon-centered radicals should not, however, be expected because nitroxide trapping of the resonance-stabilized benzyl radical is more strongly retarded by polar solvents (and hence, presumably by high nitroxide concentrations) than is the trapping of primary alkyl radicals.[15]

$$a\left(\frac{k_r}{k_T}\right)^{-1}_{T\bullet\to 0} = \left[\Delta\left(\frac{k_r}{k_T}\right)/\Delta[T^\bullet]_m\right] \Big/ \left(\frac{k_r}{k_T}\right)_{T\bullet\to 0}$$
$$= [\Delta(k_T)^{-1}/\Delta[T^\bullet]_m](k_T)_{T\bullet\to 0}$$

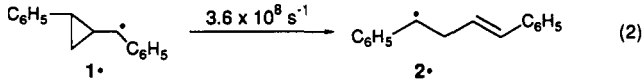
which is independent of k_r. The validity of a plot made according to eq II is, therefore, more-or-less confirmed if its slope/intercept ratio has about the "correct" value. We have previously used the ring-opening "clock" reaction of the 1,2,2-trimethylcyclopropylcarbinyl radical to measure the dependence of k_r/k_T on $[T^\bullet]_m$ for this rearrangement with Tempo[12] and ABNO[13] as traps in 1,1,2,2-tetramethylcyclopropane as solvent at 37 °C. The slope/intercept ratios[13] were 0.34 M^{-1} for Tempo and 1.2 M^{-1} for ABNO.

A plot of $([2T]/[1T])[T^\bullet]_m$ vs $[ABNO]_m$ over a range of ABNO concentrations from ca. 0.07 to 0.7 M gave a single straight line using the data obtained after 15 h at 40 °C (1 half-life of the hyponitrite) and after 150 h. The intercept, $(k_r/k_T)_{T\bullet\to 0}$ had a value of 0.45 (±0.05) M, which can be combined with $(k_T)_{T\bullet\to 0} = 7.8 \times 10^8$ M^{-1} s^{-1} to obtain $k_r = 3.5 \times 10^8$ s^{-1}. The slope/intercept ratio was 0.67 M^{-1}, which is about half the value found with the 1,1,2-trimethylcyclopropylcarbinyl radical.[13]

The results obtained with Tempo were rather different. Plots of $([2T])/[1T])[T^\bullet]_m$ vs $[Tempo]_m$ (at concentrations from ca. 0.4 to 1.9 M) gave a different straight line after 15-h reaction from the line obtained after 150-h reaction. The slopes of these two lines were about the same, viz., ca. 1.3, but the intercepts differed dramatically, viz., $(k_r/k_T)_{T\bullet\to 0}$ = 4 (±0.5) M after 15 h and 11 (±1) M after 150 h. We interpret this result as indicating that the trapping of **1**• by Tempo is *reversible* (see Scheme I), noting that the reversible trapping of **2**• by Tempo would not be observed since **2**• would simply be recaptured by Tempo. Because of this reversibility, the yield of **1T** will decrease at long reaction times while that of **2T** will increase by an equal amount. From the $(k_r/k_T)_{T\bullet\to 0}$ ratios at 15 and 150 h, we can extrapolate back to the start of the reaction to obtain an estimate for $[(k_r/k_T)_{T\bullet\to 0}]_{t\to 0}$ = 3.6 (±0.5) M. Combining this value with $(k_T)_{T\bullet\to 0} = 1.0 \times 10^8$ M^{-1} s^{-1} gives $k_r = 3.6 \times 10^8$ M^{-1} s^{-1}.

Discussion

The outstanding agreement between the k_r values calculated from the ABNO and Tempo analytical data gives us considerable confidence that $k_r(1^\bullet \to 2^\bullet) = (3.6 \pm 0.5) \times 10^8$ s^{-1} at 40 °C. The Arrhenius pre-exponential factors for the ring-opening of various cyclopropylcarbinyl radicals[12] are ca. $10^{12.85}$ s^{-1}. If we assume a similar value for reaction 2, the activation energy for this reaction can be

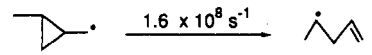


1• 2• (2)

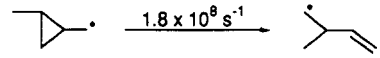
estimated to be ca. 6.1_5 kcal/mol. For comparison, we note that the parent cyclopropylcarbinyl radical undergoes ring-opening (reaction 3) with a rate constant of 1.2×10^8

(3)

s^{-1} at the same temperature[12] and with an activation energy of 7.0_5 kcal/mol.[12] More interestingly, the *trans*-2-methylcyclopropylcarbinyl undergoes 1,2 ring-opening and, 1,3 ring-opening at these temperatures with the rate constants indicated on eqs 4 and 5, respectively.[12] Of course, **1**• only undergoes 1,2 ring-opening. However, it is noteworthy that the **1**• → **2**• rearrangement occurs at a rate which is very similar to the rates of reactions 3, 4, and 5.



