Stepwise Mechanisms in Cyclopropylcarbene Reactions

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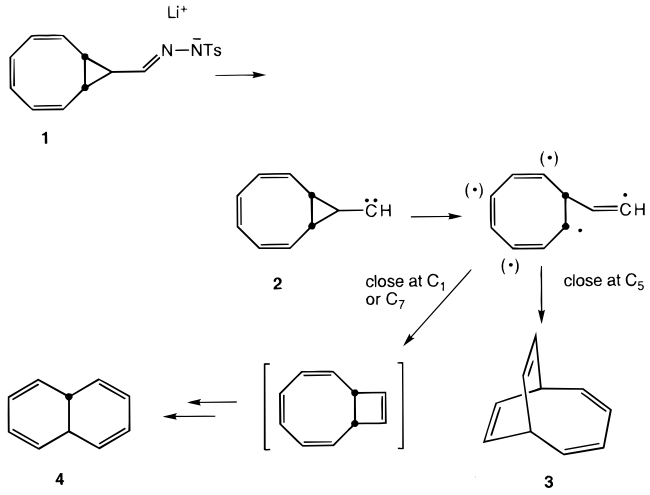
Abstract: Decomposition of a naphtho-fused cyclopropyldiazomethane leads to benzocyclooctatetraene, 1-vinylnaphthalene, 2-vinylnaphthalene, and small amounts of benzobarrelene. Diradical intermediates are postulated.

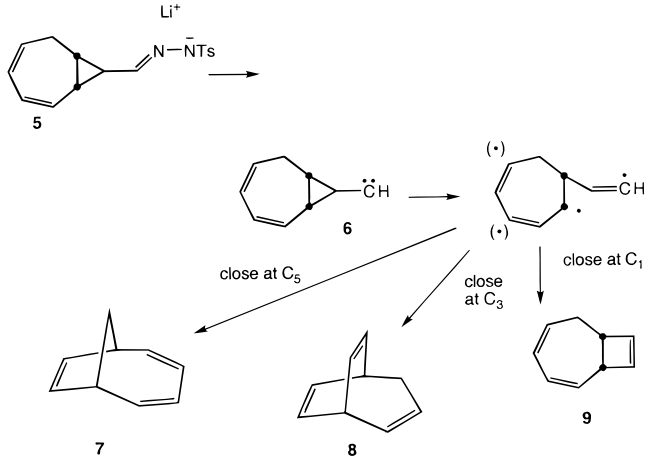
Nearly 30 years ago we described the formation of the bicyclic polyenes **3**, **4**, and **7**−**9** from thermal decomposition of the tosylhydrazone salts **1** and **5**. The mechanism we wrote is shown in Schemes 1 and 2, and accounts nicely for all the observed products. It postulates that one ring bond of the cyclopropylcarbene (**2** or **6**) breaks to give a resonance-stabilized diradical that can then close in more than one way to give the observed products, or molecules able to rearrange to them.[1]

Because this mechanism requires the stepwise fragmentation of carbenes **2** and **6** as shown in Schemes 1 and 2, over the years we grew disenchanted with it, as no firm evidence for such reactions of cyclopropylcarbenes was found despite directed searches. For example, we, and others, showed that the ring expansion and fragmentation of simple cyclopropylcarbenes, thought to be formed from intermediate diazo compounds, was stereospecific.[2] Diradicals did not seem to be viable intermediates, at least in simple cases, or even when conjugation was present.[3] Nor was there theoretical justification for the formation of diradical intermediates.[4] So, we spent much effort on fruitless experiments designed to find the "real" mechanism. Recently, however, we have learned that many of the cyclobutenes formed from "cyclopropylcarbenes" have their origin in reactions of the starting diazo compound, not the carbene.[5,6] Given that information, it seemed worthwhile to probe for other rearrangements during cyclopropylcarbene ring expansion. In this paper we present one such example, as well as the formation of other products that implicate diradical intermediates. Thus, we support our original mechanism.[1]

Scheme 1. Formation of Polyenes of the Formula $(CH)_{10}$



Scheme 2. Formation of Polyenes of the Formula C_9H_{10}



We decided to explore a system in which the putative diradical could reveal itself not only through rearrangement, as in the earlier examples,[1] but through a new reaction, a hydrogen transfer leading to aromatization. The carbene of choice was **11**, available from the tosylhydrazone salt **10**, itself produced through the unexceptional[7] sequence shown in Scheme 3.

