Radical Cyclization and Fragmentation of Azoxy Compounds

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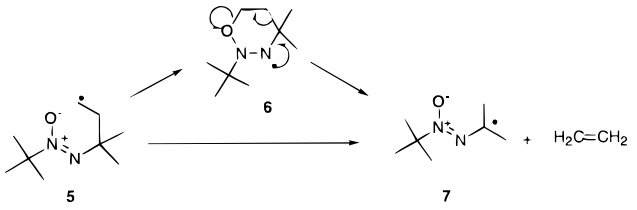
Abstract: Photolysis of azoazoxyalkane **9** and thermolysis of β-azoxyperester **13** afford β-azoxy radicals **1** and **14**, respectively. One reaction pathway of these radicals is cyclization to azoxy oxygen to form cyclic hydrazyl radicals **2** and **16** that fragment to a ketone or aldehyde plus hydrazonyl radical **3**. The analogous hydrazyl radical **6** need not be invoked in the case of γ-azoxy radical **5**, which instead undergoes a rare solution phase β-scission to lose ethylene. Surprisingly, the same β-scission was found in the 3,3-dimethyl-4-pentenyl radical (**34**), a hydrocarbon analogue of **5**.

Introduction

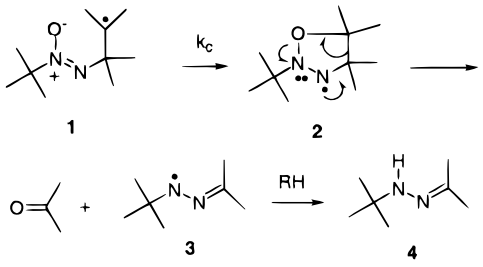
Azoxy compounds[1] are of increasing importance on account of their biological activity,[2] but the radical chemistry of azoxyalkanes is largely undeveloped.[3] Presently we report the intramolecular addition of a β-carbon radical **1** to azoxy oxygen followed by fragmentation **2** → **3**, as shown in Scheme 1. The products are acetone plus acetone *tert*-butylhydrazone **4** formed when hydrazonyl radical **3** abstracts hydrogen. The usual structure of azoxyalkanes does not permit a direct arrow-pushing mechanism for the cyclization step, but radical attack on the N═O double bond resonance structure of **1** leads to the zwitterionic form of hydrazyl radical **2**.

In principle, γ-azoxy radical **5** could also cyclize to a hydrazyl **6,** and this intermediate might fragment to α-azoxy radical **7** plus ethylene. Although ethylene is indeed a major product, it arises not via **6** but by direct β-scission of **5**. There are few previous reactions such as **5**→ **7** where a carbon-centered radical



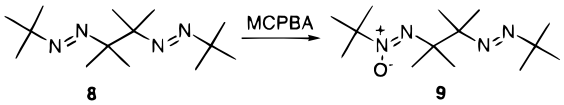
fragments to a new carbon-centered radical in solution. Herein we present evidence for the cyclization−fragmentation reaction of Scheme 1 and we demonstrate that a constrained analogue of **5** undergoes β-scission even though it cannot cyclize first. It will also be shown that the analogous olefinic radical, 3,3-dimethyl-4-pentenyl (**34**), undergoes solution phase β-scission to ethylene.

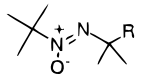
Scheme 1. Proposed Mechanism for Cyclization, Fragmentation of β-Azoxy Radical **1**



Results

Decomposition of 9. The β-azoxy radical precursor **9** was prepared by MCPBA oxidation of the known bisazoalkane **8**.[4] Thermolysis of 0.051 M **9** in C_6D_6 was carried out with 0.25 M 9,10-dihydroanthracene scavenger at 190 °C for 4 h, giving **4** (24%), acetone (74%), **10** (4%), **11** (4%), **12** (0.7%), N_2 (150%), and N_2O (10%). In contrast to the low azoxyalkane yield of the thermal reaction, photolysis at 25 °C gave a clean GC trace and quantitative product balance, as seen in Table 1.





10 R = i-Pr
11 R = C(Me)=CH$_2$
12 R = CMe$_2$-Bu-t

† Rice University.

‡ Texas Christian University.

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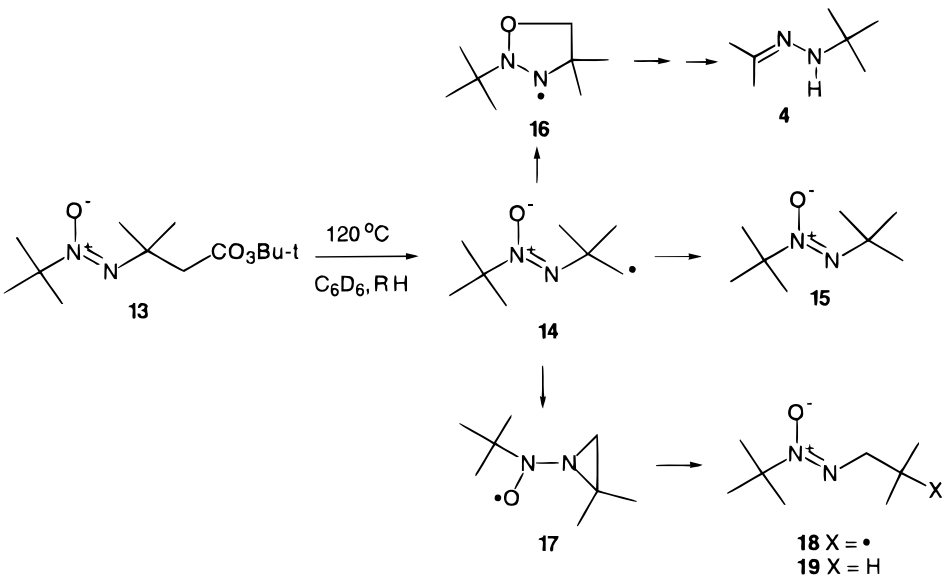


Table 1. Product Yields (%)[a] from 366 nm Photolysis of **9** in Degassed Benzene[b]

[**9**], mM	scavenger	concn, mM[c]	acetone	**10**	**11**	**12**
44	none			35	28	32
43	PhSH	200	1	72	31	5
48	CHD[d]	290	34	27	31	6
5.19	PhSH	4.66−0.58	34.5	32.3	27.1	4.8
5.19	PhSH	4.66−1.07	38.3	30.8	26.4	4.2
5.19	PhSH	6.73−1.80	32.1	36.0	27.2	4.6
5.19	PhSH	8.81−4.21	26.0	35.8	24.3	4.4
5.19	PhSH	8.81−5.34	26.3	41.9	28.2	4.4
5.19	PhSH	12.95−7.19	25.1	44.9	26.9	5.0

[a] By GC using an internal standard. [b] C_6D_6 for the first three entries, C_6H_6 for the remaining six. [c] The initial and final thiophenol concentrations are given for entries 4−9. [d] 1,4-Cyclohexadiene.

