Methylenecyclopropane Rearrangement as a Probe for Free Radical Substituent Effects. $\sigma^{\bullet}$ Values for Potent Radical-Stabilizing Nitrogen-Containing Substituents

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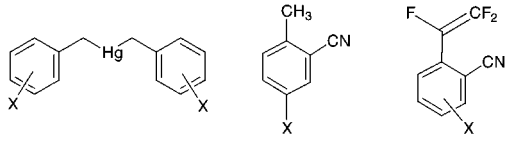
A series of nitrogen-containing 2-aryl-3,3-dimethylmethylenecyclopropanes have been prepared and rearrangement rates to the corresponding 2-arylisopropylidenecyclopropanes have been measured. These rates are dependent on the nature of the nitrogen-containing group in the *para*-position of the aryl group. Rearrangement rates have been used to calculate $\sigma^{\bullet}$ values, which are a measure of the radical stabilizing ability of the substituent. Groups such as *p*-N=N−Bu-*t*, *p*-CH=N−Bu-*t*, *p*-NH_2, *p*-CH=N−OH, and *p*-CH=N−OCH_3, are "good" radical stabilizers. We have also classified groups such as *p*-CH=N−NMe_2, *p*-N=N−Ph, *p*-N=N(O)-Bu-*t*, *p*-CH=N(O)-Bu-*t*, and *p*-CH=N−O^- M^+, which have an extraordinarily large radical stabilizing effect, as "Super Stabilizers". These substituents stabilize the transition state of the methylenecyclopropane rearrangement by extensive spin delocalization. In the case of the latter three substituents, nitroxyl type stabilization is proposed. Density functional calculations (B3LYP/6-31G*) have been carried out on a series of nitrogen-containing substituted benzylic radicals. Rates of the methylenecyclopropane rearrangement correlate with radical stabilization energies (ΔE) determined from an isodesmic reaction of substituted benzylic radicals with toluene. These calculations confirm substantial spin delocalization onto the nitrogen-containing substituents on the *para*-position of the benzylic radical.

A number of scales have been developed over the last 20 years to quantify the ability of substituents to stabilize a carbon-centered free radical. Some examples are Jackson's scale based on pyrolysis rates of dibenzylmercurials **1**,[1] Fisher's scale based on the free radical bromination of **2**,[2] and Jiang's cyclodimerization rates of **3**.[3] Neumann has evaluated radical-stabilizing effects from the dissociation equilibrium constant of substituted triphenylmethyl dimers,[4] while Bordwell has deduced bond dissociation energies from pK_a's of substituted fluorenes and the oxidation potential of their anions.[5]



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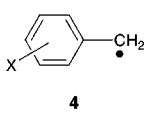

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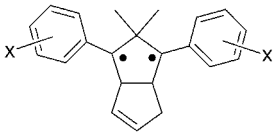

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Two of the published scales do not involve kinetics or equilibria, but instead they rely on the ESR spin density of substituted benzylic radicals **4**[6,7] and on the zero-field splitting parameter *D* of cyclopentane-1,3-diyl biradicals **5**.[8] One of the present authors proposed a $\sigma^{\bullet}$ scale based on the rearrangement rate of substituted methylenecyclopropanes **6** to their isomers **8**,[9] while another has published thermolysis rates of several α-substituted azoalkanes **9**.[10−12] The azoalkane-based scale was pioneered by Timberlake[13] and others,[14] but more recent results suggest the intervention of polar effects.[15] Theoretical calculations of increasing sophistication have also yielded reasonable radical-stabilization energies.[8,16−20]

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(1) Jackson, R. A. *J. Organomet. Chem.* **1992**, *437*, 77−83.
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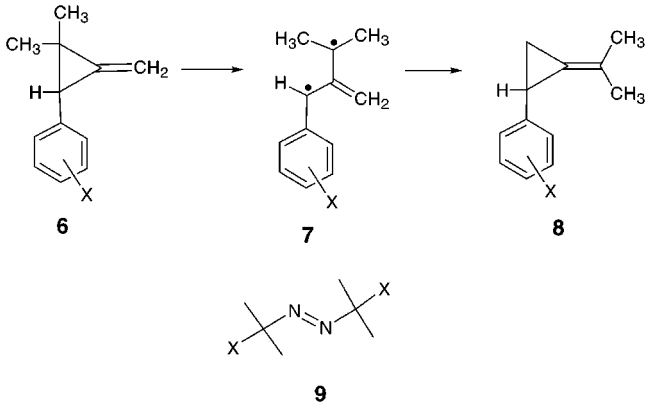
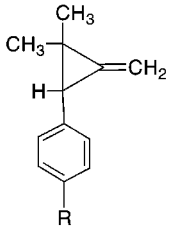
Comparison of the various scales is hampered in many cases by an insufficient number of substituents in common.



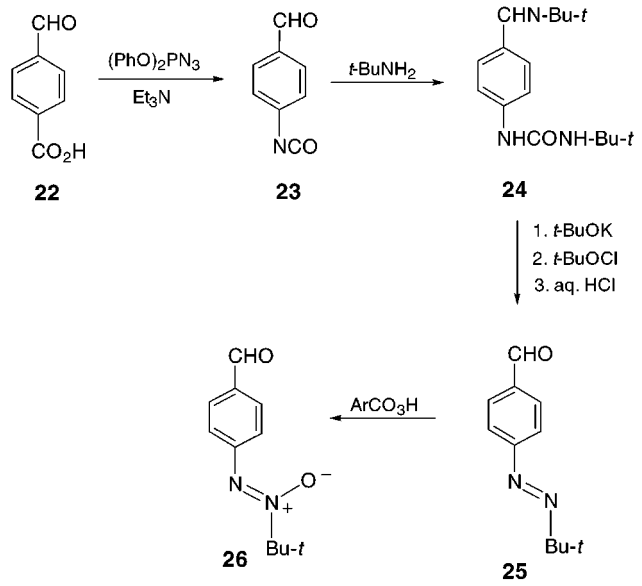
The Creary scale[9] is appealing because polar effects are minimal in breaking the strained cyclopropane bond.[3,7] The arylmethylenecyclopropanes present some synthetic challenges since the cyclopropane must be generated in the presence of the aryl substituent or the substituent must be introduced in the presence of the strained ring without heating above ~50 °C. Nevertheless, a large number of substrates of type **6** have been prepared and studied in the past. Our recent interest in the radical-stabilizing ability of the azo[21−23] and azoxy groups[24] has now led us to determine the rearrangement rates of compounds **10**−**12**. For comparison with **10**−**12**, we have also studied the nitrone derivative **13**, the Schiff base **14**, the amine **15**, the azide **16**, the hydrazone **17**, and the phenylazo compound **18**. Finally, we studied three oxime derivatives, **19**−**21**. With the exception of NH_2 and Ph−N=N, these substituents are not included in any of the existing radical stabilization scales, yet some of them had the potential to be extraordinary radical stabilizing groups. Reported here are the results of these studies.



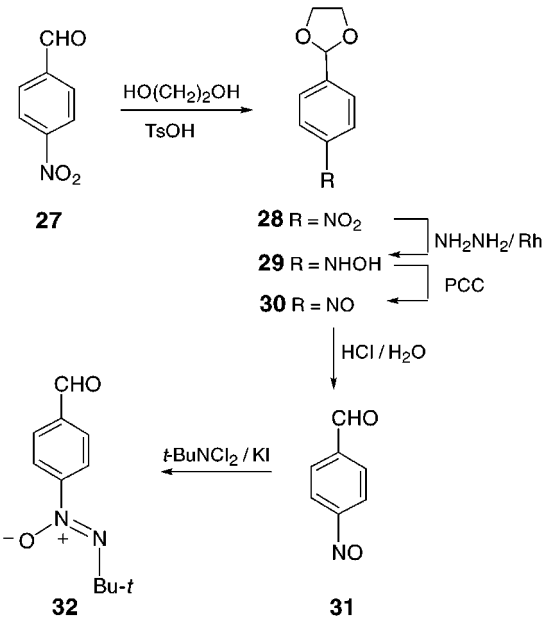
10 R = N=N-Bu-*t*
11 R = N=N(O)-Bu-*t*
12 R = N(O)=N-Bu-*t*
13 R = CH=N(O)-Bu-*t*
14 R = CH=N-Bu-*t*
15 R = NH_2
16 R = N_3
17 R = CH=N-NMe_2
18 R = N=N-Ph
19 R = CH=N-OCH_3
20 R = CH=N-OH
21 R = CH=N-O^- M^+

Results

Syntheses of 10−12. Attempts to formylate phenylazo-*tert*-butane[25−27] using $POCl_3$/DMF[28] or $SnCl_4$/$CHCl_2OMe$[29] led to recovery of starting material, but the following route gave the requisite azoaldehyde **25** in low yield. *p*-Formylbenzoic acid was converted[30] to *p*-formylphenylisocyanate **23**,[31] which was then reacted with *tert*-butylamine to form Schiff base urea **24**.[32] Hypochlorite oxidation[33] and hydrolysis afforded *p*-formylphenylazo-*tert*-butane **25**, the precursor to **10**, while treatment of **25** with *m*-chloroperbenzoic acid[34] gave azoxy compound **26**, the precursor to **11**.