Of course, we risked introducing a reaction that could shortcut rearrangements of all kinds, as fragmentation to acetylene and

(1) Jones, M, Jr.; Reich, S. D.; Scott, L. S. *J. Am. Chem. Soc*. **1970**, *92*, 3118.

(2) (a) For a summary of the chemistry of cyclopropylcarbenes see: Arct, J.; Brinker, U. H. In *Methoden der Organische Chemie (Houben-Weyl)*; Regitz, M., Ed.; G. Thieme Verlag: Stuttgart, 1989; Vol. E19b, pp 337−375. (b) Specific examples of investigations of stereochemistry can be found in: Guarino, A.; Wolf, A. P. *Tetrahedron Lett*. **1969**, 655. Berson, J. A.; Bauer, W.; Campbell, M. M. *J. Am. Chem. Soc*. **1970**, *92*, 7515. Sohn, M. B. Ph.D. Thesis, Princeton University, 1972, Bergman, R. G.; White, D. H. Private communication, 1972. Olin, S. S.; Venable, R. M. *J. Chem. Soc., Chem. Commun*. **1974**, 273. Gallucci, R. R.; Jones, M., Jr. *J. Am. Chem. Soc*. **1976**, *98*, 7704.

(3) Sasaki, T.; Eguchi, S.; Ohno, M.; Umemura, T. *J. Org. Chem*. **1973**, *38*, 4095.

(4) Schoeller, W. W. *J. Org. Chem*. **1980**, *45*, 2161. Armstrong, B. M.; McKee, M. L.; Shevlin, P. B. *J. Am. Chem. Soc*. **1995**, *117*, 3685.

(5) (a) Thamattoor, D. M.; Jones, M., Jr.; Pan, W.; Shevlin, P. B. *Tetrahedron Lett*. **1996**, *37*, 8333. (b) Huang, H.; Platz, M. S. *Tetrahedron Lett*. **1996**, *37*, 8337.

(6) We are redoing the stereochemical experiments starting from hydrocarbon carbene sources. Ruck, R. R. Unpublished work.

(7) If you do not mind doing a distillation of several hundred grams of naphthalene!

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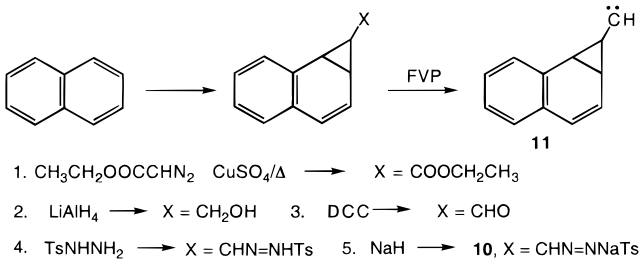
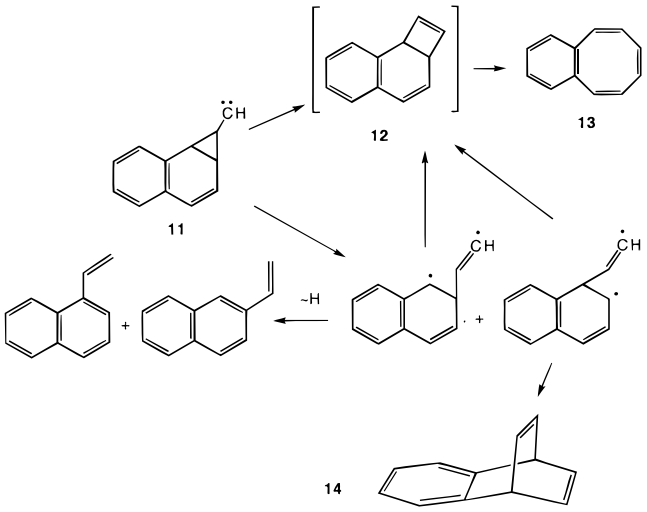
Scheme 3. Synthesis of Carbene **11**



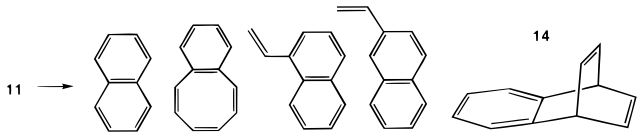
Scheme 4. Potential Reactions of Carbene **11**



naphthalene is bound to be strongly favored in **11**. If fragmentation were not the sole reaction, we expected that ring expansion would lead to cyclobutene **12**, and thence to the rearranged benzocyclooctatetraene **13**. By contrast, were a stepwise process to ensue, we hoped for rearrangement to benzobarrelene (**14**) and, perhaps, hydrogen transfers to give 1- and 2-vinylnaphthalene (Scheme 4).

