Thermolysis of Acylazo *O*-Trimethylsilyl Cyanohydrins: Azoalkanes Yielding Captodatively Substituted Radicals

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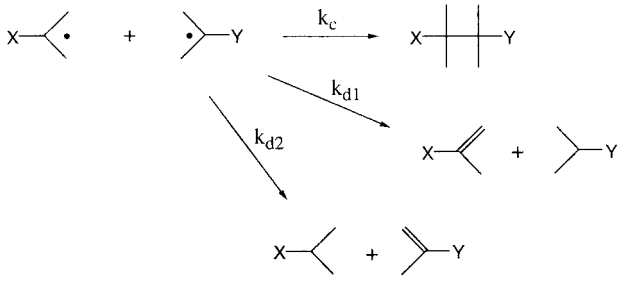
A new synthetic method has been developed for preparing azoalkanes bearing geminal α-cyano and α-trimethylsiloxy groups. While the symmetrical compound **5** decomposes near room temperature to afford, almost entirely, the C−C dimers, the unsymmetrical azoalkane **3** requires heating to 75 °C. The thermolysis activation parameters of **3** and **5** can be rationalized on steric grounds without invoking captodative radical stabilization. A ^{13}C NMR product study of photolyzed **3** in the presence of TEMPO at 21 °C shows that the fate of caged [*tert*-butyl, 1-trimethylsiloxy-1-cyanoethyl (**14**)] radical pairs is disproportionation, 17%, cage recombination, 20%, and cage escape, 63%.

The cross reactions of one reactive radical with another can be studied only if both species are generated simultaneously. Of the possible precursors to a pair of unlike radicals, azoalkanes are particularly convenient for determining such parameters as the direction of disproportionation (k_{d1}/k_{d2}) and the disproportionation-to-recombination ratio ($k_{d1} + k_{d2})/k_c$.[1,2] Potential obstacles to this approach include synthesis of the requisite azoalkane, accounting for self-reaction products of like radicals, and secondary reactions of the initial radicals with radicophilic olefin products.[3,4] In some cases, azoalkanes have been used to estimate thermodynamic radical stabilities[5] since a plot of the activation energy for symmetrical azoalkane thermolysis versus the bond dissociation energy of the corresponding hydrocarbon is a line of unit slope with correlation coefficient 0.99.[6,7]



Herein we report thermolysis kinetics and product studies of two azoalkanes, prepared by a new method, that decompose to captodative[8−14] trimethylsilyl (TMS) cyanohydrin radicals. Because of limitations in the synthetic approaches to azoalkanes,[15−17] only a single report[18] has appeared previously on their use to generate captodative radicals. Our product studies were carried out with thiophenol as hydrogen donor and with the persistent radical TEMPO to scavenge the initially formed radicals and thus prevent secondary reactions.[19]

Results

Azoalkanes **3** and **5** were synthesized from acyl diazenes **2**[20] and **4**[21] by treatment with trimethylsilyl cyanide (TMSCN).[22,23] Symmetrical compound **5** was obtained as a 50−50 mixture of meso and *dl* isomers, which were not separated. While the unsymmetrical compound **3** was stable at room temperature, **5** slowly decomposed. Nevertheless, both azoalkanes could be purified by cold-column chromatography on carefully dried silica gel. Attempts to monitor the decomposition of **3** by UV spectroscopy in toluene were foiled by the buildup of a broad, unidentified, interfering absorption at 288 nm that persisted even after heating for 15 h at 90 °C. Inclusion of 1,4-cyclohexadiene or *tert*-butanethiol as a radical

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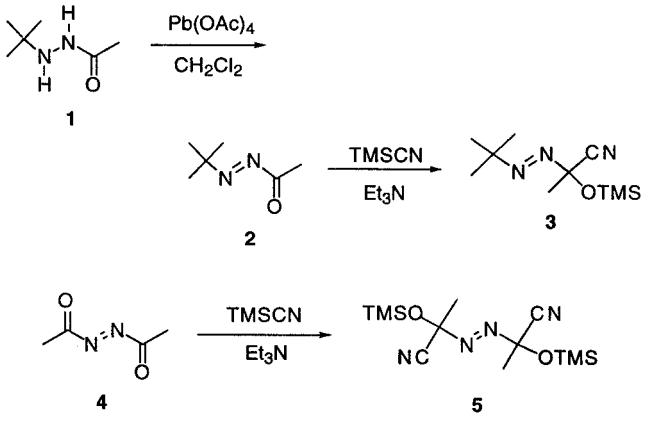
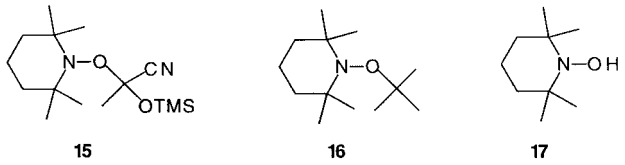


scavenger did not eliminate the problem, and thiophenol produced diphenyl disulfide, which interfered even more with UV monitoring. Although **5** showed no 288-nm band (see below), the kinetics of both azoalkanes were determined by nitrogen evolution.[24]

In the absence of a radical trap, thermolysis of **3** yielded a complex array of products, but inclusion of 0.5 M thiophenol as a scavenger led to a more tractable mixture. The identified products and their GC-peak areas relative to that of PhSSPh are as follows (compound, GC-peak area): **6**, 0.090; **7**, 0.50; **8**, 0.19; **9**, 0.013; **10a**, 0.023; **10b**, 0.019; **11**, 0.009; **12**, 0.22; **13**, 0.028; and PhSSPh, 1.00. Authentic samples of **6**, **7**, **8**, **10a**,**b**, and **12** were prepared independently, but the structures of minor products **9**, **11**, and **13** are based only on GC/MS. Their mode of formation is rationalized in Scheme 1 and in the Discussion (see below).