The transformation of *p*-nitrosobenzaldehyde **31** to **32** by Kovacic's method[35] was carried out in 78% yield. However, in our hands, the reported[36,37] synthesis of *p*-nitrosobenzaldehyde, **31**, from *p*-nitrobenzaldehyde, **27**, was not reproducible, probably because the intermediate hydroxylamine from reduction of **27** can condense with an aldehyde group. We therefore protected **27** as the ethylene acetal before converting nitro to nitroso.[38,39] In this manner, the synthesis of **32** could be achieved in 48% overall yield from **27**.



The desired methylenecyclopropanes were prepared from **25**, **26**, and **32**, in the usual manner: conversion of aldehyde to tosylhydrazone, reaction of tosylhydrazone

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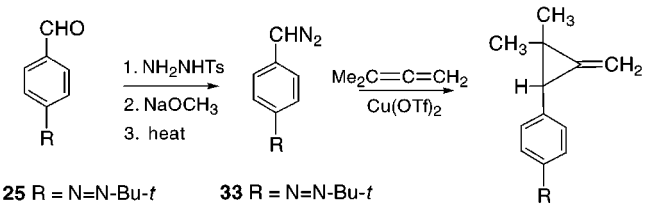
with base, pyrolysis of the tosylhydrazone salt, and Cu(OTf)$_2$-catalyzed decomposition of the resulting diazo compound in the presence of 1,1-dimethylallene.[9]



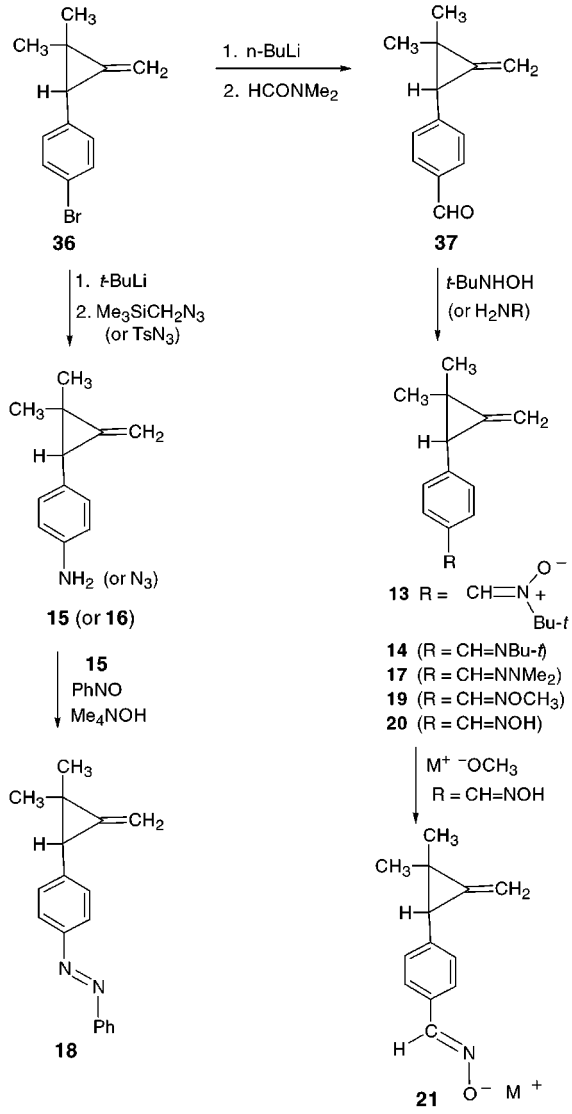
25 R = N=N-Bu-*t* **33** R = N=N-Bu-*t*
26 R = N=N(O)-Bu-*t* **34** R = N=N(O)-Bu-*t*
32 R = N(O)=N-Bu-*t* **35** R = N(O)=N-Bu-*t*

10 R = N=N-Bu-*t*
11 R = N=N(O)-Bu-*t*
12 R = N(O)=N-Bu-*t*

Syntheses of 13−21. The *p*-bromophenylmethylenecyclopropane **36**[40] provided a convenient starting material for the preparation of a variety of substrates. Lithiation of **36** with *n*-butyllithium followed by reaction with dimethylformamide gave the key aldehyde **37**. This was converted to the nitrone **13** by reaction with *N*-*tert*-butylhydroxylamine. Likewise, the imine **14** and the hydrazone **17** could be prepared by the toluenesulfonic acid-catalyzed condensation of **37** with *tert*-butylamine and 1,1-dimethylhydrazine, respectively. The O-methylated oxime derivative **19** and the simple oxime **20** were also prepared from **37** using *O*-methylhydroxylamine hydrochloride and hydroxylamine hydrochloride, respectively. Deprotonation of the oxime derivative **20** with alkali metal methoxides in DMSO gave the anions **21**.

Amine **15** and azide **16** were prepared by lithiation of **36** followed by reaction with trimethylsilylmethyl azide[41] and toluenesulfonyl azide,[42,43] respectively. Base-catalyzed condensation of **15** with nitrosobenzene afforded the phenylazo compound **18**.[44]

Kinetic Studies. Methylenecyclopropanes **10**−**19** were thermally rearranged to the corresponding isopropylidenecyclopropanes **8** in C_6D_6, while **20** and the anionic substrates **21a**−**d** were thermally rearranged in DMSO-d_6. Rate data and the corresponding $\sigma^\bullet$ values are summarized in Tables 1 and 2. To eliminate errors due to potential temperature differences in kinetic studies carried out in two different laboratories, rates of the parent compound **6** (X = H) were determined in both



laboratories. Relative rate data from each laboratory were used in determining $\sigma^\bullet$ values for compounds studied in that laboratory. All of the substrates **10**−**21** rearrange faster than the unsubstituted derivative **6** (X = H). The observed rate enhancements indicate that the nitrogen-containing substituents stabilize the developing benzylic radical intermediate **7** to varying degrees.

Discussion

Consider first the magnitude of the rate enhancements that have previously been observed in the methylenecyclopropane rearrangement. Since the developing radical center is insulated from the substituent by the aromatic ring, substituent effects are attenuated. Some rate enhancements are "small", i.e., in the range of 1.3−1.5 for groups such as *p*-CH_3 and *p*-Cl.[45] In contrast, unsaturated conjugating groups such as cyano, nitro, and vinyl are "moderate" to "good" radical stabilizers, showing rate enhancements (k_{rel}'s) of 2.87, 3.76, and 4.67, respectively.[9] On the basis of k_{rel}'s of 4.85 and 3.97 in **10** and **14**, the unsaturated groups *p*-N=N−Bu-*t* and *p*-CH=N−Bu-*t* are classified as "good" radical stabilizers. Spin delocalization in the biradical intermediate, as in **38** and **39**, accounts

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(45) Creary, X. J. *Org. Chem.* **1980**, *45*, 280−284.

Table 1. Rearrangement Rates and $\sigma^\bullet$ Values of Methylenecyclopropanes in C_6D_6

substrate	T, °C	k (s^{-1})	$\Delta H^\ddagger$ (kcal/mol)	$\Delta S^\ddagger$ (eu)	k_{rel}	$\sigma^\bullet$
6 (*p*-H)	80.0	5.57×10^{-5}	27.4	−0.8	1.00	0.00
	70.0	1.72×10^{-5}				
	60.0	5.05×10^{-6}				
6 (*p*-H)[a]	80.1	5.86×10^{-5}				
	80.0[b]	5.78×10^{-5}	27.7	0.2	1.00	0.00
	70.1	1.79×10^{-5}				
	60.2	5.23×10^{-6}				
12 (*p*-N(O)=NBu-*t*)	80.0	1.11×10^{-4}	26.3	−2.4	2.00	0.30
	70.0	3.60×10^{-5}				
	60.0	1.10×10^{-5}				
16 (*p*-N_3)[a]	80.1	1.41×10^{-4}				
	80.0[b]	1.40×10^{-4}	26.4	−1.7	2.41	0.38
	70.1	4.55×10^{-5}				
	60.2	1.41×10^{-5}				
14 (*p*-CH=NBu-*t*)	80.0	2.14×10^{-4}	26.8	0.4	3.97	0.60
	70.0	7.22×10^{-5}				
	60.0	2.04×10^{-5}				
10 (*p*-N=NBu-*t*)	80.0	2.70×10^{-4}	26.4	−0.4	4.85	0.69
	70.0	8.83×10^{-5}				
	60.0	2.66×10^{-5}				
15 (*p*-NH_2)[a]	80.1	2.85×10^{-4}				
	80.0[b]	2.82×10^{-4}	25.9	−1.8	4.88	0.69
	70.0	9.46×10^{-5}				
	60.2	2.96×10^{-5}				
19 (*p*-CH=$NOCH_3$)	80.0	2.86×10^{-4}	25.7	−2.3	5.13	0.71
	70.0	9.31×10^{-5}				
	60.0	2.99×10^{-5}				
17 (*p*-CH=$NNMe_2$)	80.0	4.61×10^{-4}	25.7	−1.3	8.27	0.92
	70.0	1.50×10^{-4}				
	60.0	4.80×10^{-5}				
11 (*p*-N=N(O)Bu-*t*)	80.0	5.26×10^{-4}	25.8	−0.8	9.45	0.98
	70.0	1.75×10^{-4}				
	60.0	5.45×10^{-5}				
18 (*p*-N=NPh)[a]	80.1	7.12×10^{-4}				
	80.0[b]	7.00×10^{-4}	25.2	−1.8	12.1	1.08
	70.0	2.38×10^{-4}				
	60.1	7.76×10^{-5}				
13 (*p*-CH=N(O)Bu-*t*)	80.0[b]	7.53×10^{-4}	25.0	−2.4	13.5	1.13
	70.0	2.60×10^{-4}				
	60.0	8.31×10^{-5}				
	50.0	2.53×10^{-5}				

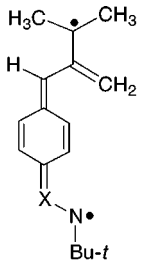
[a] Data from Rice University. Other data are from University of Notre Dame. See the Experimental Section. [b] Extrapolated from data at other temperatures.