Thermal decompositions of simple alkyl diazo compounds are far less complicated by diazo chemistry than are photochemical reactions,[8] so it seemed prudent to begin with gas-phase thermal decomposition of **10**. The salt was heated to ~120 °C at 0.005 Torr to generate the diazo compound, which was led into a quartz tube heated to 500 °C, and then to a liquid nitrogen cooled trap. Naphthalene was indeed by far the major product, but there were four other compounds of the same molecular weight as carbene **11**. Three were easily identified by comparison of retention times and spectra with those known compounds. One was the anticipated benzocyclooctatetraene.[9] Another product, 2-vinylnaphthalene, could be identified by comparison of retention time and spectra with those of a commercial sample. The third compound, 1-vinylnaphthalene, is less well-known,[10] and could not be easily separated from the 2-isomer. The compound could be identified, however, by subtraction of the ^{1}H NMR spectrum of the authentic 2-isomer. The fourth product, present in only trace amounts, had the same retention time as authentically synthesized benzobarrelene (**14**).[11]

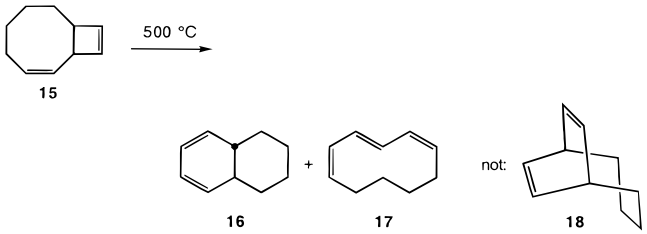
Comparison with the infrared spectrum of authentic material, obtained by GC/FTIR,[12] showed that the structural assignment of **14** was correct.



500 °C .005 torr	89	2.2	8.4	0.4	0.3
100 °C .005 torr	81	7.2	14.3	3.6	0.2
200 °C decane	58	tr	32.5	10.4	tr
hν THF, 25 °C	66	0.3	25.1	8.1	1.0

At the lower temperature of 100−120 °C, the product ratio is qualitatively similar. When the tosyl hydrazone salt is heated as a slurry in decane, the vinylnaphthalenes grow at the expense of the fragmentation product naphthalene. Presumably, decane offers a vehicle for hydrogen abstraction by the diradicals, ultimately leading to the vinyl compounds. There is precedent for the abstraction of hydrogen by vinyl radicals, even in gas-phase reactions.[13] The product of closure of the diradical, benzobarrelene, is never a major product, but it is always present.

The case for the presence of a diradical, and thus for stepwise bond breaking in the cyclopropylcarbenes, rests on the formation of the two vinylnaphthalenes and the benzobarrelene. Might these compounds come from **12**, sure to be the primary ring-expanded product of carbene **11**?[2a] Benzocyclooctatetraene is known not to form naphthalene below 625 °C, and thus **12** appears an unlikely source of the critical compounds.[14] In addition, there is also much indirect evidence that the only likely rearrangement product of **12** would be benzocycloocatetraene. For example, **15**, formed from the pyrolysis of the lithium salt of bicyclo[6.1.0]non-2-ene-9-carboxaldehyde tosyl hydrazone, gives **16** and **17**, but not **18**.[15]



Most persuasive is our observation that photolysis of salt **10** in THF at 25 °C leads to all the same products as the thermal reactions carried out at higher temperature. The vinylnaphthalenes and benzobarrelene, the compounds diagnostic for the diradical, are primary products of the reaction, not artifacts introduced by secondary reactions.

Although our results would surely seem to provide a third example in which the diradical mechanism best rationalizes the products of a cyclopropylcarbene reaction, it is important to remark how unusual this mechanistic suggestion remains. We know of only one other stepwise reaction of a (presumably)

(8) Glick, H.; Likhotvorik, I. R.; Jones, M., Jr. *Tetrahedron Lett*. **1995**, *36*, 5715 and references therein.

