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Synthesis, Thermochemistry, and Reactions of Vicinal Bis(azoalkanes). The Chemistry of α- and β-Azo Radicals

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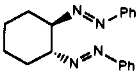
Abstract: Two vicinal bis(azo)alkanes, **8P** and **8B**, were prepared from acetone phenylhydrazone (APH) and acetone *tert*-butylhydrazone (ATBH), respectively. Thermolysis of **8P** above 130 °C in the presence of thiophenol affords APH in quantitative yield, showing that the central C–C bond of **8P** cleaves in preference to the usual C–N homolysis of azoalkanes. The resulting radicals **9P** recombine to the C–N dimer **16P** about 40 times faster than to the more stable C–C dimer **8P**. From the combustion heat of **8P**, we deduce that its strain enthalpy H_s is 5.5 kcal/mol, while the resonance stabilization energy (RSE) of **9P** is 15.3 kcal/mol. The *tert*-butyl analog **8B** loses 2 mol of N_2, showing that C–N homolysis greatly dominates over C–C homolysis. Nevertheless, we estimate that the latter process would occur with $\Delta G^{\ddagger}$ (150 °C) > 40.3 kcal/mol, which implies that the RSE of aliphatic hydrazonyl radical **9B** is at least 6 kcal/mol below that of **9P** and is little or no more than the RSE of the 1,1-dimethylallyl radical.

Although azoalkanes are general precursors for carbon-centered radicals,[1,2] compounds incorporating two azo moieties are much rarer.[3] Vicinal bis(azo)alkanes, which contain a pair of azo groups on adjacent carbons, are represented in the literature by structures **1–5**. Although no decomposition studies of **1**[4] and **2**[5a] have been reported, a recent thorough investigation of **3**[5b] and some older work on **4**[6] show that nitrogen extrusion takes place readily.



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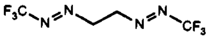

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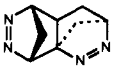

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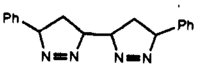

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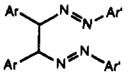

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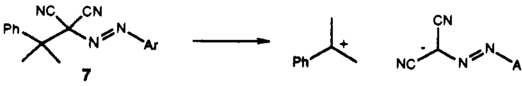
One can imagine a quite different reaction of vicinal bis(azo)alkanes: C–C homolysis with the azo group serving to stabilize an adjacent radical center. In fact compound **5**[7-13] undergoes exactly this reaction, as evidenced by crossover experiments, radical trapping, and equilibration of diastereomers.[10] Scission of the C–C bond β to an azo group has also been observed in **6**[14] and **7**,[15] where the driving force is relief of ring strain and formation of resonance-stabilized ions, respectively.

6



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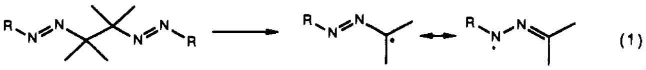
Fascinated by the early reports on the decomposition of **5**,[10,11] we resolved to understand more completely the reaction energetics of such bis(azo)alkanes. Compound **5** is not ideal for our purposes because it possesses α-hydrogens which allow tautomerization to osazones and because the α-aryl groups contribute in an unknown way to the lability of the adjacent bonds. We therefore sought to generate α-azo (hydrazonyl) radicals **9**[16-21] by homolysis of fully substituted azoalkanes **8P** and **8B**, where **P** designates the phenyl series, **B** designates the *tert*-butyl series, and no letter (e.g., **8**) leaves R unspecified (eq 1). We shall have occasion to refer to eq 1 later in connection with the stabilization energy of **9**. Though the absence of chiral carbons in **8** denies us some mechanistic information, it also simplifies the chemistry.

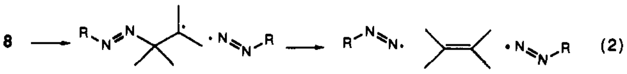


8P,B

P: R = Ph
B: R = t-Bu

9P,B

Further interest in vicinal bis(azo)alkanes arises from the possibility of ordinary C–N cleavage and the question of stepwise versus concerted loss of azo groups. Thus C–N homolysis of **8** might proceed via elimination[22,23] from a β-azo radical **10** (eq 2),



10

TME

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Table I. Summary of the Combustion Experiments[a] of **8P**

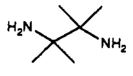
	run					
	1	2	3	4	5	6
m (**6a**) [g]	0.040 040	0.043 839	0.041 119	0.040 183	0.040 890	0.040 874
m' (cotton) [g]	0.004 39	0.000 415	0.000 384	0.000 517	0.000 474	0.000 452
ΔT_c [K][b]	1.017 48	1.112 43	1.044 06	1.021 87	1.039 87	1.039 13
$\epsilon_{calor}(-\Delta T_c)$ [cal][c]	−346.18	−378.49	−355.22	−347.68	−353.80	−353.55
$\epsilon_{cont}(-\Delta T_c)$ [cal][d]	−0.87	−0.95	−0.89	−0.87	−0.88	−0.88
ΔE_{corr} [cal][e]	0.16	0.18	0.16	0.16	0.16	0.16
$m'\Delta u'_c$ [cal]	1.78	1.68	1.56	2.10	1.92	1.83
Δu_c (**6a**) [cal/g]	−8590.1	−8585.6	−8595.5	−8586.9	−8593.5	−8593.0
ΔH_c (**6a**) [kcal/mol][f]	−2530.86	−2529.51	−2532.44	−2529.91	−2531.84	−2531.69

[a] T_h = 25 °C; V_{bomb} = 0.0820 L; p^i_{gas} = 30.00 atm (30.45 bar); m^i_{water} = 0.23 g; E_{ign} = 0.55 cal; T^i = 23.756–24.030 °C; m_{platin} = 1.159 g. [b] $\Delta T_c = T^f - T^i + \Delta T_{corr}$. [c] ϵ_{calor} = 340.234 ± 0.020 cal/K (0.0058%) calibration with benzoic acid. [d] $\epsilon_{cont}(-\Delta T_c) = \epsilon^i_{cont}(T^i - 25\ °C) + \epsilon^f_{cont}(25\ °C - T^f + \Delta T_{corr})$. [e] ΔE_{corr}: Sum of items 81–85, 87–90, 93, and 94 in ref 42; $-\Delta u'_c$ (cotton) = −4050.0 ± 4.0 cal/g. [f] Mean value of ΔH_c (**8P**) = −2531.04 ± 0.47 kcal/mol (0.019%); ΔH_f (**8P**) = 86.66 ± 0.47 kcal/mol.

or it might lead directly to tetramethylethylene (TME). Furthermore, the competition between C–C and C–N cleavage could depend on azoalkane structure, particularly on the nature of R. We shall soon see that thermolysis of **8P** and **8B** led to entirely different reactions, as **8P** mainly followed eq 1 while **8B** followed eq 2.

Results

Synthesis of Compounds. Though the usual methods of preparing azoalkanes[24] appear suitable for the synthesis of **8**, our extensive efforts along these lines were fruitless. Diamine **11**[25] is an appealing starting material, but we were unable to convert it to bis(sulfamide)[26] **12** or to the bis(azoxy) compound **13**.[27] Bis(urea) **14** was successfully prepared, but it could not be oxidized to the corresponding azoalkane.[28] Though it seemed reasonable to make **8P** by reductive coupling of acetone phenylhydrazone (APH) followed by oxidation of the bis(hydrazine),[29,30] we were unable to repeat the coupling reaction, even using active zinc metal.[31]



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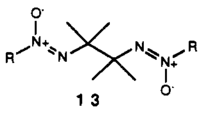
12



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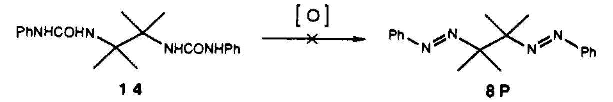
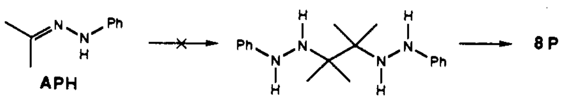
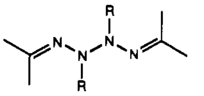


14 **8P**

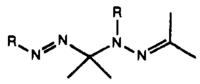


APH

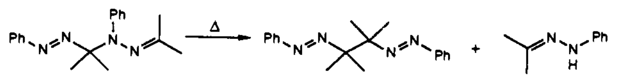
The solution to the synthesis problem arose while we were preparing an azohydrazone needed as an authentic sample in our studies of geminal bis(azo)alkanes.[32] Whyburn and Bailey[33] reported in 1928 that $KMnO_4$ in acetone oxidized APH to the N–N dimer **15P**, a yellow substance that was stable at its melting point of 89 °C. Many years later, Theilacker and Tomuschat[34] reformulated this material as C–N dimer **16P**. In fact, oxidation of hydrazones is a well-studied reaction,[35,36] the first case of oxidative coupling having been reported in 1888.[37] We discovered that heating **16P** at 125 °C for 10 h in benzene converted it to a 1:5 mixture of APH and a new compound possessing only a singlet in the upfield region of the NMR spectrum. Isolation and further spectral analysis proved this substance to be the desired compound **8P** (mp 72 °C), an isomer of **16P** formed by dissociation and allylic recombination. Although the same reaction was seen earlier in **5**,[10] it was surprising to us at first because hydrazones are usually more stable than their tautomeric azoalkanes.[38,39]



15P,B

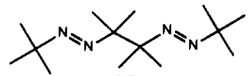


16P,B



16P **8P** **APH**

Hoping to apply this methodology to purely aliphatic cases, we oxidized acetone *tert*-butylhydrazone (ATBH) with potassium permanganate in boiling acetone and obtained exclusively C–C coupling product **8B**. A search was made for **16B** by NMR, but this C–N dimer constituted less than 5% of the oxidation product. The lower reactivity of the aliphatic hydrazone toward $KMnO_4$ is surely due to its higher oxidation and ionization potential than that of APH. For example, acetaldehyde *N*-methylhydrazone



