ARTICLE

OBC
www.rsc.org/obc

Factors affecting the selection of products from a photochemically generated singlet biradical

David A. Broyles and Barry K. Carpenter*

Department of Chemistry and Chemical Biology, Baker Laboratory, Cornell University, Ithaca, New York, 14853-1301, USA. E-mail: bkc1@cornell.edu; Fax: +1 607 255 4137; Tel: +1 607 255 3826

Received 28th January 2005, Accepted 21st March 2005
First published as an Advance Article on the web 7th April 2005

The chemistries of a monoradical of the ultrafast "radical-clock" type and a structurally related singlet biradical, generated by Norrish type II photochemistry, are compared. The monoradical is found to undergo the characteristic ring-opening reaction of its class at about 10^{10} s^{-1} at room temperature. However, the singlet biradical shows no evidence of the analogous ring-opening reaction. The contrasting chemistry is traced not to a fundamental difference in electronic structure of the two intermediates, but rather to a steric interaction that the biradical alone would have to suffer during the ring opening. Although the magnitude of the steric hindrance is small (estimated 15–20 kJ mol^{-1}), it is enough to shut down the reaction, because the biradical has other facile product-forming reactions available.

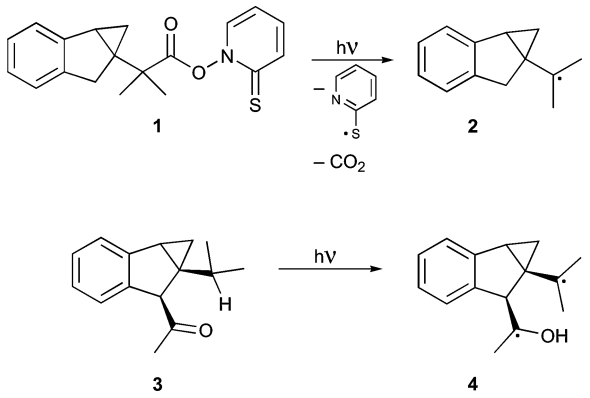
Introduction

Singlet biradicals are among the most challenging organic reactive intermediates to study. Contributing to the problems are the typically short lifetimes of these species,[1–3] the difficulties that they present to electronic-structure theory,[4–8] and the apparent susceptibility of their chemistry to nonstatistical dynamical effects.[3,9–17] Elucidation of their reactivity patterns would be facilitated if one could draw analogies between the chemistries of biradicals and monoradicals, because the latter class of intermediates has proven much more amenable to experimental investigation.[18–20]

It is probably safe in most cases to draw parallels between the chemistries of monoradicals and *triplet* biradicals,[8,21–24] because the Pauli exclusion principle ensures that the unpaired electrons in triplets behave more-or-less independently.[25] However, for *singlet* biradicals an assumed analogy with monoradical chemistry is potentially more hazardous. There certainly exist examples where singlet biradicals do behave much like their doublet-state cousins,[26–29] but there are also cases where the chemistry is quite different.[30,31] Theory can provide a guide to the factors that are likely to make the analogy valid or not. For example, singlet biradicals whose ground states involve large contributions from ionic electron configurations are unlikely to behave like monoradicals.[5,32]

However, the chemistry of singlet biradicals has proven to be susceptible to so many, often subtle, factors that its complete and confident prediction by theory remains an unattained goal. For that reason, it would appear useful to add to the list of experimental studies where a comparison of singlet biradicals with structurally related monoradicals has been made. This paper reports the results from one such investigation.

The system chosen for study was one in which the monoradical would be of the ultrafast radical-clock type (**2**).[33,34] The analogous biradical (**4**) was generated by Norrish type II photochemistry.[35] The reactive intermediates and their precursors (**1** and **3**, respectively) are shown in Scheme 1. Our expectation was that radical **2** should undergo very rapid ring opening to isomer **5**, which could then be trapped in an intermolecular reaction. By analogy, biradical **4** might be expected to ring open to isomer **6**, in addition to giving the normal ring closure and fragmentation products (**7** and **8**, respectively) expected from Norrish type II photochemistry.[35] Biradical **6**, in turn, could plausibly give products **9** and/or **10** (Scheme 2). If the chemistry occurred as anticipated, then measurement of the rate constant for ring opening of radical **2** would provide information that could be used in combination with the observed product ratios from the Norrish type II photochemistry to estimate the rate constants for the various reactions of the biradical **4**.



Scheme 1 The radical (**2**) and biradical (**4**) whose reactions are compared.

Results and discussion

Synthesis of precursor 1

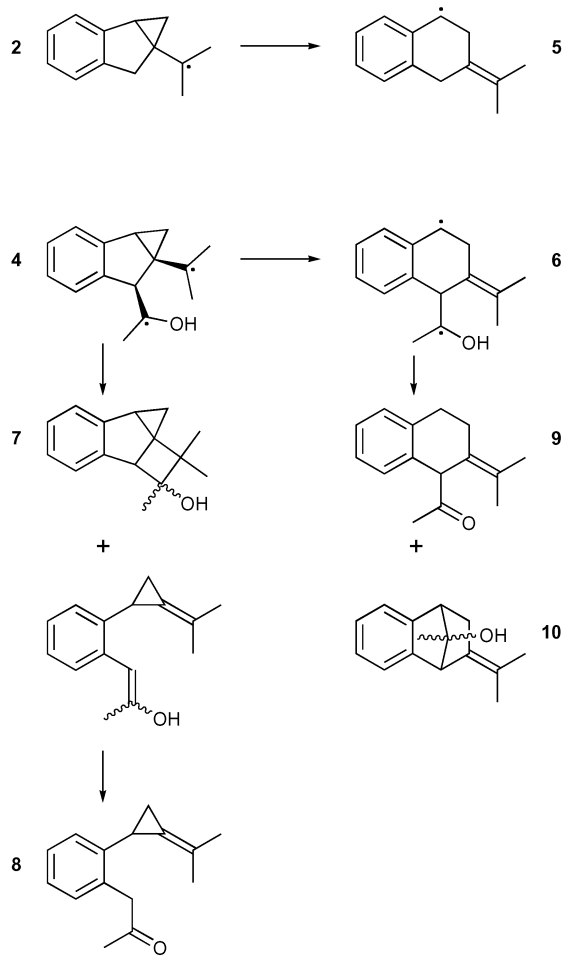
The synthesis of PTOC ester **1** was accomplished as summarized in Scheme 3.

Perhaps the only thing worthy of comment in this synthesis is the fact that the reduction of ester **12** to an alcohol, followed later by its reconversion to the carboxylic acid oxidation state, was undertaken in order to exploit the known beneficial effect of an alcohol on the Simmons–Smith and related cyclopropanation reactions.[36]

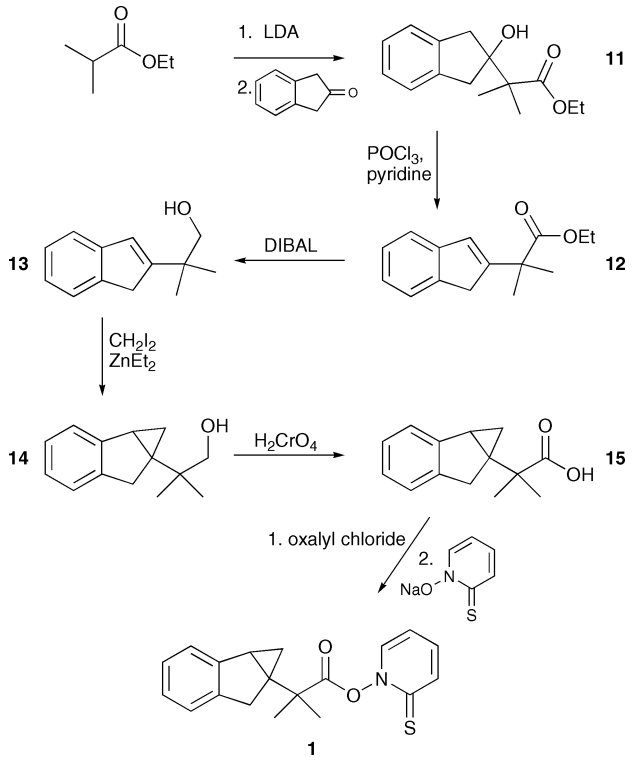
Synthesis of ketone 3

The obvious synthetic routes to ketone **3**, involving some kind of cyclopropanation of an indene derivative, were tried first, but were universally unsuccessful. No cyclopropanation method could be made to work on indenes **16a** or **16b**. Possibly a Simmons–Smith reagent, or one of its variants, could have been persuaded to cyclopropanate **16c**, but the effect of the hydroxyl ligand that leads to the desirable rate and yield effects on such reactions, also leads to a *syn* stereoselectivity,[36,37] which, in this case, would have given the wrong diastereomer of the product (Scheme 4), and so the reaction was not attempted.

DOI: 10.1039/b501422k

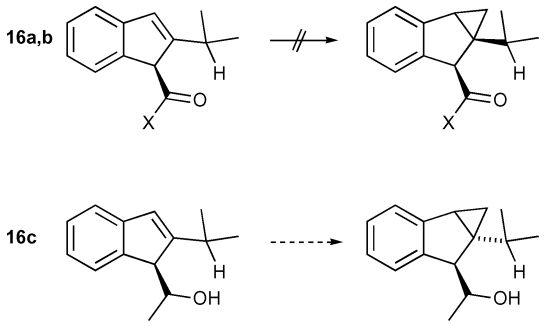


Scheme 2 Anticipated reactions of radical **2** and biradical **4**.

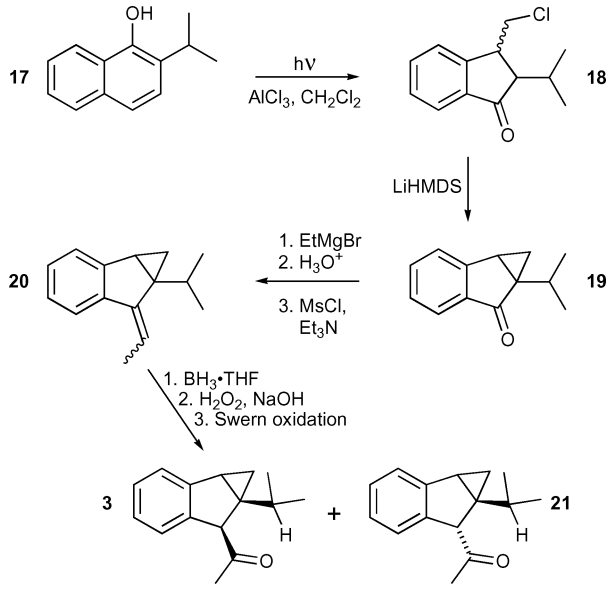


Scheme 3 Synthesis of the radical precursor **1**.

The failures of the cyclopropanation strategies prompted the pursuit of an entirely different approach, which did lead eventually to the desired product, **3**. The synthesis is summarized in Scheme 5.



