Thermolysis, Photolysis, and Acid Catalysis of an α-(Dimethylamino)azoalkane. Amino Stabilization of a Carbon Radical Center

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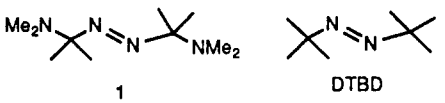
The unsymmetrical azoalkane 2-(*tert*-butylazo)-2-(dimethylamino)propane (**7**) has been synthesized cleanly by nucleophilic displacement of chloride from the corresponding α-chloroazoalkane **5** with dimethylamine. Thermolysis of **7** in hydrocarbon solvents affords typical radical-derived products and exhibits activation parameters $\Delta H^{\ddagger} = 26.6 \pm 0.4$ kcal/mol and $\Delta S^{\ddagger} = -6.6 \pm 1.1$ eu. Since the thermolysis rate of **7** is 10^4 faster than that of 1,2-di-*tert*-butyldiazene, the large stabilization of α-amino radicals is supported. Unusual products were obtained in acetonitrile, suggesting reduction of the azo linkage by 2-(dimethylamino)-2-propyl radicals and cleavage of the resulting hydrazyl radicals. In protic solvents, **7** undergoes acid catalyzed decomposition via *tert*-butyldiazene as a postulated intermediate.

The stabilizing effect of substituents on an adjacent radical center is a topic of continuing interest.[1] In attempts to quantify these effects, radical stability scales have been developed based on ESR coupling constants,[2] rearrangement of methylenecyclopropanes,[3] oxidation of fluorenide anions (Δ(AOP)),[4] equilibrium constants of triarylmethyl radicals,[5] and other techniques.[1] The dimethylamino group is missing from two of the most extensive scales[2,5] though it is found to have an unusually large radical stabilizing effect by two others[3,4] and by theoretical calculations.[6,7] Further evidence exists for the strong effect of α-amino groups; for example, the CH bond dissociation energy of Me_2NCH_2–H is 20 kcal/mol lower than that of methane,[8] and the Me_2N group lowers E_a for vinylcyclopropane rearrangement by 18.5 kcal/mol.[9]

Thermolysis rates of symmetrically α-disubstituted azoalkanes serve as another measure of radical stability, a method pioneered by Timberlake and co-workers.[10-13] By this approach, a rate comparison of compound **1** with 1,2-di-*tert*-butyldiazine (DTBD) should yield an excellent measure of the dimethylamino stabilizing effect. Azoalkane **1** is of further interest as a potentially clean source of strongly reducing[14] α-amino radicals,[15] which play a key role in amine oxidation[16,17] and in amino acid radiolysis.[18,19] Since previous attempts to prepare **1** were not successful,[20] we concentrated on an unsymmetrical analogue that ultimately provided an estimate of the desired stabilizing effect, as well as a few surprising products.



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DTBD

Table I. UV Spectral Data[a] of Selected Azoalkanes

azoalkane	hexane	acetonitrile	methanol
$Me_3CN{=}NCMe_3$	368 (13)	366 (14.8)	366 (15.0)
$NCCMe_2N{=}NCMe_2Cl$[b]	369 (17.7)[c]	363 (17.4)	362 (17.0)[d]
$Me_3CN{=}NCMe_2NMe_2$	381 (40.3)	379 (33.8)	375 (20.6)

[a] λ_{max} (ϵ). [b] Reference 29. [c] In cyclohexane. [d] In ethanol.

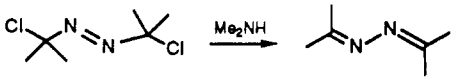
Table II. Thermolysis Rates of 7 in Hexane[a]

temp, K	10^4k, s^{-1}	$10^4\sigma$[b]	
384.75	2.236	0.030	$\Delta H^{\ddagger} = 26.6 \pm 0.4$ kcal/mol
390.58	3.800	0.031	$\Delta S^{\ddagger} = -6.6 \pm 1.1$ eu
394.80	5.780	0.052	
400.23	8.902	0.048	
403.50	11.811	0.081	

[a] By UV in sealed Pyrex curettes. [b] σ = standard deviation of k.

Results

A reasonable approach to the synthesis of **1** would be nucleophilic displacement of chloride from the readily accessible dichloroazoalkane **2**, a reaction that succeeds with such nucleophiles as carboxylate and thiomethoxide.[21-23] Unfortunately, treatment of **2** with dimethylamine affords only acetone azine.[20] Since α-chlo-



2 **3**

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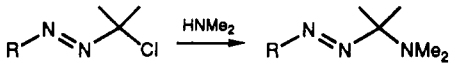
Table III. Thermolysis Rate of 7 in Various Solvents

solvent	temp, °C	10^4k, s^{-1}
hexane	113.94	2.78
methanol	113.94	15.30
hexane	121.53	5.51
methanol, OH^- [a]	121.53	1.25
DMF [b]	121.53	2.82

[a] Roughly 0.1 M NaOH added. [b] Dimethylformamide.

roazoalkane **4** undergoes facile nucleophilic displacement[24] but cannot form azine, we reacted **4** with dimethylamine.