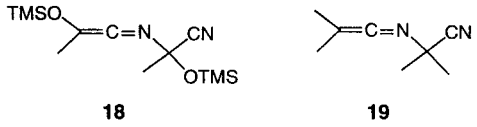
Since the 2-cyanopropyl radicals from AIBN[25] and other cyano substituted radicals[26−28] produced a sizable amount of ketenimine, a sample of **3** was thermolyzed in toluene, the solvent was evaporated, and the residue was dissolved in CCl_4. The IR spectrum of this solution showed only a small band at 2011 cm^{-1},[25,26,29] indicating either that the ketenimine hardly formed or that it decomposed.

A product study of **3**, in the presence of TEMPO, allowed us to calculate the disproportionation-to-recombination ratio for the mixed radical pair, the direction of disproportionation, and the cage effect. This clever approach was employed previously for a pair of radicals differing only in their ester side chain.[3] Because alkoxyamines are often unstable upon heating,[30,31] we decomposed our new azoalkanes near ambient temperature and employed quantitative ^{13}C NMR as the analytical method. A C_6D_6 solution of **3** and TEMPO in a sealed, degassed NMR tube was irradiated at 366 nm until the color of TEMPO had faded but not disappeared, at which point some of **3** also remained. The ^{13}C NMR spectrum of the mixture, which was acquired using gated decoupling to eliminate NOE, was not noticeably broadened by the presence of the paramagnetic compound. In fact, the residual TEMPO was beneficial because it shortened T_1 so that we were able to use a delay time of only 20 s between pulses. Although the spectrum exhibited 46 peaks (cf. Table 3), an authentic sample of nearly every product was available, allowing us to assign all but seven peaks, or all but 3% of the total area. The chemical shift of the unassigned peaks is far from that expected for a ketenimine.[29] The relative yield of each product was calculated from the intensities of all of its ^{13}C signals combined, leading to the following results: isobutane, 8%; **6**, 6%; isobutene, 3%; **7**, 2%; **8**, 11%; **15**, 34%; **16**, 35%; and **17**, 1%. Lending credence to these figures, we found nearly equal amounts of each product expected from one given pathway; e.g., cage escape afforded the same quantity of **15** as **16**.



Not surprisingly, the thermolysis products from **5** proved to be simpler than those from **3**. When a solution of **5** in C_6D_6 or $CDCl_3$ was allowed to stand for 1 day, the NMR spectrum showed, exclusively, the known[32] diastereomers **10a**,**b** and no olefin peaks. Thermolysis of **5** in the presence of excess TEMPO yielded **15**, but little of dimer **10a**,**b**, indicating that the cage effect is small. This value was determined independently by the excess scavenger technique[33] with TEMPO to be only 15%. When thiophenol was included as scavenger, one of the products was **12**, as proven by comparison with an authentic sample.[34] The major ^1H NMR peaks showed **10a**,**b**, **12**, and **7** in the molar ratio 1.0:0.5:1.6, while the GC peak area ratio was 1.0:0.3:1.0.

The IR spectrum of **5** in CCl_4 at room temperature exhibited a weak but sharp band at 2011 cm^{-1} that remained unchanged for at least 24 h. Although this band might be attributed to a small amount of ketenimine **18**, such a product would not be expected to persist.[25,35] In a



more determined effort to detect **18**, a degassed, sealed solution of **5** in hexane was heated at 40 °C with monitoring by UV. The azo band at 368 nm disappeared smoothly with no evidence of rising absorption at 290 nm, the expected λ_{max} of a ketenimine. As a control experiment, a degassed, sealed solution of AIBN at 20 °C was irradiated at 366 nm and monitored by UV. The azo band at 344 nm disappeared while a new 290-nm absorption maximum due to **19** grew in. In accord with the well-

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Scheme 1. Reactions of *tert*-Butyl and MeC·(CN)(OTMS) Radicals from Thermolysis of 3 with PhSH at 90 °C in C_6D_6