Table 2. Rearrangement Rates and $\sigma^\bullet$ Values of Methylenecyclopropanes in DMSO-d_6

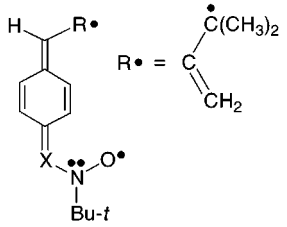
substrate	T, °C	k (s^{-1})	$\Delta H^\ddagger$ (kcal/mol)	$\Delta S^\ddagger$ (eu)	k_{rel}	$\sigma^\bullet$
6 (*p*-H)	80.0	7.90×10^{-5}	26.9	-1.5	1.00	0.00
	70.0	2.45×10^{-5}				
	60.0	7.44×10^{-6}				
20 (*p*-CH=NOH)	80.0	4.01×10^{-4}	25.6	-1.9	5.08	0.71
	70.0	1.35×10^{-4}				
	60.0	4.23×10^{-5}				
21a (*p*-CH=NO^- Li^+)	80.0[a]	1.83×10^{-3}	25.9	1.8	23	1.36
	60.0	1.90×10^{-4}				
	50.0	5.36×10^{-5}				
	40.0	1.47×10^{-5}				
21b (*p*-CH=NO^- Na^+)	80.0[a]	2.23×10^{-3}	24.3	-2.2	28	1.45
	60.0	2.57×10^{-4}				
	50.0	8.47×10^{-5}				
	40.0	2.32×10^{-5}				
21c (*p*-CH=NO^- K^+)	80.0[a]	3.35×10^{-3}	25.0	0.5	42	1.62
	60.0	3.72×10^{-4}				
	50.0	1.13×10^{-4}				
	40.0	3.15×10^{-5}				
21d (*p*-CH=NO^- Cs^+)	80.0[a]	3.55×10^{-3}	25.2	1.2	45	1.65
	60.0	3.89×10^{-4}				
	50.0	1.16×10^{-4}				
	40.0	3.22×10^{-5}				

[a] Extrapolated from data at other temperatures.

for this radical-stabilizing ability of the azo and imino groups, completely analogous to that seen in the vinyl compound **6** (X = *p*-CH=CH_2). Thus, substitution of carbon by nitrogen in a double bond has only a minor effect on radical stabilization. In previous studies of α-azo radicals, we were only able to state that an aliphatic azo group was less than 3.1 kcal/mol more stabilizing than vinyl.[21,23]



38 (X = N)
39 (X = CH)



40 (X = N)
41 (X = CH)

Unusually large k_{rel}'s of 9.45 and 13.5 are seen for the azoxy derivative **11** and the isoelectronic nitrone **13**. Prior to this paper, there were no single substituents with k_{rel} above 7.88, the value for dimethylamino.[9] Transition-state stabilization by nitroxyl forms such as **40** and **41** accounts for these rapid rearrangement rates. The high thermodynamic stability of nitroxyl radicals is apparent from the >30 kcal/mol lower O−H bond dissociation energy (BDE) of *N*,*N*-dialkylhydroxylamines relative to ordinary alcohols.[46,47]

In contrast to the large k_{rel} seen in the azoxy-substituted methylenecyclopropane **11**, the isomeric azoxy derivative **12** rearranges only 2.0 times faster than the unsubstituted system. The observation that *p*-N(O)=N−Bu-*t* is a weaker stabilizer than the isoelectronic *p*-NO_2 substituent (k_{rel} = 3.76) is attributable to the fact that the resonance structures of an α-nitro radical are identical but those of the α-azoxy radical are not. In support of this rationale, a computational study (vide infra) shows significant spin delocalization onto the nitrogen atom of a *p*-N(O)=N−Bu-*t* substituted benzylic radical, but minimal delocalization onto the oxygen atom.

According to Table 1, the amino group is a good radical stabilizer, comparable to vinyl (k_{rel} = 4.67) but it is not as strong as dimethylamino (k_{rel} = 7.88). An early mass spectroscopic study suggested that more alkyl substituents on nitrogen greatly increased the stabilization of an α-amino radical.[48] However, more recent computational[49,50] and experimental[8,51,52] work showed no such effect. The C−H BDE of 9-dimethylaminofluorene is 7 kcal/mol greater than that of the amino analogue,[52] the opposite of our k_{rel} values. While steric inhibition of resonance can rationalize the fluorene results, it is in the wrong direction to explain ours. A powerful electron donor like Me_2N may result in some ground-state destabilization of **6** (X = *p*-NMe_2), raising k_{rel}.

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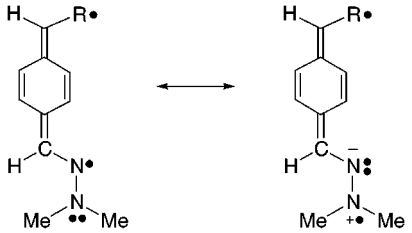
The azido group is an effective carbocation-stabilizing substituent,[53,54] being comparable to methoxy. We therefore were interested in determining whether *p*-N_3 would be a good radical-stabilizing group. However, data in Table 1 show that *p*-N_3 is only a "moderate" radical stabilizer ($k_{rel} = 2.41$), somewhat below cyano ($k_{rel} = 2.87$) but slightly better than methoxy ($k_{rel} = 1.97$).

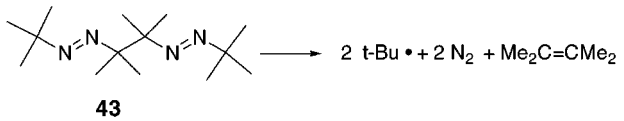
The potent carbocation-stabilizing properties of the *O*-methyloxime group[55,56] prompted us to examine the radical-stabilizing ability of *p*-CH=$NOCH_3$. On the basis of the k_{rel} values of 5.13 and 5.08 for **19** and **20**, we classify the *p*-CH=$NOCH_3$ and *p*-CH=NOH groups as "good" radical stabilizers. These groups enhance the rearrangement rate to approximately the same extent as *p*-CH=CH_2, *p*-N=N−Bu-*t*, and *p*-CH=N−Bu-*t*, indicating a similar spin delocalization mechanism.

Introduction of the dimethylamino group onto the nitrogen in the form of the hydrazone **17** (*p*-CH=N−NMe_2) gives a further rate enhancement relative to the oxime **19** (*p*-CH=$NOCH_3$). The rearrangement rate of **17** now approaches that of the azoxy and nitrone derivatives **11** and **13**. The extraordinary radical-stabilizing ability of *p*-CH=N−NMe_2 is attributed to further spin delocalization as in **42a** and **42b**, which is recognizable as a hydrazyl radical. These radicals are highly stabilized by three-electron bonding, as evidenced by the 26.5 kcal/mol difference between the N−H BDE of ammonia (107.3 kcal/mol)[57] and the most recent value for hydrazine (80.8 kcal/mol).[58] The fact that **17** rearranges faster than **19** suggests that the Me_2N group stabilizes the nitrogen-centered radical more effectively than does the MeO group of **19**. Indeed, the same trend is found in comparing the N−H BDE of phenylhydroxylamine (77.5 kcal/mol)[52] with that of 1,2-diphenylhydrazine (73.1 kcal/mol).[59] These differences are easily rationalized by the better electron-donating properties of nitrogen than oxygen.