4: R = Ph
5: R = *t*-Bu

6: R = Ph
7: R = *t*-Bu

Indeed, product **6** could be isolated, but purification was so difficult as to discourage further work. Finally, the *tert*-butyl analogue **5** was tried in the same reaction, leading easily to azoalkane **7**. Both α-chloroazoalkanes **4** and **5** were prepared cleanly from *tert*-butyl hypochlorite and the appropriate hydrazone.[25]

Although azoalkane **7** was readily accessible, one must ask whether it is a reasonable substitute for **1** for evaluating the radical stabilizing ability of the Me_2N group. The answer is affirmative because the activation free energy difference between unsymmetrical azoalkanes and their less stable symmetrical counterpart is generally small.[26] Moreover, two unsymmetrical azoalkanes closely analogous to **7** have already been studied.[27,28]

The UV spectrum of **7** (Table I) presaged its unusual chemistry in polar solvents. Not only is the λ_{max} among the longest ever reported for an α,α′-disubstituted azo-2-propane, but the value of ε drops considerably with increasing solvent polarity. The variable ε of **7** indicates a lower oscillator strength in polar solvents since the half width of the broad near-UV absorption remains constant. On the other hand, the decrease of λ_{max} in more polar solvents is typical of the azoalkane n,π* transition.[30,31]

Thermolysis kinetics of **7** were monitored by disappearance of the 381-nm band in hexane, providing the rate constants and activation parameters shown in Table II. The standard deviation (σ) of the rate constants was calculated by assuming that the absorbance was accurate to ±0.002 units. These errors were propagated in a least squares fit of ln (k/T) versus $1/T$ to obtain σ of the activation parameters. Surprisingly, the thermolysis rate of **7** is greatly accelerated in protic solvents but is slowed by the addition of hydroxide (cf. Table III).

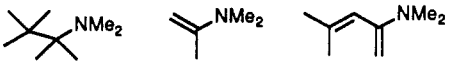
The thermolysis and photolysis products of **7** were identified by GC/MS and NMR comparison with authentic samples. Since the reactions gave mainly identifiable products with no evidence of high molecular weight materials, relative yields (Table IV) were calculated from NMR and GC peak areas.[32] The nitrogen yields, which

Scheme I. Stepwise Homolysis of Azoalkanes

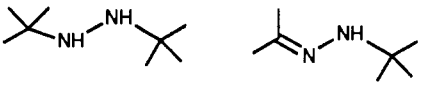
$$R_1\text{-}N{=}N\text{-}R_2 \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} R_1\text{-}N{=}N^{\bullet}\ {}^{\bullet}R_2 \xrightarrow{k_2} R_1^{\bullet} + N_2 + {}^{\bullet}R_2$$

$$k_{obs} = \frac{k_1k_2}{k_{-1} + k_2}$$

varied from 82 to 96%, were obtained using a Töpler pump and gas buret. As seen in Table IV, isobutane is a ubiquitous product, though large amounts of 2-(dimethylamino)propane and dimethylamine are often found. In acetonitrile, the nature of the thermolysis products is very sensitive to water (compare columns headed A_w and A_d) but in benzene, the main effect of water is to hydrolyze enamines **9** and **10**. Photolysis in benzene and acetonitrile affords similar product distributions, and the nitrogen quantum yield in benzene (0.41) is typical for acyclic tertiary azoalkanes.[26]



8 **9** **10**



11 **12**

The unusual kinetics and products in methanol called for a number of control experiments. Thus **7** was found to react slowly with degassed methanol at 25 °C in the dark, but it was stable if hydroxide was added. Isobutane-*d* reached a level detectable by NMR after a solution of **7** in 1:1 D_2O/CD_3CN stood in the dark for 36 h at room temperature. The azoalkane reacted slowly with acetic acid in benzene at 25 °C but rapidly at 100 °C. Dissolution of **7** in sulfuric acid/CD_3OD at 25 °C caused its instantaneous conversion to **12**-*d*, acetone-d_6, Me_2ND, $Me_2C{=}CH_2$, and **11**-d_2. These observations require the existence of an acid-catalyzed decomposition pathway.