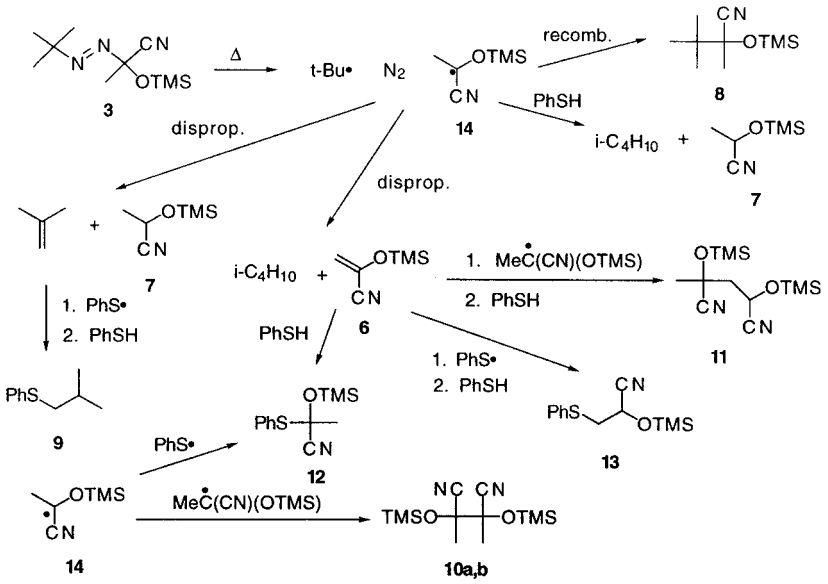

Table 1. Activation Parameters of 3 and Related Unsymmetrical Azoalkanes[a]

entry	t-Bu−N=N−R, R =	$\Delta H^{\ddagger}$	$\Delta S^{\ddagger}$	$\Delta G^{\ddagger}$ (100 °C)
1	MeC(CN)(OTMS)[b]	31.3 ± 0.3	11.8 ± 0.9	26.9
2	$Me_2C(CN)$	34.0	14.7	28.6
3	$Me_2CCH{=}CH_2$	26.8	−0.1	26.8
4	$Me_3CCH_2CMe_2$	38.1	12.3	33.5
5	$Me_3CCH_2C(CN)(Me)$	29.4	9.2	26.0

[a] Data from ref 6. [b] This work.

Table 2. Activation Parameters of 5 and Related Symmetrical Azoalkanes[a]

entry	R−N=N−R, R =	$\Delta H^{\ddagger}$	$\Delta S^{\ddagger}$	$\Delta G^{\ddagger}$ (100 °C)
1	MeC(CN)(OTMS)[b]	24.3 ± 1.2	3.9 ± 3.9	22.8
2	Me_3C	42.1	16.3	36.0
3	$Me_2C(CN)$	30.1	9.2	26.7
4	$Me_2C(OMe)$	40.9	17.7	34.3
5	$Me_2CCH{=}CH_2$	25.9	4.2	24.3
6	$Me_3CCH_2CMe_2$	32.0	2.9	30.9
	$Me_3CCH_2CMe_2$	34.6	9.5	31.1
7	$Me_3CCH_2C(CN)(Me)$			25.1[c]

[a] Data from ref 6. [b] This work. [c] $\Delta G^{\ddagger}$ (80 °C) calculated from a single rate constant in ref 6.

known behavior of AIBN,[25,36] the 290-nm band became five times more intense than the original azo band. A comparable solution of **5** was then irradiated at 0 °C, causing only a small loss of azo absorption but no buildup at 290 nm. Continued irradiation at 20 °C led to eventual destruction of **5** but still no ketenimine band. If ketenimine **18** is actually forming, it must be very labile thermally or else its UV λ_{max} is drastically blue shifted from that of **19**. Neither of these possibilities is likely.

Discussion

The thermolysis kinetics of **3** and **5** were cleanly first order. The activation parameters for **3** are compared with those of four related compounds in Table 1. Tentatively using $\Delta G^{\ddagger}$ to evaluate the stability of incipient radicals, we see that the combination of the OTMS and CN groups is more stabilizing by 1.7 kcal/mol than a CN alone (entry 2). In fact, these two groups together are nearly as effective as a methyl and vinyl moiety (entry 3). The 1.7 kcal/mol decrease in $\Delta G^{\ddagger}$ is probably of steric origin, considering that *tert*-butylazo-*tert*-octane (entry 4) is 2.5 kcal/mol more labile than azo-*tert*-butane (ATB, $\Delta G^{\ddagger}$ (100 °C) = 36.0 kcal/mol.) Similarly, replacement of methyl by neopentyl in *tert*-butylazo-2-cyanopropane lowers $\Delta G^{\ddagger}$ by 2.6 kcal/mol (cf. entries 2 and 5.)

Table 2 compares selected symmetrical azoalkanes with **5**. The lowering of $\Delta G^{\ddagger}$ by CN and OTMS, relative to ATB, is 13.2 kcal/mol, which exceeds the 11 kcal/mol combined effect of MeO (1.7 kcal/mol, entry 4) and CN (9.3 kcal/mol, entry 3). In the symmetrical series, **5** is 1.5 kcal/mol more labile than the dimethylallyl analogue (entry 5). This difference is in the opposite direction from the 0.1 kcal/mol difference in entries 1 and 3 of Table 1, but the low $\Delta S^{\ddagger}$ of entry 3 makes such a comparison risky. Once again using a hydrocarbon model for steric effects, we find that azo-*tert*-octane (entry 6) is 5.0 kcal/mol more labile than ATB (entry 2), while the cyano series (entries 3 and 7) shows a $\Delta G^{\ddagger}$ that is 1.6 kcal/mol lower. Relief of steric compression during deazatation suffices to explain the greater decrease in $\Delta G^{\ddagger}$ caused by CN and OTMS acting together than the sum of the changes in $\Delta G^{\ddagger}$ effected by them, taking MeO as an electronic model for TMSO.[37] Despite the fact that a plot of azoalkane E_a versus hydrocarbon BDE is linear,[6,7] experimental errors diminish the utility of E_a as a measure of incipient radical stability. Relative thermolysis rates or $\Delta G^{\ddagger}$ tends to be more reliable, but, as seen even in the few cases in Tables 1 and 2, $\Delta S^{\ddagger}$ varies widely. Another complication is that geminal substituents on carbon can interact to change the ground-state energy,[38,39] which is manifested as a polar effect on azoalkane thermolysis rates.[40] While the data in Tables 1 and