8B

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Table II. Summary of Vapor Pressure Measurements of **8P**[a]

T_{sat} [°C]	V_{N_2}[b] [L]	T_{cond} [°C]	m[c] [mg]	p[d] [Torr]
82.0	6.567	25.0	0.515	4.96×10^{-3}
74.2	17.483	20.0	0.645	2.34×10^{-3}
75.2	5.889	12.0	0.279	3.00×10^{-3}
82.2	4.978	8.8	0.445	5.64×10^{-3}
101.2	1.596	10.3	0.653	2.58×10^{-2}
105.4	1.178	10.1	0.658	3.53×10^{-2}
109.9	0.760	10.3	0.643	5.34×10^{-2}
114.9	0.570	10.2	0.650	7.20×10^{-2}

[a] Saturation of a flow of nitrogen (1.1 L h^{-1}) by **8P** at temperature T_{sat} and condensation of **8P** at T_{cond}. [b] Applied volume of nitrogen in liters. [c] Mass of condensed **8P** measured by GC (internal standard). [d] Equilibrium pressure of **8P** at T_{sat} calculated by iteration; see ref 43.

exhibits $IP_v = 8.22$ eV, while APH shows $IP_v = 7.42$ eV.[40] Our synthetic efforts thus provided two vicinal bis(azo)alkanes (**8P,B**) and one C–N-coupled isomer, **16P**.

Thermochemistry of 8P. The heat of formation ($\Delta H_f°(g)$) of **8P**, which was required to evaluate the stability of radicals **9P**, was determined from its heat of combustion, $\Delta H_c°(c)$, and its heat of sublimation, ΔH_{sub}. A 99.8% pure sample of **8P** was subjected to oxygen bomb calorimetry using the isoperibolic aneroid microcalorimeter and the experimental procedures described previously.[41] The density of **8P** ($d = 1.13$ g cm^{-3}) was measured to calculate its mass in vacuo, while the specific heat ($c_p = 0.194$ cal g^{-1} K^{-1} at 25 °C) was determined by differential scanning calorimetry (DSC) to calculate the isothermal bomb process. The reduction to standard state was performed in the usual manner.[42] On the basis of six calorimetric runs (Table I) the mean value of the standard heat of combustion was $\Delta H_c°(c) = -2531.04 \pm 0.47$ kcal/mol. From this value, the standard heat of formation $\Delta H_f°(c) = 86.66 \pm 0.47$ kcal/mol was derived for crystalline **8P**. The heat of fusion $\Delta H_m = 5.04 \pm 0.05$ kcal/mol was measured by DSC at the melting point of **8P** (mp 69.1 °C), while the heat of vaporization of liquid **8P** $\Delta H_{vap} = 22.17 \pm 0.37$ kcal/mol was calculated from the vapor pressure (Table II) using the Clausius–Clapeyron equation. The vapor pressure of **8P** was measured by a flow method[43] at six temperatures between 75 and 115 °C. According to the equation $\Delta H_f°(g) = \Delta H_f°(c) + \Delta H_m + \Delta H_{vap}$, our thermochemical measurements yield a gaseous heat of formation of **8P** of 113.9 ± 0.6 kcal/mol.

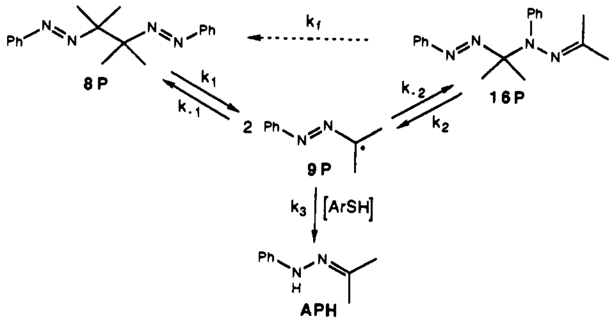
Decomposition of 8P. A sample of this bis(azo)alkane was heated at 171.7 °C with excess thiophenol in degassed toluene-d_8 until NMR showed no remaining starting material. The yield of N_2 was less than 0.5%, demonstrating that, in contrast to most azoalkanes, C–N bond homolysis in **8P** was unimportant. The thermolysis kinetics of **8P** were monitored by NMR in the temperature range 133.27–161.24 °C using thiols to scavenge radicals **9P** (cf. Table III). The activation parameters were $\Delta H^\ddagger = 30.6 \pm 0.5$ kcal/mol, $\Delta S^\ddagger = -3.5 \pm 1.1$ eu with thiophenol, and $\Delta H^\ddagger = 30.2 \pm 0.5$ kcal/mol, $\Delta S^\ddagger = -4.7 \pm 1.3$ eu with *tert*-butyl mercaptan. The agreement between the values of $\Delta G^\ddagger$ (150 °C) (32.1 and 32.2 kcal/mol, respectively) suggests that both thiols are sufficiently effective scavengers to prevent out-of-cage recombination of **9P** to **8P** and that neither one induces the decomposition of **8P**. On the other hand, selenophenol[44] and especially triphenyltin hydride[45] showed significantly enhanced rates, implying that these scavengers do induce decomposition. According to both NMR and GC comparison with authentic samples, the products of the thiophenol-scavenged runs were cleanly APH and diphenyl disulfide (**17**). A sample of **8P** in diphenyl ether

Table III. Thermolysis Kinetics of C–C Dimer **8P**

temp [°C]	solvent	scavenger	freq [MHz][a]	10^4k [s^{-1}]
133.27	C_6D_6	PhSH	250	0.544
133.27	C_6D_6	*t*-BuSH	250	0.444
141.51	C_6D_6	PhSH	90	1.22
144.30	C_6D_6	*t*-BuSH	250	0.284
153.05	C_6D_6	*t*-BuSH	250	2.81
153.12	$C_6D_5CD_3$	PhSH	90	3.35
153.12	$C_6D_5CD_3$	*t*-BuSH	90	2.93[b]
158.11	$C_6D_5CD_3$	PhSH	90	4.48
158.11	$C_6D_5CD_3$	*t*-BuSH	90	3.31[b]
161.24	C_6D_6	*t*-BuSH	250	5.26
124.7	C_6D_6	Ph_3SnH	90	19.0
139.2	C_6D_6	Ph_3SnH	90	40.3
144.30	C_6D_6	PhSeH	250	13.3

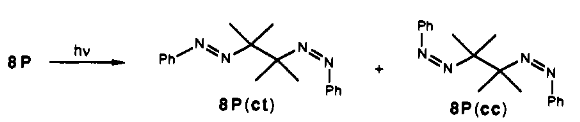
[a] Frequency of NMR spectrometer employed. [b] These points were not used in the Eyring plots because the NMR peak of **8P** partially overlapped that of *t*-BuSH at 90 MHz.

Scheme I



was heated to 170 °C in the probe of an ESR spectrometer, giving rise to a complex signal attributable to **9P**, but detailed analysis of the signal was not carried out.

Irradiation of **8P** at 435 nm in C_6D_6 at 25 or 86 °C caused only trans–cis isomerization of one or both azo groups. The cis isomers **8P(ct)** and **8P(cc)**, which were easily detected by their shifted methyl peaks in the NMR, cleanly reverted to starting *trans*-**8P** thermally (78 °C for 10 min). Slow decomposition of **8P** could



be effected using shorter wavelength light, such as that from a medium-pressure unfiltered mercury lamp through Pyrex or a 254-nm low-pressure lamp through quartz, though photoisomerization remained the major reaction. Under these conditions, the permanent products were TME and APH in a 1:2 ratio, indicating both C–N and central C–C cleavage. A number of other products were formed in these shorter wavelength experiments, but detailed analysis was not attempted.

Thermolysis of 16P. On heating, **16P** isomerized to **8P**, very likely with **9P** as the key intermediate. Scheme I shows the reactions involved, including rate constants that will be useful in the later discussion. The disappearance of **16P** was monitored by NMR, but a few percent of **16P** remained even at long reaction times. Although this result implies simply that the two isomers are in equilibrium, the kinetic analysis was complicated by a slowly drifting equilibrium point caused by buildup of APH. APH must have formed when **9P** abstracted hydrogen, but the atom donor was probably not the benzene solvent. We speculate that α, p recombination of **9P** occasionally takes place, forming a quinoid

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Table IV. Thermolysis Kinetics of **16P**

temp [°C]	K_e[a]	10^4k_f [s^{-1}][b]	$\delta k_f/k_f$[c]
80.40[d]	9.7	0.0467	0.20
120.55[e]	9.0	2.01	0.049
129.77[d]	14	4.46	0.019
129.84[e]	11	4.60	0.036
136.52[e]	8.0	9.37	0.068
140.40[e]	7.9	11.3	0.055
144.20[e]	13	16.4	0.056

[a] Equilibrium constant for **16P** ⇄ **8P**. [b] Forward rate constant for **16P** → **8P**. [c] (Standard deviation of k_f)/k_f. [d] NMR, 250 MHz. Uncertainty in peak areas = ±5%. [e] NMR, 90 MHz. Uncertainty in peak areas = ±10%.