Discussion

A few azoalkanes with saturated nitrogen on the α-carbon atom have appeared in the literature,[33-36] but very little is known about their decomposition. In the case of **7** in hexane, both the first-order plots and Eyring plot are linear, suggesting that this compound thermolyzes like other azoalkanes to give ultimately two radicals plus nitrogen. We may then compare the activation parameters for **7** with those for related azoalkanes, as shown in Table V. The difference in $\Delta G^{\ddagger}$ between the unsymmetrical azoalkane $R_1N{=}NR_2$ and its less stable symmetrical analogue $R_2N{=}NR_2$ is 1.9 kcal/mol for **13–14** and 2.5 kcal/mol for **15–16**. The small magnitude of these $\Delta G^{\ddagger}$ differences can be understood on the basis of Scheme I, which shows stepwise homolysis of an unsymmetrical azoalkane whose $R_2^{\bullet}$ is a more stable radical than $R_1^{\bullet}$. It is clear from the rate expression that the nature of R_1 is unimportant because the overall rate constant (k_{obs}) is determined mainly by k_1 when the more stable diazenyl

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(32) The 75-MHz ^{13}C NMR spectrum of **7** in C_6D_6 and the following 300-MHz ^1H spectra of **7** are available as supplementary material: (1) in C_6D_6, (2) in dry CD_3CN, (3) thermolyzed in C_6D_6, (4) photolyzed in C_6D_6, (5) thermolyzed in CD_3CN, (6) photolyzed in CD_3CN. The products responsible for most of the signals are marked on these spectra of decomposed **7**.

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Table IV. Products of Thermolysis and Photolysis of 7 (Relative Moles)

	reaction type[a] in solvent[b]									
	Δ						hν			
	Bz	A_w	A_d	Me	MeB	BzA	Bz	A_w	M_e	MeB
N_2 yield, %	89.5	90.0	c	90.1	92.8	82.7	93.0	94.8	88.0	96.0
isobutane[d]	1	1	1	1[e]	1	1	1	1	1[e]	1[e]
i-PrNMe$_2$	0.3	0.1	0.54	trace	2.2	0	2.5	2.3	0.3	0.3
tert-heptylamine (8)	0	0	0.1	0	0.4	0	0.5	0.5	0	0
enamine (9)	0.2	0	0	0	0	0	0.1	0	0	0
isobutene	trace	trace	0.12	trace	0.34	0	1.6	1.3	0.1	0.14
acetone	0.2	1.4	0.16	f	f	0.26	0.8	0.7	f	f
dimethylamine	1	1.7	1.4	2.8	2.3	1.37	0.9	0.8	2.8	2.6
mesityl oxide	0	0	0	0	0	0.39	0	0	0	0
10	0.3	0	0	0	0	0	0	0	0	0
(t-BuNH)$_2$ (11)	0.03	0.08	0.5	0.09	g	trace	0	0	0.15	0.05
t-BuNHNCMe$_2$ (12)	0.06	0.05	0.39	0.07	0.26	trace	0.13	0.09	0.02	0.1
DTBD	0	0	0.07	0	0	0	0	0	0	0

[a] Δ = thermolysis; hν = photolysis. [b] Solvent: Bz = C_6D_6 as purchased. A_w = wet CD_3CN as purchased. A_d = dried CD_3CN solution of 7, Me = CD_3OD or CH_3OD, MeB = CD_3OD/NaOH or CH_3OD/NaOH in thermolysis but CD_3OD/NaOH only in photolysis, BzA = C_6D_6/HOAc. [c] Not determined. [d] Relative moles of all compounds are referenced to isobutane. [e] Isobutane-*d* was the major isobutane product. [f] Acetone detected by GC–MS but not visible by NMR spectroscopy on account of H–D exchange with solvent. [g] NMR peak overlap obscured the product.

Table V. Activation Parameters for Thermolysis of Selected Azoalkanes $XCMe_2N{=}NCMe_2Y$