(9) Gunther, H.; Skyoakh, A.; Cremer, D.; Frisch, K.-H. *Justus Liebigs Ann. Chem.* **1978**, 150.

(10) Hashimoto, H.; Hida, M.; Miyamo, S. *J. Organomet. Chem*. **1967**, *10*, 518.

(11) Hales, N. J.; Heany, H.; Hollinshead, J. H.; Singh, P. *Org. Syn*. **1980**, *59*, 71.

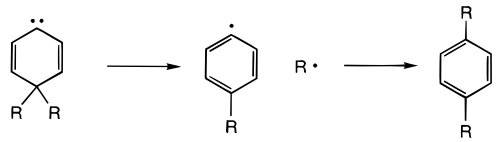
(12) We thank Dr. John Eng for assistance with this measurement.

(13) Redmond, K.; Carpenter, B. K. *J. Org. Chem*. **1997**, *62*, 5668.

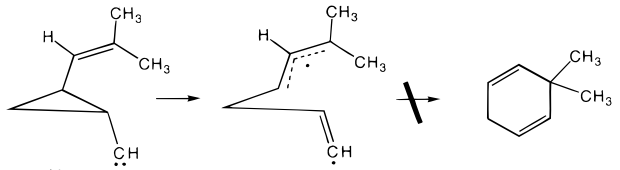
(14) Paquette, L. A.; Meisinger, R. H.; Wingard, R. E., Jr. *J. Am. Chem. Soc*. **1972**, *94*, 9224.

(15) For earlier work on this system, see: Dauben, W. G.; Michno, D. M. *J. Am. Chem. Soc*. **1981**, *103*, 2284.

singlet carbene. Crossover experiments have shown that aromatization of cyclohexadienylidenes proceeds by initial fragmentation into a pair of radicals, which then diffuse apart, finally to recombine to give the product.[16] Even here, the identity of the reacting spin state is not known with certainty.



Despite seemingly ample opportunity, rearranged products do not appear often. Thus the chrysanthemylcarbenes (**19**) give none of the cyclohexadienes that might have been anticipated from a diradical intermediate.[3] However, in an acyclic system such as this one, it seems likely that the allylic radical, if formed at all, would be primarily in the trans arrangement that is unable to close to the six-membered ring.



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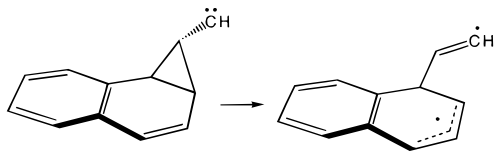
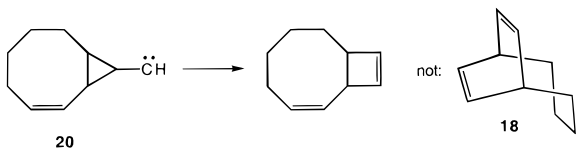
By contrast, in all the cases in which rearrangement is observed, the allylic portion of the putative diradical must be generated in the productive cis arrangement:



More puzzling is the absence of rearrangement in carbenes such as **20** in which a rearrangement-capable allylic radical is possible.[1] Perhaps the transition state for formation of the diradical requires more delocalization than the single double bond in **20** can provide; perhaps small amounts of rearranged products, or vinyl compounds, have been overlooked.



20 **18**

Finally, these days it is obligatory to bring up the question of whether carbenes are really involved at all. This problem is especially acute when intramolecular chemistry is at issue. There is ample evidence that cyclobutene formation from decomposition of cyclopropyl diazomethanes involves either complete[5b] or substantial[5a] direct rearrangement of the diazo compound. Cyclobutene **12** is surely involved in the overall reactions of **10** and **11**, particularly in the formation of benzocyclooctatetraene. It is very unlikely that **12** is the source of the vinyl compounds or benzobarrelene, which do seem to derive from cyclopropylcarbenes. Indeed, one of the reasons these stepwise reactions have been so difficult to find is that most of "cyclopropylcarbene" chemistry—ring expansion to cyclobutenes—is in reality diazo compound chemistry. Much of the intramolecular chemistry of cyclopropyldiazomethanes does not involve carbenes.

It appears that the diradical mechanism for conjugated cyclopropylcarbene rearrangements, proposed by us long ago, is correct. It remains to be seen if more simple cyclopropylcarbenes react in similar fashion.