42a **42b**

The k_{rel} of 12.1 for the phenylazo derivative **18** is nearly as large as that of nitrone **13** and greatly exceeds that of alkylazo compound **10** ($k_{rel} = 4.88$). Extended conjugation in biradical **7** is surely responsible for this rate enhancement. Only one previous radical-stability scale has included the Ph-N=N substituent and surprisingly placed it between NO_2 and CN.[2] The present result is in accord with thermolysis studies of bisazoalkanes **43** and **44**. Whereas **43** afforded nitrogen quantitatively, **44** gave no nitrogen and thermolyzed 11 times faster at 150 °C than **43**.[22] The resonance stabilization of α-azo radical **45** was estimated to be at least 6 kcal/mol greater than that of its *tert*-butyl analogue.[21]



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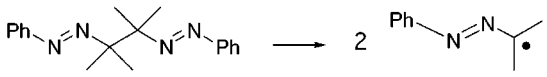
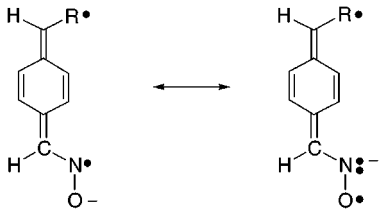


44 **45**

The best of the radical stabilizing groups in this paper is the anionic *p*-CH=N−O^- M^+ group of **21a**-**21d**. The rearrangement rates of these anionic substrates show a dependence on the counterion, with moderate increases as the metal cation becomes larger. This trend suggests that the "free anion" *p*-CH=NO^- is the best radical stabilizer. The k_{rel} of 45 exhibited by the cesium salt **21d** is exceeded by no other simple substituent on a phenyl ring; however, such large factors have been observed when the attenuating benzene ring is omitted. The $\sigma^\bullet$ value for **21d** of 1.65 is comparable to the $\gamma^\bullet$ values of the 2-thienyl ($\gamma^\bullet = 1.70$) and 2-furanyl ($\gamma^\bullet = 1.64$) groups and exceeded only by the most potent radical stabilizing group that we have reported to date, the 4-pyridyl-*N*-oxide group ($\gamma^\bullet = 1.88$).[60,61] We attribute this "super" radical stabilizing effect of *p*-CH=N−O^- to spin delocalization as in form **46a** and additional delocalization utilizing the readily available nonbonding electrons on oxygen as in **46b**.



46a **46b**

Tables 1 and 2 include activation parameters for the rearrangement of 16 arylmethylenecyclopropanes. We attribute the 4.2 eu range of $\Delta S^\ddagger$ to random experimental error and conclude that the k_{rel} values are governed by $\Delta H^\ddagger$. This outcome is as expected if k_{rel} measures stabilization of biradical **7** by the benzene ring substituents. The average $\Delta S^\ddagger$ for all entries is −0.9 eu, a figure that should be quite reliable and is consistent with $\Delta S^\ddagger$ for related methylenecyclopropane rearrangements.[62,63]

Computational Studies. To gain further insight into the radical-stabilizing nature of the nitrogen-containing substituents, density functional molecular orbital calculations were carried out on a series of benzylic radicals and the corresponding substituted toluenes. Similar calculations have been reported[20] for 15 benzylic radicals

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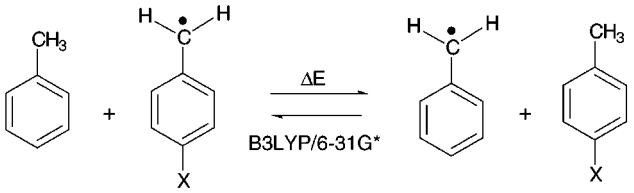
Table 3. B3LYP/6-31G* Energies of Radicals 48 and Toluenes 50 and Δ*E* Values for the Isodesmic Reaction of Substituted Benzylic Radicals 48 with Toluene

substituent	B3LYP energy (au)	ZPE (au)	Δ*E* (kcal/mol)
48 (*p*-H)	−270.915143	0.114935	0.00
48 (*p*-CH_3)	−310.233556	0.142461	0.34
48 (*p*-N(O)=NCH_3)	−494.873123	0.157968	0.60
48 (*p*-N_3)	−434.506512	0.118004	1.09
48 (*p*-CH=NCH_3)	−403.677819	0.164847	1.39
48 (*p*-NH_2)	−326.269835	0.131645	1.46
48 (*p*-NMe_2)	−404.883745	0.188564	1.72
48 (*p*-CH=CH_2)	−348.317735	0.147986	1.73
48 (*p*-N=NCH_3)	−419.687565	0.152339	1.80
48 (*p*-CH=$NOCH_3$)	−478.852187	0.168931	1.89
48 (*p*-CH=$NNMe_2$)	−498.316384	0.210117	2.34
48 (*p*-N=NPh)	−611.433669	0.205541	2.89
48 (*p*-N=$N(O)CH_3$)	−494.877912	0.158037	2.96
48 (*p*-CH=$N(O)CH_3$)	−478.851831	0.170159	3.48
48 (*p*-CH=NO^-)	−438.971717	0.127345	11.0
4-pyridyl-CH_2	−286.951160	0.103251	−1.09
3-pyridyl-CH_2	−286.951463	0.103099	−0.43
4-pyridyl-*N*-oxide-CH_2	−362.123719	0.107943	6.00
50 (*p*-H)	−271.566648	0.128296	
50 (*p*-CH_3)	−310.884526	0.155818	
50 (*p*-N(O)=NCH_3)	−495.523671	0.171280	
50 (*p*-N_3)	−435.156276	0.131334	
50 (*p*-CH=NCH_3)	−404.327110	0.178093	
50 (*p*-NH_2)	−326.919009	0.144898	
50 (*p*-NMe_2)	−405.532506	0.201748	
50 (*p*-CH=CH_2)	−348.966485	0.161228	
50 (*p*-N=NCH_3)	−420.336197	0.165622	
50 (*p*-CH=$NOCH_3$)	−479.500686	0.182089	
50 (*p*-CH=$NNMe_2$)	−498.964157	0.223281	
50 (*p*-N=NPh)	−612.080569	0.218711	
50 (*p*-N=$N(O)CH_3$)	−495.524706	0.171461	
50 (*p*-CH=$N(O)CH_3$)	−479.497792	0.183509	
50 (*p*-CH=NO^-)	−439.605655	0.139936	
4-pyridyl-CH_3	−287.604404	0.116599	
3-pyridyl-CH_3	−287.603654	0.116626	
4-pyridyl-*N*-oxide-CH_3	−362.765666	0.120791	

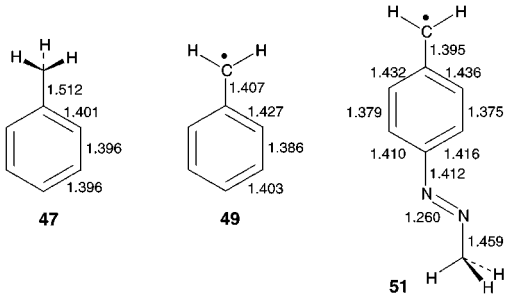
different from those included here. Table 3 summarizes our B3LYP/6-31G* energies and the corresponding values of Δ*E* for the isodesmic reaction of toluene with substituted benzylic radicals **48**. The degree of stabilization



47 **48** **49** **50**

parallels the rearrangement rates of the substituted methylenecyclopropanes. Figure 1 shows a linear free energy relationship between k_{rel} and the isodesmic reaction energy. The correlation is quite good ($r = 0.983$) and further demonstrates that density functional calculations can be useful in determining radical-stabilizing effects. The slope of the plot is 0.7 and suggests that approximately 70% of the radical-stabilizing effect is manifested in the transition state of the methylenecyclopropane rearrangement. The points for *p*-NH_2 and *p*-NMe_2 (open circles) show the greatest deviations from the line and the larger than expected k_{rel} values may indicate ground-state destabilization of the corresponding methylenecyclopropanes.

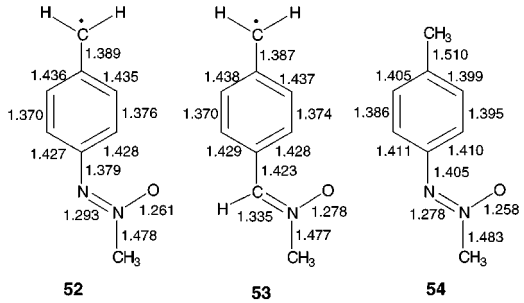
Calculated bond length and spin density data (Table 4) are in accord with extensive stabilization of the substituted radicals **48** by spin delocalization. The bond from the aromatic ring to the benzylic radical center gets progressively shorter as radical stabilization (measured by Δ*E* values) increases. For example, the C−C bond length of 1.407 Å for the unsubstituted benzyl radical **49** exceeds the 1.395 Å for the "stabilized" *p*-N=N−CH_3-substituted radical **51**, which in turn exceeds the 1.389 Å for the "super stabilized" *p*-N=N(O)CH_3-substituted radical **52**. In valence bond terms, these bond length changes indicate progressively increasing importance of forms with spin delocalized onto the para substituent.



47 **49** **51**

The spin density at the benzylic carbon also mirrors these findings. There is a progressive drop in spin density at the benzylic position with increasing radical stabilization. Substantial spin delocalization onto certain atoms of the para substituent, which is in accord with predictions based on valence bond considerations, is also indicated by these computational studies.