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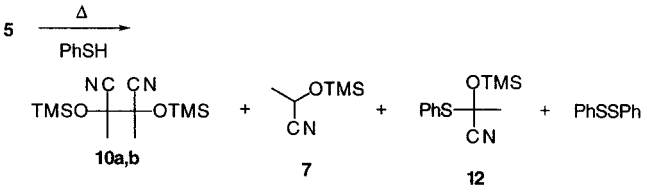
2 and in ref 18 are not without interest, they cannot be taken as evidence for or against the captodative effect.

The thermolysis products of **5** consisted solely of dimers **10a**,**b**, whose formation is in accord with the tendency of delocalized radicals to recombine rather than disproportionate.[41] Similar behavior was seen in *tert*-butoxy(cyano)methyl radicals[9] and in the radical formed by addition of 2-cyanopropyl to silyl enol ether **6**.[34] Thermolysis of **5** with thiophenol led to sulfide **12**, which arises by cross recombination of phenylthiyl radicals and **14**. A similar cross recombination product, the alkoxyamine, was formed upon thermolysis of azo-α-phenylethane with diethylhydroxylamine.[30] An alternate source of **12** is the known reaction[34] of **6** with thiophenol, but the absence of **6** without the scavenger precludes this



pathway. The relatively large amount of **10a**,**b** in the presence of PhSH is only partly due to cage recombination; the rest is attributed to inefficient scavenging of **14** by PhSH, judging from the fact that **3** also affords **10a**,**b** with PhSH (see below).

The low cage effect (15%) seen with **5** can be attributed to steric hindrance to radical recombination[9,42] but then recombination should preferentially occur at cyano nitrogen. Not only did we find no evidence for ketenimine **18**, but azo-*tert*-octane at 20 °C exhibited a normal cage effect of 30%, despite the similar geometry of the *tert*-octyl radical to **14**. No appealing rationale for this dilemma comes to mind. In contrast to **5**, the cage effect of the mixed radical pair *t*-Bu•/**14** is also normal (37%).

The thermolysis products of **3** can be explained on the basis of Scheme 1. In addition to the expected thiophenol-scavenging product, **7**, we find a sizable amount of recombination product **8**. The *tert*-butyl/**14** radical pair undergoes disproportionation in both directions, but the resulting olefins isobutene and **6** suffer some attack by other radicals to afford **9**, **11**, and **13**. The addition of **14** to **6** to yield **11** is analogous to the reported addition of 2-cyanopropyl to **6**,[34] while the presence of **10a**,**b** shows that 0.5 M thiophenol is not a completely effective scavenger of **14**. Unlike **5**, the radicals from **3** disproportionate, in part, to give **6**, which therefore cannot be ruled out as the source of **12** for the unsymmetrical case.

Photolysis of **3** in the presence of TEMPO eliminates the secondary reactions and allows us to assess the relative importance of the three reaction pathways of the caged *tert*-butyl/**14** radical pair. Cage recombination to afford **8** accounts for 20% of the radicals, as calculated from %**8**/[%**8** + 0.5(%isobutane + %**6**) + 0.5(%isobutene + %**7**) + 0.5(%**15** + %**16**)], while cage disproportionation accounts for 17%. Disproportionation to **6** and isobutane is more important than that to **7** and isobutene, presumably because **14** is more hindered than *tert*-butyl and is therefore more sensitive to steric effects.[3] The remaining 63% of the radicals escape the solvent cage, which is an entirely reasonable figure by comparison to related systems.[43] A small amount of hydroxylamine **17** was found among the products, suggesting the possibility that TEMPO disproportionates with either *tert*-butyl radical or with **14**. A sample of **5** was allowed to decompose thermally in the presence of TEMPO, and the product mixture was analyzed by ^{13}C NMR. Since no **17** was detectable, this minor product from **3** must come either from *tert*-butyl radicals plus TEMPO or from another source altogether. Comparison of the present results with the cumyl−cyclohexyl case, where recombination is also the dominant self-reaction of the delocalized radical, shows distinct similarities. Our total cage disproportionation-to-recombination ratio (0.9) is lower than that of cumyl−cyclohexyl (1.3) while the ratio of disproportionation to the conjugated olefin **6** relative to the nonconjugated one (isobutene) is 3 in **3** versus 5 in the literature example.[1]

In summary, we have developed a method to convert acyldiazenes to hitherto inaccessible azoalkanes **3** and **5**. The thermolysis rates of these azoalkanes do not support captodative stabilization of TMS cyanohydrin radical **14**. The low cage effect for **5** (15%) is at odds with our failure to detect ketenimine **18**. Judging from the observation that thiophenol does not completely prevent **3** from dimerizing to **10a**,**b**, we suggest that this hydrogen donor is only partially effective in trapping **14**. Finally, photolysis of **3** in the presence of excess TEMPO followed by ^{13}C NMR analysis allowed us to quantify the competing processes in a pair of unlike radicals.