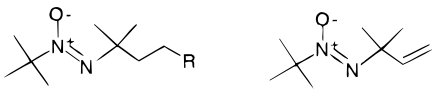
Entries 4−9 show the effect on product composition of varying the thiophenol scavenger concentration in a set of otherwise identical degassed, sealed samples. The general trend is toward more thiol trapping product **10** and less cyclization−fragmentation product, acetone, at higher thiophenol concentration.

The temperature dependence of the competing reactions of radical **1** was evaluated as follows. A solution of 0.046 M **9** and 0.5 M 1,4-cyclohexadiene in C_6D_6 was degassed and sealed into four NMR tubes. Each tube was irradiated at 366 nm at a different temperature ranging from 0 °C to 150 °C. GC and ^{1}H NMR analysis of the solutions showed clearly that higher temperatures led to a greater yield of acetone and **4** relative to **10**−**12**. An Eyring plot of the **4**/(**10** + **11** + **12**) ratio gave $\Delta\Delta H^{\ddagger} = 3.6$ kcal/mol, while the corresponding plot for acetone gave $\Delta\Delta H^{\ddagger} = 2.3$ kcal/mol. Thus the activation enthalpy for cyclization−fragmentation of **1** is about 3 kcal/mol higher than that for radical−radical reactions.

Thermolysis of *β*-azoxyperester 13. Further support for the cyclization−fragmentation mechanism was sought by independent generation of a *β*-azoxy radical like **1**. We previously reported that thermolysis of azoxyperester **13** leads to such a radical **14** which rearranges to **18**, presumably via aziridinylnitroxyl **17**.[3,5] Closer examination of the product mixture from the 120 °C thermolysis of **13** with 1.1 M 1,4-cyclohexadiene revealed **4** in 6.5% GC yield, smaller than the ∼40% calculated at the same temperature from **9**, yet still supportive of the mechanism in Scheme 1.

Thermolysis of Azoxy-tert-butane. Suspecting that the low yield of **10**−**12** from thermolysis of **9** was due to their thermal lability, we carried out a control experiment with azoxy-*tert*-butane (**15**). A solution of 0.14 M **15** in C_6D_6 was heated at 190 °C for 19.2 h, yielding on a mole per mole basis 0.81 N_2, 0.20 N_2O, 0.052 isobutane, and 2.14 isobutene. The high yields of nitrogen and isobutene imply that a Cope elimination mechanism predominates over extrusion of N_2O to give radicals, as reported earlier for azoxycumene.[6]

Thermolysis of *γ*-azoxyperester 20. Since the carbon-centered radical of **14** attacked both azoxy nitrogen and oxygen, we decided to investigate these competing processes in the next homolog. The requisite *γ*-azoxyperester **20** was prepared analogously to **13** from 4-amino-4-methyl pentanoic acid.[7] Heating **20** in C_6D_6 to 120° for 3 h gave a mixture whose GC/MS trace showed eleven significant peaks after the solvent, the most intense of which were toluene-d_5 and ether **22**. The structure of this ether was verified by co-injection of a sample prepared independently from **25**. Other products identified by co-injection were **23** and **25**. On the basis of GC/MS, one of the later peaks was assigned as the product **24** of radical **5** attacking solvent benzene. This structure is supported by the fact that the mass of **24** and the expected fragment ions decreased by 5 AMU when **20** was thermolyzed in C_6H_6 instead of C_6D_6.



20 R = CO_3Bu-t
21 R = COOH
22 R = OBu-t
23 R = H
24 R = Ph

25

The ^{1}H NMR spectrum of the crude thermolyzate from **20** exhibited a sharp singlet at 5.30 ppm, exactly the chemical shift of ethylene. This assignment was verified by GC analysis of the evolved gases, which showed the yield of C_2H_4 to be 61% and that of CO_2 to be 70%. When 7.38 M 1,4-cyclohexadiene was included in the initial solution of **20**, no ethylene and very

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Scheme 2. Synthesis of Pyrazoline Oxide Perester **30**

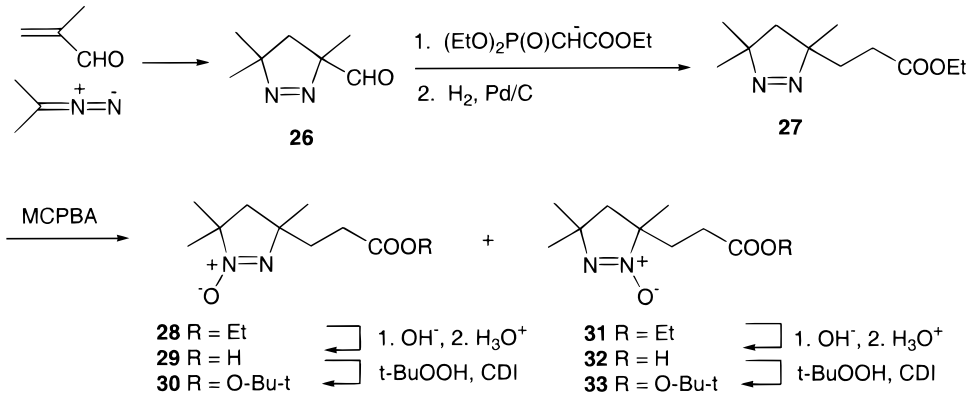


Table 2. Calculated QCISD Energy and Selected Bond Distances of Structures in Figure 1 and Table 4

species	energy, Hartrees	*r*(N−O), Å	*r*(N−N), Å	energy, kcal/mol
Z−A	−263.019974	1.234	1.286	(0)
B	−263.073218	1.408	1.352	−33.4
A → B TS	−263.019700	1.245	1.295	0.2
C	−263.077330		1.214	−36.0
D	−148.885418		1.316	
E	−114.188805			
D+E	−263.074223			−34.0
C → (D + E) TS	−263.050433		1.213	−19.1
B → (D + E) TS	−263.060487	1.729	1.303	−25.4
F	−263.038144	1.257	1.395	−11.4
A → F TS	−263.017576	1.241	1.347	1.5
G	−302.224369	1.229	1.223	(0)
H[a]	−302.252127	1.406	1.351	−17.4
G → H TS	−302.153841	1.320	1.410	44.3
I	−223.904189	1.239	1.334	
J	−78.317777			
I+J	−302.221966			1.5
G → (I + J) TS	−302.183080	1.237	1.311	25.9
H → (I + J) TS	−302.189247	1.238	1.308	22.0

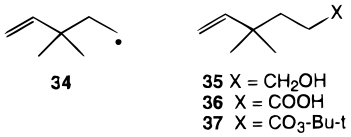
[a] H is the six-membered homolog of B.

little **24** was formed. Now **23** was the major product but **22** was still present along with a small amount of **25** and **21**. These results indicate that 1,4-cyclohexadiene mostly trapped γ-azoxy radical **5** before it could attack benzene.