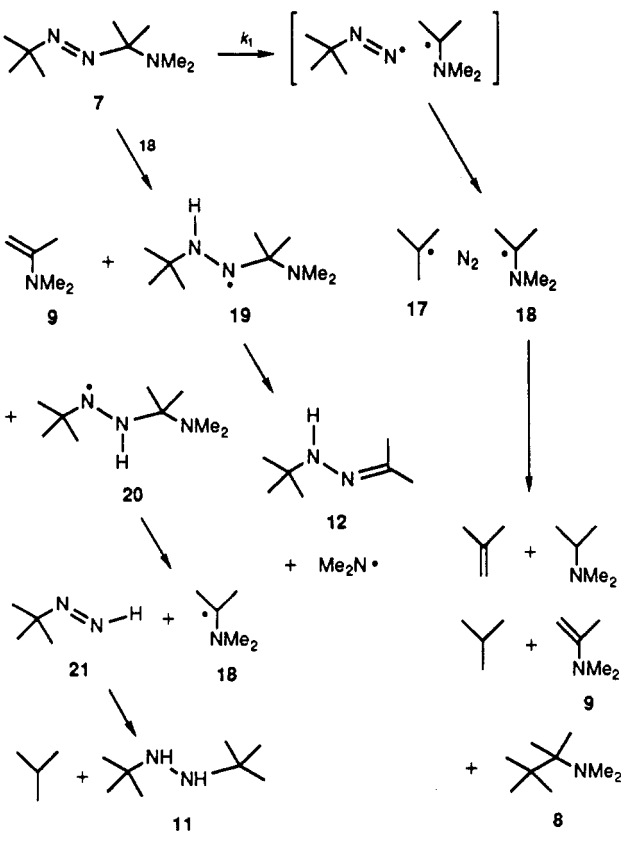
compd	X	Y	$\Delta H^{\ddagger}$, kcal/mol	$\Delta S^{\ddagger}$, eu	$\Delta G^{\ddagger}$,[a] kcal/mol	k_{rel}[a]	ref
DTBD	Me	Me	42.1	16.3	36.0	(1.0)[b]	26
13	Me	CN	34.0	14.7	28.6	2.2×10^4	28
14	CN	CN	30.4	9.8	26.7	2.8×10^5	26
15	Me	CH=CH$_2$	26.8	−0.1	26.8	2.5×10^5	26
16	H$_2$C=CH	CH=CH$_2$	25.6	3.4	24.3	7.1×10^6	26
7	Me	NMe$_2$	26.6	−6.6	29.1	1.1×10^4	this work
1	Me$_2$N	NMe$_2$			(26.9)[c]	(2.1×10^5)[c]	this work

[a] At 100 °C. [b] The absolute rate constant for DTBD is 6.36×10^9 s^{-1}. [c] Estimated; see text.

radical $R_1N{=}N^{\bullet}$ undergoes deazatation (k_2) faster than cage recombination (k_{-1}). As we have already shown[37], this kinetic situation holds for **15** where R_1 = *tert*-butyl and R_2 = 1,1-dimethylallyl. If the $\Delta G^{\ddagger}$ difference between **7** and **1** is also 2.2 kcal/mol, we can calculate $\Delta G^{\ddagger}$ for **1** to be 26.9 kcal/mol, implying that **1** decomposes 2.1×10^5 times faster than DTBD at 100 °C. Since azoalkane thermolysis rates reflect incipient radical stability, this relative rate constant indicates that *N,N*-dimethylamino is nearly as good a radical stabilizing substituent as cyano. We have of course ignored any elevation of ground-state energy[38,39] due to the α-substituent but this effect is not large in geminal bisazoalkanes[40] and is unlikely to dominate in **7**.

Most of the decomposition products of **7** (cf. Table IV) are just as expected from the usual mechanism of azoalkane homolysis. Heterolysis[41] giving *tert*-butyldiazenyl anions plus 2-(dimethylamino)-2-propyl cations is conceivable, but the slower thermolysis rate in DMF than hexane (Table III) argues against this mechanism (the exceptional rate acceleration in methanol is discussed below). Furthermore, addition of cyanide anion to **7** did not trap the expected α-amino cation. Thus inclusion of the useful organic-soluble tetrabutylammonium cyanide[42] in a thermolysis of **7** in acetonitrile gave no 2-(dimethylamino)-2-cyanopropane, a compound demonstrated independently to be stable under the reaction conditions. As

Scheme II. Homolysis Mechanism of 7



shown in Scheme II, *tert*-butyl radicals **17** and 2-(dimethylamino)-2-propyl radicals **18** undergo disproportionation and recombination to afford isobutane, isobutene, 2-(dimethylamino)propane, acetone *N,N*-dimethylenamine

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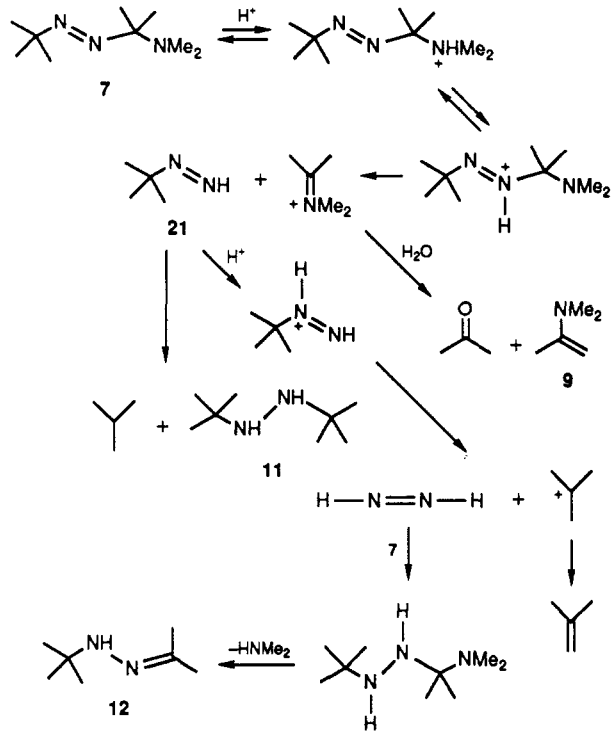
(9), and 2-(dimethylamino)-2,3,3-trimethylbutane (8). The enamine is hydrolyzed by adventitious water to dimethylamine and acetone, which can then undergo self-condensation, giving mesityl oxide, or condensation with 9 to afford conjugated enamine 10 (another precursor of mesityl oxide). Formation of 9 was observed at early thermolysis times in dry MeCN but it later disappeared, perhaps due to polymerization.