Experimental Section

General. Photolysis was carried out with a 450-W medium-pressure mercury arc (Hanovia lamp). Melting points were determined on a Thomas-Hoover Uni-melt capillary melting point appartus and are uncorrected. ^{1}H NMR spectra were obtained on a General Electric QE 300 spectrometer at 300 MHz. Gas chromatographic/mass spectrometric analyses were performed on a Hewlett-Packard 5890/5971 Series II gas chromatograph/mass spectrometer with a HP-1701 capillary column (30 m × 0.25 mm i.d., 0.25 mm film thickness). Preparative gas chromatography was performed on a Gow-Mac 580 gas chromatograph with an aluminum column (6 ft × $^1/_4$ in.) packed with 10% OV-101 on Chromosorb WHP. Precise masses were measured on a KRATOS MS50 RFA high-resolution mass spectrometer. GC/FTIR measurements were made on a Hewlett-Packard HP 5898 gas chromatograph (30 m × 0.32 mm id, 0.5 mm film thickness) with a Restek rtx-1 column connected to a Nicolet 730 FTIR spectrometer. Ethyl diazoacetate, 2-vinylnaphthalene, *p*-toluenesulfonhydrazide, PCC, and NaH were purchased from Aldrich Chemical Co. Solvents (Et_2O, CH_2Cl_2, THF) were dried and distilled prior to use.

Ethyl 1-Benzonorcaradienecarboxylate.[17] To molten naphthalene (750 g, 5.78 mol) and anhydrous $CuSO_4$ (140 g, 880 mmol), at 150 °C under argon, was added dropwise ethyl diazoacetate (100 g, 867 mmol) over 1 h with mechanical stirring. The dark slurry was stirred for 4 h at 150 °C and then cooled to ambient temperature. The mixture was distilled under reduced pressure to remove naphthalene: bp 110−130 °C (25 Torr). The ester was collected as a yellow oil: bp 140−160 °C (2.5 Torr). Redistillation of this material yielded 37 g (20%) of ethyl 1-benzonorcaradienecarboxylate as a pale yellow oil: ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.87 (q, 2H), 1.30 (t, 3H), 2.65 (m, 1H), 3.08 (m, 1H), 4.2 (d, 1H), 6.32 (m, 1H), 6.41 (d, 1H), 7.0−7.5 (m, 4H).

1-(Hydroxymethyl)benzonorcaradiene. Ethyl 1-benzonorcaradienecarboxylate (37 g, 173 mmol) was dissolved in anhydrous Et_2O (35 mL) and added dropwise to a mixture of $LiAlH_4$ (10 g, 263 mmol) in refluxing anhydrous Et_2O (70 mL) over 1.5 h. Reaction was followed by TLC (50/50 EtOAc/hexanes). Reflux was maintained for another 1.5 h, at which time 10% NH_4Cl (10 mL) was added to quench the reaction. The mixture was filtered to remove the product (a white precipitate) which was washed with excess ether and CH_2Cl_2. The aqueous layer was extracted with Et_2O (30 mL), and the combined organic layers were dried over Na_2SO_4. The product was concentrated to yield 25.5 g (mp 64−67 °C, 86.6%). This material was used without further purification in the next step: ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.34 (m, 1H), 1.17 (m, 1H), 1.39 (s, 1H), 1.86 (m, 1H), 2.27 (m, 1H), 3.68 (m, 2H), 6.18 (m, 1H), 7.0−7.5 (m, 4H); IR (neat) 3300 (br) cm^{-1}.

1-Benzonorcaradienecarboxaldehyde. Crude 1-(hydroxymethyl)-benzonorcaradiene (25.5 g, 148 mmol) dissolved in dry CH_2Cl_2 (150 mL) was rapidly charged into a heterogeneous mixture of PCC (47.9 g, 1.5 equiv) in dry CH_2Cl_2 (300 mL). The mixture immediately turned black. The reaction was followed by TLC (50/50 EtOAc/hexanes) and diluted with 3 × 400 mL of Et_2O upon completion (1 h). Crude product was filtered through Flourisil and concentrated under reduced pressure to yield 22 g (87%) of a black liquid. A sample of 5 g of this crude material was purified by flash column chromatography (90/10 hexanes/EtOAc). A total of 3.5 g of pure material, mp 34−36 °C, was recovered: ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.18 (m, 1H), 2.86 (m, 1H), 3.28 (m, 1H), 6.33 (q, 1H), 6.47 (d, 1H), 7.0−7.5 (m, 4H), 9.91 (s, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) d 202.7, 132.4, 131.0, 128.7, 128.2, 128.0, 127.2, 126.7, 125.9, 32.7, 31.3, 29.8. HRMS (EI) calcd for $C_{12}H_{10}O$ 170.07315, found 170.07341.