Interestingly, the calculated structure of the azoxy-substituted benzylic radical **52** shows a shorter C−N bond and a longer N=N bond than the corresponding substituted toluene **54**. Analogous trends are seen in the nitrone-substituted radical **53**, and both radicals **52** and **53** show high calculated spin densities on nitrogen and oxygen. In valence bond terms, these bond length changes



52 **53** **54**

and spin density trends are consistent with substantial contributions from nitroxyl radical forms. These computational results are in line with the observed large rate enhancements seen in the azoxy and nitrone derivatives **11** and **13**.

The calculated structure of the radical anion **55** also merits further discussion. A high degree of spin delocalization is indicated by a large calculated spin density on oxygen as well as smaller spin density on nitrogen relative to the other entries in Table 4. Also of interest are calculated charge densities in **55**, where the benzylic carbon has considerable negative charge. In valence bond terms, nitroxyl form **55a** has major importance. The value of Δ*E* for the reaction of **55** with toluene (11 kcal/mol)[64] is the largest of the substituents studied and indicative of major stabilization in the radical **55**. The experimental observation that the anionic systems **21** are

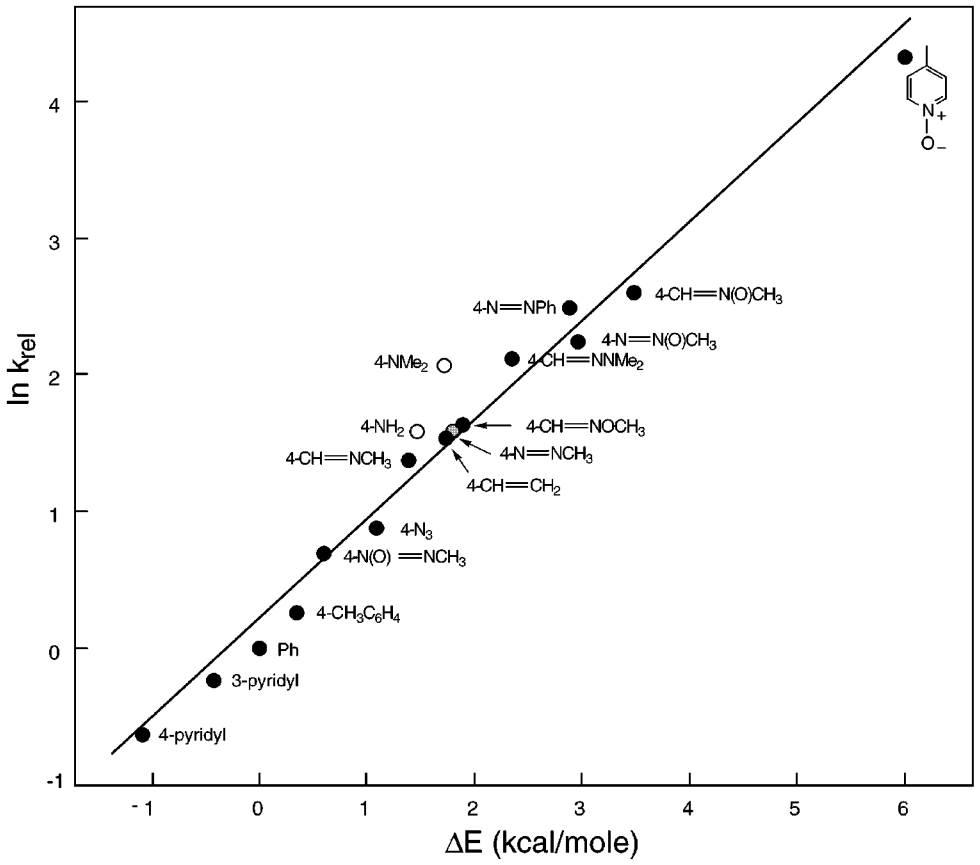


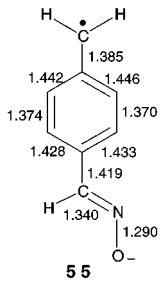
Figure 1. Plot of ln k_{rel} for rearrangement of substituted methylenecyclopropanes **6** vs calculated (B3LYP/6-31G*) ΔE values for the isodesmic reaction of toluene with substituted benzylic radicals **48**.

Table 4. B3LYP/6-31G* Bond Lengths (C_1−Aryl Bond) and Spin Densities of Radicals 48

substituent	bond length (Å)	spin density at C_1 (benzylic carbon)	spin density on X (N, O, or C atoms)
4-pyridyl-CH_2	1.4086	0.814	
48 (*p*-H)	1.4067	0.792	
3-pyridyl-CH_2	1.4047	0.795	
48 (*p*-CH_3)	1.4052	0.783	
48 (*p*-N(O)=NCH_3)	1.4011	0.754	N, 0.108; O, −0.021
48 (*p*-NH_2)	1.4028	0.757	N, 0.064
48 (*p*-NMe_2)	1.4021	0.750	N, 0.075
48 (*p*-N_3)	1.4002	0.746	$N_{(2)}$, 0.009; $N_{(3)}$, 0.098
48 (*p*-CH=NCH_3)	1.3981	0.732	N, 0.162
48 (*p*-CH=CH_2)	1.3966	0.721	C, 0.223
48 (*p*-CH=NOH)	1.3956	0.714	N, 0.178; O, 0.036
48 (*p*-CH=$NOCH_3$)	1.3952	0.710	N, 0.178; O, 0.038
48 (*p*-N=NCH_3)	1.3951	0.709	N, 0.198
48 (*p*-CH=$NNMe_2$)	1.3944	0.699	N, 0.148; N, 0.074
48 (*p*-N=NPh)	1.3888	0.653	N, 0.223
48 (*p*-N=N(O)CH_3)	1.3887	0.656	N, 0.144; O, 0.205
48 (*p*-CH=N(O)CH_3)	1.3867	0.637	N, 0.166; O, 0.234
48 (*p*-CH=NO^-)	1.3852	0.495	N, 0.066; O, 0.300
4-pyridyl-*N*-oxide-CH_2	1.3776	0.571	N, 0.190; O, 0.371

the fastest rearranging methylenecyclopropanes in the present study confirms this suggestion.

Conclusions. The radical-stabilizing ability of a variety of nitrogen containing groups has been evaluated by measuring their effect on the rearrangement rate of 2-aryl-3,3-dimethylmethylenecyclopropanes. The fastest rearrangement occurred when the aryl substituent was the anionic *p*-CH=NO^- group. The azoxy, nitrone, and phenylazo groups, (*p*-N=N(O)-Bu-*t*, *p*-CH=N(O)-Bu-*t*, and *p*-N=N−Ph) were also outstanding rate enhancers. We classify these groups as "super radical stabilizers". Radical stabilization by spin delocalization in the transition state for the rearrangement accounts for these large rate enhancements. Computational studies (B3LYP/6-31G*) on substituted benzylic radicals reveal an excellent linear free energy relationship between rate of the methylenecyclopropane rearrangement and radical-stabilization energy. These calculations confirm extensive spin delocalization in many nitrogen-substituted benzylic radicals. Carbocation studies would be lacking without inclusion of substituents, such as *p*-methoxy, which have special cation-stabilizing features. By the same token, we suggest that correlations of radical reactions should include substituents that have special radical-stabilizing properties. Some of the nitrogen-containing substituents described in this paper provide excellent examples of potent radical stabilizers that could be employed as criteria for evaluation of radical processes.



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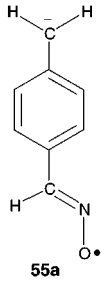

55a

(64) The anionic *p*-CH=NO^- substituent is not included in the correlation in Figure 1. The comparison of calculated energies of charged molecules in the gas phase with neutral molecules is unwarranted.

Experimental Section

***p*-Formylphenyl isocyanate (23)** was prepared using a modification of Yamada's method.[30] To 4-carboxybenzaldehyde (3 g, 20 mmol) suspended in dry methylene chloride (50 mL) was added triethylamine (2.78 mL, 20 mmol). When all of the solid had dissolved, diphenylphosphoryl azide (4.3 mL, 20 mmol) was added dropwise. The resulting solution was refluxed for 6 h, and the solvent was removed by rotary evaporation. The resulting light yellow solid was dissolved in 50 mL of ether and washed with 2 × 50 mL portions of aqueous $NaHCO_3$ (pH 9). The ether layer was dried over K_2CO_3, and the solvent was evaporated to give **23** as a white solid (3 g, 20 mmol, yield: 100%): ^{1}H NMR ($CDCl_3$) δ 8.00 (d, 2 H, J = 8.2 Hz), 8.27 (d, 2 H, J = 8.2 Hz), 10.12 (s, 1 H); ^{13}C NMR ($CDCl_3$) δ 129.65, 130.0, 135.27, 139.96, 171.68, 191.32; IR 3096, 2918, 2855, 2173, 2140, 1676, 1250 cm^{-1}.