Thermolysis of 1-oxy-3-(2-*tert*-butylperoxycarbonylethyl)-3,5,5-trimethyl-1-pyrazoline 30. In an effort to determine whether **5** cyclized to **6** prior to fragmentation, we prepared a cyclic analogue (**30**) of **20**. Attempts to make the precursor pyrazoline **28** by the method[8] used in the acyclic case,[9] namely, conjugate addition to ethyl acrylate of the anion derived from 3,5,5-trimethyl-2-pyrazoline, led only to N-alkylation. This problem was overcome by prior assembly of the quaternary carbon α to the azo group as shown in Scheme 2. While the 1,3-dipolar cycloaddition of diazo compounds to electron-deficient olefins is a standard synthetic method for 1-pyrazolines,[10] we are unaware of any case involving an unsaturated aldehyde. Because **26** was somewhat unstable, it was immediately subjected to the Horner-Emmons reaction. Catalytic hydrogenation selectively reduced the olefin, but MCPBA oxidation afforded a 2:1 mixture of **28** and **31** that could be separated only by preparative HPLC. The isomers were converted separately to their *tert*-butyl peresters.[11] The structure assignment of **28** and **31** is based on an HMBC NMR experiment and the fact that the ^{13}C nearest azoxy oxygen falls downfield from the one away from oxygen. In **28**, this downfield ^{13}C was long-range coupled to the protons of two methyl groups and the upfield α carbon was long-range coupled to one methyl. In **31**, the opposite situation was found: the $^{13}C-N(O)=N$ was long-range coupled to one methyl while the $^{13}C-N=N(O)$ was coupled to two.

Thermolysis of **30** and **33** was carried out separately in C_6D_6 at 120 °C but the NMR spectra revealed ethylene only from **30**. One would not expect ethylene from **33** because unlike **7**, $R-N=N(O)CR_2^{\bullet}$ is little stabilized.[3,12] GC analysis of the evolved gases from incompletely decomposed samples of **30** showed CO_2 (59% yield), N_2 (13%) and C_2H_4 (39%).

***β*-Scission of the 3,3-Dimethyl-4-pentenyl Radical 34.** The perester precursor to **34** was prepared by oxidizing the known alcohol **35**[13] to acid **36** and converting the acid to **37**.[11] Complete thermolysis of **37** in C_6D_6 afforded CO_2 (100% yield) and ethylene (29%), showing that **34** undergoes β-scission in solution.



Theoretical Calculations. Ab initio calculations were undertaken to better understand the energetics of the cyclization and fragmentation reactions described above. While the activation energies were less useful than we had hoped, the reaction energies were reasonable and the computational results led to additional experiments on several occasions. To shorten computational times, we replaced methyl groups by hydrogen wherever possible; these species will be designated by boldface letters. As in our previous work,[9] the geometry was optimized at the UHF/6-31G* level and then UQCISD/6-31+G* energies were determined. The total electronic energies and relative energies are summarized in Table 2 and are displayed as an energy diagram in Figure 1. The energies of the species needed for evaluating β-scission of the 4-pentenyl radical (**38**) and **34** are included in Tables 3 and 4.

Discussion

In view of the resonance stabilization of fragments **3** and **7**[12] and of our earlier results on thermolysis of a vicinal bis-

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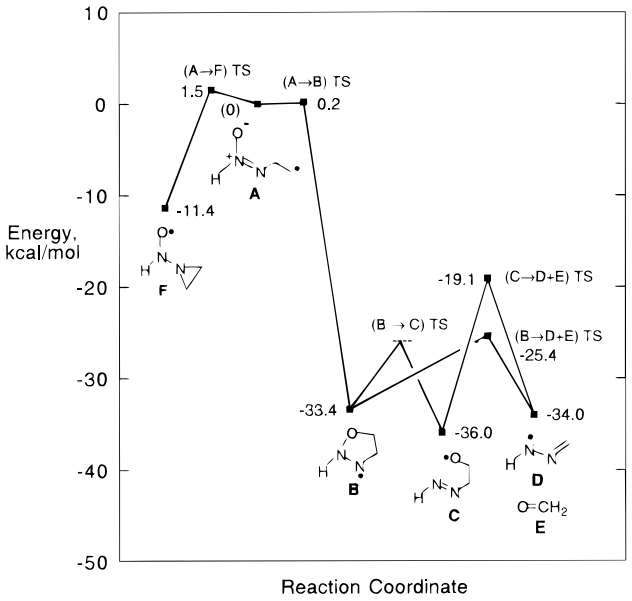

Figure 1. Energy Diagram for Reactions of A.

Table 3. Calculated Energies of Hydrocarbon Radical Fragmentation

species	energy, Hartrees
4-pentenyl•(**38**)	−195.188838
allyl•	−116.865875
4-pentenyl TS	−195.145894
3,3-diMe-4-pentenyl•(**34**)	−273.561897
1,1-diMe allyl•	−195.231116
3,3-diMe-4-pentenyl TS	−273.527566

Table 4. Calculated Reaction Energetics (kcal/mol)

			ΔH[a]	ΔH‡[a]	ΔH, UHF
38	+ C_2H_4 **J**		3.3	27.0	5.7
G	+ C_2H_4 **I**		1.5	25.9	
34	+ C_2H_4		8.2[b]	21.5	0.04

[a] UQCISD. [b] Too high; see text.

phenylazoalkane,[4] we initially expected **9** to undergo central C−C bond cleavage (Scheme 3, path a). While this path explains the production of **4**, it cannot lead to products **10**−**12**, which instead arise by the expected reactions of the **1**−*tert*-butyl radical pair. Pathway (a) must actually be very minor, as judged from the fact that **9** underwent thermolysis at the same corrected rate as that of **8** (**9**, $\Delta G^{\ddagger}$ (190 °C) = 34.85 kcal/mol; **8**, $\Delta G^{\ddagger}$ (190 °C) = 33.9 kcal/mol). The presence of two azo groups in **8** doubles its thermolysis rate; if it contained only one, its $\Delta G^{\ddagger}$ would equal that of **9** and azo-*tert*-butane ($\Delta G^{\ddagger}$ (190 °C) = 34.6 kcal/mol).[14] The essentially equal $\Delta G^{\ddagger}$'s suggest that all three compounds undergo the same reaction, namely, C−N bond cleavage, and that **1** must therefore be the precursor of **4**. The proposed cyclization−fragmentation mechanism shown in Scheme 3 correctly predicts that acetone should be the other product. The first step (**1** → **2**) is a 5-endo cyclization, which is rare in olefinic radicals[13,15] but more common when the double bond contains heteroatoms.[9,15−18] Our mechanism involves a 1,2,3-oxadiazolidine ring, the first example of which was recently generated by intramolecular photocycloaddition of an azoxy moiety to a double bond.[19] The decomposition mode of this unstable heterocycle closely resembles that depicted in Scheme 3 for **2**.