The last three products in Table IV cannot be rationalized on the basis of this simple mechanism. Instead, we were attracted to the idea that one of these products, *s*-di-*tert*-butylhydrazine 11, came from *tert*-butyldiazene 21. According to Kosower,[43] two molecules of 21 disproportionate to 11, nitrogen, and isobutane. Our initial hypothesis was that radical 18 transferred an electron followed by a proton to *tert*-butyldiazenyl radicals in the solvent cage, leading to 21. Since α-aminoalkyl radicals are known to have very low oxidation potentials,[44] electron transfer to the electron-deficient diazenyl radical[45] could be fast. Moreover, cage electron transfer between two neutral radicals has been observed in solution.[46,47] We became disenchanted with this hypothesis on realizing that the estimated lifetime of *tert*-butyldiazenyl radicals was 4.6 ps at room temperature and is expected to be shorter at higher temperature.[37] It then seemed highly unlikely that even caged electron transfer would compete with such a fast deazatation. Furthermore, addition of cyanide anion failed to trap the α-amino cation expected from 18 following electron loss (see above).

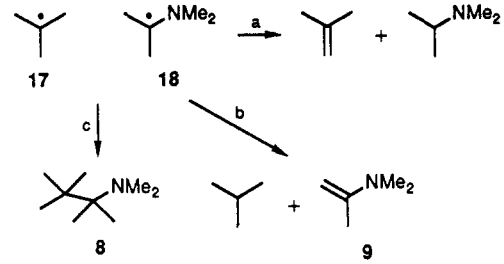
We therefore propose an alternate mechanism wherein 18 transfers a hydrogen atom to 7, similar to our recently reported reduction of azoalkanes by benzhydryl radicals.[48] In fact aminoalkyl radicals are known to donate hydrogen atoms to such acceptors as α-diketones.[14] The proposed hydrogen atom transfer leads to hydrazyl radicals 19 and 20, which then undergo β-scission. Transfer of an electron then a proton from 18 to 7 would also give hydrazyl radicals, but the first process is calculated to be endothermic.[49] As shown in Scheme II, these reactions can explain not only product 11 but also 12 if one allows fragmentation of 19. The third product, DTBD, arises on thermolysis of 7 in dry CH_3CN. We speculate that addition of *tert*-butyl radicals to the azo linkage of 7 and β-scission of the resulting hydrazyl radical gives DTDB and acetone di-*tert*-butylhydrazone, whose presence was suspected on the basis of GC/MS. It is important to note that the last three products in Table IV are minor when benzene is the solvent. We assume that the hydrogen atom transfer mechanism in Scheme II is negligible in hexane, the solvent used for thermolysis kinetics of 7. Though we have no explanation for this solvent dependence, it is unlikely that the kinetics in Table II are complicated by induced decomposition.

Except in methanol solvent, the photolysis products are indicative of a purely radical process. In fact, considerably more of the typical radical products isobutene, 2-(dimethylamino)propane, and 8 were found at the much lower temperature used for photolysis (25 °C) than thermolysis (130 °C), perhaps because the cage effect is greater at lower temperature. The temperature-dependent cage effect contributes to the absence of 11 in photolysis because less 18 is available to donate H• at 25 °C. Moreover, hydrogen transfer from 18 to 7 should be an activated process. The photolability of 21[51] also decreases the yield of 11.