***N*-*tert*-Butyl-*N*′-(*p*-formylphenyl)urea, *tert*-butylimine (24)** was prepared according to a method modified from Fowler.[32] To *p*-formylphenyl isocyanate (3 g, 20 mmol) in 100 mL of benzene was added dry *tert*-butylamine (2 equiv, 2.93 g, 4.20 mL), and the solution was heated to reflux for 5.5 h. The solvent was removed by rotary evaporation, and the residual white solid was recrystallized from ether. Purification was difficult due to partial Schiff base hydrolysis. The yield of **24** was 65%: ^{1}H NMR ($CDCl_3$) δ 1.29 (s, 9 H), 1.37 (s, 9 H), 7.33 (d, 2 H, J = 8.6 Hz), 7.66 (δ, 2 H, J = 8.6 Hz), 8.18 (s, 1 H). For *N*-*tert*-butyl, *N*′-(*p*-formylphenyl) urea: ^{1}H NMR ($CDCl_3$) δ 1.39 (s, 9 H), 5.08 (s, 1 H), 7.09 (s, 1 H), 7.49 (d, 2 H, J = 8.5 Hz), 7.77 (d, 2 H, J = 8.5 Hz), 9.85 (s, 1 H); ^{13}C NMR δ 29.20, 51.13, 118.03, 130.61, 131.41, 145.49, 191.27.

***p*-(*tert*-Butylazo)benzaldehyde (25)** was prepared by Porter's method.[33] Potassium *tert*-butoxide (49 mg, 0.44 mmol, 1.2 equiv) was dissolved in 2 mL of *tert*-butyl alcohol, and 0.1 g (0.364 mmol) of the urea **24** in 2 mL of *tert*-butyl alcohol was then added. After the slurry was stirred for 35 min at room temperature, a solution of 69 mL (1.6 equiv) of *t*-BuOCl in 1 mL of *tert*-butyl alcohol was added over 10 min. Stirring was continued for another 30 min. Ice (5 g) was added, the solution was stirred for 5 min, and then ether (25 mL) was added. The organic layer was separated and washed with 3 × 50 mL of ice−water. The water layer was extracted with hexane, and the ether and hexane solutions were combined and treated with aqueous HCl (15 mL). After being stirred for 1 h at room temperature, the organic layer was separated and dried over K_2CO_3. The solvent was removed by rotary evaporation, and the crude product **25** was purified by column chromatography on silica gel with 20% ethyl acetate in hexane as eluent. The yield of **25** was 30%: mp 43−45 °C; ^{1}H NMR ($CDCl_3$) δ 1.37 (s, 9 H), 7.75 (d, 2 H, J = 8.4 Hz), 7.98 (d, 2 H, J = 8.4 Hz), 10.08 (s, 1 H); ^{13}C NMR ($CDCl_3$) δ 26.85, 68.83, 122.40, 130.612, 136.89, 155.85, 191.69; HRMS (70 eV, EI) calcd for $C_{11}H_{14}N_2O$ 190.1106, found 190.1105. Anal. Calcd for $C_{11}H_{14}N_2O$: C, 69.44; H 7.42; N, 14.72. Found: C, 69.36; H, 7.42; N, 14.76.

***p*-(*tert*-Butyl-ONN-azoxy)benzaldehyde (26)** was prepared by a modification of the method of Kovacic.[34] A solution of 1 g of *p*-(*tert*-butylazo)benzaldehyde, **25**, in 30 mL of methylene chloride was cooled to 0 °C, and 1.8 g of 50% *m*-chloroperbenzoic acid (1.0 equiv) was added. The mixture was stirred for 3 h in an ice bath, and the solid *m*-chlorobenzoic acid was removed by filtration. Sodium hydroxide (3 M, 15 mL) was added dropwise to the filtrate cooled in an ice bath, and the solution was stirred for 15 min. The methylene chloride was removed by rotary evaporation, and the crude product was purified by column chromatography on silica gel with 20% ethyl acetate in hexane as eluent. The aldehyde **26** was then recrystallized from pentane at low temperature. The yield of **26** was 40%: mp 47−48 °C; ^{1}H NMR ($CDCl_3$) δ 1.68 (s, 9 H), 7.87 (d, 2 H, J = 8.6 Hz), 7.94 (d, 2 H, J = 8.6 Hz), 10.01 (s, l H); ^{13}C NMR ($CDCl_3$) δ 28.38, 78.59, 124.68, 130.15, 135.33, 149.11, 191.28. Anal. Calcd for $C_{11}H_{14}N_2O_2$: C, 64.06; H, 6.84; N, 13.58. Found: C, 64.21; H, 6.93; N, 13.47.

***p*-Nitrosobenzaldehyde (31)** was made by reduction of the nitro group to the hydroxylamine according to Entwistle's method[39] followed by PCC oxidation of the hydroxylamine.[38] A mixture of 2.5 g of *p*-nitrobenzaldehyde ethylene acetal (**28**)[65] (0.0128 mol) in 25 mL of THF containing 40 mg of 5% Rh/C was stirred as 15 mL of 65% aqueous hydrazine solution was added dropwise. Gas evolution was immediate. After 1 h, TLC showed no remaining starting material. The mixture was poured into 80 mL of distilled water and quickly extracted with 3 × 50 mL of ether. The combined organic extracts were dried over Na_2SO_4 under nitrogen. The ether was rapidly removed by rotary evaporation to give crude *p*-hydroxylaminobenzaldehyde ethylene acetal (**29**). To a solution of this crude product in 25 mL of freshly distilled, dry THF was added 2.98 g of pyridimium chlorochromate (1.05 equiv). After 10 min, the dark brown slurry was filtered through a dry pad of silica gel, and the silica gel was washed with THF. The solvent was removed, and the crude *p*-nitrosobenzaldehyde ethylene acetal (**30**) was further purified by column chromatography on silica gel with 30% ethyl acetate in hexane as eluent. Compound **30** (60% yield) was a green solid that turned yellow on standing due to dimerization: ^{1}H NMR ($CDCl_3$) δ 4.10 (m, 4 H), 5.89 (s, 1 H), 7.73 (d, 2 H, J = 8.5 Hz), 7.91 (d, 2 H, J = 8.5 Hz); ^{13}C NMR ($CDCl_3$) δ 65.45, 102.57, 120.92, 127.39, 145.12, 165.56.

Compound **30** (1.4 g) was hydrolyzed by stirring with 100 mL of 4 M HCl under nitrogen for 50 min. The bright yellow solid (dimer of **31**) was collected by filtration, washed five times with distilled water, and recrystallized from THF at −5 °C. The yield of **31** (as the dimer) was 90%, mp 135−136 °C. This compound was found to be sensitive to dry potassium carbonate. The dimer of **31** slowly dissolved in $CDCl_3$ to give the monomer in solution: ^{1}H NMR of **31** ($CDCl_3$) δ 8.03 (d, 2 H, J = 8.4 Hz), 8.16 (d, 2 H, J = 8.4 Hz), 10.19 (s, 1 H); ^{13}C NMR ($CDCl_3$) δ 121.05, 131.04, 139.42, 163.71, 191.26.

***p*-(*tert*-Butylazoxy-NNO)benzaldehyde (32)** was prepared by a modification of Kovacic's method.[35] *p*-Nitrosobenzaldehyde, **31** (0.5 g, 3.7 mmol), was dissolved in 20 mL of acetonitrile with stirring and heat (monomer formation). Solid potassium iodide (0.615 g) was then added followed by the dropwise addition of 0.52 g (3.7 mmol) of freshly prepared *tert*-butyl *N*,*N*-dichloroamine[66] at room temperature. The solution turned brown immediately. The mixture was stirred overnight at room temperature under nitrogen. The solvent was removed by rotary evaporation, and the aldehyde **32** was purified by silica gel chromatography, eluting with 10% ethyl acetate in hexane. The yield of **32** (brown oil) was 78%: ^{1}H NMR ($CDCl_3$) δ 1.45 (s, 9 H), 7.95 (d, 2 H, J = 8.7 Hz), 8.26 (d, 2 H, J = 8.7 Hz), 10.09 (s, 1 H); ^{13}C NMR ($CDCl_3$) δ 25.61, 59.45, 123.01, 129.97, 137.92, 152.22, 190.93; HRMS (CI) (M^+ + H) calcd for $C_{11}H_{15}N_2O_2$ 207.1133, found 207.1142.

Aryldiazomethanes (33−35) were prepared by the previously described tosylhydrazone salt solution pyrolysis method.[67] Approximately 0.78 mmol of tosylhydrazine was suspended in 3 mL of methanol containing about 5 mg of pyridine, and 0.74 mmol of the appropriate aldehyde **25**, **26**, or **32** was added to the stirred solution. After 8 h at room temperature, 0.80 mmol of $NaOCH_3$ in methanol was added. The methanol was removed using a rotary evaporator, and 8 mL of ethylene glycol was added. The mixture was stirred until the tosylhydrazone salt dissolved, and then the solution was heated in an oil bath at 80−90 °C with periodic extraction with ether. When no more diazo compound formed, the combined ether extracts were washed with water and dried over $MgSO_4$. Solvent removal left the corresponding diazo compounds **33**, **34**, and **35**, which were used without further purification. The thermally labile, light-sensitive diazo compounds were stored in the dark at −20 °C.