The accessibility of the Cope elimination of azoxy-*tert*-butane indicates that this reaction destroys the more crowded and presumably more labile **10**−**12**, accounting for their low yield (9% total) in thermolysis. Moreover, our observation that the N_2 yield from **9** was far greater than 100% can be rationalized as a secondary reaction of these products. Unless Cope elimination is surprisingly accelerated in **9**, this process should hardly contribute to its thermolysis because $\Delta G^{\ddagger}$ (190 °C) for azoxy-*tert*-butane (38.9 kcal/mol) considerably exceeds that of **9** (34.8 kcal/mol).

Since thermolysis of **9** required high enough temperatures to destroy several of the products, we studied its 366 nm photolysis under milder conditions (cf. Table 1). Inclusion of 0.29 M 1,4-cyclohexadiene increased the yield of **4** from 0% to 9% without significantly altering the distribution of the other products. We propose that **2** always cleaves to acetone but that a hydrogen atom donor is needed to convert **3** to **4**; otherwise, **3** goes to unknown products. One might suppose that a better hydrogen donor would afford more **4**, but 0.20 M thiophenol again gave none of this hydrazone. Instead, there was a considerable increase in the yield of **10** and a corresponding decrease in acetone (cf. Table 1), suggesting that PhSH trapped **1** before it could cyclize. The cyclization is apparently slow enough that irradiation of **9** with more dilute PhSH should allow the determination of the cyclization rate constant k_c.

The product compositions from irradiating **9** with low concentrations of thiophenol are displayed in entries 4−9 of Table 1. As seen in Scheme 3, radicals **1** that are trapped by thiophenol appear as **10** in excess of that formed by disproportionation, while each cyclization−cleavage event (**1** → **3**) produces one molecule of acetone. According to the usual radical clock method,[20−22] a plot of the yield of (**10** − **11**)/acetone versus the average thiophenol concentration should be linear with a slope of k_t/k_c. The actual plot exhibited a slope of 81 and a correlation coefficient of 0.99. Since k_t at 25 °C is known to be 1.4×10^8 M^{-1} s^{-1},[22] we calculate that k_c is 1.7×10^6 s^{-1} at 25 °C. This value is faster than 5-exo cyclization of the 5-hexenyl radical,[21] but it is much slower than cyclization to the azo group.[9] Our implicit assumption that hydrazyl radical **2** always goes to acetone appears safe since neither NMR nor GC/MS of any photolysis of **9** produced evidence for **40**, the 1,2,3-oxadiazolidine corresponding to **2**. Moreover, our theoretical calculations predict that fragmentation of hydrazyl radical **B** is activated by only 8 kcal/mol (cf. Figure 1).

Thermolysis of azoxyperester **13** yielded β-azoxy radical **14** whose 3-exo cyclization to nitrogen, unlike that from **1**, is not degenerate. Since much of **14** must undergo essentially irreversible cyclization to **17**, attack at oxygen is less likely than in **1**, accounting for the lower yield of **4** from **13** than from **9**. The

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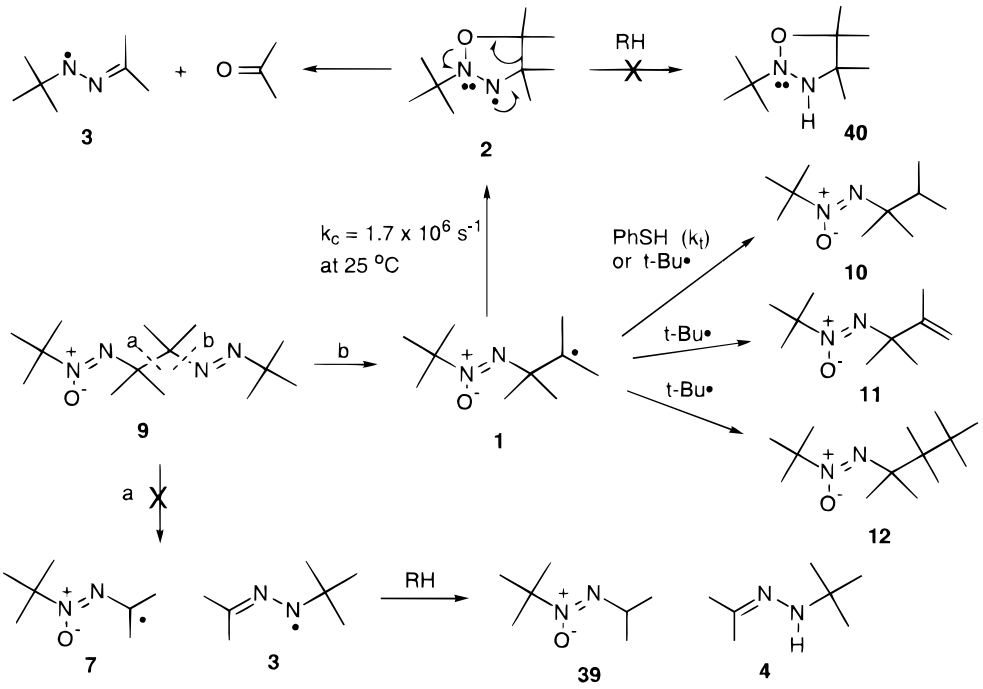
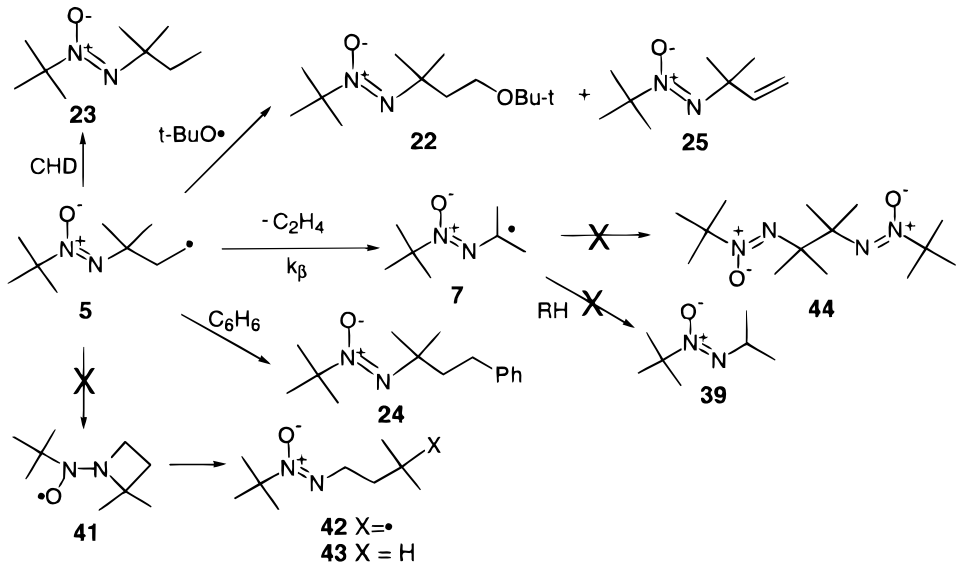
Scheme 3. C−C Versus C−N Cleavage of Azoazoxyalkane 9