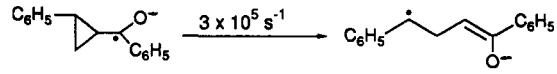
(4)



(5)

This would appear to be quite reasonable for reactions 2, 3, and 5, since there can be very little difference in the degree of thermodynamic stabilization between the reactant and product radicals.

After the present work had been submitted, Tanner et al.[20] reported the rate constant for ring-opening at 22 °C of the ketyl radical analogous to **1**• (reaction 6). This



(6)

reaction is much slower than reaction 2 as would be expected in view of the considerable thermodynamic stabilization of ketyl radicals relative to structurally related alkyl radicals. Moreover, reaction 6 was found to be reversible ($K \sim 2 \times 10^3$ at 61 °C) whereas reaction 2 should be essentially irreversible.

The trapping of resonance-stabilized radicals by Tempo is known to be a reversible process even at ambient temperatures.[14,21,22] For example,[21] oxygen-trapping of the carbon-centered radical has been used to determine the rate constant for decomposition of the trialkylhydroxylamine formed from Tempone and the 1,1-diphenylethyl radical. From the data given[23] we can estimate that the rate constant for this (reverse trapping) reaction will be ca. 5×10^{-3} s^{-1} at 40 °C. As would be expected, the hydroxylamine formed by coupling of the less stabilized radical **1**• with Tempo is more resistant to decomposition and our (limited) data suggest that for this compound $k_{-T} \sim 1.5 \times 10^{-6}$ s^{-1} at 40 °C. The adduct of **1**• with ABNO is yet more stable, a result which is consistent with the known greater strength of the O–H bond in the dialkylhydroxylamine formed by reduction of ABNO relative to that formed by reduction of Tempo.[24] Thus, ABNO is the nitroxide trap of choice for resonance-stabilized radicals.

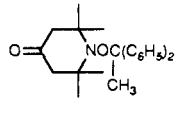
The cis isomer of **1H** was also synthesized during the present work, our intention being to obtain a second, "fast" benzylic radical clock. Unfortunately, our synthetic procedure yielded *cis*-**1H** contaminated with 16% of *trans*-**1H** (and 15% of $(C_6H_5CH_2)_2$). When this mixture was subjected to *tert*-butoxyl attack in the presence of a nitroxide trap, the hydroxylamine products showed that *trans*-**1H**

(20) Tanner, D. D.; Chen, J. J.; Luelo, C.; Peters, P. M. *J. Am. Chem. Soc.* **1992**, *114*, 713–717. **Note added in proof**: For a related study of the reversible ring opening of arylcyclopropylketyl anions, see: Tanko, J. M.; Drumright, R. E. *J. Am. Chem. Soc.* **1992**, *114*, 1844–1854.

(21) Howard, J. A.; Tait, J. C. *J. Org. Chem.* **1978**, *43*, 4279–4283.

(22) Gratton, D. W.; Carlsson, D. J.; Howard, J. A.; Wiles, D. M. *Can. J. Chem.* **1979**, *57*, 2834–2842.

(23) The rate constant for the decomposition of i in the presence of O_2 at temperatures from 20 to 50 °C could be described by[21] log (k/s^{-1}) = 14.8 – 5348/*T*.



(24) *D*[ABNO-H] = 76.2 kcal/mol,[25] *D*[Tempone-H] = 71.8 kcal/mol.[25]

(25) Mahoney, L. R.; Mendenhall, G. D.; Ingold, K. U. *J. Am. Chem. Soc.* **1973**, *95*, 8610–8614.

was a much better hydrogen atom donor than *cis*-**1H**. While this is simple to rationalize in terms of differences in steric hindrance of the benzylic hydrogen atoms, it prevented even an estimation of k_r for *cis*-**1**$^{\bullet}$ → **2**$^{\bullet}$. Unfortunately, all our attempts to separate pure *cis*-**1H** were unsuccessful.