Scheme 4 Unsuccessful synthetic approaches to ketone **3**. **16a**: X = OH; **16b**: X = CH_3.



Scheme 5 Successful synthetic route to ketone **3**.

The key to this approach was the photochemical ring contraction reported by Kakiuchi and coworkers.[38] The yield of the transformation with naphthol **17** as reactant was found to be rather variable (30–60%), possibly because the work-up in the presence of large amounts of $AlCl_3$ was quite difficult. Various methods for converting ketone **19** into the desired product were explored, including Wittig reaction with 1-methoxyethylidene–triphenylphosphorane,[39,40] but none turned out to afford a yield better than that from the sequence shown in Scheme 5. The desired product, **3**, and its diastereomer, **21**, were formed in about a 1 : 1 ratio, but could be separated by chromatography.

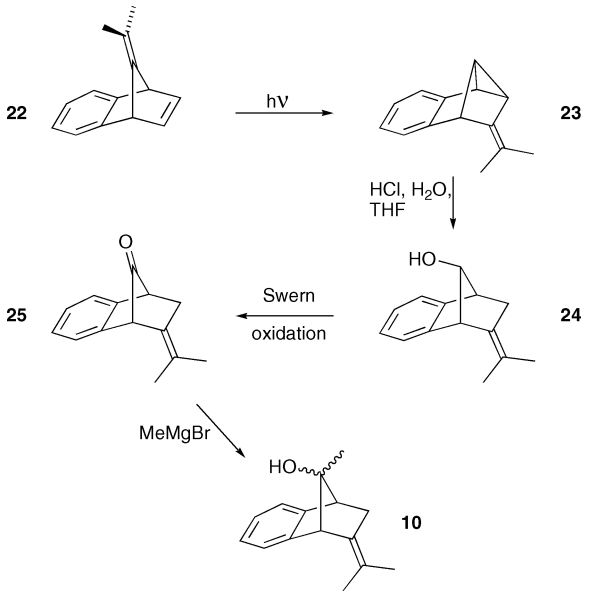
Independent synthesis of potential photochemical products 10

In an effort to aid in the detection of small amounts of compounds **10** that may be formed from the photolysis of ketone **3**, an independent synthesis was undertaken (Scheme 6). The availability of compounds **10** also permitted a check of their stability to the photochemical reaction conditions.

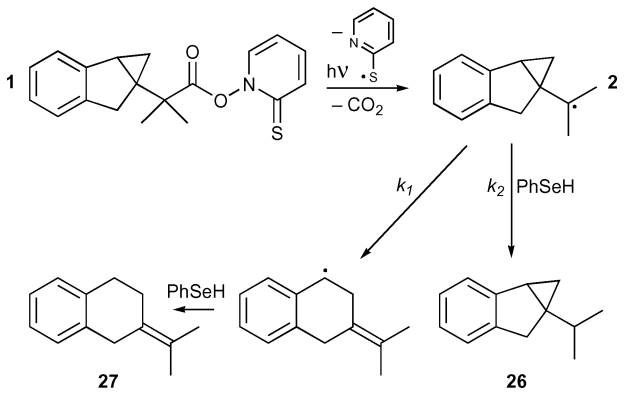
Again, the sequence depended for its first step on some known photochemistry – this time converting the benzyne/dimethylfulvene Diels–Alder adduct, **22**, to polycyclic isomer **23** by a di-π-methane rearrangement.[41]

Determination of the activation parameters for ring opening of radical 2

The activation parameters for ring opening of radical **2** were determined by a procedure pioneered by Newcomb and coworkers.[42] It involved generation of the radical in the presence of varying concentrations of PhSeH over a range of temperatures, and measurement of the ratio of ring-closed and ring-opened products, **26** and **27**, respectively (Scheme 7).



Scheme 6 Synthetic route to potential photochemical products **10**.



Scheme 7 Reactions used in the determination of activation parameters for ring opening of radical **2**.

Since the reaction was run with a large stoichiometric excess of PhSeH, its concentration could be considered effectively constant. Measurement of the ratio of products **26** and **27** therefore gave the ratio k_2[PhSeH]/k_1. Since [PhSeH] was measured, and k_2 could be determined at each temperature from the known activation parameters for reaction of PhSeH with tertiary alkyl radicals, values for k_1 could be deduced. They are listed in Table 1.

A weighted, nonlinear least-squares fit of the Eyring equation to these data gave the following activation parameters for ring opening of radical **2**: $\Delta H^{\ddagger} = 3.6 \pm 0.5$ kJ mol^{-1}, $\Delta S^{\ddagger} = -37.6 \pm 1.6$ J mol^{-1} K^{-1}.

Electronic structure calculations on the ring opening of radical 2

The activation enthalpy and entropy determined for the ring opening of radical **2** are both significantly lower than those found for other "ultrafast" radical clocks. For example, the *trans*-2-phenylcyclopropylcarbinyl radical has reported activation parameters[33] for ring opening that translate to $\Delta H^{\ddagger} = 10.9$ kJ mol^{-1}, $\Delta S^{\ddagger} = +11.0$ J mol^{-1} K^{-1} at 298 K. The differences of the present results from these reference values seem somewhat surprising. First, the σ orbital of the cyclopropane C–C bond to be broken in radical **2** appears to have a poor overlap with the π orbitals of the benzene ring, which might be expected to raise the enthalpic barrier with respect to that found for ring opening of the *trans*-2-phenylcyclopropylcarbinyl radical. Second, it is not obvious why the activation entropy would be positive for the ring opening of *trans*-2-phenylcyclopropylcarbinyl radical but negative for the ring opening of **2**.

Table 1 Rate constants for ring opening of radical **2** as a function of temperature. Uncertainty estimates were derived from 3–6 measurements with different concentrations of PhSeH at each temperature

Temperature/K	k_1/s^{-1}
229	$8.86 \pm 1.52 \times 10^9$
253	$1.04 \pm 0.20 \times 10^{10}$
276	$1.40 \pm 0.29 \times 10^{10}$
298	$1.72 \pm 0.27 \times 10^{10}$
321	$1.92 \pm 0.20 \times 10^{10}$
329	$2.14 \pm 0.11 \times 10^{10}$

In an effort to understand these results, electronic structure calculations were undertaken. Optimized geometries and harmonic vibration frequencies for radical **2** and its ring-opening transition structure were determined at the UB3LYP/cc-pVDZ level.[43] In addition, single-point CASPT2(9,9)/cc-pVDZ calculations were carried out,[44] from a CASSCF(9,9) reference wavefunction involving the singly-occupied orbital of the radical, the σ and σ* orbitals of the breaking cyclopropane bond, and the π and π* orbitals of the benzene ring. The G3(MP2,B3) model[45,46] was also investigated, but the UMP2 wavefunction for the ring-opening transition state, which forms part of this composite method, was so highly spin contaminated ($\langle S^2 \rangle = 1.42$) that the activation parameters computed by this model were judged to be unreliable.

The UB3LYP optimized transition structure showed a 31° dihedral angle between the planes C3–C2–C7 and C6–C1–H14 (Fig. 1). Thus, the orbital overlap in the transition structure (which is where it matters for the kinetics) made the problem appear less severe than it did from inspection of the reactant geometry. Nevertheless, this analysis did still predict that there should be an overlap penalty on the barrier for ring opening, even if its magnitude may be modest. That expectation was born out in the directly computed activation enthalpies. The UB3LYP calculations found $\Delta H^{\ddagger} = 11.2$ kJ mol^{-1}, $\Delta S^{\ddagger} = -13.3$ J mol^{-1} K^{-1}, while the CASPT2 calculations (using UB3LYP geometries and harmonic vibration frequencies) gave $\Delta H^{\ddagger} = 13.4$ kJ mol^{-1}. The activation enthalpy was therefore higher than that calculated for the ring opening of *trans*-2-phenylcyclopropylcarbinyl radical at the same levels of theory (UB3LYP: $\Delta H^{\ddagger} = 4.2$ kJ mol^{-1}, $\Delta S^{\ddagger} = -8.8$ J mol^{-1} K^{-1}; CASPT2: $\Delta H^{\ddagger} = 7.2$ kJ mol^{-1}). There is consequently a clear disagreement between theory and experiment for the ring opening of radical **2**, as revealed in Fig. 2. Neither of the computational predictions fits the data points within the estimates of random error.

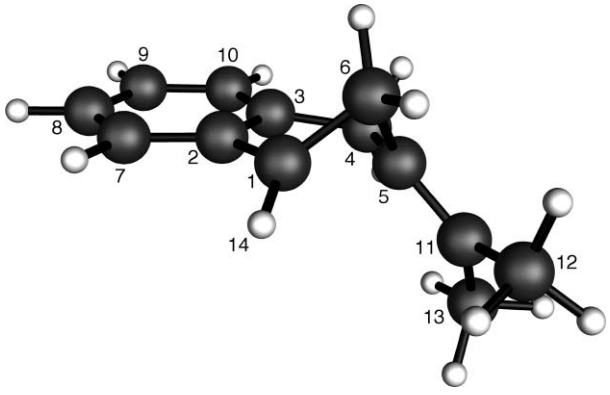


Fig. 1 UB3LYP/cc-pVDZ optimized transition structure for ring opening of radical **2**.

Two sources of this discrepancy seem possible. The more obvious is that the levels of electronic-structure theory used are simply not up to the task. However, two arguments lead us not to place all of the responsibility for the disagreement on the theoretical side. The first is that the models employed *under*estimate

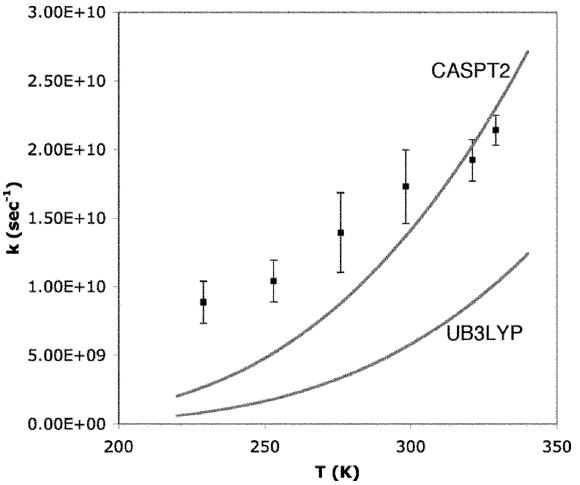


Fig. 2 Comparison of theoretical (lines) and experimental (points) estimates of the rate constant k_1 as a function of temperature.