Scheme 4. Possible Reaction Pathways of γ-azoxy radical **5**[a]



[a] CHD is 1,4-cyclohexadiene.

cyclization rate of **14** to hydrazyl **16** can be roughly estimated as 3×10^6 s^{-1} at 120 °C from the relative yields of **4** and **19** (0.21:1) and the previously determined rearrangement rate of 1.5×10^7 s^{-1} for **14** → **18** at 120 °C.[23] In view of the many uncertainties in this estimate, we are much more confident in the figure $k_c = 1.7 \times 10^6$ s^{-1} for the cyclization of **1** at 25 °C.

Our computational results depicted in Figure 1 show that cyclization of β-azoxy radical **A** to hydrazyl radical **B** is highly favorable both kinetically and thermodynamically. However the calculated activation energies are too low, and they erroneously predict that 5-endo cyclization will dominate over 3-exo. The computational results do not distinguish between concerted fragmentation of **B** to **D** + **E** and stepwise fragmentation via **C**.

γ-Azoxy radical **5** led to expected products **22**−**25** but not to **43**, the product of a rare 4-exo cyclization followed by ring opening (cf. Scheme 4).[24,25] In contrast to the cases of **1** and **14** where azoxy oxygen is attacked even in the presence of 1,4-cyclohexadiene, we are dealing here with a radical whose unimolecular pathway is at least 10 times slower and which therefore measurably attacks not only 1,4-cyclohexadiene but also benzene. The most surprising product from **5** is ethylene, whose formation rate can be roughly estimated by using the attack of **5** on benzene as a radical clock. The pseudo-first-order rate of this "clock" reaction[26,27] at 120 °C is about 3×10^4 s^{-1}, and the absolute GC yield of **24** is 10%. Thus the ratio

(23) See ref 3.
(24) Park, S.-U.; Varick, T. R.; Newcomb, M. *Tetrahedron Lett.* **1990**, *31*, 2975−2978.
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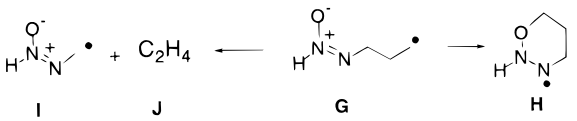
of ethylene to **24** is 6, and the ethylene-forming reaction proceeds with a rate constant of about 2×10^5 s^{-1} at 120 °C. This figure is an upper limit because some minor products remain unidentified; hence, other pathways might consume the cyclohexadienyl radical from attack of **5** on benzene.

β-Scission of **5** must yield **7**, but as in the case of similar radicals,[28−30] its fate is unknown. Azoxyalkanes **39** and **44** are two plausible products of **7**, but GC comparison with authentic samples showed these compounds to be absent with and without 1,4- cyclohexadiene (cf. Scheme 4). Since an allylic nitroxide undergoes α-cleavage,[31] **7** might fragment to $Me_2C{=}N^{\bullet}$ + t-BuNO, a process that we calculate at the Becke3LYP/6-31G* level to be endothermic by 30.7 kcal/mol. The alternate fragmentation of **7** to t-Bu$^{\bullet}$ and the unstable $Me_2C{=}N{-}NO$[32] is calculated to be less favorable, ΔH = 41.7 kcal/mol.

The large amount of ethylene from **20** could arise directly by β-scission of **5** or by prior cyclization to **6**.[33] Extensive efforts to evaluate the possible intermediacy of **6** by ab initio calculations yielded no low-energy transition structure (TS) for the cyclization of **G** to **H**. Since the lowest-lying TS found was 44.3 kcal/mol above **G** (cf. Table 2), we conclude that **G** fragments directly to **I** + **J** (ethylene). However, even that



process is considerably activated ($\Delta H^{\ddagger}$ = 25.9 kcal/mol), in accord with our experimental results that showed the attack of **5** on benzene.

To determine experimentally whether cyclization of **5** to **6** was necessary for ethylene formation, we synthesized an azoxyperester **30** that cannot cyclize without engendering about 22 kcal/mol of ring strain. The fact that **30** yielded ethylene supports the β-scission mechanism. This type of reaction is seen most often at high temperatures[34,35] and in the gas phase;[34,36−38] however, highly stabilized radicals bearing CN or COOEt groups can arise by β-scission at 80 °C[39,40] and β-aminoalkyl radicals can lose ethylene in solution even at 27 °C.[41]

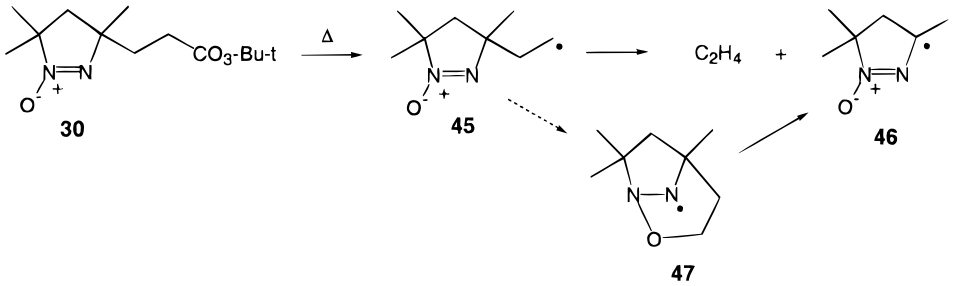
The behavior of **45** and, by association, of **5** led us to ask whether the olefin analogue might also undergo β-scission. We therefore calculated the energy of the 4-pentenyl and γ-azoxy radical (**G**) that would allow such a comparison (cf. Tables 3, 4). The reaction and activation enthalpies in Table 4 show that both ΔH and $\Delta H^{\ddagger}$ for loss of ethylene are increased only slightly (1.8 and 1.1 kcal/mol, respectively) on replacing the azoxy group in **G** by an olefin. Since **5** contains a *gem* dimethyl group that is likely to have a large effect on k_{β}, we studied **34** computationally and found that its $\Delta H^{\ddagger}$ was lower than that of **38** by 5.5 kcal/mol. The calculated ΔH for β-scission of **34** was unreasonably high (8.2 kcal/mol) at the UQCISD level, but at the UHF/6-31G* level, it was 5.7 kcal/mol below ΔH of **38** at that level. $\Delta H^{\ddagger}$ for **34** (21.5 kcal/mol) is low enough that β-scission could well compete with its attack on benzene.