Experimental Section

1-Benzyl-*trans*-2-phenylcyclopropane (1H). Following a literature procedure,[26] 95% ethanol (70 mL), KOH (10 g), and phenylacetaldehyde (20 g) were refluxed for 4 h and the resultant solution was then washed with brine, followed by extraction with ether, water washing, and drying over Na_2SO_4. Removal of the ether and purification by column chromatography (silica gel, hexane eluent) gave 6.5 g (40% yield) of a clear oil, *trans*-1,3-diphenylpropene, 99% pure by GC-MS, *m/z* (relative abundance): 194 (M^+, 99), 193 (60), 179 (50), 178 (42), 115 (100).

Again following a literature procedure,[27] a mixture of zinc dust (10.5 g, 0.15 mol) and cuprous chloride (1.59 g, 0.016 mol) in ether (30 mL) was stirred and refluxed under N_2 for 1 h, after which diiodomethane (6.47 mL, 0.080 mol) was added and refluxing was continued for 15 min. The diphenylpropene (6.0 g, 0.080 mol) was added and refluxing was continued for 5 days, it being necessary to add more of the Zn/Cu couple after 2 days in order to force the reaction to completion (as determined by GC-MS). Filtration through Celite, followed by removal of the ether and chromatographic purification (silica gel/hexane) gave 5.0 g (78% yield) of **1H** as a clear oil, 98% pure by GC-MS. ^{1}H NMR: δ 0.85–1.10 (m, 2 H, cyclopropyl CH_2), 1.21–1.48 (m, 1 H, CH_2CHCH_2), 1.67–1.87 (m, 1 H, C_6H_5-*CH*), 2.55–2.82 (m, 2 H, $C_6H_5CH_2$), 6.85–7.30 (m, 10 H, aromatic H's). ^{13}C NMR: δ 16.10 (cyclopropyl CH_2), 22.96 (CH_2CHCH_2), 24.71 (C_6H_5CH), 39.99 ($C_6H_5CH_2$). GC-MS: *m/z* (relative abundance) 208 (M^+, 7), 178 (13), 117 (100), 115 (30), 104 (31).

1-Benzyl-*cis*-2-phenylcyclopropane (*cis*-1H). Since this compound was not prepared in a pure and "useful" form, only the general procedure, following literature precedents,[27-29] is given: (1) $C_6H_5C{\equiv}CH$ ($+CH_3CH_2MgBr + CuCl + C_6H_5CH_2Br$)[28] → $C_6H_5C{\equiv}CCH_2C_6H_5$ (68% yield, 99% purity by GC-MS). (2) $C_6H_5C{\equiv}CCH_2C_6H_5$ (+5% $Pd/BaSO_4$/quinoline + H_2(gas))[29] → $C_6H_5CH{=}CHCH_2C_6H_5$(81% cis, 5% trans, and 14% $(C_6H_5C-H_2)_2CH_2$ by GC-MS). (3) $C_6H_5CH{=}CHCH_2C_6H_5$ (+Zn + CuCl + CH_2I_2)[27] → $C_6H_5\overline{CHCH_2CHCH_2}C_6H_5$ (69% *cis*-**1H**, 16% *trans*-**1H**, 15% $(C_6H_5CH_2)_2CH_2$ by GC-MS and ^{13}C NMR).

Surprisingly, this last reaction was *much* slower than the corresponding reaction with the pure trans olefin, the reaction taking 9 days instead of 5 days. We assume that under these reaction conditions there is appreciable cis to trans conversion of the olefin and that this accounts for the unexpectedly high yield of *trans*-**1H**. From this mixture of products we can extract the following analytical data about *cis*-**1H**. ^{1}H NMR: δ 0.85–1.25 (m, 2 H, cyclopropyl CH_2), 2.10–2.25 (m, 2 H, $C_6H_5CH_2CH$ and C_6H_5CH), 2.45–2.75 (m, 2 H, $C_6H_5CH_2$). ^{13}C NMR: δ 9.87 (cyclopropyl CH_2), 19.93 (CH_2CHCH_2), 21.33 (C_6H_5CH), 34.42 ($C_6H_5CH_2$).

Procedures. The nitroxide trap (Tempo or ABNO at final concentrations in the range ca. 0.4–1.9 M and ca. 0.07–0.7 M, respectively) and di-*tert*-butyl hyponitrite [at ca. 20–25% of the trap concentration for experiments run for only 1 half-life (15 h) of this compound or at half this concentration for experiments run for 10 half-lives] were dissolved in **1H** (20 μL) and cyclopentane (380 μL). The solution was degassed by several freeze–pump–thaw cycles, sealed under vacuum, and heated at 40 °C for 1 or 10 half-lives of the hyponitrite. After the reaction vessel was opened, the cyclopentane was blown off under N_2 and an equivalent volume of ethanol was added. Analysis was by LC-MS as previously described[12,13] with selective ion monitoring for **1T** and **2T** at $(M + 1)^+$. The ^{1}H and ^{13}C NMR spectra were measured on a 200-MHz Bruker instrument in $CDCl_3$ with tetramethylsilane as an internal standard.