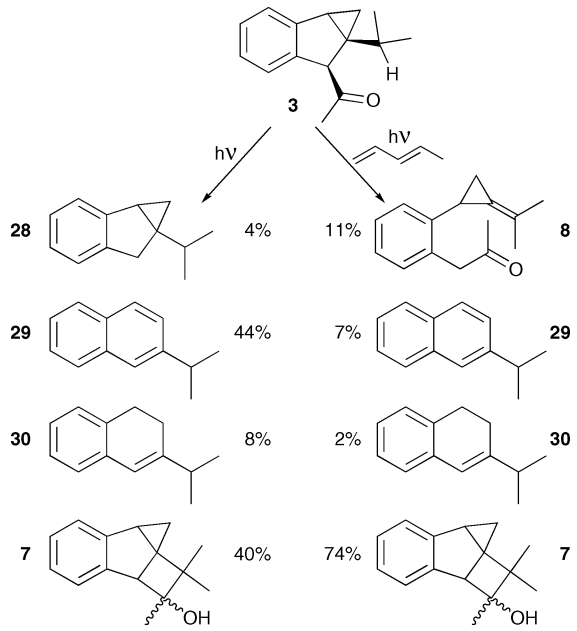
both $\Delta H^{\ddagger}$ and $\Delta S^{\ddagger}$ for ring opening of the *trans*-2-phenylcyclopropylcarbinyl radical, and so it seems unlikely that they would *over*estimate those quantities for the apparently very similar reaction of radical **2**. The second is that the experimental activation parameters found for the ring opening of radical **2** differ not only quantitatively from the values directly calculated, but also qualitatively from those expected on the basis of the physical differences between **2** and *trans*-2-phenylcyclopropylcarbinyl, as discussed above.

The other potential source of the discrepancy would obviously be a systematic error in the experimental values. Unidentified systematic errors are always possible, of course, but in this case one potential problem does stand out. It is the adoption of the published activation parameters for trapping of tertiary alkyl radicals by phenylselenol. As the authors of that work took pains to point out, the reaction is partly diffusion controlled, and so the transferability of the activation parameters from one tertiary radical to another is open to doubt, since structurally disparate radicals may well have different diffusion constants.[42] In principle, this issue could be explored by running the trapping reactions in solvents of different viscosity, but an investigation of that kind was deemed to be beyond the scope of the present study.

In summary, while perfect agreement between experiment and theory at the levels used here cannot be expected, there is reason to believe that the agreement ought to be better than it turns out to be. We suspect that a systematic error could have made both the experimental activation enthalpy and activation entropy too low. Since these effects will tend to cancel, the estimated rate constant for ring opening of radical **2** of $\sim 10^{10}$ s^{-1} at room temperature is probably still reasonably accurate. For example, if one assumed the CASPT2//UB3LYP model to be accurate in reproducing the *difference* in activation parameters between ring openings of radical **2** and *trans*-2-phenylcyclopropylcarbinyl, one would arrive at $\Delta H^{\ddagger} = 17.1$ kJ mol^{-1}, $\Delta S^{\ddagger} = +6.5$ J mol^{-1} K^{-1} for the former reaction. Although these values look very different from the ones deduced experimentally, the two sets lead to quite similar rate constants at 298 K: 1.37×10^{10} s^{-1} from the values just quoted and $1.72 \pm 0.27 \times 10^{10}$ s^{-1} from the experiment.

Photochemistry of ketone 3

Irradiation of ketone **3**, as a solution in degassed pentane, was carried out with a 450 W medium-pressure mercury lamp and a Pyrex filter. Reaction was essentially complete after 1 h. Four products could be identified (Scheme 8). Minor products, totaling about 4%, were present in individual quantities too small to permit characterization. Since hydrocarbons **28–30** were apparently products of a Norrish type I reaction, and since



Scheme 8 Principal products from UV photolysis of ketone **3** with and without the triplet quencher piperylene present.

reactions of that class often occur preferentially from the $^3(n,\pi^*)$ states of aliphatic ketones,[35] the effect of adding piperylene, a triplet quencher, was examined. As expected, addition of piperylene did reduce the yield of Norrish type I products, although even at a concentration of 330 mM it could not suppress them completely. This might indicate that some of the Norrish type I chemistry occurred also in the singlet manifold. With the piperylene present, a new product, identified as **8**, appeared. The failure to detect **8** in the absence of the triplet quencher suggested that it might be unstable with respect to direct photolysis. That was confirmed by experiment: photolysis of **8** in the absence of piperylene led to its rapid disappearance, apparently by Norrish type I photochemistry.

The increase in yield of the Norrish type II products **7** and **8** in the presence of piperylene indicated that they were formed from a singlet excited state, as desired. Product **7** appeared to be a single diastereomer. It was tentatively assigned the structure in which the hydroxyl group was *endo*, by comparison of its observed ^{1}H NMR chemical shifts with those predicted for the two epimers by GIAO calculations[47] at the B3LYP/6-311+G(2d,p)//B3LYP/6-31G(d) level, using the polarizable-continuum model[48] for $CHCl_3$ as the solvent (Fig. 3).

The photochemical instability of compound **8** led to a search for other primary photoproducts that might prove unstable to the reaction conditions. Photolysis to low conversion did reveal another product, which was found to disappear at longer reaction times. It proved to be ketone **31**. This product could arise by Norrish type I chemistry, but it might also be a secondary photoproduct of the benzonorbornenols **10** (Scheme 9). However, when the independently synthesized sample of **10** was subjected to the photolysis conditions it was found to be stable, and so the Norrish type II mechanism could be ruled out.

Electronic structure calculations on the reactions of singlet biradical 4

The photochemistry of ketone **3** revealed that the singlet biradical **4** underwent only "normal" Norrish type II ring closure and fragmentation. No products arising from the ring opening of the cyclopropane could be detected, despite the high rate constant for such a process deduced for the apparently related monoradical, **2**. In an effort to understand this observation, electronic structure calculations were undertaken. Ideally for a singlet biradical one would use a multireference method,

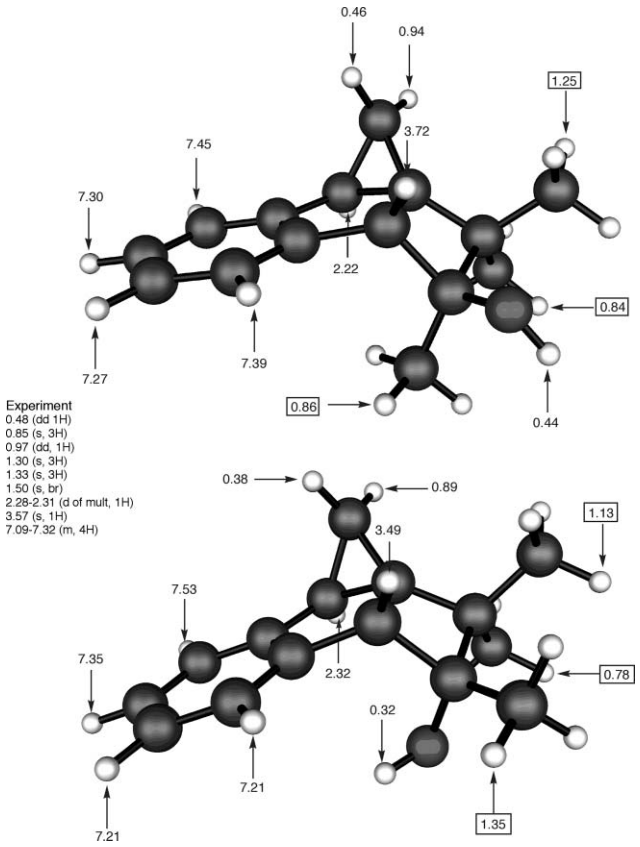
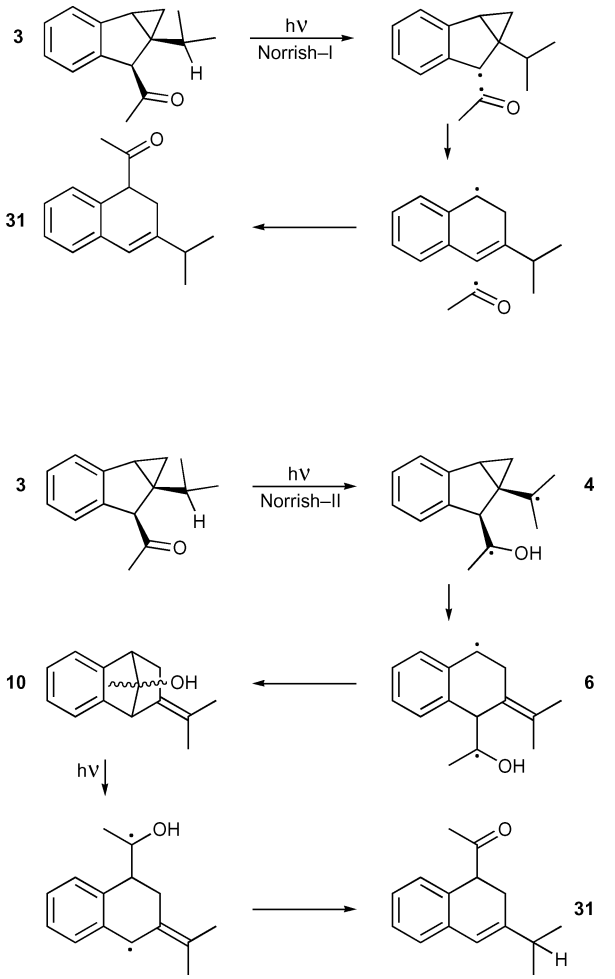


Fig. 3 Comparison of experimental ^{1}H NMR chemical shifts (ppm downfield from TMS in $CDCl_3$) for compound **7** with those calculated for the two diastereomers. Calculations were of the GIAO type, conducted at the B3LYP/6-311+G(2d,p)//B3LYP/6-31G(d) level, using a polarizable-continuum model for $CHCl_3$ solvent. Chemical shifts for the individual protons of each methyl group were averaged to represent the fast-exchange limit.



Scheme 9 Norrish type I and type II mechanisms for the formation of ketone **31**.

such as CASPT2, which can provide a reasonably balanced treatment of dynamic and nondynamic electron correlation. Unfortunately, biradical **4** proved to be too big for CASPT2 to be employed with a credible active space and basis set. Consequently, a broken-symmetry UB3LYP/6-31 + G(d) model was used. This approach for treating singlet biradicals has problems, partly associated with the unphysical mixing of singlet and triplet (plus higher multiplicity) spin states. However, there exist classes of biradical for which the UB3LYP model is likely to be appropriate; these have been described by Cremer.[49] We judge the biradical **4** to be within the group for which this model should provide a reasonable description. The primary intent of the calculations was to find out whether the reluctance of biradical **4** to undergo cyclopropane ring opening could be understood.