When **34** was generated from perester **37**, we found that it indeed fragmented to C_2H_4. Solution phase β-scission of **38** and **34** was not mentioned when these radicals were studied years ago to explore the scope of free radical cyclization.[13] The fact that **37** afforded ethylene suggests that the Bu_3SnH employed earlier[13] trapped **34** before it could undergo β-scission. Since the perester method of generating **34** does not involve a radical chain, slow β-scission is not overwhelmed by chain transfer. Our observation that the ratio of ethylene to CO_2 is 2−3 times greater in the azoxy cases than in **34** suggests that their activation energy for fragmentation is lower than that of the olefinic radical.

In summary, our study of C−C versus C−N homolysis of **9** (Scheme 3, paths a and b, respectively) produced evidence only for path b, leading to the expected products of radical disproportionation and recombination **10**, **11**, and **12**. The additional products acetone and **4**, coupled with the thermolysis activation parameters of **9**, support a new mechanism involving 5-endo attack of the β-carbon-centered radical **1** on azoxy oxygen, which proceeds with $k_c = 1.7 \times 10^6$ s^{-1} at 25 °C. The hydrazyl intermediate **2** then fragments to acetone and a hydrazonyl radical **3**. Re-examination of azoxyperester **13** uncovered a second case of the new mechanism in competition with the previously reported cyclization to azoxy nitrogen. Thermolysis of the homologous γ-azoxyperester **20** led to no 4-exo and probably no 6-endo cyclization of **5** but instead afforded ethylene in 61% yield. On the basis of the results with constrained γ-azoxy radical **45**, we suggest that ethylene arises by direct β-scission of **5**, a reaction that also takes place in hydrocarbon analogue **34**. The computed activation enthalpies for these β-scissions are low enough that they can compete with alkyl radical attack on benzene solvent. Despite the results described herein, much remains to be learned about the radical chemistry of the azoxy group.

Experimental Section

2-*tert*-Butylazo-3-*tert*-butylazoxy-ONN-2,3-dimethylbutane 9. 2,3-Bis(*tert*-butylazo)-2,3-dimethylbutane **8** was synthesized as described previously.[4] MCPBA (104 mg, 0.6 mmol) was added to a solution of **8** (108 mg, 0.4 mmol) in CH_2Cl_2 (10 mL) at 0 °C, and the mixture was stirred for 3 h at 0 °C. Water (10 mL) was added and the organic layer was separated. The aqueous solution was extracted with CH_2Cl_2 (2 × 30 mL). The combined organic layer was washed with aq $NaHCO_3$, water, and brine. After being dried over $MgSO_4$, the solvent was rotary evaporated and the products were isolated by column chromatography (5% ether in hexane). Azoazoxy compound **9** was obtained as pale yellow crystals (51 mg, 47%), accompanied by the over-oxidation product, 2,3-bis-(*tert*-butylazoxy ONN)-2,3-dimethyl-butane **44** (26 mg, 23%). **9** mp 76.0−76.5 °C. ^{1}H NMR (C_6D_6): δ 1.19 (s, 9H), 1.25 (s, 6H), 1.32 (s, 9H), 1.67 (s, 6H). ^{13}C NMR (C_6D_6): δ 16.81, 20.96, 26.92, 28.22, 65.52, 66.91, 74.13, 77.08. UV (95% MeOH) 372 nm (ϵ 20). Anal. calcd for $C_{14}H_{30}N_4O$ C, 62.18; H, 11.18; N, 20.72. Found C,



62.28; H, 11.17; N, 20.04. HRMS calcd for $C_{14}H_{31}N_4O$ (M + H) 271.2498, found 271.2497.

Isolation of 2-*tert*-Butylazoxy-ONN-2,3-dimethylbutane 10, 3-*tert*-Butylazoxy-ONN-2,3-dimethylbut-1-ene 11, and 2-*tert*-Butylazoxy-ONN-2,3,3,4,4-pentamethyl-pentane 12. A 0.42 M solution of **9** in benzene was irradiated at 366 nm for 1.5 h. Azoxyalkene **11** was isolated by preparative TLC (K6F silica gel 60 A, 20 × 20 cm, 250 μm). Azoxyalkanes **10** and **12** were collected together and separated by preparative GC (column OV-101, 1/4 in. × 10 in., inj. 180 °C, det. 180 °C, oven 125 °C). **10** ^{1}H NMR ($CDCl_3$): δ 0.89 (d, 6H, J = 6.7 Hz), 1.23 (s, 6H), 1.49 (s, 9H), 2.10 (m, 1H). ^{13}C NMR ($CDCl_3$): δ 17.41, 19.48, 28.31, 36.45, 62.84, 77.20. MS *m*/*e* 187 (M + H, 25), 131 (38), 85 (100), 57 (33). HRMS calcd for $C_{10}H_{23}N_2O$ (M + H) 187.1810, found 187.1815. **11** ^{1}H NMR ($CDCl_3$): δ 1.38 (s, 6H), 1.51 (s, 9H), 1.62 (t, 3H, J = 0.8 Hz), 4.76 (m, 2H). ^{13}C NMR ($CDCl_3$): δ 19.22, 24.31, 28.20, 63.40, 77.20, 108.05, 149.66. MS *m*/*e* 185 (M + H, 5), 129 (20), 101 (40), 83 (100), 57 (60). HRMS calcd for $C_{10}H_{21}N_2O$ (M + H) 185.1654, found 185.1658. **12** ^{1}H NMR ($CDCl_3$): δ 0.95 (s, 6H), 1.00 (s, 9H), 1.41 (s, 6H), 1.48(s, 9H). ^{13}C NMR ($CDCl_3$): δ 19.40, 21.08, 23.80, 28.15, 29.14, 29.68, 62.90, 77.21. MS *m*/*e* 243 (M + H, 5), 185 (10), 171 (20), 85 (20), 57 (100).