In a typical procedure, reaction of 153 mg of aldehyde **32** with 145 mg of tosylhydrazine gave 146 mg (90% yield) of diazo

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Table 5. ^{1}H NMR Spectral Data (δ) for Methylenecyclopropanes 10−21 in $CDCl_3$

compd	CH_3	CH	CH_2	aromatic	other
10 *p*-N=NBu-*t*	0.853, 1.357	2.499	5.56, 5.50	7.25, 7.56	1.327
11 *p*-N=N(O)Bu-*t*	0.850, 1.348	2.481	5.55, 5.58	7.21, 7.87	1.648
12 *p*-N(O)=NBu-*t*	0.835, 1.359	2.501	5.56, 5.60	7.22, 7.99	1.463
13 *p*-CH=N(O)Bu-*t*	0.836, 1.348	2.487	5.55, 5.59	7.22, 8.19	1.606, 7.506
14 *p*-CH=NBu-*t*	0.835, 1.349	2.484	5.55, 5.59	7.21, 7.64	1.287, 8.249
15 *p*-NH_2	0.831, 1.306	2.369	5.51, 5.54	6.61, 6.98	3.552
16 *p*-N_3	0.830, 1.334	2.432	5.53, 5.58	6.93, 7.17	
17 *p*-CH=NNMe_2	0.838, 1.337	2.451	5.54, 5.57	7.14, 7.47	2.947, 7.257
18 *p*-N=NPh	0.897, 1.382	2.541	5.58, 5.62	7.32, 7.49	7.82−7.92
19 *p*-CH=NOCH_3	0.846, 1.348	2.464	5.54, 5.59	7.18, 7.47	3.959, 8.037
20 *p*-CH=NOH	0.856, 1.353	2.472	5.55, 5.59	7.20, 7.47	8.116
21 *p*-CH=NO^- K^+ [a]	0.793, 1.283	2.436	5.51, 5.54	6.94, 7.28	7.811

[a] In DMSO-d_6.

Table 6. ^{13}C NMR Spectral Data (δ) for Methylenecyclopropanes 10−21 in $CDCl_3$

compd	CH_3	CH	CH_2	aromatic	other
10 *p*-N=NBu-*t*	18.43, 26.16	32.13	103.62	121.58, 129.39, 145.45, 150.65	24.32, 27.05, 67.42, 140.76
11 *p*-N=N(O)Bu-*t*	18.40, 26.15	32.26	103.58	124.54, 128.90, 142.35, 145.42	24.38, 28.44, 77.38, 139.49
12 *p*-N(O)=NBu-*t*	18.35, 26.11	31.86	103.95	121.75, 128.91, 142.32, 144.90	24.60, 25.85, 58.91
13 *p*-CH=N(O)Bu-*t*	18.28, 26.11	32.39	103.61	128.46, 128.87, 141.02, 145.18	24.47, 28.31, 70.41, 128.70, 129.81
14 *p*-CH=NBu-*t*	18.39, 26.17	32.26	103.55	127.56, 129.10, 140.93, 145.46	24.24, 29.80, 57.13, 134.99, 155.14
15 *p*-NH_2	18.44, 25.94	31.44	102.90	114.88, 128.24, 129.79, 144.31	22.96, 146.35
16 *p*-N_3	18.37, 25.97	31.53	103.54	118.57, 130.23, 135.25, 137.52	23.78, 145.37
17 *p*-CH=NNMe_2	18.40, 26.14	32.17	103.31	125.28, 129.10, 137.78, 145.79	23.90, 42.95, 133.35, 134.58
18 *p*-N=NPh	18.37, 26.18	32.35	103.71	129.04, 129.53, 130.68, 145.32, 151.02, 152.80	24.77, 142.24
19 *p*-CH=NOCH_3	18.38, 26.17	32.25	103.64	126.68, 129.28, 140.68, 145.30	24.37, 61.97, 129.79, 148.65
20 *p*-CH=NOH	18.38, 26.15	32.22	103.67	126.71, 129.35, 140.98, 145.23	24.43, 129.53, 150.31
21 *p*-CH=NO^- K^+ [a]	18.29, 25.65	31.50	103.26	122.78, 128.33, 133.04, 137.31	22.72, 141.50, 145.70

[a] In DMSO-d_6.

compound **35**: ^{1}H NMR of **35** ($CDCl_3$) δ 1.461 (s, 9 H), 5.034 (s, 1 H), 6.91 and 8.04 (AA′BB′ quartet, 4 H); ^{13}C NMR of **35** ($CDCl_3$) δ 25.91, 48.08, 58.88, 120.69, 123.06, 134.09; ^{1}H NMR of **33** ($CDCl_3$) δ 1.322 (s, 9 H), 5.014 (s, 1 H), 7.63 and 6.96 (AA′BB′ quartet, 4 H); ^{13}C NMR of **33** ($CDCl_3$) δ 27.10, 48.01, 67.20, 121.42, 123.15, 132.17; ^{1}H NMR of **34** ($CDCl_3$) δ 1.641 (s, 9 H), 5.011 (s, 1 H), 8.00 and 6.92 (AA′BB′ quartet, 4 H); ^{13}C NMR of **34** ($CDCl_3$) δ 28.43, 48.43, 77.21, 120.92, 126.26, 130.76.

Cu(OTf)$_2$-Catalyzed Reaction of Aryldiazomethanes 33−35 with 1,1-Dimethylallene. General Procedure. Approximately 15 mg of $Cu(OTf)_2$ was stirred in 2.5 mL of 1,1-dimethylallene as a solution of approximately 80−100 mg of aryldiazomethanes **33**−**35** in 13 mL of 1,1-dimethylallene was added dropwise over a 1 h period. The color of the diazo compound disappeared during the addition. The excess allene was removed at 15 mm pressure (and recovered), and the residue was chromatographed on approximately 7 g of silica gel. The product **10** eluted with hexanes, while the products **11** and **12** eluted with 5% ether in hexanes. Solvent removal gave **10**, **11**, or **12**, which contain varying amounts of the "rearranged" methylenecyclopropane **8** (formed by carbene addition to the less substituted double bond of the allene). Satisfactory high-resolution mass spectral data (EI) were obtained for **10**, **11**, and **12**. ^{1}H and ^{13}C NMR data are summarized in Tables 5 and 6.

2-(*p*-Formylphenyl)-3,3-dimethylmethylenecyclopropane 37. A solution of 795 mg of the 2-(*p*-bromophenyl)-3,3-dimethylmethylenecyclopropane **36** (which contained 10% of the isomeric methylenecyclopropane)[40] in 4 mL of dry THF was cooled to −78 °C, and 3.2 mL of 1.6 M *n*-BuLi in hexane was added dropwise to the stirred solution. The mixture was warmed to −50 °C for 5 min and then recooled to −78 °C. After 30 min at −78 °C, a solution of 360 mg of dimethylformamide in 3 mL of ether was added dropwise. The mixture was allowed to slowly warm to 0 °C, and water was then added. The organic phase was separated, and the aqueous phase was extracted with an additional portion of ether. The combined organic extracts were washed with saturated NaCl solution and then dried over $MgSO_4$. After filtration, the organic solvents were removed using a rotary evaporator. The residue was chromatographed on 22 g of silica gel, and the column was eluted with increasing amounts of ether in hexanes. A small amount of debrominated product (**6**, X = H) eluted with pure hexane. The aldehyde **37** (containing increasing amounts of the isomeric aldehyde **8** (X = *p*-CHO) eluted with 4% ether in hexanes. The purest fraction contained 95% of **37** along with 5% of the isomeric aldehyde **8** (X = *p*-CHO). The total yield of products was 433 mg (78% yield): ^{1}H NMR of **37** ($CDCl_3$) δ 0.869 (s, 3 H), 1.376 (s, 3 H), 2.526 (m, 1 H), 5.56 (m, 1 H), 5.62 (m, 1 H), 7.78 and 7.33 (AA′BB′ quartet, 4 H), 9.961 (s, 1 H); ^{13}C NMR of **37** ($CDCl_3$) δ 18.25, 25.32, 26.18, 32.55, 104.04, 129.39, 129.47, 134.37, 144.64, 146.28, 191.93. Anal. Calcd for $C_{13}H_{14}O$: C, 83.83; H, 7.58. Found: C, 83.61; H, 7.42.

Preparation of Aldehyde Derivatives 13, 19, and 20. General Procedure. The methylenecyclopropanes **13**, **19**, and **20** were prepared by the reaction of aldehyde **37** with either *N-tert*-butylhydroxylamine hydrochloride, *O*-methylhydroxylamine hydrochloride, or hydroxylamine hydrochloride in pryidine. A mixture of 0.30 mmol of aldehyde **37**, and 0.60 mmol of the appropriate hydroxylamine hydrochloride in 1 mL of pyridine was stirred at room temperature for 24 h. The mixture was then taken up into ether, washed with water, dilute HCl solution, and saturated NaCl solution, and dried over $MgSO_4$. After filtration, the ether solvent was removed using a rotary evaporator, and the residue was chromatographed on silica gel and eluted with increasing amounts of ether in hexanes. Solvent removal gave **13**, **19**, or **20** in 92, 96, and 96% yields, respectively. Satisfactory high-resolution mass spectral data (EI) were obtained for **13**, **19**, and **20**. ^{1}H and ^{13}C NMR data are summarized in Tables 5 and 6.