Table V. Thermolysis of **16P** at 80.40 °C in the Presence of Thiols

thiol	concn, M	10^4k_{obsd} [s^{-1}]
2,6-$Me_2C_6H_3SH$[a]	1.58	1.59
PhSH	1.66	1.82
t-BuSH	0.191	0.099[b]

[a] Impurities in the commercial sample of 2,6-dimethylthiophenol and the proximity of the aromatic methyl signal to that of **16P** made NMR quantification difficult. [b] Uncertainty greater than for the other *k* values.

dimer that would be an excellent hydrogen atom donor. The kinetic data for **16P** → **8P** were treated as those of a reversible first-order reaction, and the equilibrium point was taken as the concentration of **16P** after 7 half-lives (98.4% conversion). Due to the difficulty of measuring the small NMR peaks from **16P**, the values of K_e varied from 7.9 to 14 (Table IV). However, the rate constants should be reliable because only points early in the run were used for the first-order plot of log $[(A - A_\infty)/(A_0 - A_\infty)]$ versus time. The rate constants at each temperature and their associated uncertainties were fitted by a weighted least-squares treatment to yield the following activation parameters for the observed process **16P** → **8P**: $\Delta H^\ddagger = 27.3 \pm 0.7$ kcal/mol, $\Delta S^\ddagger = -6.6 \pm 1.7$ eu, $\Delta G^\ddagger$ (150 °C) = 30.1 kcal/mol. The average value of K_e over the experimental temperature range was 10 ± 2, corresponding to a free energy change for **16P** going to **8P** of $\Delta G = -1.9 \pm 0.2$ kcal/mol at 150 °C.

Because the values of K_e in Table IV varied so widely, another experiment was undertaken to confirm K_e.[46] A 7:1 mixture of **8P** and **16P** (corresponding roughly to the equilibrium ratio) was dissolved in C_6D_6, and portions of the solution were thermolyzed at 80.4, 120.4, and 144.2 °C. NMR assay after several half-lives showed less than 9% APH and a ratio of **8P** to **16P** of 8.9, 10.3, and 8.8, respectively. Thus K_e is close to the average value of 10 deduced from Table IV and is quite independent of temperature.

Since the kinetic dimerization product of **9P** is **16P**, a large fraction of the radicals from thermolysis of **16P** must return to starting material rather than proceeding to **8P** (cf. Scheme I). Therefore k_f, which represents the *observed overall thermolysis rate constant of 16P without added thiol*, is less than the initial bond cleavage rate constant. In order to determine the latter value (k_2), thermolysis of **16P** was carried out in the presence of thiols to prevent radical return (cf. Table V). We know that PhSH is an effective scavenger of **9P** because inclusion of this thiol during thermolysis of **16P** was found to prevent the formation of **8P**. Since the rate is 14% faster with thiophenol than with its 2,6-dimethyl analog, the steric effect seen with cyclopropylcarbinyl radicals[47] apparently operates with **9P** as well.

As found for **8P**, thermolysis of **16P** with added PhSH gave only APH, even though **9P** might conceivably abstract hydrogen on carbon to yield azoalkane **18**. Two control experiments were run to ensure that **18** was stable under the reaction conditions. A C_6D_6 solution of **16P** (40 μmol), authentic **18** (7 μmol), and PhSH (170 μmol) was heated at 127.0 °C for 2 h, after which all **16P** had gone to APH. None of the **18** was destroyed, though PhS• was certainly formed during the reaction. A similar solution without PhSH was heated until **16P** had nearly reached equilibrium with **8P**. Although radicals **9P** were generated, no loss of **18** was observed. These results establish that neither **9P** nor PhS• is reactive enough to abstract α-hydrogen from **18**. Thus thermolysis of **8P** with PhSH leads to APH directly, not via **18**. In the Discussion, we shall offer an explanation of why hydrogen is transferred only to the nitrogen of **9P**.

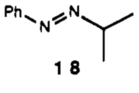

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Table VI. Product Ratios from Coupling of Radical **9P**

temp [°C]	**16P/8P**	precursor
−72	38	APH + NiO_2
−57.5	39	APH + NiO_2
−10.0	47	APH + NiO_2
0	45	APH + $KMnO_4$
2.0	46	APH + NiO_2
5.0	29	**19**, *hν*[a,b]
23.5	41	APH + $KMnO_4$
24.5	40	APH + NiO_2
43.5	39	APH + NiO_2
45.0	42	APH + NiO_2
47.1	28	**19**, Δ[a,c]
55.5	42	APH + NiO_2
58	32	APH + $KMnO_4$
78.0	37	APH + NiO_2
84.6	26	**19**, Δ[a,c]

[a] Analysis by NMR; all other analyses were by HPLC. [b] Photolysis of **19**. [c] Thermolysis of **19**.

C–C versus C–N Recombination of 9P. Although **16P** was the only product isolated from the $KMnO_4$ oxidation of APH, we found by HPLC and NMR analysis of the crude reaction mixtures that a small amount of **8P** was also produced. Both compounds surely arose by coupling[10] of radical **9P**, the likely intermediate in the oxidation of APH. In order to confirm that the product ratio did not depend on the mode of radical generation, a sample of geminal bis(azo)alkane **19**[32] was thermolyzed in benzene at two temperatures and photolyzed at a third, lower temperature. This radical precursor is much more labile than **8P** or **16P** so that it could be decomposed to substantial conversion without causing equilibration of **8P** and **16P**. Due to the complexity of the product mixture, HPLC analysis was unpromising, but 250-MHz NMR allowed us to obtain the product compositions shown in Table VI. Even here, the precision was compromised by the small size of the δ = 1.5 ppm NMR singlet of **8P** and its proximity to another peak. APH was then oxidized with NiO_2[9b] over a wide temperature range, giving a ratio of **16P** to **8P** similar to that obtained from the other methods for generating **9P**. Unfortunately, the small area of the HPLC peak due to **8P** caused errors large enough to obscure any temperature dependence of the ratio. Using only the NiO_2 data, which were the most reliable, we obtain the average ratio **16P**/**8P** = 41 ± 4 over the temperature range from −72 to 78 °C and presumably at 150 °C, so that $\Delta G^\ddagger$ (150 °C) for the recombination of **9P** to **8P** is 3.1 ± 0.1 kcal/mol greater than for the recombination of **9P** to **16P**. Although the scatter in the plot of ln (**16P**/**8P**) versus $1/T$ prevents an exact determination of $\Delta\Delta H^\ddagger$, the data show that its value is below 2 kcal/mol. Moreover, $\Delta H^\ddagger$ for radical recombination is generally small, implying that $\Delta\Delta H^\ddagger$ for competing recombinations is even smaller. If we assume that $\Delta\Delta H^\ddagger$ is essentially 0, the entire difference in $\Delta G^\ddagger$ for competing dimerizations becomes a matter of entropy ($\Delta\Delta S^\ddagger = -7.4$ eu), as is the usual case in radical dimerizations.[48a]

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[46] We thank a referee for suggesting this experiment.

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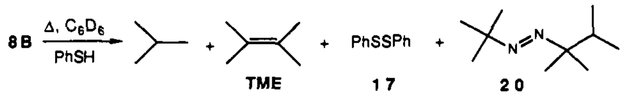
Table VII. Decomposition Products of **8P** (Moles Relative to TME)[a]

product	thermolysis [156.6 °C, C_7D_8, PhSH][b]	thermolysis [161 °C, C_6D_6]	photolysis [25 °C, C_6D_6]	photolysis [−78 °C, C_7D_8, PhSH]
isobutane, isobutene[c]	1.73[d]	1.5	2.4	13.7
2,3-dimethylbutane, 2,3-dimethyl-1-butene[c]		0.058	0.42	4.8
TME[e]	(1.00)	(1.00)	(1.00)	(1.00)
2,2,4-trimethylpentane		0.13	trace	
2,4,4-trimethyl-1-pentene[f]		0.15	0.028	
2,2,3,3-tetramethylbutane		0.15	0.12	
2,3,3,4,4-pentamethyl-1-pentene[f]		0.29	0.58	3.6
20		0.018	trace	2.0
2,2,3,3,4-pentamethylpentane[f]			0.083	0.66
isobutyl phenyl sulfide[f]				2.6
2,3-dimethyl-3-(phenylthio)-1-butene[f]				0.34

[a] Analysis by GC. [b] Analyzed by ^{1}H NMR after reaction was complete. [c] Not separable under our GC conditions. [d] No isobutene was present. The low relative yield of isobutane may arise from its being partly in the gas phase. [e] Tetramethylethylene. [f] Identified only by GC/MS.

Decomposition of 8B. In the presence of thiophenol, thermolysis of **8B** at 156.6 °C in C_7D_8 gave cleanly isobutane, TME, and **17**. A small peak shown by comparison with an authentic sample to be due to **20** built up in the NMR spectrum and later disappeared.

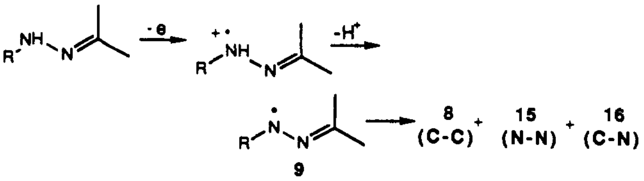


The nitrogen yield was 1.99 mol/mol, corresponding to quantitative C–N rather than C–C bond cleavage. Because it was important to verify the absence of C–C homolysis, a careful GC search for acetone *tert*-butylhydrazone (ATBH) was made. A miniscule peak was observed at the correct retention time, but its area in a thiophenol-scavenged run at 162 °C was less than 0.04% of the TME peak area. Unfortunately, we could not distinguish whether the ATBH was a thermolysis product or a trace contaminant in **8B**. In C_6D_6 without thiophenol, many additional products formed in the mole ratios shown in Table VII. Though we were able to identify most of the hydrocarbons by GC comparison with authentic materials, five unknowns of long retention time accounted for about 15% of the total peak area. The thermolysis rate of **8B** at several temperatures in toluene allowed determination of the activation parameters $\Delta H^{\ddagger} = 35.2 \pm 0.3$ kcal/mol, $\Delta S^{\ddagger} = 2.8 \pm 0.6$ eu, and $\Delta G^{\ddagger}$ (150 °C) = 34.0 kcal/mol. The analogous results for **20** were $\Delta H^{\ddagger} = 40.3 \pm 0.2$ kcal/mol, $\Delta S^{\ddagger} = 12.5$ eu, and $\Delta G^{\ddagger}$ (150 °C) = 35.0 kcal/mol.