Experimental Section

General Methods. Most of these have been described earlier.[30] The NMR solvents $CDCl_3$ and C_6D_6 from Cambridge Isotope Laboratory were used without further purification. The 250 MHz NMR chemical shifts (δ, ppm) are stated relative to internal TMS, hexamethyldisiloxane (^1H $\delta = 0.115$), or solvent signal ($CDCl_3$ ^1H $\delta = 7.26$, ^{13}C $\delta = 77.0$; C_6D_6 ^1H $\delta = 7.15$, ^{13}C $\delta = 128.0$). Analytical GC was carried out with a DB-5 capillary column (0.25 mm × 30 m) and FID. The GC conditions were as follows: head pressure, 16 psi; He split flow, 53 mL/min; injector, 210 °C; detector, 250 °C; initial oven temperature, 35 °C; initial time, 2.5 min; program rate, 10 °C/min; final oven temperature, 250 °C; final time, 10 min.

***N*-Acetyl *N′*-*tert*-Butyl Hydrazide (1).** A 1-L three-neck round-bottom flask equipped with a mechanical stirrer, inert gas inlet adapter, and rubber septum was charged with 6.24 g of *tert*-butylhydrazine hydrochloride (50 mmol, 1.0 equiv), 500 mL of dry CH_2Cl_2, and 15.6 mL of distilled Et_3N (11.3 g, 112 mmol, 2.24 equiv). After the suspension was cooled to approximately −90 °C, a solution of 3.6 mL (3.97 g, 51 mmol, 1.0 equiv) of acetyl chloride in 25 mL of CH_2Cl_2 was added with vigorous stirring. The suspension was stirred for 20 min and then allowed to warm to room temperature. A 90-mL portion of 1.0 M aqueous KOH (90 mmol, 1.8 equiv) was added to liberate Et_3N from its salt, the CH_2Cl_2 layer was separated, and NaCl was added to the aqueous layer, which was then extracted five times with Et_2O. The combined organic layers were washed with brine and passed through a pad of Na_2SO_4 and then silica gel. After removal of solvent and Et_3N in vacuo, the product remained as a water-soluble yellow oil that crystallized with difficulty (4.07 g, 63% yield). Although this material was sufficiently pure, as ascertained by NMR, for use in the next step, the hydrazide can be purified by column chromatography ($R_f = 0.13$ in 100% EtOAc). Mp 61−64.5 °C.

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NMR shows that the hydrazide exists as two geometrical isomers because of restricted rotation about the amide linkage.[44] ^{1}H NMR ($CDCl_3$): 1.09 (9H, s), 2.00, 2.11 (3H, s) 3.4 (b s), 4.7 (b s), 6.8 (b s), 6.9 (b s). ^{13}C NMR ($CDCl_3$) (smaller *Z*-isomer peaks are in parentheses): 21.09 (19.54), 27.14 (26.94), 54.98 (54.21), 169.33 (177.18).

***N*-Acetyl *N*′-*tert*-Butyl Diazene (2).** Under nitrogen, a 2.10 g (16.1 mmol, 1.0 equiv) portion of hydrazide **1** was dissolved in 80 mL of dry, distilled CH_2Cl_2 with stirring. The mixture was cooled to approximately −78 °C, and a solution of 7.85 g (17.7 mmol, 1.1 equiv) of $Pb(OAc)_4$ in 30 mL of CH_2Cl_2 was added over 5 min with stirring. The orange mixture was allowed to warm to room temperature and stirred for 1 h. The CH_2Cl_2 was decanted off, and the residue in the flask was washed with more CH_2Cl_2. The combined organic layer was then washed twice with chilled, saturated NaCl, once with 75 mL of chilled, saturated $NaHCO_3$, and again with 75 mL of chilled, saturated aqueous NaCl. The solution was dried over $MgSO_4$, the solid residue was filtered off, and the solvent was removed in vacuo. Flash distillation into a liquid nitrogen cold trap removed any nonvolatile impurities, and the moderately pure yellow oil (1.84 g, 89% yield) was carried on directly to be used in the next step. ^{1}H NMR ($CDCl_3$): 1.28 (9H, s), 2.25 (3H, s). ^{13}C NMR ($CDCl_3$): 20.9, 26.1, 69.7, 189.7. TLC: R_f = 0.29 (10% EtOAc/hexane).