Acknowledgment. We thank D. A. Lindsay for valuable technical assistance in the analyses of the hydroxylamine product mixtures.

Registry No. 1$^{\bullet}$, 141375-04-4; *trans*-**1H**, 14213-83-3; *cis*-**1H**, 30627-65-7; ABNO, 31785-68-9; TEMPO, 2564-83-2; $PhCH_2CHO$, 122-78-1; *trans*-$PhCH{=}CHCH_2Ph$, 3412-44-0; *cis*-$PhCH{=}CHCH_2Ph$, 1138-83-6; $PhC{\equiv}CH$, 536-74-3; $PhCH_3Br$, 100-39-0; $PhC{\equiv}CCH_2Ph$, 4980-70-5; $(PhCH_2)_2CH_2$, 1081-75-0.

(26) Stoermer, R.; Thier, C.; Laage, E. *Ber.* **1925**, *58*, 2607–2615.
(27) Rawson, R. J.; Harrison, I. T. *J. Org. Chem.* **1970**, *35*, 2057–2058.
(28) Johnson, J. R.; Jacobs, T. L.; Schwartz, A. M. *J. Am. Chem. Soc.* **1938**, *60*, 1885–1889. See also: Taniguchi, H.; Mathai, I. M.; Miller, S. I. *Tetrahedron* **1966**, *22*, 867–878.
(29) Augustine, R. L. *Catalytic Hydrogenation*; Marcel Dekker: New York, 1965; pp 69–71.

Electrochemical Reduction of 2-(Arylideneamino)furans: An Unexpected Stable Anion-Radical

F. Barba* and J. R. Díaz

Departamento de Química Orgánica, Universidad de Alcalá de Henares, 28805-Madrid, Spain

A. Sánchez

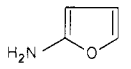
Departamento de Química-Física Aplicada, Universidad Autónoma, 28049-Madrid, Spain

C. Seoane

Departamento de Química Orgánica, Universidad Complutense, 28040-Madrid, Spain

Received November 14, 1991

The parent 2-aminofuran ring system (1), although thermodynamically stable,[1] is not isolable.[2] In fact, 2-aminofuran itself has been only identified as a transient species.[3,4]



1

Recently, a general procedure has been developed for the synthesis of substituted 2-furanamines, by stabilizing them as Schiff bases **2** through in situ condensation with aromatic aldehydes.[5-7] Attempts to obtain the free furanamine from the Schiff base by reduction or hydrolysis failed, leading to cleavage of the furan ring.[6,8]

Given the above situation, we thought that the electrochemical reduction of the arylideneamino derivative in the presence of a proton donor could be a sensible route to furanamines **3**. However, the electrochemical reduction of compound **2a** (R = *p*-ClC_6H_4) took place in an unusual manner. In the pale yellow initial solution (DMF–H_2O/

(1) Poquet, E.; Reisch, J. Communication to 6th International Congress of Heterocyclic Chemistry, Teheran 1977.
(2) Katritzky, A. R.; Rees, C. W. *Comprehensive Heterocyclic Chemistry*; Pergamon Press: Oxford, New York, 1984; Vol. 4.
(3) Johnson, F.; Heeschen, J. P. *J. Org. Chem.* **1967**, *32*, 1126.
(4) Katritzky, A. R.; Rees, C. W. Comprehensive Heterocyclic Chemistry; Pergamon Press: Oxford, New York, 1984; Vol. 4, p 647.
(5) Ciller, J. A.; Seoane, C.; Soto, J. L. *Liebig Ann. Chem.* **1985**, 51.
(6) Ciller, J. A.; Seoane, C.; Soto, J. L.; Yruretagoyena, B. *J. Heterocycl. Chem.* **1986**, *23*, 1583.
(7) Ciller, J. A.; Martin, N.; Seoane, C.; Soto, J. L. *J. Chem. Soc., Perkin Trans. I* **1985**, 2581.
(8) Ciller, J. A. Ph.D. Thesis, Universidad Complutense, Madrid, 1985.

0022-3263/92/1957-4287$03.00/0