As in the case of **8P**, bis(azo)alkane **8B** is expected to undergo photochemical trans–cis isomerization. Indeed, 366-nm irradiation of **8B** at −78 °C deepened the yellow color of the sample and caused a new NMR peak to appear at 1.58 ppm. On warming of the sample to −33 °C, the color and the peak disappeared with concomitant formation of permanent products. When irradiated at 25 °C, **8B** gave mainly the same hydrocarbons as in the thermolysis (cf. Table VII) along with a trace of **20**. The latter azoalkane became a major product when **8B** was irradiated at −78 °C in the presence of thiophenol, though **20** was destroyed on further photolysis. The product distribution at an intermediate time is shown in Table VII.

Discussion

Recombination of Hydrazonyl Radicals. Permanganate or NiO_2 oxidation of ketone hydrazones proceeds via hydrazonyl radicals **9**,[13] which in principle can lead to C–C, C–N, or N–N coupling.



During the course of the present work, we searched in vain for N–N dimers **15P,B** both in hydrazone oxidations and in decomposition of vicinal bis(azo)alkanes, including low-temperature photolyses. In retrospect, there is reason to believe that **15P** would be exceedingly unstable. Subtracting twice the phenylhydrazonyl radical resonance energy (15.3 kcal/mol relative to *tert*-butyl; see below) from the N–N BDE of hydrazine (68–70 kcal/mol)[49,50] leaves a N–N bond energy of at most 40 kcal/mol for **15P**. The low central N–N BDE of H_2N–NH–NH–NH_2 (27 kcal/mol)[50] may carry over to **15P**, possibly decreasing its BDE to 0.

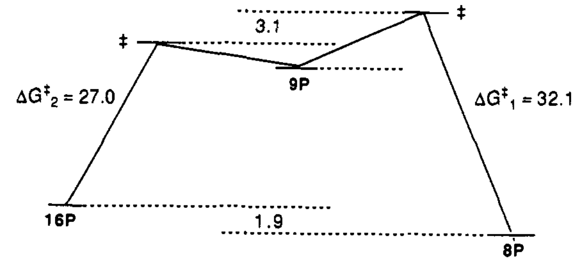


Figure 1. Free energy diagram (kcal/mol) for **9P** and its dimers.

The products obtained from the oxidation of ketone hydrazones vary with the structure of R. Thus one obtains mainly **16** when R = Ph, only **8** when R = *t*-Bu, and a mixture of **8** and **16** when R = Me.[32] In the simplest analysis, the nature of the coupling products under kinetic control should be governed by both steric and electronic effects, as in the case of allylic and propargylic radicals.[51,52] The spin density is higher on N than on C,[16–18,53] favoring product **16** over **8**. On the other hand, bulky R groups would favor **8**, which places those groups very far apart. Since **9** (R = Me) gives both isomers,[32] it is not surprising that the *tert*-butyl-substituted radical **9B** affords only **8B**. However, phenyl is also larger than methyl,[54] so that one would expect **9P** to couple mostly to **8P** rather than to the observed **16P**. Since the dominant C–N coupling of **9P** cannot be explained on steric grounds, the spin density on N may be higher in **8P** than in **8B**. An ESR study of **9P,B** coupled with the earlier work on hydrazonyl radicals[16,17] would serve to test this hypothesis. The high propensity for C–N coupling only in the aromatic radical **9P** may also be related to the possible intervention of a radical complex.[48a,55]

Thermochemistry and Kinetics of 9P and Its Dimers. A free energy diagram for the phenylhydrazonyl radical dimers **8P** and **16P** (Figure 1) is constructed from the thermodynamic and kinetic data presented above. The thermolysis kinetics of **8P** in the presence of thiols (Table III) gave $\Delta G^{\ddagger}$ (150 °C) = 32.1 kcal/mol. Radical return of **9P** to **8P** does not diminish the overall disappearance rate of **8P** since caged radicals should afford **16P**, which is more labile than **8P**. (Cf. Scheme I; $k_{-2} \gg k_{-1}$, $k_2 \gg k_1$.)

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Neither do free radicals **9P** return to **8P** because they are scavenged by the added thiols (k_3[ArSH] ≫ k_{-1}). Therefore $\Delta G^{\ddagger}$ of **8P** applies to the C–C bond dissociation step k_1. The value of $\Delta G^{\ddagger}$ (150 °C) obtained for **16P** is 30.1 kcal/mol, but in this more complicated case, radical return (k_{-2}) greatly decreases the disappearance rate and raises the apparent $\Delta G^{\ddagger}$.

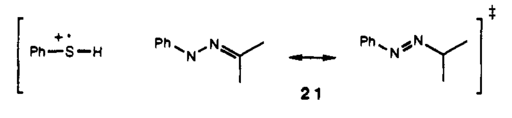
From the kinetic ratio of products formed by the oxidation of APH (cf. Table VI), we calculate $\Delta\Delta G^{\ddagger}$ (150 °C) = 3.1 kcal/mol, which is the difference in activation free energy for C–N versus C–C coupling of **8P**. The $\Delta G^{\ddagger}$ obtained for thermolysis of **16P** is the energy needed to reach the highest transition state in Figure 1, $\Delta G^{\ddagger}$ (**16P** → **8P**) = $\Delta G^{\ddagger}$ (**16P** → **9P**) + $\Delta G^{\ddagger}$ (**9P** → **8P**) – $\Delta G^{\ddagger}$ (**9P** → **16P**), implying that the true $\Delta G^{\ddagger}$ for C–N bond dissociation of **16P** (k_2 in Scheme I) is 30.1 – 3.1 = 27.0 kcal/mol. A cage effect in the recombination of **9P** to **16P** would provide an additional mechanism for decreasing k_f for **16P** → **8P** below k_2 (cf. Scheme I). However, thermolysis of **16P** in the presence of PhSH affords no detectable **8P**. If caged radical pairs of **9P** yield **16P** and **8P** in the same 41:1 ratio as do free radical pairs, cage formation of **16P** cannot be a major reaction. Even a cage effect of the usual magnitude would reduce k_f by only a factor of 2.

The equilibrium constant for **16P** ⇄ **8P** is 10, which indicates that **8P** is 1.9 ± 0.2 kcal/mol more stable in ΔG than **16P**. Since K_e is temperature independent, this ΔG difference is entirely entropic. We were pleased that the directly measured $\Delta G^{\ddagger}$ for **8P** → **9P** (32.1 kcal/mol) agreed with the sum of $\Delta G^{\ddagger}$ (**16P** → **8P**) + ΔG (**8P** → **16P**) = 30.1 + 1.9 = 32.0 kcal/mol. An enthalpy diagram analogous to Figure 1 cannot be constructed from our data because we could not determine $\Delta\Delta H^{\ddagger}$ (**9P** → **16P** vs **9P** → **8P**). This interesting case of kinetic versus thermodynamic control resembles the recombination of benzylic radicals[56–58] and of 2-cyanopropyl radicals[48a,59,60] except that K_e for dimers **8P** ⇄ **16P** is small enough to allow determination of their free energy difference.

Intrigued by the recent discovery of azo-Cope rearrangements,[61,62] we considered this possibility in our compounds; however, they are unsuitable for observing such a reaction. Conversion of **8** to the labile **15** would be difficult to detect, while Cope rearrangement of **16** is degenerate. Despite the slightly negative $\Delta S^{\ddagger}$ for **8P** (Table VIII), we doubt that N–N dimer **15P** lies on the pathway from **8P** to radicals **9P**. Based purely on data for **16P** [$\Delta G^{\ddagger}$ (**16P** → **8P**) + ΔG (**8P** → **16P**)], Figure 1 shows that $\Delta G^{\ddagger}$ (**8P** → **9P**) is 32.1 kcal/mol. If Cope rearrangement of **8P** were the rate-determining step in forming **9P**, this rearrangement must coincidentally exhibit the same $\Delta G^{\ddagger}$ as for C–C bond homolysis. Even if **8P** affords **15P** rapidly and reversibly, the activation energies for formation and destruction of **15P** must coincidentally add up to 32.1 kcal/mol.

Thiol Scavenging of Hydrazonyl Radicals. As mentioned earlier, thermolysis of **16P** is complicated by radical return. According to Scheme I, the rate constant for the disappearance of **16P** can be expressed as $k_f = k_2[k_{-1}/(k_{-1} + k_{-2})] = k_2F$, where F is the fraction of **9P** that proceeds to **8P**. Adding thiols diverts **9P** from recombination (mainly to **16P**) and raises the observed rate constant. Indeed, this rate enhancement is so large that we initially attributed it to induced decomposition. From the NiO$_2$ data in Table VI, the average value of **16P**/**8P** under kinetic control is 41. Since **16P**/**8P** = k_{-2}/k_{-1}, we can calculate the value of F, which is assumed to be independent of temperature.[48a] Thus k_{-1}/k_{-2} is 0.0244, F is 0.0238, and k_f at 80.4 °C is 4.67 × 10^{-6} s^{-1} (Table IV). Since $k_f = k_2F$, we find that k_2 is 2.0 × 10^{-4} s^{-1}, which should equal the observed thermolysis rate constant of **16P** (k_{obsd}) in the presence of a good radical scavenger. Indeed, the aryl mercaptans in Table V give rate constants quite close to this value, showing that we have correctly extracted the value of k_2 from Scheme I. On the other hand, k_{obsd} for *tert*-butyl mercaptan is 9.9 × 10^{-6} s^{-1}, which is only twice the value in the absence of scavenger (cf. Table IV). *tert*-Butyl mercaptan is clearly a poor scavenger of **9P** since it hardly inhibits recombination to **16P**.