Two different rotomers of biradical **4** could be found as local minima on the potential energy surface (PES). However, when zero-point and thermal corrections were included, the enthalpic barriers for their ring-closures to alcohols **7** disappeared. The rotomer of **4** that would close to the epimer of **7** with the *exo* hydroxyl was found to be lower in enthalpy by 2.5 kJ mol^{-1}, but this is well within the likely error of the calculations and so cannot be taken as a reason to reverse the tentative product assignment based on NMR chemical shifts (Fig. 3). Furthermore, when the PES is as flat as it seems to be in the vicinity of biradical **4**, one must consider the possibility that nonstatistical dynamical effects could perturb the product ratios significantly. For example, the parent tetramethylene biradical in its singlet state seems to be strongly influenced by such effects.[50]

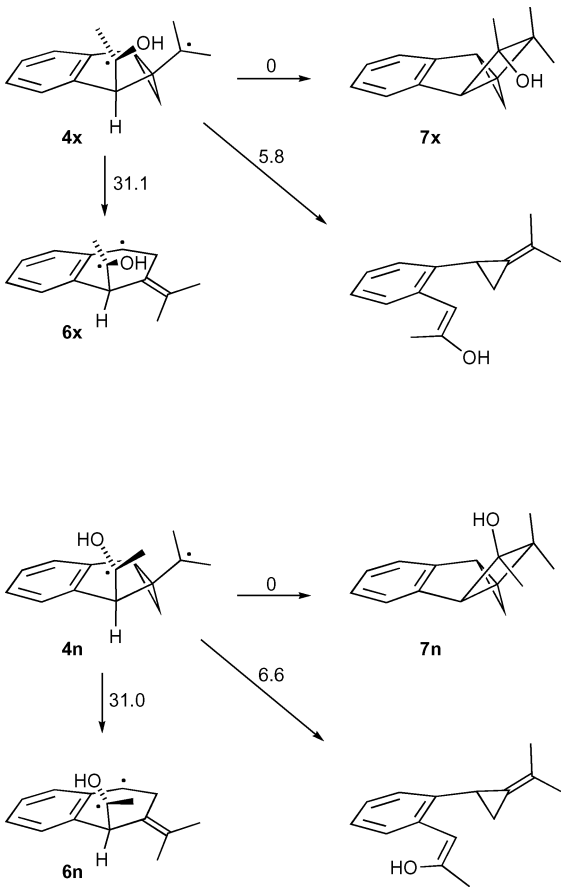
The two rotomers of biradical **4** were found to be connected to distinct transition states for cyclopropane ring opening and for the cleavage that leads eventually to product **8**. The reactions and computed activation enthalpies are summarized in Scheme 10.

The calculated activation enthalpies were found to reproduce, at least qualitatively, most of the experimental observations on the Norrish type II photochemistry of ketone **3**. Specifically, the closure to alcohol **7** was found to be favored, with the cleavage leading eventually to product **8** competing as a minor channel, since it faces a small barrier. Of obvious relevance to the purpose of the study, was the discovery that the ring opening of biradical **4** to biradical **6** should face a much larger barrier than that found for the formally analogous reaction of monoradical **2**. The barrier facing **4** was calculated to be large enough that it could explain the virtual absence of products derived from this pathway in the photochemistry of ketone **3**. The question then became whether the difference in ring-opening barriers for the monoradical and biradical derived from fundamentally distinct electronic structures of the two intermediates, or whether some alternative explanation could be found. An answer became apparent as soon as the geometries of the rotomeric transition structures for ring opening of **4** were examined in detail. They are shown in Fig. 4. One can see that in both cases, the isopropylidene substituent is forced into a steric interaction with the vicinal hydroxyethylidene substituent, because of the orbital alignment required to form the new exocyclic C=C bond. Simple MM2 molecular-mechanics estimates suggest that these steric interactions are worth 15–20 kJ mol^{-1}, which is just about the difference between the computed activation enthalpies for ring opening of **2** and **4**.

Experimental

General

All reagents were purchased from Aldrich Chemical Company, Acros, or Fluka. All solvents were obtained from Fisher



Scheme 10 UB3LYP/6-31+G(d) computed activation enthalpies (kJ mol^{-1}) for the ring opening of two rotomers of biradical **4**. Rotomer **4x** was found to be lower in enthalpy than **4n** by 2.5 kJ mol^{-1}.

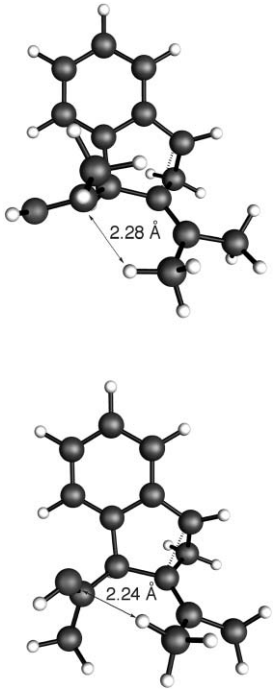


Fig. 4 UB3LYP/6-31+G(d) optimized transition structures for the cyclopropane ring opening of *exo* and *endo* rotomers of biradical **4**.

Scientific and were used as received except as noted below. When needed dry, acetonitrile and dichloromethane were dried by distillation from calcium hydride. THF was dried by distillation from potassium benzophenone ketal, and diethyl ether was dried by distillation from sodium benzophenone ketal. Methanol was dried by distillation from magnesium methoxide, generated in situ. Diisopropylamine and triethylamine were dried by distillation from and stored over potassium hydroxide. Dimethyl sulfoxide was distilled under reduced pressure from calcium hydride and was either stored over more calcium hydride or 4 Å molecular sieves. Solvents were sometimes dried over 4 Å molecular sieves. Piperylene (90% *cis–trans* mixture) was distilled from sodium borohydride before use and stored under Ar.

^{1}H NMR spectra were obtained with a Varian XL-200 spectrometer, a Varian MERCURY-300 spectrometer Varian INOVA-400 spectrometer, a Varian INOVA-500 spectrometer, or a Varian INOVA-600. ^{13}C NMR spectra were obtained with a Varian MERCURY-300 spectrometer or a Varian INOVA-500 spectrometer operating at 75.4 or 125.7 MHz respectively.

Infrared spectra were obtained with a Nicolet Impact 410 FT-IR spectrometer. Samples were either prepared as thin films on salt plates or *via* a flattened potassium bromide mix (KBr pellet).

Mass spectrometry data were obtained with GC/MS using a Hewlett Packard 5890 chromatograph equipped with a 0.25 mm × 30 m DB-5 capillary column and a Hewlett Packard 5970 series mass selective detector.

Analytical gas chromatography was carried out with either (1) a Hewlett Packard 5880A gas chromatograph with a 0.25 m × 15 m RTX-5 ((5%-phenyl)methylpolysiloxane) column, a flame ionization detector, and a Hewlett Packard 5880 GC plotter-integrator; or (2) a Hewlett-Packard 6890 gas chromatograph having a 0.32 mm × 30 m HP-1 (crosslinked methyl polysiloxane) column, a flame ionization detector, and using a computer with HP ChemStation software (revision 6.03).

Hydrogenations were carried out in high-pressure bottles on a Parr Model 3911 High Pressure Reactor.

Photolysis reactions were run using an Ace-Hanovia 450 W medium-pressure mercury arc lamp, cooled with a Pyrex (or quartz) jacket. The PTOC ester photolyses were run using a standard sun lamp with a tungsten filament at 250 W.

Thin-layer chromatography was performed using glass plates coated with a 0.25 mm layer of silica gel 60 F254. Plates were visualized by visual inspection, UV light (254 nm) and then either iodine or stain (most commonly anisaldehyde). The anisaldehyde stain was prepared from 5 mL *p*-anisaldehyde, 90 mL 95% ethanol, 2 mL glacial acetic acid, and 5 mL concentrated sulfuric acid. TLC plates were then dipped in the stain and heated with a heat gun.

All column chromatography followed the flash chromatography protocol,[51] using silica gel 60 (0.04–0.063 mm, 230–400 mesh, E. M. Merck). Chromatographic solvents, as well as those for workup procedures were used without purification.

Melting points were determined using a Thomas-Hoover capillary melting point apparatus. Temperatures were uncorrected.

Purities of key compounds were confirmed by elemental analysis. However, in the case of PTOC ester **1**, its photochemical lability made this impossible. Consequently the elemental analysis was conducted on its immediate precursor, carboxylic acid **15**.

Synthesis of PTOC ester 1

2-(2-Hydroxyindan-2-yl)-2-methylpriopionic acid ethyl ester (11). In a 250 mL round bottom flask, flame-dried under Ar, diisopropylamine (5.161 g, 51.0 mmol) was placed in dry THF (50 mL). The solution was cooled to −78 °C. *n*Buli (7.168 mL, 1.6 M, 51.0 mmol) was slowly added and the solution was stirred for 15 min. Ethyl isobutyrate (5.808 g, 50.0 mmol) was added and the mixture was stirred for 20 min, at which point 2-indanone (6.608 g, 50.0 mmol) was added. The solution was stirred for 2 h at the low temperature. After warming the solution to 0 °C, HCl (3 M) was carefully added to quench the reaction. The organic layer was then washed twice with a saturated aqueous sodium chloride solution and was dried with magnesium sulfate. GC analysis showed forming of a new peak thought to be the product, but also showed around 50% of the starting indanone

remaining. The solvent was removed and the mixture was carried onto the next step without purification.

2-(1*H*-Inden-2-yl)-2-methylpropionic acid ethyl ester (12). The material from the previous reaction was dissolved in pyridine (100 mL) and the solution was cooled to 0 °C. Phosphorus oxytrichloride (15 g) was then added. The solution turned dark and a precipitate formed. The solution was heated to reflux for 2 h, and the color darkened further. The mixture was poured onto 300 g of ice and then placed into a separatory funnel with diethyl ether. An emulsion ensued that did not clear until it had been filtered through a Buchner funnel. Extractions with diethyl ether and pentane, with plenty of washings with water eventually led to a solution that was dried with magnesium sulfate. The solvent was removed and the material was purified by column chromatography (in a 100 mm column, 100% hexane for 200 mL, 10% diethyl ether for 200 mL, 20% diethyl ether for 200 mL and then the remainder with 33% diethyl ether, the material with the higher R_f was collected) to yield compound **12** (6.7 g, 58% over two steps).

^{1}H NMR (500 MHz, $CDCl_3$): δ 1.23 (t, $J = 7.0$ Hz, 3H), 1.53 (s, 6H), 3.42 (s, 2H), 4.13 (q, $J = 7.0$ Hz, 2H), 6.68 (s, 1H), 7.14 (t, $J = 7.5$ Hz, 1H), 7.24 (t, $J = 8.0$ Hz, 1H), 7.32 (d, $J = 7.0$ Hz, 1H), 7.40 (d, $J = 7.5$ Hz, 1H).

^{13}C NMR (125.7 MHz, $CDCl_3$): δ 14.13, 25.70, 38.67, 44.65, 60.87, 120.63, 123.48, 124.29, 126.32, 126.59, 143.13, 144.59, 152.51, 175.94.