1-Benzonorcaradienecarboxaldehyde Tosylhydrazone. The aldehyde (3.5 g, 20.6 mmol, 1.0 equiv) dissolved in a minimal amount

(16) Berdick, T. E.; Levin, R. H.; Wolf, A. D.; Jones, M., Jr. *J. Am. Chem. Soc.* **1973**, *95*, 5087.

(17) Doering, W. v. E.; Goldstein, M. J. *Tetrahedron*, **1959** *5*, 53.

of EtOH was added dropwise to *p*-toluenesulfonylhydrazide (4.22 g, 22.6 mmol, 1.1 equiv) in EtOH (20 mL) and glacial acetic acid (2 mL) with stirring at 50 °C. The heterogeneous mixture was allowed to stir for 12 h. The mixture was warmed to 70 °C, and EtOH was added to the flask until all the solids were dissolved. The flask was cooled to room temperature and crystals appeared. The white crystals were filtered and washed with cold EtOH. The product was dried in vacuo for 6 h. A total of 3.1 g of tosylhydrazone (mp 131−141 °C, dec, 42%) was recovered: δ ^{1}H NMR (DMSO) 1.33 (m, 1H), 2.47 (s, 3H), 2.50 (m, 1H), 2.97 (m, 1H), 3.44 (s, 1H), 6.44 (m, 2H), 7.30 (m, 3H), 7.48, (m, 2H), 7.77 (d, 2H), 10.71 (m, 1H). ^{13}C NMR (75 MHz, acetone-d_6) δ 153.2, 143.8, 136.9, 133.4, 130.9, 129.6, 129.5, 128.4, 128.2, 128.0, 127.7, 126.7, 126.6, 125.2, 26.6, 24.2, 20.8. The methyl group is presumably lost under residual acetone. In DMSO there is an additional signal at 28.6, but the rest of the spectrum is less well resolved. HRMS (EI) calcd for $C_{19}H_{18}O_2N_2S$ 338.10801, found 338.10890.

Sodium Salt of 1-Benzonorcaradienecarboxaldehyde Tosylhydrazone (10). A solution of the tosylhydrazone (100 mg, 0.282 mmol, 1 equiv) in a minimum amount of dry THF (2 mL) was added by syringe to NaH (12 mg, 1.1 equiv) in small flask flushed with argon (with vent for evolved H_2). After the addition, the solvent was evaporated with a stream of argon, resulting in a white film coating the bottom of the flask. The salt was allowed to dry for 15 h.

Flash Vacuum Pyrolysis of 10 at 500 °C. Salt **10** as prepared above was equilibrated at 0.005 Torr (25 min) and then heated to 120 °C to generate the diazo compound, which was led into a heated quartz tube at 500 °C. The reaction product was condensed in a liquid N_2 trap at the end of the oven. In this run 15 mg combined products were recovered after 0.5 h of pyrolysis. The products were dissolved in CH_2Cl_2 (1 mL) and identified by comparison with spectra of authentic samples or from the literature.

Flash Vacuum Pyrolysis of 10 at 100 °C. The same procedure as in the reaction at 500 °C above was used except for the temperature of the pyrolysis tube.

Pyrolysis of 10 in Decane at 200 °C. To dry salt **10** was added $C_{10}H_{22}$ (10 mL). The reaction flask was evacuated, sealed with a wired-down septum cap, and heated to 200 °C with magnetic stirring for 0.5 h. The flask was allowed to cool, and the products were filtered to remove solid debris. Analysis by GC/MS yielded the relative product ratios.

Photolysis of 10 at 25 °C. Salt **10** was transferred under argon into a quartz tube and washed with dry THF (3 mL). The sealed quartz tube was degassed by the freeze/pump/thaw procedure three times before photolysis. The slurry was photolyzed for 4 h at 25 °C at which time the reaction products were analyzed by GC/MS.

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