Because the spin density in hydrazonyl radicals is higher on terminal nitrogen than on carbon,[17,18,53] one can understand why APH would be the dominant thiophenol scavenging product. The fact that APH is the *exclusive* product suggests that some factor in addition to spin density comes into play, for example, initial hydrogen bonding from nitrogen to thiol or contribution of a polar effect to the selectivity.[63] Thus the transition state for hydrogen transfer probably possesses the character of **21**, implying that the more electronegative end of the hydrazonyl radical would receive the hydrogen.



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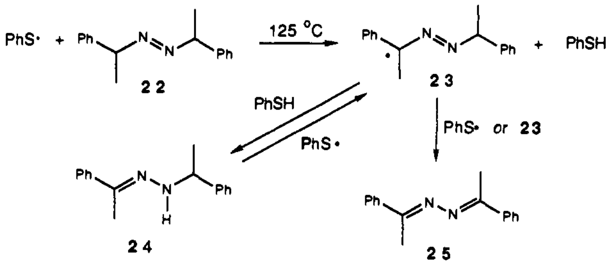
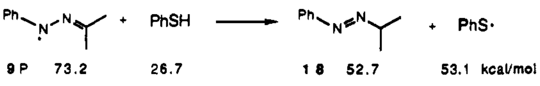
We find that thiophenol is an adequate scavenger of **9P** but that PhS• does not abstract hydrogen from **18**. The latter result differs from the much earlier report[64] that PhS• converts azo-α-phenylethane **22** to the azine **25**. If the postulated mechanism **22** → **23** → **25** is correct, we find it surprising not only that PhS• reacts with **22** but also that hydrazonyl radical **23** attacks another radical instead of PhSH to give **24**. Perhaps PhS• regenerates **23** from **24**, and **23** eventually goes to **25**.



Sufficient data are now available to consider the thermochemistry of the system PhSH, **9P**. Reaction 3 is endothermic by 0.4 kcal/mol, based on the 78.5 kcal/mol BDE of PhSH[65] and the 78.1 kcal/mol BDE of APH (see below). Hydrogen transfer

 (3)

to form 18 (eq 4) is less favorable (ΔH_4 = 5.9 kcal/mol) on account of the high energy of the azo tautomer relative to APH.[32]

 (4)

To the reasons given above for the dominance of eq 3 over eq 4, we may add the greater thermodynamic driving force of eq 3. Although thiophenol scavenging of **9P** (eq 3) is endothermic, ΔH for the overall reaction (eq 5) is calculated to be –14.5 kcal/mol.

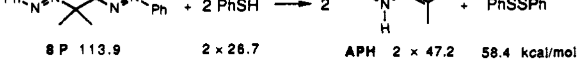
 (5)

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Table VIII. Thermodynamic Parameters for Calculating Radical Stabilization Energies

compound	$\Delta H^{\ddagger}$ [a]	$\Delta S^{\ddagger}$ [a]	$\Delta G^{\ddagger}$ [a,c]	H_s [a,d]	$\Delta G^{\ddagger}_s$ [a,e]	$\Delta G^{\ddagger}_e$ [a,f]	RSE[a,g]
Me_3CCMe_3[h]	67.4	13	61.9	6.9	−4.4	66.3	(0)
$PhMe_2CCMe_2Ph$[h]	45.7	13.7	39.9	10.5[i]	−6.7	46.6	9.9
8P	30.6	−3.5	32.2	5.5	−3.5	35.7	15.3
5[j]	24.6	−6.5	27.3	(3.6)[k]	−2.3[l]	29.6	18.4

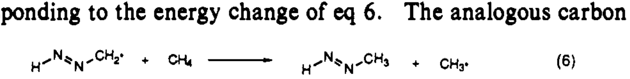
[a] In kcal/mol. [b] In eu. [c] At 150 °C. [d] Strain enthalpy; values in parentheses are assumed. [e] Free energy change due to ground-state strain; slope of $\Delta G^{\ddagger}$ vs H_s is −0.64; see ref 48a, Figures 2 and 3. [f] Electronic contribution to $\Delta G^{\ddagger}$, $\Delta G^{\ddagger}_e = \Delta G^{\ddagger} - \Delta G^{\ddagger}_s$. [g] Resonance energy of 2-substituted 2-propyl radical relative to *tert*-butyl. RSE = $(66.3 = \Delta G^{\ddagger}_e)/2$. [h] Reference 48a. [i] Reference 80. [j] Activation parameters recalculated from data in ref 10. [k] Estimated. [l] Slope of $\Delta G^{\ddagger}$ vs H_s is −0.65.

The enthalpy of formation (ΔH_f) of **8P** shown in eq 5 is the experimental value determined in this work, ΔH_f of PhSH and PhSSPh are literature values,[66] and that of APH is derived from the 5.5 kcal/mol tautomerization enthalpy[32] of **18** → APH. ΔH_f of **18** (52.7 kcal/mol) is taken as the average of the ΔH_f values of azobenzene (96.83 kcal/mol)[67] and azo-2-propane (8.5 kcal/mol),[1] as is usual in group additivity.[68] In each case, gas-phase ΔH_f values have been used as an approximation to the values in nonpolar solvents.

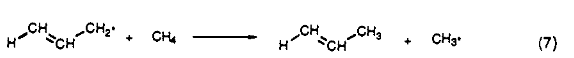
C–N Bond Homolysis of 8B to a β-Azo Radical. The thermal chemistry of **8B** is remarkably different from that of **8P**, for exclusive central C–C bond cleavage changes to nearly pure C–N homolysis. We have already shown that the β-azo radical **10B** is an intermediate in this reaction and that its lifetime is only 0.26 ns at 153.5 °C (cf. Scheme II).[69] An energy diagram for **8B**[68] reveals that breaking of the first C–N bond is endothermic by 30.9 kcal/mol while cleavage of the second azo group is exothermic by 33.7 kcal/mol.

It is clear that **10B** is much more labile than a model azoalkane such as **20**. Most likely, **10B** is destabilized by the substantial exothermicity of its fragmentation in contrast to the endothermicity of ordinary azoalkane thermolysis. The origin of the homolysis products in Table VII is shown in Scheme II. *tert*-Butyl radicals run rampant in this system, adding to isobutene and TME besides giving their usual disproportionation, recombination, and hydrogen abstraction products. The much higher yield of 2,3-dimethylbutane and 2,3-dimethyl-1-butene at −78 °C with thiophenol is in accord with their origin as secondary photolysis products of **20**. Any radicals **10B** that do not fragment or get scavenged are likely to disproportionate to **26**. However, **26** is allylic, and it should be much more labile than either **8B** or **20** and, hence, undetectable.

Stabilization Energy of Hydrazonyl Radicals. According to theoretical calculations,[18] the resonance stabilization energy (RSE) of $^{\bullet}CH_2{-}N{=}N{-}H$ relative to $CH_3^{\bullet}$ is 13.4 kcal/mol, corresponding to the energy change of eq 6. The analogous carbon



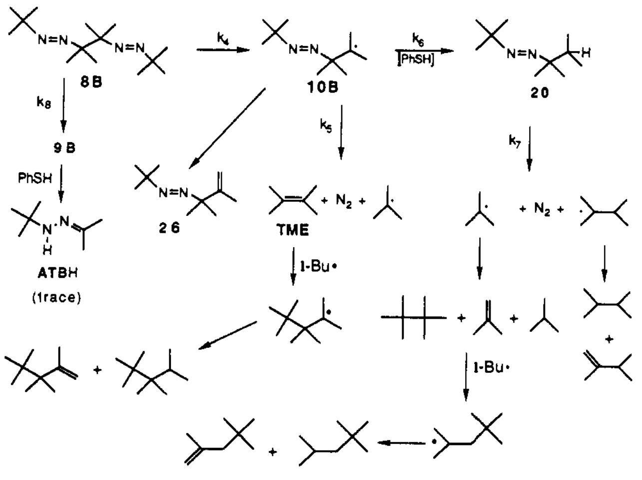
$$\mathrm{H{-}N{=}N{-}CH_2^{\bullet} + CH_4 \longrightarrow H{-}N{=}N{-}CH_3 + CH_3^{\bullet}} \qquad (6)$$



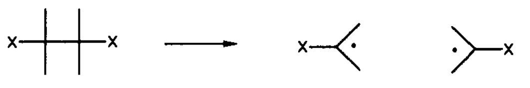
$$\mathrm{H{-}CH{=}CH{-}CH_2^{\bullet} + CH_4 \longrightarrow H{-}CH{=}CH{-}CH_3 + CH_3^{\bullet}} \qquad (7)$$

system (eq 7) at the same level of theory (MP2/6-31G*) gives RSE = 18.6 kcal/mol.[70] Comparison of eqs 6 and 7 then indicates that the RSE of allyl is 18.6 − 13.4 = 5.2 kcal/mol greater than that of 2,3-diazaallyl. As will be described below, our experimental results provide some information on the RSE of substituted 2,3-diazaallyl radicals.