2-(1*H*-Inden-2-yl)-2-methylpropan-1-ol (13). Ester **12** (6.7 g, 29.1 mmol) was dissolved in dry diethyl ether (150 mL) and the solution was cooled to −78 °C. A solution of DIBALH (1 M in toluene, 78 mL, 78 mmol) was slowly added and the resulting mixture was stirred for 1 h. The solution was warmed to room temperature and stirred overnight (20 h total), after which it was carefully poured into aqueous NaOH (180 mL, 3 M). The mixture was extracted three times with diethyl ether. The aqueous layer was then acidified using 3 M HCl and then it was extracted once more with diethyl ether. These fractions were dried with magnesium sulfate and the solvent removed to give a white solid (5.34 g, 97%) that was only very slightly yellow. The material was pure by GC and TLC and so was carried onto the next step without purification.

Mp 62–64 °C.

^{1}H NMR (300 MHz, $CDCl_3$): δ 1.25 (s, 6H), 1.42 (br s, 1H), 3.38 (s, 2H), 3.54 (s, 2H), 6.65 (s, 1H), 7.10–7.26 (m, 2H), 7.31 (d, $J = 6$ Hz, 1H), 7.40 (d, $J = 7.5$ Hz, 1H).

^{13}C NMR (75 MHz, $CDCl_3$): δ 24.78, 38.16, 39.12, 71.64, 120.35, 123.50, 124.11, 126.36, 126.99, 143.07, 144.93, 155.12.

2-(1a,6-Dihydro-1*H*-cycloprop[*a*]inden-6a-yl)-2-methylpropan-1-ol (14). Methylene chloride (300 mL) was placed in a 500 mL round bottom flask with a magnetic stir bar and the vessel was cooled using an ice–NaCl bath. Diethyl zinc (14.9 mL, 145.5 mL) was slowly added dropwise to the solvent followed by the addition of diiodomethane (11.74 mL, 145.5 mmol). The solution was stirred for 30 min and a white precipitate formed. The olefin from the previous reaction (**13**, 5.34 g, 28.4 mmol) was added in methylene chloride (15 mL) and the mixture was warmed to room temperature and stirred overnight. The solution was then cooled to 0 °C and very carefully quenched by the addition of a solution of saturated aqueous ammonium chloride. More water was added along with some dilute HCl (3 M). The aqueous layer was extracted three times with methylene chloride, and then the combined organic layers were washed successively with saturated aqueous solutions of sodium carbonate, sodium bicarbonate and sodium chloride. The solution was dried with magnesium sulfate and filtered. GC analysis showed only 3% of the starting olefin remained. Removal of the solvent yielded 5.4 g of a slightly green oil.

^{1}H NMR (500 MHz, $CDCl_3$): δ 0.12 (t, $J = 4.5$ Hz, 1H), 0.91 (s, 3H), 0.93 (s, 3H), 1.34 (dd, $J = 4.5$, 8.5 Hz, 1H), 1.48 (br s, 1H), 2.26 (d of m, $J = 8.5$ Hz, 1H), 2.87 (d, $J = 16.5$ Hz, 1H), 3.24 (d, $J = 16.5$ Hz, 1H), 3.53 (s, 2H), 7.07 (m, 2H), 7.14 (m, 1H), 7.25 (m, 1H).

^{13}C NMR (125 MHz, $CDCl_3$): δ 20.14, 22.16, 22.33, 25.95, 34.16, 35.94, 37.01, 70.86, 122.90, 125.10, 125.22, 125.81, 141.86, 147.25.

2-(1a,6-Dihydro-1*H*-cycloprop[*a*]inden-6a-yl)-2-methylpropionic acid (15). The alcohol **14** (5.2 g, 25.7 mmol) was dissolved in acetone (150 mL) and the solution was cooled to 0 °C. Jones' reagent (20 mL) was added dropwise (prepared by dissolving 5.44 CrO_3 in 20 mL H_2O, cooling to 0 °C and adding 4.5 mL of H_2SO_4). The mixture was stirred for 4 h total until the starting material and the intermediate aldehyde had completely vanished by TLC. The solvent was removed and water added, and the mixture was extracted three times with EtOAc. The organic layers were combined and washed twice with water and once with saturated aqueous sodium chloride. After drying with Na_2SO_4 and filtering, the solvent was removed to give 5.64 g of an orange–white solid. The solid was subjected to column chromatography (100 mm column, 1 : 1 hexanes–EtOAc, the material was not very soluble and required a lot of solvent to dissolve), enough to leave behind an orange band and give 5.05 g of a light, yellow solid. The material was then recrystallized from benzene–hexanes, gathering up to 5 crops of crystals and a total recovery of 4.12 g (38% from 2-indanone) of **15** as an off-white solid with a melting point of 126–128 °C.

^{1}H NMR (500 MHz, $CDCl_3$): δ 0.22 (dd, $J = 4$, 5 Hz, 1H), 1.18 (s, 3H), 1.24 (s, 3H), 1.36 (dd, $J = 5$, 7.5 Hz, 1H), 2.44 (d of m, $J = 8.5$ Hz, 1H), 2.98 (d, $J = 17.5$ Hz, 1H), 3.17 (d, $J = 17.5$ Hz, 1H), 7.07 (m, 3H), 7.24 (m, 1H), 11.5 (vbr, 1H).

^{13}C NMR (125.7 MHz, $CDCl_3$): δ 20.26, 22.73, 23.12, 27.78, 34.95, 38.20, 43.46, 123.00, 125.19, 125.27, 125.89, 141.68, 146.86, 183.39.

IR: br –COOH, 1695.6 cm^{-1}.

Calc. for $C_{14}H_{16}O_2$: C, 77.75; H, 7.46. Found: C, 77.71; H, 7.55%.

2-(1a,6-Dihydro-1*H*-cycloprop[*a*]inden-6a-yl)-2-methylpropionic acid 2-thioxo-2*H*-pyridin-1-yl ester (1). This material was prepared immediately before use. The carboxylic acid **15** (1.000 g, 4.624 mmol) was dissolved in benzene (30 mL) along with 10 drops of DMF. Under Ar, oxalyl chloride (0.994 mL, 11.574 mmol) was added *via* syringe. The solution bubbled initially and was stirred for 1 h. The solvent was then removed by vacuum to give a syrup. Benzene (20 mL) was added to redissolve this material. *The material from this point becomes light sensitive, and all precautions must be taken to keep the material from direct light.* All flasks and beakers were coated with aluminium foil. This solution of the acid chloride was added to a mixture of benzene (20 mL), DMAP (0.059 g, 0.48 mmol) and 2-mercaptopyridine 1-oxide sodium salt (0.716 g, 4.8 mmol). The reaction was stirred for 2 h in the dark at which point it was washed with saturated aqueous sodium bicarbonate, brine, dried with magnesium sulfate and filtered. The solvent was removed and the material was purified by column chromatography (1 : 1 methylene chloride–ether), yielding 620 mg of a gummy, yellow foam after solvent removal.

^{1}H NMR (500 MHz, $CDCl_3$): δ 0.36 (dd, $J = 4.0$, 5.5 Hz, 1H), 1.41 (s, 3H), 1.48 (s, 3H), 1.49 (m, 1H), 2.56 (d of m, $J = 8.5$ Hz, 1H), 3.09 (d, $J = 17.0$ Hz, 1H), 3.23 (d, $J = 16.5$ Hz, 1H), 6.51 (dt, $J = 2.0$, 7.0 Hz, 1H), 7.05–7.15 (m, 4H), 7.25 (m, 1H), 7.64 (m, 1H).

^{13}C NMR (125.7 MHz, $CDCl_3$): δ 20.29, 22.51, 23.40, 28.27, 35.12, 38.36, 44.21, 123.23, 125.18, 125.58, 126.17, 133.15, 137.38, 137.63, 141.23, 146.17, 157.29.

Synthesis of 1-(6a-isopropyl-1,1a,6,6a-tetrahydrocycloprop[*a*]-inden-6-yl)ethanone (3)

1-Hydroxynaphthalene-2-carboxylic acid methyl ester. In dry THF (60 mL) was placed 1-hydroxy-2-naphthoic acid

(20.01 g, 106.3 mmol), and to this solution was added lithium hydroxide monohydrate (4.46 g, 106.3 mmol). This mixture was allowed to stir for 30 min under an argon atmosphere, at which point dimethyl sulfate (10 mL, 106 mmol) was added slowly *via* syringe. The solution was stirred for 1 h and then heated at reflux for 3 h. Some of the THF was removed by distillation (about 35 mL) and then a saturated aqueous sodium bicarbonate solution (40 mL) was added. The mixture was placed in a separatory funnel with more diethyl ether and H_2O and the aqueous layer was extracted four times with diethyl ether. The diethyl ether layers were combined, dried with magnesium sulfate, filtered, and the solvent removed to give 21.5 g of a peach solid. This material was dissolved in 25 mL benzene, applying heat to dissolve all of the material. White crystals formed upon cooling, and these were removed by filtration (they were mostly starting material). The solvent was removed on the solution to give 20.62 g of the product (95.9% yield, 99.4% yield with recovery of starting material).

Mp 72–73.5 °C, (lit.[52] 76–77 °C).

^{1}H NMR (400 MHz, $CDCl_3$): δ 1.54 (br s, 1H), 3.98 (s, 3H), 7.27 (d, $J = 8.8$ Hz, 1H), 7.51 (t, $J = 7.2$ Hz, 1H), 7.59 (t, $J = 7.2$ Hz, 1H), 7.75 (d, $J = 8.8$ Hz, 2H), 8.40 (d, $J = 8$ Hz, 1H).

2-(1-Hydroxy-1-methylethyl)naphthalen-1-ol. A 3-L three-neck flask was equipped with a reflux condenser, a mechanical stirring rod and an addition funnel, and the entire apparatus was flame-dried under an argon atmosphere. The flask was charged with methylmagnesium bromide (3 M in diethyl ether, 540 mL, 1.62 mol). Stirring was started while a solution of 1-hydroxy-2-naphthoic acid methyl ester (30.0 g, 148 mmol) in 500 mL dry diethyl ether was added dropwise (in two batches). The mixture stirred for 6 h and then was quenched by the addition of dilute HCl (3 M, 500 mL) and finally concentrated HCl until the salts dissolved. The mixture was placed in a 2 L separatory funnel and the aqueous layer was washed three times with diethyl ether. The organic layers were combined, dried with magnesium sulfate and filtered. The mixture was carried onto the next step without purification or removal of solvent.

^{1}H NMR (200 MHz, $CDCl_3$): δ 1.74 (br s, 1H), 1.74 (s, 6H), 7.1–7.7 (m, 6H).