Scheme III. Acid-Catalyzed Decomposition of 7



Since the photolysis of 7 is mainly a simple homolysis, we have an opportunity to observe the cross disproportionation (k_d) and recombination (k_c) of two different radicals.[52,53] According to the photolysis results in Table IV for benzene and acetonitrile, reactions a–c of 17 and 18 proceed with relative rates of about 4:2:1. The k_d/k_c ratio is 6:1, which is much closer to that of *tert*-butyl ($k_d/k_c \sim 5$) than it is to the low k_d/k_c ratios for cumyl (0.06) and 1,1-dimethylallyl (<0.003).[54] Since both 18 and $Me_2CCOOMe$[55] are substantially stabilized but give much disproportionation, k_d/d_c has little to do with radical stabilization. Instead, formation of an oriented complex that lowers k_d/k_c was recently supported for cumyl[56] and



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calculated even for methyl radicals.[57] This concept may extend to allylic radicals but not to 18 and $Me_2CCOOMe$. The greater importance of reaction a than b is in accord with the previously noted generalization[52] that increasing substitution causes a preference for hydrogen atom acceptance rather than donation. However the opposite outcome was obtained in some α-carboalkoxy radicals[55] and disproportionation of cumyl–cyclohexyl pairs gives far more α-methylstyrene plus cyclohexane than cumene plus cyclohexene.[58] Attempts to model alkyl radical disproportionation theoretically have appeared in the recent literature,[59,60] but polar substituents have not been considered. Clearly, more work remains to be done.

The most unusual aspect of azoalkane **7** is its sensitivity to protons,[34] manifested as both a rate acceleration (cf. Table III) and a decrease in such radical-derived products as i-$PrNMe_2$, enamine **9**, isobutene, and **8**. The sensitivity of **7** to water and acid is rationalized as acid-catalyzed hydrolysis as shown in Scheme III. This scheme correctly predicts isobutane-*d* as the major isobutane product in MeOD. Although the amino nitrogen is more basic, protonation of the azo group is analogous to acid decomposition of α-azo carbinols[61] and 3,4-dihydroformazans.[33] Protonation of alkyldiazenes to give diimide is precented[62] and diimide reduction of azoalkanes was known previously.[48] The presence of diimide in the system was proved by GC detection of norbornane when H_2SO_4 was added to a solution of 0.4 M norbornene and 0.1 M **7** in CD_3OD. Thermolysis in methanol without base seems to be acid-catalyzed decomposition since the addition of base drastically slowed the thermolysis rate and increased the amount of i-$PrNMe_2$ and isobutene, both of which are radical derived.

If **7** generates *tert*-butyldiazene in polar solvents at elevated temperature, we expect that **1** would do the same to give diimide at lower temperature in the presence of water. The diimide produced from **1** would then reduce **1** or more likely **2** to give acetone azine. This scheme rationalizes the failure[20] to prepare **1** from **2**.

The similar deazatation quantum yield of DTBD and **7** in benzene suggests that **7** probably photolyzes by prior isomerization to the cis isomer, which then undergoes thermolysis. Since *trans*-**7** is unstable in methanol at ambient temperature, the fact that photolysis under these conditions gives a similar product distribution to thermolysis (isobutane-*d* as major isobutane product when CH_3OD was used, much dimethylamine, presence of **12** but little to no i-$PrNMe_2$, isobutene or **8**) suggests that *cis*-**7** is readily protonated by methanol. Indeed, *cis*-azoalkanes are much more polar than trans.[63] Noting that the product distribution hardly changes on addition of base, we propose that *cis*-**7** is at least hydrogen bonded to methanol and may be in significant equilibrium with the protonated form even in the presence of base. Although excited singlet cyclic azoalkanes are quenched by protic solvents,[64] the reactivity of *cis*-**7** to methanol is remarkable in light of its thermolability, which can be estimated as follows. Assume that the internal steric strain of *cis*-**7** is the same as *cis*-DTBD (though it is surely greater). At 298 K, $\Delta G^{\ddagger}_{t\text{-DTBD}}$ = 37.2 kcal/mol in Ph_2O,[26] $\Delta G^{\ddagger}_{c\text{-DTDB}}$ = 19.2 kcal/mol in methanol,[65] ΔG(strain) = $\Delta G^{\ddagger}_{t\text{-DTBD}} - \Delta G^{\ddagger}_{c\text{-DTDB}}$ = 37.2 − 19.2 = 18.0 kcal/mol. Therefore, $\Delta G^{\ddagger}_{c\text{-}7}$ = 28.6 − 18.0 = 10.6 kcal/mol, which corresponds to a maximum half-life of 6.6 μs at 298 K for *cis*-**7** undergoing homolysis.

Since Schemes II and III both involve *tert*-butyldiazene, an attempt was made to trap this reactive intermediate. Aliphatic aldehydes react with **21** in weakly basic solution,[66] and benzaldehyde supposedly reacts with **21** in neutral organic solvents and in acid.[67] We were unable to detect the expected hydrazide *t*-Bu-NH-NH-CO-Ph by GC/MS on inclusion of PhCHO in a thermolysis of **7** in benzene or in acidic methanol. However, this result does not speak against **21** because diazenes are sensitive to acid[62,68] and because the α-azo carbinol initial adducts are reactive towards radicals.[69] Even the trapping of **21** with aldehydes has been questioned,[69] leaving our negative result with no significance.