Scheme II



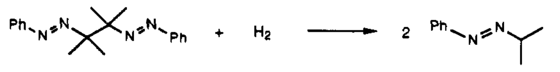
Unlike most azoalkanes, **8P** undergoes exclusive C–C homolysis with no loss of nitrogen. The compound is therefore a hindered ethane **27** of the type studied extensively by Rüchardt and coworkers.[47,73,74] If the strain enthalpy (H_s) of **27** is determined



(8)

27

by combustion calorimetry or force field calculations,[75] its thermolysis rate (eq 8) can be used to calculate the RSE of the substituted 2-propyl radicals relative to *tert*-butyl radical. In the case of **8P**, H_s can be calculated by considering the hypothetical hydrogenation of **8P** to **18** (eq 9). The hydrogenation heat (ΔH_H)



(9)

8P 113.9 **18** 52.7

is −8.5 kcal/mol based on our estimated ΔH_f (**18**) (see above) and the experimental ΔH_f (**8P**). Since most of the group contributions cancel in eq 9, we may also express ΔH_H as $2\{[C-(N_A)(C)_2(H)] - [C-(N_A)(C)_3]\} - H_s$ (**8P**). The remaining group contributions are known from earlier combustion work on azoalkanes.[1] Thus $\Delta H_H = 2(-1.74 + 0.26) - H_s\,(\mathbf{8P}) = -8.5$, and H_s (**8P**) = 5.5 kcal/mol, which is lower than H_s of hexamethylethane.[76] Using this value, we may compare the stabilization energy of **9P** with that of analogous benzylic radicals, as shown in Table VIII. The

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(68) By analogy, ΔH_f (styrene) is predicted exactly as the average of the experimental ΔH_f (*trans*-stilbene) and ΔH_f (ethylene).

(69) Engel, P. S.; Chen, Y.; Wang, C. *J. Am. Chem. Soc.* **1991**, *113*, 4355.

(70) We thank Professor Michael L. McKee of Auburn University for this calculation.

(71) The RSE of allyl radical has been calculated very recently relative to ethyl as 13.9 kcal/mol.[72]

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(76) The experimental ΔH_f(g) of −53.82 ± 0.49 kcal/mol of hexamethylethane[77] leads to H_s = 5.7 kcal/mol using Benson's group values[78] and to H_s = 7.1 kcal/mol using Schleyer's single-conformation group increments.[79] The MM2 value of H_s is 6.9 kcal/mol.[48a]

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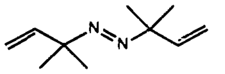
value of H_s for the model compound hexamethylethane is from a force field calculation,[48a,76] while H_s for bicumyl is an experimental value.[80] To obtain the strain energy contribution to $\Delta G^{\ddagger}$ ($\Delta G^{\ddagger}_s$), we have simply used the slope of the published plots[48a] of $\Delta G^{\ddagger}$ versus H_s. Subtracting $\Delta G^{\ddagger}_s$ from $\Delta G^{\ddagger}$ gives $\Delta G^{\ddagger}_e$, the activation free energy for C–C bond homolysis if resonance stabilization of the radicals were the only influence. Finally, we calculated the RSE of the azo substituent relative to the methyl substituent as one-half of the decrease in $\Delta G^{\ddagger}_e$ caused by replacing X = CH_3 in **27** with a new substituent.

Before discussing the RSEs we must point out that the compounds in Table VIII were thermolyzed in temperature ranges from 70 to 470 °C. If $\Delta S^{\ddagger}$ for all homolyses were the same, the difference in $\Delta G^{\ddagger}$ would be independent of temperature. Even though $\Delta S^{\ddagger}$ varies from one compound to the next, the error in RSE is minimized by calculating $\Delta G^{\ddagger}$ at 150 °C, which is not far from the experimental temperature range for all compounds except hexamethylethane. RSE should really be based on activation enthalpies, so that an entropy correction[48a] should be applied to the last column of Table VIII. However, because $\Delta S^{\ddagger}$ values are notoriously sensitive to errors, we have employed only $\Delta G^{\ddagger}$ in calculating RSE.

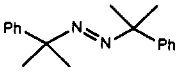
According to Table VIII, the RSE of phenyl is 9.9 kcal/mol, while that of radical **9P** is considerably greater at 15.3 kcal/mol. Using the reported rate constants for various *p*-methoxy-substituted compounds **5**,[10] we calculated an average value of $\Delta H^{\ddagger}$ and $\Delta S^{\ddagger}$ for the series, assuming that the substituent effect was much less than the experimental error in the kinetics of each particular member. The RSE of a phenyl group and an α-arylazo group acting together is seen to be only 3.1 kcal/mol greater than the α-arylazo group alone. It might be argued that because **9P** benefits from two methyl groups, the RSE of Ph—N=N—$CH_2^{\bullet}$ would be less than 15.3 kcal/mol, so that the effect of α-phenyl in Ph—N=N—$CH^{\bullet}$-Ph actually exceeds 3.1 kcal/mol. However, the effect of the methyls would surely be no more than a few kilocalories/mole, leading us to suggest that the unusually small stabilization by α-phenyl in **5** is due to the lower spin density on carbon than on nitrogen in the hydrazonyl radical.[16-18,53]

In order to compare the RSE of **9P** with that of dimethylallyl, we require $\Delta G^{\ddagger}_e$ for **27** (X = vinyl). Although this compound would undergo the Cope rearrangement[82-84] before dissociating, the reliable activation parameters[1] for **28** and **29** coupled with the known relationship between azoalkane lability and radical stability[1] suggest that dimethylallyl is 0.6 kcal/mol more stable than cumyl. According to this treatment, the RSE of **9P** (15.3 kcal/mol) including its phenyl group is 4.8 kcal/mol greater than the (9.9 + 0.6) kcal/mol RSE of α,α-dimethylallyl. It would be desirable to study the C–C homolysis of a compound lacking the phenyl group, but **8B** mainly breaks the wrong bond. Nevertheless, we shall see shortly that a lower limit on the phenyl contribution to the RSE of **9P** can be deduced from our results on **8B**.



28

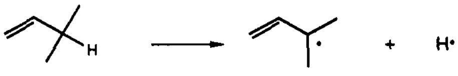
$\Delta G^{\ddagger}$ (25 °C) = 24.6 kcal/mol



29

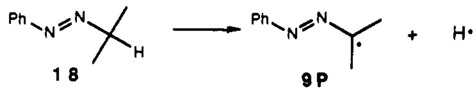
$\Delta G^{\ddagger}$ (25 °C) = 25.7 kcal/mol

Another approach to comparing the phenylazo and vinyl substituents is simply to determine the C–H bond dissociation energy of the analogous compounds **30** and **18**.[85] The BDE of **30** (D_{10}) has been reported as 80.3 ± 1.5 kcal/mol[86] and 81.7 ± 1.2 kcal/mol,[87] while that of **18** (D_{11}) is calculable from a thermochemical cycle and our thermolysis data for **8P**: $D_{11} = (D_1 + 104.2 - \Delta H_H)/2$. D_1 is the C–C BDE of **8P** (cf. eq 1, R = Ph), 104.2 kcal/mol is the BDE of hydrogen, and ΔH_H is the hydrogenation heat of **8P** (eq 9). The greatest uncertainty in the above equation is associated with D_1, which equals $\Delta H^{\ddagger}$ of **8P** → **9P** if there is no activation energy associated with recombination, as is the usual case.[48a,b] Our data show that $\Delta H^{\ddagger}$ (**8P** → **9P**) is 30.6 ± 0.5 kcal/mol and $\Delta S^{\ddagger} = -4.1 \pm 1.7$ eu, but if $\Delta S^{\ddagger}$ were +10 eu, as is usually observed in the thermolysis of compounds **27**, $\Delta H^{\ddagger}$ would be 36.4 kcal/mol. However, the low $\Delta S^{\ddagger}$ of **8P** → **9P** should be more correct since several bond rotations are frozen out during radical formation, bond scission reactions that afford delocalized radicals often have low activation entropies,[1] and the activation parameters are based on 8 kinetic points spanning 28°. Weighting the lower $\Delta H^{\ddagger}$ more heavily, we obtain $D_{11} = (32.5 \pm 3 + 104.2 + 8.5)/2 = 72.6 \pm 1.5$ kcal/mol, which is 8.4 ± 2.5 kcal/mol less than D_{10}. While this uncertainty seems large, it is actually no greater than that of most BDE differences,[88] especially considering that several precisely stated BDEs turned out to be inaccurate.[81]



30

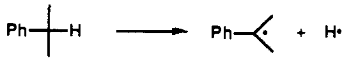
(10)



18 **9P**

(11)

As an aside, we may apply the same procedure to bicumyl and cumene. ΔH_H of the central C–C bond of bicumyl is $2\Delta H_f$ (cumene) − ΔH_f (bicumyl)[80] = 2(0.9) − 13.7 = −11.9 kcal/mol, while the BDE of this bond (D_{13}) is $\Delta H^{\ddagger}$ (bicumyl → 2cumyl) = 45.7 kcal/mol.[48a] Thus $D_{12} = (45.7 + 104.2 + 11.9)/2 = 80.9$ kcal/mol, which is below the reported value of $D_{12} = 84.4 \pm 1.5$ kcal/mol[88] but is encouragingly similar to D_{10}.