***N*-*t*-Butyl *N*′-(1-[(Trimethylsilyl)oxy]-1-cyano)ethyl Diazene (3).** A 1.84-g (14.4 mmol, 1.0 equiv) portion of crude **2** was dissolved with stirring in 70 mL of dry, distilled CH_2Cl_2 under N_2. The solution was cooled to approximately −78 °C, and 1.71 g of trimethylsilyl cyanide (TMSCN) (17.2 mmol, 1.2 equiv) in 40 mL of CH_2Cl_2 was added over one min. The Et_3N catalyst (150 mg, 1.4 mmol, 0.1 equiv) was added, and the mixture was stirred and allowed to warm overnight. After the reaction was complete as ascertained by TLC (R_f = 0.39 50% CH_2Cl_2/hexane), all volatiles were removed in vacuo. The crude **3** was quite pure but was subjected to column chromatography on dry silica gel, eluting with dry 50% CH_2Cl_2/hexane. The diazene was a faintly yellow oil. ^{1}H NMR ($CDCl_3$): 0.24 (9H, s), 1.27 (9H, s), 1.60 (3H, s), (C_6D_6) 0.221 (9H, s), 1.06 (9H, s), 1.39 (3H, s). ^{13}C NMR (C_6D_6): 1.6, 26.2, 27.6, 68.5, 93.5, 118.7. UV: λ_{max} = 366 nm, ϵ = 22.4.

Diacetyl Diazene (4).[21] To a solution of 1,2-diacetyl hydrazine (5.0 g, 1.0 equiv) in CH_2Cl_2 (215 mL) chilled in an ice−water bath was added $Pb(OAc)_4$ (21.0 g, 1.1 equiv) in CH_2Cl_2 (80.0 mL). The mixture was immediately allowed to warm to 25 °C, was stirred for 2 h, was recooled to 0 °C, and was filtered into a chilled separatory funnel. The solid was rinsed with CH_2Cl_2, and the solution was quickly washed with chilled 50% brine (150 mL), chilled 50% brine/saturated $NaHCO_3$ (200 mL), and chilled brine once more (150 mL). After drying over $MgSO_4$, filtration, and removal of solvent in vacuo, the crude product was reasonably pure. Yield: 1.77 g, 36%. ^{1}H and ^{13}C NMR spectra showed the only impurity to be acetic anhydride. Diacetyl diazene is extremely electrophilic and is rapidly decomposed by water with gas evolution. Attempted nonaqueous workups gave higher yields but more impurities. Because purification by distillation proved futile and chromatographic media consumed the desired product, **4** was carried on to the next step without purification. ^{1}H NMR ($CDCl_3$): 2.36 (s), 2.22 (acetic anhydride). ^{13}C NMR ($CDCl_3$): 187.0, 20.4.

***N*,*N*′-bis(1-[Trimethylsilyl)oxy]-1-cyano)ethyl Diazene (5).** To a solution of crude diacetyl diazene (~0.68 g, 1.0 equiv) contaminated with acetic anhydride (~0.075 g) in CH_2Cl_2 (30 mL) cooled to −78 °C was slowly added TMSCN (1.3 mL, 2.0 equiv) in CH_2Cl_2 (10 mL) followed by the dropwise addition of Et_3N (0.2 mL, 0.25 equiv). After 0.5 h, the bath was removed, and the reaction was allowed to warm to 0 °C. All volatiles were removed in vacuo at 0 °C. Cold (ice−water) chromatography on very dry silica gel with CH_2Cl_2/hexanes (20−50%) provided 1.17 g (63%) of **5** as a roughly 50/50 mixture of diastereomers that can be stored at <−80 °C. ^{1}H NMR ($CDCl_3$): 0.27 and 0.29 (9H, s), 1.77 and 1.72 (3H, s). ^{13}C NMR ($CDCl_3$): 1.16, 1.20, 27.3, 27.7, 92.7, 92.8, 117.0. UV: λ_{max} 368 nm.

Isobutane. ^{13}C NMR (C_6D_6): δ 23.6, 24.8.

Isobutene. ^{13}C NMR (C_6D_6): δ 24.0, 111.0, 141.8.

2-[(Trimethylsilyl)oxy]propenenitrile (6) was prepared from pyruvonitrile and N,O-bis(trimethylsilyl)acetamide.[45] ^{1}H NMR (C_6D_6): 0.00 (9H, s), 4.47 (1H, d, J = 2.3 Hz), 4.52 (1H, d, J = 2.3 Hz). ^{1}H NMR ($CDCl_3$): 0.30 (9H, s), 5.03 (d, 1H, J = 2.3 Hz), 5.10 (1H, d, J = 2.3 Hz). The reported J of 0.23 Hz is erroneous, but we used the published ^{13}C shifts to identify **6** in the product mixture from **3**. ^{13}C NMR (C_6D_6): −0.5, 108.9, 116.1, 131.2. lit.[45] ^{13}C NMR ($CDCl_3$): −0.50, 109.06, 115.91, 130.81.

2-[(Trimethylsilyl)oxy]propanenitrile (7)[46] was prepared from distilled acetaldehyde, trimethylsilyl cyanide, and catalytic Et_3N in dry CH_2Cl_2 at 0 °C.[23] ^{1}H NMR (C_6D_6): 0.00 (9H, s), 1.02 (3H, d, J = 6.6 Hz), 3.84, (2H, q, J = 6.6 Hz). ^{13}C NMR (C_6D_6): −0.6, 22.8, 57.4, 120.4.