2-Isopropenylnaphthalen-1-ol. A solution containing the starting material (usually not purified from the previous step, in this case, approximately 148 mmol of 2-(1-hydroxy-1-methylethyl)naphthalen-1-ol) had the solvent volume adjusted to about 400 mL diethyl ether. Sulfur trioxide pyridine complex (100. g, 628 mmol) was added and the solution was stirred for 8 h, monitoring the reaction by TLC. Concentrated HCl (about 500 mL) was added to quench the reaction and the mixture was poured into a separatory funnel with diethyl ether and H_2O. The aqueous layer was extracted three times with diethyl ether, and the combined organic layers were then washed with dilute HCl (1 M), dried with magnesium sulfate, and filtered to give a dark yellow solution. This solution was usually carried onto the next step (see below) without further purification, though some solvent was often removed to reduce the volume. The solvent was removed during a smaller-scale reaction to give a yellow oil (98% for that small-scale reaction). The alcohol could be dehydrated with phosphorus pentoxide, but the solution had to be thoroughly washed to avoid slowing the hydrogenation step.

^{1}H NMR (400 MHz, $CDCl_3$): δ 2.09 (s, 3H), 5.17 (m, 1H), 5.43 (m, 1H), 6.31 (s, 1H, –OH), 7.15–8.19 (m, 6H).

2-Isopropylnaphthalen-1-ol. A solution containing the starting material (not purified from the previous reaction, but containing roughly 148 mmol of 2-isopropenylnaphthalen-1-ol in about 800 mL of diethyl ether and THF) was split into three batches for hydrogenation (each about 250–300 mL). Each batch was prepared by placing 0.450 g Pd/C (10%) in the reaction bomb, adding the solution of 2-isopropenylnaphthalen-1-ol and then charging the H_2 reactor at about 55 psi. The bomb was agitated for 1 h, the flask recharged to 50 psi, and then allowed to shake 30 min to 1 h more. The solution was then filtered through Celite to remove the Pd/C and give a yellow solution. The solvent was removed on the combined batches to give 22.55 g of a red-colored oil of 2-isopropylnaphthalen-1-ol (typical yield from three steps, 75–85%).

^{1}H NMR (200 MHz, $CDCl_3$): δ 1.35 (d, $J = 6.8$ Hz, 6H), 3.32 (sept., 1H), 5.2 (br s, 1H), 7.32–8.08 (m, 6H).

3-Chloromethyl-2-isopropylindan-1-one (18). In a typical sequence, the reaction was run in 24/40 joint-size traps (roughly 100 mL volume). Each tube was filled with methylene chloride (*ca*. 30 mL) and aluminium trichloride (21.5 g) and a stir bar. While on ice, a solution of 2-isopropylnaphthalen-1-ol (22.55 g, 121.1 mmol) in methylene chloride (45 mL) was slowly added to the vials (in this case, split in three, 15 mL of the solution added to each). The solutions often started out black–green, but ended up a black–red by the end of the photolysis. The solutions were swished around to help mix in the aluminium trichloride, but often a large amount of solid was left on the bottom. Each tube was then subjected to three cycles of freeze–pump–thaw. Finally, the tubes were photolyzed under vacuum for 11 days with a Hg medium-pressure lamp. After that time, the tubes were cooled on ice and the solutions were very carefully quenched with H_2O, adding diethyl ether when necessary. The quenched mixtures were combined and the aqueous layer was extracted five times with diethyl ether. The combined organic layers were dried with magnesium sulfate, filtered and the solvent removed to give 24 g of a dark, maroon sludge. This residue was purified by Kugelrohr distillation under vacuum to give 14.5 g of a translucent yellow oil. This oil was then subjected to column chromatography to give 10.8 g of 3-chloromethyl-2-isopropylindan-1-one (**18**) as a slightly yellow oil (90% pure by GC, 36%). Typical yields ranged from 30–60%.

^{1}H NMR (400 MHz, $CDCl_3$): δ 0.83 (d, $J = 6.8$ Hz, 3H), 1.05 (d, $J = 7.2$ Hz, 3H), 2.37 (dsept, $J = 4$, 6.8 Hz, 1H), 2.55 (dd, $J = 3.6$, 4 Hz, 1H), 3.52 (m, $J = 2.8$ Hz, 1H), 3.80 (m, 2H), 7.42 (t, 1H), 7.60 (m, 2H), 7.73 (d, 1H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 18.0, 20.0, 29.6, 42.6, 54.9, 56.7, 123.1, 125.3, 128.1, 134.6, 137.3, 153.2, 206.4.

6a-Isopropyl-1a,6a-dihydro-1*H*-cycloprop[*a*]inden-6-one (19). A 250 mL round-bottomed flask with a stir bar was flame dried under an argon atmosphere. It was then charged with dry THF (70 mL) and 1,1,1,3,3,3-hexamethyldisilazane (15.5 mL, 73.5 mmol) and cooled to −78 °C. A solution of *n*BuLi (1.6 M in hexanes, 45.9 mL, 73.5 mmol) was added slowly and the solution was stirred for 40 min at the low temperature. A solution of the chloride (**18**, 10.8 g, 48.5 mmol) in 40 mL dry THF was then added by syringe, whereupon the solution turned bright yellow and then darkened. The reaction was stirred at −78 °C for 1.5 h, then it was warmed to room temperature and stirred for 1.2 h. The reaction was then quenched with H_2O and 3 M HCl, and the mixture was poured into a separatory funnel where it was extracted three times with diethyl ether. The combined diethyl ether layers were washed with 1 M HCl, then a saturated aqueous sodium bicarbonate solution, dried with magnesium sulfate and filtered. The solvent was removed to give a yellow–orange liquid which was then subjected to column chromatography to give 8.27 g of **19** (90% pure by GC, 82% yield).

^{1}H NMR (200 MHz, $CDCl_3$): δ 1.03 (d, $J = 7.0$ Hz, 3H), 1.10 (d, $J = 7.0$ Hz, 3H), 1.26 (dd/t, $J = 3.6$, 4.2 Hz, 1H), 1.48 (dd, $J = 4.2$, 7.2 Hz, 1H), 2.25 (septet, $J = 6.8$ Hz, 1H), 2.68 (dd, $J = 3.4$, 7.2 Hz, 1H), 7.21–7.62 (m, 4H).

6-Ethyl-6a-isopropyl-1,1a,6,6a-tetrahydrocycloprop[*a*]inden-6-ol. A flask flame-dried under argon atmosphere was charged with ethylmagnesium bromide (3 M, 45 mL, 130 mmol) and compound **19** (8.27 g, 44.4 mmol) in dry diethyl ether (25 mL) was added slowly *via* syringe. The solution was stirred for 2 h and then it was carefully quenched on ice with H_2O and

1 M HCl. The aqueous layer was extracted five times with diethyl ether, and the combined organic layers were washed with a saturated aqueous sodium bicarbonate solution, dried with magnesium sulfate, and filtered. The solvent was removed *via* rotary evaporation and the yellow oil was subjected to column chromatography to give 6-ethyl-6a-isopropyl-1,1a,6,6a-tetrahydrocycloprop[*a*]inden-6-ol (7.78 g, 73%).

^{1}H NMR (400 MHz, $CDCl_3$): δ 0.16 (t, $J = 3.2$ Hz, 1H), 0.53 (t, $J = 7.6$ Hz, 3H), 0.70 (d, $J = 6.8$ Hz, 3H), 0.93 (dd, $J = 4$ Hz, 1H), 1.13 (d, $J = 6.8$ Hz, 3H), 1.5 (br s, 1H), 2.0 (diast m, $J \sim 7$ Hz, 2H), 2.40 (m, 1H), 2.41 (m, $J \sim 7$ Hz, 1H), 7.1–7.2 (m, 4H).

6-Ethylidene-6a-isopropyl-1,1a,6,6a-tetrahydrocycloprop-[*a*]-indene (20). 6-Ethyl-6a-isopropyl-1,1a,6,6a-tetrahydrocycloprop[*a*]inden-6-ol (7.87 g, 36.4 mmol) was dissolved in methylene chloride (175 mL), and to this was added distilled triethylamine (36.9 g, 363.8 mmol), and 4-dimethylaminopyridine (0.178 g, 1.5 mmol). The reaction was stirred under argon for 10 min. Then a solution of methanesulfonyl chloride (11.26 mL, 146 mmol) in methylene chloride (30 mL) was very slowly added to the stirring mixture; the solution quickly turned yellow. After the addition was complete, the reaction was stirred for 30 min, and then quenched by the addition of water. The aqueous layer was extracted three times with pentane, the combined organic layers washed with very dilute HCl, dried with magnesium sulfate and filtered. Removal of the solvent gave a yellow oil that was subjected to column chromatography (100% pentane), collecting the bright-yellow band to give 6.95 g of **20**, both *E* and *Z* isomers, as a yellow oil (90% pure by GC, 87% yield).

Major isomer: ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.45 (t, 1H), 0.96 (d, 6H), 2.10 (d, 3H), 2.82 (septet, 1H), 6.13 (q, 1H).

Minor isomer: ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.63 (t, 1H), 0.90 (d, 6H), 2.01 (d, 3H), 3.15 (septet, 1H), 5.84 (q, 1H).

1-(6a-Isopropyl-1,1a,6,6a-tetrahydrocycloprop[*a*]inden-6-yl)-ethanol. The alkene mixture, **20**, (6.95 g, 35.0 mmol) was dissolved in dry THF (300 mL) under an argon atmosphere, and a solution of BH_3·THF (1 M, 36 mL, 36 mmol) was slowly added by syringe. The solution turned clear and colorless (from bright yellow) after 1 h. The reaction was allowed to stir overnight (18 h total, since early quenching of an aliquot revealed 27% starting material around after 3 h). A solution was prepared of sodium hydroxide (3 M, 50 mL) and hydrogen peroxide (30% in water, 50 mL), and this solution was slowly added to the cooled (by ice) reaction vessel. The mixture was then warmed to room temperature and stirred for 3 h, put in a separatory funnel, and dilute HCl was added to dissolve some of the solid that had formed. The aqueous layer was extracted four times with diethyl ether (checking the extracts by TLC for any remaining spots), and the combined organic layers were dried with magnesium sulfate and filtered. The solvent was removed to give a slightly yellow, very thick oil, which was then subjected to column chromatography to give 1-(6a-isopropyl-1,1a,6,6a-tetrahydrocycloprop[*a*]inden-6-yl)ethanol (5 g, ~70%) a clear, colorless, thick oil. It was difficult to determine exact purity and yield by GC owing to the presence of four diastereomers. NMR spectra could not be assigned, for the same reason.