(12)

(13)

The totally different thermolysis behavior of **8P** versus **8B** suggests that the central C–C bond of **8P** is weakened by resonance stabilization of **9P** that is lacking in **9B**. An estimate of the radical stabilization due to the phenyl group can be obtained from $\Delta G^{\ddagger}$ for C–C homolysis of compounds **8P** and **8B** (cf. Figure 2). Although C–C scission of **8B** is a very minor reaction pathway, a minimum $\Delta G^{\ddagger}$ for this process is calculated as follows. The observed GC peak area ratio of ATBH to TME was less than 1:2450, corresponding to a molar ratio of <1:1800 if estimated FID factors are applied. From Scheme II, we derive the expression $[\mathrm{TME}]/[\mathrm{ATBH}] = (k_4/k_8)(k_5/(k_5 + k_6[\mathrm{PhSH}]))$, but the thiol term is negligible because so little **10B** is diverted to **20**. The molar ratio of ATBH to TME then corresponds to $k_4/k_8 > 1800$, which translates to a value of $(\Delta G_8^{\ddagger} - \Delta G_4^{\ddagger}) = 6.3$ kcal/mol at 150 °C. (All subscripts here refer to Scheme II.) Since C–N cleavage of **8B** exhibits $\Delta G_4^{\ddagger}$ (150 °C) = 34.0, $\Delta G_8^{\ddagger}$ for C–C homolysis is at least 40.3 kcal/mol at 150 °C. We do not know $\Delta S_8^{\ddagger}$ for **8B** → **9B**, but it is surely above the ∼−4.1 eu found for **8P**, because formation of **9B** freezes out fewer bond rotations than formation of **9P**, and because $\Delta S^{\ddagger}$ often parallels $\Delta H^{\ddagger}$ for a series of reactions, even bond homolyses.[89] If we assume that $\Delta S^{\ddagger}$ = 10 eu, D_1 for R = *t*-Bu exceeds 44.5 kcal/mol. Then D_{14} > (44.5

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(85) Caution is necessary in using BDE values as a measure of radical stability because relative BDEs depend on the type of bond being cleaved. See: Nicholas, A. M. P.; Arnold, D. R. *Can. J. Chem.* **1984**, *62*, 1850.

(86) Trenwith, A. B. *Trans. Faraday Soc.* **1970**, *66*, 2805; Trenwith, A. B.; Wrigley, S. P. *J. Chem. Soc., Faraday Trans. 1* **1977**, *73*, 817.

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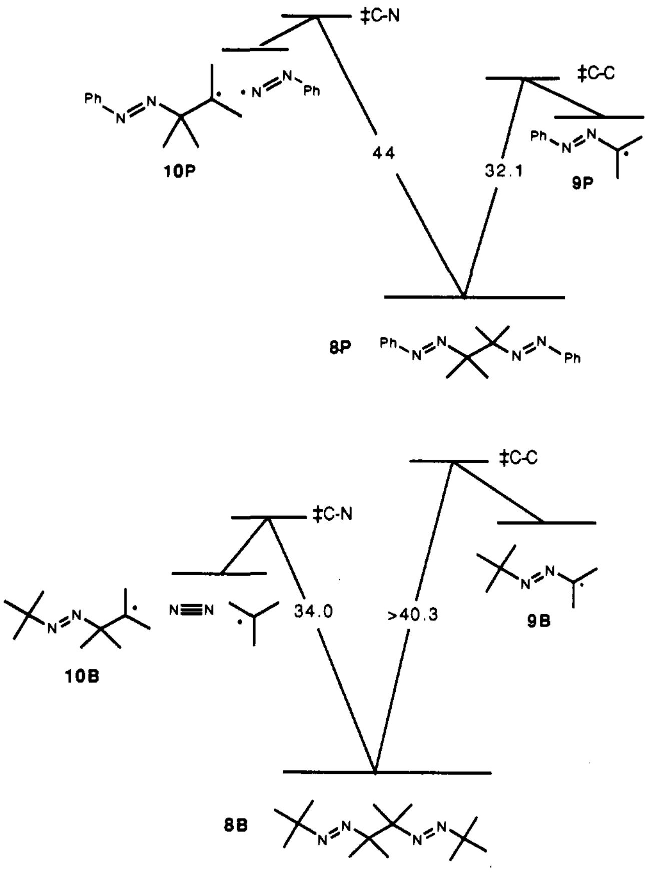
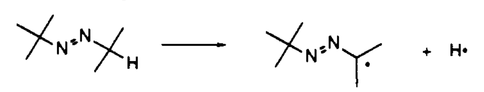


Figure 2. Free energy diagram (kcal/mol, 150 °C) for C–C and C–N cleavage of **8P** and **8B**.

+ 104.2 + 8.5)/2 = 78.6 kcal/mol, where the ΔH_H of **8B** is assumed to equal that of **8P**. The resonance stabilization due to phenyl in **9P** must therefore exceed (78.6 – 72.6) = 6 kcal/mol. This figure, which is admittedly crude, is similar to the 5.4 kcal/mol RSE difference between the allyl and 1-phenylallyl radicals[90] and may well account for the roughly 8.4 kcal/mol difference between D_{10} and D_{11}. Since D_{14} is similar to D_{10}, the α-azo group is little or no more stabilizing of a radical center than is a vinyl group.[85] Our results do not allow us to state whether azo is less stabilizing than vinyl, as predicted by theory (see above), because the miniscule ATBH peak, on which this analysis is based, may be left over from the preparation of **8B** rather than being a thermolysis product. By changing the *tert*-butyl groups in **8B** to poorer incipient radicals, we expect in future work to raise $\Delta G^{\ddagger}$ for deazatation. Quantifying the hydrazone produced on thermolysis should then allow us to calculate activation parameters for the central C–C bond homolysis of a purely aliphatic vicinal bis(azo)alkane and thus evaluate D_{14} more reliably.



(14)

To complete the discussion of Figure 2, we consider the C–N homolysis of **8P** and **8B**. This process in **8B** requires 34.0 kcal/mol, according to our kinetic measurements. Since C–N homolysis does not occur in **8P**, we can only estimate that it would require 44 kcal/mol, by comparison with other phenylazo *tert*-alkanes.[91] The second azo group of **8B** does not accelerate C–N homolysis relative to **20**; hence, the same should hold true for **8P**.

In summary, vicinal bis(azo)alkanes can undergo two thermolytic reactions: (a) cleavage of the central C–C bond to generate hydrazonyl radicals (e.g., **8P** → **9P**) or (b) the usual homolysis of one C–N bond to generate a short-lived β-azo radical (e.g., **8B** → **10B**). C–C cleavage dominates in **8P** because the phenyl group of radical **9P** imparts at least 6 kcal/mol additional resonance stabilization. Without the phenyl group, an azo group stabilizes a carbon-centered radical little or no better than does a vinyl group. The free energy diagram for the system **8P** ⇄ **9P** ⇄ **16P** quantifies the observation that **16P** is the kinetic product of radical dimerization while **8P** is the thermodynamic product.

Experimental Section

General Methods. Melting points (uncorrected) were obtained on a Mel-Temp apparatus. Thiophenol, *tert*-butyl mercaptan, benzene, and toluene were purified by distillation. The NMR solvents $CDCl_3$, C_6D_6, and $C_6D_5CD_3$ from Cambridge Isotope Laboratory were used without further purification.

NMR spectra were obtained on a JEOL FX-90Q, an IBM AF-300, or an IBM AF-250 spectrometer; chemical shifts (δ, ppm) were based on internal TMS, hexamethyldisiloxane (^1H δ = 0.115), or solvent signal ($CDCl_3$ ^1H δ = 7.25, ^{13}C δ = 77.0; C_6D_6 ^1H δ = 7.15, ^{13}C δ = 128.5) as reference. UV–vis spectra were run on either a Cary 17 or a Hewlett-Packard 8452A diode array spectrometer. Low-resolution mass spectra were obtained on a Finnigan 3300 spectrometer, and high-resolution mass spectra were obtained on a CEC Du Pont 21-110B spectrometer. The elemental analysis was done at Desert Analytics laboratory. Differential scanning calorimetry was carried out on a Perkin-Elmer DSC-2.

HPLC analyses were conducted with a Beckman Model 342 HPLC system equipped with a Model 165 dual variable wavelength UV detector whose output was interfaced to a PC-AT computer. A 25-cm Alltech Silica 600-Si column was used for general HPLC work, and a 25-cm Alltech C_{18} 5μ column was used for reverse-phase HPLC. GC analyses were carried on a Hewlett-Packard 5890 instrument with FID and TC detectors. This GC was interfaced to an IBM-XT-compatible computer to allow storage, peak integration, and manipulation of chromatograms. Preparative GC was carried out on an Antek 300 with a TC detector.

All samples for thermolysis or photolysis were freeze–thaw degassed three times and sealed on a vacuum line, using liquid nitrogen (–196 °C) or dry ice–2-propanol (–78 °C) as a cooling bath. Samples for thermolysis were immersed completely in a DC-200 silicone oil bath contained in a 1.5-gal Dewar flask with a mechanical stirrer. The temperature was regulated by a Bayley Model 123 temperature controller and was measured with a Hewlett-Packard Model 3456A digital voltameter and a platinum thermometer.

An Oriel 500-W high-pressure mercury lamp was usually employed in photolysis work except where otherwise specified. The filters are summarized as follows: >254 nm direct irradiation in a quartz NMR tube or UV cell; >280 nm, direct irradiation in a Pyrex NMR tube or UV cell; 313 nm, a 10-cm length of aqueous potassium chromate (5.0 × 10^{-4} M) with a Corning 7-54 glass filter; 366 nm, a 5-cm length of 2,7-dimethyl-3,6-diazacyclohepta-1,6-diene perchlorate (10 mg/100 mL water) with a Corning 7-60 glass filter; and 435 nm, a 10-cm length of aqueous sodium nitrite (7.5 g/100 mL).

Gas yields were measured with a Töpler pump and a gas buret. A liquid nitrogen trap between the sample and the Töpler pump was used to ensure that only nitrogen was collected. The collected gas could be analyzed on the Antek 300 GC equipped with a Porapak-Q column at 25 °C to check for contamination of the nitrogen.