3,3-Dimethyl-2-[(trimethylsilyl)oxy]-2-cyanobutane (8).[47] A 0.25-mL portion of pinacolone (200 mg, 1.0 equiv) and 20 mL of CH_2Cl_2 freshly distilled from CaH_2 were placed into a 50 mL flask. Under Ar, the solution was cooled in an ice bath, and 0.3 mL (220 mg, 1.1 equiv) of TMSCN in 10 mL of CH_2Cl_2 was added via cannula. A catalytic amount of ZnI_2 was added, and the solution was allowed to warm and stir overnight under Ar. The ^{1}H NMR spectrum of the crude reaction mixture showed complete conversion to **8**, whose chemical shifts were correlated with those of the product mixture from decomposition of **3**. ^{1}H NMR (C_6D_6): 0.19 (9H, s), 0.90 (9H, s), 1.19 (3H, s).^{13}C NMR (C_6D_6): 1.1, 23.7, 24.5, 38.8, 76.3, 121.8.

2,3-Dicyano-2,3-bis[(trimethylsilyl)oxy]butane 10a[32] (lower R_f). ^{1}H NMR ($CDCl_3$): 0.3 (18 H, s), 1.59 (3 H, s). ^{13}C NMR ($CDCl_3$): 0.9, 22.6, 75.1, 119.4. **10b** (higher R_f). ^{1}H NMR ($CDCl_3$): 0.29 (18 H, s), 1.78 (3H, s). ^{13}C NMR ($CDCl_3$): 1.02, 24.2, 75.5, 118.8. **10a**,**b**. ^{1}H NMR (C_6D_6): 0.13 (18 H, s), 0.26 (18 H, s), 1.21 (6 H, s), 1.56 (6H, s). ^{13}C NMR (C_6D_6): 0.90, 22.72, 24.16, 75.38, 75.72, 118.99, 119.66.

2-Phenylthio-2-[(trimethylsilyl)oxy]propanenitrile (12) was synthesized from pyruvonitrile and phenyltrimethylsilyl sulfide.[34] ^{1}H NMR ($CDCl_3$): 0.14 (9H, s), 1.91 (3H, s), 7.37−7.68 (5H, m).

1-(1,1-Dimethylethoxy)-2,2,6,6-tetramethylpiperidine (16)[48] was prepared by 366-nm irradiation of a freeze−thaw degassed C_6D_6 solution of azo-*tert*-butane in the presence of 1 molar equiv of TEMPO. The tube was opened, and the mixture was chromatographed on silica gel to yield 3 mg of pure material. ^{1}H NMR ($CDCl_3$): 1.29 (6H, s), 1.31 (6H, s), 1.42 (9H, s), 1.5 (6H, m). ^{13}C NMR (C_6D_6): 17.5, 20.6, 29.6, 35.1, 41.1, 59.3, 77.5.

1-(1-(Trimethylsilyl)oxy-1-cyanoethoxy)-2,2,6,6-tetramethylpiperidine (15) was prepared by allowing an excess of **5** to decompose overnight in the presence of TEMPO. ^{1}H NMR (C_6D_6): 0.25 (9H, s), 1.05 (3H, s), 1.09 (3H, s), 1.22 (3H, s), 1.36 (3H, s), 1.65 (3H, s), 1.0−1.5 (6H, m). ^{13}C NMR (C_6D_6): 1.0, 16.9, 20.5, 20.7, 28.34, 33.4, 33.9, 40.1, 40.2, 59.9, 60.28, 98.16, 118.8. Calcd for $C_{15}H_{30}N_2O_2Si + H^+$: 299.21548. Found: 299.21603.

Thermolysis of 3 with PhSH. A dry NMR tube equipped with a 7/25 joint was charged with 59 mg of **3** (0.26 mmol) and 51 mg of thiophenol (0.46 mmol, 0.9 equiv) in 1 mL of C_6D_6. The tube was freeze−thaw degassed, sealed, and then heated at 90 °C for 15 h. After the tube was opened its contents were analyzed promptly by GC/MS. Besides the products mentioned in the text, unknowns were found at 16.63, 22.32, and 22.67 min.

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Thermolysis of 5 with Thiophenol. A sealed, degassed solution of **5** (0.11 mmol) and PhSH (0.22 mmol) in 0.5 mL of C_6D_6 was allowed to stand overnight at 40 °C. The contents of the tube were analyzed by GC comparison with authentic compounds and by CI/GC/MS. The products, their retention times, and their relative areas as follows: were **7**, 7.78, (176); PhSH, 10.68, (573); **10a**,**b**, 17.33, 17.72 (174); **12**, 20.16, (57); PhSSPh, 23.91, (100). Two unknowns, at 25.44 and 25.53 min, had peak areas of 52 and 56, respectively. The GC conditions were 0.25 mm × 30 m DB5, 40 °C for 5 min, 10 °C/min to 250 °C with 5 min final time; injector, 180 °C; detector, 250 °C.