1-(6a-Isopropyl-1,1a,6,6a-tetrahydrocycloprop[*a*]inden-6-yl)-ethanone (3 + 21). A 100 mL flask with a stir bar was flame-dried under an argon atmosphere, charged with oxalyl chloride (2 M in methylene chloride, 4.62 mL, 9.25 mmol), and cooled to −78 °C. Dimethyl sulfoxide (1.13 mL, 18.49 mmol) was added *via* syringe, taking care not to let it freeze in the needle-tip, and this mixture was stirred for 2 min. A solution of 1-(6a-isopropyl-1,1a,6,6a-tetrahydrocycloprop[*a*]inden-6-yl)ethanol (1.00 g, 4.62 mmol) in CH_2Cl_2 (10 mL) was slowly added *via* syringe, and the reaction was stirred for 15 min. Distilled triethylamine (5.15 mL, 36.98 mmol) was added *via* syringe and the solution was stirred for 5 min, warmed to room temperature and stirred for 15 min. The solution had a cloudy, yellow color. Water was added (20 mL) to dissolve the solid, and the aqueous layer was washed three times with methylene chloride. The combined organic layers was washed with a saturated aqueous sodium chloride solution, dried with magnesium sulfate, and filtered. The solvent was removed to give a dark yellow liquid, which was subjected to column chromatography (30 : 1 pentane–ether) to give 630 mg of a mixture of **3** and **21** (64%), which could be separated by a second column chromatography.

^{1}H NMR of **3** (400 MHz, $CDCl_3$): δ 0.00 (t, $J = 3.8$ Hz, 1H), 0.73 (d, $J = 6.8$ Hz, 3H), 1.07 (d, $J = 6.4$ Hz, 3H), 1.14 (dd, $J = 4.8$, 8.2 Hz, 1H), 1.78 (s, 3H), 2.01 (septet, $J = 6.6$ Hz, 1H), 2.49 (m, $J = 3.0$ Hz, 1H), 3.98 (s, 1H), 7.01–7.07 (m, 2H), 7.15 (t, $J = 7.4$ Hz, 1H), 7.30 (d, $J = 7.2$ Hz, 1H).

^{13}C NMR of **3** (125.7 MHz, $CDCl_3$): δ 17.7, 18.2, 21.7, 26.7, 27.0, 28.1, 35.8, 65.6, 123.2, 125.5, 125.7, 127.4, 139.6, 149.3, 196.4.

^{1}H NMR of **21** (400 MHz, $CDCl_3$): δ 0.70 (dd, $J = 3.2$, 4.8 Hz, 1H), 0.94 (d, $J = 6.8$ Hz, 3H), 0.99 (d, $J = 6.8$ Hz, 3H), 1.12 (dd, $J = 4.8$, 8.2 Hz, 1H), 1.80 (septet, $J = 6.8$ Hz, 1H), 2.21 (dd, $J = 3.6$, 8.2 Hz, 1H), 2.24 (s, 3H), 4.32 (s, 1H), 7.03 (d, $J = 7.2$ Hz, 1H), 7.08 (t, $J = 7.4$ Hz, 1H), 7.14 (t, $J = 7.4$ Hz, 1H), 7.23 (d, $J = 7.2$ Hz, 1H).

^{13}C NMR of **21** (100 MHz, $CDCl_3$): δ 19.7, 20.1, 20.7, 27.6, 29.6, 32.2, 36.3, 61.1, 123.2, 125.3, 125.6, 127.1, 139.9, 147.2, 209.8.

Photolysis of ketone 3

The photolysis studies on the Norrish-II radical clock precursors were first accomplished by creating a solution of **3** in pentane around 7 mM. The solution was divided into Pyrex tubes (0.5–1.0 mL) that already had one end sealed; the tubes had a 6 mm outer diameter and a 4 mm inner diameter. The tubes were then subjected to three freeze–pump–thaw cycles and finally sealed under vacuum. Using tape, the sealed tubes were attached to the cooling jacket of a Hg-arc lamp and allowed to irradiate for various lengths of time.

As the studies progressed, piperylene was added as a triplet quencher to reduce the amount of Norrish-I products forming. Piperylene came as a 90% tech grade (remainder was cyclopentene), and was distilled from sodium borohydride before use. The concentration of piperylene was varied in the range 30–330 mM. The principal new compounds formed were as follows:

1-(3-Isopropyl-1,2-dihydronaphthalen-1-yl)ethanone (31). ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.09 (d, $J = 7.0$ Hz, 3H), 1.10 (d, $J = 7.0$ Hz, 3H), 1.98 (s, 3H), 2.42 (septet, $J = 7.0$ Hz, 1H), 2.46 (ddd, $J = 1.5$, 9.5 Hz, 1H), 2.71 (dd, $J = 3.5$, 16.5 Hz, 1H), 3.59 (dd, $J = 3.5$, 7.5 Hz, 1H), 6.16 (s, 1H), 7.02–7.23 (m, 4H).

1-[2-(Isopropylidenecyclopropyl)phenyl]propan-2-one (8). ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.63 (t, 1H), 1.85 (s, 3H), 1.89 (s, 3H), 2.15 (s, 3H), 2.46 (m, 1H), 3.87 (s, 2H), 6.97–7.2 (m, 4H).

MS: *m/z* 214 (<1), 199 (22), 171 (12), 157 (27), 129 (34), 115 (29), 43 (100%).

Alcohol 7. ^{1}H NMR (500 MHz, $CDCl_3$): δ 0.48 (dd, $J = 4.0$, 5.3 Hz, 1H), 0.85 (s, 1H), 0.97 (dd, $J = 5.5$, 8.5 Hz, 1H), 1.30 (s, 3H), 1.33 (s, 3H), 1.50 (br s, 1H), 2.30 (d of m, 1H), 3.57 (s, 1H), 7.09–7.32 (m, 4H).

MS: *m/z* 214 (<1), 199 (1), 171 (17), 155 (12), 141 (17), 129 (100), 115 (20), 86 (57%).

3-Isopropyl-1,2-dihydronaphthalene (30). ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.09 (d, $J = 6.8$ Hz, 6H), 2.23 (t, $J = 8.0$ Hz, 2H), 2.41 (septet, $J = 6.8$ Hz, 1H), 2.77 (t, $J \sim 8$ Hz, 2H), 6.20 (s, 1H), 7.01–7.14 (m, 4H).

MS: *m/z* 172 (43), 157 (89), 142 (19), 129 (100), 115 (39%).

The other principal product, 2-isopropylnaphthalene, is a known compound.[53]

Synthesis of alcohols 10

Hydrocarbon 23. Hydrocarbon **22**[41] (0.250 g, 1.4 mmol) was dissolved in acetone (18 mL), and Ar was bubbled through the solution in a Pyrex test tube for 1 min. The solution was irradiated on a medium-pressure Hg lamp (with a quartz jacket) for 6 h, at which point GC analysis showed the reaction to be complete. The solvent was removed and the residue was purified *via* pipet column chromatography (2 : 1 pentane–methylene chloride) giving **23** (201 mg, 80%) as a slightly milky liquid.

^{1}H NMR (400 MHz, $CDCl_3$): δ 1.49 (s, 3H), 1.52 (s, 3H), 2.58 (m, 1H), 2.77 (t, $J = 5.2$ Hz, 1H), 3.56 (m, 1H), 3.74 (br t, 1H), 7.02–7.1 (m, 3H), 7.34 (d, $J = 7.2$ Hz, 1H).

2-Isopropylidene-1,2,3,4-tetrahydro-1,4-methanonaphthalen-9-ol (24). The starting hydrocarbon **23** (0.025 g, 0.14 mmol) was dissolved in 0.5 mL THF and 0.5 mL water. A small amount of hydrochloric acid (0.5 mL, 3 M) was added and this mixture was stirred vigorously. The reaction was monitored by TLC, indicating the formation of two products with R_fs low on the plate in 8 : 1 : 1 hexanes–benzene–EtOAc. The reaction was then extracted four times with diethyl ether, dried with magnesium sulfate and the solvent removed to give 36 mg of a residue. This material was purified by pipet column chromatography using a 3:1 pentane-methylene chloride mixture, affording the product, **24** (26 mg total).

^{1}H NMR (400 MHz, $CDCl_3$): δ 1.46 (s, 3H), 1.59 (br s, 1H), 1.73 (m, very fine splitting, 3H), 1.81 (d, $J = 15.2$ Hz, 1H), 2.47 (d of m, $J = 14.2$ Hz, 1H), 3.32 (s, 1H), 3.82 (m, 1H), 4.18 (m, 1H), 7.13–7.17 (m, 2H), 7.23–7.25 (m, 1H), 7.29–7.31 (m, 1H).

2-Isopropylidene-1,2,3,4-tetrahydro-1,4-methanonaphthalen-9-one (25). A round bottom flask with stir bar was flame-dried under Ar, cooled to −78 °C and then charged with oxalyl chloride (0.130 mL, 3 M, 0.260 mmol). DMSO was added slowly *via* syringe (0.037 mL, 0.519 mmol) and the solution was stirred for 2 min. A solution of the alcohol **24** (0.026 g, 0.130 mmol) in 1 mL dry methylene chloride was added, and the solution was stirred for 15 min. Triethylamine (0.145 mL, 1.039 mmol) was added and the solution stirred for 5 min at low temperature, then 15 min at room temperature; the solution was cloudy white. Water was added (3 mL) along with five drops of HCl (3 M) to dissolve the salts. The mixture was the extracted four times with methylene chloride and the combined organic layers were washed with saturated aqueous ammonium chloride and dried with magnesium sulfate. The solvent was removed and the residue was purified using pipet column chromatography with 1 : 1 pentane–methylene chloride as the eluent ($R_f \sim 0.5$, purple spot with anisaldehyde stain) to give 15 mg of the product **25** as a clear, colorless oil (60%).

^{1}H NMR (400 MHz, $CDCl_3$): δ 1.52 (s, 3H), 1.79 (s, 3H), 2.06 (d, $J = 15$ Hz, 1H), 3.26 (br d, $J = 15.5$ Hz, 1H), 3.53 (d, $J = 3.9$ Hz, 1H), 4.02 (br s, 1H), 7.19–7.32 (m, 4H).

^{13}C NMR (75.4 MHz, $CDCl_3$): δ 20.0, 20.9, 32.2, 50.1, 54.2, 121.0, 121.9, 123.6, 125.3, 126.7, 127.0, 139.5, 140.5, 185.4.

2-Isopropylidene-9-methyl-1,2,3,4-tetrahydro-1,4-methanonaphthalen-9-ol (10). To a solution of ketone **25** in 1 mL THF (approx. 12 mg, 0.061 mmol) was added MeMgBr (0.200 mL, 3 M). This solution was stirred overnight, whereupon it was carefully quenched with water and a small amount of HCl (3 M). The mixture was extracted with diethyl ether and the combined organic layers were dried with magnesium sulfate. Upon removal of the solvent, the residue was purified *via* pipet column chromatography (1 : 1 pentane–methylene chloride, $R_f \sim 0.2$ in 8 : 1 : 1 hexanes–benzene–EtOAc, greenish-blue spot with anisaldehyde stain). Purification gave 9 mg of a colorless oil-residue (70%), with GC and NMR analysis showing roughly a 5 : 1 ratio of the diastereomers.

Major isomer: ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.06 (s, 3H), 1.57 (s, 3H), 1.78 (s, very fine splitting, 3H), 1.8 (d, blends in with 1.78, 1H), 2.74 (d of m, $J = 13.6$ Hz, 1H), 3.01 (dm, $J = 4.2$ Hz, 1H), 3.56 (br s, 1H), 7.05–7.16 (m, 4H).