***tert*-Butyl 4-*tert*-butylazoxy-ONN-4-methylperpentanoate 20.** Following a published procedure,[7] 4-methyl-4-nitro-pentanoic acid[42] (820 mg, 5 mmol) and ammonium formate (1.6 g, 24 mmol) were added to a suspension of Pd/C (10%, 100 mg) in 15 mL of MeOH. The suspension was stirred at room temperature for 6 h. After filtration through Celite, MeOH was removed by rotary evaporation. The ammonium salt of 4-amino-4-methylpentanoic acid (600 mg, 90%) was obtained as a white solid, mp > 250 °C. ^{1}H NMR (D_2O): δ 1.31 (s, 6H), 1.89 (dd, 2H, J = 7.8, J = 10.1 Hz), 2.28 (dd, 2H, J = 7.8, J = 10.1 Hz). Conversion to the azoxyacid was effected by adding commercial bleach (5% NaOCl, 8 mL) over 15 min to a solution of this ammonium salt (380 mg, 2.6 mmol) and nitroso *tert*-butane (260 mg, 3 mmol) in MeOH (50 mL). Then KOH (160 mg) was added, causing the solution to warm spontaneously to 40 °C. After the blue solution was stirred at room temperature for 4 h, the solvent was rotary evaporated and the residue was acidified and extracted with CH_2Cl_2 (3 × 60 mL). The combined organic layers were dried over $MgSO_4$. After filtration and solvent evaporation, 4-*tert*-butylazoxy ONN-4-methylperpentanoic acid **21** was obtained by flash chromatography (28% ether in hexane) (372 mg, 66%). ^{1}H NMR ($CDCl_3$): δ 1.30 (s, 6H), 1.49 (s, 9H), 2.01 (m, 2H), 2.39 (m, 2H). ^{13}C NMR ($CDCl_3$): δ 22.07, 28.25, 29.36, 36.52, 59.44, 77.25, 180.10. The acid was converted to the perester by the procedure of Staab.[11] A solution of the azoxyacid (216 mg, 1 mmol) in 2 mL of THF was added to carbonyl diimidazole (170 mg, 1.1 mmol) in THF (15 mL) under argon at room temperature. The reaction mixture was stirred for 30 min, and then, *tert*-butyl hydroperoxide (100 mg, 1.1 mmol) was added dropwise at 0 °C. After stirring for 10 h, ether (20 mL) was added and the solution was washed with aq NaOH (5%), water, and brine. The organic solution was dried over $MgSO_4$, filtered, and rotary evaporated. The product **20** (220 mg, 78%) was isolated by flash chromatography (9% ether in hexane). ^{1}H NMR ($CDCl_3$): δ 1.29 (s, 6H), 1.32 (s, 9H), 1.49 (s, 9H), 2.01 (m, 2H), 2.38 (m, 2H). ^{13}C NMR ($CDCl_3$): δ 22.00, 26.06, 26.54, 28.22, 36.62, 59.35, 77.25, 83.19, 176.7. Anal. calcd for $C_{14}H_{28}N_2O_4$: C, 58.31; H, 9.79; N, 9.71. Found: C, 58.34; H, 9.49; N, 9.46.

3-Formyl-3,5,5-trimethyl-1-pyrazoline 26. To an ether solution of 2-diazopropane[43] from 1.5 g acetone hydrazone at −78 °C was added methacrolein (1.47 g, 21 mmol) until the red color disappeared. The reaction mixture was stirred at −78 °C for 30 min and then warmed to room temperature. Ether (15 mL) was added, and the mixture was washed with water and brine. The ether solution was dried over Na_2SO_4. After filtration and solvent evaporation, the product **26** was purified by flash column chromatography. The yield was 1.1 g (55%). ^{1}H NMR ($CDCl_3$): δ 1.21 (d, 1H, J = 13.1 Hz), 1.35 (s, 3H), 1.48 (s, 3H), 1.62 (s, 3H), 2.01 (d, 1H, J = 13.1 Hz), 9.81 (s, 1H). Because this compound was unstable to storage, it was carried on directly to the next step.

3-(2-Ethoxycarbonyl)ethyl-3,5,5-trimethyl-1-pyrazoline 27. Triethyl phosphonoacetate (1.7 g, 8 mmol) was added to a suspension of NaH (390 mg, 50%, 8.1 mmol) in THF (50 mL) at room temperature. After 1 h, gas evolution had subsided and aldehyde **26** (1.0 g, 7.1 mmol) was added dropwise. The mixture was stirred for 3 h and then ether (20 mL) was added. The organic layer was separated and was washed with water and brine. After being dried over Na_2SO_4, filtration, and solvent evaporation, the product was isolated by column chromatography (17% ether in hexane). ^{1}H NMR ($CDCl_3$): δ 1.29 (t, 3H, J = 6.95 Hz), 1.34 (s, 3H), 1.40 (d, 1H, J = 12.9 Hz), 1.46 (s, 3H), 1.54 (s, 3H), 1.64 (d, 1H, J = 12.9 Hz), 4.20 (q, 2H, J = 7.02 Hz), 5.92 (d, 1H, J = 15.8 Hz), 7.07 (d, 1H, J = 15.8 Hz). ^{13}C NMR ($CDCl_3$): δ 14.14, 26.19, 26.93, 27.46, 42.95, 60.57, 90.89, 92.96, 119.75, 149.65, 166.21. A 45 mg portion of Pd/C (10%) was added to a solution of the ester (450 mg, 2.1 mmol) in ethanol (20 mL), and the mixture was hydrogenated at 1 atm. After one equivalent of hydrogen had been consumed, the catalyst was removed by filtration. Evaporation of the ethanol gave **27** as an oil (400 mg, 92%). ^{1}H NMR ($CDCl_3$): δ 1.27 (t, 3H, J = 7.07 Hz), 1.36 (s, 3H), 1.37 (s, 3H), 1.42 (s, 3H), 2.06 (m, 4H), 2.37 (m, 2H), 4.20 (q, 2H, J = 7.14 Hz). ^{13}C NMR ($CDCl_3$) δ 14.12, 25.59, 27.54, 27.74, 29.76, 35.00, 42.16, 60.53, 89.84, 92.30, 173.10. UV (ether) 330 nm (ϵ 129).

1-*N*-Oxy and 2-*N*-Oxy 3-(2-Ethoxycarbonyl)ethyl-3,5,5-trimethyl-1-pyrazoline 28 and 31. MCPBA (688 mg, 50−60%, 2 mmol) was added slowly to a solution of **27** (390 mg, 1.87 mmol) in dry CH_2Cl_2 (20 mL) at 0 °C. The mixture was stirred at 0 °C for 30 min and then warmed to room temperature for 4 h. Additional CH_2Cl_2 was added, and the solution was washed with water (2 × 30 mL) and brine. After being dried over Na_2SO_4, filtration, and solvent evaporation, a 2:1 mixture of two regioisomers was obtained (356 mg, 83%). The separation of the two isomers was carried out by preparative HPLC on silica gel (33% EtOAc in hexane). Major isomer **28** ^{1}H NMR ($CDCl_3$, 500 MHz): δ 1.19 (t, 3H, J = 7.2 Hz), 1.31 (s, 3H), 1.50 (s, 3H), 1.51 (s, 3H), 1.90 (ddd, 1H, J = 14.0, 10.1, 6.1 Hz), 1.96 (ddd, 1H, J = 14.0, 10.0, 6.1 Hz), 2.05 (d, 1H, J = 13.2 Hz), 2.08 (d, 1H, J = 13.2 Hz), 2.34 (ddd, 1H, J = 16.1, 10.2, 6.0 Hz), 2.40 (ddd, 1H, J = 16.1 10.2, 6.0 Hz), 4.06 (q, 2H, J = 7.2 Hz). ^{13}C NMR ($CDCl_3$): δ 14.16, 26.68, 28.24, 28.47, 29.48, 36.80, 45.77, 60.62, 68.17, 83.68, 172.99. IR (neat): 2979, 1738, 1510. CI-MS (%) 229 (M + H, 55), 137 (100),