In summary, thermolysis of **7** in hexane provides reliable activation parameters for production of *tert*-butyl and 2-(dimethylamino)propyl radicals. The previously reported large radical stabilizing effect of the dimethylamino substituent is strongly supported. The decreasing thermolysis rate of **7** in more polar solvents coupled with the nature of the products argue for a simple homolysis mechanism in hydrocarbon solvents. However, di-*tert*-butylhydrazine (**11**) must arise by a new pathway, which is postulated to be hydrogen atom transfer from **18** to the azo linkage followed by β-scission to *tert*-butyldiazene, **21**. In protic solvents and acidic solution, yet another decomposition mechanism comes into play, as evidenced by both a rate acceleration and a decrease in radical-derived products. Thus protonation of azo nitrogen leads to *tert*-butyldiazene and an iminium cation that is rapidly hydrolyzed to acetone plus dimethylamine.

Experimental Section

General. NMR spectra were recorded on an IBM AF-300 spectrometer. Analytical GC was carried out on a Hewlett-Packard 5890 instrument equipped with a data system while GC–MS was carried out on a Finnigan 3300 spectrometer. UV spectra were obtained on a Cary 17 spectrophotometer.

Materials. All of the solvents were used without further purification unless otherwise specified. NMR solvents were obtained from Cambridge Isotope Laboratories (CIL, C_6D_6, C_7D_8, 99.6% D; CD_3OD, 99.8% D) or Aldrich (CD_3CN, 99% D; CH_3OD, 99.5% D). Hexane and methanol used for kinetic studies were Burdick & Jackson high purity solvent. The same brand of DMF was dried with $MgSO_4$ and vacuum distilled. Authentic samples of **11** were made for NMR and GC comparison by reduction of DTBD with benzpinacol in C_6D_6, CD_3CN, and CD_3OD.[46] 2-(Dimethylamino)propane was synthesized by methylation of isopropylamine with formaldehyde and formic acid.

2-(*tert*-Butylazo)-2-(dimethylamino)propane (7). To a solution of 5.0 g of acetone *tert*-butylhydrazone[70] in 30 mL of dichloromethane cooled with a dry ice bath was added dropwise over 15 min 4.2 g of *tert*-butylhypochlorite in 5 mL of dichloromethane. After the mixture was stirred at −78 °C for 5 h, volatiles were removed from the yellow mixture by rotary evaporation in the dark. The NMR spectrum of the residue was relatively clean, showing the following peaks: δ 1.62 (s, 6 H), 1.14 (s, 9 H). Without further purification, excess 40% aqueous dimethylamine was added dropwise to the yellow residual liquid at 0 °C. After being

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Table VI. NMR Data of 7 in Various Solvents

	^1H	^{13}C
C_6D_6	2.44 (s, 6 H), 1.23 (s, 6 H), 1.18 (s, 9 H)	83.78, 67.26, 38.87, 27.02, 22.95
C_7D_8	2.44 (s, 6 H), 1.21 (s, 6 H), 1.18 (s, 9 H)	83.79, 67.32, 38.88, 27.07, 23.03
CD_3CN	2.36 (s, 6 H), 1.14 (s, 9 H), 1.10 (s, 6 H)	84.41, 67.75, 38.95, 27.11, 22.57
CD_3OD	2.42 (s, 6 H), 1.19 (s, 9 H), 1.14 (s, 6 H)	85.21, 68.44, 38.90, 27.11, 21.77

stirred at 0 °C for 5 min, the mixture was stirred with ether at room temperature for 2 h. The ether layer was separated and dried with K_2CO_3 and Na_2SO_4. After rotary evaporation of the solvent, the yellow residue (6 g) was relatively clean 7 as shown by NMR analysis. Vacuum distillation gave the pure azoalkane, bp 66.5–67.5 °C (~25 mm). NMR data in four solvents are listed in Table VI. MS (45 eV): 85 (60), 70 (100), 59 (12), 57 (17), 56 (42), 55 (25), 44 (13), 43 (13), 42 (23), 41 (37), 39 (18), 28 (25), 15 (30).