MS: *m/z* 214 (7), 199 (2), 171 (47), 129 (100), 115 (**12**).

Minor isomer: ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.34 (s, 3H), 1.47 (s, 3H), 1.74 (s, very fine splitting, 3H), 2.53 (dm, $J \sim 20$ Hz, 1H), 3.06 (d, $J = 3.2$ Hz, 1H), 3.61 (br s, 1H), 7.20–7.27 (m, 4H); one proton hidden.

Conclusions

The studies reported here suggest that the radical **2** ring opens at about 10^{10} s^{-1} at 298 K. Nevertheless, the apparently similar singlet biradical, **4**, generated by Norrish type II photochemistry, showed no evidence of ring opening at all. The theoretical work that has accompanied this experimental investigation suggests that the distinction arises not from a fundamental difference in electronic structure between the monoradical and biradical, but rather from the fact that the transition state for ring opening of biradical **4** faces a steric interaction that has no counterpart in the ring opening of **2**. Although the magnitude of this steric interaction is modest (estimated 15–20 kJ mol^{-1}), it is enough to shut the reaction down because the biradical has two other product-forming channels that experience little or no barrier. Thus one learns that even when theory leads to an expectation of similar physical properties of monoradicals and singlet biradicals, the chemistry can nonetheless be quite different because singlet biradicals will often decay by very fast unimolecular reactions that are unavailable to monoradicals.

Acknowledgements

Support of this research by the U.S. National Science Foundation (grant CHE-0212149) is gratefully acknowledged.

References

1 C. P. Casey and R. A. Boggs, *J. Am. Chem. Soc.*, 1972, **94**, 6457.
2 S. De Feyter, E. W. G. Diau and A. H. Zewail, *Angew. Chem., Int. Ed.*, 2000, **39**, 260.
3 M. B. Reyes and B. K. Carpenter, *J. Am. Chem. Soc.*, 2000, **122**, 10163.
4 L. Salem, *Pure Appl. Chem.*, 1973, **33**, 317.
5 L. Salem and C. Rowland, *Angew. Chem., Int. Ed. Engl.*, 1972, **11**, 92.
6 P. J. Hay, W. J. Hunt and W. A. Goddard, III, *J. Am. Chem. Soc.*, 1972, **94**, 638.
7 W. T. Borden, *React. Intermed. (Wiley)*, 1985, **3**, 151.
8 A. D. Dutoi, Y. Jung and M. Head-Gordon, *J. Phys. Chem. A*, 2004, **108**, 10270.
9 S. L. Debbert, B. K. Carpenter, D. A. Hrovat and W. T. Borden, *J. Am. Chem. Soc.*, 2002, **124**, 7896.
10 C. Doubleday, G. Li and W. L. Hase, *Phys. Chem. Chem. Phys.*, 2002, **4**, 304.
11 M. B. Reyes, E. B. Lobkovsky and B. K. Carpenter, *J. Am. Chem. Soc.*, 2002, **124**, 641.
12 J. E. Baldwin and E. J. Keliher, *J. Am. Chem. Soc.*, 2002, **124**, 380.
13 C. Doubleday, Jr., K. Bolton and W. L. Hase, *J. Phys. Chem. A*, 1998, **102**, 3648.
14 D. A. Hrovat, S. Fang, W. T. Borden and B. K. Carpenter, *J. Am. Chem. Soc.*, 1997, **119**, 5253.
15 C. Doubleday, Jr., K. Bolton, G. H. Peslherbe and W. L. Hase, *J. Am. Chem. Soc.*, 1996, **118**, 9922.
16 B. K. Carpenter, *J. Am. Chem. Soc.*, 1995, **117**, 6336.
17 D. C. Sorescu, D. L. Thompson and L. M. Raff, *J. Chem. Phys.*, 1995, **102**, 7910.
18 B. A. Thrush, *J. Chem. Soc., Faraday Trans. 2*, 1986, **82**, 2125.
19 K. A. McLauchlan, *Chem. Soc. Rev.*, 1993, **22**, 325.
20 D. Beckert, *Electron Paramag. Res.*, 2002, **18**, 74.
21 M. V. Encinas, P. J. Wagner and J. C. Scaiano, *J. Am. Chem. Soc.*, 1980, **102**, 1357.
22 P. J. Wagner, K.-C. Liu and Y. Noguchi, *J. Am. Chem. Soc.*, 1981, **103**, 3837.

23 W. Adam, C. van Barneveld, O. Emmert, H. M. Harrer, F. Kita, A. S. Kumar, W. Maas, W. M. Nau, S. H. K. Reddy and J. Wirz, *Pure Appl. Chem.*, 1997, **69**, 735.
24 C. J. Cramer and J. Thompson, *J. Phys. Chem. A*, 2001, **105**, 2091.
25 For a caution against literal acceptance of this simple notion, see: C. F. Logan and P. Chen, *J. Am. Chem. Soc.*, 1996, **118**, 2113.
26 T. H. Peterson and B. K. Carpenter, *J. Am. Chem. Soc.*, 1992, **114**, 1496.
27 T. H. Peterson and B. K. Carpenter, *J. Am. Chem. Soc.*, 1993, **115**, 5466.
28 K. Redmond and B. K. Carpenter, *J. Org. Chem.*, 1997, **62**, 5668.
29 A. Maiti, J. B. Gerken, M. R. Masjedizadeh, Y. S. Mimieux and R. D. Little, *J. Org. Chem.*, 2004, **69**, 8574.
30 E. D. Nelson, A. Artau, J. M. Price, S. E. Tichy, L. Jing and H. I. Kenttaemaa, *J. Phys. Chem. A*, 2001, **105**, 10155.
31 M. Abe, W. Adam, M. Hara, M. Hattori, T. Majima, M. Nojima, K. Tachibana and S. Tojo, *J. Am. Chem. Soc.*, 2002, **124**, 6540.
32 K. Jug and C. Koelle, *J. Phys. Chem. B*, 1998, **102**, 6605.
33 M. Newcomb, *Tetrahedron*, 1993, **49**, 1151.
34 A. A. Martin-Esker, C. C. Johnson, J. H. Horner and M. Newcomb, *J. Am. Chem. Soc.*, 1994, **116**, 9174.
35 N. J. Turro, *Modern Molecular Photochemistry*, Benjamin/Cummings, Menlo Park, California, 1978.
36 A. B. Charette and A. Beauchemin, *Org. React.*, 2001, **58**, 1.
37 M. Nakamura, A. Hirai and E. Nakamura, *J. Am. Chem. Soc.*, 2003, **125**, 2341.
38 K. Kakiuchi, B. Yamaguchi and Y. Tobe, *J. Org. Chem.*, 1991, **56**, 5745.
39 D. R. Coulson, *Tetrahedron Lett.*, 1964, 3323.
40 U. Schubert and E. O. Fischer, *Chem. Ber.*, 1973, **106**, 1062.
41 W. Eberbach, P. Wuersch and H. Prinzbach, *Helv. Chim. Acta*, 1970, **53**, 1235.
42 S.-Y. Choi, P. H. Toy and M. Newcomb, *J. Org. Chem.*, 1998, **63**, 8609.
43 UB3LYP calculations were carried out with the Gaussian 03 program package: *Gaussian 03*; Rev. B.05: M. J. Frisch, G. W. Trucks, H. B. Schlegel, G. E. Scuseria, M. A. Robb, J. R. Cheeseman, J. A. Montgomery, Jr., T. Vreven, K. N. Kudin, J. C. Burant, J. M. Millam, S. S. Iyengar, J. Tomasi, V. Barone, B. Mennucci, M. Cossi, G. Scalmani, N. Rega, G. A. Petersson, H. Nakatsuji, M. Hada, M. Ehara, K. Toyota, R. Fukuda, J. Hasegawa, M. Ishida, T. Nakajima, Y. Honda, O. Kitao, H. Nakai, M. Klene, X. Li, J. E. Knox, H. P. Hratchian, J. B. Cross, V. Bakken, C. Adamo, J. Jaramillo, R. Gomperts, R. E. Stratmann, O. Yazyev, A. J. Austin, R. Cammi, C. Pomelli, J. W. Ochterski, P. Y. Ayala, K. Morokuma, G. A. Voth, P. Salvador, J. J. Dannenberg, V. G. Zakrzewski, S. Dapprich, A. D. Daniels, M. C. Strain, O. Farkas, D. K. Malick, A. D. Rabuck, K. Raghavachari, J. B. Foresman, J. V. Ortiz, Q. Cui, A. G. Baboul, S. Clifford, J. Cioslowski, B. B. Stefanov, G. Liu, A. Liashenko, P. Piskorz, I. Komaromi, R. L. Martin, D. J. Fox, T. Keith, M. A. Al-Laham, C. Y. Peng, A. Nanayakkara, M. Challacombe, P. M. W. Gill, B. Johnson, W. Chen, M. W. Wong, C. Gonzalez, and J. A. Pople, Gaussian, Inc., Wallingford, CT, 2004.
44 CASPT2 calculations were carried out with the MOLCAS program package: *MOLCAS 5.4*: K. Andersson, M. Barysz, A. Bernhardsson, M. R. A. Blomberg, D. L. Cooper, T. Fleig, M. P. Fulscher, C. de Graaf, B. A. Hess, G. Karlstrom, R. Lindh, P.-Å. Malmqvist, P. Neogrady, J. Olsen, B. O. Roos, A. J. Sadlej, M. Schutz, B. Schimmelpfennig, L. Seijo, L. Serrano-Andres, P. E. M. Siegbahn, J. Stalring, T. Thorsteinsson, V. V. Pidmark, and P.-O. Widmark, University of Lund, Sweden, 2002.
45 A. G. Baboul, L. A. Curtiss, P. C. Redfern and K. Raghavachari, *J. Chem. Phys.*, 1999, **110**, 7650.
46 L. A. Curtiss, P. C. Redfern, K. Raghavachari, V. Rassolov and J. A. Pople, *J. Chem. Phys.*, 1999, **110**, 4703.
47 K. Wolinski, J. F. Hinton and P. Pulay, *J. Am. Chem. Soc.*, 1990, **112**, 8251.
48 B. Mennucci and J. Tomasi, *J. Chem. Phys.*, 1997, **106**, 5151.
49 D. Cremer, *Mol. Phys.*, 2001, **99**, 1899.
50 C. Doubleday, Jr., *Chem. Phys. Lett.*, 1995, **233**, 509.
51 W. C. Still, M. Kahn and A. Mitra, *J. Org. Chem.*, 1978, **43**, 2923.
52 N. J. P. Broom and P. G. Sammes, *J. Chem. Soc., Perkin Trans. 1*, 1981, 465.
53 L. Ernst and P. Schulz, *Magn. Res. Chem.*, 1992, **30**, 73.