1,4-Diphenyl-3,3,6-trimethyl-1,2,4,5-tetraazahepta-1,5-diene (16P) was made by the method of Whyburn[33] and Theilacker.[34] The crude product was purified by recrystallization from methanol at –15 °C, giving **16P** as yellow crystals in 95% yield: mp 83.0–87.0 °C. UV (hexane): λ_{max} = 422 nm; ϵ = 131. ^1H NMR (250 MHz, C_6D_6): δ (ppm) 1.56 (3 H, s), 1.66 (6 H, s), 1.72 (3 H, s), 7.08–7.14 (3 H, m), 7.46 (1 H, d), 7.89 (1 H, d).

2,3-Dimethyl-2,3-bis(phenylazo)butane (8P). Three grams of **16P** and 15 mL of C_6H_6 were placed into a 25-mL glass tube fitted with a 14/30 standard taper joint, and the solution was degassed three times and sealed under vacuum. The tube was immersed in a 110 °C oil bath and heated over 40 h. After removal of the benzene by rotary evaporation, the brown oil was purified by recrystallization from methanol at –15 °C. **8P** was obtained in 80% yield: mp 68.8–69.3 °C. UV (hexane): λ_{max} = 410 nm; ϵ = 258. ^1H NMR (250 MHz, C_6D_6): δ (ppm) 1.51 (12 H, s), 7.10 (4 H, m), 7.80 (6 H, m). ^{13}C NMR (C_6D_6): δ (ppm) 21.55, 75.32, 129.58, 130.28, 152.82. Anal. Calcd: C, 73.44; H, 7.53; N, 19.03. Found: C, 73.53; H, 7.84; N, 19.00. For combustion calorimetry, the sample was purified by multiple recrystallizations from methanol and removal of residual solvent under vacuum. As measured by DSC, the purity of the sample was about 99.8%.[92]

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2,3-Dimethyl-2,3-bis(*tert*-butylazo)butane (8B). In a 100-mL flask equipped with a magnetic stirrer and a water condenser, 0.5 g of acetone *tert*-butylhydrazone[93] (3.9 mmol) was mixed with 15 mL of acetone. A 1.0-g portion of $KMnO_4$ (6.3 mmol) dissolved in 40 mL of acetone was added dropwise under refluxing. After refluxing for 3 h, the solution was filtered to remove all solids. The residue was rotary evaporated and was extracted with Et_2O to obtain crude product. After removal of the ether, the crude product (28% yield based on *tert*-butylhydrazine) was purified by recrystallization from methanol: mp 43.5–44.2 °C. UV(hexane): $\lambda_{max} = 372$ nm; $\epsilon = 36$. ^1H NMR (300 MHz, C_6D_6): δ (ppm) 1.21 (18 H, s), 1.32 (12 H, s). ^{13}C NMR (C_6D_6): δ (ppm) 73.15, 66.87, 26.92, 21.01. Anal. Calcd for $C_{14}H_{30}N_4$: 254.2470. Found: 254.2468.

Thermolysis kinetics of **8B** monitored by UV spectroscopy gave the following rate constants: T (°C), 10^4k (s^{-1}); 153.46, 0.327; 164.29, 0.953; 171.68, 1.93; 174.13, 2.20. The decomposition products of **8B** (cf. Table VII) were analyzed by GC under the following conditions: injector temperature 140 °C, detector temperature 160 °C initial oven temperature 35 °C, initial time 10 min, program rate 10 deg/min, final oven temperature 150 °C.

2,3-Dimethyl-2-(*tert*-butylazo)butane (20). Into a three-necked flask equipped with a magnetic stirrer, a nitrogen inlet, and an addition funnel and containing a solution of 1.97 g (19.3 mmol) of 2,3-dimethyl-2-butanol in 25 mL of hexane cooled in ice was added dropwise with stirring 5 mL of a hexane solution of 2.74 g (19.4 mmol) of chlorosulfonyl isocyanate. After the addition was complete, the reaction mixture was stirred in the cold for 1.5 h and was then allowed to stand at room temperature overnight under nitrogen. The following day, the white precipitate that formed during the addition had disappeared and two liquid layers were present. The bottom layer, a reddish oil, was the sulfamoyl chloride. ^1H NMR (300 MHz, $CDCl_3$): δ (ppm) 0.98 (6 H, d), 1.45 (6 H, s), 1.90 (1 H, septet), 5.56 (1 H, br s).

Under nitrogen, 1.54 g (21.1 mmol of *tert*-butylamine, 2.1 g (19.1 mmol) of triethylamine, and 50 mL of ether were placed into a 250-mL three-necked flask cooled to −78 °C. The above crude sulfamoyl chloride (both layers) in 20 mL of ether was added dropwise to the flask with stirring over 50 min, causing formation of a white precipitate. The reaction mixture was stirred at −78 °C for 2.5 h and at room temperature for 1.5 h. The product mixture was washed with water (3 × 25 mL), dried over sodium sulfate, rotary evaporated, and evacuated. The white solid weighed 1.4 g (5.9 mmol), corresponding to a 31% yield based on 2,3-dimethyl-2-butanol. ^1H NMR (300 MHz, $CDCl_3$): δ (ppm) 0.92 (6 H, d), 1.32 (6 H, s), 1.37 (9 H, s), 1.85 (1 H, septet), 4.04 (2 H, br m).

To 0.65 g of the above sulfamide in a 100-mL three-necked flask were added 10 g of Clorox (5.25% NaClO) and 40 mL of pentane. A 7.0-mL portion of 1 N aqueous NaOH was then added dropwise to the stirred suspension over 3 min, and the reaction mixture was stirred at room temperature for 80 min. The pentane layer was washed with water (3 × 15 mL), dried over potassium carbonate, and rotary evaporated to yield a pale yellow liquid. The crude product was purified by silica gel column chromatography using hexane as eluent. The pure product weighed 0.26 g (56.5% yield). UV (hexane): $\lambda_{max} = 372$ nm; $\epsilon = 14.5$ ^1H NMR (300 MHz, C_6D_6): δ (ppm) 0.89 (6 H, d), 1.09 (9 H, s), 1.22 (6 H, s), 2.21 (1 H, m). ^{13}C NMR (C_6D_6): δ (ppm) 17.54, 25.92, 36.57, 66.32, 70.87. Thermolysis kinetics on **20** gave the following rate constants: T (°C), 10^4k (s^{-1}): 172.35, 0.832; 178.49, 1.59; 183.90, 2.72; 190.90, 5.35.

2-(Phenylazo)propane (18). In a three-necked flask equipped with a mechanical stirrer and a nitrogen inlet was dissolved 2 g (14 mmol) of acetone phenylhydrazone in 15 mL of methanol. The pH of the methanol solution was adjusted to 3 with 20% HCl. Then 1 g (0.016 mol) of $NaBH_3CN$ was added in small portions with stirring. The reaction was monitored by TLC (silica), using 15% EtOAc in hexane as eluent. After the reaction was complete, the product was extracted with ether (3 × 15 mL), washed with water, and dried over $MgSO_4$. The solution was filtered and was then treated with HgO (3 g, 0.014 mol) followed by stirring at room temperature for 30 min. The product mixture was filtered and rotary evaporated to yield an orange-colored liquid weighing 1.8 g (90% yield). Further purification was achieved by short-path distillation under vacuum (4–5 mmHg, bath at 40 °C). UV (hexane): $\lambda_{max} = 406$ nm; $\epsilon = 145$. ^1H NMR ($CDCl_3$): δ (ppm) 1.39 (6 H, d), 3.91 (1 H, septet), 7.43 (3 H, m), 7.66 (2 H, m). ^{13}C NMR (250 MHz, $CDCl_3$): δ (ppm) 20.61, 68.50, 122.06, 128.91, 130.16, 152.12.

Oxidation of Acetone Phenylhydrazone by NiO_2. Into a three-necked flask equipped with a magnetic stirrer, a nitrogen inlet, and a thermometer were placed 0.5 g (3.38 mmol) of acetone phenylhydrazone and 10 mL of toluene. The solution was held at a known temperature (cf. Table IV), and 0.61 g (6.73 mmol) of NiO_2[94] was added with stirring. After 10–60 min, the suspension was filtered, and the filtrate was analyzed by HPLC using the following conditions: column, Alltech C_{18}, ODS (reverse phase), particle size 5 μm, 4.6-mm i.d. × 25 cm; solvent, 18% (99.5% CH_3CN/0.5% Et_3N)/82% (85% MeOH/15% H_2O); flow rate, 1 mL/min; detector, UV, 280-nm wavelength. In order to quantify the ratio of C–N to C–C dimer, a calibration line was made by analyzing mixtures of known molar ratio.

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Polysaccharides as Amphiphiles

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Abstract: Polysaccharide chains are usually considered to be highly hydrophilic, since they contain no obvious apolar moieties but a large number of hydroxyl groups. However, it is possible even for these chains to display hydrophobic character, arising out of stereochemical constraints on the chain. We present experimental and theoretical evidence which show that the α-1*a*,4*e*-D-glucopyranose chains, namely linear dextrin, display amphiphilic properties, since all the hydroxyl groups are disposed on one side or face of the chain and the hydrogens disposed on the other. As a result, dextrin solubilizes lipophilic compounds in water, retards organic reactions that are hydrophobically accelerated in water, destabilizes globular protein chains, and binds to a fluorescent probe dye and enhances its emission. In contrast, the β-1,4-linked glucoside cellulose and the α-1,6-linked dextran chains exhibit only hydrophilicity. Several other oligosaccharide chains are also predicted to display amphiphilic properties. This is expected to be relevant to intermolecular recognition on cell surfaces, lectin-sugar binding, antigen–antibody interactions, and the like.

Sugar molecules are usually thought of as essentially hydrophilic, because of their high water solubility, multiple hydroxyl groups, and lack of alkyl or aryl groups. Yet, as the cyclic oligosaccharides called cyclodextrins[1,2] exemplify, appropriate ste-

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