2-(*p*-Formylphenyl)-3,3-dimethylmethylenecyclopropane, *t*-Butyl Imine. A solution of 98 mg of aldehyde **37** and 80 mg of *tert*-butylamine in 1.0 mL of CCl_4 was stirred at room temperature as 13 mg of *p*-toluenesulfonic acid was added. Anhydrous $MgSO_4$ (356 mg) was then added, and the mixture was stirred at room temperature for 140 h. The mixture was then diluted with 2 mL of hexane and centrifuged. The solvent was carefully decanted and removed by rotary evaporator to give 113 mg (89% yield) of imine **14**, which was used without further purification for kinetic studies. ^{1}H and ^{13}C NMR data

are given in Tables 5 and 6: HRMS (EI^+) calcd for $C_{17}H_{23}N$ 241.1831, found 241.1859.

2-(*p*-Formylphenyl)-3,3-dimethylmethylenecyclopropane, *N*,*N*-Dimethyl Hydrazone 17. A solution of 34.6 mg of aldehyde **37** and 31 mg of 1,1-dimethylhydrazine in 1.0 mL of ether was stirred at room temperature, and 3.3 mg of *p*-toluenesulfonic acid was added. After 6 h, about 20 mg of Na_2CO_3 was added followed by a small amount of anhydrous $MgSO_4$. The mixture was then filtered, and the solvent was removed using a rotary evaporator leaving 41.2 mg of hydrazone **17** (97% yield), which was used without further purification for kinetic studies. ^1H and ^{13}C NMR data are given in Tables 5 and 6: HRMS (EI^+) calcd for $C_{15}H_{20}N_2$ 228.1626, found 228.1625.

Oxime Anions 21a−d were prepared by reaction of 1.2 equiv of the corresponding metal methoxide (prepared by dissolving the appropriate alkali metal in absolute methanol) with 1.0 equiv of oxime **20**. In a typical procedure, 82 μL of 1.03 M $NaOCH_3$ in methanol was placed a 5 mL flask under nitrogen, and the solvent was carefully removed under aspirator vacuum. The dry $NaOCH_3$ (under nitrogen) was dissolved with stirring in 1.5 mL of DMSO-d_6, and a solution of 14.2 mg of oxime **20** in 0.6 mL of DMSO-d_6 was added. The DMSO-d_6 solution was kept under nitrogen at all times and carefully transferred to three NMR tubes. The tubes were sealed under nitrogen and used directly for kinetic studies. ^1H and ^{13}C NMR data for **21c** in DMSO-d_6 are given in Tables 5 and 6.

2-(*p*-Aminophenyl)-3,3-dimethylmethylenecyclopropane (15) was synthesized by a modification of Nishiyama's method.[41] *tert*-Butyllithium (2.0 eq of 1.7 M in pentane) was slowly added into a solution of 0.22 g of 2-(*p*-bromophenyl)-3,3-dimethylmethylenecyclopropane **36** in 2 mL of dry THF at −78 °C under nitrogen. The solution was stirred at −78 °C for 40 min, and then the temperature was allowed to rise and the solution was stirred for another 5 min at 0 °C. After 1.2 equiv of trimethylsilylmethyl azide in 3 mL of dry THF was added dropwise at −78 °C, the mixture was allowed to warm slowly to room temperature; then it was stirred for another 3 h. Water (2 mL) and then ether (2 mL) were added dropwise at 0 °C, and the aqueous solution was drained off and then washed with 3 × 3 mL of Et_2O. The organic phases were combined and dried sequentially over Na_2SO_4 and $MgSO_4$. A 0.5 g portion of silica gel was added to the organic phase, and the mixture was stirred at room temperature until the bubbling subsided (2−3 h). The silica gel was removed by filtration and was washed with 3 × 5 mL of EtOAc. Rotary evaporation of the combined organic phases yielded the crude **15**, which was purified by silica gel chromatography using 20% EtOAc in hexane as eluent. The yield of light brown oil was 49%. The NMR data can be found in Tables 5 and 6: HRMS (EI^+) calcd for $C_{12}H_{15}N$ 173.12045, found 173.1205.

2-(*p*-Azidophenyl)-3,3-dimethylmethylenecyclopropane (16) was prepared by a modification of the method of Smith.[42] A 0.21 g portion of 2-(*p*-bromophenyl)-3,3-dimethylmethylenecyclopropane **36** was dissolved in 2.5 mL of dry ether. Under argon, 2.0 equiv of *tert*-butyllithium (1.7 M in pentane) was added dropwise with stirring at −78 °C. After 40 min, the bath temperature was raised to 0 °C, and the mixture was stirred for 5 min. A solution of *p*-toluenesulfonyl azide (1.1 equiv in 1.5 mL of Et_2O) was added dropwise at −78 °C, and the mixture was stirred for 1 h at −78 °C. The bath was allowed to warm slowly to room temperature, and the mixture was stirred for another 5 h, during which time a precipitate formed. The ether was removed by rotary evaporation, and the solid was washed with 3 × 3 mL dry hexane and redissolved in 3 mL of ether. Sodium pyrophosphate (0.24 g, 1 equiv) in 2 mL of H_2O was added at 0 °C, and stirring was continued overnight. The organic layer was separated, and the aqueous solution was extracted with 3 × 2 mL of ether. The pure azide **16** was obtained in 50% yield by silica gel chromatography, eluting with hexane. The NMR data can be found in Tables 5 and 6: IR 3064, 3038, 2953 (s), 2862, 2431 (w), 2260 (w), 2129 (s), 2089 (s), 1514, 1454 (m), 1376 (w), 1291(s), 1115(m); HRMS (CI^+) calcd for ($C_{12}H_{13}N_3$ + 1H) 200.11877, found 200.11926.

2-(*p*-Phenylazo)-3,3-dimethylmethylenecyclopropane (18) was prepared according to Brown's method.[44] 2-(*p*-Aminophenyl)-3,3-dimethylmethylenecyclopropane (**15**) (60 mg) was dissolved in a mixture of 4.5 mL of pyridine and 1.1 mL of distilled water in an ice−water bath. Then 2 equiv of nitrosobenzene and 4 equiv of tetramethylammonium hydroxide pentahydrate were added into the mixture. The ice−water bath was removed, and the solution was allowed to stand at room temperature for 48 h. After 1 mL of distilled water was added, the solution was extracted with 3 × 3 mL toluene. The toluene was removed by rotary evaporation. Purification by silica gel chromatography using 5% EtOAc in hexane afforded **18** as a thick, orange-red liquid in 38% isolated yield. The NMR data can be found in Tables 5 and 6: UV λ_{max} 440 nm; HRMS (EI^+) calcd for $C_{18}H_{18}N_2$ 262.1470, found 262.1469.

Kinetics Procedures. Kinetics procedures for the thermal rearrangements of **10**−**21** were analogous to those previously described.[9,61] A solution of approximately 3.0 mg of the appropriate methylenecyclopropane and 1.5 mg of dimethyl maleate in 0.75 mL of C_6D_6 was sealed under nitrogen in an NMR tube. The tube was immersed in a constant-temperature bath (allowing 30 s to reach the bath temperature) for a given amount of time. The tube was withdrawn from the bath, immediately quenched in cold water, and then analyzed for unreacted methylenecyclopropane by 300 MHz NMR at 22 °C (where the rate is negligible). The olefinic singlet of the dimethyl maleate at δ 5.66 served as the internal standard, and the relative area of the vinyl region of the unreacted methylenecyclopropane at δ 5.56−5.35 was determined as a function of time. In determining peak areas, care was taken to use 90° pulses, long relaxation delays, as well as well-phased spectra. First-order rate constants were determined by standard least-squares methods. Correlation coefficients were greater than 0.9995. The kinetics of **15**, **16**, and **18** were carried out similarly at Rice University but without the 30 s equilibration period, which has no effect on relative rate constants. To ensure the accuracy of our k_{rel} values, the kinetics of **6** (X = H) were repeated at Rice. Both values for **6** (X = H) are shown in Table 1, and they differ by 3.8% at 80 °C. In an alternative kinetics procedure, the relative area of the methyl signals of unreacted methylenecyclopropane (δ 1.1−1.3) and the area of the methyl signal of the rearranged product (δ 1.8−1.9) was determined as a function of time. Rate constants were determined by standard methods. Rates in DMSO-d_6 were determined using this method.

Computational Studies. Molecular orbital calculations were performed using the Gaussian 94 series of programs.[68] Structures were characterized as energy minima via frequency calculations that showed no negative frequencies.

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