Acetone Dimethylenamine (9) was prepared according to the literature procedure,[71] NMR (C_6D_6) δ 3.88 (br s, 1 H), 3.73 (s, 1 H), 2.38 (s, 6 H), 1.72 (d, 3 H, J = 0.6 Hz). Crude 9 polymerized on attempted distillation, and it degraded into a mixture on standing for 4 days in the freezer under nitrogen. Attempts to purify 9 by GC gave 10 instead: NMR (C_6D_6) δ 5.78 (m, 1 H), 4.06 (s, 1 H), 4.01 (d, 1 H, J = 0.8 Hz), 2.45 (s, 6 H), 1.79 (d, 3 H, J = 1.1 Hz), 1.61 (d, 3 H, J = 1.3 Hz); MS (70 eV) 125 (17), 110 (100), 95 (30), 94 (22), 42 (27), 39 (20), 15 (43).

2-(Dimethylamino)-2,3,3-trimethylbutane (8) was synthesized as described in the literature.[72] The crude product was purified by preparative GC: ^1H NMR (C_6D_6) δ 2.30 (s, 6 H), 0.96 (s, 9 H), 0.93 (s, 6 H); ^{13}C NMR (C_6D_6) δ 59.96, 42.29, 40.49, 27.07, 21.09.

Thermolysis Kinetics. Thermolysis kinetics were done in sealed 1-cm Pyrex UV cells in a constant-temperature oil bath shielded from fluorescent lights. Solutions were degassed by at least three freeze–thaw cycles. The bath temperature was recorded by a platinum thermometer and a HP Model 3456 $6^1/_2$ digit volmeter. The reaction was followed by the decay of the UV absorption maximum around 380 nm.

Thermolysis Product Study. All solutions for thermolysis were degassed by at least three freeze and thaw cycles. Product analysis was done in sealed NMR tubes heated at an appropriate temperature (110–130 °C) in the same bath as used for kinetics. A dry solution of 7 in CD_3CN was obtained by stirring the wet solution with CaH_2 followed by trap to trap distillation on the vacuum line into an NMR tube. In the trapping experiment, tetrabutylammonium cyanide was first placed in the NMR tube and pumped to dryness. Dried 7 solution (see above) in CD_3CN was then distilled into the NMR tube, and the reaction was followed by NMR spectroscopy. In the reaction of 7 with acetic acid, the HOAc–C_6D_6 solution and the solution of 7–C_6D_6 were degassed separately. The acetic acid solution was then distilled into the frozen 7 solution at −196 °C. The combined solution was first allowed to react at room temperature for 30 h in the dark and was then heated at 100 °C for 20 min to complete the reaction. For GC–MS analysis, the tube was usually opened after thermolysis, and the reaction mixture was analyzed immediately to avoid air oxidation of the products and escape of volatile components. Products were identified by ^1H and ^{13}C NMR analyses, or by GC–MS comparison with authentic material. The product ratio was estimated from NMR peak area or peak height. Nitrogen volumes were obtained on a Töpler pump and the gas purity was checked by GC on a 5-Å molecular sieves column. An NMR tube sealed to a 7/25 standard taper joint was used for the nitrogen yields.

Photolysis of 7. All photolyses were done in degassed solution in sealed NMR tubes using an Oriel 500-W high-pressure mercury lamp with a 2,7-dimethyl-3,6-diazacyclohepta-1,6-diene perchlorate filter. Products were identified and quantified by the same methods used in thermolysis.

Quantum Yield. A Hanovia 450-W medium-pressure mercury lamp with 366-nm light filter was used for this purpose. The quantum yield was obtained from the nitrogen volume ratio of 7 relative to DTBD standard with NMR tubes on a merry-go-round apparatus at an average temperature of 20 °C. Solutions of 0.3 M 7–C_6D_6 and 0.82 M DTBD–C_6D_6 were used. The tubes were removed frequently for NMR analysis. Caution was exercised to make sure that all light was absorbed by the samples during the photolysis. After the photolysis, about 25% of DTBD and 63% of 7 were decomposed.

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Supplementary Material Available: NMR spectra of 7 and its decomposition products as described in ref 32 (7 pages). Ordering information is given on any current masthead page.

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Synthesis of Polyquinanes. 3. Total Synthesis of (±)-Hirsutene: The Intramolecular Diels–Alder Approach[1,2]

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The highly efficient (19% overall yield) 20-step synthesis of the linearly fused triquinane (±)-hirsutene (11) is described. The key step in this sequence is an intramolecular Diels–Alder reaction of the substituted cyclopentadiene **16d**, which contains all but two of the carbon atoms found in hirsutene. During this intramolecular Diels–Alder reaction, two of the three carbocyclic rings found in hirsutene are formed. The third ring is formed by the aldol cyclization of **29**. The successful synthesis of (±)-hirsutene demonstrates the synthetic utility of the intramolecular Diels–Alder strategy for the synthesis of linearly fused triquinanes.

Over the last 15 years much effort has been devoted to the syntheses of polyquinane natural products as well as to the application of the intramolecular Diels–Alder reaction to problems of general synthetic interest. In the

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