NMR TEMPO Tolerance Experiment. Solutions of 8, 4, and 2 mg/mL of TEMPO in $CDCl_3$ were prepared. To 0.5 mL of each solution was added 0.11 mL (100 mg) of ethyl acetate. All three samples exhibited ^{1}H NMR spectra with some line broadening, but the 8 mg/mL spectrum was so distorted that the ethyl-group coupling was difficult to observe. A quantitative ^{13}C NMR experiment (see below) on the most concentrated solution gave sharp peaks with the proper area ratios, indicating that ^{13}C integrals should be reliable at TEMPO concentrations below 8 mg/mL.

Photolysis of 3 with TEMPO. To a dry 5-mm NMR tube equipped with a 7/25 joint was added 127 mg of azoalkane **3** (0.56 mmol) and 90 mg of TEMPO (0.58 mmol) as a solution in 0.6 mL of C_6D_6. The orange-red solution was freeze−thaw degassed three times in liquid nitrogen and then sealed. The sample was irradiated at 366 nm and 21 °C with periodic manual agitation until the orange-red color of the TEMPO had been reduced to an intensity corresponding to 4−8 mg/mL, as judged by visual comparison to standard solutions. The proton and nonquantitative carbon NMR spectra were acquired to determine the spectrometer and decoupler offset. A delay of 20 s was established between pulses to allow for complete relaxation. The number of data points was set at the maximum of 128K for accurate line-shape definition, and the spectral width was set at 160 ppm to encompass the entire spectrum. The experiment was performed with gated decoupling to eliminate NOE. After a total of 1922 scans were acquired, the FID was processed with slight line broadening (0.5 Hz) to reduce noise, and, was then phased. The chemical shifts were referenced to C_6D_6 at 128.0 ppm. By comparison with the ^{13}C spectra of the authentic products, nearly all of the peaks were assigned. The peaks were integrated in windows of about 10−20 ppm, so that accurate baseline corrections could be applied. Correcting the integrals for multiple carbons led to numbers proportional to the concentration of products. Table 3 summarizes the chemical shifts, areas, total area for each compound, and percent yield.

***N*-Hydroxy-2,2,6,6-tetramethylpiperidine (17)** was generated by reduction of TEMPO with phenylhydrazine.[49] Carbons 2, 3, and 4 appear at 18.04, 40.42, and 59.18 ppm, respectively, but the methyl groups could not be seen on account of rapid conformational interconversion.[50] To confirm the presence of **17** from thermolyzed **3**, the NMR tube was opened and 5 mg of TEMPO and a slight excess of phenylhydrazine were added. The orange-red color of TEMPO disappeared, but the tube retained a slight yellow tint due to excess **3**. The NMR tube was capped with a rubber septum, and a conventional ^{13}C spectrum was acquired. No new peak in the window near 18 ppm appeared, indicating that the previously seen peaks corresponded to **17**.

Decomposition of 5 with TEMPO. To an NMR tube equipped with a 7/25 joint and a sealing constriction was added 20 mg of TEMPO (0.13 mmol) and 11 mg of **5** (0.035 mmol) in 0.4 mL of C_6D_6. Because **5** is extremely water and heat sensitive, anhydrous techniques were employed while keeping the sample under 10 °C. The tube was freeze−thaw degassed as described above and sealed. After the solution had stood at 25 °C for 1 day, the color had faded noticeably, but a conventional ^{13}C spectrum revealed that no **17** was present.

Thermolysis kinetics of 3 and 5 were carried out on a constant-volume, variable-pressure gas-evolution apparatus.[24] The rate constants for ∼0.25 M **3** in Ph_2O were (temp (°C), 10^4k (s^{-1}), method) 74.9, 0.582 ± 0.003, I; 80.0, 1.11 ± 0.003, I; 90.0, 3.85 ± 0.016, I; 95.1, 7.38 ± 0.076, G; while those for 0.2 M **5** in $PhCH_3$ were 24.9, 0.664 ± 0.001, I; 29.3, 1.41 ± 0.02, G; 29.2, 1.37 ± 0.004, I; 33.7, 2.46 ± 0.01, I; 39.4, 4.83 ± 0.01, I. "I" indicates that the experimental infinity point was used while "G" signifies the Guggenheim method.

Cage Effects. The cage effect of **5** was determined using a hexane solution of 0.0846 M TEMPO and <0.04 M **5**. The solution was kept cool to prevent azoalkane thermolysis as it was degassed and sealed into a Pyrex tube attached to a cuvette. The absorbance of TEMPO was determined with the cool solution; then this solution was allowed to decompose at approximately 40 °C for several hours. The final absorbance of TEMPO was determined, and the amount of nitrogen evolved was measured on a vacuum line and Töpler pump. The nitrogen yield gave the amount of **5** that decomposed (0.126 mmol), while the change in TEMPO absorbance counted the escaped radicals (0.215 mmol). On the basis of these numbers, the efficiency was 85%, and the cage effect was 15%. The same technique was employed for azo-*t*-octane, but, since this compound is thermally stable,[51] it was not necessary to keep the solution cool.

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Supporting Information Available: Table 3, a tabulation of ^{13}C NMR chemical shifts and areas for all products of the photolysis of **3** in the presence of Tempo (2 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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