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107 (40). HRMS calcd for $C_{11}H_{20}N_2O_3$, 228.1474; found, 228.1468. Minor isomer **31** ^{1}H NMR ($CDCl_3$, 500 MHz): δ 1.19 (t, 3H, J = 7.2 Hz), 1.33 (s, 3H), 1.34 (s, 3H), 1.51 (s, 3H), 2.01 (d, 1H, J = 13.3 Hz), 2.04 (d, 1H, J = 13.3 Hz), 2.07 (ddd, 1H, J = 14.4, 10.3, 6.0 Hz), 2.15 (ddd, 1H, J = 14.3, 10.5, 5.3 Hz), 2.23 (ddd, 1H, J = 15.9, 10.5, 5.3 Hz), 2.32 (ddd, 1H, J = 16.1 10.3, 5.9 Hz), 4.06 (q, 2H, J = 7.2 Hz). ^{13}C NMR ($CDCl_3$): δ 14.04, 26.85, 29.11, 29.20, 34.22, 44.25, 60.66, 66.31, 86.27, 172.15. IR (neat): 2976, 1737, 1510.

1-*N*-Oxy and 2-*N*-Oxy 3-(2-Carboxy)ethyl-3,5,5-trimethyl-1-pyrazoline 29, 32. The azoxy acids were obtained by base hydrolysis of the above esters. The yield of the 1-*N*-oxy isomer was 60 mg (81%). ^{1}H NMR ($CDCl_3$): δ 1.33 (s, 3H), 1.52 (s, 6H), 1.95 (m, 2H), 2.09 (bs, 2H), 2.43 (m, 2H). ^{13}C NMR ($CDCl_3$): δ 26.56, 28.19, 28.39, 36.48, 45.76, 68.23, 83.82, 178.4. The yield of the 2-*N*-oxy isomer was 35 mg (89%). ^{1}H NMR ($CDCl_3$): δ 1.35 (s, 6H), 1.55 (s, 3H), 2.07 (bs, 2H), 2.14 (m, 2H), 2.38 (m, 2H). ^{13}C NMR ($CDCl_3$) δ 26.82, 28.97, 29.14, 29.21, 34.01, 44.39, 66.64, 86.29, 177.5.

1-*N*-Oxy and 2-*N*-Oxy 3-(2-*tert*-Butylperoxycarbonyl)ethyl-3,5,5-trimethyl-1-pyrazoline 30 and 33. The peresters were made by the procedure of Staab using CDI and t-BuOOH.[11] 1-*N*-Oxy **30** ^{1}H NMR (C_6D_6): δ 0.86 (s, 3H), 1.06 (s, 3H), 1.08 (s, 3H), 1.16 (s, 9H), 1.23 (d, 1H, J = 13.2 Hz), 1.33 (d, 1H, J = 13.2 Hz), 1.70 (m, 2H), 2.15 (m, 2H). ^{13}C NMR ($CDCl_3$): δ 26.07, 26.40, 26.51, 28.29, 28.40, 36.76, 45.95, 67.96, 83.56, 83.73, 170.1. 2-*N*-Oxy **33** ^{1}H NMR (C_6D_6): δ 0.93 (s, 3H), 0.97 (s, 3H), 1.04 (s, 3H), 1.12 (s, 9H), 1.20 (d, 1H, J = 13.3 Hz), 1.34 (d, 1H, J = 13.3 Hz), 1.82 (m, 2H), 2.09 (m, 2H). ^{13}C NMR ($CDCl_3$) δ 26.07, 26.24, 26.82, 29.25, 34.23, 44.57, 66.52, 83.70, 86.15, 169.9.

4,4-Dimethylhex-5-en-1-ol 35. This compound was prepared by the literature procedure.[13] ^{1}H NMR ($CDCl_3$): δ 0.99 (s, 6H), 1.33 (m, 2H), 1.48 (m, 2H), 3.60 (t, 2H, J = 6.4 Hz), 4.89 (d, 1H, J = 16.3 Hz), 4.93 (d, 1H, J = 10.4), 5.75 (dd, 1H, J = 16.3, 10.4 Hz). ^{13}C NMR ($CDCl_3$) δ 26.66, 27.99, 36.24, 38.50, 63.63, 110.52, 148.15.

4,4-Dimethyl-5-hexenoic acid 36. The alcohol **35** was oxidized by PDC in DMF to the acid **36**.[44] ^{1}H NMR ($CDCl_3$): δ 1.00 (s, 6H), 1.64 (m, 2H), 2.28 (m, 2H), 4.94 (dd, 1H, J = 17.4, 1.2 Hz), 4.97 (dd, 1H, J = 10.8, 1.2 Hz), 5.72 (dd. 1H, J = 17.4, 10.8 Hz). ^{13}C NMR ($CDCl_3$): δ 26.41, 29.87, 36.16, 36.66, 111.59, 146.88, 180.79. HRMS calcd for $C_8H_{15}O_2$ (M + H), 143.1072; found, 143.1071.

4,4-Dimethyl-*tert*-butylperoxy-5-hexenoate 37. The perester was made by the procedure of Staab using CDI and t-BuOOH.[11] ^{1}H NMR ($CDCl_3$): δ 1.00 (s, 6H), 1.31 (s, 9H), 1.66 (m, 2H), 2.21 (m, 2H), 4.95 (d, 1H, J = 17.4 Hz), 4.97 (d, 1H, J = 10.7, 1.2 Hz), 5.70 (dd, 1H, J = 17.4, 10.7 Hz). ^{13}C NMR ($CDCl_3$): δ 26.12, 26.38, 27.03, 36.30, 36.88, 83.25, 111.71, 146.73, 171.49.

Theoretical Calculations. Ab initio calculations were carried out either with SPARTAN,[45] G94,[46] or G98.[47] Stable structures were minimized for energy and geometry first at the UHF/6-31G* level. Similarly, transition structures were first optimized at this level with the requirement that each must have one imaginary frequency corresponding to the reaction coordinate. The latter was determined visually via SPARTAN or Gaussview.[46] The final energy for each structure was then derived from a UQCISD/6-31+G* calculation.

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Supporting Information Available: General experimental methods, synthesis, and spectral data of authentic compounds **10**, **15**, **22**, **23**, **39**, and **43**, thermolysis and photolysis procedures, and a table of Gaussian quantum chemical results. This material is available free of charge via the Internet at http://pubs.acs.org.

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